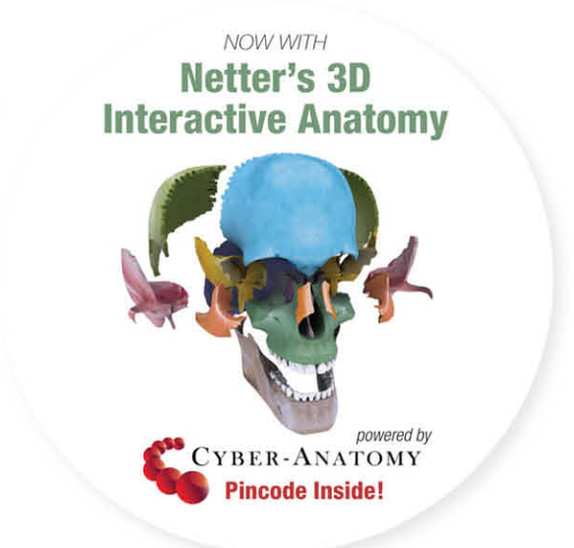
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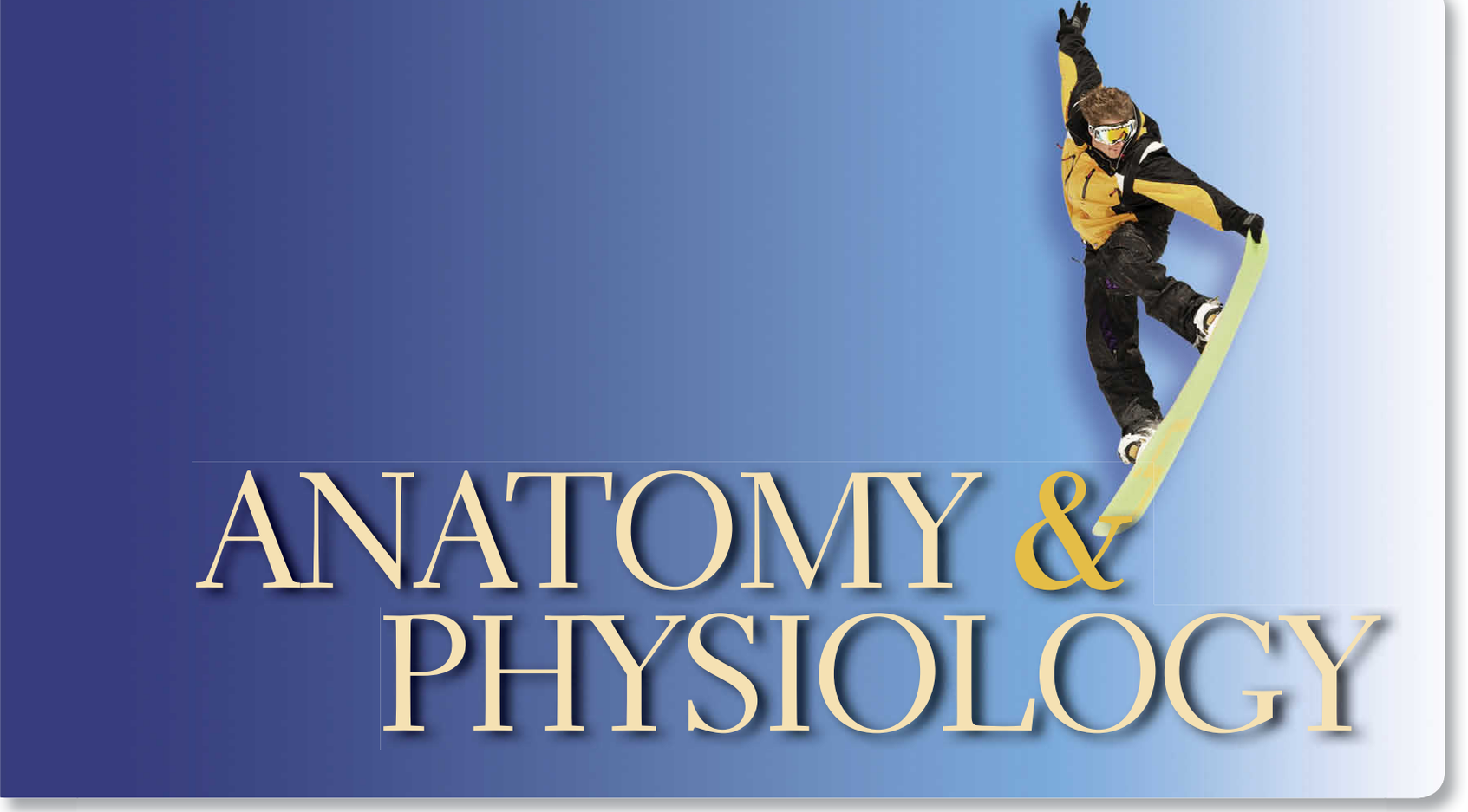


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ANATOMY & PHYSIOLOGY

8th Edition

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About the Authors



Kevin Patton has taught anatomy and physiology to high school, community college, and university students from various backgrounds for three decades. Kevin found that the work that led him to a PhD in vertebrate anatomy and physiology instilled in him an appreciation for the "Big Picture" of human structure and function. This experience has helped him produce a text that will be easier to understand for all students. He has earned several citations for teaching anatomy and physiology, including the Missouri Governor's Award for Excellence in Teaching. "One thing I've learned," says Kevin, "is that most of us learn scientific concepts more easily when we can see what's going on." His talent for using imagery to teach is evident throughout this edition with its extensive array of visual resources. Kevin's interest in promoting excellence in teaching anatomy and physiology has led him to take an active role in the Human Anatomy and Physiology Society (HAPS), where he is a President Emeritus and was the founding director of the HAPS Institute. In 2008, he was awarded the HAPS President's Medal for outstanding contributions in promoting the mission of excellence in A&P teaching and learning. Kevin also teaches graduate courses to prospective and current A&P professors and produces online resources for A&P students and teachers, including *theAPstudent.org* and *theAPprofessor.org*.

To my family and friends, who never let me forget the joys of discovery, adventure, and good humor.

To the many teachers who taught me more by who they were than by what they said.

To my students who help me keep the thrill of learning fresh and exciting.

Kevin T. Patton



Gary Thibodeau has been teaching anatomy and physiology for more than three decades. Since 1975, *Anatomy & Physiology* has been a logical extension of his interest and commitment to education. Gary's teaching style encourages active interaction with students, and he uses a wide variety of teaching methodologies—a style that has been incorporated into every aspect of this edition. He is considered a pioneer in the introduction of collaborative learning strategies to the teaching of anatomy and physiology. Recent conferral of Emeritus status in the University of Wisconsin System has provided him with additional time to interact with students and teachers across the country and around the world. His focus continues to be successful student-centered learning—leveraged by text, Web-based, and ancillary teaching materials. Over the years, his success as a teacher has resulted in numerous awards from both students and professional colleagues. Gary is active in numerous professional organizations including the Human Anatomy and Physiology Society (HAPS), The American Association of Anatomists, and the American Association of Clinical Anatomists. His biography is included in numerous publications, including *Who's Who in America*; *Who's Who in American Education*; *Outstanding Educators in America*; *American Men and Women of Science*; and *Who's Who in Medicine and Healthcare*. While earning master's degrees in both zoology and pharmacology, as well as a PhD in physiology, Gary says that he became "fascinated by the connectedness of the life sciences." That fascination has led to this edition's unifying themes that focus on how each concept fits into the "Big Picture" of the human body.

To my parents, M.A. Thibodeau and Florence Thibodeau, who had a deep respect for education at all levels and who truly believed that you never give up being a student.

To my wife, Emogene, an ever-generous and uncommonly discerning critic, for her love, support, and encouragement over the years.

To my children, Douglas and Beth, for making it all worthwhile.

Gary A. Thibodeau

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Preface

Success in both teaching and learning is, in many ways, determined by how effective we are in transforming information into knowledge. This is especially true in scientific disciplines, such as anatomy and physiology, where both student and teacher continue to be confronted with an enormous accumulation of factual information. *Anatomy & Physiology* is intended to help transform that information into a manageable knowledge base by effective use of unifying themes and by focusing on the significant and on what is truly relevant in both disciplines.

This textbook is intended for use as both a teaching tool and a learning tool. It was written to help students unify information, stimulate critical thinking, and acquire a taste for knowledge about the wonders of the human body. This textbook will help students avoid becoming lost in a maze of facts in a complex learning environment. It will encourage them to explore, to question, and to look for relationships, not only between related facts in a single discipline, but also between fields of academic inquiry and personal experience. It is our hope that *Anatomy & Physiology* will help both students and teachers transform information into knowledge.

This new edition of the text has been extensively revised. We built upon the successful art revision program begun in the previous edition by adding several new illustrations and photographs. Several of the longer chapters were split into smaller chapters to improve comprehension and better organize study. We also improved our execution of a page design and layout that maximizes learning effectiveness. As with each new edition, we added carefully selected new information on both anatomy and physiology to provide an accurate and up-to-date presentation. We have retained the basic philosophy of personal and interactive teaching that characterized previous editions. In addition, essential, accurate, and current information continues to be presented in a comfortable writing style. Emphasis is placed on concepts rather than descriptions, and the "connectedness" of human structure and function is repeatedly reinforced by unifying themes.

UNIFYING THEMES

Anatomy and physiology encompasses a body of knowledge that is large and complex. Students are faced with the need to know and understand a multitude of individual structures and functions that constitute a bewildering array of seemingly disjointed information. Ultimately, the student of anatomy and physiology must be able to "pull together" this information to view the body as a whole—to see the "Big Picture." If a textbook is to be successful as a teaching tool in such a complex learning environment, it must help unify information, stimulate critical thinking, and motivate students to master a new vocabulary.

To accomplish this synthesis of information, unifying themes are required. In addition, a mechanism to position and implement these themes must be an integral part of each chapter. Unit One begins with "Seeing the Big Picture," an overview that encourages students to place individual structures or functions into an integrated framework. Then, throughout the book, the specific information presented is highlighted in a special "The Big Picture" section so that it can be viewed as an integral component of a single multifaceted organism.

Anatomy & Physiology is dominated by two major unifying themes: (1) the complementarity of normal structure and function and (2) homeostasis. The student is shown, in every chapter of the book, how organized anatomical structures of a particular size, shape, form, or placement serve unique and specialized functions. The integrating principle of homeostasis is used to show how the "normal" interaction of structure and function is achieved and maintained by counterbalancing forces within the body. Repeated emphasis of these principles encourages students to integrate otherwise isolated factual information into a cohesive and understandable whole. "The Big Picture" summarizes the larger interaction between structures and functions of the different body systems. As a result, anatomy and physiology emerge as living and dynamic topics of personal interest and importance to students.

AIMS OF THE REVISION

As in past editions, our revision efforts focused on identifying the need for new or revised information and for additional visual presentations that clarify important, yet sometimes difficult, content areas.

In this eighth edition, we have included information on new concepts in many areas of anatomy and physiology. For example, new data on the description of cranial nerves, protein structure, and updates in terminology have been included. Most of these changes are subtle adjustments to our current understanding of human science. However, the accumulation of all of these subtle changes makes this edition the most up-to-date textbook available.

One of the most apparent changes that you will notice in this new edition is a reorganization of chapters. Three of the longer chapters have been split into small chapters. In cell biology, we moved *cell growth and reproduction* to its own chapter (Chapter 5). In the nervous system, we moved the *autonomic nervous system* into its own chapter (Chapter 16). And the endocrine system was split into an introductory chapter on *endocrine regulation*

(Chapter 18) followed by a survey of major *endocrine glands* (Chapter 19). A hallmark of our textbook has been its effective "chunking" of material into manageable chapters and these changes reflect our continuing commitment to that approach.

The previous edition featured a complete redesign of the page layouts and the art program. This enabled us to make the textbook easier to use by putting the illustrations, graphs, and tables closer to the related text. In this edition, we have improved the creative layout even more. Additional tables help students visually organize important concepts and complement the improved design to provide a multisensory learning tool. We have expanded the art program, while preserving a style as consistent as possible throughout the book. In this edition, we have expanded and improved the use of a consistent Color Key (pp. xxiv-xxv) for certain cell parts, tissue types, and biomolecules to help make learning easier for beginning students.

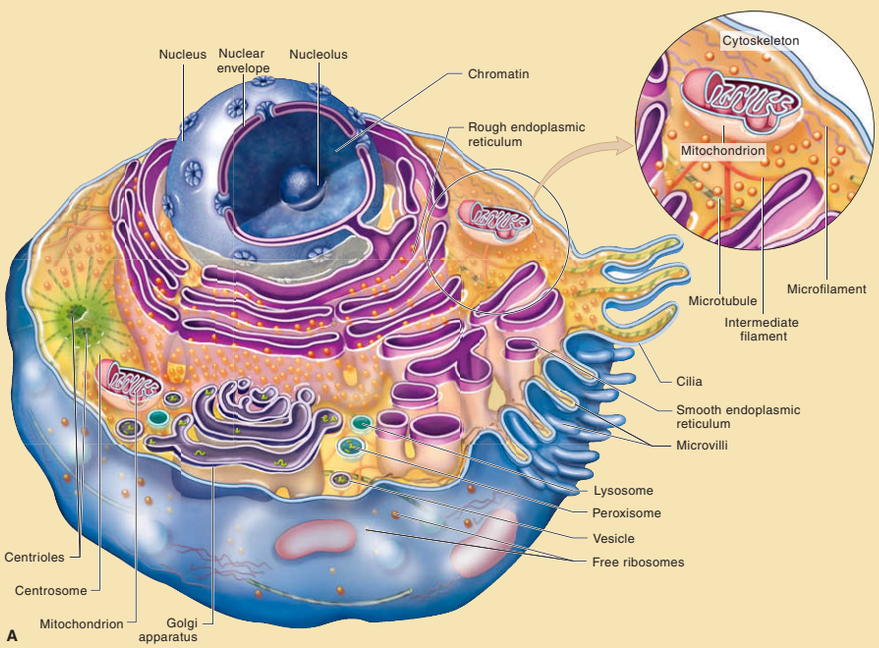
In this edition, great effort has been made to make this text accessible to students whose first language is not English. After consulting with ESL specialists and ESL learners, we have continued to enhance our word lists and improve our readability to make the concepts of human structure and function more understandable for all students.

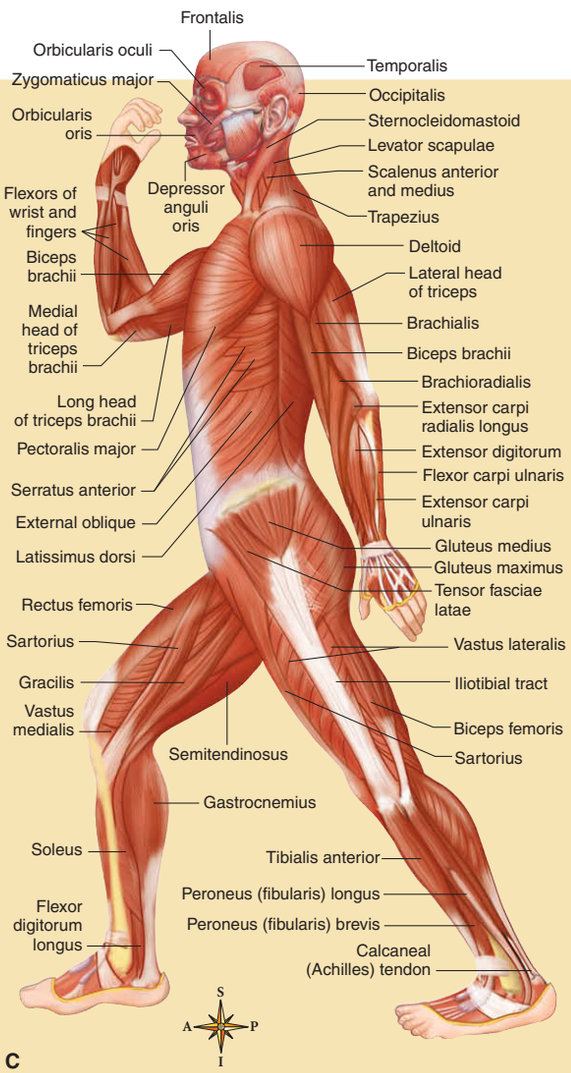
As teachers of anatomy and physiology, we know that to be effective a text must be readable, and it must challenge and excite the student. This text remains one that students will read—one designed to help the teacher teach and the student learn. To accomplish this end, we facilitated the comprehension of difficult material for students with thorough, consistent, and nonintimidating explanations that are free of unnecessary terminology and extraneous information. This easy access to complex ideas remains the single most striking hallmark of our textbook.

ILLUSTRATIONS AND DESIGN

A major strength of this text has always been the exceptional quality, accuracy, and beauty of the illustration program. It is the original "visual" anatomy and physiology textbook. We have worked very closely with scientific illustrators to provide attractive and colorful images that clearly and accurately portray the major concepts of anatomy and physiology.

The truest test of any illustration is how effectively it can complement and strengthen the written information in the text and how successfully it can be used by the student as a learning tool. Each illustration is explicitly referred to in the text and is designed to support the text discussion. Careful attention has been





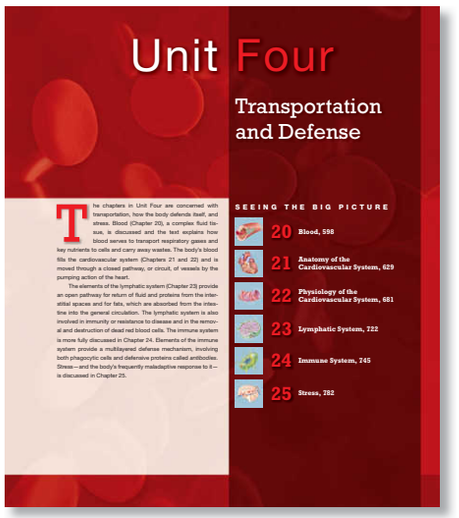
LEARNING AIDS

Anatomy & Physiology is a student-oriented text. Written in a readable style, the text is designed with many different pedagogical aids to motivate and maintain interest. The special features and learning aids listed below are intended to facilitate learning and retention of information in the most effective and efficient manner.

No textbook can replace the direction and stimulation provided by an enthusiastic teacher to a curious and involved student. However, a full complement of innovative pedagogical aids that are carefully planned and implemented can contribute a great deal to the success of a text as a learning tool. An excellent textbook can and should be enjoyable to read and should be helpful to both student and teacher. We hope you agree that the learning aids in *Anatomy & Physiology* meet the high expectations we have set.

Unit Introductions

Each of the six major units of the text begins with a brief overview statement. The general content of the unit is discussed, and the chapters and their topics are listed. Before beginning the study of material in a new unit, students are encouraged to scan the introduction and each of the chapter outlines in the unit to understand the relationship and "connectedness" of the material to be studied. Each unit has a color-coded tab at the outside edge of every page to help you quickly find the information you need.


Unit Four
Transportation and Defense
SEEING THE BIG PICTURE
20 Blood, 598
21 Anatomy of the Cardiovascular System, 629
22 Physiology of the Cardiovascular System, 681
23 Lymphatic System, 722
24 Immune System, 745
25 Stress, 782

paid to placement and sizing of the illustrations to maximize usefulness and clarity. Each figure and all labels are relevant to—and consistent with—the text discussion. Each illustration has a boldface title for easy identification. Most illustrations also include a concise explanation that guides the student through the image as a complement to the nearby text narrative.



The artistically drawn, full-color artwork is both aesthetically pleasing and functional. Color is used to highlight specific structures in drawings to help organize or highlight complex material in illustrated tables or conceptual flow charts. The text is also filled with dissection photographs, exceptional light micrographs, and scanning (SEM) and transmission (TEM) electron micro-graphs, some of which are new to this edition. In addition, examples of medical imagery, including CT scans, PET scans, MRIs, and x-ray photographs, are used throughout the text to show structural detail, explain medical procedures, and enhance the understanding of differences that distinguish pathological conditions from normal structure and function. All illustrations used in the text are an integral part of the learning process and should be carefully studied by the student.

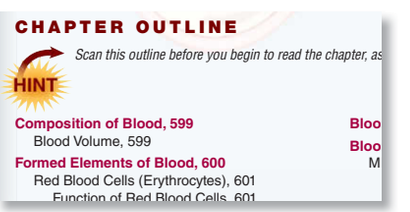


Chapter Learning Aids

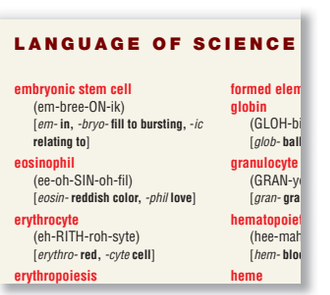
- **Study Hints**—*give specific suggestions for using many of the learning aids found in each chapter.* Because many readers have never learned the special skills needed to make effective use of pedagogical resources found in science textbooks, helpful tips are embedded within each Chapter Outline, Language of Science & Medicine list, Case Study, Chapter Summary, Review Question set, and Critical Thinking section. Answers for all of the case study questions and also the review and critical thinking questions are in the Instructor's Resource Manual, the Instructor's Electronic Resource DVD, and the instructor's EVOLVE site for *Anatomy & Physiology*. Teachers can then choose to use the questions as homework assignments or include them on tests.


HINT

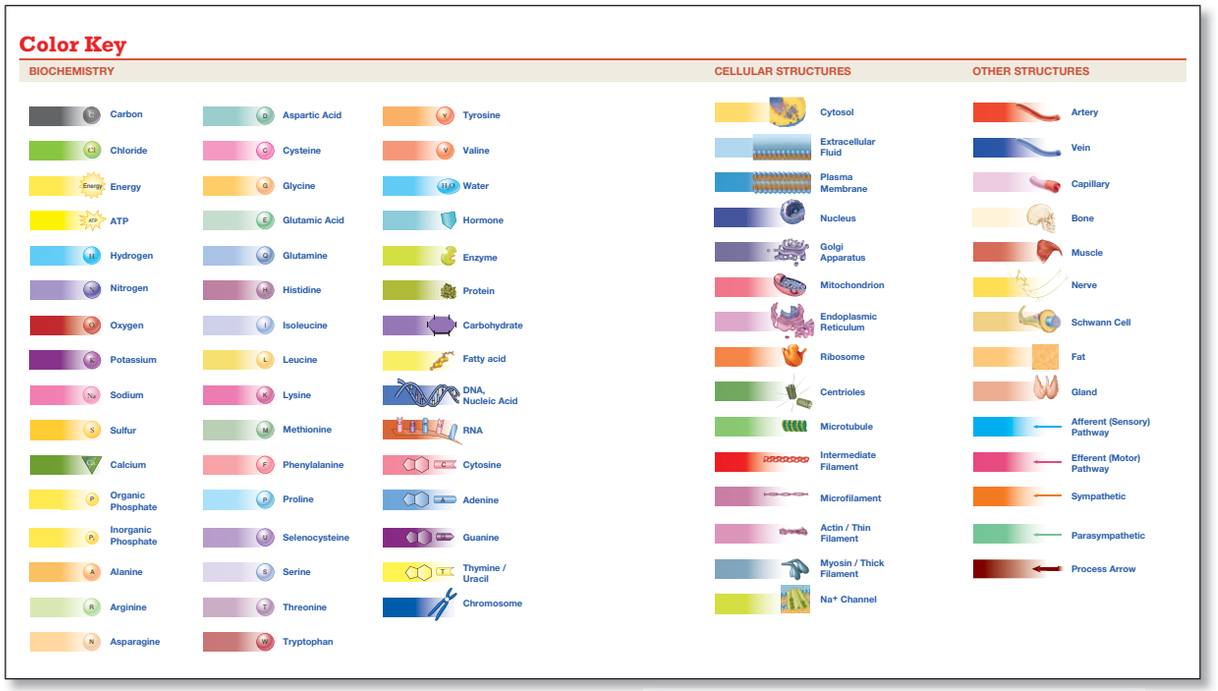
- **Chapter Outline**—*summarizes the contents of a chapter at a glance.* An overview outline introduces each chapter and enables the student to preview the content and direction of the chapter at the major concept level before beginning a detailed reading. Page references enable students to quickly locate topics in the chapter.


CHAPTER OUTLINE
Scan this outline before you begin to read the chapter, as
HINT
Composition of Blood, 599
Blood Volume, 599
Formed Elements of Blood, 600
Red Blood Cells (Erythrocytes), 601
Function of Red Blood Cells, 601
Bloo
Bloo
M

- **Language of Science**—*introduces you to new scientific terms in the chapter.* A comprehensive list of new terms is presented at the beginning of the chapter. Each term in the list has an easy-to-use pronunciation guide to help the learner easily "own" the word by being able to say it. Literal translations of the term or its word parts are included to help students learn how to deduce the meaning of new terms themselves. The listed terms are defined in the text body, where they appear in boldface type, and may also be found in the glossary at


LANGUAGE OF SCIENCE
embryonic stem cell
(em-bree-ON-ik)
[*em-* in, *-bryo-* fill to bursting, *-ic* relating to]
eosinophil
(ee-oh-SIN-oh-fil)
[*eosin-* reddish color, *-phil* love]
erythrocyte
(eh-RITH-roh-syte)
[*erythro-* red, *-cyte* cell]
erythropoiesis
formed elem
globin
(GLOH-bi
[*glob-* ball
granulocyte
(GRAN-y
[*gran-* gra
hematopoiet
(hee-mah
[*hem-* bloo
heme

the back of the book. The boldface type feature enables students to scan the text for new words before beginning their first detailed reading of the material, so they may read without having to disrupt the flow to grapple with new words or phrases. The Language of Science word list includes terms related to the essential anatomy and physiology presented in the chapter. Another word list near the end of the chapter, a feature described below as the Language of Medicine, is an inventory of all the new clinical terms introduced in the chapter.



- **Color-Coded Illustrations**—*help beginning students appreciate the "Big Picture" of human structure and function.* A special feature of the illustrations in this text is the careful and consistent use of color to identify important structures and substances that recur throughout the book. Consistent use of a color key helps beginning students appreciate the "Big Picture" of human structure and function each time they see a familiar structure in a new illustration. For an explanation of the color scheme, see the Color Key on pp. xxiv-xxv.

- **Directional Rosettes**—*help students learn the orientation of anatomical structures.* Where appropriate, small orientation diagrams and directional rosettes are included as part of an illustration to help students locate a structure with reference to the body as a whole or orient a small structure in a larger view.



- **Quick Check questions**—*test your knowledge of material just read.* Short objective-type questions are located immediately following major topic discussions throughout the body of the text. These questions cover important information presented in the preceding section. Students unable to answer the questions should reread that section before proceeding. This feature therefore enhances reading comprehension. Quick Check items are numbered by chapter, and a numerical listing of their answers can be found on the EVOLVE site (http://evolve.elsevier.com/Patton/AP/).

| QUICK CHECK |

1. Name the fluid portion of whole blood.
2. What constitutes the formed elements of blood?
3. What factors influence blood volume?
4. Identify the component percentages of the normal hematocrit.

- **A&P Connect features**—*call the reader's attention to online articles that illustrate, clarify, and apply concepts encountered in the text.* Embedded within the text narrative, these boxes connect you with interesting, brief online articles that stimulate thinking, satisfy your curiosity, and help you apply important concepts. They are often illustrated with micrographs, medical images, and medical illustrations.

| A&P CONNECT |

Blood transfusions are an important therapeutic tool. Learn more about blood transfusions, blood banking, and even *artificial* blood in ***Blood Transfusions*** online at ***A&P Connect.***

evolve

- **Cycle of Life**—*describes major changes that occur over a person's lifetime.* In many body systems, changes in structure and function are frequently related to a person's age or state of development. In appropriate chapters of the text, these changes are highlighted in this special section.

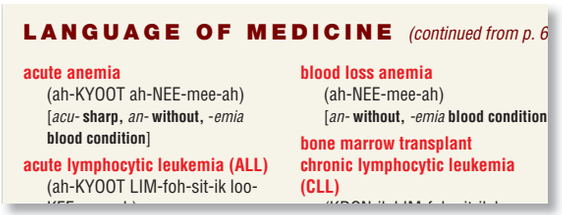


- **The Big Picture**—*explains the interactions of the system discussed in a particular chapter with the body as a whole.* This helps students relate information about body structures or functions that are discussed in the chapter to the body as a whole. The Big Picture feature helps you improve critical thinking by focusing on how structures and functions relate to one another on a global basis.



- **Mechanisms of Disease**—*helps you understand the basic principles of human structure and function by showing what happens when things go wrong.* Examples of pathology, or disease, are included in many chapters of the book to stimulate student interest and to help students understand that the disease process is a disruption in homeostasis, a breakdown of normal integration of form and function. The intent of the ***Mechanisms of Disease*** section is to reinforce the normal structures and mechanisms of the body while highlighting the general causes of disorders for a particular body system.

- **Language of Medicine**—*introduces you to new clinical terms in the chapter.* A brief list of clinical terms is presented near the end of each chapter. As in the ***Language of Science***


LANGUAGE OF MEDICINE (continued from p. 6

acute anemia
(ah-KYOOT ah-NEE-mee-ah)
[*acu-* **sharp**, *an-* **without**, *-emia* **blood condition**]

acute lymphocytic leukemia (ALL)
(ah-KYOOT LIM-foh-sit-ik loo-

blood loss anemia
(ah-NEE-mee-ah)
[*an-* **without**, *-emia* **blood condition**]

bone marrow transplant

chronic lymphocytic leukemia (CLL)

list at the beginning of the chapter, each term has a phonetic pronunciation guide and translations of word parts. The listed terms are defined in the text body, where they appear in boldface type.

- **Case Study**—*challenges you with "real-life" clinical or other practical situations so you can creatively apply what you have learned.* Every chapter has a case study preceding the chapter summary. The case study consists of a description of a real-life situation and a series of questions that require the student to use critical thinking skills to determine the answers.
- **Chapter Summary**—*outlines essential information in a way that helps you organize your study.* Detailed end-of-chapter summaries provide excellent guides for students as they review the text materials before examinations. Many students also find the summaries to be useful as a chapter preview in conjunction with the chapter outline.
- **Audio Chapter Summaries**—*allow you to listen and learn wherever you may be.* For the first time, the chapter summaries are now available in MP3 format for download at the EVOLVE site. You can play them on your computer, import them into your portable media device, or burn them onto a CD for playback in your stereo or car.
- **Review Questions**—*help you determine whether you have mastered the important concepts of each chapter.* Review questions at the end of each chapter give students practice in using a narrative format to discuss the concepts presented in the chapter.
- **Critical Thinking Questions**—*actively engage and challenge you to evaluate and synthesize the chapter content.* Critical thinking questions require students to use their higher level reasoning skills and demonstrate their understanding of, not just their repetition of, complex concepts.

Boxed Information

As always, we made every effort to update factual information and incorporate the most current anatomy and physiology research findings in this edition. Although there continues to be an incredible explosion of knowledge in the life sciences, not all new information is appropriate for inclusion in a fundamental-level textbook. Therefore we were selective in choosing new clinical, pathological, or special-interest material to include in this edition. This text remains focused on normal anatomy and physiology. The addition of new boxed content is intended to stimulate student interest and provide examples that reinforce the immediate personal relevance of anatomy and physiology as important disciplines for study.

- **General Interest Boxes**—*provide an expanded explanation of specific chapter content.* Many chapters contain boxed essays, occasionally clinical in nature, that expand on or relate to material covered in the text. Examples of subjects include the RNA revolution and the enteric nervous system.
- **Health Matters**—*present current information on diseases, disorders, treatments, and other health issues related to normal structure and function.* These boxes contain information related to health issues or clinical applications. In some instances, examples of structural anomalies or pathophysiology are presented. Information of this type is often useful in helping students understand the mechanisms involved in maintaining the "normal" interaction of structure and function.
- **Diagnostic Study**—*keep you abreast of developments in diagnosing diseases and disorders.* These boxes deal with specific diagnostic tests used in clinical medicine or research. Lumbar puncture, angiography, and antenatal diagnosis and treatment are examples.
- **FYI**—*give you more in-depth information on interesting topics mentioned in the text.* Topics of current interest, such as new advances in anatomy and physiology research, are covered in these "for your information" boxes.
- **Sports and Fitness**—*highlight sports-related topics.* Exercise physiology, sports injury, and physical education applications are highlighted in these boxes.
- **Career Choices**—*highlight individuals in health-related careers.* A Career Choices box appears at the end of each unit. These boxes describe some of the diverse opportunities currently available in health-related occupations and also demonstrate the importance of how an understanding of anatomy and physiology will be useful to students in their futures.

Glossary

A comprehensive glossary of terms is located at the end of the text. Accurate, concise definitions and phonetic pronunciation guides are provided. In this edition, word parts have also been added to each glossary entry. An audio glossary is also available on the expanded EVOLVE site (http://evolve.elsevier.com/Patton/AP/) with definitions and audio pronunciations for most of the key terms in the text.

LEARNING SUPPLEMENTS FOR STUDENTS

Brief Atlas of Human Anatomy

A full-color *Brief Atlas of Human Anatomy* containing cadaver dissections, osteology, organ casts, histology specimens, and surface anatomy photographs is packaged with every new copy of this edition of *Anatomy & Physiology*. This helpful supplement serves as a handy reference for students as they study the human body in class and in the laboratory—and even later on in clinical and career contexts.

summaries of landmark features used to distinguish microscopic specimens. Each exercise concludes with a lab report that may also serve as a homework assignment or self-test.

The new edition of the lab manual includes *eLabs for Anatomy & Physiology*, an online lab program designed to complement traditional lab exercises. The lab exercises, both anatomy and physiology based, are separated into modules. Each lab is composed of a variety of learning activities, animations, simulations, and quizzes. The labs are designed so that students can easily navigate between activities, allowing them the freedom to focus on the areas where they need the most help.

TEACHING SUPPLEMENTS FOR INSTRUCTORS

Instructor Resources on Evolve

The *Instructor's Resource* was written and developed specifically for this new edition of *Anatomy & Physiology*. Available on Evolve, it provides critical thinking questions, learning objectives and activities, teaching tips for the text, synopses of difficult concepts, and clinical applications exercises. To make lecture preparations a little easier, the Instructor's Resource also includes lesson plans that allow you to hit the ground running. The Evolve website for instructors also includes a **Computerized Test Bank** with more than 7000 multiple choice, true/false, short answer, and challenge questions (which you can also import into your **Classroom Performance System** to quickly assess student comprehension and monitor your classroom's response), an **Electronic Image Collection** to accompany *Anatomy & Physiology*, featuring hundreds of full-color illustrations and photographs, with labels and lead lines that you can turn off and on, **Powerpoint Presentations**, and much more!

Instructor's Guide for the Laboratory Manual

The Instructor's Guide for the ***Laboratory Manual*** on Evolve offers detailed information to help the instructor prepare for the laboratory exercises. Alternate activities, substitutions, student handouts, and other resources help instructors tailor the use of the ***A&P Laboratory Manual*** to their own course. Answers for all questions on the lab reports in the ***A&P Laboratory Manual*** are also provided either to check student work or to provide for students who use lab reports as self tests. Also included is a **cadaver dissection video**—shot in high definition— that you can use in lecture or lab.

Acknowledgments

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Kevin T. Patton
Gary A. Thibodeau

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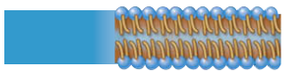
BIOCHEMISTRY

- C — Carbon
- Cl — Chloride
- Energy — Energy
- ATP — ATP
- H — Hydrogen
- N — Nitrogen
- O — Oxygen
- K — Potassium
- Na — Sodium
- S — Sulfur
- Ca — Calcium
- P — Organic Phosphate
- P_i — Inorganic Phosphate
- A — Alanine
- R — Arginine
- N — Asparagine
- D — Aspartic Acid
- C — Cysteine
- G — Glycine
- E — Glutamic Acid
- Q — Glutamine
- H — Histidine
- I — Isoleucine
- L — Leucine
- K — Lysine
- M — Methionine
- F — Phenylalanine
- P — Proline
- U — Selenocysteine
- S — Serine
- T — Threonine
- W — Tryptophan
- Y — Tyrosine
- V — Valine
- H_2O — Water
- Hormone
- Enzyme
- Protein
- Carbohydrate
- Fatty acid
- DNA, Nucleic Acid
- RNA
- C — Cytosine
- A — Adenine
- G — Guanine
- T — Thymine / Uracil
- Chromosome

CELLULAR STRUCTURES


Cytosol


Extracellular Fluid


Plasma Membrane


Nucleus


Golgi Apparatus


Mitochondrion


Endoplasmic Reticulum


Ribosome


Centrioles


Microtubule


Intermediate Filament


Microfilament


Actin / Thin Filament


Myosin / Thick Filament


Na^+ Channel

OTHER STRUCTURES


Artery


Vein


Capillary


Bone


Muscle


Nerve


Schwann Cell


Fat


Gland


Afferent (Sensory) Pathway


Efferent (Motor) Pathway


Sympathetic


Parasympathetic


Process Arrow

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Chapter 17

17-1, 17-13, *B*: Adapted from Guyton A, Hall J: *Textbook of medical physiology*, ed 11, Philadelphia, 2006, Saunders. **17-2, *A*:** From Seidel HM, Ball JW, Dains JE, Benedict GW: *Mosby's guide to physical examination*, ed 6, St Louis, 2006, Mosby. **17-2, *B*:** From Swartz MH: *Textbook of physical diagnosis*, ed 4, Philadelphia, 2002, Saunders. **17-3, 17-30:** Adapted from Boron W, Boulpaep E: *Medical physiology*, updated version, ed 1, Philadelphia, 2005, Saunders. **17-8, *D*:** Photo Researchers Inc. **17-10, *A*:** From Swartz MH: *Textbook of physical diagnosis*, ed 5, Philadelphia, 2006, Saunders. **17-10, *B*:** From Wilson SF, Giddens J: *Health assessment for nursing practice*, ed 3, St Louis, 2005, Mosby. **17-10, *C*:** Courtesy Richard A. Buckingham, Clinical Professor, Otolaryngology, Abraham Lincoln School of Medicine, University of Illinois, Chicago. **17-16:** Copyright Kevin Patton, Lion Den Inc, Weldon Spring, MO. **17-18, 17-24:** From Newell FW: *Ophthalmology: principles and concepts*, ed 7, St Louis, 1992, Mosby. **17-23, *C*:** Courtesy Dr. Scott Mittman, Johns Hopkins Hospital, Baltimore, MD. **17-28:** From Seidel HM, Ball JW, Dains JE, Benedict GW: *Mosby's guide to physical examination*, ed 3, St Louis, 2003, Mosby. **17-32:** From Bingham BJG, Hawke M, Kwok P, *Atlas of clinical otolaryngology*, St Louis, 1992, Mosby–Year Book. **17-34, 17-35, A, Box 17-3:** From Swartz MH: *Textbook of physical diagnosis*, ed 4, Philadelphia, 2002, Saunders. **Box 17-5:** From Barkauskas V, Baumann L, Stoltenberg-allen K, Darling-Fisher C: *Health and physical assessment*, ed 2, St Louis, 1998, Mosby. **Box 17-6:** From *Ishihara's tests for colour deficiency*, Tokyo, Japan, 1973, Kanehara Trading Co, Copyright Isshinkai Foundation.

Chapter 18

18-13: Adapted from Hinson J, Raven P: *The endocrine system*, Edinburgh, 2007, Churchill Livingstone.

Chapter 19

19-2: From Erlandsen SL, Magney J: *Color atlas of histology*, St Louis, 1992, Mosby. **19-7:** Adapted from Boron W, Boulpaep E: *Medical physiology*, updated version, ed 1, Philadelphia, 2005, Saunders. **19-9, *B*:** From Jacob S: *Atlas of human anatomy*, Edinburgh, 2002, Churchill Livingstone. **19-12, *B*:** From Abrahams P, Marks S, Hutchings R: *McMinn's color atlas of human anatomy*, ed 3, Philadelphia, 2003, Mosby. **19-13:** Dennis Strete. **19-15:** From Gosling J, Harris P, Whitmore I, Willan P: *Human anatomy*, ed 4, Philadelphia, 2002, Mosby. **19-17:** From Kierszenbaum A: *Histology and cell biology*, Philadelphia, 2002, Mosby. **19-23:** From Brissova M, et al: Assessment of Human Pancreatic Islet Architecture and Composition by Laser Scanning Confocal Microscopy, J Histochem Cytochem 2005 53:1087. **Box 19-5, *A*:** From Swartz MH: *Textbook of physical diagnosis*, ed 4, Philadelphia, 2002, Saunders. **Box 19-5, *B*:** From Stein Ha, Slatt BJ, Stein RM: *The ophthalmic assistant: fundamentals and clinical practice*, ed 7, Philadelphia, 2000, Mosby. **Box 19-5, *C*:** From Swartz MH: *Textbook of physical diagnosis history and examination*, ed 5, Philadelphia, 2006, Saunders. **Box 19-8:** Courtesy Gower Medical Publishers. **Career Choices (Inset):** From Fritz S, Chaitow L, Hymel G: *Mosby's massage career development series: clinical massage in the healthcare setting*, St Louis, 2008, Mosby.

Chapter 20

20-3, *D*: From Zakus SM: *Clinical procedures for medical assistants*, ed 3, St Louis, 1995, Mosby. **20-4, Box 20-2:** Courtesy Bevelander G, Ramalay Ja: *Essentials of histology*, ed 8, St Louis, 1979, Mosby. **20-8 (Inset), 20-15:** From Carr J, Rodak B: *Clinical hematology atlas*, St Louis, 1999, Elsevier. **20-9, 20-10, 20-11, 20-12, 20-13:** Dennis Strete. **20-14:** From Turgeon M: *Linne & Ringsud's clinical laboratory science*, ed 5, St Louis, 2007, Mosby. **20-18 (Inset):** From Belcher AE: *Blood disorders*, St Louis 1993, Mosby. **20-21, *B*:** Copyright Dennis Kunkel Microscopy Inc. **20-24:** From Cotran R, Kumar V, Collins T: *Robbins pathologic basis of disease*, ed 6, Philadelphia, Saunders, 1999. **20-25, 20-26D, 20-27:** From Kumar V, Abbas A, Fausto N: *Robbins and Cotran pathologic basis of disease*, ed 7, Philadelphia, 2005, Saunders. **20-26, *A*:** Courtesy Dr. J. V. Melo. **20-26, *B*:** From Copstead-Kirkhorn L, Banasik J: *Pathophysiology*, ed 2, St Louis, 2005, Saunders. **20-26, *C*:** From Skarin A: *Atlas of diagnostic oncology*, ed 2, Philadelphia, 1996, Mosby. **Case Study Box:** From Stevens ML: *Fundamentals of clinical hematology*, Philadelphia, 1997, Saunders.

Chapter 21

21-1: Courtesy Patricia Kane, Indiana University Medical School. **21-9 (Drawing):** From Wilson SF, Giddens JF: *Health assessment for nursing practice*, ed 2, St Louis, 2001, Mosby. **21-9 (Inset):** From Seidel HM, Ball JW, Dains JE, Benedict GW: *Mosby's guide to physical examination*, ed 6, St Louis, 2006, Mosby. **21-17:** Adapted from McCance K, Huether S: *Pathophysiology*, ed 5, St Louis, 2006, Mosby. **21-21, *C*, 21-23, *A*, *C*, 21-25, *B*, *C*:** From Abrahams P, Marks S, Hutchings R: *McMinn's color atlas of human anatomy*, ed 5, Philadelphia, 2003, Mosby. **21-38, 21-45, *B*:** From Kumar V, Abbas A, Fausto N: *Robbins and Cotran pathologic basis of disease*, ed 7, Philadelphia, 2005, Saunders. **21-41, 21-42, 21-46:** From Cotran R, Kumar V, Collins T: *Robbins pathologic basis of disease*, ed 6, Philadelphia, 1999, Saunders. **21-43 (Photo):** From Swartz MH: *Textbook of physical diagnosis*, ed 4, Philadelphia, 2002, Saunders. **Box 21-1:** From Warekois R, Robinson R: *Phlebotomy*, ed 2, St Louis, 2007, Saunders. **Box 21-2:** From Goldman L, Ausiello D: *Cecil textbook of medicine*, ed 23, Philadelphia, 2008, Saunders. **Box 21-3:** Courtesy Simon C, Janner M: *Color atlas of pediatric diseases with differential diagnosis*, ed 2, Hamilton, Ontario, 1990, BC Decker. **Case Study Box:** Courtesy Dr. Daniel Simon and Mr. Paul Zambino.

Chapter 22

22-1: From Harvey W: *The anatomical exercises*, London, 1995, Dover Publishing. **22-6:** From Noble A, Johnson R, Thomas A, Bass P: *The cardiovascular system*, Edinburgh, 2005, Churchill Livingstone. **22-13:** From Rhoades R, Pflanzer R: *Human physiology*, ed 3, Philadelphia, 1995, Perennial. **22-16:** Adapted from Guyton A, Hall J: *Textbook of medical physiology*, ed 11, Philadelphia, 2006, Saunders. **22-18, 22-26, *B*:** Adapted from Boron W, Boulpaep E: *Medical physiology*, updated version, ed 1, Philadelphia, 2005, Saunders. **22-25:** Adapted from McCance K, Huether S: *Pathophysiology*, ed 4, St Louis, 2002, Mosby. **22-32:** Adapted from Canobbio MM: *Cardiovascular disorders*, St Louis, 1990, Mosby. **22-35:** Courtesy Guzzetta and Dossey, 1984. **22-36:** From Aehlert B: *ACLS Quick Review Study Cards*, ed 2, St Louis, 2004, Mosby.

Case Study Box: From Hicks GH: *Cardiopulmonary anatomy and physiology*, Philadelphia, 2000, Saunders.

Chapter 23

23-6: Courtesy Ballinger P, Frank E: *Merrill's atlas of radiographic positions and radiologic procedures*, vol 1, ed 10, St Louis, 2003, Mosby. **23-7:** Adapted from McCance K, Huether S: *Pathophysiology*, ed 4, St Louis, 2002, Mosby. **23-8:** Adapted from Boron W, Boulpaep E: *Medical physiology*, updated version, ed 1, Philadelphia, 2005, Saunders. **23-9, *A*:** Adapted from Mathers L, Chase R, Dolph J, Glasgow E: *CLASS clinical anatomy principles*, Philadelphia, 1996, Mosby. **23-9, *B*:** From Nielsen M: *Human anatomy lab manual and workbook*, ed 4, Dubuque, Ia, 2002, Kendall/Hunt Publishing Company. **23-10, *B*, 23-18, *B*:** Dennis Strete. **23-11, 23-12, 23-16, 23-25:** From Seidel HM, Ball JW, Dains JE, Benedict GW: *Mosby's guide to physical examination*, ed 6, St Louis, 2006, Mosby. **23-15:** From National Institute of allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD. **23-17, *B*:** Courtesy Dr. Edward L. Applebaum, Head, Department of Otolaryngology, University of Illinois Medical Center, Chicago, IL. **23-19:** Adapted from Rhoades R, Pflanzer R: *Human physiology*, ed 3, Philadelphia, 1995, Perennial. **23-20:** Courtesy Vidic B, Suarez FR: *Photographic atlas of the human body*, St Louis, 1984, Mosby. **23-22:** Courtesy Walter Tunnesen, MD, The American Board of Pediatrics, Chapel Hill, NC. **23-23:** From Goldstein B, editor: *Practical dermatology*, ed 2, St Louis, 1997, Mosby. **23-24:** From Zitelli B, Davis H: *Atlas of pediatric physical diagnosis*, ed 4, Mosby, 2002. **Case Study Box:** From Cohen J, Powderly WG: *Infectious diseases*, ed 2, St Louis, 2004, Mosby.

Chapter 24

24-1, 24-8, 24-13, 24-14, 24-15, 24-19, 24-24, 24-24, 24-26, 24-27, 24-28, 24-30, Box 24-1, *B*, Box 24-8: From Abbas A, Lichtman A: *Cellular and molecular immunology*, ed 5, Philadelphia, 2003, Saunders. **24-4:** From Roitt IM, Brostoff, Male DK: *Immunology*, ed 3, St Louis, 1993, Mosby. **24-6:** Adapted from McCance K, Huether, S: *Pathophysiology*, ed 5, St Louis, 2006, Mosby. **24-10, 24-23, 24-31, Box 24-1, *A*:** From Copstead-Kirkhorn L, Banasik J: *Pathophysiology*, ed 2, St Louis, 1999, Saunders. **24-11:** Copyright Dennis Kunkel Microscopy Inc. **Box 24-5:** From Stinchcombe JC, Griffiths GM: The role of the secretory immunological synapse in killing by $CD8^+$ CTL, *Semin Immunol* 15(6):301-305, 2003. **Box 24-7:** Adapted from McCance K, Huether S: *Pathophysiology*, ed 4, St Louis, 2002, Elsevier. **Case Study Box:** From Mason DJ, Leavitt J, Chaffee M: *Policy and politics in nursing and health care*, ed 5, St Louis, 2007, Saunders.

Chapter 25

25-1, *A*: J Gebhardt/The Image Bank. **25-1, *B*:** Koch/Constrasto Picture Group. **25-1, *C*:** Mickey Gibson/Tom Stack and associates. **25-1, *D*:** Global Warming Art. **25-8:** Copyright Kevin Patton, Lion Den Inc, Weldon Spring, MO (courtesy National Tiger Sanctuary).

Chapter 26

26-4: From Stevens A, Lowe J: *Human histology*, ed 3, Philadelphia, 2005, Mosby. **26-8, *B*:** Custom Medical Stock Photo Inc. **26-9:** Adapted from Thompson JM, Wilson SF: *Health assessment for nursing practice*, St Louis, 1996, Mosby. **26-10 (Electron micrograph), 26-13, *B*:** From Erlandsen SL, Magney J: *Color atlas of histology*, St Louis, 1992, Mosby. **26-12:** From Hutchings RT, McMinn RM: *McMinn's color atlas of human anatomy*, ed 2, Chicago, 1988, Year Book Medical Publishers. **26-14:** From Epstein O, Perkin GD, Cookson J, de Bono D: *Clinical examination*, ed 3, Philadelphia, 2003, Mosby. **26-16:** Courtesy Vidic B, Suarez RF: *Photographic atlas of the human body*, St Louis, 1984, Mosby. **26-19:** From Zitelli B, Davis H: *Atlas of pediatric physical diagnosis*, ed 4, Philadelphia, 2002, Mosby. **26-20, 26-21:** From Kumar V, Abbas A, Fausto N: *Robbins and Cotran pathologic basis of disease*, ed 7, Philadelphia, 2005, Saunders.

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27-6: From Drake R, Vogl AW, Mitchell A: *Gray's anatomy for students*, Philadelphia, 2005, Churchill Livingstone. **27-10, *A*, 27-17, 27-26, 27-32:** Adapted from Boron W, Boulpaep E: *Medical physiology*, updated version, ed 1, Philadelphia, 2005, Saunders. **27-10, *B*:** From Wilson SF, Thompson JM: *Respiratory disorders*, St Louis, 1990, Mosby. **27-13, Box 27-2:** Adapted from Davies A, Moores C: *The respiratory system*, Edinburgh, 2004, Churchill Livingstone. **27-18:** From Rhoades R, Pflanzer R: *Human physiology*, ed 3, Philadelphia, 1995, Perennial. **Box 27-8:** Copyright Kevin Patton, Lion Den Inc, Weldon Spring, MO. **Box 27-9:** Adapted from Guyton A, Hall J: *Textbook of medical physiology*, ed 11, Philadelphia, 2006, Saunders.

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Chapter 29

29-4, Box 29-1: Adapted from Boron W, Boulpaep E: *Medical physiology*, updated version, ed 1, Philadelphia, 2005, Saunders. **29-19, *B*:** Courtesy Dr. Andrew Evan, Indiana University. **Box 29-2, *B*:** Adapted from Smith M, Morton D: *The digestive system*, Edinburgh, 2001, Churchill Livingstone. **Box 29-4, *B*, *C*:** From Stevens A, Lowe J: *Human histology*, ed 3, Philadelphia, 2005, Mosby.

Chapter 30

30-14, *B*: Courtesy Brenda Russell, PhD, University of Illinois at Chicago. **30-18, *B*:** Adapted from Carroll R: *Elsevier's integrated physiology*,

Philadelphia, 2007, Mosby. **30-20:** Adapted from Report of the Expert Panel for Population Strategies for Blood Cholesterol Reduction: Bethesda, MD, November 1990, The National Cholesterol Education Program, National Heart Lung and Blood Institute, Public Health Service, US Department of Health and Human Services, NIH Publication No. 90-3046. **30-25, 30-26, 30-29, 30-32, Box 30-9, *B*:** Adapted from Mahan LK, Escott-Stump S: *Krause's food, nutrition and diet therapy*, ed 11, St Louis, 2004, Saunders. **30-31:** Adapted from Guyton A, Hall J: T*extbook of medical physiology*, ed 11, Philadelphia, 2006, Saunders. **30-33:** From Zitelli B, Davis H: *Atlas of pediatric physical diagnosis*, ed 3, Philadelphia, 1997, Mosby. **Box 30-2:** Courtesy Bevelander G, Ramalay Ja: *Essentials of histology*, ed 8, St Louis, 1979, Mosby.

Chapter 31

31-1, *A*: Barbara Cousins. **31-1, *B*, 31-2, *B*:** From Abrahams P, Marks S, Hutchings R: *McMinn's color atlas of human anatomy*, ed 5, Philadelphia, 2003, Mosby. **31-2, A, 31-10:** Adapted from Brundage DJ: Renal disorders. *Mosby's clinical nursing series*, St Louis, 1992, Mosby. **31-3, *B*:** From Weir J, Abrahams P: *Imaging atlas of the human anatomy*, ed 2, Philadelphia, 1997, Mosby. **31-6:** From Heylings D, Spence R, Kelly B: *Integrated anatomy*, Edinburgh, 2007, Churchill Livingstone. **31-7, 31-11, 31-16:** From Stevens A, Lowe J: *Human histology*, ed 3, Philadelphia, 2005, Mosby. **31-8:** From Gosling J, Harris P, Whitmore I, Willan P: *Human anatomy*, ed 4, Philadelphia, 2002, Mosby. **31-9:** Adapted from Guyton A, Hall J: T*extbook of medical physiology*, ed 11, Philadelphia, 2006, Saunders. **31-14, 31-15, *B*:** From Boron W, Boulpaep E: *Medical physiology*, updated version, ed 1, Philadelphia, 2005, Saunders. **31-29:** From Kumar V, Abbas A, Fausto N: *Robbins and Cotran pathologic basis of disease*, ed 7, Philadelphia, 2005, Saunders. **Box 31-2:** From Schmidbauer J, Remzi M, Memarsadeghi M et al: Diagnostic accuracy of computed tomography-guided percutaneous biopsy of renal masses, *Eur Urol* 53(5):869-1100, 2007.

Chapter 32

32-7: Copyright Kevin Patton, Lion Den Inc, Weldon Spring, MO. **32-9, 32-18:** Adapted from Mahan LK, Escott-Stump S: *Krause's food, nutrition and diet therapy*, ed 12, St Louis, 2007, Saunders. **32-11:** From Bloom A, Ireland J: *Color atlas of diabetes*, ed 2, St Louis, 1992, Mosby. **Box 32-2:** From Barkauskas V, Baumann L, Stoltenberg-allen K, Darling-Fisher C: *Health and physical assessment*, ed 2, St Louis, 1998, Mosby.

Chapter 33

Box 33-1: Courtesy Kevin Patton, Lion Den Inc, Weldon Spring, MO.

Chapter 34

34-3, A, 34-8, *E*: Lennart Nilsson. **34-4, 34-8, *F*:** From Stevens A, Lowe J: *Human histology*, ed 3, Philadelphia, 2005, Mosby. **34-5:** Courtesy Dr. Mark Ludvigson, US Army Medical Corps, St Paul, MN. **34-9, 34-10, 34-13:** From Erlandsen SL, Magney J: *Color atlas of histology*, St Louis, 1992, Mosby. **34-11:** Barbara Cousins. **34-12:** From Abrahams P, Marks S, Hutchings R: *McMinn's color atlas of human anatomy*, ed 5, Philadelphia, 2003, Mosby. **34-14, *B*:** Courtesy Vidic B, Suarez RF: *Photographic atlas of the human body*, St Louis, 1984, Mosby. **34-15:** Adapted from Guyton A, Hall J: *Textbook of medical physiology*, ed 11, Philadelphia, 2006, Saunders. **34-16:** Adapted from Boron W, Boulpaep E: *Medical physiology*, updated version, ed 1, Philadelphia, 2005, Saunders. **34-17, Box 34-1:** From Seidel HM, Ball JW, Dains JE, Benedict GW: *Mosby's guide to physical examination*, ed 6, St Louis, 2006, Mosby.

Chapter 35

35-1, *B*: From Moses K, Nava P, Banks J, Petersen D: *Moses atlas of clinical gross anatomy*, Philadelphia, 2005, Mosby. **35-3, *B*, 35-6, 35-7:** From Gosling J, Harris P, Whitmore I, Willan P: *Human anatomy*, ed 4, Philadelphia, 2002, Mosby. **35-5C:** From Familiari G, et al: Ultrastructural Dynamics of Human Reproduction, from Ovulation to Fertlization and Early Embryo Development, Int Rev Cytol, 249:53-141, 2006. **35-10:** From Stevens A, Lowe J: *Human histology*, ed 3, Philadelphia, Mosby, 2005. **35-11:** Courtesy Dr. Richard Blandau, Department of Biological Structure, University of Washington School of Medicine, Seattle, Wa, from his film *Ovulation and Egg Transport in Mammals*, 1973. **35-17:** Adapted from Boron W, Boulpaep E: *Medical physiology*, updated version, ed 1, Philadelphia, 2005, Saunders. **35-20, 35-22:** From Mettler F: *Essentials of radiology*, ed 2, Philadelphia, 2005, Saunders. **35-21, *A*:** From Abrahams P, Marks S, Hutchings R: *McMinn's color atlas of human anatomy*, ed 5, Philadelphia, 2003, Saunders. **35-21, *B*:** From Symonds EM, MacPherson MBa: *Color atlas of obstetrics and gyneocolgy*, London, 1994, Mosby Wolfe. **35-23:** From Kumar V, Abbas A, Fausto N: *Robbins and Cotran pathologic basis of disease*, ed 7, Philadelphia, 2005, Saunders. **35-24, *B*, *C*,** From Cotran R, Kumar V, Collins T: *Robbins pathologic basis of disease*, ed 6, Philadelphia, 1999, Saunders. **Box 35-5 (Photo):** Ferri FF: Ferri's Color Atlas and Text of Clinical Medicine, 2009, Saunders/Elsevier.

Chapter 36

36-5 (Photo), 36-13: Lennart Nilsson. **36-7:** Courtesy Lucinda L. Veeck, Jones Institute for Reproductive Medicine, Norfolk, Va. **36-11, *B*:** From Cotran R, Kumar V, Collins T: *Robbins pathologic basis of disease*, ed 6, Philadelphia, 1999, Saunders. **36-12, *B*:** Adapted from Hinson J, Raven P, *The endocrine system*, Edinburgh, 2007, Churchill Livingstone. **36-14:** From Moore KL, Persand TVa: *The developing human*, ed 6, Philadelphia, 1998, Saunders. **36-17, 36-18, 36-25:** Adapted from Boron W, Boulpaep E: *Medical physiology*, updated version, ed 1, Philadelphia, 2005, Saunders. **36-23:** Courtesy Ron Edwards, Chesterfield, MO. **36-24**: Copyright Kevin Patton, Lion Den Inc, Weldon Spring, MO. **36-26:** Adapted from Mahan LK, Escott-Stump S: *Krause's food, nutrition and diet therapy*, ed 12, St Louis, 2007, Saunders. **36-27:** Adapted from McCance K, Huether S: *Pathophysiology*, ed 5, St Louis, 2005, Mosby. **36-29, *B*:** Adapted from Ignatavicius D, Bayne MV: *Medical-surgical nursing: a nursing process approach*, Philadelphia, 1991, Saunders. **36-30:** From Andersen JL, Schjerling P, Saltin B: Muscle, genes, and athletic performance, *Sci Am*, 283(3):49-55, 2000. **Box 36-2, *B*:** Courtesy Kevin Patton, Lion Den Inc, Weldon Spring, MO. **Case Study Box:** From Hagen-ansert SL: *Textbook of diagnostic ultrasonography*, Vol 2, ed 6, St Louis, 2007, Mosby.

Chapter 37

37-1: Adapted from Boron W, Boulpaep E: *Medical physiology*, updated version, ed 1, Philadelphia, 2005, Saunders. **37-5:** From Jorde L, Carey J, Bamshad M: *Medical genetics*, ed 3, Philadelphia, 2004, Saunders. **37-10:** From McCance K, Huether S: *Pathophysiology*, ed 4, St Louis, 2002, Mosby. **37-13, *B*:** From Kumar V, Abbas A, Fausto N: *Robbins and Cotran pathologic basis of disease*, ed 7, Philadelphia, 2005, Saunders. **37-14, *A*:** Courtesy Lois McGavran, Denver Children's Hospital. **37-14, *B*:** Richard Hutching/Photo Researchers Inc. **37-15, 37-16, 37-17, *B*:** Courtesy Nancy S. Wexler, PhD, Columbia University.

Unit One

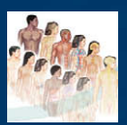
The Body as a Whole

The six chapters in Unit One "set the stage" for the study of human anatomy and physiology. They provide the unifying information required to understand the "connectedness" of human structure and function. They will help you understand how organized anatomical structures of a particular size, shape, form, or placement serve important functions. The illustration that opens this unit shows the body not as a jumble of isolated parts but as an integrated whole.

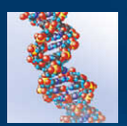
In Chapter 1 the concept of levels of organization in the body is presented, and the unifying theme of homeostasis is introduced to explain how the interaction of structure and function at chemical, organelle, cellular, tissue, organ, and system levels is achieved and maintained by dynamic counterbalancing forces within the body. The material presented in Chapter 2—The Chemical Basis of Life—provides an understanding of the basic chemical interactions that influence the control, integration, and regulation of these counterbalancing forces in every organ system of the body.

Unit One concludes with information that builds on the organizational and biochemical information presented in the first two chapters. The structure and function of cells presented in Chapters 3, 4, and 5 explain why physiologists often state that "all body functions are cellular functions." Grouping similar cells into functioning tissues is accomplished in Chapter 6. Subsequent chapters of the text focus on the remaining organ systems of the body.

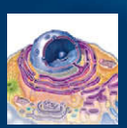
SEEING THE BIG PICTURE



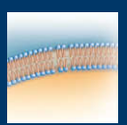
1 **Organization of the Body, 3**



2 **The Chemical Basis of Life, 33**



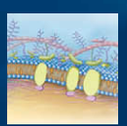
3 **Anatomy of Cells, 66**



4 **Physiology of Cells, 90**



5 **Cell Growth and Reproduction, 113**



6 **Tissues, 131**

the BIG picture

Seeing the BIG picture

Before reading this introduction, you probably spent a few minutes flipping through this book. Naturally, you are curious about your course in human anatomy and physiology, and you wanted to see what lies ahead. It is more than that. You are curious about the human body—about yourself, really. We all have that desire to learn more about how our bodies are put together and how all the parts work. Unlike many other people, though, you now have the opportunity to gain an understanding of the underlying scientific principles of human structure and function.

To truly understand the nature of the human body requires an ability to appreciate "the parts" and "the whole" at the same time. As you flipped through this book for the first time, you probably looked at many different body parts. Some were microscopic—such as muscle cells—and some were very large—such as arms and legs. In looking at these parts, however, you gained very little insight about how they worked together to allow you to sit here, alive and breathing, and read and comprehend these words.

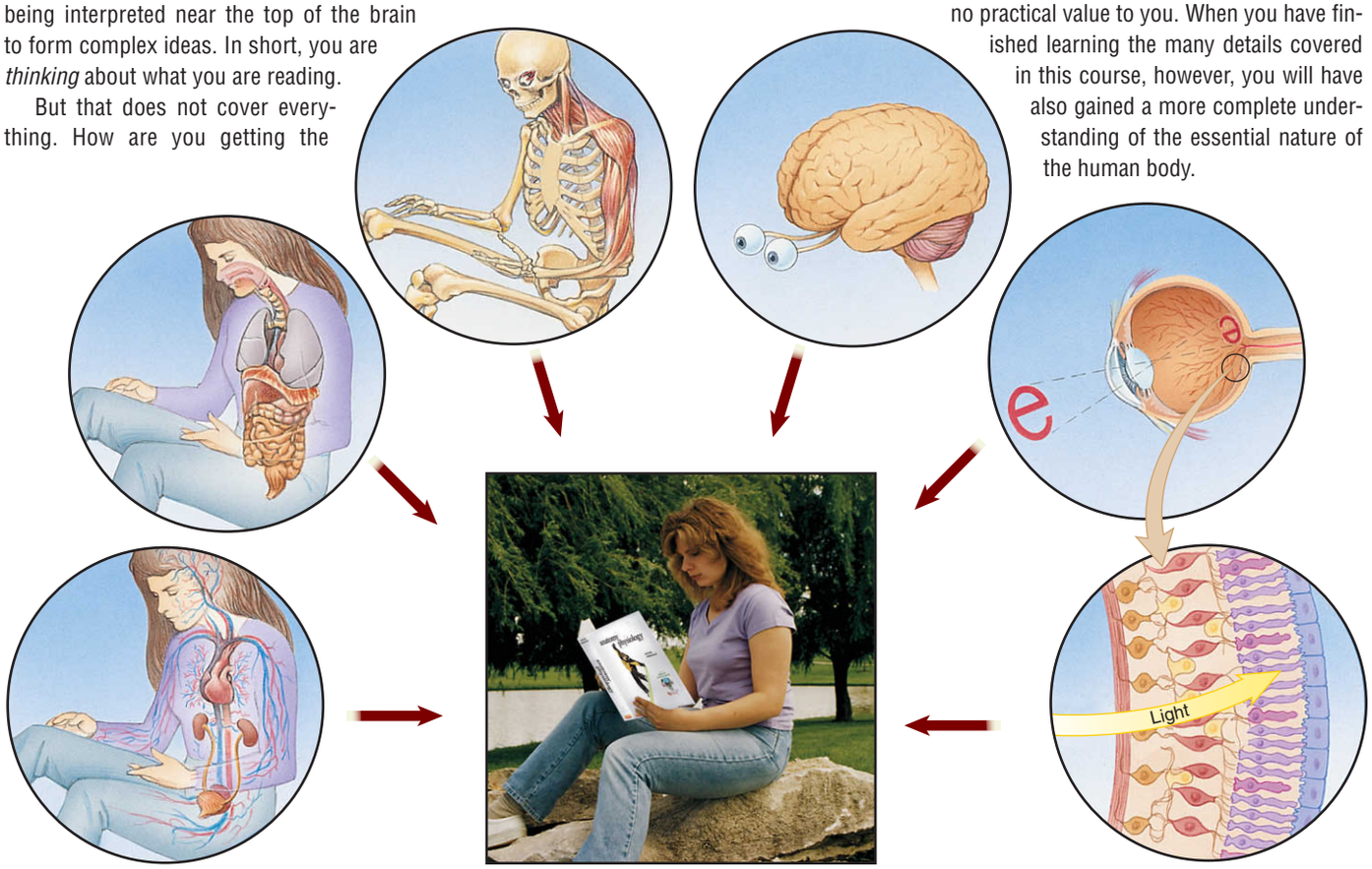
Think about it for a moment. What does it take to be able to read these words and understand them? You might begin by thinking about the eye. How do all of its many intricate parts work together to form an image? The eye is not the only organ you are using right now. What about the bones, joints, and muscles you are using to hold the book, to turn the pages, and to move your eyes as they scan this paragraph? Let's not forget the nervous system. The brain, spinal cord, and nerves are receiving information from the eyes, evaluating it, and using it to coordinate the muscle movements. The squiggles we call letters are being interpreted near the top of the brain to form complex ideas. In short, you are *thinking* about what you are reading.

But that does not cover everything. How are you getting the energy to operate your eyes, muscles, brain, and nerves? Energetic chemical reactions inside each cell of these organs require oxygen and nutrients captured by the lungs and digestive tract and delivered by the heart and blood vessels. These chemical reactions produce wastes that are handled by the liver, kidneys, and other organs. All these functions must be coordinated, a feat accomplished by regulation of body organs by hormones, nerves, and other mechanisms.

Learning to name the various body parts, to describe their detailed structure, and to explain the mechanisms that produce their functions is an essential step that leads to the goal of understanding the human body. To actually reach that goal, however, you must be able to draw together isolated facts and concepts. In other words, understanding the nature of individual body parts becomes more meaningful when you understand how the parts work together in a living, whole person.

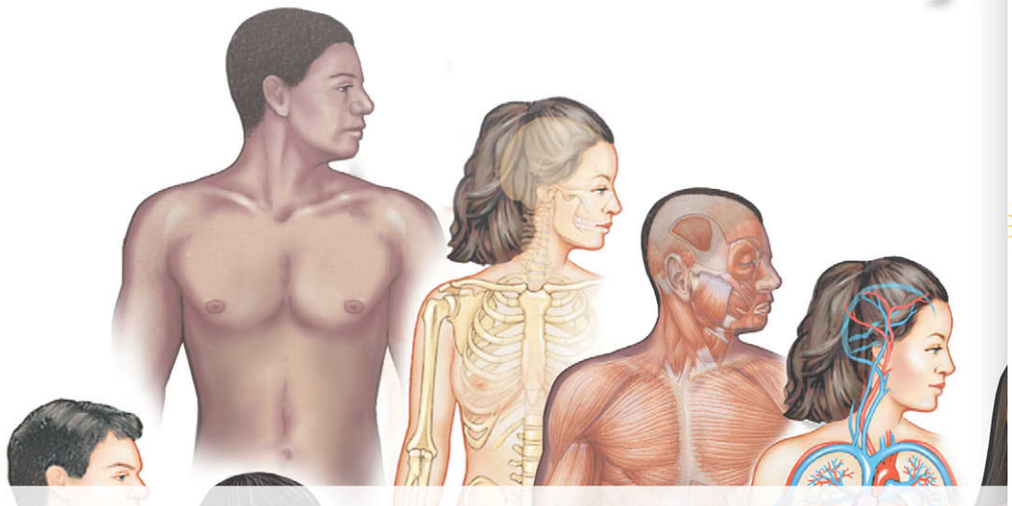
Many textbooks are written like reference books—dictionaries, for example. They provide detailed descriptions of the structure and function of individual body parts, often in logical groupings, while rarely stopping to step back and look at the whole person. In this book, however, we have incorporated the "whole body" aspect into the discussion of every major topic. In chapter and unit introductions, in appropriate paragraphs within each section, and in specific sections near the end of each chapter, we have stepped back from the topic at hand and refocused attention to the broader view.

We are confident that the "whole body" approach will help you put each new fact or concept you learn into its proper place within a larger framework of understanding. You may also better appreciate why it is important to learn some detailed facts that may at first seem to have no practical value to you. When you have finished learning the many details covered in this course, however, you will have also gained a more complete understanding of the essential nature of the human body.



Organization of the Body

1



CHAPTER OUTLINE

HINT *Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.*

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LANGUAGE OF SCIENCE

HINT *Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.*

abdominopelvic cavity
(ab-DOM-i-no-PEL-vik KAV-ĭ-tee)
[*abdomin-* **belly,** *-pelv-* **basin,** *cav-* **hollow,** *-ity* **state]**

anatomical position
(an-ah-TOM-i-kal po-ZISH-un)
[*ana-* **apart,** *-tom-* **cut,** *-ical-* **relating to,** *posit-* **place,** *-tion* **state]**

anatomy
(ah-NAT-o-mee)
[*ana-* **apart,** *-tom-* **cut,** *-y* **action]**

anterior
(an-TEER-ee-or)
[*ante-* **front,** *-er-* **more,** *-or* **quality]**

apical
(AY-pik-al)
[*apic-* **tip,** *-al* **relating to]**

autopoiesis
(aw-toe-poy-EE-sis)
[*auto-* **self,** *-poiesis* **making]**

basal
(BAY-sal)
[*bas-* **base,** *-al* **relating to]**

bilateral symmetry
(bye-LAT-er-al SIM-e-tree)
[*bi-* **two,** *-later-* **side,** *-al* **relating to,** *sym-* **together,** *-metr-* **measure,** *-ry* **condition of]**

body plane
(BOD-ee playn)

cadaver
(kah-DAV-er)
[*cadaver* **dead body]**

cell
(sell)
[*cell* **storeroom]**

cell theory
(sell THEE-o-ree)
[*cell* **storeroom,** *theor-* **look at,** *-y* **act of]**

continued on p. 28

You have just begun the study of one of nature's most wondrous structures—the human body. ***Anatomy*** *(ah-NAT-o-mee) and* ***physiology*** *(fiz-ee-OL-o-jee) are branches of biology that are concerned with the form and functions of the body. Anatomy is the study of body structure, whereas physiology deals with body function. As you learn about the complex interdependence of structure and function in the human body, you become, in a very real sense, the subject of your own study.*

Regardless of your field of study or your future career goals, acquiring and using information about your body structure and functions will enable you to live a more knowledgeable, involved, and healthy life in this science-conscious age. Your study of anatomy and physiology provides a unique and fascinating understanding of self, and this knowledge allows for more active and informed participation in your own personal health care decisions. If you are pursuing a health or science-related athletic career, your study of anatomy and physiology takes on added significance. It provides the necessary concepts you will need to understand your professional courses and succeed in clinical experiences.

SCIENCE AND SOCIETY

Before we get to the details, we should emphasize that everything you will read in this book is in the context of a broad field of inquiry called *science*. Science is a style of inquiry that attempts to understand nature in a rational, logical manner. Using detailed observations and vigorous tests, or *experiments*, scientists winnow out each element of an idea or **hypothesis** (hye-POTH-eh-sis) until a reasonable conclusion about its validity can be made. Rigorous experiments that eliminate any influences or biases not being directly tested are called *controlled experiments*. If the results of observations and experiments are repeatable, they may verify a hypothesis and eventually lead to enough confidence in the concept to call it a *theory*. Theories in which scientists have an unusually high level of confidence are sometimes called *laws*. Experiments may disprove a hypothesis, a result that often leads to the formation of new hypotheses (hye-POTH-eh-seez) to be tested.

Figure 1-1 summarizes some of the basic concepts of how new scientific principles are developed. As you can see, science is a dynamic process of getting closer and closer to the truth about nature, including the nature of the human body. Science is definitely not a set of unchanging facts as many people in our culture often assume.

We should also take this opportunity to point out the social and cultural context of the science presented in this book. Scientists drive the process of science, but our culture drives the kinds of questions we ask about nature and how we attempt to answer them. For example, cutting apart human *cadavers* (dead bodies) for the purpose of studying them has not always been an acceptable activity in all cultures. Today the debate faced by our culture concerns the acceptability of using live animals in scientific experiments. Because our culture does not condone most experiments involving living humans, we have until now often conducted testing on animals that are similar to humans. In fact, most of the theories presented in this book are based on animal experimentation, but cultural influences now are pulling scientists in other experimental directions they otherwise may not have taken.

Similarly, science affects culture. Recent advances in understanding human genes and technological advances in our ability to use so-called "stem cells" and other tissues from human embryos, human cadavers, and living donors to treat devastating diseases have sparked new debates concerning how our culture defines what it means to be a human being.

As you study the concepts presented in this book, keep in mind that they are not set in stone. Science is a rapidly changing set of ideas and processes that not only is influenced by our cultural biases but also affects our cultural awareness of who we are.

| A&P CONNECT |

For a quick peek at the major scientific breakthroughs that have changed our lives—and serve as the core concepts of this book—check out ***The Nobel Legacy*** online at ***A&P Connect.***

evolve

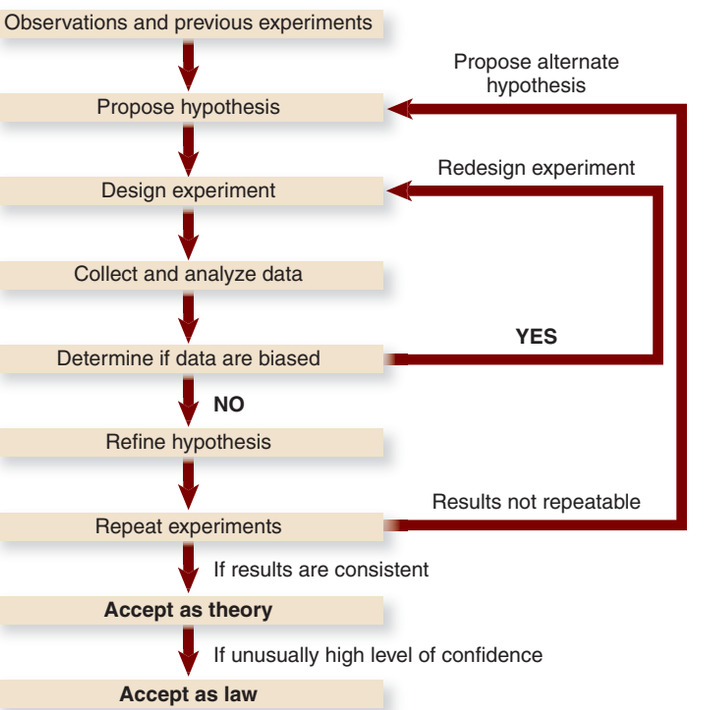


FIGURE 1-1

The scientific method. This flowchart summarizes the classic ideal of how new principles of science are developed. Initial observations or results from other experiments may lead to the formation of a new hypothesis. As more testing is performed to eliminate outside influences or biases and ensure consistent results, scientists begin to have more confidence in the principle and call it a *theory* or *law.*

ANATOMY AND PHYSIOLOGY

Anatomy

Anatomy is often defined as study of the structure of an organism and the relationships of its parts. The word *anatomy* is derived from Greek word parts that mean "to cut apart." Students of anatomy still learn about the structure of the human body by literally cutting it apart. This process, called *dissection*, remains a principal technique used to isolate and study the structural components or parts of the human body.

Biology is defined as the scientific study of life. Both anatomy and physiology are subdivisions of this very broad area of inquiry. Each of these subdivisions can be further divided into smaller areas of study. For example, the term **gross anatomy** is used to describe the study of body parts visible to the naked eye. Before invention of the microscope, anatomists had to study human structure relying only on the eye during dissection. These early anatomists could make only a gross, or whole, examination, as you can see in Figure 1-2. With the use of modern microscopes, many anatomists now specialize in **microscopic anatomy,** including the study of cells, called *cytology* (sye-TOL-o-jee), and tissues, called *histology* (hiss-TOL-o-jee).

Other branches of anatomy include the study of human growth and development (*developmental anatomy*) and the study of diseased body structures (*pathological anatomy*). In the chapters that follow, you will study the body by systems—a process called *systemic anatomy*. Systems are groups of organs that have a common function, such as the bones in the skeletal system and the muscles in the muscular system.

Physiology

Physiology is the science that deals with the functions of the living organism and its parts. The term is a combination of two Greek words (*physis*, "nature," and *logos*, "words or study"). Simply stated, it is the study of physiology that helps us understand how the body works. Physiologists attempt to discover and understand the intricate control systems that permit the body to operate and survive in an often hostile environment.

As a scientific discipline, physiology can be subdivided according to (1) the type of organism involved, such as human physiology or plant physiology; (2) the organizational level studied, such as molecular or cellular physiology; or (3) a specific or *systemic* function being studied, such as neurophysiology, respiratory physiology, or cardiovascular physiology.

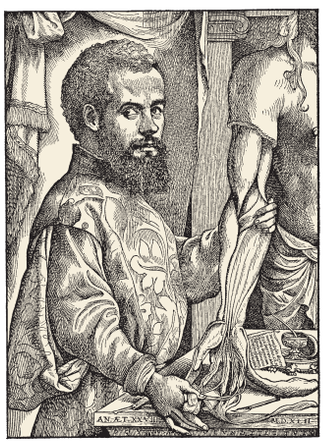


FIGURE 1-2

Gross anatomy. This famous woodcut of a gross dissection appeared in the world's first modern anatomy textbook, *De Humani Corporis Fabrica (On the Structure of the Human Body)* in 1543. This woodcut features the book's author, Andreas Vesalius, who is considered to be the founder of modern anatomy. The body being dissected is called a *cadaver*.

In the chapters that follow, both anatomy and physiology are studied by dividing the human body into specific organ systems. This unit begins with an overview of the body as a whole. In subsequent chapters the body is dissected and studied, both structurally (anatomy) and functionally (physiology), into "levels of organization" so that its component parts can be more easily understood and then "fit together" into a living and integrated whole. It is knowledge of anatomy and physiology that allows us to understand how nerve impulses travel from one part of the body to another; how muscles contract; how light energy can be transformed into visual images; how we breathe, digest food, reproduce, excrete wastes, and sense changes in our environment; and even how we think and reason.

| QUICK CHECK |

1. Describe how science develops new principles.
2. Define anatomy and physiology.
3. List the three ways in which physiology can be subdivided as a scientific discipline.
4. What name is used to describe the study of the body that focuses on groups of organs that have a common function?

LANGUAGE OF SCIENCE AND MEDICINE

You may have noticed by now that many scientific terms, such as anatomy and physiology, are made up of non-English word parts. Many such terms make up the core of the language used to communicate ideas in science and medicine. Learning in science thus begins with learning a new vocabulary, just as when you learn a new language to help you understand and communicate in a region of the world other than the one you call home.

To help you learn the vocabulary of anatomy and physiology, we have provided several helpful tools for you. Within each chapter, lists of new terms titled *Language of Science* and *Language of Medicine* give you each new key (boldface) term that you will be learning in that chapter. Each term in the list has a pronunciation guide and an explanation (or meaning) of each of the word parts that make up the term.

We have also included a separate compact reference called *Language of Science and Medicine* with this textbook. Take a moment now to locate it. After you have finished reading this chapter, quickly review the tips for learning scientific language. Then keep it nearby so that you will have a handy list of commonly used word parts at your fingertips.

You will see that most scientific terms are made up of word parts from Latin or Greek. Most Western scientists first began corresponding with each other in these languages, because it was commonly the first written language learned by educated people. Other languages such as German, French, and Japanese are also sources of some scientific word parts.

As with any language, scientific language changes constantly. This is useful because we often need to fine-tune our terminology to reflect changes in our understanding of science and to accommodate new discoveries. But it also sometimes leads to confusion. In an attempt to clear up some of the confusion, the International Federation of Associations of Anatomists (IFAA) formed a worldwide committee to publish a list of "universal" or standard anatomical terminology. The list for *gross anatomy*, the structure we can see without magnification, was published in 1998 as *Terminologia Anatomica (TA)*. In 2008

the *Terminologia Histologica (TH)* was published for *microscopic anatomy*—the study of body structure requiring significant magnification for the purpose of visualization.

Although there remain some alternate (and newer) terms used in anatomy, the lists are useful standard references. The lists show each term in Latin and English (based on the Latin form), along with a reference number. In this textbook we use the English terms from the published lists as our standard reference, but we do occasionally refer to the pure Latin form or an alternate term when appropriate for beginning students.

One of the basic principles of the standardizing terminology is the avoidance of **eponyms** (EP-o-nimz), or terms that are based on a person's name. Instead, a more descriptive Latin-based term is always preferred. Thus the term *eustachian tube* (tube connected to the middle ear, named after the famed Italian anatomist Eustachius) is now replaced with the more descriptive *auditory tube*. Likewise, the *islets of Langerhans* (in the pancreas) are now simply *pancreatic islets*. In the rare cases where eponyms do appear in a standard list, we now avoid the possessive form. Thus *Bowman's capsule* (in kidney tissue) is now either *glomerular capsule* or *Bowman capsule*.

There are no such standard lists of physiological terms. However, many principles used in anatomical terminology are used in physiology. For example, most terms have an English spelling but are based on Latin or Greek word parts. And, as in anatomy, eponyms are less favored than descriptive terms.

This may all seem like a lot more than you want to know right now. However, if you focus on learning the new words as you begin each new topic, as though you are in a foreign land and need to pick up a few phrases to get by, you will find your study of anatomy and physiology easy and enjoyable.

CHARACTERISTICS OF LIFE

Anatomy and physiology are important disciplines in biology—the study of life. But what is life? What is the quality that distinguishes a vital and functional being from a dead body? We know that a living organism is endowed with certain characteristics not associated with inorganic matter. However, it is sometimes hard to find a single criterion to define life. One could say that living organisms are self-organizing or self-maintaining and nonliving structures are not. This concept is called autopoiesis (aw-toe-poy-EE-sis), which literally means "self making." Another idea, called the *cell theory*, states that any independent structure made up of one or more microscopic units called *cells* is a living organism.

Instead of trying to find a single difference that separates living and nonliving things, scientists sometimes define life by listing what are often called *characteristics of life*. Lists of characteristics of life may differ from one physiologist to the next, depending on the type of organism being studied and the way in which life functions are grouped and defined. Attributes that characterize life in bacteria, plants, or animals may vary. Characteristics of life that are considered most important in humans are described in Table 1-1.

Each characteristic of life is related to the sum total of all the physical and chemical reactions occurring in the body. The term **metabolism** is used to describe these various processes. They include the steps involved in the breakdown of nutrient materials to produce energy and the transformation of one material into another. For example, if we eat and absorb more sugar than needed for the body's immediate energy requirements, it is converted into an alternate form, such as fat, that can be stored in the body. Metabolic reactions are also required for making complex compounds out of simpler ones, as in tissue growth, wound repair, or manufacture of body secretions.

Each characteristic of life—its functional manifestation in the body, its integration with other body functions and structures, and its mechanism of control—is the subject of study in subsequent chapters of the text.

| QUICK CHECK |

5. What is an *eponym*?
6. What single criterion might be used to define life?
7. Define the term *metabolism* as it applies to the characteristics of life.

TABLE 1-1 Characteristics of Human Life

CHARACTERISTIC	DESCRIPTION
Responsiveness	Ability of an organism to sense, monitor, and respond to changes in both its external and internal environments
Conductivity	Capacity of living cells to transmit a wave of electrical disturbance from one point to another within the body
Growth	Organized increase in the size and number of cells and therefore an increase in size of the individual or a particular organ or part
Respiration	Exchange of respiratory gases (oxygen and carbon dioxide) between an organism and its environment
Digestion	Process by which complex food products are broken down into simpler substances that can be absorbed and used by individual body cells
Absorption	Movement of molecules, such as respiratory gases or digested nutrients through a membrane and into the body fluids for transport to cells for use
Secretion	Production and release of important substances, such as digestive juices and hormones, for diverse body functions
Excretion	Removal of waste products from the body
Circulation	Movement of body fluids containing many substances from one body area to another in a continuous, circular route through hollow vessels
Reproduction	Formation of new individual offspring

LEVELS OF ORGANIZATION

Before you begin the study of the structure and function of the human body and its many parts, it is important to think about how the parts are organized and how they might logically fit together and function effectively. The differing levels of organization that influence body structure and function are illustrated in Figure 1-3.

Chemical Level—Basis for Life

Note that organization of the body begins at the chemical level (see Figure 1-3). There are more than 100 different chemical building blocks of nature called *atoms*—tiny spheres of matter so small they are invisible. Every material thing in our universe, including the human body, is composed of atoms.

Combinations of atoms form larger chemical groupings, called *molecules*. Molecules, in turn, often combine with other atoms and molecules to form larger and more complex chemicals, called *macromolecules*.

The unique and complex relationships that exist between atoms, molecules, and macromolecules in living material form a gel-like material made of fluids, particles, and membranes called *cytoplasm* (SYE-toe-plaz-em)—the essential material of human life. Unless proper relationships between chemical elements are

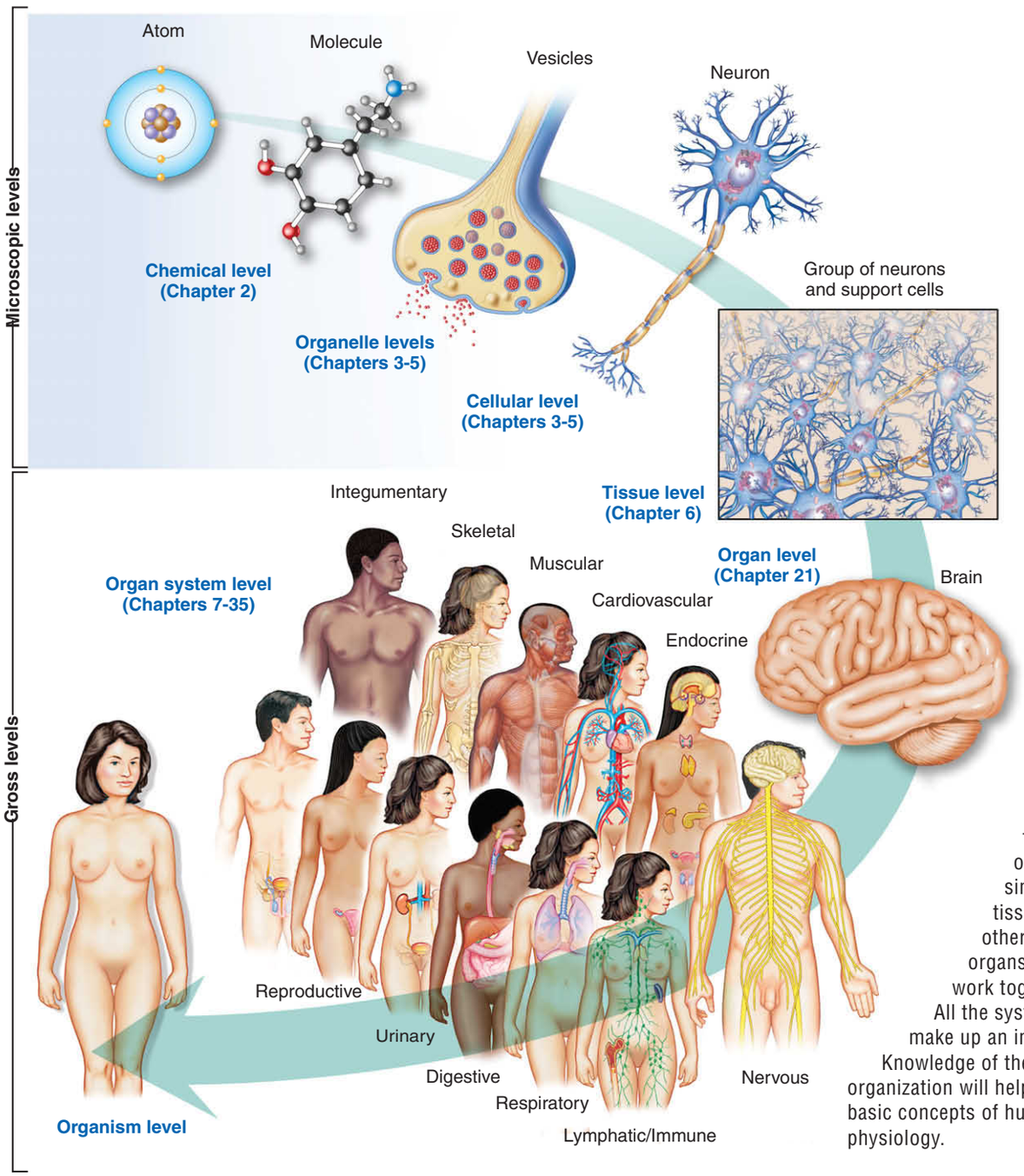


FIGURE 1-3

Levels of organization. The smallest parts of the body are the atoms that make up the chemicals, or molecules, of the body. Molecules, in turn, make up microscopic parts called organelles that fit together to form each cell of the body. Groups of similar cells are called tissues, which combine with other tissues to form individual organs. Groups of organs that work together are called systems. All the systems of the body together make up an individual organism. Knowledge of the different levels of organization will help you understand the basic concepts of human anatomy and physiology.

maintained, death results. Maintaining the type of chemical organization in cytoplasm required for life requires the expenditure of energy. In Chapter 2 important information related to the chemistry of life is discussed in more detail.

Organelle Level

Chemical structures may be organized within larger units called *cells* to form various structures called **organelles** (or-gah-NELLZ), the next level of organization (see Figure 1-3). An organelle may be defined as a structure made of molecules organized in such a way that it can perform a specific function. Organelles are the "tiny organs" that allow each cell to live. Organelles cannot survive outside the cell, but without organelles the cell itself could not survive either.

Dozens of different kinds of organelles have been identified. A few examples include *mitochondria* (my-toe-KON-dree-ah), the "power houses" of cells that provide the energy needed by the cell to carry on day-to-day functioning, growth, and repair; *Golgi* (GOL-jee) *apparatus*, which provides a "packaging" service to the cell by storing material for future internal use or for export from the cell; and *endoplasmic reticulum*, the network of transport channels within the cell that act as "highways" for the movement of chemicals. Chapter 3 contains a complete discussion of organelles and their functions.

Cellular Level

The characteristics of life ultimately result from a hierarchy of structure and function that begins with the organization of atoms, molecules, and macromolecules. Further organization that results in organelles is the next step. However, in the view of the anatomist, the most important function of the chemical and organelle levels of organization is that of furnishing the basic building blocks required for the next higher level of body structure—*the cellular level.*

Cells are the smallest and most numerous structural units that possess and exhibit the basic characteristics of living matter. How many cells are there in the body? One estimate places the number of cells in a 150-pound adult human body at 100,000,000,000,000.

In case you are having trouble translating this number—1 with 14 zeroes after it—it is 100 trillion! or 100,000 billion! or 100 million million!

Each cell is surrounded by a membrane and is characterized by a single nucleus surrounded by cytoplasm that includes the numerous organelles required for the normal processes of living. Although all cells have certain features in common, they specialize or *differentiate* to perform unique functions. Fat cells, for example, are structurally modified to permit the storage of fats, whereas other cells, such as cardiac muscle cells, are able to contract with great force (see Figure 1-3). Muscle, bone, nerve, and blood cells are other examples of structurally and functionally unique cells.

Tissue Level

The next higher level of organization beyond the cell is the *tissue level* (see Figure 1-3). Tissues represent another step in the progressive organization of living matter. By definition, a **tissue** is a group of a great many similar cells that all developed together from the same part of the embryo and all perform a certain function. Tissue cells are surrounded by varying amounts and kinds of nonliving, intercellular substances, or the matrix. Tissues are the "fabric" of the body.

There are four major or principal tissue types: *epithelial*, *connective*, *muscle*, and *nervous*. Considering the complex nature of the human body, this is a surprisingly short list of major tissues. Each of the four major tissues, however, can be subdivided into several distinct subtypes. Together the body tissues are able to meet all the structural and functional needs of the body.

The tissue used as an example in Figure 1-3 is a type of muscle called *cardiac muscle*. Note how the cells are branching and interconnected. The details of tissue structure and function are covered in Chapter 6.

Organ Level

Organ units are more complex than tissues. An **organ** is defined as a structure made up of several different kinds of tissues arranged so that, together, they can perform a special function.

If tissues are the "fabric" of the body, an organ is like an item of clothing with a specific function made up of different fabrics. The heart is an example of the *organ level:* muscle and connective tissues give it shape and pump blood; epithelial tissues line the cavities, or chambers; and nervous tissues permit control of the pumping contractions of the heart.

Tissues seldom exist in isolation. Instead, joined together, they form organs that represent discrete, but functionally complex, operational units. Each organ has a unique shape, size, appearance, and placement in the body, and each can be identified by the pattern of tissues that form it. The lungs, heart, brain, kidneys, liver, and spleen are all examples of organs.

System Level

Systems are the most complex of the organizational units of the body. The **system** level of organization involves varying numbers and kinds of organs arranged so that, together, they can perform complex functions for the body.

Eleven major systems compose the human body: integumentary, skeletal, muscular, nervous, endocrine, circulatory, lymphatic/immune, respiratory, digestive, urinary, and reproductive. Systems that work together to accomplish the general needs of the body are summarized in Table 1-2.

Take a few minutes to read through Table 1-2. The left column points out that several different systems often work together to accomplish some overall goal. For example, the first three systems

TABLE 1-2 Body Systems (With Unit and Chapter References)

FUNCTIONAL CATEGORY	SYSTEM	PRINCIPAL ORGANS	PRIMARY FUNCTIONS
Support and movement (Unit One)	Integumentary (Chapter 7)	Skin	Protection, temperature regulation, sensation
	Skeletal (Chapters 8–10)	Bones, ligaments	Support, protection, movement, mineral and fat storage, blood production
	Muscular (Chapters 11–12)	Skeletal muscles, tendons	Movement, posture, heat production
Communication, control, and integration (Unit Two)	Nervous (Chapters 13–17)	Brain, spinal cord, nerves, sensory organs	Control, regulation, and coordination of other systems, sensation, memory
	Endocrine (Chapters 18–19)	Pituitary gland, adrenals, pancreas, thyroid, parathyroids, and other glands	Control and regulation of other systems
Transportation and defense (Unit Three)	Cardiovascular (Chapters 20–22)	Heart, arteries, veins, capillaries	Exchange and transport of materials
	Lymphatic (Chapters 23–25)	Lymph nodes, lymphatic vessels, spleen, thymus, tonsils	Immunity, fluid balance
Respiration, nutrition, and excretion (Unit Four)	Respiratory (Chapters 26–27)	Lungs, bronchial tree, trachea, larynx, nasal cavity	Gas exchange, acid-base balance
	Digestive (Chapters 28–30)	Stomach, small and large intestines, esophagus, liver, mouth, pancreas	Breakdown and absorption of nutrients, elimination of waste
	Urinary (Chapters 31–33)	Kidneys, ureters, bladder, urethra	Excretion of waste, fluid and electrolyte balance, acid-base balance
Reproduction and development (Unit Five)	Reproductive (Chapters 34–37)	*Male:* Testes, vas deferens, prostate, seminal vesicles, penis *Female:* Ovaries, fallopian tubes, uterus, vagina, breasts	Reproduction, continuity of genetic information, nurturing of offspring

listed (integumentary, skeletal, muscular) make up the framework of the body and therefore provide support and movement. Notice also that this table corresponds to the organization of this book. Once we get to the system level of organization, we will study each system one by one, chapter by chapter. To help you navigate through the book, we have organized the chapters into units of several systems each—units that group the systems by common or overlapping functions.

You are probably aware that some systems can be grouped together or split apart. We use those groupings that are most useful to us. For example, because both the skeletal and muscular systems work together to produce athletic movements, an athletic trainer may study them together as the *skeletomuscular system.* A physical therapist may also include concepts of nervous control of movement and study the *neuroskeletomuscular system.* On the other hand, a neurologist may find it useful to keep in mind a distinction between the sensory nervous system and the motor nervous system. In any case, the idea of levels of organization is universal, and once you know how it works, you can adapt it to suit your own changing needs. The plan of dividing the body into 11 major systems is widely used among biologists, so we will use it as the basis of our study too.

Organism Level

The living human **organism** is certainly more than the sum of its parts. It is a marvelously coordinated team of interactive structures that is able to survive and flourish in an often hostile environment. Not only can the human body reproduce itself (and its genetic information) and maintain ongoing repair and replacement of worn or damaged parts, it can also maintain—in a constant and predictable way—an incredible number of variables required for a human to lead a healthy, productive life.

We are able to maintain a "normal" body temperature and fluid balance under widely varying environmental extremes. We maintain constant blood levels of many important chemicals and nutrients. We experience effective protection against disease, elimination of waste products, and coordinated movement. We correctly and quickly interpret sound, visual images, and other external stimuli with great regularity. These are a few examples of how the different levels of organization in the human organism permit expression of the characteristics associated with life.

As you study the structure and function of the human body, it is too easy to think of each part or function in isolation from the

body as a whole. Always remember that you are ultimately dealing with information related to the entire human organism—not information limited to an understanding of the structure and function of a single organelle, cell, tissue, organ, or organ system. Do not limit your learning to the memorization of facts. Instead, connect and integrate factual information so that your understanding of human structure and function is related not to a part of the body but to the body as a whole.

| QUICK CHECK |

8. List the seven levels of organization.
9. Identify three organelles.
10. List the four major tissue types.
11. List the 11 major organ systems.

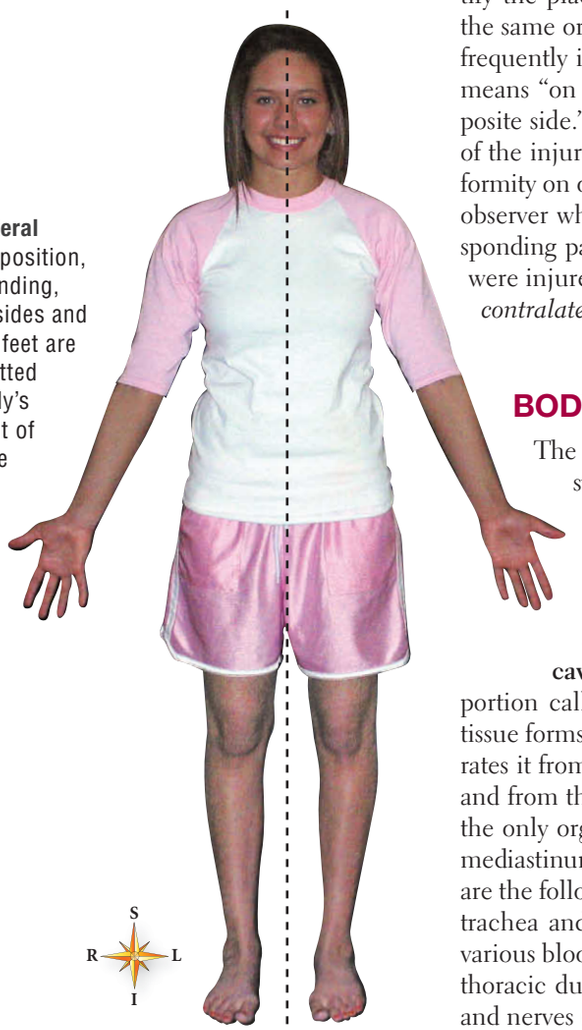


FIGURE 1-4

Anatomical position and bilateral symmetry. In the anatomical position, the body is in an erect, or standing, posture with the arms at the sides and palms forward. The head and feet are also pointing forward. The dotted line shows the axis of the body's bilateral symmetry. As a result of this organizational feature, the right and left sides of the body are mirror images of each other.

ANATOMICAL POSITION

Discussions about the body, how it moves, its posture, or the relationship of one area to another, assume that the body as a whole is in a specific position called the **anatomical position.** In this reference position the body is in an erect, or standing, posture with the arms at the sides and palms turned forward (Figure 1-4). The head and feet are also pointing forward. The anatomical position is a reference position that gives meaning to the directional terms used to describe the body parts and regions.

Bilateral symmetry is one of the most obvious of the external organizational features in humans. The person shown in Figure 1-4 is divided by a line into bilaterally symmetrical sides. To say that humans are bilaterally symmetrical simply means that the right and left sides of the body are mirror images of each other and only one plane can divide the body into left and right halves. One of the most important features of bilateral symmetry is balanced proportions. There is a remarkable correspondence in size and shape when comparing similar anatomical parts or external areas on opposite sides of the body.

The terms *ipsilateral* and *contralateral* are often used to identify the placement of one body part with respect to another on the same or opposite side of the body. These terms are used most frequently in describing injury to an extremity. *Ipsilateral* simply means "on the same side," and *contralateral* means "on the opposite side." Injuries to an arm or leg require careful comparison of the injured with the noninjured side. Minimal swelling or deformity on one side of the body is often apparent only to a trained observer who compares a suspected area of injury with its corresponding part on the opposite side of the body. If the right knee were injured, for example, the left knee would be designated the *contralateral knee.*

BODY CAVITIES

The body, contrary to its external appearance, is not a solid structure. It contains two major sets of cavities that each house compact, well-ordered arrangements of internal organs. The location and outlines of the body cavities are illustrated in Figure 1-5.

The **ventral cavities** include the *thoracic*, or *chest, cavity* and the *abdominopelvic cavity*. The **thoracic cavity** includes a right and a left *pleural cavity* and a midportion called the *mediastinum* (mee-dee-ass-TI-num). Fibrous tissue forms a wall around the mediastinum that completely separates it from the right pleural cavity, in which the right lung lies, and from the left pleural cavity, in which the left lung lies. Thus the only organs in the thoracic cavity that are not located in the mediastinum are the lungs. Organs located in the mediastinum are the following: the heart (enclosed in its pericardial cavity), the trachea and right and left bronchi, the esophagus, the thymus, various blood vessels (e.g., thoracic aorta, superior vena cava), the thoracic duct and other lymphatic vessels, various lymph nodes, and nerves (such as the phrenic and vagus nerves).

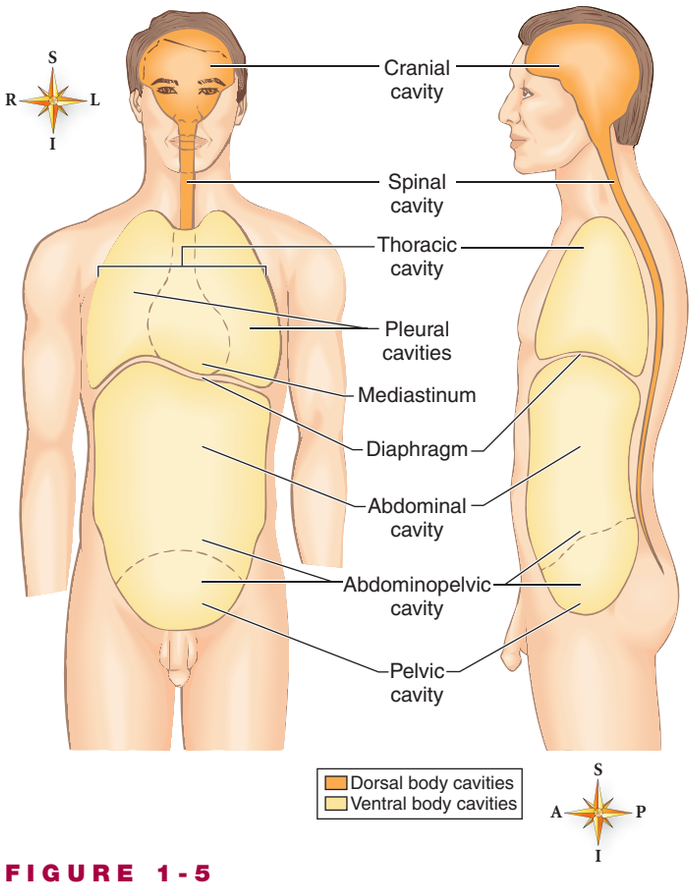


FIGURE 1-5

Major body cavities. The dorsal body cavity is in the dorsal (back) part of the body and is subdivided into a cranial cavity above and a spinal cavity below. The ventral body cavity is on the ventral (front) side of the trunk and is subdivided into the thoracic cavity above the diaphragm and the abdominopelvic cavity below the diaphragm. The thoracic cavity is subdivided into the mediastinum in the center and pleural cavities to the sides. The abdominopelvic cavity is subdivided into the abdominal cavity above the pelvis and the pelvic cavity within the pelvis.

TABLE 1-3 Organs in Ventral Body Cavities

AREAS	ORGANS
Thoracic Cavity	
Right pleural cavity	Right lung
Mediastinum	Heart
	Trachea
	Right and left bronchi
	Esophagus
	Thymus gland
	Aortic arch and thoracic aorta
	Venae cavae
	Various lymph nodes and nerves
	Thoracic duct
Left pleural cavity	Left lung
Abdominopelvic Cavity	
Abdominal cavity	Liver
	Gallbladder
	Stomach
	Pancreas
	Intestines
	Spleen
	Kidneys
	Ureters
Pelvic cavity	Urinary bladder
	Female reproductive organs
	Uterus
	Uterine tubes
	Ovaries
	Male reproductive organs
	Prostate gland
	Seminal vesicles
	Part of vas deferens
	Part of large intestine, namely, sigmoid colon and rectum

The **abdominopelvic cavity** has an upper portion, the *abdominal cavity*, and a lower portion, the *pelvic cavity*. The abdominal cavity contains the liver, gallbladder, stomach, pancreas, intestines, spleen, kidneys, and ureters. The bladder, certain reproductive organs (uterus, uterine tubes, and ovaries in females; prostate gland, seminal vesicles, and part of the vas deferens in males), and part of the large intestine (namely, the sigmoid colon and rectum) lie in the pelvic cavity (Table 1-3).

The **dorsal cavities** include the *cranial* and *spinal cavities*. The cranial cavity lies in the skull and houses the brain. The spinal cavity lies in the spinal column and houses the spinal cord (see Figure 1-5).

The thin filmy membranes that line body cavities or cover the surfaces of organs within body cavities also have special names. The term **parietal** refers to the actual wall of a body cavity or the lining membrane that covers its surface. **Visceral** refers not to the wall or lining of a body cavity but to the thin membrane that covers the organs, or viscera, within a cavity.

The membrane lining the inside of the abdominal cavity, for example, is called the *parietal peritoneum*. The membrane that covers the organs within the abdominal cavity is called the *visceral peritoneum*. If you skip ahead to Figure 1-10, you will see that there is a space or opening between the two membranes in the abdomen. This is called the *peritoneal cavity*. Body membranes are discussed in greater detail in Chapter 6.

BODY REGIONS

Identification of an object begins with overall recognition of its structure and form. Initially, it is in this way that the human form can be distinguished from other creatures or objects. Recognition occurs as soon as you can identify the overall shape and basic outline. For more specific identification to occur, details of size, shape, and appearance of individual body areas must be described. Individuals differ in overall appearance because specific body areas, such as the face or torso, have unique identifying characteristics. Detailed descriptions of the human form require that specific regions be identified and appropriate terms be used to describe them (Figure 1-6 and Table 1-4).

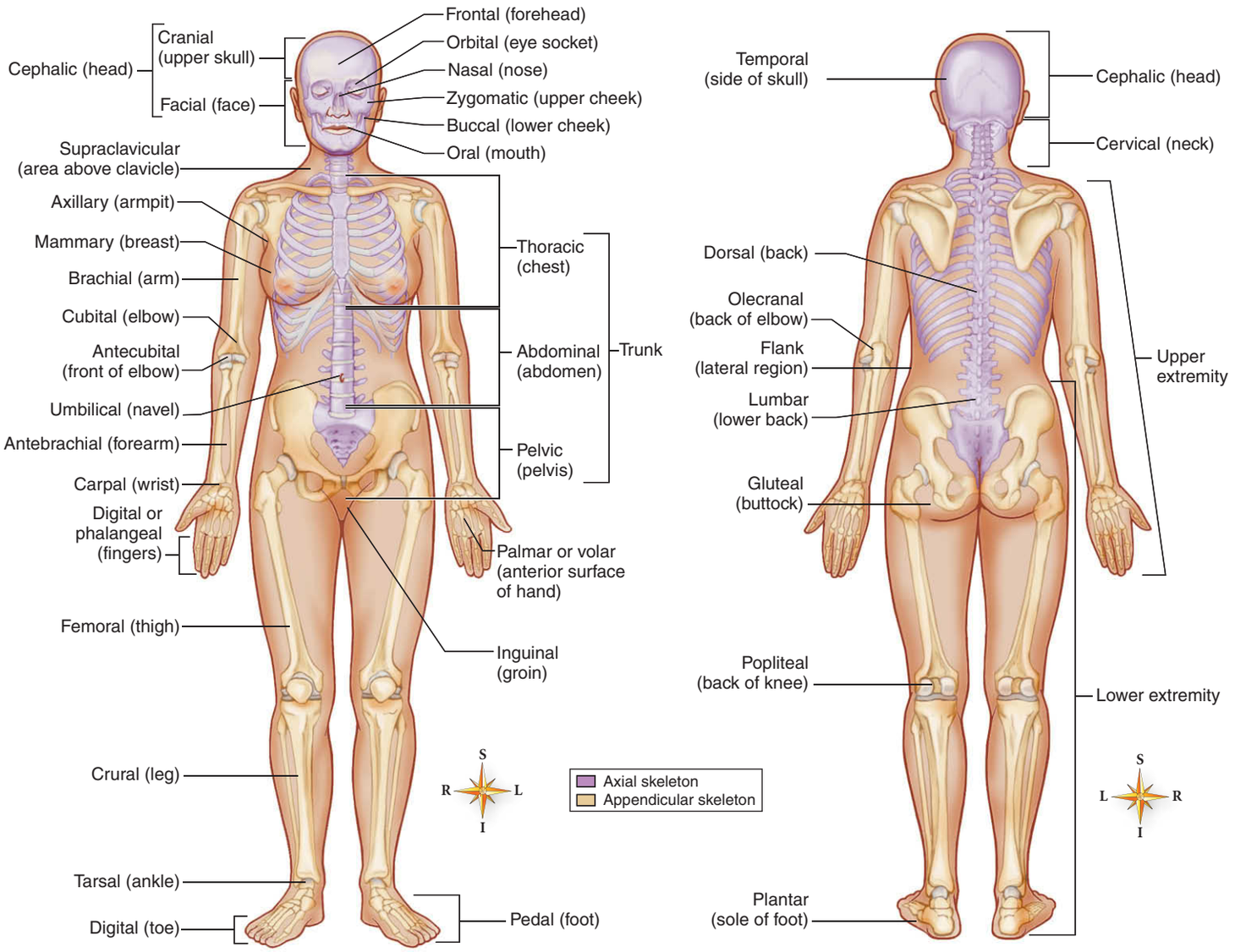


FIGURE 1-6

Specific body regions. Note that the body as a whole can be subdivided into two major portions: axial (along the middle, or *axis,* of the body) and appendicular (the arms and legs, or *appendages*). Names of specific body regions follow the Latin form, with the English equivalent in parentheses.

The body as a whole can be subdivided into two major portions or components: *axial* and *appendicular*. The axial portion of the body consists of the head, neck, and torso, or trunk; the appendicular portion consists of the upper and lower extremities and their connections to the axial portion. Each major area is subdivided as shown in Figure 1-6. Note, for example, that the torso is composed of the thoracic, abdominal, and pelvic areas and the upper extremity is divided into arm, forearm, wrist, and hand components. Although most terms used to describe gross body regions are familiar, misuse is common. The term *leg* is a good example. To an anatomist, "leg" refers to the area of the lower extremity between the knee and ankle and not to the entire lower extremity.

TABLE 1-4 Latin-Based Descriptive Terms for Body Regions*

BODY REGION	AREA OR EXAMPLE	BODY REGION	AREA OR EXAMPLE
Abdominal (ab-DOM-in-al)	Anterior torso below diaphragm	**Mammary** (MAM-er-ee)	Breast
Acromial (ah-KRO-mee-al)	Shoulder	**Manual** (MAN-yoo-al)	Hand
Antebrachial (an-tee-BRAY-kee-al)	Forearm	**Mental** (MEN-tal)	Chin
Antecubital (an-tee-KYOO-bi-tal)	Depressed area just in front of elbow (cubital fossa)	**Nasal** (NAY-zal	Nose
Axillary (AK-si-lair-ee)	Armpit (axilla)	**Navel** (NAY-vel)	Area around navel, or umbilicus
Brachial (BRAY-kee-al)	Arm	**Occipital** (ok-SIP-i-tal)	Back of lower part of skull
Buccal (BUK- al)	Cheek (inside)	**Olecranal** (o-LECK-ra-nal)	Back of elbow
Calcaneal (cal-CANE-ee-al)	Heel of foot	**Oral** (OR-al)	Mouth
Carpal (KAR-pal)	Wrist	**Orbital** or **ophthalmic** (OR-bi-tal *or* op-THAL-mik)	Eyes
Cephalic (se-FAL-ik)	Head	**Otic** (O-tick)	Ear
Cervical (SER-vi-kal)	Neck	**Palmar** (PAHL-mar)	Palm of hand
Coxal (COX-al)	Hip	**Patellar** (pa-TELL-er)	Front of knee
Cranial (KRAY-nee-al)	Skull	**Pedal** (PED-al)	Foot
Crural (KROOR-al)	Leg	**Pelvic** (PEL-vik)	Lower portion of torso
Cubital (KYOO-bi-tal)	Elbow	**Perineal** (pair-i-NEE-al)	Area (perineum) between anus and genitals
Cutaneous (kyoo-TANE-ee-us)	Skin (or body surface)	**Plantar** (PLAN-tar)	Sole of foot
Digital (DIJ-i-tal)	Fingers or toes	**Pollex** (POL-ex)	Thumb
Dorsal (DOR-sal)	Back or top	**Popliteal** (pop-li-TEE-al)	Area behind knee
Facial (FAY-shal)	Face	**Pubic** (PYOO-bik)	Pubis
Femoral (FEM-or-al)	Thigh	**Supraclavicular** (soo-pra-cla-VIK-yoo-lar)	Area above clavicle
Frontal (FRON-tal)	Forehead	**Sural** (SUR-al)	Calf
Gluteal (GLOO-tee-al)	Buttock	**Tarsal** (TAR-sal)	Ankle
Hallux (HAL-luks)	Great toe	**Temporal** (TEM-por-al)	Side of skull
Inguinal (ING-gwi-nal)	Groin	**Thoracic** (tho-RAS-ik)	Chest
Lumbar (LUM-bar)	Lower part of back between ribs and pelvis	**Zygomatic** (zye-go-MAT-ik)	Cheek

*The left column lists English adjectives based on Latin terms that describe the body parts listed in English in the right column.

Abdominopelvic Regions

For convenience in locating abdominopelvic organs, anatomists divide the abdominopelvic cavity like a tic-tac-toe grid into nine imaginary regions. The following is a list of the nine regions (Figure 1-7) identified from right to left and from top to bottom:

1. Right hypochondriac region
2. Epigastric region
3. Left hypochondriac region
4. Right lumbar region
5. Umbilical region
6. Left lumbar region
7. Right iliac (inguinal) region
8. Hypogastric region
9. Left iliac (inguinal) region

The most superficial organs located in each of the nine abdominopelvic regions are shown in Figure 1-7. In the right hypochondriac region the right lobe of the liver and the gallbladder are visible. In the epigastric area, parts of the right and left lobes of the liver and a large portion of the stomach can be seen. Viewed superficially, only a portion of the stomach and a small portion of the large intestine is visible in the left hypochondriac area. Note that the right lumbar region includes parts of the large and small intestines (see Figure 1-7). The superficial organs seen in the umbilical region include a portion of the transverse colon and loops of the small intestine. Additional loops of the small intestine and a part of the colon can be seen in the left lumbar region. The right iliac region contains the cecum and parts of the small intestine. Only loops of the small intestine, the urinary bladder, and the appendix are seen in the hypogastric region. The left iliac region shows portions of the colon and the small intestine.

Abdominal Quadrants

Physicians and other health professionals frequently use a simpler method and divide the abdomen into four quadrants to describe the site of abdominopelvic pain or locate some type of internal pathology such as a tumor or abscess (Figure 1-8). One horizontal line and one vertical line passing through the umbilicus (navel) divide the abdomen into *right* and *left upper quadrants* and *right* and *left lower quadrants* (see Figure 1-8).

| QUICK CHECK |

12. Define the term *anatomical position* and explain its importance.
13. Name the two major subdivisions of the body as a whole.
14. Identify the two major body cavities and the subdivisions of each.
15. List the nine abdominopelvic regions and four abdominal quadrants.

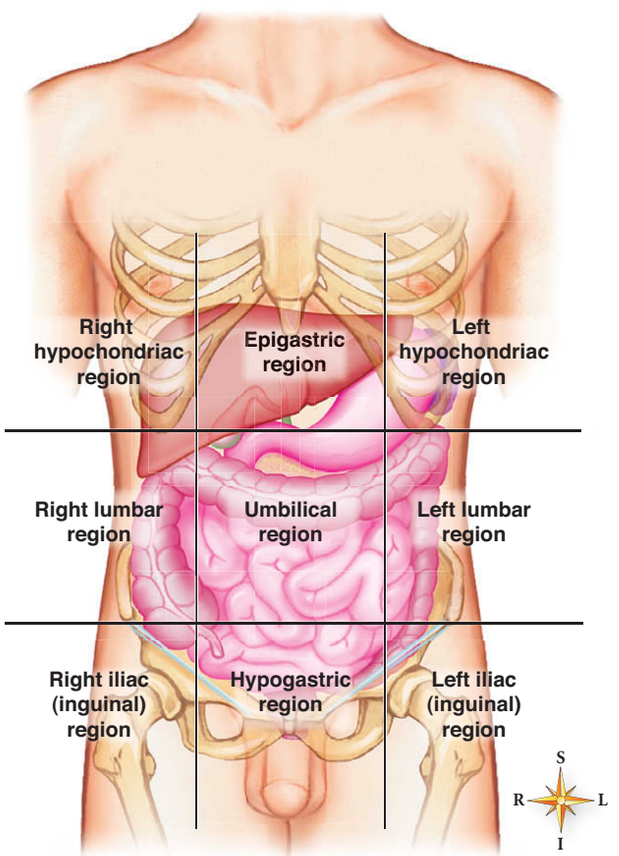


FIGURE 1-7

Nine regions of the abdominopelvic cavity. Only the most superficial structures of the internal organs are shown here.

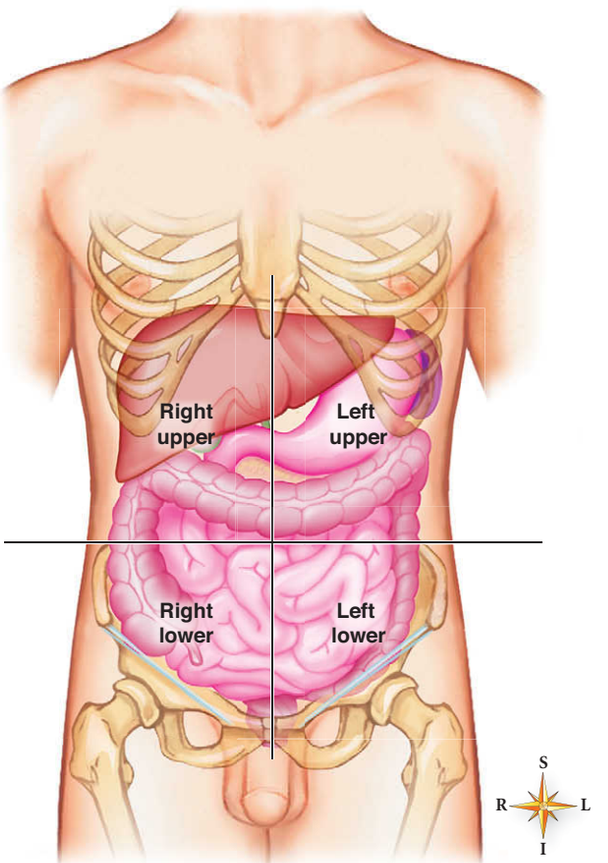


FIGURE 1-8

Division of the abdomen into four quadrants. The diagram shows the relationship of internal organs to the four abdominal quadrants.

TERMS USED IN DESCRIBING BODY STRUCTURE

Directional Terms

To minimize confusion when discussing the relationship between body areas or the location of a particular anatomical structure, specific terms must be used. When the body is in the anatomical position, the following directional terms can be used to describe the location of one body part with respect to another (Figure 1-9).

Superior and ***inferior.*** **Superior** means "toward the head," and **inferior** means "toward the feet." Superior also means "upper" or "above," and inferior means "lower" or "below." For example, the lungs are located superior to the diaphragm, whereas the stomach is located inferior to it.

Anterior and ***posterior.*** **Anterior** means "front" or "in front of"; **posterior** means "back" or "in back of." In humans—who walk in an upright position—*ventral* (toward the belly) can be used in place of anterior, and *dorsal* (toward the back) can be used for posterior. For example, the nose is on the anterior surface of the body, and the shoulder blades are on its posterior surface.

Medial and ***lateral.*** **Medial** means "toward the midline of the body"; **lateral** means "toward the side of the body, or away from its midline." For example, the great toe is at the medial side of the foot, and the little toe is at its lateral side. The heart lies medial to the lungs, and the lungs lie lateral to the heart.

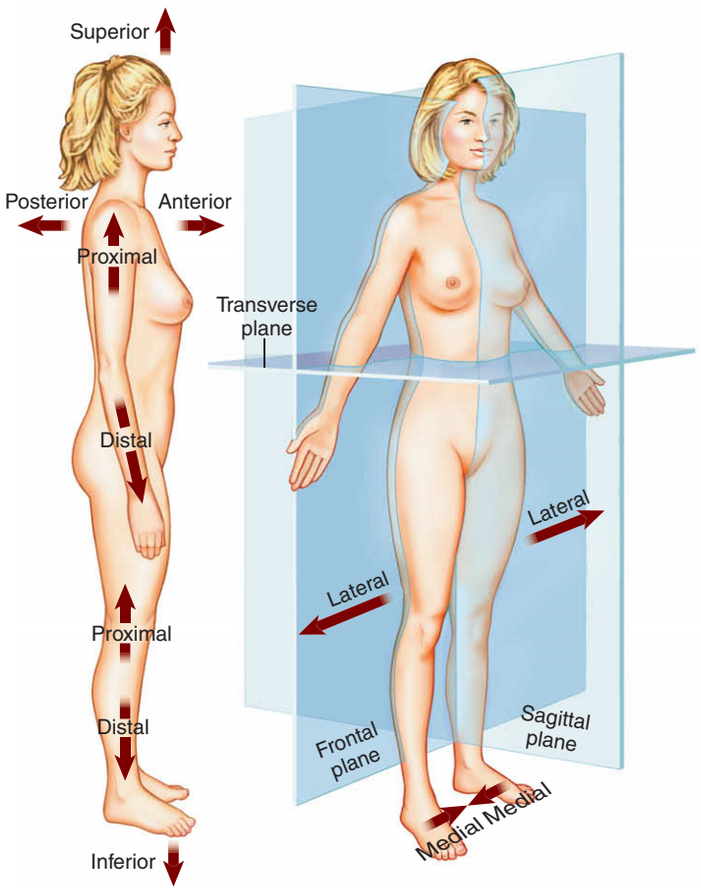


FIGURE 1-9
Directions and planes of the body.

Proximal and ***distal.*** **Proximal** means "toward or nearest the trunk of the body, or nearest the point of origin of one of its parts"; **distal** means "away from or farthest from the trunk or the point of origin of a body part." For example, the elbow lies at the proximal end of the forearm, whereas the hand lies at its distal end.

Superficial and ***deep.*** **Superficial** means "nearer the surface"; **deep** means "farther away from the body surface." For example, the skin of the arm is superficial to the muscles below it, and the bone of the upper part of the arm is deep to the muscles that surround and cover it. Refer often to the table of anatomical directions on the inside front cover. It is intended to serve as a useful and ready reference for review.

Terms Related to Organs

When discussing anatomical relationships among organs in a system or region, or anatomical relationships within an organ, additional terms are often useful.

Lumen. Many organs of the body are hollow, such as the stomach, small intestine, blood vessels, urinary organs, and so on. The hollow area of any of these organs is called the **lumen**. The term *luminal* means "of or near the lumen."

Central and ***peripheral.*** **Central** means "near the center;" **peripheral** means "around the boundary." For example, the central nervous system includes the brain and spinal cord, which are near the center of the body. The peripheral nervous system, on the other hand, includes the nerves of the muscles, skin, and other organs that are nearer the periphery, or outer boundaries, of the body.

Medullary and ***cortical.*** **Medullary** refers to an inner region of an organ; **cortical** refers to an outer region or layer of an organ. For example, the inner region of the kidney is the *medulla*, and any structures there are described as medullary. Similarly, the term *cortical* describes structures found in the outer layer of kidney tissue (the *cortex* of the kidney).

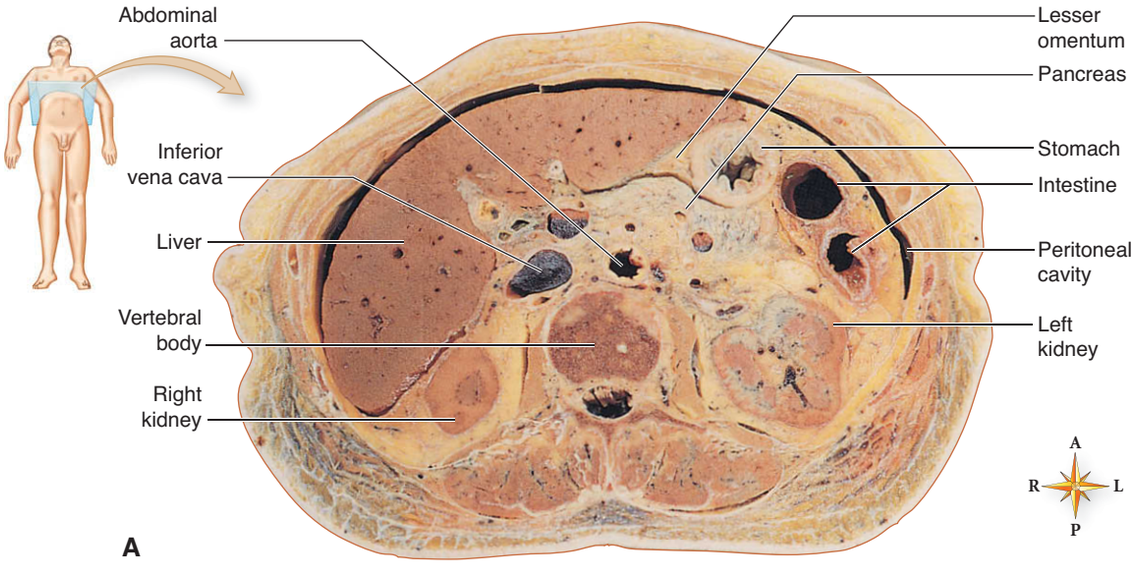
Basal and apical. Some organs, such as the heart and each lung, are somewhat cone-shaped. Thus we borrow terms that describe the point or *apex* of a cone and the flat part or *base* of a cone. **Basal** refers to the base or widest part of an organ; **apical** refers to the narrow tip of an organ. For example, in the heart the term *apical* refers to the "point" of the heart that rests on the diaphragm. Basal and apical may also refer to individual cells: the apical surface faces the lumen of a hollow organ, and the basal surface of the cell faces away from the lumen. Many of the more common directional terms that you will use in this course are listed in a handy table inside the front cover of the book.

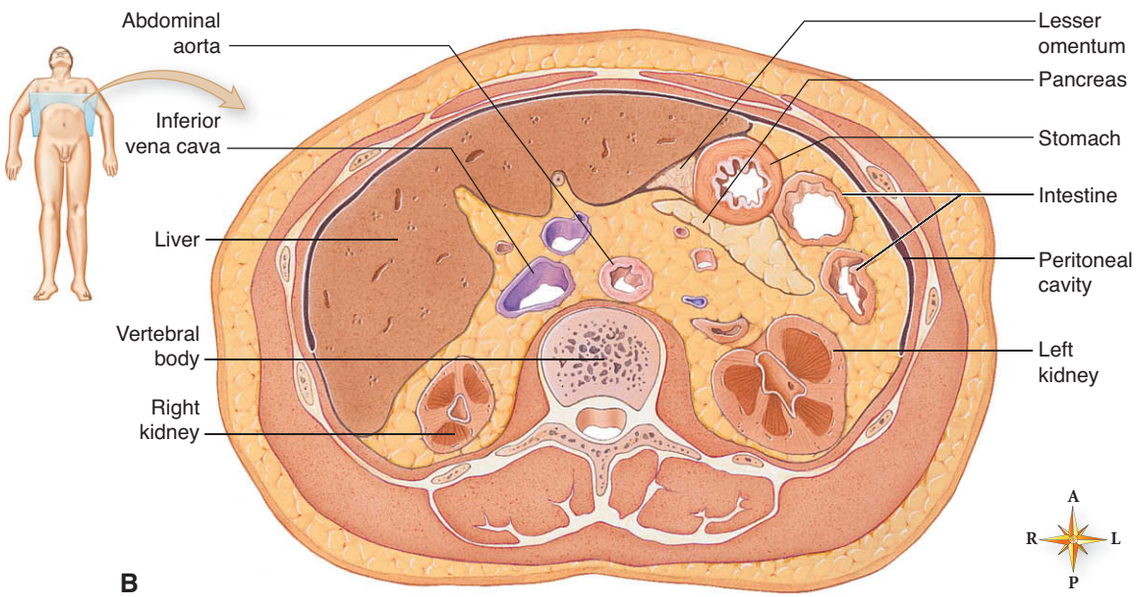
BODY PLANES AND SECTIONS

The transparent glasslike plates in Figure 1-9 that divide the body into parts represent cuts, or *sections*, that can be made along a particular axis, or line of orientation, called a *plane*. There are three major **body planes** that lie at right angles to each other. They are called the *sagittal* (SAJ-i-tal), *coronal* (ko-RO-nal), and *transverse* (or *horizontal*) planes. Literally hundreds of sections can be made in each plane, and each section made is named after

FIGURE 1-10

Transverse section of the abdomen. A, A transverse, or horizontal, plane through the abdomen shows the position of various organs within the cavity. **B,** A drawing of the photograph helps clarify the photo. Compare these views, both seen from below, with the medical image shown in the box on p. 17.





the particular plane along which it occurs. For example, the transverse plane in Figure 1-9 is shown dividing the individual into upper and lower parts at about the level of the umbilicus. Many other transverse sections are possible in parallel transverse planes. A transverse section through the knee would amputate the lower extremity at that joint, and a transverse section through the neck would result in decapitation.

Read the following definitions and identify each term in Figure 1-9:

Sagittal plane. A lengthwise plane running from front to back; divides the body or any of its parts into right and left sides. If a sagittal section is made in the exact midline, resulting in equal and symmetrical right and left halves, the plane is called a *median sagittal plane* or *midsagittal plane* (see Figure 1-9).

Coronal plane. A lengthwise plane running from side to side; divides the body or any of its parts into anterior and posterior portions; also called a *frontal plane.*

Transverse plane. A crosswise plane; divides the body or any of its parts into upper and lower parts; also called a *horizontal plane.*

Figure 1-10 shows the organs of the abdominal cavity as they would appear in the transverse, or horizontal, plane or "cut" through the abdomen represented in Figure 1-9. In addition to the actual photograph, a simplified line diagram helps in identifying the primary organs. Note that organs near the bottom of the photo or line drawing are in a posterior position. The cut vertebra of the spine, for example, can be identified in its position behind, or posterior, to the stomach. The kidneys are located on either side of the vertebra—they are *lateral* and the vertebra is *medial.* To make the reading of anatomical figures a little easier, an *anatomical rosette* is used throughout this book. On many figures, you will notice a small compass rosette similar to those on geographical maps. Rather than being labeled N, S, E, and W, the anatomical rosette is labeled with abbreviated anatomical directions:

A = Anterior	**P** (opposite A) = Posterior
D = Distal	**P** (opposite D) = Proximal
I = Inferior	**S** = Superior
L (opposite M) = Lateral	**M** = Medial
L (opposite R) = Left	**R** = Right

For your convenience, the compass rosette and its possible directions, a helpful diagram of the planes and directions of the body, and a summary table are found on the inside front cover of this book. Refer to it frequently until you are familiar enough with anatomy to do without it.

| QUICK CHECK |

16. Define and contrast each term in these pairs: superior/inferior, anterior/posterior, medial/lateral, dorsal/ventral.
17. How is anatomical left different from your left?
18. List and define the three major planes that are used to divide the body into parts.
19. Explain how an anatomical rosette is used in anatomical illustrations.

INTERACTION OF STRUCTURE AND FUNCTION

One of the most unifying and important concepts of the study of anatomy and physiology is the principle of *complementarity of structure and function*. In the chapters that follow, you will note again and again that anatomical structures are adapted to perform specific functions. Each structure has a particular size, shape, form, or placement in the body that makes it especially efficient at performing a unique and important activity.

The relationships between the levels of structural organization will take on added meaning as you study the various organ systems in the chapters that follow. For example, as you study the respiratory system in Chapter 27, you will learn about a special chemical substance secreted by cells in the lungs that help to keep tiny air sacs in these organs from collapsing during respiration. Hereditary material called *DNA* (a macromolecule) "directs" the differentiation of specialized cells in the lungs during development so that they can effectively contribute to respiratory function. As a result of DNA activity, special chemicals are produced, cells are modified, and tissues appear that are uniquely suited to this organ system. The cilia (organelles), which cover the exposed surface of cells that form the tissues lining the respiratory passageways, help trap and eliminate inhaled contaminants such as dust. The structures of the respiratory tubes and lungs assist in efficient and rapid movement of air and also make possible the exchange of critical respiratory gases such as oxygen and carbon dioxide between the air in the lungs and the blood. Working together as the respiratory system, specialized chemicals, organelles, cells, tissues, and organs supply every cell of the human body with necessary oxygen and constantly remove carbon dioxide.

Structure determines function, and function influences the actual anatomy of an organism over time. Understanding this fact helps students better understand the mechanisms of disease and the structural abnormalities often associated with pathology. Box 1-1 gives one example of the relationship between body structure, function, and disease. Current research in the study of human biology is now focused in large part on integration, interaction, development, modification, and control of functioning body structures.

By applying the principle of complementarity of structure and function as you study the structural and functional levels of the body's organization in each organ system, you will be able to integrate otherwise isolated factual information into a cohesive and understandable whole. A memorized set of individual and isolated facts is soon forgotten—the parts of an anatomical structure that can be related to its function are not.

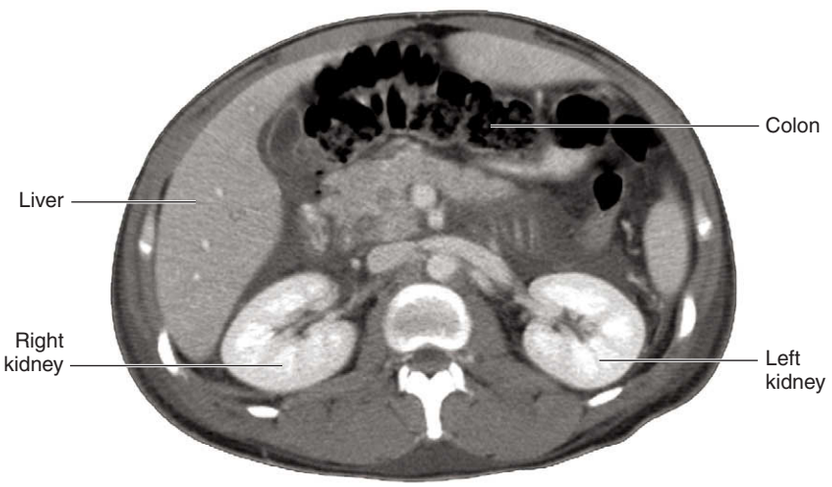
| QUICK CHECK |

20. Define what is meant by "complementarity of structure and function."
21. Give an example of how the chemical macromolecule DNA can have an influence on body structure.

| A&P CONNECT |

Why bother to learn about sections of the body? In the short term, you'll need to understand how to interpret the many illustrations like Figure 1-10 in this book. In the long term, you will use them in clinical settings—as in medical imaging.

Cadavers (preserved human bodies used for scientific study) can be cut into sagittal, frontal, or transverse sections for easy viewing of internal structures, but living bodies, of course, cannot. This fact has been troublesome for medical professionals who must determine whether internal organs are injured or diseased. In some cases the only sure way to detect a lesion or variation from normal is extensive exploratory surgery. Fortunately, advances in medical imaging allow physicians to visualize internal structures of the body without risking the trauma or other complications associated with extensive surgery. This figure shows a CT (computed tomography) scan similar to the perspective of Figure 1-10. CT scanning and some of the other widely used techniques are illustrated and described in ***Medical Imaging of the Body*** online at ***A&P Connect.***



Box 1-1 | DIAGNOSTIC study

Body Type and Disease

The concept of body types is a good example of how structure and function are interrelated. The term **somatotype** is used to describe a particular category of body build, or physique. Although the human body comes in many sizes and shapes, every individual can be classified as belonging to one of three basic body types, or somatotypes. The names used to describe these body types are as follows:

Ectomorph: thin, fragile physique characterized by little body fat accumulation

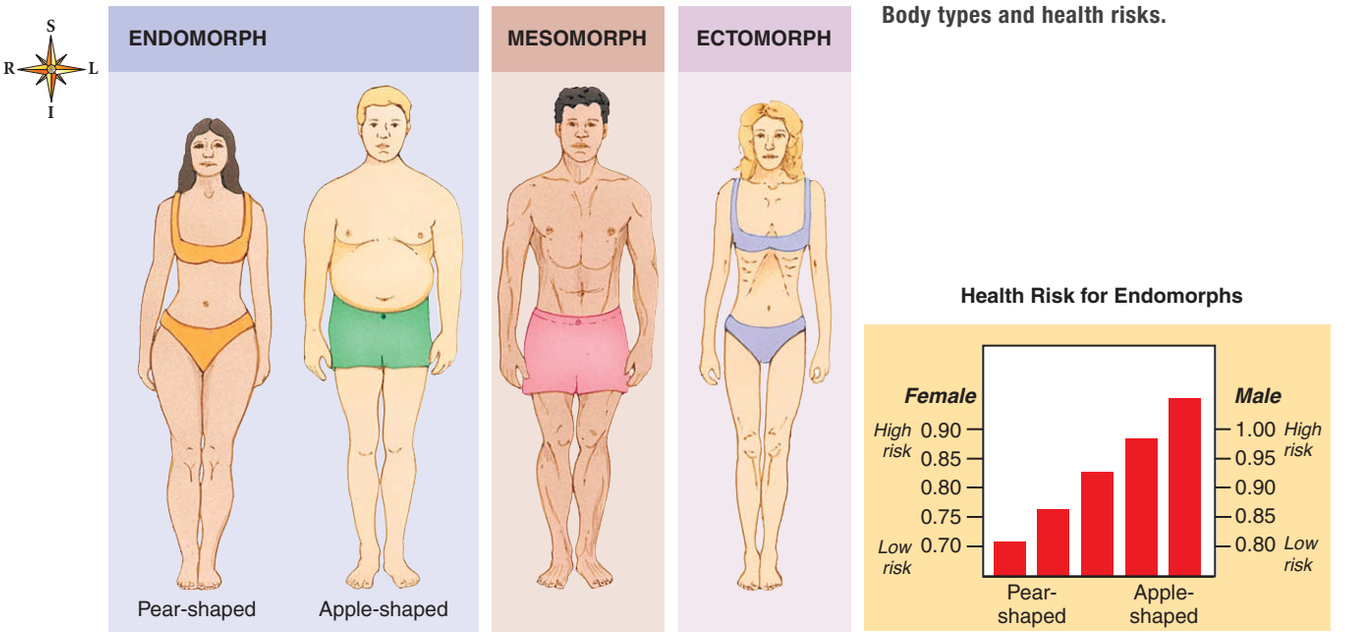
Mesomorph: muscular physique

Endomorph: heavy, rounded physique characterized by large accumulations of fat in the trunk and thighs

The figure shows extreme examples of the three somatotypes. By carefully studying the body build of numerous individuals, scientists have found that the basic components that determine the different categories of physique occur in varying degrees in every person—both men and women. Only in very rare instances does an individual show almost total dominance by a single somatotype component.

Until recently the concept of somatotype was considered largely "historical" and of relatively little practical importance. However, new research findings have rekindled interest in this area. We now know, for example, that knowledge of physique can provide health care professionals and educators with vital information useful in such areas as disease screening procedures, programs designed to identify individuals who may be at risk for certain diseases, and prediction of performance capability in selected physical education programs.

Researchers have discovered that individuals (especially endomorphs) who have large waistlines and are "apple-shaped," or fattest in the abdomen, have a greater risk for heart disease, stroke, high blood pressure, and diabetes than do individuals with a lower "pear-shaped" distribution pattern of fat in the hips, thighs, and buttocks. Breast cancer in postmenopausal women is also associated with storage of fat in the abdomen and upper body area (apple shape). In both sexes, endomorphic individuals of the same height and weight but with a lower, or pear-shaped, body fat distribution pattern contracted these diseases more frequently than mesomorphs and ectomorphs but less frequently than endomorphs with an apple-shaped, or high body fat distribution pattern.



Body types and health risks.

HOMEOSTASIS

More than a century ago a great French physiologist, Claude Bernard (1813-1878), made a remarkable observation. He noted that body cells survived in a healthy condition only when the temperature, pressure, and chemical composition of their fluid environment remained relatively constant. He called the environment of cells the *internal environment*, or *milieu intérieur*. Bernard realized that although many elements of the external environment in which we live are in a constant state of change, important elements of the internal environment, such as body temperature, remain remarkably stable. For example, Bernard's neighbor, who travels from his Paris home heated with a fireplace to the snowy slopes of the Alps in January, is exposed to dramatic changes in air temperature within a few hours.

Fortunately, in a healthy individual, body temperature will remain at or very near normal regardless of temperature changes that may occur in the external environment. Just as the external environment surrounding the body as a whole is subject to

change, so too is the fluid environment surrounding each body cell. The remarkable fluid that bathes each cell contains literally dozens of different substances. Good health, indeed life itself, depends on the correct and constant amount of each substance in the blood and other body fluids. The precise and constant chemical composition of the internal environment must be maintained within very narrow limits ("normal ranges"), or sickness and death will result.

In 1932 a famous American physiologist, Walter B. Cannon, suggested the name **homeostasis** (ho-me-o-STAY-sis) for the relatively constant states maintained by the body. Homeostasis is a key word in modern physiology. It comes from two Greek words (*homoios*, "the same," and *stasis*, "standing"). "Standing or staying the same," then, is the literal meaning of homeostasis. In his classic publication titled *The Wisdom of the Body*, Cannon advanced one of the most unifying and important themes of physiology. He suggested that every regulatory mechanism of the body existed to maintain homeostasis, or constancy, of the body's internal fluid environment.

However, as Cannon emphasized, homeostasis does not mean something set and immobile that stays exactly the same all the time. In his words, homeostasis "means a condition that may vary, but which is relatively constant." It is the maintenance of relatively constant internal conditions despite changes in either the internal or the external environment that characterizes homeostasis. For example, even if external temperatures vary, homeostasis of body temperature means that it remains relatively constant at about 37° C (98.6° F), although it may vary slightly above or below that point and still be "normal." The fasting concentration of blood glucose, an important nutrient, can also vary somewhat and still remain within normal limits (Figure 1-11).

This normal reading or range of normal is called the **set point** or **set point range.** A value between 80 and 100 mg of glucose per milliliter of blood, depending on dietary intake and timing of meals, is typical. Although levels of the important gases oxygen and carbon dioxide also vary with the respiratory rate, these substances, like body temperature and blood glucose levels, must be maintained within very narrow limits.

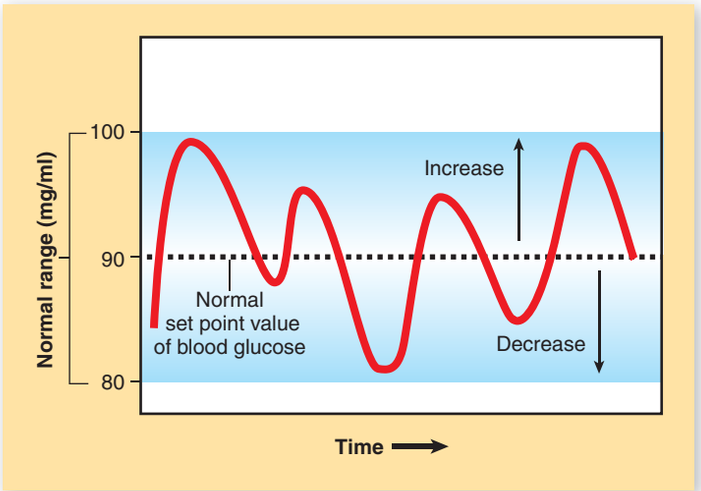


FIGURE 1-11

Homeostasis of blood glucose. The range over which a given value, such as the blood glucose concentration, is maintained is accomplished through homeostasis. Note that the concentration of glucose fluctuates above and below a normal set point value (90 mg/ml) within a normal set point range (80 to 100 mg/ml).

| A&P CONNECT |

What are the normal set point values for the concentration of clinically important substances found in the body? Check out ***Clinical and Laboratory Values*** online at ***A&P Connect.***

evolve

Specific regulatory mechanisms are responsible for adjusting body systems to maintain homeostasis. This ability of the body to "self-regulate," or "return to normal" to maintain homeostasis, is a critically important concept in modern physiology and also serves as a basis for understanding mechanisms of disease. Each cell of the body, each tissue, and each organ system plays an important role in homeostasis. Each of the diverse regulatory systems described in subsequent chapters of the text is explained as a function of homeostasis. You will learn how specific regulatory activities such as temperature control or carbon dioxide elimination are accomplished. In addition, an understanding of the relationship of homeostasis to healthy survival helps explain why such mechanisms are necessary.

Take a moment to study Figure 1-12. This diagram is a classic way of envisioning the idea of the body as a "bag of fluid." The fluid inside the bag is our internal environment, and it is this fluid that must be kept at a relatively constant temperature, glucose level, and so on, if the cells that make up the body are to survive. It is like a big, walking fishbowl, and our cells are the fish. All the little tubes and gizmos you see in Figure 1-12 are the systems that keep the "water in the fishbowl"—your internal fluid environment—stable. For example, the tube representing the digestive tract is a way for food in the external environment to be absorbed into the internal environment. So, just as you feed your goldfish every day, keeping the nutrient level in the fishbowl relatively constant over the years, your digestive tract keeps your body's nutrient levels relatively constant over the years.

All the other "accessories" in Figure 1-12 are like the accessories you may use in your fishbowl. The urinary system is like a filter that keeps waste levels constantly low. The respiratory system is like an aquarium's air pump and gets oxygen deep into the body to keep oxygen levels high for your cells. Throughout the book, we will regularly refer back to this diagram and the idea it represents—because this idea is the foundation for understanding all of physiology. If you know that everything functions to keep your "fishbowl" of a body constant so that your "fish," or cells, will stay alive, you can understand the basic function of every organ of every system!

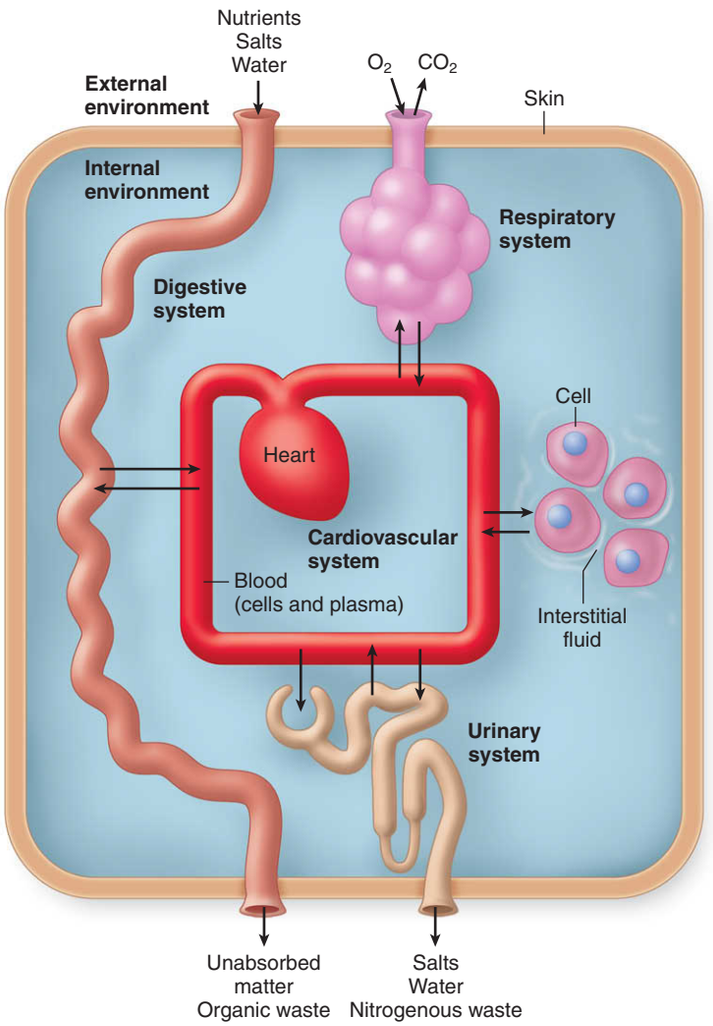


FIGURE 1-12

Diagram of the body's internal environment. The human body is like a bag of fluid separated from the external environment. Tubes, such as the digestive tract and respiratory tract, bring the external environment to deeper parts of the bag where substances may be absorbed into the internal fluid environment or excreted into the external environment. All the "accessories" somehow help maintain a constant environment inside the bag that allows the cells that live there to survive.

HOMEOSTATIC CONTROL MECHANISMS

Maintaining homeostasis means that the cells of the body are in an environment that meets their needs and permits them to function normally under changing external conditions. Processes for maintaining or restoring homeostasis are known as *homeostatic control mechanisms*. They involve virtually all of the body's organs and systems. If circumstances occur that require changes or more active regulation in some aspect of the internal environment, the body must have appropriate control mechanisms available that respond to these changing needs and then restore and maintain a healthy internal environment. For example, exercise increases the need for oxygen and results in accumulation of the waste product carbon dioxide. By increasing our breathing rate above its average of about 17 breaths per minute, we can maintain an adequate blood oxygen level and also increase the elimination of carbon dioxide. When exercise stops, the need for an increased respiratory rate no longer exists and the frequency of breathing returns to normal.

To accomplish this self-regulation, a highly complex and integrated communication control system or network is required. This type of network is called a **feedback control loop.** Different networks in the body control such diverse functions as blood carbon dioxide levels, temperature, heart rate, sleep cycles, and thirst. Information may be transmitted in these control loops by nervous impulses or by specific chemical messengers called *hormones*, which are secreted into the blood. Regardless of the body function being regulated or the mechanism of information transfer (nerve impulse or hormone secretion), these feedback control loops have the same basic components and work in the same way.

Basic Components of Control Mechanisms

There is a minimum of four basic components in every feedback control loop:

1. Sensor mechanism
2. Integrating, or control, center
3. Effector mechanism
4. Feedback

The terms *afferent* and *efferent* are important directional terms frequently used in physiology. They are used to describe movement of a signal from a sensor mechanism to a particular integrating or control center and, in turn, movement of a signal from that center to some type of effector mechanism. *Afferent* means that a signal is traveling toward a particular center or point of reference, and *efferent* means that the signal is moving away from a center or other point of reference. These terms are of particular importance in the study of the nervous and endocrine systems in Unit Three.

The process of regulation and the concept of return to normal require that the body be able to "sense" or identify the variable being controlled. Sensory nerve cells or hormone-producing (endocrine) glands frequently act as homeostatic sensors. To function in this way, a sensor must be able to identify the element being controlled. It must also be able to respond to any changes that may occur from the normal set point range. If deviations from the normal set point range occur, the sensor generates an afferent signal (nerve impulse or hormone) to transmit that information to the second component of the feedback loop—the integration or control center (Box 1-2).

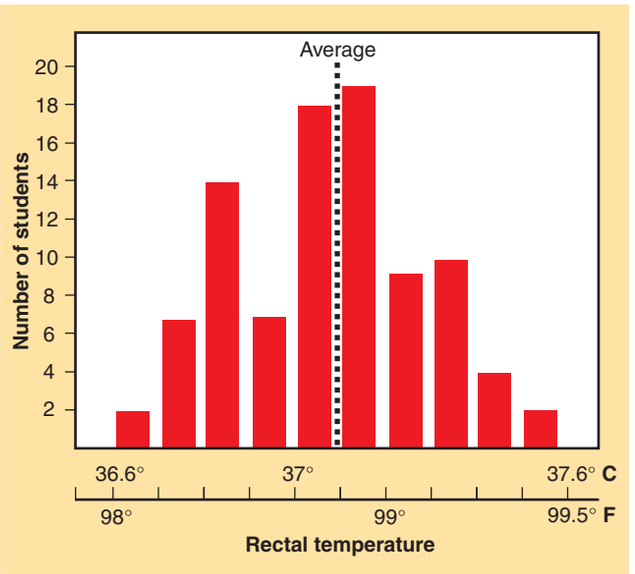
When the integration or control center of the feedback loop (often a discrete area of the brain) receives input from a homeostatic sensor, that information is analyzed and integrated with input from other sensors, and then an efferent signal travels from the center to some type of effector mechanism, where a specific action is initiated, if necessary, to maintain homeostasis. First, the level or magnitude of the variable being measured by the sensor is compared with the normal set point level that must be maintained for homeostasis. If significant deviation from that predetermined level exists, the integration/control center sends its own signal to the third component of the control loop—the effector mechanism.

Effectors are organs, such as muscles or glands, that directly influence controlled physiological variables. For example, it is

Box 1-2 | FYI

Changing the Set Point

Like the set point on a furnace, the physiological set points in your body can be changed. Your body's set point temperature is a good example. First, not everyone's set point, or "normal," body temperature is the same. The figure at right shows the difference in body temperatures observed in a group of healthy students. You can see that temperatures varied widely. This explains why some people are comfortable at a temperature that is too cold for others around them—their temperature set point must be lower. However, your set point can also change under varying circumstances. For example, we know a fellow who once turned up the thermostat in his house to get the temperature warm enough to get some unwelcome visitors to leave. Likewise, during a bacterial infection, your immune system sends chemicals to signal the brain's hypothalamus to "turn up the set point temperature." Your body shivers, and you may ask for a blanket as your body tries to reach this new higher set point. You now have a fever. The bacteria that have invaded your body did so because they liked the temperature of your body. When you are experiencing a fever, your body becomes uncomfortably warm for the bacteria, and they slow down their reproductive rate, which slows the infection. At the same time, the warmer temperature helps improve the immune system's function as it deals with the bacteria. After the infection is over, the hypothalamus returns to its usual set point and your fever goes away.



Range of normal body temperatures. In a well-controlled experiment, a group of healthy students show a wide range of normal rectal temperatures. The average (mean) temperature of the group is 37.1° C (98.8° F).

effector action that increases or decreases variables such as body temperature, heart rate, blood pressure, or blood sugar concentration to keep them within their normal range. The activity of effectors is ultimately regulated by feedback of information regarding their own effects on a controlled variable.

Many instructors use the example of a furnace controlled by a thermostat to explain how feedback control systems work. This analogy is a good one because it parallels the homeostatic mechanism used to control body temperature. Note that changes in room temperature (the controlled variable) are detected by a thermometer (sensor) attached to the thermostat (integrator) (Figure 1-13, A). The thermostat contains a switch that controls the furnace (effector). When cold weather causes a decrease in room temperature, the change is detected by the thermometer and relayed to the thermostat. The thermostat compares the actual room temperature with the set point temperature. After the integrator determines that the actual temperature is too low, it sends a "correction" signal by switching on the furnace. The furnace produces heat and thus increases room temperature back toward normal. As the room temperature increases above normal, feedback information from the thermometer causes the thermostat to switch off the furnace. Thus by intermittently switching the furnace off and on, a relatively constant room temperature can be maintained.

Body temperature can be regulated in much the same way as room temperature is regulated by the furnace system just described (see Figure 1-13, B). Here, sensory receptors in the skin and other tissues act as sensors by monitoring body temperature. When cold weather causes the body temperature to decrease, feedback information is relayed through the nerves to the "thermostat" in a part of the brain called the *hypothalamus* (hye-poh-THAL-ah-muss). The hypothalamic integrator compares the actual body temperature with the "built-in" set point body temperature and subsequently sends a nerve signal to effectors. In this example, the skeletal muscles act as effectors by shivering and thus producing heat. Shivering increases body temperature back to normal, at which point it stops as a result of feedback information that causes the hypothalamus to shut off its stimulation of the skeletal muscles. More specifics of body temperature control are discussed in Chapter 7.

The impact of effector activity on sensors may be positive or negative. Therefore, homeostatic control mechanisms are categorized as negative or positive feedback systems. By far the most important and numerous of the homeostatic control mechanisms are negative feedback systems.

Negative Feedback Control Systems

The example of temperature regulation by action of a thermostatically regulated furnace is a classic example of **negative feedback.** Negative feedback control systems are inhibitory. They oppose a change (such as a drop in temperature) by creating a response (production of heat) that is opposite in direction to the initial disturbance (fall in temperature below a normal set point). All negative feedback mechanisms in the body respond in this way regardless of the variable being controlled. They produce an action that is opposite to the change that activated the system. It is important to emphasize that negative feedback control systems

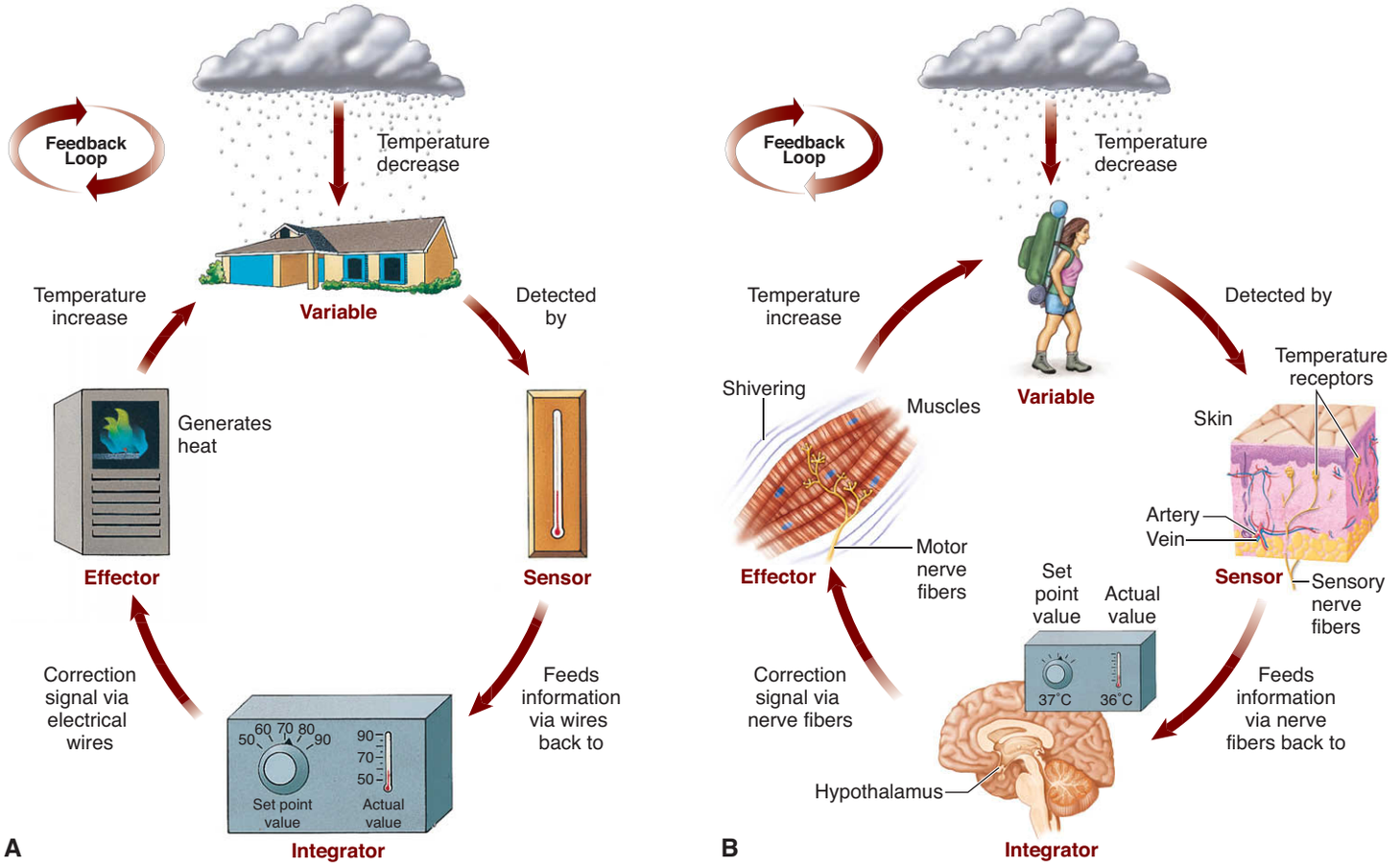


FIGURE 1-13

Basic components of homeostatic control mechanisms. **A,** Heat regulation by a furnace controlled by a thermostat. **B,** Homeostasis of body temperature. Note that in both examples **A** and **B,** a stimulus (drop in temperature) activates a sensor mechanism (thermostat or body temperature receptor) that sends input to an integrating, or control, center (on-off switch or hypothalamus), which then sends input to an effector mechanism (furnace or contracting muscle). The resulting heat that is produced maintains the temperature in a "normal range." Feedback of effector activity to the sensor mechanism completes the control loop. Both are examples of negative feedback loops.

stabilize physiological variables. They keep variables from straying too far outside their normal ranges. Negative feedback systems are responsible for maintaining a constant internal environment.

Positive Feedback Control Systems

Positive feedback is also possible in control systems. However, because positive feedback does not operate to help the body maintain a stable, or homeostatic, condition, it is often harmful, even disastrous, to survival. Positive feedback control systems are stimulatory.

Instead of opposing a change in the internal environment and causing a return to normal, positive feedback tends to amplify or reinforce the change that is occurring. In the example of the furnace controlled by a thermostat, a positive feedback loop continues to increase the temperature. It does so by stimulating the furnace to produce more and more heat. Each increase in heat production is followed by a positive stimulation to increase the temperature even more. Typically, such responses result in instability and disrupt homeostasis because the variable in question continues to deviate further and further away from its normal range.

Only a few examples of positive feedback operate in the body under normal conditions. In each case, positive feedback accelerates the process in question. The feedback causes an ever-increasing rate of events to occur until something stops the process. In other words, positive feedback loops tend to amplify or accelerate a change—in contrast to negative feedback loops, which reverse a change. Although positive feedback is not the usual type of feedback in the body, it is no less important (Box 1-3).

Events that lead to a simple sneeze, the birth of a baby, an immune response to an infection, or the formation of a blood clot are all examples of positive feedback.

Feed-Forward in Control Systems

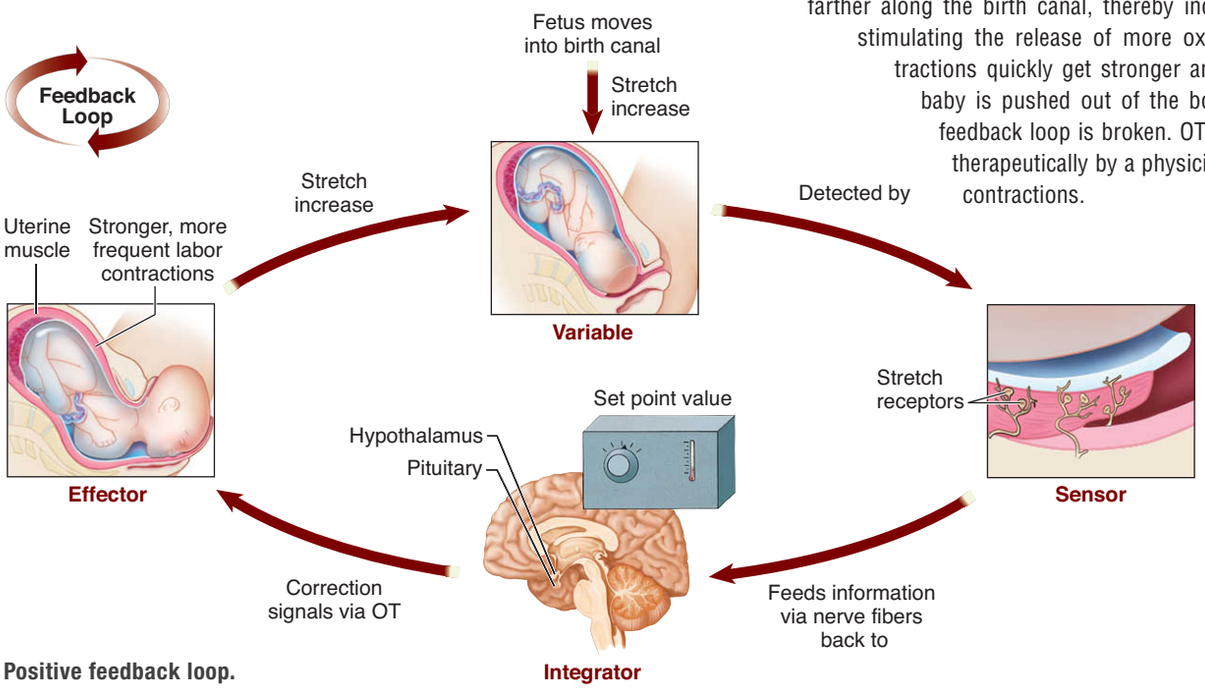
As you study the complexity of control systems throughout the body, you will no doubt run into cases of *feed-forward* in control systems. Feed-forward is the concept that information may flow ahead to another process to trigger a change in anticipation of an event that will follow. For example, when you eat a meal, the stomach stretches and this triggers stretch sensors in the stomach wall. As you would expect, the stretch sensors trigger a feedback response that causes the release of digestive juices and contraction of stomach muscles. This is normal negative feedback because secretion and muscle activity eventually get rid of the food and bring the stretch of the stomach back down to normal. It will continue as long as there is food to

Box 1-3 | FYI

Positive Feedback During Childbirth

One of the mechanisms that operates during delivery of a newborn illustrates the concept of positive feedback. As delivery begins, the baby is pushed from the *womb,* or *uterus,* into the birth canal, or *vagina.* Stretch receptors in the wall of the reproductive tract detect the increased stretch caused by movement of the baby. Information regarding increased stretch is fed back to the brain, which triggers the pituitary gland to secrete a hormone called *oxytocin* (OT).

Oxytocin travels through the bloodstream to the uterus, where it stimulates stronger contractions. Stronger contractions push the baby farther along the birth canal, thereby increasing stretch and stimulating the release of more oxytocin. Uterine contractions quickly get stronger and stronger until the baby is pushed out of the body and the positive feedback loop is broken. OT can also be injected therapeutically by a physician to stimulate labor contractions.



Positive feedback loop.

stretch the stomach. At the same time, the stretch stimulus is triggering the small intestine and related organs to increase secretion there as well—*before* the food has arrived. In other words, information from one feedback loop (in the stomach) has leaped ahead to the next logical feedback loop (in the intestines) to get the second loop ready ahead of time. Feed-forward causes a feedback loop to anticipate a stimulus (in this case, stretch of the intestinal wall caused by food moving down from the stomach) before it actually happens.

Levels of Control

One of the first principles that will occur to you as you study human physiology is that the functions of cells, tissues, organs, and systems are integrated into a coordinated whole. This is accomplished by many different feedback loops and feed-forward systems operating at many different levels of organization within the body (Figure 1-14).

Intracellular control mechanisms operate at the cell level. These mechanisms regulate functions within the cell, often by means of genes and enzymes. The role of genes and enzymes is discussed further in Chapters 4 and 5.

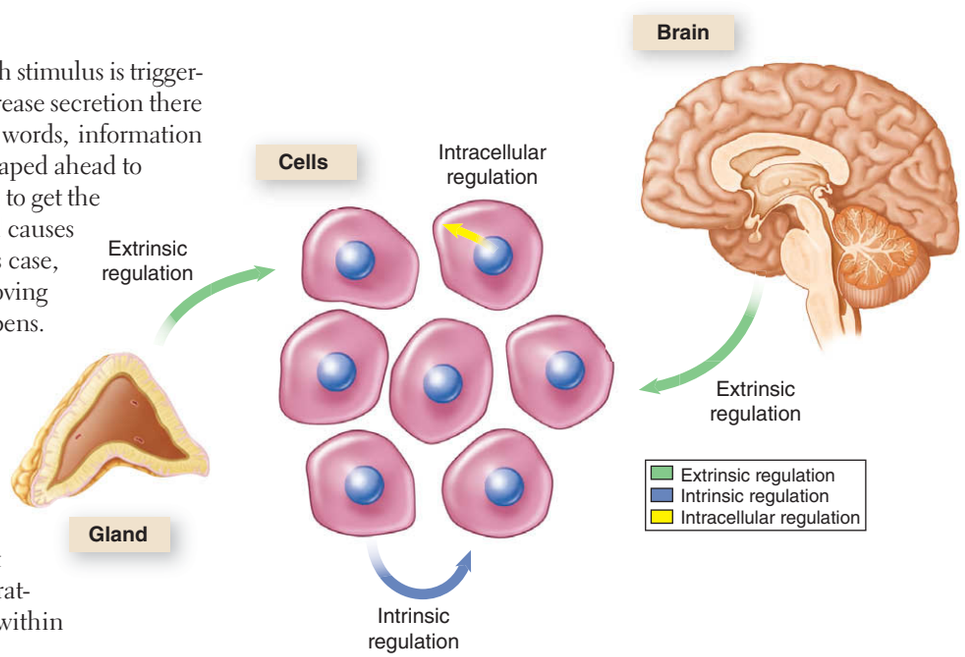


FIGURE 1-14

Levels of control. The many complex processes of the body are coordinated at many levels: intracellular (within cells), intrinsic (within tissues/organs), and extrinsic (organ to organ).

Intrinsic control mechanisms operate at the tissue and organ levels. Sometimes also called local control or *autoregulation*, intrinsic mechanisms often make use of chemical signals. For example, prostaglandins are molecules sent as signals to other nearby cells. Intrinsic regulation may also be "built in" to the tissue or organ. For instance, when cardiac muscle in the heart is stretched, the muscle automatically contracts with more force. Prostaglandins are discussed further in Chapters 2 and 18. Many other examples of intrinsic control are discussed throughout the book.

Extrinsic control means "outside" control and operates at the system and organism levels. Extrinsic control usually involves nervous and endocrine (hormonal) regulation. It is called "extrinsic" control because the nerve signals and hormones originate outside the controlled organ. Nervous regulation is introduced in more detail in Chapters 13 through 17 and endocrine regulation is introduced in Chapter 18.

Summary of Homeostasis

In summary, many homeostatic mechanisms operate on the negative feedback principle. They are activated, or turned on, by changes in the environment that surround every body cell. Negative feedback systems are inhibitory. They reverse the change that initially activated the homeostatic mechanism. By reversing the initial change, a homeostatic mechanism tends to maintain or restore internal constancy. Occasionally, a positive (stimulatory) feedback mechanism helps promote survival. Such positive or stimulatory feedback systems may be required to bring specific body functions to swift completion (see Box 1-3). Feed-forward occurs when sensory information "jumps ahead" to a feedback loop to get it started before the stimulus actually changes the controlled physiological variable.

Homeostatic control systems can operate at any (or all) of several different levels: within the cell, from cell to cell within a tissue, and throughout the body. This layering of regulation allows for precise coordination of functions within organs as well as in the whole body.

| QUICK CHECK |

22. Define the term *homeostasis.*
23. List the basic components of every feedback control system.
24. Explain the mechanism of action of negative and positive feedback control systems.
25. Contrast intracellular, intrinsic, and extrinsic levels of control.



Cycle of LIFE

Life Span Considerations

An important generalization about body structure is that every organ, regardless of location or function, undergoes change over the years. In general, the body performs its functions least well at both ends of life—in infancy and in old age. Organs develop and grow during the years before maturity, and body functions gradually become more and more efficient and effective. In a healthy young adult all body systems are mature and fully operational. Homeostatic mechanisms tend to function most effectively during this period of life to maintain the constancy of one's internal environment.

After maturity, effective repair and replacement of the body's structural components often decrease. The term **atrophy** is used to describe the wasting effects of advancing age. In addition to structural atrophy, the functioning of many physiological control mechanisms also decreases and becomes less precise with advancing age. The changes in functions that occur during the early years are called *developmental processes.* Those that occur during the late years are called *aging processes.* The study of aging processes and other changes that occur in our lives as we get older is called *gerontology.* Many specific age changes are noted in the chapters that follow.



the BIG picture

Organization of the Body

Ultimately, your success in the study of anatomy and physiology, your ability to see the "big picture," will require understanding, synthesis, and integration of structural information and functional concepts. After you have completed your study of the individual organ systems of the body presented in the chapters that follow, you must be able to reassemble the parts and view the body in a holistic, integrated way.

The body is truly more than the sum of the parts, and understanding the connectedness of human structure and function is the real challenge—and the greatest reward—in the study of anatomy and physiology. Your ability to integrate otherwise isolated factual information about bones, muscles, nerves, and blood vessels, for example, will allow you to view anatomical components of the body and their functions in a more cohesive and understandable way. This chapter introduces the principle of homeostasis as the glue that integrates and explains how the normal interaction of structure and function is achieved and maintained and how a breakdown of this integration results in disease. Furthermore, it provides the basis for understanding and integrating the body of knowledge, both factual and conceptual, that anatomy and physiology encompass.

Mastery of any academic discipline or achieving success in any health care–related work environment requires the ability to communicate effectively. The ability to understand and appropriately use the vocabulary of anatomy and physiology allows you to accurately describe the body itself, the orientation of the body in its surrounding environment, and the relationships that exist between its component parts in both health and disease. This chapter provides you with information necessary to be successful in seeing "the big picture" as you master the details of each organ system that, although presented separately in subsequent chapters of the text, are in reality part of a marvelously integrated whole.

MECHANISMS of DISEASE

SOME GENERAL CONSIDERATIONS

A clearer understanding of the normal function of the body often comes from our study of disease (Box 1-4). **Pathophysiology** is the organized study of the underlying physiological processes associated with disease. Pathophysiologists attempt to understand the mechanisms of a disease and its course of development, or *pathogenesis*. Near the end of each chapter of this book we briefly describe some important disease mechanisms that illustrate the breakdown of normal functions described in that chapter.

Many diseases are best understood as disturbances to homeostasis, the relative constancy of the body's internal environment. If homeostasis is disturbed, various negative feedback mechanisms usually return the body to normal. When a disturbance goes beyond the normal fluctuation of everyday life, we can say that a disease condition exists. In acute conditions the body recovers its homeostatic balance quickly. In chronic diseases a normal state of balance may never be restored. If the disturbance keeps the body's internal environment too far from normal for too long, death may result.

Basic Mechanisms of Disease

Disturbances to homeostasis and the body's responses are the basic mechanisms of disease. Because of their variety, disease mechanisms can be categorized for easier study:

Genetic mechanisms. Altered, or mutated, genes can cause abnormal proteins to be made. These abnormal proteins often do not perform their intended function—resulting in the absence of an essential function. On the other hand, such proteins may instead perform an abnormal, disruptive function. Either case poses a potential threat to the constancy of the body's internal environment. The action of genes is first discussed in Chapter 3, and the mechanisms by which genes are inherited are discussed in Chapter 37.

Pathogenic organisms. Many important disorders are caused by pathogenic (disease-causing) organisms or particles that damage the body in some way (Figure 1-15). Any organism that lives in or on another organism to obtain its nutrients is called a *parasite*.

Box 1-4 | HEALTH matters

Disease Terminology

Everyone is interested in **pathology**—the study of disease. Researchers want to know the scientific basis of abnormal conditions. Health practitioners want to know how to prevent and treat various diseases. Every one of us, when we suffer from the inevitable head cold or something more serious, want to know what is going on and how best to deal with it. Pathology has its own terminology, as in any specialized field. Just as with other scientific terms, most disease-related terms are derived from Latin and Greek word parts. For example, patho- comes from the Greek word for disease (*pathos*) and is used in many terms, including "pathology" itself.

Disease conditions are usually *diagnosed* or identified by **signs** and **symptoms.** Signs are objective abnormalities that can be seen or measured by someone other than the patient, whereas symptoms are the subjective abnormalities that are felt only by the patient. Although *sign* and *symptom* are distinct terms, we often use them interchangeably. A **syndrome** is a collection of different signs and symptoms that occur together. When signs and symptoms appear suddenly, persist for a short time, and then disappear, we say that the disease is **acute.** On the other hand, diseases that develop slowly and last for a long time (perhaps for life) are labeled **chronic** diseases. The term *subacute* refers to diseases with characteristics somewhere between acute and chronic.

The study of all the factors involved in causing a disease is its **etiology.** The etiology of a skin infection often involves a cut or abrasion and subsequent invasion and growth of a bacterial colony. Diseases with undetermined causes are said to be **idiopathic. Communicable** diseases are those that can be transmitted from one person to another.

The term *etiology* refers to the theory of a disease's cause, but the actual pattern of a disease's development is called its **pathogenesis.** The common cold, for example, begins with a *latent,* or "hidden," stage during which the cold virus establishes itself in the patient. No signs of the cold are yet evident. In infectious diseases, the latent stage is also called **incubation.** The cold may then manifest itself as a mild nasal drip and trigger a few sneezes. It subsequently progresses to its full fury and continues for a few days. After the cold infection has run its course, a period of *convalescence,* or recovery, occurs. During this stage, body functions return to normal. Some chronic diseases, such as cancer, exhibit a temporary reversal that seems to be a recovery. Such reversal of a chronic disease is called a **remission.** If a remission is permanent, we say that the person is "cured."

Epidemiology is the study of the occurrence, distribution, and transmission of diseases in human populations. A disease that is native to a local region is called an **endemic** disease. If the disease spreads to many individuals in a relatively short time, the situation is called an **epidemic. Pandemics** are epidemics that affect large geographic regions, perhaps spreading worldwide. Because of the speed and availability of modern air travel, pandemics are more common than they once were. Almost every flu season we see a new strain of influenza virus quickly spreading from continent to continent.

Names of specific diseases are often descriptive, such as *rheumatoid arthritis* (meaning "autoimmune inflammation of joints"). Some disease names are eponyms, with a person's name incorporated into the term, as in *Parkinson disease (PD).* Notice that we follow the American Medical Association (AMA) format for eponyms in this textbook, which prohibits adding the possessive ('s) to a person's name. Notice also that some disease names are abbreviated with an acronym such as *DMD* (for *Duchenne muscular dystrophy*).

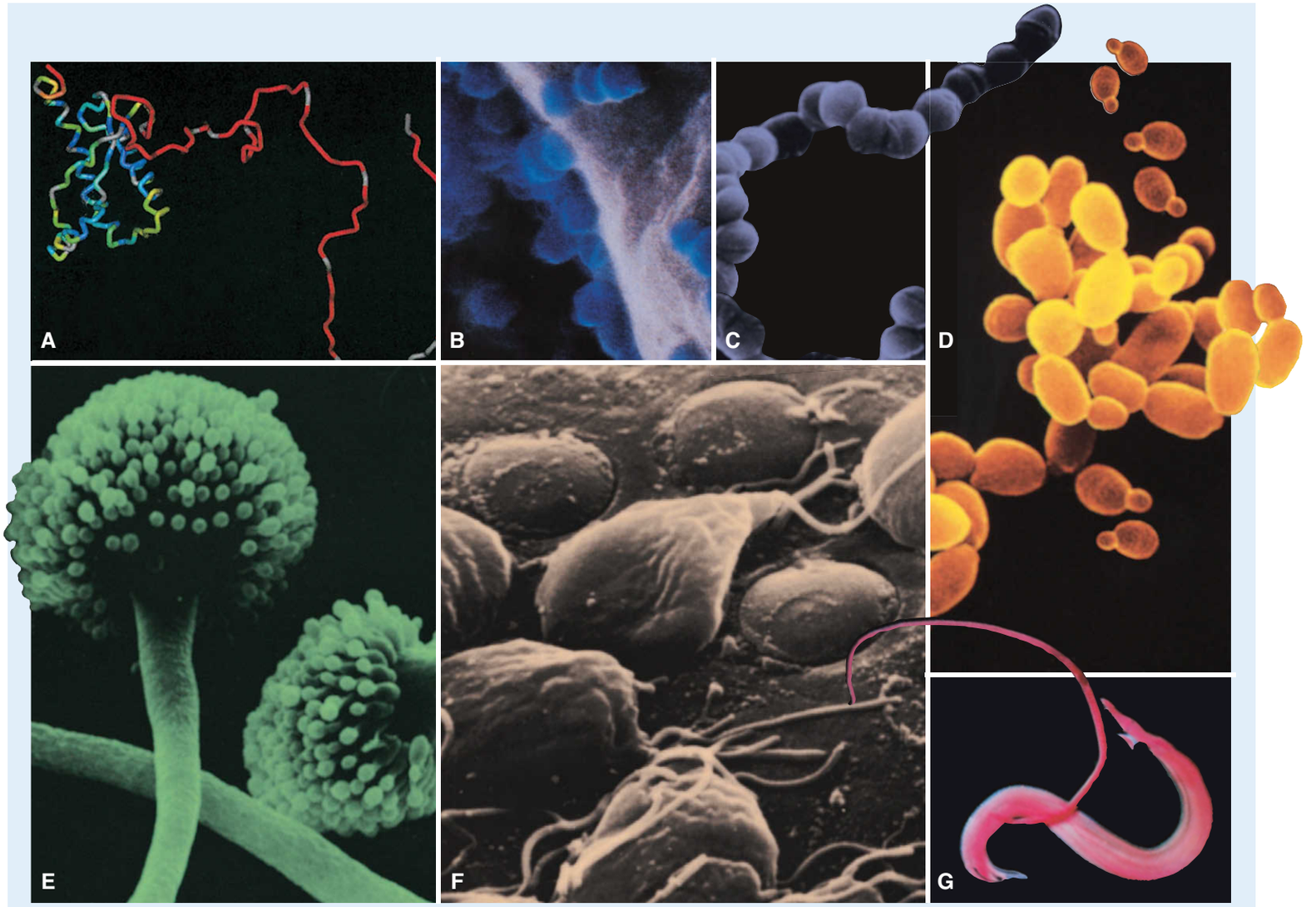


FIGURE 1-15

Pathogenic organisms. A, Prion (cause of variant Creutzfeldt-Jakob disease). **B,** Viruses (the human immunodeficiency virus [HIV] that causes AIDS). **C,** Bacteria (Streptococcus bacteria that cause strep throat and other infections). **D,** Fungi (yeast cells that commonly infect the urinary and reproductive tracts). **E,** Fungi (the mold that causes aspergillosis). **F,** Protozoans (the flagellated cells that cause traveler's diarrhea). **G,** Pathogenic animals (the parasitic worms that cause snail fever).

The presence of microscopic or larger parasites may interfere with normal body functions of the host and cause disease. Besides parasites, there are organisms that poison or otherwise damage the human body to cause disease. Some of the major pathogenic organisms and particles include the following:

Prions (proteinaceous infectious particles) are proteins that convert normal proteins of the nervous system into abnormal proteins, thereby causing loss of nervous system function. The abnormal form of the protein may also be inherited. Prion protein (also called *PrP*) molecules are a newly discovered type of pathogen, and not much is known about how the prion works to cause such diseases as bovine spongiform encephalopathy (BSE; "mad cow disease") or variant Creutzfeldt-Jakob disease (vCJD). However, not all prions cause disease. Some are now known to be involved in memory formation and the normal maintenance of the insulating sheath around many nerve fibers.

Viruses are intracellular parasites that consist of a DNA or RNA core surrounded by a protein coat and, sometimes, a lipoprotein envelope. They are particles that invade human cells and cause them to produce viral components. Sometimes, the term *virion* is used to designate the complete virus particle as it exists outside the host cell.

Bacteria are tiny, primitive cells that lack nuclei. They cause infection by parasitizing tissues or otherwise disrupting normal function.

Fungi are simple organisms similar to plants but lack the chlorophyll pigments that allow plants to make their own food. Because they cannot make their own food, fungi must parasitize other tissues, including those of the human body. **Protozoa** are protists, one-celled organisms larger than bacteria whose DNA is organized into a nucleus. Many types of protozoa parasitize human tissues. **Pathogenic animals** are large, multicellular organisms such as

insects and worms. Such animals can parasitize human tissues, bite or sting, or otherwise disrupt normal body function.

Examples of infections or other conditions caused by pathogenic organisms are given in many chapters throughout this book.

- **Tumors and cancer.** Abnormal tissue growths, or neoplasms, can cause various physiological disturbances, as described in Chapter 6.
- **Physical and chemical agents.** Agents such as toxic or destructive chemicals, extreme heat or cold, mechanical injury, and radiation can each affect the normal homeostasis of the body. Examples of healing of tissues damaged by physical agents are discussed in Chapters 6, 7, and a few other chapters.
- **Malnutrition.** Insufficient or imbalanced intake of nutrients causes various diseases; these are outlined in Chapters 29 and 30.
- **Autoimmunity.** Some diseases result from the immune system attacking one's own body (*autoimmunity*) or from other mistakes or overreactions of the immune response. Autoimmunity, literally "self-immunity," is discussed in Chapter 24 along with other disturbances of the immune system.
- **Inflammation.** The body often responds to disturbances with an *inflammatory response*. The inflammatory response, which is described in Chapters 6 and 24, is a normal mechanism that usually speeds recovery from an infection or injury. However, when the inflammatory response occurs at inappropriate times or is abnormally prolonged or severe, normal tissues may become damaged. Thus some disease symptoms are caused by the inflammatory response.
- **Degeneration.** By means of many still unknown processes, tissues sometimes break apart or *degenerate*. Although a normal consequence of aging, degeneration of one or more tissues resulting from disease can occur at any time. The degeneration of tissues associated with aging is discussed in nearly every chapter of this book.

Risk Factors

Other than direct causes or disease mechanisms, certain predisposing conditions may exist that make a disease more likely to develop. Usually called *risk factors*, they often do not actually cause a disease but just put one "at risk" for it. Risk factors can combine and increase a person's chance for contracting a specific disease even more. Some of the major types of risk factors are as follows:

Genetic factors. There are several types of genetic risk factors. Sometimes an inherited trait puts one at greater than normal risk for development of a specific disease. For example, light-skinned people are more at risk for certain forms of skin cancer than are dark-skinned people. This occurs because light-skinned people have less pigment in their skin to protect them from cancer-causing ultraviolet radiation (see Chapter 7). Membership in a certain ethnic group, or *gene pool*, involves the "risk" of inheriting a disease-causing gene that is common in that gene pool. For example, certain Africans and their descendants are at greater than average risk of inheriting *sickle cell anemia*—a serious blood disorder.

Age. Biological and behavioral variations during different phases of the human life cycle put us at greater risk for certain diseases at certain times in our life. For example, middle ear infections are more common in infants than in adults because of the difference in ear structure at different ages.

Lifestyle. The way we live and work can put us at risk for some diseases. People whose work or personal activity puts them in direct sunlight for long periods have a greater chance for development of skin cancer because this puts them in more frequent contact with ultraviolet radiation from the sun. Some researchers believe that the high-fat, low-fiber diet common among people in the "developed" nations increases the risk for certain types of cancer.

Stress. Physical, psychological, or emotional stress can put one at risk for problems such as chronic high blood pressure (hypertension), peptic ulcers, and headaches. Conditions caused by psychological factors are sometimes called *psychogenic* (mind-caused) disorders. Chapter 25 discusses the concept of stress and its effect on health.

Environmental factors. Although environmental factors such as climate and pollution can actually cause injury or disease, some environmental situations simply put us at greater risk for getting certain diseases. For example, because some parasites survive only in tropical environments, we are not at risk of being infected with them if we live in a temperate climate.

Microorganisms. Different types of pathological organisms, such as viruses and bacteria, are now suspected of being "infectious cofactors" in the development of certain noninfectious diseases that in the past were not considered to result directly from their presence in the body. For example, we now have very strong evidence to link infections caused by hepatitis B virus with liver cancer and human papillomavirus with cervical cancer. We also know that the bacterium *Helicobacter pylori*, which causes ulcers, is in some way also a factor in the development of certain types of stomach cancer.

Preexisting conditions. A preexisting condition can adversely affect our capacity to defend ourselves against an entirely different condition or disease. Thus the *primary* (preexisting) condition can put a person at risk for development of a *secondary* condition. For example, in individuals with AIDS the primary condition is characterized by a suppressed immune system. As a result, secondary or "opportunistic" infections such as pneumonia often develop. Obesity is a risk factor for many conditions, including heart disease, diabetes, stroke, some forms of cancer, and high blood pressure.

| A&P CONNECT |

World events have shown us that the intentional transmission of disease can be used as a weapon of terror. For example, the bacterial infection anthrax usually infects grazing animals such as sheep, but has been used as a weapon against people. For more, check out ***Disease as a Weapon*** online at ***A&P Connect.***



LANGUAGE OF SCIENCE *(continued from p. 3)*

central
(SEN-tral)
[*centr-* **center,** *-al* **relating to]**

coronal plane
(ko-RO-nal plane)
[*corona-* **crown,** *-al* **relating to]**

cortical
(KOR-tik-al)
[*cortic-* **bark,** *-al* **relating to]**

deep

distal
(DIS-tal)
[*dist-* **distance,** *-al* **relating to]**

dorsal cavities
(DOR-sal KAV-i-teez)
[*dors* **back,** *-al* **relating to,** *cav-* **hollow,** *-ity* **state]**

eponym
(EP-o-nim)
[*epo-* **above,** *-nym* **name]**

extrinsic control
(eks-TRIN-sik kon-TROL)
[*extr-* **outside or beyond,** *-insic* **beside]**

feedback control loop

gross anatomy
(grohs ah-NAT-o-mee)
[*gross* **large,** *ana-* **apart,** *-tom-* **cut,** *-y* **action]**

homeostasis
(ho-mee-o-STAY-sis)
[*homeo- same or equal, -stasis* **standing still]**

Ohypothesis
(hye-POTH-eh-sis)
[*hypo-* **under or below,** *-thesis* **placing or proposition];** *pl.,* **hypotheses**
(hye-POTH-eh-seez)

inferior
(in-FEER-ee-or) [*infer-* **lower,** *-or* **quality]**

intracellular control
(in-tra-SELL-yoo-lar kon-TROL)
[*intra- inside or within, -cell* **storeroom]**

intrinsic control
(in-TRIN-sik kon-TROL)
[*intr-* **inside or within,** *-insic* **beside]**

lateral
(LAT-er-al)
[*later* **side,** *-al* **relating to]**

lumen
(LOO-men)
[*lumen* **light];** *pl.,* **lumina**

medial
(MEE-dee-al)
[*media-* **middle,** *-al* **relating to]**

medullary
(MED-oo-lar-ee)
[*medulla-* **middle,** *-ry* **state]**

metabolism
(me-TAB-o-liz-em)
[*metabol-* **change,** *-ism* **condition]**

microscopic anatomy
(my-kroh-SKOP-ik ah-NAT-o-mee)
[*micro-* **small,** *-scop-* **see,** *-ic* **relating to,** *ana-* **apart,** *-tom-* **cut,** *-y* **action]**

negative feedback
[*negative* **opposing or prohibitive]**

organ
(OR-gan)
[*organ* **instrument]**

organelle
(or-gah-NELL)
[*organ-* **tool or instrument,** *-elle* small]

organism
(OR-gah-niz-im)
[*organ-* **instrument,** *-ism* **condition]**

parietal
(pah-RYE-i-tal)
[*pariet-* **wall,** *-al* **relating to]**

pathology
(pah-THOL-o-jee)
[*patho-* **disease,** *-o-* **combining form,** *-log-* **words (study of),** *-y* **activity]**

peripheral
(pe-RIF-er-al)
[*peri-* **around,** *-phera-* **boundary,** *-al* **relating to]**

physiology
(fiz-ee-OL-o-jee)
[*physio-* **nature (function),** *-o-* **combining form,** *-log-* **words (study of),** *-y* **activity]**

positive feedback
[*positive* **to place or to amplify]**

posterior
(pos-TEER-ee-or)
[*poster-* **behind,** *-or* **quality]**

proximal
(PROK-si-mal)
[*proxima-* **near,** *-al* **relating to]**

sagittal plane
(SAJ-i-tal plane)
[*sagitta-* **arrow,** *-al* **relating to]**

set point

somatotype
(so-MAT-o-type)
[*soma-* **body,** *-to-* **combining form,** *-type* **mark]**

superficial
(soo-per-FISH-al)
[*super-* **over or above,** *-fici-* **face,** *-al* **relating to]**

superior
(soo-PEER-ee-or)
[*super-* **over or above,** *-or* **quality]**

system
(SIS-tem)
[*system* **organized whole]**

thoracic cavity
(thoh-RASS-ik)
[*thorac-* **chest (thorax),** *-ic* **relating to]**

tissue
(TISH-yoo)
[*tissue* **fabric]**

transverse plane
(TRANS-vers plane)
[*trans-* **across or through,** *-vers* **turn]**

ventral cavities
(VEN-tral KAV-ih-teez)
[*ventr-* **belly,** *-al* **relating to,** *cav-* **hollow,** *-ity* **state]**

viscera, visceral
(VISS-er-ah) (VISS-er-al)
[*visc-* **internal organ,** *-al* **relating to];** *sing.,* **viscus**

LANGUAGE OF MEDICINE

acute
(ah-KYOOT)
[*acute* **sharp]**

atrophy
(AT-ro-fee)
[*a-* **without,** *-troph* **nourishment,** *-y* **state]**

bacterium
(bak-TEE-ree-um)
[*bacterium* **small staff];** *pl.,* **bacteria**

chronic
(KRON-ik)
[*chron-* **time,** *-ic* **relating to]**

communicable
(kom-MYOO-ni-kah-bil)
[*communic* **common,** *-able* **capacity for]**

ectomorph
(EK-toh-morf)
[*ecto-* **outside,** *-morph* **form]**

endemic
(en-DEM-ik)
[*en-* **in,** *-dem-* **people,** *-ic* **relating to]**

endomorph
(EN-doh-morf)
[*endo-* **within,** *-morph* **shape]**

epidemic
(ep-i-DEM-ik)
[*epi-* **upon,** *-dem-* **people,** *-ic* **relating to]**

epidemiology
(EP-i-dee-mee-OL-o-jee)
[*epi-* **upon,** *-dem-* **people,** *-o-* **combining form,** *-log-* **words (study of),** *-y* **activity]**

etiology
(e-tee-OL-o-jee)
[*etio-* **cause,** *-o-* **combining form,** *-log-* **words (study of),** *-y* **activity]**

fungus
(FUNG-us)
[*fungus* **mushroom];** *pl.,* **fungi**
(FUNG-eye)

idiopathic
(id-ee-o-PATH-ik)
[*idio-* **peculiar,** *-path-* **disease,** *-ic* **relating to]**

incubation
(in-kyoo-BAY-shun)
[*in-* **in or on,** *-cuba-* **lie,** *-tion* **condition of]**

mesomorph
(MEZ-oh-morf)
[*meso-* **middle,** *-morph* **form]**

pandemic
(pan-DEM-ik)
[*pan-* **all,** *-dem-* **people,** *-ic* **relating to]**

pathogenesis
(path-o-JEN-e-sis)
[*patho-* **disease,** *-genesis* **origin]**

pathogenic animal
(path-o-JEN-ik)
[*patho-* **disease,** *-gen-* **produce,** *-ic* **condition of]**

pathophysiology
(path-o-fiz-ee-OL-o-jee)
[*patho-* **disease,** *-physio-* **nature (function),** *-o-* **combining form,** *-log-* **words (study of),** *-y* **activity]**

prion
(PREE-ahn)
[condensed from proteinaceous infectious particle]

protozoan
(pro-toe-ZO-an)
[*proto-* **first,** *-zoan* **animal];** *pl.,* **protozoa**

remission
(ree-MISH-un)
[*re-* **back or again,** *-miss-* **to send,** *-sion* **condition of]**

sign
(syn)
[*sign* **mark]**

somatotype
(so-MAT-o-type)
[*soma-* **body,** *-type* **kind]**

symptom
(SIMP-tum)
[*sym-* **together,** *-tom* **fall]**

syndrome
(SIN-drome)
[*syn-* **together,** *-drome* **running or (race)course]**

virus
(VYE-rus)
[*virus* **poison]**

CASE study

Seamus is just starting his first year in college, and he's been thinking about going into the medical field—maybe nursing. To find out what nursing is really like, Seamus signed up for a "shadow a nurse" day at the local hospital. He's scheduled to follow a nurse in the emergency department to see what the job involves.

Everything is rather boring and quiet for the first hour; then suddenly an ambulance pulls into the bay and a paramedic rushes a patient in on a stretcher. The paramedic gives a quick patient report, and Seamus hears, "Stab wound to the right upper quadrant. He has additional cuts to his brachial region and a large contusion on his right lower extremity just proximal to the knee."

Seamus feels like he's listening to a foreign language! Can you help him interpret the paramedic's report?

1. Where was the patient stabbed?
   a. In his thoracic cavity
   b. In his abdominopelvic cavity
   c. In his pericardial cavity
   d. In his pleural cavity
2. What organ is most likely to have been damaged by the attack?
   a. His heart
   b. His lungs
   c. His liver
   d. His spleen
3. Where is the bruise (contusion) on the patient's body?
   a. Near his groin
   b. Just above his ankle
   c. His lower thigh
   d. Behind his knee
4. Where is the patient's brachial region?
   a. His femoral region
   b. His crural region
   c. His humoral region
   d. His popliteal region

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*



CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

SCIENCE AND SOCIETY

A. Science involves logical inquiry based on experimentation (Figure 1-1)
   1. Hypothesis—idea or principle to be tested in experiments
   2. Experiment—series of tests of a hypothesis; a controlled experiment eliminates biases or outside influences

3. Theory—a hypothesis that has been proved by experiments to have a high degree of confidence
4. Law—a theory that has an unusually high level of confidence

B. The process of science is active and changing as new experiments add new knowledge
C. Science is affected by culture and culture is affected by society

ANATOMY AND PHYSIOLOGY

A. Anatomy and physiology are branches of biology concerned with the form and functions of the body
B. Anatomy—science of the structure of an organism and the relationship of its parts
   1. Gross anatomy—study of the body and its parts relying only on the naked eye as a tool for observation (Figure 1-2)
   2. Microscopic anatomy—study of body parts with a microscope
      a. Cytology—study of cells
      b. Histology—study of tissues
   3. Developmental anatomy—study of human growth and development
   4. Pathological anatomy—study of diseased body structures
   5. Systemic anatomy—study of the body by systems
C. Physiology—science of the functions of organisms; subdivisions named according to:
   1. Organism involved—human or plant physiology
   2. Organizational level—molecular or cellular physiology
   3. Systemic function—respiratory physiology, neurophysiology, or cardiovascular physiology

LANGUAGE OF SCIENCE AND MEDICINE

A. Scientific terms are often based on Latin or Greek word parts
B. A terminology tool is provided in the pull-out section near the front of this textbook
C. *Terminologia Anatomica (TA)* and *Terminologia Histologica (TH)*
   1. Official lists of anatomical terms (*TA*, gross anatomy; *TH*, microscopic anatomy)
   2. Terms listed in Latin, English, and by number
   3. Avoids use of eponyms (terms based on a person's name)
D. Physiology terms do not have an official list but follow the same principles as *TA* and *TH*

CHARACTERISTICS OF LIFE

A. A single criterion may be adequate to describe life, for example:
   1. Autopoiesis—living organisms are self-organized and self-maintaining
   2. Cell theory—if it is made of one or more cells, it is alive
B. Characteristics of life considered most important in humans are summarized in Table 1-1
C. Metabolism—sum total of all physical and chemical reactions occurring in the living body

LEVELS OF ORGANIZATION (FIGURE 1-3)

A. Chemical level—basis for life
   1. Organization of chemical structures separates living material from nonliving material
   2. Organization of atoms, molecules, and macromolecules results in living matter—a gel called *cytoplasm*
B. Organelle level
   1. Chemical structures organized to form organelles that perform individual functions
   2. It is the functions of the organelles that allow the cell to live
   3. Dozens of organelles have been identified, including:
      a. Mitochondria
      b. Golgi apparatus
      c. Endoplasmic reticulum
C. Cellular level
   1. Cells—smallest and most numerous units that possess and exhibit characteristics of life
   2. Each cell has a nucleus surrounded by cytoplasm within a limiting membrane
   3. Cells differentiate to perform unique functions
D. Tissue level
   1. Tissue—an organization of similar cells specialized to perform a certain function
   2. Tissue cells are surrounded by nonliving matrix
   3. Four major tissue types
      a. Epithelial tissue
      b. Connective tissue
      c. Muscle tissue
      d. Nervous tissue
E. Organ level
   1. Organ—organization of several different kinds of tissues to perform a special function
   2. Organs represent discrete and functionally complex operational units
   3. Each organ has a unique size, shape, appearance, and placement in the body
F. System level
   1. Systems—most complex organizational units of the body
   2. System level involves varying numbers and kinds of organs arranged to perform complex functions (Table 1-2):
      a. Support and movement
      b. Communication, control, and integration
      c. Transportation and defense
      d. Respiration, nutrition, and excretion
      e. Reproduction and development
G. Organism level
   1. The living human organism is greater than the sum of its parts
   2. All of the components interact to allow the human to survive and flourish

ANATOMICAL POSITION (FIGURE 1-4)

A. Reference position
B. Body erect with arms at sides and palms forward

C. Head and feet pointing forward
D. *Bilateral symmetry*—a term meaning that right and left sides of the body are mirror images
   1. Bilateral symmetry confers balanced proportions
   2. Remarkable correspondence of size and shape between body parts on opposite sides of the body
   3. Ipsilateral structures are on the same side of the body in anatomical position
   4. Contralateral structures are on opposite sides of the body in anatomical position

BODY CAVITIES (FIGURE 1-5; TABLE 1-3)

A. Ventral body cavity
   1. Thoracic cavity
      a. Right and left pleural cavities
      b. Mediastinum
   2. Abdominopelvic cavity
      a. Abdominal cavity
      b. Pelvic cavity
B. Dorsal body cavity
   1. Cranial cavity
   2. Spinal cavity

BODY REGIONS (FIGURE 1-6; TABLE 1-4)

A. Axial subdivision
   1. Head
   2. Neck
   3. Torso, or trunk, and its subdivisions
B. Appendicular subdivision
   1. Upper extremity and subdivisions
   2. Lower extremity and subdivisions
C. Abdominopelvic regions (Figure 1-7)
   1. Right hypochondriac region
   2. Epigastric region
   3. Left hypochondriac region
   4. Right lumbar region
   5. Umbilical region
   6. Left lumbar region
   7. Right iliac (inguinal) region
   8. Hypogastric region
   9. Left iliac (inguinal) region
D. Abdominal quadrants (Figure 1-8)
   1. Right upper quadrant
   2. Left upper quadrant
   3. Right lower quadrant
   4. Left lower quadrant

TERMS USED IN DESCRIBING BODY STRUCTURE

A. Directional terms (Figure 1-9)
   1. Superior and inferior
   2. Anterior (ventral) and posterior (dorsal)
   3. Medial and lateral
   4. Proximal and distal
   5. Superficial and deep
B. Terms related to organs
   1. Lumen (luminal)
   2. Central and peripheral
   3. Medullary (medulla) and cortical (cortex)
   4. Apical (apex) and basal (base)
C. Many directional terms are listed inside the front cover of the book

BODY PLANES AND SECTIONS (FIGURES 1-9 AND 1-10)

A. Planes are lines of orientation along which cuts or sections can be made to divide the body, or a body part, into smaller pieces
B. There are three major planes, which lie at right angles to each other:
   1. Sagittal plane runs front to back so that sections through this plane divide the body (or body part) into right and left sides
      a. If section divides the body (or part) into symmetrical right and left halves, the plane is called *midsagittal* or *median sagittal*
   2. Frontal (coronal) plane runs lengthwise (side to side) and divides the body (or part) into anterior and posterior portions
   3. Transverse (horizontal) plane is a "crosswise" plane and it divides the body (or part) into upper and lower parts

INTERACTION OF STRUCTURE AND FUNCTION

A. Complementarity of structure and function is an important and unifying concept in the study of anatomy and physiology
B. Anatomical structures are adapted to perform specific functions because of their unique size, shape, form, or body location
C. Understanding the interaction of structure and function assists in the integration of otherwise isolated factual information

HOMEOSTASIS (FIGURE 1-13)

A. Term *homeostasis* coined by American physiologist Walter B. Cannon
B. *Homeostasis* is used to describe the relatively constant states maintained by the body—internal environment around body cells remains constant
C. Body adjusts important variables from a normal "set point" in an acceptable or normal range
D. Examples of homeostasis
   1. Temperature regulation
   2. Regulation of blood carbon dioxide level
   3. Regulation of blood glucose level

HOMEOSTATIC CONTROL MECHANISMS

A. Devices for maintaining or restoring homeostasis by self-regulation through feedback control loops
B. Basic components of control mechanisms

1. Sensor mechanism—specific sensors detect and react to any changes from normal
2. Integrating, or control, center—information is analyzed and integrated, and then if needed, a specific action is initiated
3. Effector mechanism—effectors directly influence controlled physiological variables
4. Feedback—process of information about a variable constantly flowing back from the sensor to the integrator

C. Negative feedback control systems
1. Are inhibitory
2. Stabilize physiological variables
3. Produce an action that is opposite to the change that activated the system
4. Are responsible for maintaining homeostasis
5. Are much more common than positive feedback control systems

D. Positive feedback control systems
1. Are stimulatory
2. Amplify or reinforce the change that is occurring
3. Tend to produce destabilizing effects and disrupt homeostasis
4. Bring specific body functions to swift completion

E. Feed-forward control systems occur when information flows ahead to another process or feedback loop to trigger a change in anticipation of an event that will follow

F. Levels of control (Figure 1-14)
1. Intracellular control
   a. Regulation within cells
   b. Genes or enzymes can regulate cell processes
2. Intrinsic control (autoregulation)
   a. Regulation within tissues or organs
   b. May involve chemical signals (e.g., prostaglandins)
   c. May involve other "built in" mechanisms
3. Extrinsic control
   a. Regulation from organ to organ
   b. May involve nerve signals
   c. May involve endocrine signals (hormones)

CYCLE OF LIFE: LIFE SPAN CONSIDERATIONS

A. Structure and function of body undergo changes over the early years (developmental processes) and late years (aging processes)

B. Infancy and old age are periods when the body functions least well

C. Young adulthood is period of greatest homeostatic efficiency

D. Atrophy—term to describe the wasting effects of advancing age

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Define the terms *anatomy* and *physiology.*
2. List and briefly describe the levels of organization that relate the structure of an organism to its function. Give examples characteristic of each level.
3. Give examples of each system level of organization in the body and briefly discuss the function of each.
4. What is meant by the term *anatomical position?* How do the specific anatomical terms of position or direction relate to this body orientation?
5. What is *bilateral symmetry?* What terms are used to identify placement of one body part with respect to another on the same or opposite sides of the body?
6. What does the term *somatotype* mean? Name the three major somatotype categories and briefly describe the general characteristics of each.
7. Define briefly each of the following terms: anterior, distal, sagittal plane, medial, dorsal, coronal plane, organ, parietal peritoneum, superior, tissue.
8. Locate the mediastinum.
9. What does the term *homeostasis* mean? Illustrate some generalizations about body function using homeostatic mechanisms as examples.
10. Define *homeostatic control mechanisms* and *feedback control loops.*
11. Identify the four basic components of a control loop.
12. Discuss in general terms the *principle of complementarity of structure and function.*
13. Briefly describe medical imaging techniques that allow physicians to examine internal structures in a noninvasive manner.
14. List the major types of risk factors that may increase a person's chance of a specific disease developing.

CRITICAL THINKING QUESTIONS

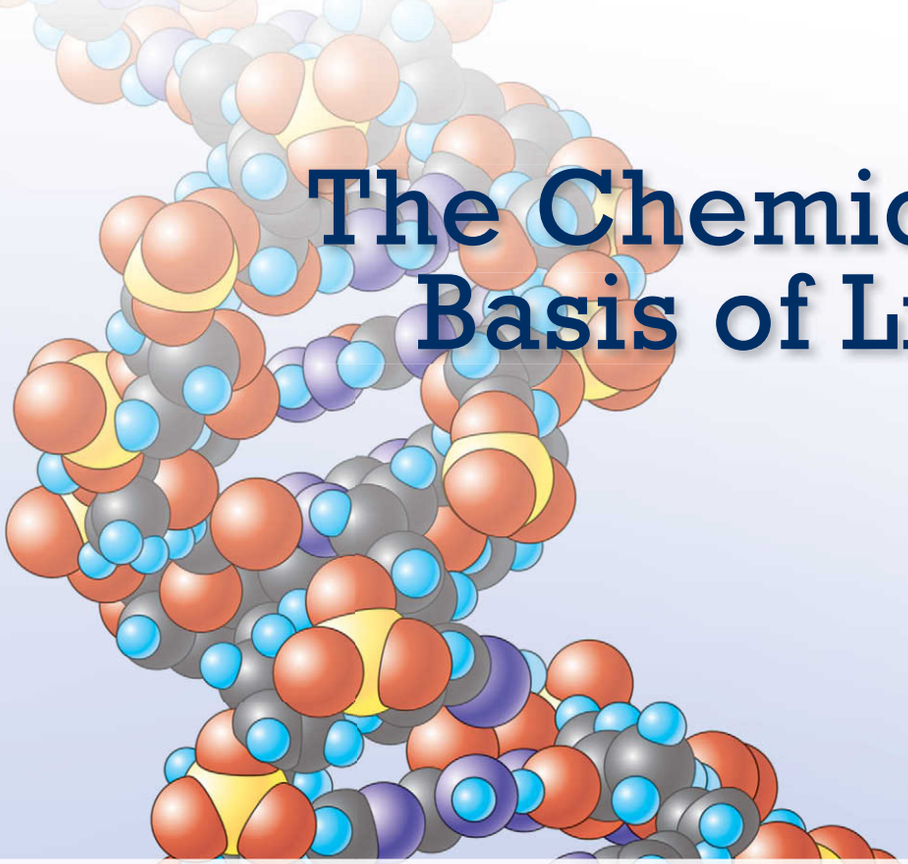


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Each characteristic of life is related to body metabolism. Explain how digestion, circulation, and growth are metabolically related.
2. What diseases may result in a patient with an endomorph somatotype and a waist-to-hip ratio of 1:2?
3. An x-ray technician has been asked to take x rays of the entire large intestine (colon), including the appendix. Which of the nine abdominopelvic regions must be included in the x ray?
4. Body cavities can be subdivided into smaller and smaller sections. Identify, from largest to smallest, the cavities in which the urinary bladder can be placed.
5. When driving in traffic, it is important to stay in your own lane. If you see that you are drifting out of your lane, your brain tells your arms and hands to move in such a way that you get back in your lane. Identify the three components of a control loop in this example. Explain why this would be a negative feedback loop.

The Chemical Basis of Life

2



CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

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LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

acid
(ASS-id)
[*acid* **sour**]

adenosine triphosphate (ATP)
(ah-DEN-o-seen try-FOS-fate)
[blend of *adenine* and *ribose*, *tri-* **three**, *-phosph-* **phosphorus**, *-ate* **oxygen**]

amino acid
(ah-MEE-no ASS-id)
[*amino* **NH2**, *acid* **sour**]

anabolism
(ah-NAB-o-lizem)
[*anabol-* **build up**, *-ism* **action**]

atom
(AT-om)
[*atom* **indivisible**]

base
(BAYS)
[*bas* **base**]

buffer
(BUFF-er)
[*buffe-* **cushion**, *-er* **actor**]

carbohydrate
(kar-bo-HYE-drate)
[*carbo-* **carbon**, *-hydr-* **hydrogen**, *-ate* **oxygen**]

catabolism
(kah-TAB-o-lizem)
[*catabol-* **throw down**, *-ism* **action**]

compound
(KOM-pownd)
[*compoun-* **put together**]

covalent bond
(ko-VAYL-ent bond)
[*co-* **with**, *-valen-* **power**, *bond* **band**]

energy
[*en-* **in**, *-erg-* **work**, *-y* **state**]

continued on p. 60

Anatomy and physiology are subdivisions of biology—the study of life. To best understand the characteristics of life, what living matter is, how it is organized, and what it can do, we must appreciate and understand certain basic principles of chemistry that apply to the life process.

Life itself depends on proper levels and proportions of chemical substances in the cytoplasm of cells. The various structural levels of organization described in Chapter 1 are ultimately based on the existence and interrelationships of atoms and molecules. Chemistry, like biology, is a very broad scientific discipline. It deals with the structure, arrangement, and composition of substances and the reactions they undergo. Just as biology may be subdivided into many sub-disciplines or branches, like anatomy and physiology, chemistry may also be divided into focused areas. Biochemistry is the field of chemistry that deals with living organisms and life processes. It deals directly with the chemical composition of living matter and the processes that underlie life activities such as growth, muscle contraction, and transmission of nervous impulses.

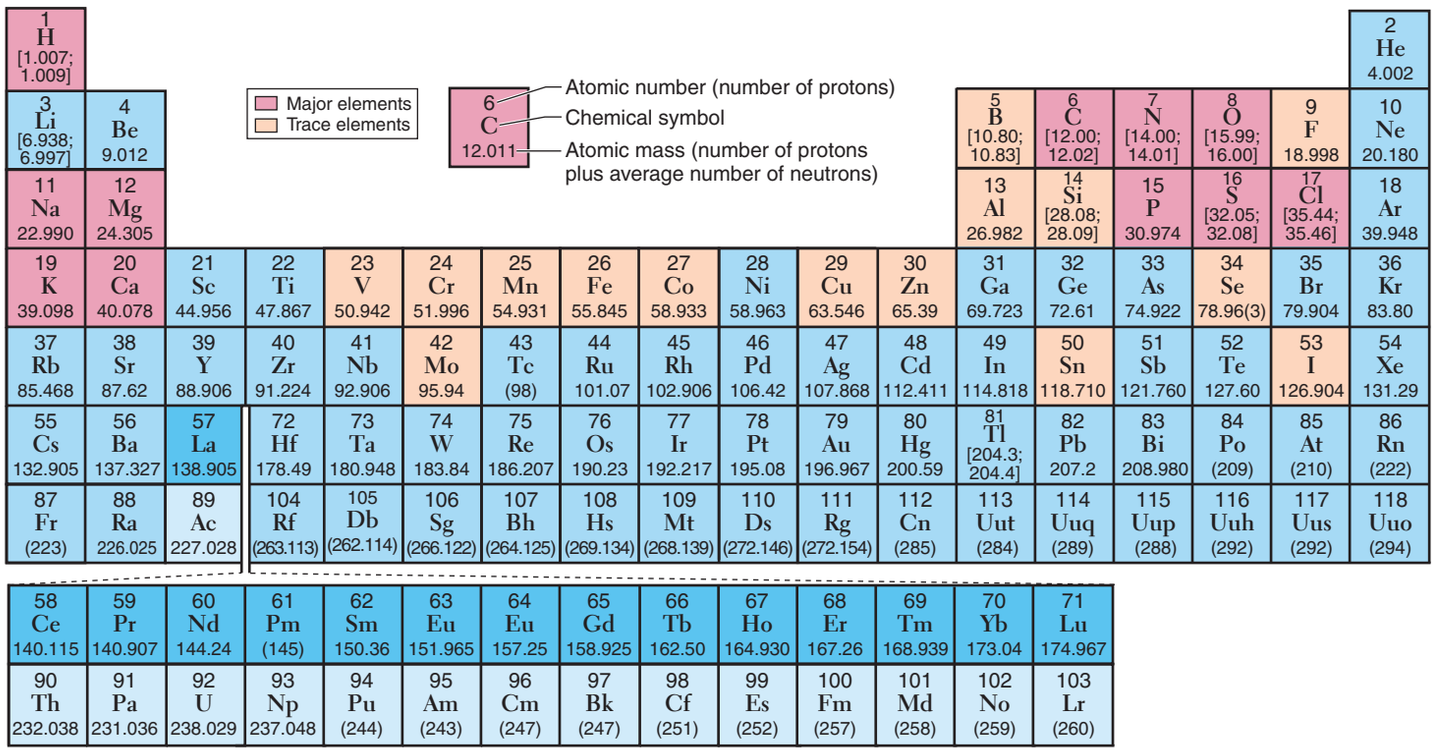
BASIC CHEMISTRY

Elements and Compounds

Chemists use the term *matter* to describe in a general sense all of the materials or substances around us. Anything that has mass and occupies space is matter.

Substances are either **elements** or **compounds.** An element is said to be "pure" in the sense that it cannot be broken down or decomposed into two or more different substances. Carbon and oxygen are good examples of elements. In most living material, elements do not exist alone in their pure state. Instead, two or more elements are joined to form chemical combinations called *compounds.* Compounds can be broken down or decomposed into the elements that are contained within them. Water is a compound (H_2O). It can be broken down into atoms of hydrogen and atoms of oxygen in a 2:1 ratio.

Other examples of elements include phosphorus, copper, and nitrogen (Figure 2-1). For convenience in writing chemical formulas and in other types of notation, chemists assign a symbol to each element, usually the first letter or two of the English or Latin name of the element: P, phosphorus; Cu, copper (Latin *cuprum*); N, nitrogen (see Figure 2-1). Note in Table 2-1 that 26 elements



1 H [1.007; 1.009]																	2 He 4.002
3 Li [6.938; 6.997]	4 Be 9.012											5 B [10.80; 10.83]	6 C [12.00; 12.02]	7 N [14.00; 14.01]	8 O [15.99; 16.00]	9 F 18.998	10 Ne 20.180
11 Na 22.990	12 Mg 24.305											13 Al 26.982	14 Si [28.08; 28.09]	15 P 30.974	16 S [32.05; 32.08]	17 Cl [35.44; 35.46]	18 Ar 39.948
19 K 39.098	20 Ca 40.078	21 Sc 44.956	22 Ti 47.867	23 V 50.942	24 Cr 51.996	25 Mn 54.931	26 Fe 55.845	27 Co 58.933	28 Ni 58.963	29 Cu 63.546	30 Zn 65.39	31 Ga 69.723	32 Ge 72.61	33 As 74.922	34 Se 78.96(3)	35 Br 79.904	36 Kr 83.80
37 Rb 85.468	38 Sr 87.62	39 Y 88.906	40 Zr 91.224	41 Nb 92.906	42 Mo 95.94	43 Tc (98)	44 Ru 101.07	45 Rh 102.906	46 Pd 106.42	47 Ag 107.868	48 Cd 112.411	49 In 114.818	50 Sn 118.710	51 Sb 121.760	52 Te 127.60	53 I 126.904	54 Xe 131.29
55 Cs 132.905	56 Ba 137.327	57 La 138.905	72 Hf 178.49	73 Ta 180.948	74 W 183.84	75 Re 186.207	76 Os 190.23	77 Ir 192.217	78 Pt 195.08	79 Au 196.967	80 Hg 200.59	81 Tl [204.3; 204.4]	82 Pb 207.2	83 Bi 208.980	84 Po (209)	85 At (210)	86 Rn (222)
87 Fr (223)	88 Ra 226.025	89 Ac 227.028	104 Rf (263.113)	105 Db (262.114)	106 Sg (266.122)	107 Bh (264.125)	108 Hs (269.134)	109 Mt (268.139)	110 Ds (272.146)	111 Rg (272.154)	112 Cn (285)	113 Uut (284)	114 Uuq (289)	115 Uup (288)	116 Uuh (292)	117 Uus (292)	118 Uuo (294)

58 Ce 140.115	59 Pr 140.907	60 Nd 144.24	61 Pm (145)	62 Sm 150.36	63 Eu 151.965	64 Eu 157.25	65 Gd 158.925	66 Tb 162.50	67 Ho 164.930	68 Er 167.26	69 Tm 168.939	70 Yb 173.04	71 Lu 174.967
90 Th 232.038	91 Pa 231.036	92 U 238.029	93 Np 237.048	94 Pu (244)	95 Am (243)	96 Cm (247)	97 Bk (247)	98 Cf (251)	99 Es (252)	100 Fm (257)	101 Md (258)	102 No (259)	103 Lr (260)

FIGURE 2-1

Periodic table of elements. The major elements found in the body are highlighted in pink. The trace elements, found in very tiny quantities in the body, are highlighted in orange. (Atomic mass numbers in brackets show the natural range of isotopes; those in parentheses are uncertain or theoretical.)

TABLE 2-1 Elements in the Human Body

ELEMENT	SYMBOL	HUMAN BODY WEIGHT (%)	IMPORTANCE OR FUNCTION
Major Elements			
Oxygen	O	65.0	Necessary for cellular respiration; component of water
Carbon	C	18.5	Backbone of organic molecules
Hydrogen	H	9.5	Component of water and most organic molecules; necessary for energy transfer and respiration
Nitrogen	N	3.3	Component of all proteins and nucleic acids
Calcium	Ca	1.5	Component of bones and teeth; triggers muscle contraction
Phosphorus	P	1.0	Principal component in the backbone of nucleic acids; important in energy transfer
Potassium	K	0.4	Principal positive ion within cells; important in nerve function
Sulfur	S	0.3	Component of many energy-transferring enzymes
Sodium	Na	0.2	Important positive ion surrounding cells
Chlorine	Cl	0.2	Important negative ion surrounding cells
Magnesium	Mg	0.1	Component of many energy-transferring enzymes
Trace Elements			
Silicone	Si	<0.1	Uncertain
Aluminum	Al	<0.1	Uncertain
Iron	Fe	<0.1	Critical component of hemoglobin in the blood
Manganese	Mn	<0.1	Component of many energy-transferring enzymes
Fluorine	F	<0.1	Hardens crystals that form teeth and bones
Vanadium	V	<0.1	Uncertain
Chromium	Cr	<0.1	Alters insulin (hormone) effects which regulates carbohydrate lipid and protein metabolism
Copper	Cu	<0.1	Key component of many enzymes
Boron	B	<0.1	May strengthen cell membranes; plays a role in brain and bone development
Cobalt	Co	<0.1	Component of vitamin B_{12}
Zinc	Zn	<0.1	Key component of some enzymes
Selenium	Se	<0.1	Component of an antioxidant enzyme
Molybdenum	Mo	<0.1	Key component of some enzymes
Tin	Sn	<0.1	Uncertain
Iodine	I	<0.1	Component of thyroid hormone

are listed as being present in the human body. Although all are important, 11 are called *major elements*. Four of these major elements—carbon, oxygen, hydrogen, and nitrogen—make up about 96% of the material in the human body (Figure 2-2). The 15 remaining elements are present in amounts that are less than 0.1% of body weight and are called *trace elements*. The unique "aliveness" of a living organism does not depend on a single element or mixture of elements but on the complexity, organization, and interrelationships of all elements required for life.

| QUICK CHECK |

1. What is biochemistry?
2. What is the difference between an element and a compound?
3. What elements make up 96% of the material in the human body?

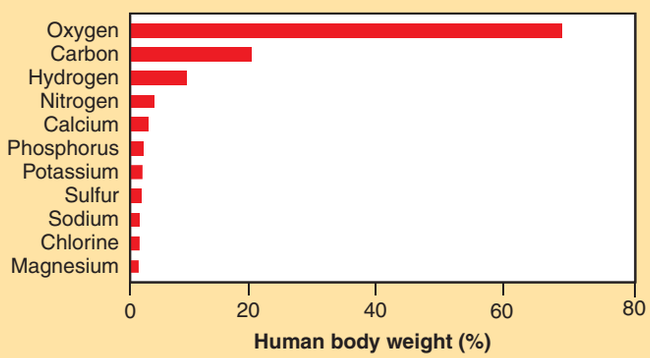


FIGURE 2-2

Major elements of the body. These elements are found in great quantity in the body (see Figure 2-1). The graph shows the relative abundance of each in the body. Notice that oxygen (O), carbon (C), hydrogen (H), and nitrogen (N) predominate.

Atoms

The most important of all chemical theories was advanced in 1805 by the English chemist John Dalton. He proposed the concept that matter is composed of **atoms** (from the Greek *atomos*, "indivisible"). His idea was revolutionary and yet simple—that all matter, regardless of the form it may assume (liquid, gas, or solid), is composed of units he called *atoms*.

Dalton conceived of atoms as solid, indivisible particles, and for about 100 years this was believed to be true. We now know that atoms are divisible into even smaller or *subatomic* particles, some of which exist in a "cloud" surrounding a dense central core called a *nucleus*. More than 100 million atoms of even very dense and heavy substances, if lined up, would measure barely an inch and would consist mostly of empty space! Our knowledge about the number and nature of subatomic particles and the central nucleus around which they move continues to grow as a result of ongoing research.

ATOMIC STRUCTURE

Atoms contain several different kinds of smaller or subatomic particles that are found in either a central nucleus or its surrounding "electron cloud" or "field." Figure 2-3, A, shows an atomic model of carbon illustrating the most important types of subatomic particles:

- Protons (p^+)
- Neutrons (n^0)
- Electrons (e^-)

Note that the carbon atom in Figure 2-3 has a central corelike *nucleus*. It is located deep inside the atom and is made up of six positively charged *protons (p)* and six uncharged *neutrons (n)*. Note also that the nucleus is surrounded by a cloud or field of six negatively charged *electrons (e)*. Because protons are positively charged and neutrons are neutral, the nucleus of an atom bears a positive electrical charge equal to the number of protons that are present in it. Electrons move around the atom's nucleus in what can be represented as an electron cloud or field (Figure 2-3, B). The number of negatively charged electrons moving around an atom's nucleus equals the number of positively charged protons in the nucleus. The opposite charges therefore cancel or neutralize each other, which means atoms are electrically neutral particles.

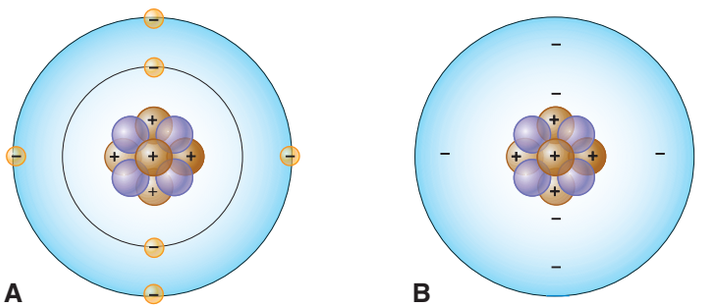


FIGURE 2-3

Models of the atom. The nucleus—protons (+) and neutrons—is at the core. Electrons inhabit outer regions called electron *shells* or energy levels **(A)** or probability distributions called electron clouds **(B)**. This drawing depicts a carbon atom. All carbon atoms (and *only* carbon atoms) have six protons. (Not all of the protons in the nucleus are visible in this illustration.)

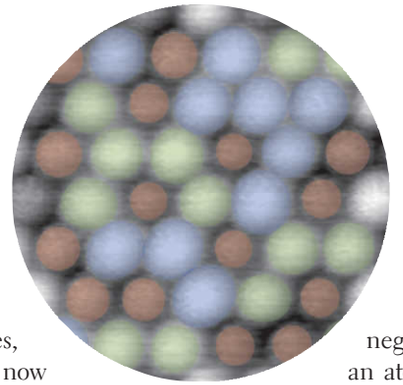


FIGURE 2-4

Atoms. The cloudlike structures seen here were recorded using an atomic force microscope (AFM) and represent the outer surfaces of individual atoms along the flat surface of a crystal. Different colors represent different kinds of atoms.

The so-called electron clouds are really just areas where the electrons are most likely to be found moving about rapidly. However, they can sometimes be visualized with a special form of microscope, as you can see in Figure 2-4.

ATOMIC NUMBER AND MASS NUMBER

Elements differ in their chemical and physical properties because of differences in the number of protons in their atomic nuclei. The number of protons in an atom's nucleus, called its *atomic number*, is therefore critically important—it identifies the kind of element it is.

Look again at the elements important in living organisms listed in Table 2-1. Each element is identified by its symbol and atomic number. Hydrogen, for example, has an atomic number of 1; this means that all hydrogen atoms—and *only* hydrogen atoms—have one proton in their nucleus. All carbon atoms—and *only* carbon atoms—contain six protons and have an atomic number of 6. All oxygen atoms, and only oxygen atoms, have eight protons and an atomic number of 8. In short, each element is identified by its own unique number of protons, that is, by its own unique atomic number. If two atoms contain a different number of protons, they are different elements.

There are 92 elements that occur naturally on earth. Because each element is characterized by the number of protons in its atoms (atomic number), there are atoms that contain from 1 to 92 protons. Additional elements have been discovered as a result of sophisticated research in the area of particle physics.

The term *mass number* refers to the mass of a single atom. The mass number is sometimes called the *atomic mass*. It equals the number of protons plus the number of neutrons in the atom's nucleus. The weight of electrons is, for practical purposes, negligible. Because protons and neutrons weigh almost exactly the same, the equation for determining mass number is as follows:

$$\text{Mass number} = (p + n)$$

The largest naturally occurring atom is uranium. It has a mass number of 238, with a nucleus containing 92 protons and 146 neutrons. In contrast, hydrogen, which has only one proton and no neutrons in its nucleus, has a mass number of 1.

ENERGY LEVELS

The total number of electrons in an atom equals the number of protons in its nucleus (see Figure 2-3). These electrons are known to exist in regions surrounding the atom's nucleus.

No single model of the atom sufficiently explains all we know about atomic structure. However, two simple models of atoms may be useful here to begin our discussion.

The cloud model suggests that any one electron cannot be exactly located at a specific point at any particular time. This concept is called a *probability distribution* and refers to the probability of finding an electron at any specific location outside the nucleus. Earlier models based on the work of a Danish physicist, Niels Bohr, who won the 1922 Nobel Prize in Physics for his groundbreaking contributions, suggested that electrons moved in regular patterns around the nucleus much like the planets in our solar system move around the sun. A simplified version of the Bohr model of the atom (see Figure 2-3, A) is perhaps most useful in visualizing the structure of atoms as they enter into chemical reactions.

In the Bohr model, the electrons are shown in shells or concentric circles. The different shells show the relative distances of the electrons from the nucleus. The electrons surrounding the atom's nucleus are seen in this model as existing in simple rings or shells. Each ring represents a different **energy level,** and each can hold only a certain maximum number of electrons (Figure 2-5). The number and arrangement of electrons orbiting in an atom's energy levels are important because they determine whether the atom is chemically reactive.

In chemical reactions between atoms, it is the electrons in the outermost energy level that participate in the formation of chemical bonds. In each energy level, electrons tend to group in pairs. As a rule, an atom can be listed as chemically stable and unable to react with another atom if its outermost energy level has four pairs of electrons, or a total of eight. Such an atom is said to have a stable electron configuration. The pairing of electrons is important. If the outer energy level contains single, unpaired electrons, the atom will be chemically reactive. Atoms with fewer than eight electrons in the outer energy level will attempt to lose, gain, or share electrons with other atoms to achieve stability. This tendency is called the **octet rule.**

Consider an atom of oxygen, which has a total of six electrons in its outer energy level. As you can see in Figure 2-6, it has two unpaired electrons so it is two electrons short of satisfying the octet rule. Oxygen is likely to enter into chemical reactions to gain or share electrons with other atoms. By doing so, the oxygen atom will fill in its outer energy level and thus satisfy the octet rule.

The octet rule holds true except for atoms that are limited to a single energy level that is filled by a maximum of two electrons. For example, hydrogen has but one electron in its single energy level. It therefore has an incomplete energy level with an unpaired electron. The result is a highly reactive tendency of hydrogen to enter into many chemical reactions. Helium, however, has two electrons in its single energy level. Because this is the maximum number for this energy level, no chemical activity is possible, and no naturally occurring compound containing helium exists. Helium is an *inert*, or stable, element.

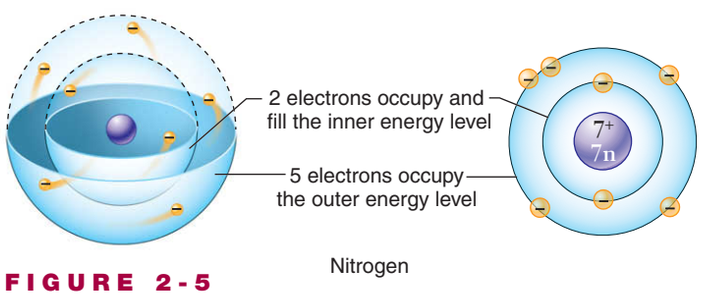


FIGURE 2-5

Energy levels (electron shells) surrounding the nucleus of an atom. Each concentric shell represents a different electron energy level.

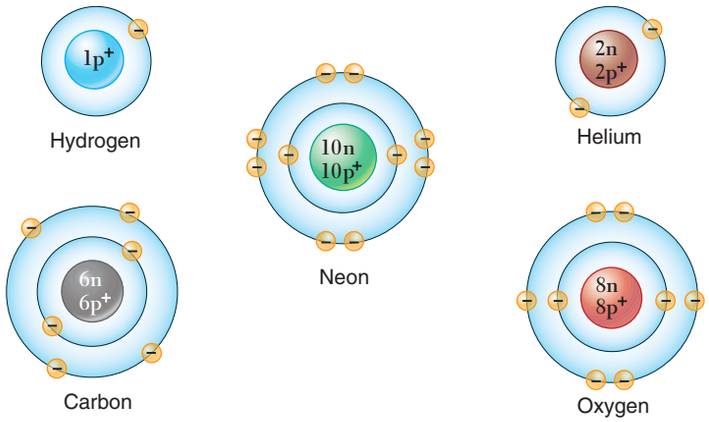


FIGURE 2-6

Energy levels (shells) of five common elements. All atoms are balanced with respect to positive and negative charges. In atoms with a single energy level, two electrons are required for stability. Hydrogen with its single electron is reactive, whereas helium with its full energy level is not. In atoms with more than one energy level, eight electrons in the outermost energy level are required for stability. Neon is stable because its outer energy level has eight electrons. Oxygen and carbon, with six and four electrons, respectively, in their outer energy levels, are chemically reactive.

The atoms shown in Figure 2-6 illustrate several of the most important facts related to energy levels. Note that even in the hydrogen atom with its very basic structure, positive and negative charges balance. Hydrogen, carbon, and oxygen will react chemically because they do not satisfy the octet rule.

| QUICK CHECK |

4. List and define the three most important types of subatomic particles.
5. How are the atomic number and atomic weight of an atom defined?
6. What is an energy level?
7. Explain what is meant by the *octet rule.*

ISOTOPES

All atoms of the same element contain the same number of protons but do not necessarily contain the same number of neutrons. **Isotopes** of an element contain the same number of protons, but different numbers of neutrons.

Isotopes have the same basic chemical properties as any other atom of the same element, and they also have the same atomic number. However, because they have a different number of neutrons, they differ in mass number. Usually a hydrogen atom has only one proton and no neutrons (atomic number, 1; mass number, 1). Figure 2-7 illustrates this most common type of hydrogen and two of its isotopes. Note that the isotope of hydrogen called

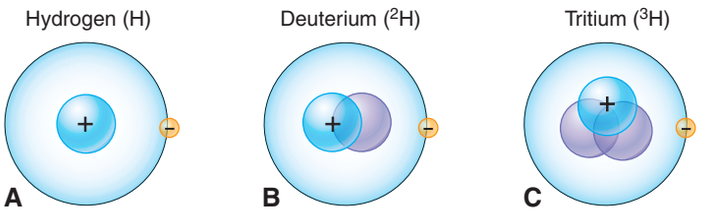


FIGURE 2-7

Structure of hydrogen and two of its isotopes. A, The most common form of hydrogen. **B,** An isotope of hydrogen called *deuterium (^2H).* **C,** The hydrogen isotope *tritium (^3H).* Note that isotopes of an element differ only in the number of its neutrons.

deuterium (^2H) has one proton and one neutron (mass number, 2). *Tritium (^3H)* is the isotope of hydrogen that has one proton and two neutrons (mass number, 3).

The term *atomic weight* refers to the average mass number for a particular element based on the typical proportion of different isotopes found in nature. Atomic weights are shown in the periodic table of elements illustrated in Figure 2-1, below each chemical symbol. Notice that the atomic weights for some elements, such as hydrogen and carbon, are listed as ranges instead of averages. For elements with isotope proportions that vary widely in nature, chemists find ranges more useful than averages.

The atomic nuclei of more than 99% of all carbon atoms in nature have six protons and six neutrons (atomic number, 6; mass number, 12). An important isotope of carbon has seven neutrons instead of six and is called *carbon-13 (^{13}C)*. Carbon-13 makes up about 1% of the world's carbon atoms. The presence of carbon-13 in human tissues is useful in molecular studies of metabolic processes in the body. Another important carbon isotope has eight neutrons instead of six; it is called *carbon-14 (^{14}C)*. Carbon-14 is an example of a special type of isotope that is unstable and undergoes nuclear breakdown—it is designated as a *radioactive isotope*, or **radioisotope.** During breakdown, radioactive isotopes emit nuclear particles and radiation—a process called *decay.*

| A&P CONNECT |

Radioactivity is the emission of radiation from an atom's nucleus. Alpha particles, beta particles, and gamma rays are the three kinds of radiation.

Alpha particles are relatively heavy particles consisting of two protons plus two neutrons. They shoot out of a radioactive atom's nucleus at a reported speed of 18,000 miles per second. *Beta particles* are electrons formed in a radioactive atom's nucleus by one of its neutrons breaking down into a proton and an electron. The proton remains behind in the nucleus, and the electron is ejected from it as a beta particle. Beta particles, because they are electrons, are much smaller than alpha particles, which consist of two protons and two neutrons. In addition, beta particles travel at a much greater speed than alpha particles do. *Gamma rays* are electromagnetic radiation, a form of light energy.

Radioactivity differs from chemical activity because it can change the number of protons in an atom, thus changing the atom from one element to another!

Check out ***Radioactivity*** online at ***A&P Connect*** to find out how radioactivity affects the human body.

Attractions Between Atoms—Chemical Bonds

Interactions between two or more atoms occur largely as a result of activity between electrons in their outermost energy level. The result, called a *chemical reaction*, most often involves unpaired electrons.

Ultimately, in atoms with fewer or more than eight electrons in the outer energy level, reactions will occur that result in the loss, gain, or sharing of one atom's unpaired electrons with those of another atom to satisfy the octet rule for both atoms. The result of such reactions between atoms is the formation of larger chemical structures such as *crystals* and **molecules.** For example, two atoms of oxygen can combine with one carbon atom to form molecular carbon dioxide, or CO_2. If atoms of more than one element combine, the result, as defined earlier, is a compound. In other words, oxygen exists as a molecule (O_2) and is an element. Water exists as a molecule (H_2O) and is a compound. Reactions that hold atoms together do so by the formation of *chemical bonds.* There are two types of chemical bonds that unite atoms into larger structures: ionic (or electrovalent) bonds and covalent bonds.

IONIC BONDS

A chemical bond formed by the transfer of electrons from one atom to another is called an *ionic*, or *electrovalent, bond.* Such a bond occurs as a result of the attraction between atoms that have become electrically charged by the loss or gain of electrons. When dissolved in water (Figure 2-8), such atoms are separate into **ions.** It is important to remember that ions can be positively or negatively charged and that ions with opposite charges are attracted to each other.

Note in Figure 2-8, A, that in the outer energy level of the sodium atom there is a single unpaired electron. If this electron were "lost," the outer ring would be stable because it would have a full outer octet (four pairs of electrons). The loss of the electron would result in the formation of a sodium ion (Na^+) with a positive charge. This is because there is now one more proton (+) than electron (–).

The chlorine atom, in contrast, has one unpaired electron plus three paired electrons, or a total of seven electrons, in its outer energy level. By the addition of another electron, chlorine would satisfy the octet rule—its outer energy level would have a full complement of four paired electrons. The addition of another electron would result in the formation of a negatively charged chloride ion (Cl^-).

Sodium transfers or donates its one unpaired electron to chlorine and becomes a positively charged sodium ion (Na^+). Chlorine accepts the electron from sodium and pairs it with its one unpaired electron, thereby filling its outer energy level with the maximum of four electron pairs and becoming a negatively charged chloride ion (Cl^-). The positively charged sodium ion (Na^+) is attracted to the negatively charged chloride ion (Cl^-), and the formation of NaCl crystals, ordinary table salt, results. This process illustrates ionic or electrovalent bonding.

The electron transfer changed the two atoms of the elements sodium and chlorine into ions. An **ionic bond** is simply the strong electrostatic force that binds the positively and negatively charged ions together in a crystal.

COVALENT BONDS

Just as atoms can be held together in crystals by ionic bonds formed when atoms gain or lose electrons, atoms can also be bonded together into molecules by *sharing* electrons. A chemical bond

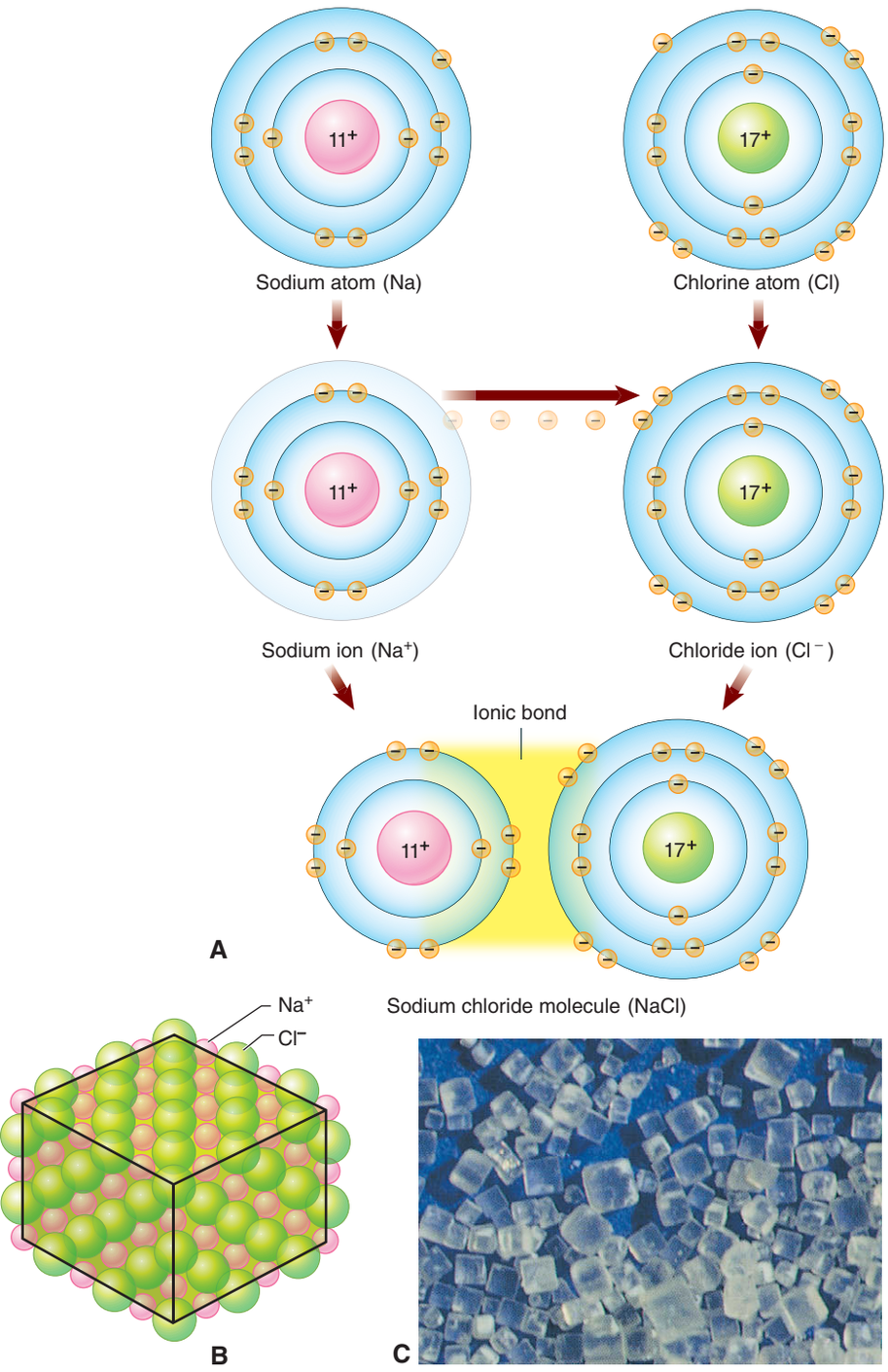


FIGURE 2-8

Example of an ionic bond. A, Energy-level models show the steps involved in forming an ionic bond between atoms of sodium and chlorine within the internal fluid environment of the body (water). Sodium "donates" an electron to chlorine, thereby forming a positive sodium ion and a negative chloride ion. The electrical attraction between the now oppositely charged ions forms an ionic bond. **B,** The space-filling model shows a crystal of sodium chloride (table salt) in the typical cube-shaped formation. **C,** Photomicrograph showing cubic crystals of sodium chloride after the removal of water.

formed by the sharing of one or more pairs of electrons between the outer energy levels of two atoms is called a **covalent bond.** This type of chemical bonding is of great significance in physiology.

The major elements of the body (carbon, oxygen, hydrogen, and nitrogen) almost always share electrons to form covalent bonds. For example, if two atoms of hydrogen are bound together by the sharing of one electron pair, a *single* covalent bond is said to exist, and a molecule of hydrogen gas results (Figure 2-9, A). Covalent bonds that bind atoms together by sharing *two* pairs of electrons are called *double bonds* (Figure 2-9, B). The example shown illustrates two atoms of oxygen, each sharing two electrons with a carbon atom to acquire a complete outer energy level of eight electrons and thus satisfy the octet rule. A molecule of carbon dioxide results.

Attractions Between Molecules

HYDROGEN BONDS

In addition to ionic and covalent bonds, another type of attractive force, called a *hydrogen bond*, can exist between biologically important molecules. Hydrogen bonds are much weaker forces than ionic or covalent bonds because they require less energy to break. Although an individual hydrogen bond is weak, large numbers of these bonds can collectively exert a strong attractive force. Instead of forming as a result of transfer or sharing of electrons between atoms, hydrogen bonds result from unequal charge distribution on a molecule. Such molecules are said to be **polar.**

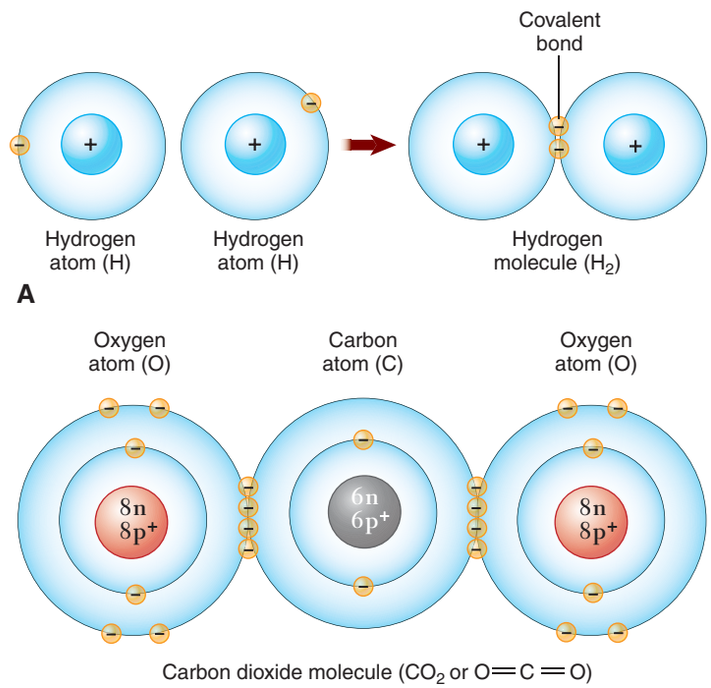


FIGURE 2-9

Types of covalent bonds. A, A single covalent bond formed by the sharing of one electron pair between two atoms of hydrogen results in a molecule of hydrogen gas. **B,** A double covalent bond (double bond) forms by the sharing of *two* pairs of electrons between two atoms. In this case, two double bonds form—one between carbon and *each* of the two oxygen atoms forming a molecule of carbon dioxide.

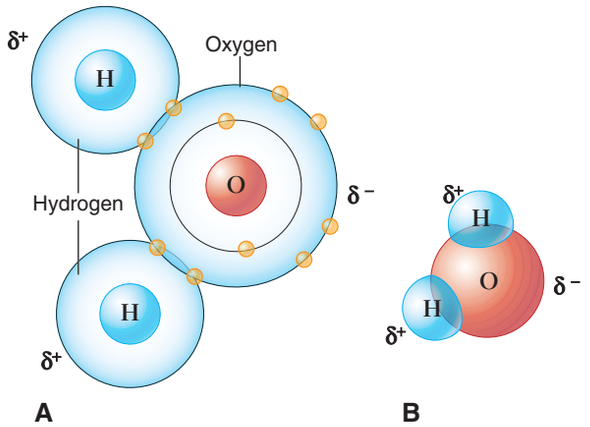


FIGURE 2-10

Water—example of a polar molecule. The polar nature of water is represented in an energy-level model **(A)** and a space-filling model **(B)**. The two hydrogen atoms are nearer one end of the molecule and give that end a partial positive charge (δ+). The "oxygen end" of the molecule attracts the electrons more strongly and thus has a partial negative charge(δ–). Notice that a lowercase Greek letter delta (δ) represents a partial charge.

Water is a good example of a polar molecule. Note in Figure 2-10 that although an atom of water is electrically neutral (the number of negative charges equals the number of positive charges), it has a partial positive charge (the hydrogen side) and a partial negative charge (the oxygen side). That is, the water molecule has a positive pole and a negative pole. The partial charges result from the electrons having a higher probability of being found nearer the highly positive oxygen nucleus than either hydrogen nucleus. That is, the electrons are not shared equally within the molecule. Thus water is said to be "polar" because it has regions with different partial charges. Hydrogen bonds serve to weakly attach the partially negative (oxygen) side of one water molecule to the partially positive (hydrogen) side of an adjacent water molecule.

Figure 2-11 illustrates hydrogen bonding between water molecules. Depending on how many of these hydrogen bonds are intact at one instant, the water may be either liquid (few bonds) or solid (many bonds). If the water molecules are too far apart to form any hydrogen bonds, then the water is a gas, such as steam.

Hydrogen bonds form only between H atoms that are covalently bonded to an oxygen, nitrogen, or fluorine atom. In water molecules H is bonded to O, thus producing the polarity that permits the formation of hydrogen bonds between water molecules.

The ability of water molecules to form hydrogen bonds between molecules accounts for many of the unique properties of water that make it an ideal medium for the chemistry of life. Hydrogen bonds are also important in maintaining the three-dimensional structure of proteins and nucleic acids, also described later in the chapter.

OTHER WEAK ATTRACTIONS

Other weak attractions sometimes attract molecules to each other, even if only temporarily. Shifts in the locations of electrons within each molecule result in fleeting changes in the partial electrical charge of some regions of the molecule. This change in electrical charge may result in attraction to oppositely charged regions of another molecule. In the scope of our course, however, we will not concern ourselves with the different varieties of weak attractions or how they are produced. It is important to know only that they exist and sometimes play an underlying role in holding the material of the body together.

Chemical Reactions

Chemical reactions involve interactions between atoms and molecules, which in turn involves the formation or breaking of chemical bonds. Three basic types of chemical reactions that you will learn to recognize as you study physiology are the following:

1. Synthesis reactions
2. Decomposition reactions
3. Exchange reactions

To the chemist, reactions can be symbolized by variations on a simple formula. In *synthesis reactions*, two or more substances called *reactants* combine to form a different, more complex substance called a *product*. Synthesis literally means "putting together." The process can be summarized by the following formula:

$$\underset{\text{(Reactants)}}{A + B} \xrightarrow{\text{Energy}} \underset{\text{(Product)}}{AB}$$

Synthesis reactions result in the formation of new bonds, and energy is required for the reaction to occur and the new product to form. Many such reactions occur in the body. Every cell, for example, combines amino acid molecules as reactants to form complex protein compounds as products. The ability of the body to synthesize new tissue in wound repair is a good example of this type of reaction.

Decomposition reactions result in the breakdown of a complex substance into two or more simpler substances. In this type of reaction, chemical bonds are broken and energy is released. Energy can be released in the form of heat, or it can be captured

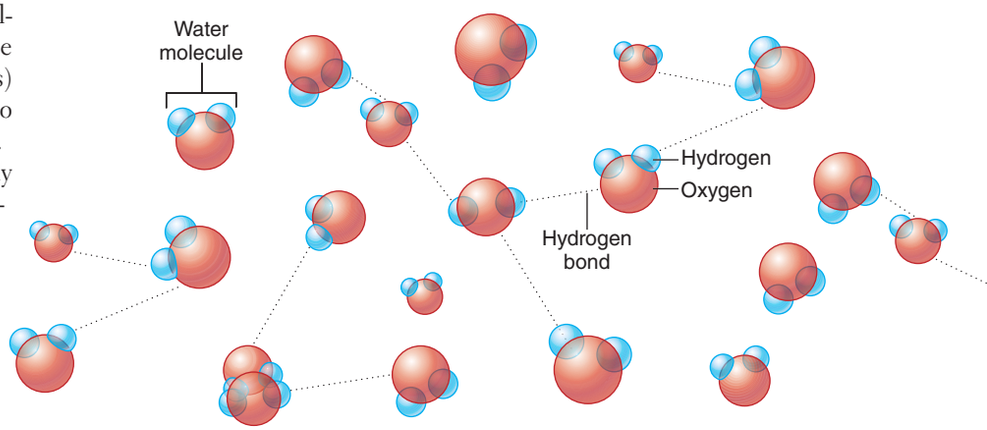


FIGURE 2-11

Hydrogen bonds between water molecules. Hydrogen bonds serve to weakly attach the negative (oxygen) side of one water molecule to the positive (hydrogen) side of a nearby water molecule. This diagram depicts a few bonded molecules, as one would expect in liquid water. Ice would instead have more hydrogen bonds; steam would have no such bonds.

for storage and future use. Decomposition reactions can be summarized by the following formula:

$$AB \longrightarrow A + B + \text{Energy}$$

Decomposition reactions occur when a complex nutrient is broken down in a cell to release energy for other cellular functions. The products of such a reaction are ultimately waste products. Decomposition and synthesis are opposites. Synthesis builds up; decomposition breaks down. Synthesis forms chemical bonds; decomposition breaks chemical bonds. Decomposition and synthesis reactions are often coupled with one another in such a way that the energy released by a decomposition reaction can be used to drive a synthesis reaction.

The nature of **exchange reactions** permits two different reactants to exchange components and, as a result, form two new products. An exchange reaction is often symbolized by the following formula:

$$AB + CD \longrightarrow AD + CB$$

Exchange reactions break down, or decompose, two compounds and, in exchange, synthesize two new compounds. Certain exchange reactions take place in the blood. One example is the reaction between lactic acid and sodium bicarbonate. The decomposition of both substances is exchanged for the synthesis of sodium lactate and carbonic acid. These changes can be seen more easily in the following equation:

$$H \cdot Lactate + NaHCO_3 \longrightarrow Na \cdot Lactate + H \cdot HCO_3$$

The formula $H \cdot Lactate$ represents lactic acid; $NaHCO_3$ is the formula for sodium bicarbonate; $Na \cdot Lactate$ represents sodium lactate; and $H \cdot HCO_3$ represents carbonic acid.

Reversible reactions, as the name suggests, proceed in both directions. A great many synthesis, decomposition, or exchange reactions are reversible, and a number of them are cited in later chapters of this book. An arrow pointing in both directions is used to denote a reversible reaction:

$$A + B \rightleftharpoons AB$$

| QUICK CHECK |

8. List the two types of chemical bonds between atoms and explain how they are formed.
9. What type of bonds attract one molecule to another?
10. Diagram the three basic types of chemical reactions.

METABOLISM

The term **metabolism** is used to describe all the chemical reactions that occur in body cells. The important topics of nutrition and metabolism are discussed fully in Chapter 30. Nutrition and metabolism are described together because the total of all the chemical reactions or *metabolic activity* occurring in cells is associated with the use the body makes of foods after they have been digested, absorbed, and circulated to cells. The terms *catabolism* and *anabolism* are used to describe the two major types of metabolic activity.

Catabolism describes chemical reactions that break down larger food molecules into smaller chemical units and, in so doing, often *release energy*. The release of energy is related to the disruption of chemical bonds. This breakdown of bonds in the chemical compounds contained in the foods and beverages that we consume provides the energy to power all of our activities.

Anabolism involves the many chemical reactions that build larger and more complex chemical molecules from smaller subunits (Figure 2-12). Anabolic chemical reactions *require energy*—energy most often made available by the breakdown of **adenosine triphosphate (ATP).**

Catabolism

Catabolism consists of chemical reactions that not only break down relatively complex compounds into simpler ones but also release energy from them. This breakdown process represents a type of chemical reaction called **hydrolysis** (see Figure 2-12). As a result of hydrolysis occurring during catabolism, a water molecule is added to break a larger compound into smaller subunits. For example, hydrolysis of a fat molecule breaks it down into its subunits—glycerol and fatty acid molecules; a disaccharide such as sucrose breaks down into its monosaccharide subunits—glucose and fructose; and the subunits of protein hydrolysis are amino acids.

Ultimately, catabolic reactions will further degrade these building blocks of food compounds—glycerol, fatty acids, monosaccharides, and amino acids—into the end products carbon dioxide, water, and other waste products. During this process, energy is released. Some of the energy released by catabolism is heat energy, the heat that keeps our bodies warm. However, more than half the energy released is immediately recaptured and transferred

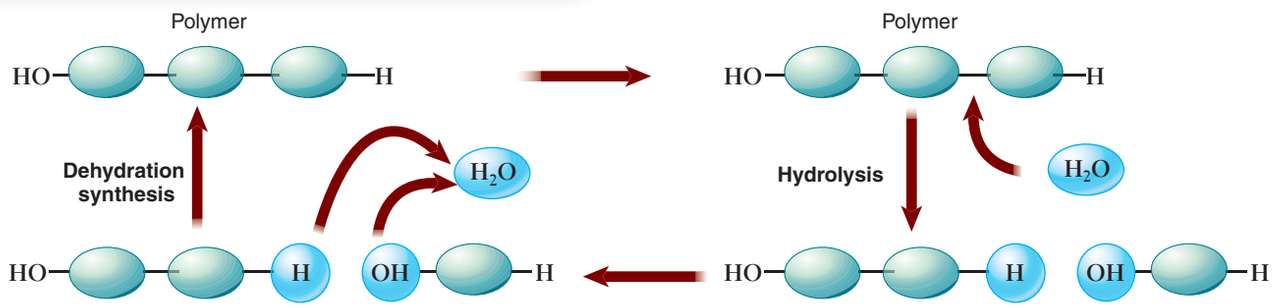


FIGURE 2-12

Metabolic reactions. Hydrolysis is a catabolic reaction that adds water to break down large molecules into smaller molecules, or subunits. Dehydration synthesis is an anabolic reaction that operates in the reverse fashion: small molecules are assembled into large molecules by removing water. Note that specific examples of dehydration synthesis are shown in Figures 2-18 and 2-27.

to a molecule called *ATP*, which transfers the energy to cell components that need it to do work. ATP is discussed in more detail later in this chapter.

Anabolism

Anabolism is the term used to describe chemical reactions that join simple molecules together to form more complex biomolecules—notably, carbohydrates, lipids, proteins, and nucleic acids. Literally thousands of anabolic reactions take place continually in the body. The type of chemical reaction responsible for this joining together of smaller units to form larger molecules is called *condensation* or **dehydration synthesis** (see Figure 2-12). It is a key reaction during anabolism. As a result of dehydration synthesis, water is removed as smaller subunits are fused together.

Anabolism requires energy, which is transferred from ATP molecules. Anabolic reactions use energy to join monosaccharide units to form larger carbohydrates, fuse amino acids into peptide chains, and form fat molecules from glycerol and fatty acid subunits.

| QUICK CHECK |

11. What does the term *metabolism* mean?
12. What is the difference between *anabolism* and *catabolism?*
13. What is the role of *ATP* in the body?

ORGANIC AND INORGANIC COMPOUNDS

In living organisms, there are two kinds of compounds: *organic* and *inorganic*. Organic compounds are generally defined as compounds composed of molecules that contain carbon–carbon (C–C) covalent bonds or carbon–hydrogen (C–H) covalent bonds—or both kinds of bonds. Few inorganic compounds have carbon atoms in them, and none have C–C or C–H bonds. Organic molecules are generally larger and more complex than inorganic molecules.

The term **functional groups** is often used to describe certain arrangements of atoms attached to the carbon core of many organic molecules. Different functional groups confer unique chemical properties. Our later discussions will occasionally involve some of these functional groups. Take a moment now to preview the examples shown in Figure 2-13.

The human body has inorganic and organic compounds because both are equally important to the chemistry of life.

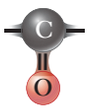
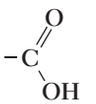
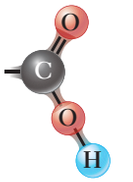
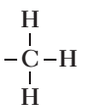
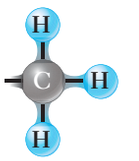
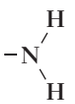
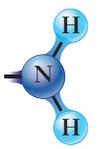
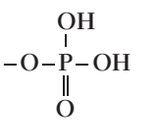
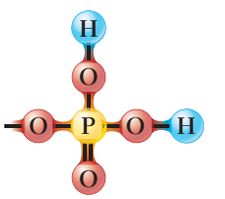
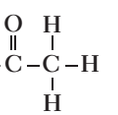
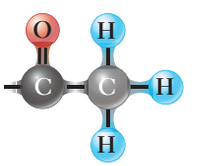
Functional Group	Structural Formula	Models
Hydroxyl	–OH	
Carbonyl		
Carboxyl		
Methyl		
Amino		
Sulfhydryl	–SH	
Phosphate		
Acetyl		

FIGURE 2-13

The principal functional chemical groups. Each functional group confers specific chemical properties on the molecules that possess them.

INORGANIC MOLECULES

Water

Water has been called the "cradle of life" because all living organisms require water to survive. Each body cell is bathed in fluid, and it is only in this precisely regulated and homeostatically controlled environment that cells can function. In addition to water surrounding the cell, the basic substance of each cell, *cytoplasm*, is itself largely water. Water is certainly the body's most abundant and important compound. Fifty percent or more of a normal adult's body weight is water, which serves a host of vital functions. Because of water's pervasive importance in all living organisms, an understanding of the basics of water chemistry is important. In a very real sense, *water chemistry forms the basis for the chemistry of life.*

PROPERTIES OF WATER

The chemist views water as a simple and stable compound. It has an atomic structure that results from the combination of two covalent bonds between a single oxygen atom and two hydrogen atoms.

Recall that water molecules are polar molecules and interact with one another because they have a partial positive charge at one end and a partial negative charge at their other end. Take a moment to go back and review Figure 2-10. This simple chemical property, called *polarity*, allows water to act as a very effective *solvent*. Proper functioning of a cell requires the presence of many chemical substances. Many of these compounds are quite large and must be broken into smaller and more reactive particles (ions) for reactions to occur. Because of its polar nature, water tends to dissociate ionic compounds in solution and surround any molecule that has an electrical charge (Figure 2-14). The fact that so many substances dissolve in water is of utmost importance in the life process.

The critical role that water plays as a solvent permits the *transportation* of many essential materials within the body. By dissolving nutrient molecules in blood, for instance, water enables these materials to enter and leave the blood capillaries in the digestive organs and eventually enter cells in every area of the body. In turn, waste products are transported from where they are produced to excretory organs for elimination from the body.

Another important function of water stems from the fact that water both absorbs and gives up heat slowly. These properties of water enable it to maintain a relatively constant temperature. This allows the body, which has a large water content, to resist sudden changes in temperature. Chemists describe this property by saying that water has a high *specific heat*; that is, water can lose and gain large amounts of heat with little change in temperature. As a result, excess body heat produced by the contraction of muscles during exercise, for example, can be transported by blood to the body surface and dissipated into the environment with little actual change in core temperature.

Chemists and biologists recognize water's high *heat of vaporization* as another important physical quality. This characteristic requires the absorption of significant amounts of heat to change water from a liquid to a gas. The energy is required to break the many hydrogen bonds that hold adjacent water molecules together in the liquid state. Thus the body can dissipate excess heat and maintain a normal temperature by evaporation of water (sweat) from the skin surface whenever excess heat is being produced.

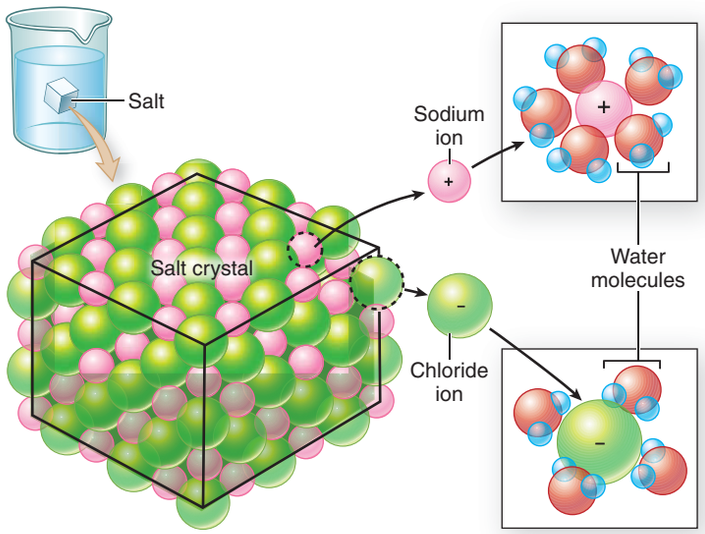


FIGURE 2-14

Water as a solvent. The polar nature of water (blue) favors ionization of substances in solution. Sodium (Na^+) ions (pink) and chloride (Cl^-) ions (green) dissociate in the solution.

Understanding and appreciating the importance of water in the life process are critical. Water does more than act as a solvent, produce ionization, and facilitate chemical reactions. It has essential chemical roles of its own in addition to the many important physical qualities it brings to body function (Table 2-2). It plays a key role in such processes as cell permeability, active transport of materials, secretion, and membrane potential, to name a few.

Oxygen and Carbon Dioxide

Oxygen (O_2) and carbon dioxide (CO_2) are important inorganic substances that are closely related to cellular respiration.

Molecular oxygen in the body is present as two oxygen atoms joined by a double covalent bond. Oxygen is required to complete the decomposition reactions required for the release of energy from nutrients burned by the cell.

TABLE 2-2 Properties of Water

PROPERTY	DESCRIPTION	EXAMPLE OF BENEFIT TO THE BODY
Strong polarity	Polar water molecules attract other polar compounds, which causes them to dissociate	Many kinds of molecules can dissolve in cells, thereby permitting a variety of chemical reactions and allowing many substances to be transported
High specific heat	Hydrogen bonds absorb heat when they break and release heat when they form, thereby minimizing temperature changes	Body temperature stays relatively constant
High heat of vaporization	Many hydrogen bonds must be broken for water to evaporate	Evaporation of water in perspiration cools the body
Cohesion	Hydrogen bonds hold molecules of water together	Water works as lubricant or cushion to protect against damage from friction or trauma

Carbon dioxide is considered one of a group of very simple carbon-containing inorganic compounds. It is an important exception to the "rule of thumb" that inorganic substances do not contain carbon. Like oxygen, carbon dioxide is involved in cellular respiration. It is produced as a waste product during the breakdown of complex nutrients and also serves an important role in maintaining the appropriate acid-base balance in the body.

Electrolytes

Other inorganic substances include acids, bases, and salts. These substances belong to a large group of compounds called **electrolytes** (e-LEK-tro-lites). Electrolytes are substances that break up, or *dissociate*, in solution to form charged particles, or ions. Sometimes the ions themselves are also called electrolytes. Ions with a positive charge are called *cations*, and those with a negative charge are called *anions*. Figure 2-14 shows the way in which water molecules work to dissociate a common electrolyte, sodium chloride (NaCl), into Na^+ cations and Cl^- anions.

ACIDS AND BASES

Acids and bases are common and very important chemical substances in the body. Early chemists categorized acids and bases by such characteristics as taste or the ability to change the color of certain dyes. Acids, for example, taste sour and bases taste bitter. The dye *litmus* will turn blue in the presence of a base and red when exposed to an acid. These and other observations illustrate a fundamental point, namely, that acids and bases are chemical opposites. Although acids and bases dissociate in solution, both release different types of ions. The unique chemical properties of acids and bases when they are in solution are perhaps the best way to differentiate them.

Acids

By definition, an **acid** is any substance that will release a hydrogen ion (H^+) when in solution. A hydrogen ion is simply a bare proton—the nucleus of a hydrogen atom. Therefore, acids are frequently called *proton donors*. It is the concentration of hydrogen ions that accounts for the chemical properties of acids. The level of "acidity" of a solution depends on the number of hydrogen ions a particular acid will release.

One particular point should be understood about water. Water molecules dissociate continually in a reversible reaction to form hydrogen ions (H^+) and hydroxide ions (OH^-):

$$H_2O \rightleftharpoons H^+ + OH^-$$

Recall from our discussion of ionic bonds (p. 38) that having a single unpaired electron in the outer energy level makes an atom unstable and that losing that electron results in a more stable structure. This is precisely the reason dissociation of water occurs. In pure water, the balance between these two ions is equal. However, when an acid such as hydrochloric acid (HCl) dissociates into H^+ and Cl^-, it shifts the H^+/OH^- balance in favor of excess H^+ ions, thus increasing the level of acidity. The more hydrogen ions (H^+) produced, the stronger the acid.

A *strong acid* is an acid that completely, or almost completely, dissociates to form H^+ ions. A *weak acid*, on the other hand, dissociates very little and therefore produces few excess H^+ ions in solution. There are many important acids in the body, and they perform many functions. Hydrochloric acid, for example, is the acid produced in the stomach to aid the digestive process.

Bases

Bases, or *alkaline* compounds, are electrolytes that when dissociated in solution, shift the H^+/OH^- balance in favor of OH^-. This can be accomplished by increasing the number of hydroxide ions (OH^-) in solution or decreasing the number of H^+ ions present. The fact that bases will combine with or accept H^+ ions (protons) is the reason the term *proton acceptor* is used to describe these substances. The dissociation of a common base, sodium hydroxide, yields the cation Na^+ and the OH^- anion.

Like acids, bases are classified as strong or weak, depending on how readily and completely they dissociate into ions. Important bases in the body, such as the bicarbonate ion (HCO_3^-), play critical roles in the transportation of respiratory gases, maintaining normal pH balance, and in the elimination of waste products from the body.

The pH Scale

The term **pH** is literally an abbreviation for a phrase meaning "the power of hydrogen" and is used to mean the relative H^+ ion concentration of a solution. As you can see at the left side of Figure 2-15, the pH value is the negative of the base-10 logarithm of the H^+ ion concentration. The pH indicates the degree of *acidity* or *alkalinity* of a solution. As the concentration of H^+ ions increases, the pH goes down and the solution becomes more acidic; a decrease in H^+ ion concentration makes the solution more alkaline and the pH goes up:

- A pH of 7 indicates neutrality (equal amounts of H^+ and OH^-)
- A pH of less than 7 indicates acidity (more H^+ than OH^-)
- A pH greater than 7 indicates alkalinity (more OH^- than H^+)

The overall pH range is often expressed numerically on a logarithmic scale of 1 to 14. Keep in mind that a change of 1 pH unit on this type of scale represents a 10-fold difference in actual concentration of H^+ ions (Box 2-1).

BUFFERS

The normal pH range of blood and other body fluids is extremely narrow. For example, venous blood (pH 7.36) is only slightly more



Box 2-1 | FYI

The pH Unit

A pH value of 7, for example, means that a solution with that measurement contains 10^{-7} grams of hydrogen ions per liter. Translating this logarithm into a number, a pH of 7 means that such a solution contains 0.0000001 (that is, 1/10,000,000) gram of hydrogen ions per liter. A solution with a measurement of pH 6 contains 0.000001 (1/1,000,000) gram of hydrogen ions per liter, and one of pH 8 contains 0.00000001 (1/100,000,000) gram of hydrogen ions per liter. Note that a solution with pH 7 contains *10 times* as many hydrogen ions as a solution with pH 8 and that pH decreases as the hydrogen ion concentration increases.

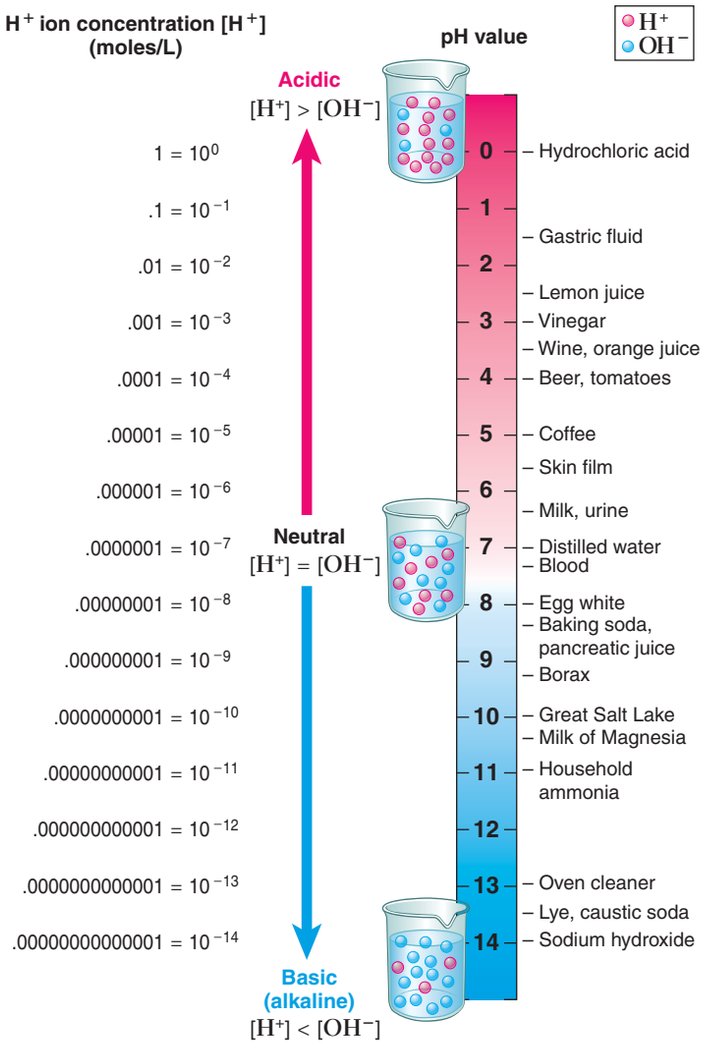


FIGURE 2-15

The pH scale. Note that as the concentration of H^+ increases, the solution becomes increasingly acidic and the pH value decreases. As the H^+ concentration decreases, the pH value increases, and the solution becomes more and more basic, or alkaline. (The scale on the left side of the diagram shows the actual concentrations of H^+ in moles per liter, or molar concentration, as an ordinary number and expressed as an exponent [logarithm] of 10. You can see that the pH scale is simply the negative of the exponent of 10.)

acidic than arterial blood (pH 7.41). The difference results primarily from carbon dioxide entering venous blood as a waste product of cellular metabolism. Carbon dioxide is carried as carbonic acid (H_2CO_3) and therefore lowers the pH of venous blood. More than 30 *liters* of carbonic acid is transported in venous blood each day and eliminated as carbon dioxide by the lungs, and yet 1 liter of venous blood contains only about 1/100,000,000 gram more H^+ ions than 1 liter of arterial blood does!

The incredible constancy of the pH homeostatic mechanism relies partly on the presence of substances, called **buffers,** that minimize changes in the concentrations of H^+ and OH^- ions in our body fluids. Buffers are said to act as a "reservoir" for H^+ ions. They donate, or remove, H^+ ions to a solution if that becomes necessary to maintain a constant pH. Examples of important buffer systems and specifics of buffer action are discussed in Chapter 33.

SALTS

A salt is any compound that results from the chemical interaction of an acid and a base. Salts, like acids and bases, are electrolyte compounds and dissociate in solution to form positively and negatively charged ions. Ions exist in solution. If the water is removed, the ions will crystallize and form salt. When mixed and allowed to react, the positive ion (cation) of a base and the negative ion (anion) of an acid will join to form a salt and additional water in the manner of a typical exchange reaction. The reaction between an acid and base to form a salt and water is called a *neutralization reaction:*

AB	+	CD	⟶	CB	+	AD
HCl	+	NaOH	⟶	NaCl	+	H_2O
Acid		Base		Salt		Water

Note that the sodium and the chloride join to form the salt whereas the hydroxide ion "accepts" or combines with a hydrogen ion to form water.

The sources of many of the major and trace mineral elements listed in Table 2-1 are inorganic salts, which are common in many body fluids and certain tissues such as bone. These elements often exert their full physiological effects only when present as charged atoms or ions in solution.

The proper amount and concentration of such mineral ions as potassium (K^+), calcium (Ca^{++}), and sodium (Na^+) are required for proper functioning of nerves and for contraction of muscle tissue. See Chapter 32 for specific homeostatic control mechanisms that regulate electrolyte balance in blood and other body fluids.

| QUICK CHECK |

14. Discuss the properties of water that make it so important in living organisms.
15. What is an electrolyte?
16. How do acids and bases react with each other when in solution?
17. What is pH?

ORGANIC MOLECULES

The term *organic* is used to describe the enormous number of compounds that contain carbon—specifically C–C or C–H bonds. Recall that carbon atoms have only four electrons in their outer energy level (see Figure 2-3, A); it requires four electrons to satisfy the octet rule. As a result, each carbon atom can join with up to four other atoms to form literally thousands of molecules of varying size and shape. Although some organic molecules are small and have only one or two functional groups, the large *macromolecules* often have many functional groups attached to one another or to other chemical compounds (Figure 2-16). In the human body, the following four major groups of organic substances are very important:

1. Carbohydrates
2. Lipids
3. Proteins
4. Nucleic acids and related molecules

Figure 2-16 shows examples of the four major organic substances represented by three-dimensional models. Many macromolecules are composed of basic building blocks, such as glucose or amino acids, that are joined in chains of varying length by covalent bonds. Table 2-3 identifies important biological molecules (or biomolecules), including macromolecules and combined forms, shows the type of subunit present, gives a typical function, and lists one or more examples of each. Refer to this table as you read about the large biological molecules in the paragraphs that follow.

Carbohydrates

All **carbohydrate** compounds contain the elements carbon, hydrogen, and oxygen—usually in the ratio of 1 to 2 to 1. The carbon atoms link to one another in chains or rings. Carbohydrates include the substances commonly called *sugars* and *starches* and represent the primary source of chemical energy needed by every body cell. In addition, carbohydrates serve a structural role as components of such critically important molecules as RNA and DNA, which are involved in cell reproduction and protein synthesis.

As a group, carbohydrates are divided into three types or classes that are characterized by the length of their carbon chains. The three types are named as follows:

1. Monosaccharides (simple sugars)
2. Disaccharides (double sugars)
3. Polysaccharides (complex sugars)

MONOSACCHARIDES

Monosaccharides, or simple sugars, are relatively small carbohydrates. The most important simple sugar is *glucose*. It is a six-carbon sugar with the formula $C_6H_{12}O_6$. The chemical formula indicates that each molecule of glucose contains 6 atoms of carbon, 12 atoms of hydrogen, and 6 atoms of oxygen. Because it has six carbon atoms, it is called a *hexose* (*hexa*, "six"). Glucose is present in the dry state as a *straight chain* but forms a *cyclic* compound (ring) when dissolved in water. In Figure 2-17 the straight chain and cyclic arrangements are shown with a three-dimensional model of the molecule. However, it is important to remember that all forms of glucose represented in models or illustrations are the same molecule.

In addition to glucose, other important hexoses, or six-carbon simple sugars, include fructose and galactose. Not all monosaccharides, however, are hexoses. Some are *pentoses* (from *penta*, five), so named because they contain five carbon atoms. *Ribose* and *deoxyribose* are pentose monosaccharides of great importance in the body—they are covered further when we study nucleic acids later in this chapter. Like all monosaccharides, ribose and deoxyribose are simple sugars—but strange sugars in that they are not sweet.

DISACCHARIDES AND POLYSACCHARIDES

Substances classified as *disaccharides* (double sugars) or *polysaccharides* (complex sugars) are carbohydrates composed of two or more simple sugars that are bonded together through a dehydration synthesis reaction that involves the removal of water. Sucrose (table sugar), maltose, and lactose are all disaccharides. Each consists of two monosaccharides linked together. Figure 2-18 shows the formation of sucrose from glucose and fructose. Note that a hydrogen atom from the glucose molecule combines with a hydroxyl group (OH) from the fructose molecule to form water, with an oxygen atom left to bind the two subunits together. Lactose is likewise synthesized from glucose and galactose. Two glucose molecules join to form maltose.

Polysaccharides consist of many monosaccharides chemically joined to form straight or branched chains. Once again, water is removed as the many monosaccharide subunits are joined. Any large molecule made up of many identical small molecules is called a *polymer*. Polysaccharides are polymers of monosaccharides. *Glycogen*, a polymer of glucose, is sometimes referred to as *animal starch*. It is the main polysaccharide in the body and has an estimated molecular weight of several million—truly a macromolecule.

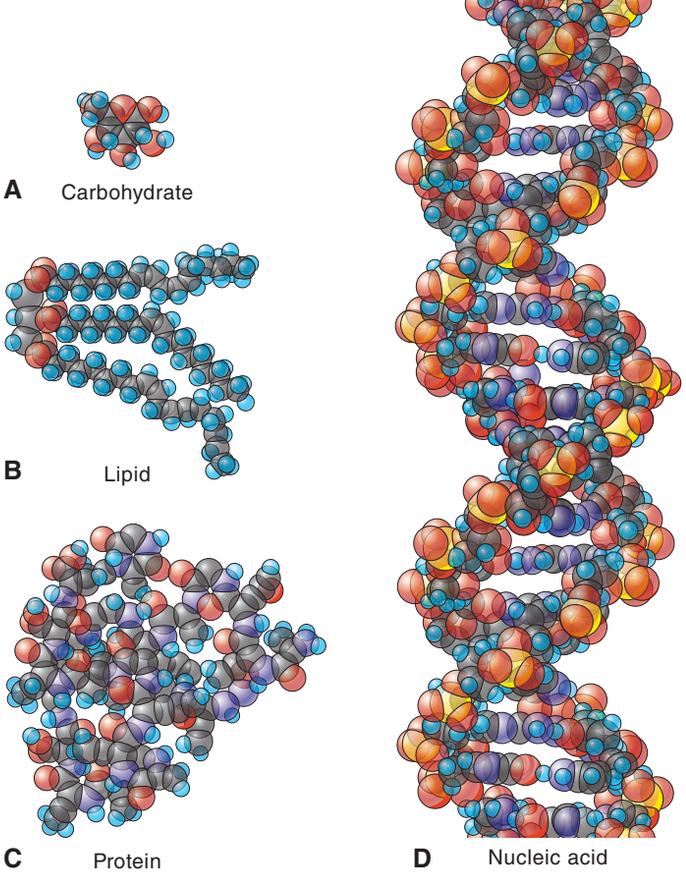


FIGURE 2-16

Important organic molecules. Molecular models showing examples of the four major groups of organic substances: **A,** carbohydrate; **B,** lipid; **C,** protein; **D,** nucleic acid.

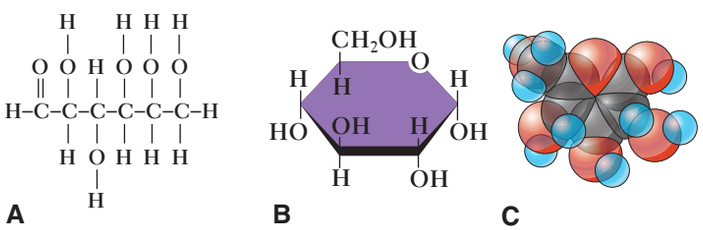


FIGURE 2-17

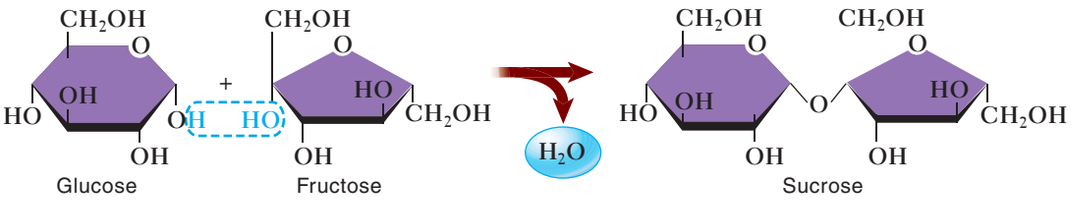
Structure of glucose. **A,** Straight chain, or linear model, of glucose. **B,** Ring model representing glucose in solution. **C,** Three-dimensional, or space-filling, model of glucose.

TABLE 2-3 Examples of Important Biomolecules

MACROMOLECULE	SUBUNIT	FUNCTION	EXAMPLE
Carbohydrates			
Glucose	Simple sugar (hexose: $C_6H_{12}O_6$)	Stores energy	Blood glucose
Ribose	Simple sugar (pentose: $C_5H_{10}O_5$)	Plays role in expression of hereditary information	Component of RNA
Deoxyribose	Simple sugar (pentose: $C_5H_{10}O_4$)	Plays role in storage and transmission of hereditary information	Component of DNA
Glycogen	Glucose	Stores energy	Liver glycogen
Lipids			
Triglycerides	Glycerol + 3 fatty acids	Store energy	Body fat
Phospholipids	Glycerol + phosphate + 2 fatty acids	Make up cell membranes	Plasma membrane of cell
Steroids	Steroid nucleus (4-carbon ring)	Make up cell membranes Hormone synthesis	Cholesterol, various steroid hormones Estrogen
Prostaglandins	20-carbon unsaturated fatty acid containing 5-carbon ring	Regulate hormone action; enhance immune system; affect inflammatory response	Prostaglandin E, prostaglandin A
Proteins			
Functional proteins	Amino acids	Regulate chemical reactions	Hemoglobin, antibodies, enzymes
Structural proteins	Amino acids	Component of body support tissues	Muscle filaments, tendons, ligaments
Nucleic Acids			
DNA	Nucleotides (sugar, phosphate, base)	Encodes hereditary information	Chromatin, chromosomes
RNA	Nucleotides (sugar, phosphate, base)	Helps decode hereditary information; acts as "RNA enzyme"; silencing of gene expression	Transfer RNA (tRNA), messenger RNA (mRNA), double-strand RNA (dsRNA)
Nucleotides and Related Molecules			
Adenosine triphosphate (ATP)	Phosphorylated nucleotide (adenine + ribose + 3 phosphates)	Transfers energy from fuel molecules to working molecules	ATP present in every cell of the body
Creatine phosphate (CP)	Amino acid derivative + phosphate	Transfers energy from fuel to ATP	CP present in muscle fiber as "backup" to ATP
Nicotinic adenine dinucleotide (NAD)	Combination of two ribonucleotides	Acts as coenzyme to transfer high-energy particles from one chemical process to another	NAD present in every cell of the body
Combined or Altered Forms			
Glycoproteins	Large proteins with small carbohydrate groups, attached	Similar to functional proteins	Some hormones, antibodies, enzymes, cell membrane components
Proteoglycans	Large polysaccharides with small polypeptide chains attached	Lubrication; increases thickness of fluid	Component of mucous fluid and many tissue fluids in the body
Lipoproteins	Protein complex containing lipid groups	Transport lipids in the blood	LDLs (low-density lipoproteins); HDLs (high-density lipoproteins)
Glycolipids	Lipid molecule with attached carbohydrate group	Component of cell membranes	Component of membranes of nerve cells
Ribonucleoprotein	Combination of RNA nucleotide and protein	Enzyme-like actions such as splicing mRNA	Small nuclear ribonucleoproteins (snRNPs or "snurps") that make up the spliceosome structure in a cell

FIGURE 2-18

Formation of sucrose. Glucose and fructose are joined in a synthesis reaction that involves the removal of water.



| QUICK CHECK |

18. List the four major groups of organic substances.
19. Identify the most important monosaccharide, or simple sugar.
20. Identify a carbohydrate polymer and explain how it is formed.

Lipids

Lipids, according to one definition, are water-insoluble organic biomolecules. Lipids ordinarily do not dissolve in water because lipid molecules are generally **nonpolar.** Because electrons are shared equally within a molecule there are no partially charged regions and thus lipids do not cling to the partially charged areas of the polar water molecules. Although insoluble in water, most lipids, many with an oil-like consistency and greasy feel, dissolve readily in some organic solvents such as ether, alcohol, or benzene.

Like the carbohydrates, lipids are composed largely of carbon, hydrogen, and oxygen. However, the proportion of oxygen in lipids is much lower than that in carbohydrates. Many lipids also contain other elements such as nitrogen and phosphorus. As a group, lipids include a large assortment of compounds that have been classified in several ways. Classification of lipids includes triglycerides or fats, phospholipids, steroids, and prostaglandins.

Lipids are critically important biological compounds and have several major roles in the body (Table 2-4). Many are used for energy purposes, whereas others serve a structural role and function as integral parts of cell membranes. Other important lipid compounds serve as vitamins or protect vital organs by serving as "fat pads," or shock absorbers, in certain body areas. One type of lipid material actually serves as "insulator material" around nerves, thus serving to prevent "short circuits" and speed nervous impulse transmissions.

TABLE 2-4 Major Functions of Human Lipid Compounds

FUNCTION	EXAMPLE
Energy	Lipids can be stored and broken down later for energy; they yield more energy per unit of weight than carbohydrates or proteins do
Structure	Phospholipids and cholesterol are required components of cell membranes
Vitamins	Fat-soluble vitamins: vitamin A forms retinal (necessary for night vision); vitamin D increases calcium uptake; vitamin E promotes wound healing; and vitamin K is required for the synthesis of blood-clotting proteins
Protection	Fat surrounds and protects organs
Insulation	Fat under the skin minimizes heat loss; fatty tissue (myelin) covers nerve cells and electrically insulates them
Regulation	Steroid hormones regulate many physiological processes; for example, estrogen and testosterone are responsible for many of the differences between females and males; prostaglandins help regulate inflammation and tissue repair

TRIGLYCERIDES OR FATS

Triglycerides (triacylglycerols), or fats, are the most abundant lipids, and they function as the body's most concentrated source of energy. Two types of building blocks are needed to synthesize or build a fat molecule: *glycerol* and *fatty acids.* Each glycerol unit is joined to three fatty acids, and the glycerol building block is the same in each fat molecule. Therefore, it is the specific type of fatty acid molecule or component that identifies and determines the chemical nature of any fat.

Types of Fatty Acids

Fatty acids vary in the length of their carbon chains (number of carbon atoms) and in the number of hydrogen atoms that are attached to, or "saturate," the available bonds around each carbon in the chain. Naturally occurring fatty acids have an even number of carbons, usually numbering between 12 and 18. Figure 2-19 shows a structural formula and three-dimensional model for a saturated (palmitic) and unsaturated (linolenic) fatty acid.

By definition, a *saturated fatty acid* is one in which all available bonds of its hydrocarbon chain are filled, that is, saturated, with hydrogen atoms. The chain contains no double bonds (Figure 2-19, A). In contrast, an *unsaturated fatty acid* has one or more double bonds in its hydrocarbon chain because not all the chain's carbon atoms are saturated with hydrogen atoms. Looking at Figure 2-19, B, you can easily see that some of the hydrogens are missing from the carbon backbone of the unsaturated fatty acid.

The degree of saturation is the most important factor in determining the physical and chemical properties of fatty acids. For example, animal fats such as tallow and lard are solids at room temperature, whereas vegetable oils are typically liquids. The difference lies in the extent of unsaturation—animal fats are mostly saturated, whereas most vegetable oils are not. Note in Figure 2-19, B, that the presence of double bonds in a fatty acid molecule will cause the chain to kink or bend.

Fats become more oily and liquid as the number of unsaturated double bonds increases. The kinks and bends in the unsaturated molecules keep them from fitting closely together. In contrast, the lack of kinks in saturated fatty acids allows the molecules to fit tightly together to form a solid mass at higher temperatures.

Formation of Triglycerides

Figure 2-20 shows the formation of a triglyceride. Its name, *glycerol tricaproate,* suggests that it contains three molecules of the

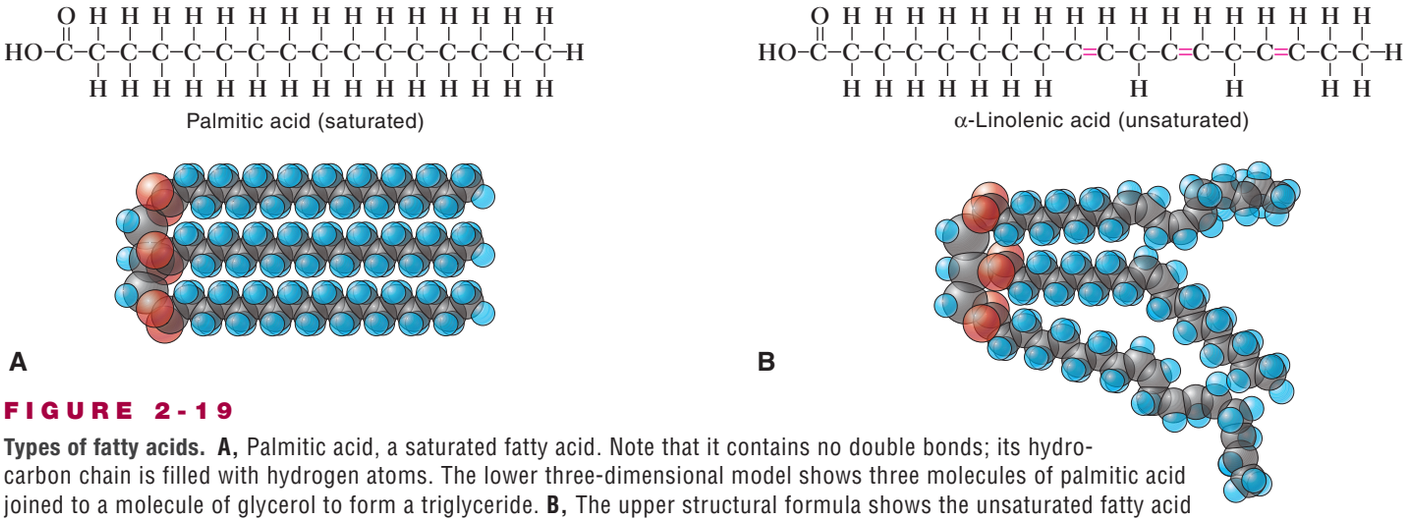


FIGURE 2-19

Types of fatty acids. A, Palmitic acid, a saturated fatty acid. Note that it contains no double bonds; its hydrocarbon chain is filled with hydrogen atoms. The lower three-dimensional model shows three molecules of palmitic acid joined to a molecule of glycerol to form a triglyceride. **B,** The upper structural formula shows the unsaturated fatty acid α-linolenic acid (double bonds shown in red). The lower three-dimensional model shows triglyceride exhibiting "kinks" caused by the presence of double bonds in the component fatty acids.

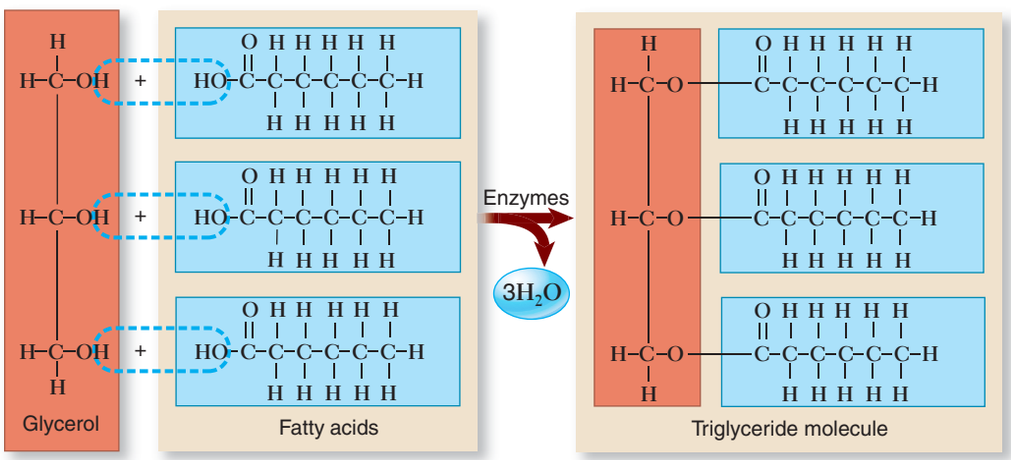


FIGURE 2-20

Formation of triglyceride. Glycerol tricaproate is a composite molecule made up of three molecules of caproic acid (a six-carbon fatty acid) coupled in a dehydration synthesis reaction to a single glycerol backbone. In addition to the triglyceride, this process results in the formation of three molecules of water.

six-carbon fatty acid *caproic acid* attached to a glycerol molecule. Note that the three caproic acid building blocks attach by their carboxyl groups (COOH) to the three hydroxyl groups (OH) of the glycerol molecule to form the triglyceride and three molecules of water. The process is one you are now familiar with—it is a dehydration synthesis reaction. Keep in mind that although some fats, such as glycerol tricaproate, contain three molecules of the same fatty acid, others may have two or three different fatty acids attached to glycerol. Caproic acid is considered to be a *short-chain* fatty acid; some triglycerides contain fatty acids with a carbon backbone several times longer, thus forming *long-chain* fatty acids.

PHOSPHOLIPIDS

Phospholipids are fat compounds similar to triglycerides. They are modified, however, in that one of the three fatty acids attached to glycerol in a triglyceride is replaced in a phospholipid by another type of chemical structure containing phosphorus and nitrogen. The structural formula of a phospholipid is shown in Figure 2-21. Observe that the phospholipid molecule contains glycerol. Joined to the glycerol at one end of the molecule are two fatty acids. Attached to glycerol but extending in the opposite direction is the phosphate group, which is attached to a nitrogen-containing compound.

The head, or end of the molecule containing the phosphorus group, in a phospholipid molecule is polar and is therefore water

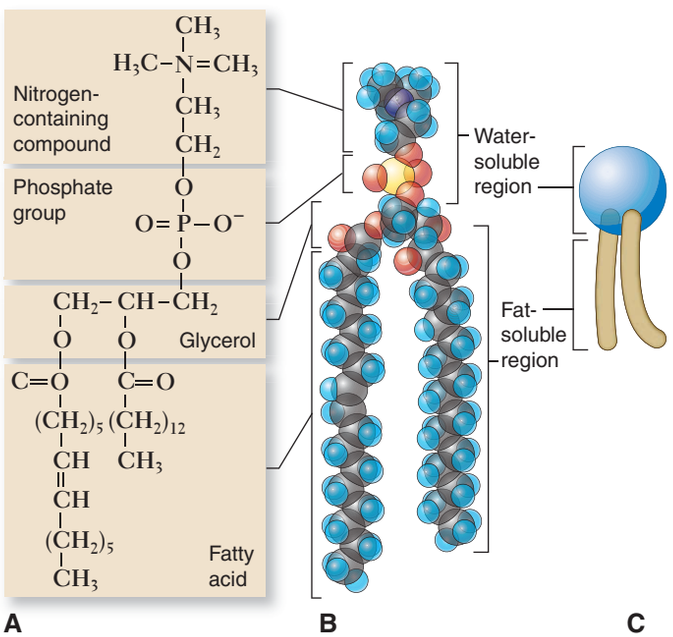


FIGURE 2-21

Phospholipid molecule. A, Chemical formula of a phospholipid molecule. **B,** Molecular model showing water- and fat-soluble regions. **C,** Cartoon often used to represent the double-tailed phospholipid molecule.

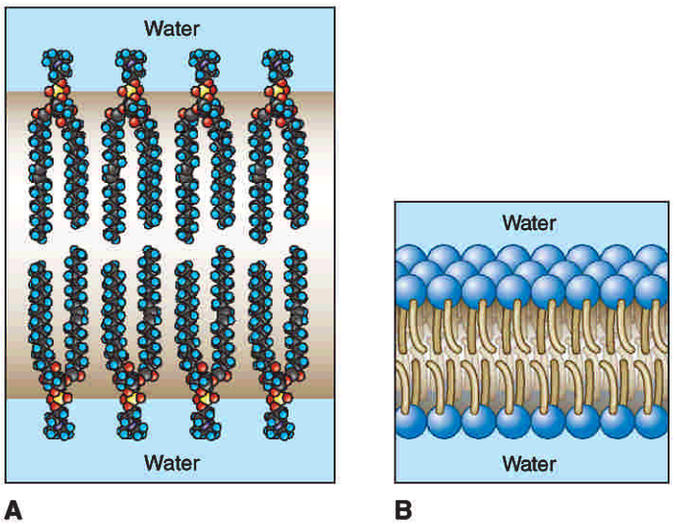


FIGURE 2-22

Phospholipid bilayer. A, Orientation of phospholipid molecules when surrounded by water and forming a bilayer. **B,** Cartoon commonly used to depict a phospholipid bilayer.

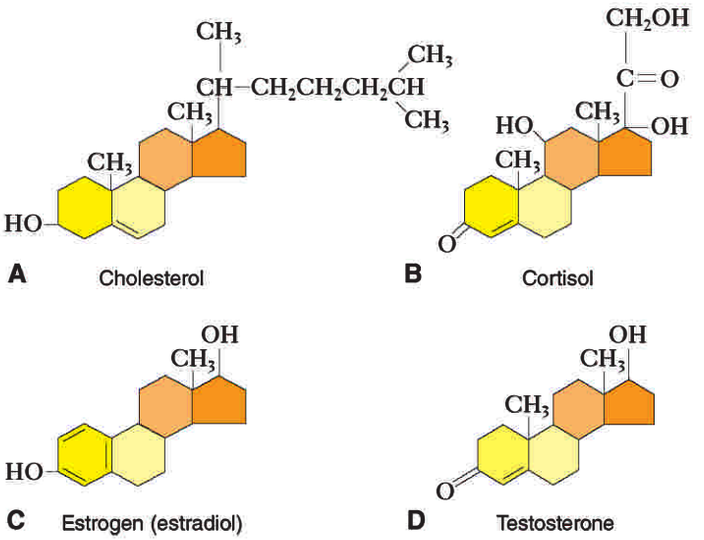


FIGURE 2-23

Steroid compounds. The steroid nucleus—highlighted in yellow—found in cholesterol **(A)** forms the basis for many other important compounds such as cortisol **(B)**, estradiol (an estrogen) **(C)**, and testosterone **(D)**.

soluble. The term *hydrophilic*, meaning "water loving," also applies to the phospholipid head. The end formed by the two fatty acids is nonpolar and is therefore fat soluble or *hydrophobic* ("water fearing"). This unique property means that phospholipid molecules can bridge, or join, two different chemical environments—a water environment on one side and a lipid environment on the other. Thus in water they often form bilayers (double layers) with the fatty tails facing toward one another and the heads forming sheets that face the water on either side of the bilayer (Figure 2-22). For this reason, phospholipids are a primary component of cell membranes (which are bilayers); they are discussed further in Chapter 3.

STEROIDS

Steroids are a large and important class of lipids whose molecules have as their main feature the *steroid nucleus* (Figure 2-23). The steroid nucleus is composed of four attached rings that are structurally similar but may have widely diverse functions related to the differing functional groups that are attached to them.

Steroids, some of which are called *sterols*, are widely distributed in the body and are involved in many important structural and functional roles. Cholesterol is a steroid found in the plasma membrane surrounding every body cell (see Chapter 3 and Box 2-2). Its presence helps stabilize this important cellular structure and is required for many reactions that cells must perform to survive. In addition, the body slightly modifies cholesterol molecules to form such important hormones as cortisone, estrogen, and testosterone. It is also used to make the bile salts needed for digestion. The steroid nucleus is also a part of the active hormone form of vitamin D called *calcitriol*.

PROSTAGLANDINS

Prostaglandins, often called *tissue hormones*, are lipids composed of a 20-carbon unsaturated fatty acid that contains a five-carbon ring (Figure 2-24). Many different kinds of prostaglandins exist in the body. We now classify 16 prostaglandin types (PGs) into nine broad categories, called PGA to PGI. Each major grouping of prostaglandins can be further subdivided according to chemical structure and function.

Prostaglandins were first associated with prostate tissue and were named accordingly. Subsequent discoveries, however, have shown that these biologically powerful chemical substances are produced by cell membranes located in almost every body tissue. They are formed and then released from cell membranes in response to a particular stimulus. Once released, they have a very local effect and are then inactivated.

The effects of prostaglandins in the body are many and varied. They play a crucial role in regulating the effects of several hormones, influence blood pressure and the secretion of digestive juices, enhance the body's immune system and inflammatory response (Box 2-3), and have an important role in blood clotting and respiration, to name a few. The use of prostaglandins and prostaglandin inhibitors as drugs is an exciting and rapidly growing area in clinical medicine.

| QUICK CHECK |

21. What are the building blocks of a triglyceride, or fat?
22. Give an example of a dehydration synthesis reaction.
23. What is a phospholipid, and why is it an important type of molecule?
24. Identify an important steroid.

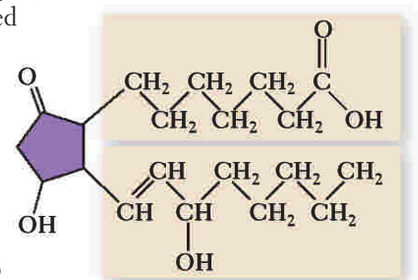


FIGURE 2-24

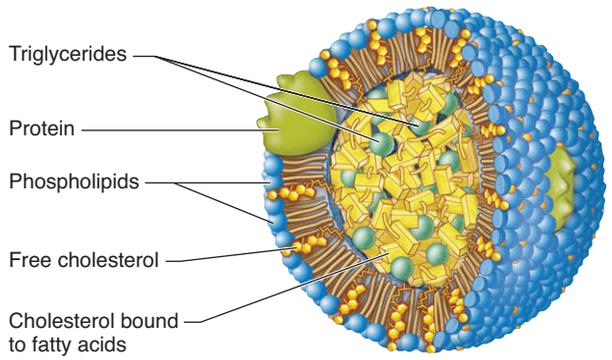
Prostaglandin. Prostaglandins such as this example of prostaglandin E (PGE) are 20-carbon unsaturated fatty acids with a 5-carbon ring. Prostaglandins act as local regulators in the body.

Box 2-2 | HEALTH matters

Blood Lipoproteins

A lipid such as cholesterol can travel in the blood only after it has attached to a protein molecule—forming a lipoprotein. Some of these molecules are called *high-density lipoproteins* (HDLs) because they have a high density due to having more protein than cholesterol. Another type of molecule contains less protein than cholesterol, so it is called *low-density lipoprotein* (LDL). The composite nature of a lipoprotein molecule is shown in the figure.

The cholesterol in LDLs is often called "bad" cholesterol because high blood levels of LDL are associated with *atherosclerosis,* a life-threatening blockage of arteries. LDLs carry cholesterol to cells, including the cells that line blood vessels. HDLs, on the other hand, carry so-called "good" cholesterol *away from cells* and toward the liver for elimination from the body. A high proportion of HDL in the blood is associated with a low risk for atherosclerosis.



Structure of a lipoprotein.

Proteins

All **proteins** have four elements: carbon, oxygen, hydrogen, and nitrogen. Many proteins also contain small amounts of sulfur, iron, magnesium, zinc, and other trace metals. Some also contain phosphorus. Proteins (from word parts meaning "first-rank substance") are the most abundant of the organic compounds in the body. As their name implies, their functions are of first-rank importance. Protein molecules are among the giant sized macromolecules, along with many of the polysaccharides and nucleic acids.

The many roles played by proteins in the body can be divided into two broad categories: *structural* and *functional*. Structural proteins form the structure of the cells, tissues, and organs of the body. Various unique shapes and compositions such as flexible strands, elastic strands, and waterproof layers allow structural proteins to form the many different building blocks of the body. Functional proteins are chemists. The unique shape of each functional protein allows it to fit with certain other chemicals and cause some change in the molecules. For example, **enzymes** are functional proteins that bring molecules together or split them apart in chemical reactions. Protein hormones such as insulin trigger chemical changes in cells to produce the hormone's effects.

It is the *shape* of a protein that determines how it performs. The main principle in understanding how proteins work is that form and function go hand in hand—the right shape for the right job.

Compared with water with a total mass number of of 18, giant protein molecules may have a total mass number of several million! However, all protein molecules, regardless of size, have a similar basic structure. They are chainlike polymers composed of multiple subunits, or building blocks, linked end to end. The building blocks of all proteins are called *amino acids.*

AMINO ACIDS

The elements that make up a protein molecule are bonded together to form chemical units called **amino acids.** Proteins are composed

Box 2-3 | FYI

Aspirin and Prostaglandins

In the presence of an appropriate stimulus such as irritation or injury, fatty acids required for prostaglandin synthesis are released by cell membranes. If a specific type of enzyme, *cyclooxygenase (COX),* is present to interact with these fatty acids, prostaglandins will be synthesized and released from the cell membrane into the surrounding tissue fluid.

Prostaglandins sometimes serve as inflammatory agents. They cause local dilation of blood vessels with resulting heat (fever), swelling, redness, and pain. Aspirin (acetylsalicylic acid [ASA]) is a *COX inhibitor* and thus works to relieve these symptoms by blocking the activity of the COX–1 and COX–2 enzymes. If these enzymes cannot function properly, prostaglandin synthesis will be inhibited, and symptoms will be relieved.

Prostaglandins sometimes serve to regulate blood clotting. Again, aspirin can inhibit prostaglandin synthesis and play a therapeutic role in preventing abnormal blood clots or reducing abnormal clots that have already begun forming. For this reason, some people at risk for a heart attack triggered by abnormal blood clots are advised to take daily low-dose aspirin to reduce the formation of abnormal clots. If a heart attack has already begun, full-dose aspirin taken immediately may stop the clotting and thus increases a person's chances of surviving the episode by about 25%.

The functions of prostaglandins and the actions of other COX enzyme inhibitors are discussed further in Chapter 18.

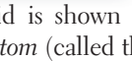


Aspirin. Acetylsalicylic acid (aspirin) is a commonly used COX inhibitor that reduces prostaglandin effects in the body such as inflammation, fever, and blood clotting.

of 21 naturally occurring amino acids, and nearly all of the 21 amino acids are usually present in every protein. Of these 21, 8 are known as *essential amino acids*. They cannot be produced by the body and must be included in the adult diet. The 13 remaining *nonessential amino acids* can be produced from other amino acids or from simple organic molecules readily available to the body cells.

| A&P CONNECT |

Some scientists state that there are 20 amino acids making up proteins, and others 21 or 22. Why is this? Find out in ***Amazing Amino Acids*** online at ***A&P Connect.***



The basic structural formula for an amino acid is shown in Figure 2-25. As you can see, it consists of a *carbon atom* (called the *alpha* carbon) to which are bonded a positive *amino group* (NH_3^+), a negative *carboxyl group* (COO^-), a *hydrogen atom*, and a *side group* of elements designated by the letter *R*. It is this side group that constitutes the unique, identifying part of an amino acid.

The 21 amino acids that make up most human proteins are shown in Figure 2-26. You can see that each individual amino acid has its own chemical nature because of its unique side group. Some are more acid, some more basic. Some tend to ionize and thus have an electric charge. Others have regions of different partial charges and are therefore polar. On the other hand, some amino acids tend to be nonpolar. Some are large and some are small. Individual amino acids are often compared with the letters of the alphabet. Just as combinations of individual letters form word combinations, different amino acids form protein chains. Think of amino acids as the alphabet of proteins.

The ability of amino acids to "link up" in all possible combinations allows the body to build or synthesize an almost infinite variety of different protein "words" or chains that may contain a dozen, several hundred, or even thousands of amino acids. Each of these chains can have different regions with different chemical characteristics.

Amino acids frequently become joined by peptide bonds. A **peptide bond** is one that binds the carboxyl group of one amino acid to the amino group of another amino acid. O from the negative carboxyl group of one amino acid and two H atoms from the positive amino group of another amino acid split off to form water plus a new compound called a *peptide*. A peptide made up of only two amino acids linked by a peptide bond is a *dipeptide*. A *tripeptide* consists of three amino acids linked by two bonds. The linkage of four amino acids by these peptide bonds is shown in Figure 2-27, A. A long sequence or chain of amino acids—usually 100 or more—linked by peptide bonds constitutes a *polypeptide*. When the length of the polymer chain exceeds about 100 amino acids, the molecule is called a *protein* rather than a polypeptide.

Do you see a similarity between the formation of a polysaccharide, such as glycogen, from simple sugar "building blocks" and the formation of a polypeptide from amino acid building blocks? In both processes, many subunits are joined together, resulting in the loss of water molecules. Thus, both are examples of the *condensation* or *dehydration synthesis* reactions that are very common in living organisms. A decomposition reaction called *hydrolysis* requires the addition of a water molecule to break a bond. During hydrolysis of a peptide chain, the peptide linkages between adjacent amino acids in the sequence are broken by the addition of water, and individual amino acids are released (Figure 2-27, B).

LEVELS OF PROTEIN STRUCTURE

Biochemists often describe four levels of increasing complexity in protein organization:

1. Primary (first level)
2. Secondary (second level)
3. Tertiary (third level)
4. Quaternary (fourth level)

The four levels of protein structure are illustrated in Figure 2-28.

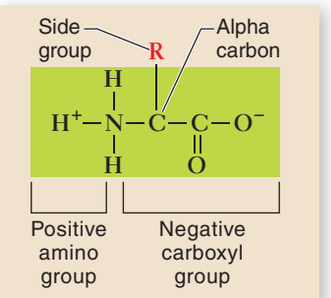
The *primary structure* of a protein refers simply to the number, kind, and sequence of amino acids that make up the polypeptide chain. The hormone of the human parathyroid gland, parathyroid hormone (PTH), is a protein that retains its primary structure—it is a noodle-like molecule consisting of only one polypeptide chain of 84 amino acids.

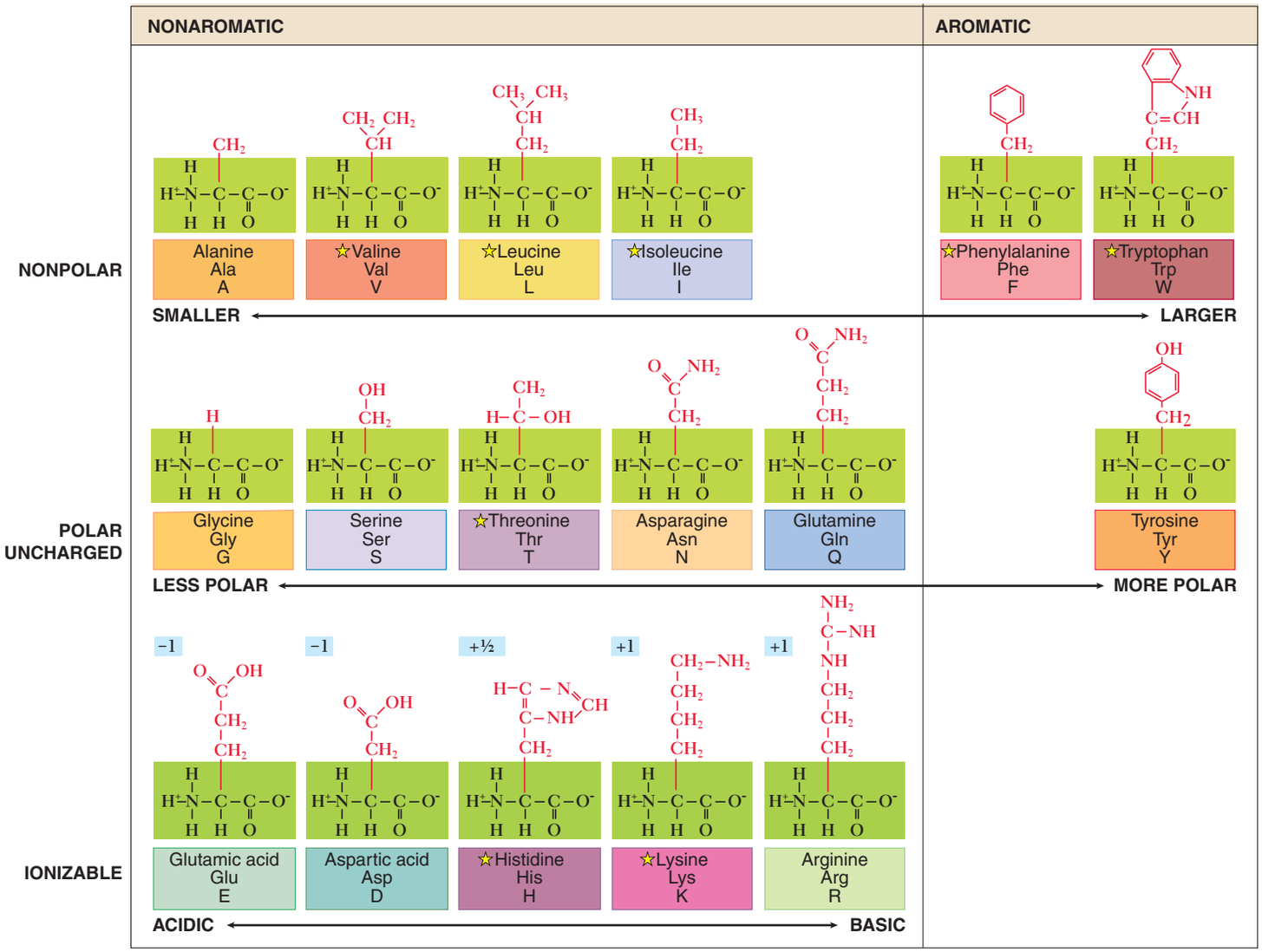
Most polypeptides do not exist as a straight chain. Instead, they show a *secondary structure* in which the chains are coiled or bent into pleated sheets. The most common type of coil takes a clockwise direction and is called an *alpha helix*. In this type of secondary structure, the coils of the protein chain resemble a spiral staircase, with the coils stabilized by hydrogen bonds between successive turns of the spiral. Pleated *beta sheets* are likewise stabilized by hydrogen bonds. This stabilizing function of hydrogen bonding in protein structure is critical. A commonly occurring pattern of alpha helices and/or beta sheets within the secondary structure is called a *motif*. A motif often imparts a specific function to each protein in which it appears.

Just as a primary structure polypeptide chain can pleat or bend into a helical secondary structure, so too can a secondary structure protein chain undergo other contortions and be further twisted so that a globular-shaped *tertiary structure* of a protein is formed. In this structure, the polypeptide chain is so twisted that its coils touch one another in many places, and "spot welds," or interlocking connections, occur. Some of these linkages may be strong covalent bonds between amino acid units that exist in the same chain (Box 2-4). Most of the linkages are ionic bonds. Hydrogen bonds, and other weak attractions also help stabilize the twisted and convoluted loops of the structure. A tertiary structure may include several complicated "knots" called *domains*. Each specific type of domain has specific functions that contribute to the overall function of a protein.

FIGURE 2-25

Basic structural formula for an amino acid. Note relationship of the side group (R), amino group, and carboxyl group to the alpha carbon. The amino group (NH_2) is depicted in the Figure as H_2N to show that the *nitrogen* atom of the group bonds to the alpha carbon.





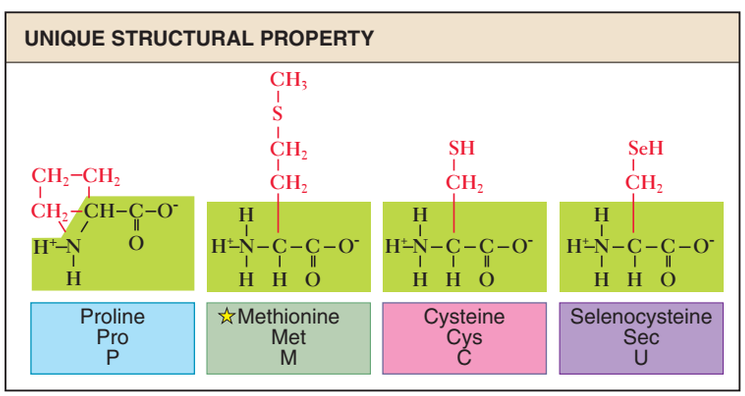


FIGURE 2-26

The standard amino acids of the human body. The full name for each is given, followed by the three-letter abbreviation and the one-letter symbol. The structural formulas show that each amino acid has the same chemical backbone (green highlight) but differs from the others in the side, or R, group that it possesses (red). Essential amino acids are indicated by a star preceding the name. Notice the great variety of sizes among the amino acids, the different polarities or charges, the different levels of acidity, and the other differing chemical characteristics. Like different kinds of blocks in a set of toy blocks, this makes it possible to build different proteins with a wide variety of chemical characteristics and functions. (Additional types of amino acids may be added to proteins after their initial structure is formed.)

The red muscle protein myoglobin, which is discussed in Chapter 12 is an example of a protein with a tertiary structure.

A *quaternary structure* protein is one that contains clusters of more than one polypeptide chain, all linked together into one giant molecule. Antibody molecules that protect us from disease (see Chapter 24) and hemoglobin molecules in red blood cells (see Chapter 20) are examples.

A group of proteins called *chaperones*, which are present in every body cell, acts to direct the steps required for many proteins to fold into the twisted and convoluted shape required for them to function properly (Box 2-5). Some of these chaperone proteins are called *chaperonins*. Inappropriate folding of some proteins is known to be associated with certain diseases. The critically important chemical reactions that permit chaperonins to organize proteins into the different organizational levels required for a particular function can occur only within a very narrow pH range. Maintaining acid-base balance and normal pH in body cells and fluids is discussed in depth in Chapter 33.

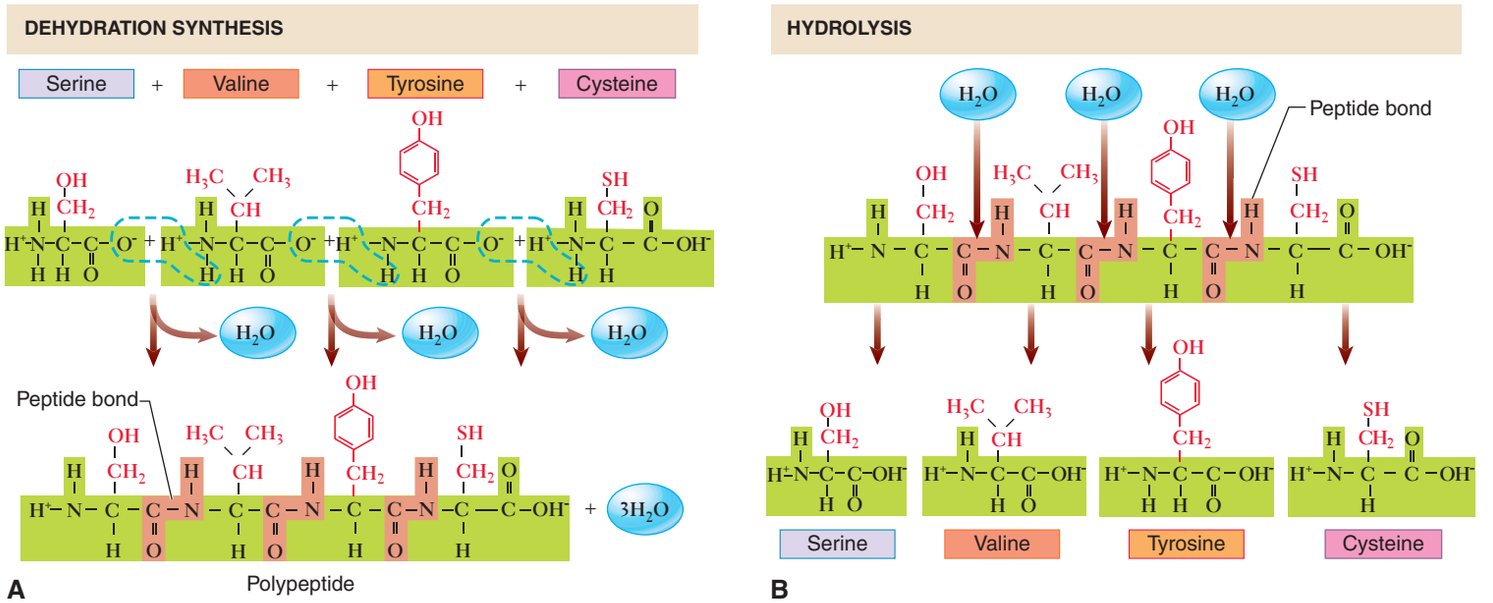


FIGURE 2-27

Formation (dehydration synthesis) and decomposition (hydrolysis) of a polypeptide. A, Linkage of four amino acids by three peptide bonds resulting in the dehydration synthesis of a polypeptide chain and three molecules of water. **B,** Decomposition (hydrolysis) reaction resulting from the addition of three molecules of water. Peptide bonds are broken and individual amino acids are released.

IMPORTANCE OF PROTEIN SHAPE

Properly folded protein molecules are highly organized in their structure and show a very definite relationship between their shape and their function. The final, functioning shape for a protein is often called its *native state.* The native states of the strong **structural proteins** found in tendons and ligaments are fibrous, or threadlike, insoluble, and very stable (Figure 2-29). In contrast, **functional proteins** such as enzymes, certain protein hormones, antibodies, albumin, and hemoglobin have native states that are globular (ball-shaped), often soluble, and have chemically reactive regions. Table 2-5 summarizes some of the important roles played by proteins.

Simply stated, proteins perform their roles by having the right shape for their job—whatever that job is. Given the nearly infinite variety of different amino acid sequences and the complexity of how proteins are folded, you can see that the body can make just about any tool or building block it needs for a variety of jobs. Consider also that if one of the body's proteins loses its shape, or **denatures,** it will lose its function (Figure 2-30). If a protein is built incorrectly or it denatures, the whole body may be in peril (Box 2-6). Factors that can cause a protein to denature include changes in temperature, changes in pH, radiation, and the presence of certain hazardous

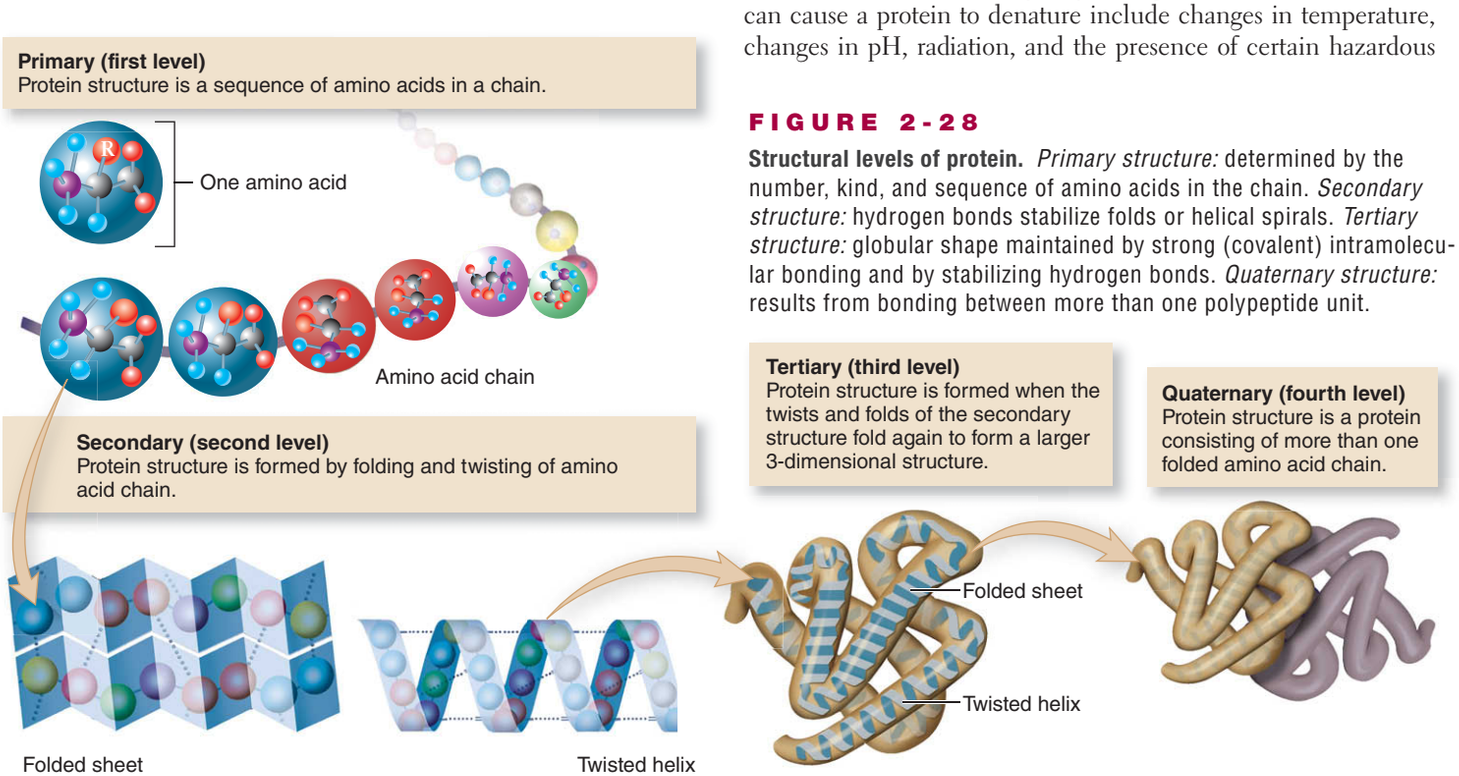


FIGURE 2-28

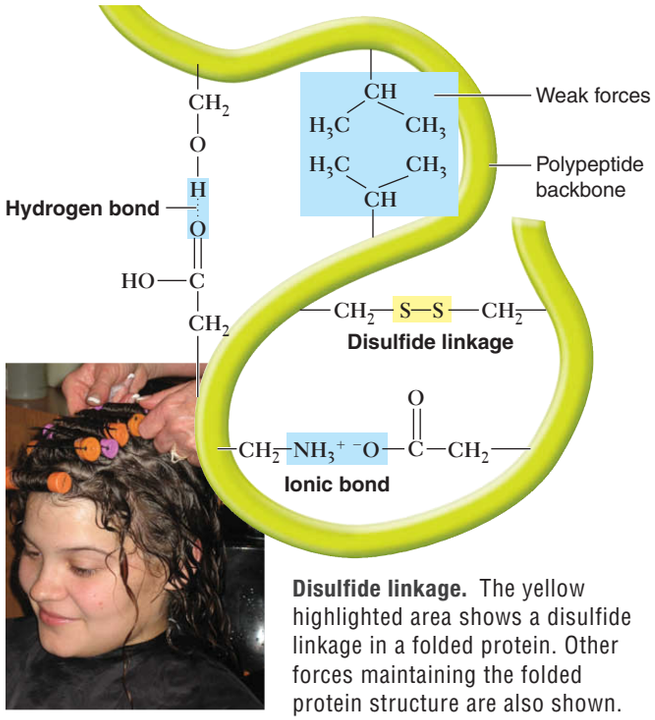
Structural levels of protein. *Primary structure:* determined by the number, kind, and sequence of amino acids in the chain. *Secondary structure:* hydrogen bonds stabilize folds or helical spirals. *Tertiary structure:* globular shape maintained by strong (covalent) intramolecular bonding and by stabilizing hydrogen bonds. *Quaternary structure:* results from bonding between more than one polypeptide unit.

Box 2-4 | FYI

Disulfide Linkages

Hair contains a threadlike fibrous protein called *keratin* that is rich in the sulfur-containing amino acid cysteine. The protein chains in keratin are linked in numerous places by S—S bonds that form between cysteines within each hair shaft. These bonds are called *disulfide linkages*.

The object of a "permanent wave" is to change the arrangement of these bonds by breaking the naturally occurring disulfide linkages and then causing them to reform in another pattern. Strong chemicals are applied to the hair that break the existing or "natural" disulfide linkages. The hair is then curled on some type of roller and then another chemical is applied that causes the disulfide bridges to become reestablished in the new or reoriented configuration.

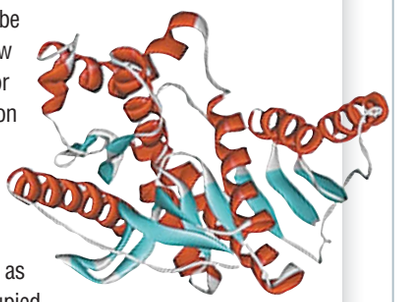


Disulfide linkage. The yellow highlighted area shows a disulfide linkage in a folded protein. Other forces maintaining the folded protein structure are also shown.

Box 2-5 | FYI

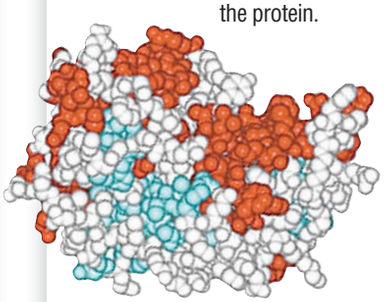
Visualizing Proteins

Only a few decades ago, the usual way for a biochemist to demonstrate the three-dimensional structure of a protein molecule was by building wooden ball-and-stick models. These models were less than ideal because they took a long time to build, often fell apart, and were not easy to handle. Now there are many sophisticated, but easy-to-use, computer programs that can "build" protein molecules on the monitor screen. These *virtual protein molecules* can be rotated and viewed from nearly any angle. They can also be changed when trying to design a new protein molecule for therapeutic or other purposes. Here, three common types of protein models are shown. The *ribbon model* shows the areas where alpha helices and folded sheets form within the molecule. The *space-filling model* shows each atom as a "cloud" filling up the space occupied by that atom. The *surface-rendering model* shows the three-dimensional boundaries of the whole protein molecule, often also color-coding for charged regions on the surface of the protein.



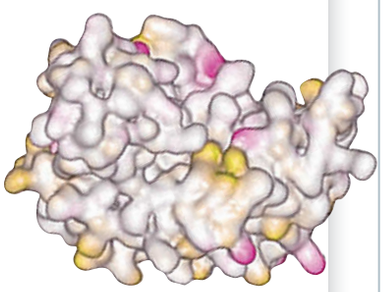
Ribbon model

Helix
Folded sheet
Unorganized area



Space-filling model

Helix
Folded sheet
Unorganized area



Surface-rendering model

Positive charge
Negative charge
Unchanged area

Three ways to visualize the same folded protein molecule.

chemicals. Depending on the circumstances, restoring the proper chemical environment of a protein may allow it to *renature* to its native state and begin functioning normally once again.

One last thing to remember about protein shape is that it is often dynamic. That is, proteins often move as they perform their functions. Besides the occasional bend or twist, many proteins have moving parts that resemble hinges, spinning rotors, and grabbing pinchers that permit proteins to move in interesting and useful ways—as you shall see in later chapters.

| QUICK CHECK |

25. What element is present in all proteins but not in carbohydrates?
26. Identify the building blocks of proteins and explain what common chemical features they all share.
27. Explain the four levels of protein structure.

Nucleic Acids and Related Molecules

DNA AND RNA

Survival of humans as a species—and survival of every other species—depends largely on two kinds of **nucleic acid** molecules. Almost everyone has heard or seen their abbreviated names, DNA and RNA, but their full names are much less familiar. They are deoxyribonucleic and ribonucleic acids (i.e., DNA and RNA). Nucleic acid molecules are polymers of thousands and thousands of smaller molecules called **nucleotides**—deoxyribonucleotides in DNA molecules and ribonucleotides in RNA molecules.

A *deoxyribonucleotide* consists of the pentose sugar named *deoxyribose*, a nitrogenous base (either adenine, cytosine, guanine, or thymine), and a phosphate group (Figure 2-31). *Ribonucleotides* are similar but contain the sugar ribose instead of deoxyribose and the nitrogenous base uracil instead of thymine (Table 2-6).

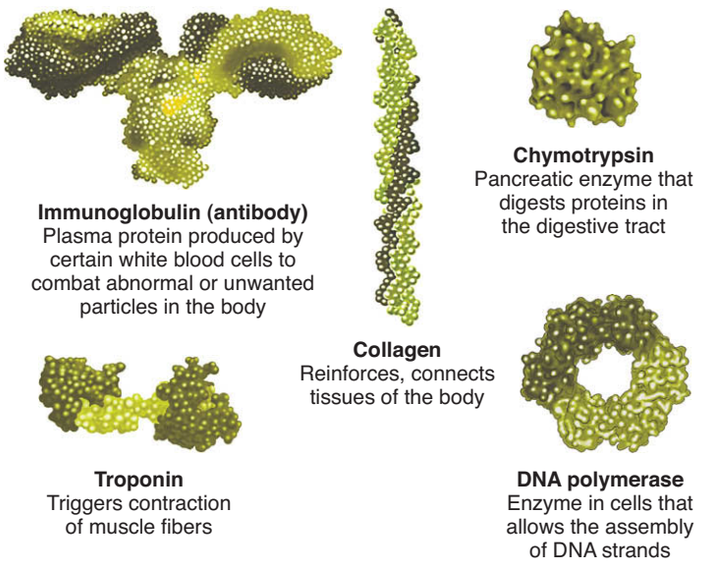


FIGURE 2-29

Variety of protein shapes. These images of folded protein structures provide examples of the wide variety of shapes that proteins have in the human body.

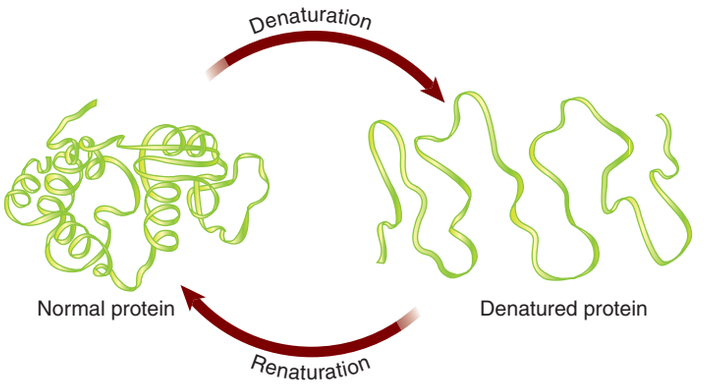


FIGURE 2-30

Denatured protein. When a protein loses its normal folded organization and thus loses its functional shape, it is called a *denatured protein.* Denatured proteins are not able to function normally. However, if the protein shape is restored, the *renatured protein* may resume its normal function.

Two of the bases in a deoxyribonucleotide, specifically adenine and guanine, are called *purine bases* because they derive from *purine.* Purines have a double ring structure. Cytosine and thymine derive from *pyrimidine*, so they are known as *pyrimidine bases.* Pyrimidines have a single ring structure. The pyrimidine base uracil replaces thymine in RNA. More about the differences between DNA and RNA is discussed in Chapter 5.

DNA molecules, the largest molecules in the body, are very large polymers composed of many nucleotides. The nucleotides

TABLE 2-5 Major Functions of Human Protein Compounds

FUNCTION	EXAMPLE
Provide structure	Structural proteins include keratin of skin, hair, and nails; parts of cell membranes; tendons
Catalyze chemical reactions	Lactase (enzyme in intestinal digestive juice) catalyzes chemical reaction that changes lactose to glucose and galactose
Transport substances in blood	Proteins classified as albumins combine with fatty acids to transport them in form of lipoproteins
Communicate information to cells	Insulin, a protein hormone, serves as chemical message from islet cells of the pancreas to cells all over the body
Act as receptors	Binding sites of certain proteins on surfaces of cell membranes serve as receptors for insulin and various other hormones
Defend body against many harmful agents	Proteins called *antibodies* or *immunoglobulins* combine with various harmful agents to render those agents harmless
Provide energy	Proteins can be metabolized for energy

Box 2-6 | HEALTH matters

Phenylketonuria

Phenylketonuria (PKU) is a genetic disease caused by the lack of a single enzyme *(phenylalanine hydroxylase)* required to break down or metabolize the amino acid phenylalanine. PKU is one example of a group of genetic diseases called *inborn errors of metabolism,* which are discussed in Chapter 37. In this instance, phenylalanine metabolism is impaired because the gene required to produce the necessary enzyme for its breakdown is defective. The disease occurs in 1 of every 12,000 births in North America and, if untreated, causes a buildup of phenylalanine in the tissues that results in severe mental retardation and other neurobehavioral symptoms. Traditional treatment of PKU consisted of strict dietary restriction of phenylalanine-containing foods during the first 4 to 8 years of life, followed by some liberalization of diet. Continuation of the diet into adulthood may be necessary (see Figure).



PKU Diet. A preadolescent girl with PKU prepares a special diet low in phenylalanine.

Since the mid-1960s every state has mandated testing of newborn infants for PKU before discharge from the nursery. As a result, the number of undiagnosed and untreated PKU cases that formerly resulted in mental retardation has decreased dramatically. A phenylalanine level above 4 mg/dl is considered positive for the disease. However, the screening procedure, called the *Guthrie test,* is less accurate if blood is drawn before the infant is 48 hours old. Because early discharge of both the mother and baby from the hospital after childbirth is becoming more common, a second, or repeat, screening test at 2 weeks of age may be necessary. The test is performed on a drop of blood, which is obtained from the baby by a *heel stick* and adsorbed onto a piece of filter paper.

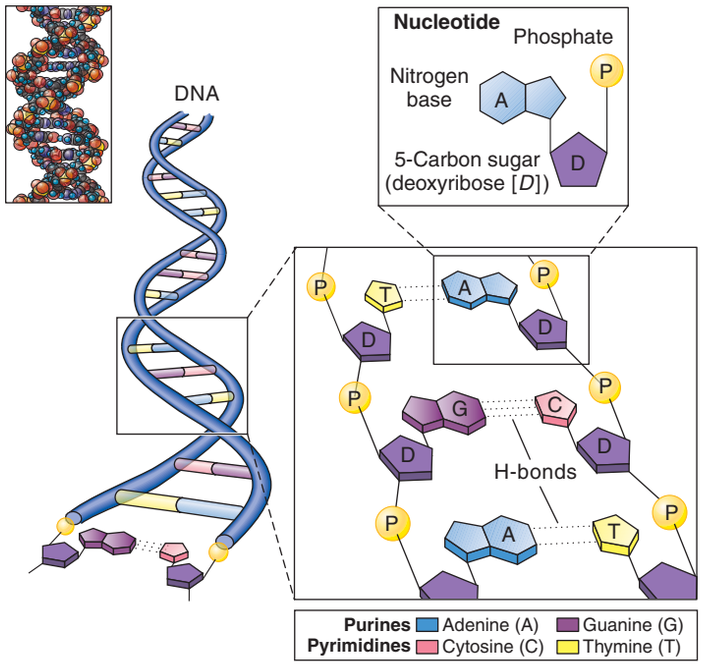


FIGURE 2-31

The DNA molecule. Representation of the DNA double helix showing the general structure of a nucleotide and the two kinds of *base pairs:* adenine (A) (blue) with thymine (T) (yellow) and guanine (G) (purple) with cytosine (C) (red). Note that the G–C base pair has three hydrogen bonds and an A–T base pair has two. Hydrogen bonds are extremely important in maintaining the structure of this molecule.

are joined together, saccharide group to phosphate group, by dehydration synthesis (condensation) to form a long sugar-phosphate backbone. Two of these long polynucleotide chains compose a single DNA molecule. The chains coil around each other to form a double helix. A helix is a spiral shape similar to the shape of a wire in a spring. Figure 2-31 is a diagram of the double-helix DNA.

Each helical chain in a DNA molecule has its phosphate-sugar backbone toward the outside and its bases pointing inward toward the bases of the other chain. More than that, each base in one chain is joined to a base in the other chain by means of either two or three hydrogen bonds to form what is known as a *base pair.* The two polynucleotide chains of a DNA molecule are thus held together by hydrogen bonds between the two members of each base pair (see Figure 2-31).

One important principle to remember is that only two kinds of base pairs are present in DNA. What are they? Symbols used to represent them are A≡T and G≡C. Although a DNA molecule contains only these two kinds of base pairs, it contains millions of them—more than 100 million pairs estimated in one human DNA molecule! Two other impressive facts are that the millions of base pairs occur in the same sequence in all the millions of DNA molecules in one individual's body but in a slightly different sequence in the DNA of all other individuals. In short, the base pair sequence in DNA is unique to each individual. This fact has momentous significance because DNA functions as the molecule of heredity. It has a weighty responsibility: that of passing the traits of one generation to the next. DNA accomplishes this feat by acting as an "information molecule" that stores the master code of all the recipes (the *genes*) needed to make the various RNA and protein molecules of the body.

The details of how the information is stored and retrieved by the cells is introduced in Chapter 5, and then Chapter 37 features even more discussion of the processes of heredity.

Most types of RNA molecules consist of a single strand, but the strand often folds on itself to form a compact folded structure. Each RNA strand is a sequence of ribonucleotides that is essentially copied from a portion of a DNA molecule. Thus RNA molecules act as "temporary copies" of the master code of hereditary information in the DNA molecules. These RNA "copies" are involved in the process of protein synthesis.

Figure 2-32 shows a type of RNA called *transfer RNA (tRNA).* tRNA is used by the cell to "grab" a specific amino acid and place it in the correct sequence when building a primary protein strand. The correct location in the sequence is guaranteed by matching tRNA's three-base *anticodon* to the complementary *codon* copied from a gene (a "protein recipe" in the genetic code). Chapter 5 outlines the process by which all of this takes place in the cell.

Instead of acting as "information molecules," some RNA molecules regulate cell function. For example, a type of RNA enzyme sometimes called a *ribozyme* is involved in editing the code of RNA strands by removing sections of the code and joining the remaining pieces. A recently discovered type of *double-strand RNA (dsRNA)* is now known to regulate cell function by silencing gene expression in a process called *RNA interference (RNAi).* These processes are discussed further in Chapter 5.

Thus we can say that RNA can act as either an "information molecule" or as a regulatory molecule.

TABLE 2-6 Comparison of DNA and RNA Structure

	DNA	RNA
Polynucleotide strands	Double; very long	Single or double; short
Sugar	Deoxyribose	Ribose
Base pairing	Adenine-thymine (A-T)	Adenine-uracil (A-U)
	Guanine-cytosine (G-C)	Guanine-cytosine (G-C)

NUCLEOTIDES AND RELATED MOLECULES

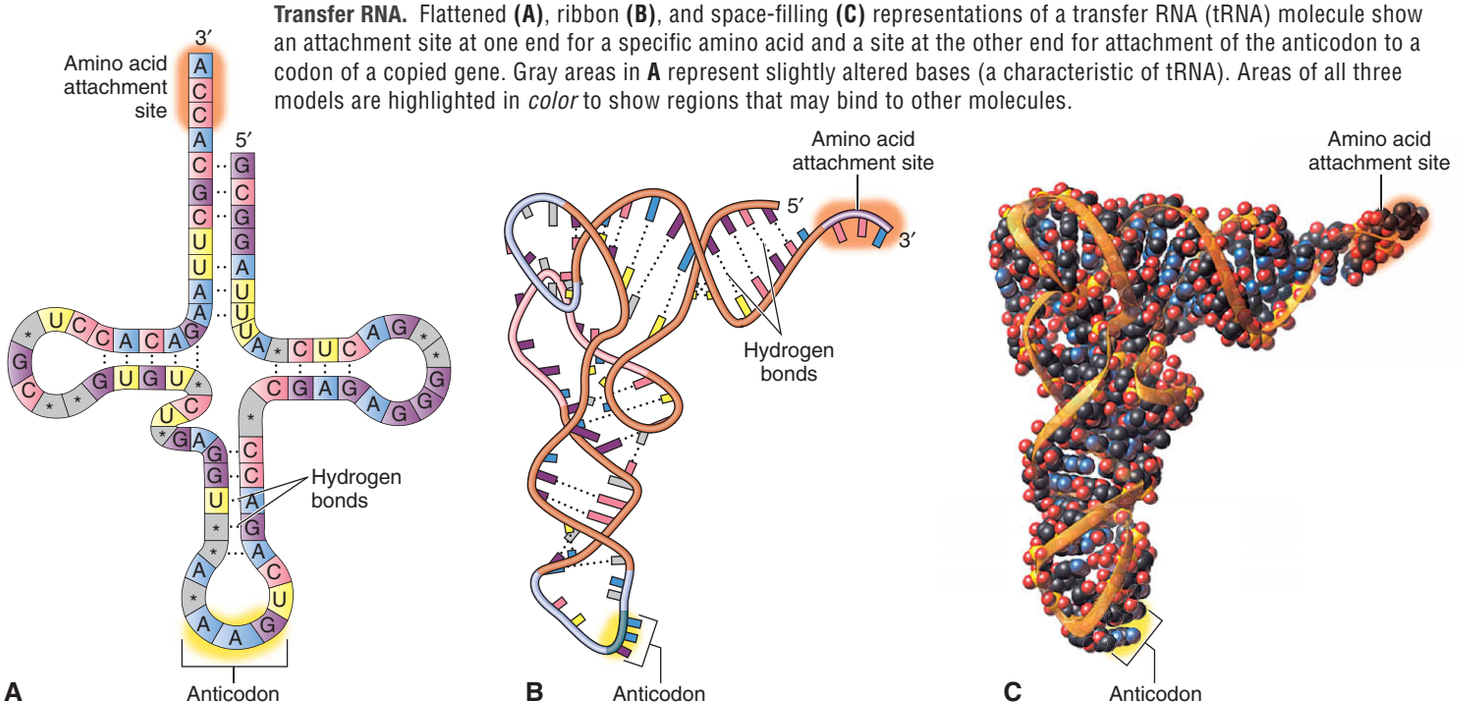
Besides joining together to form nucleic acids, nucleotides and related molecules also play other important roles in the body.

Adenosine triphosphate (ATP) is a very important molecule composed of an adenine and ribose sugar (a combination called *adenosine*) to which are attached a string of three phosphate groups (Figure 2-33, A). Thus ATP is really an adenine ribonucleotide with two "extra" phosphate groups attached. The "squiggle" lines indicate covalent bonds that link the phosphate groups. These bonds are called **high-energy bonds** because when they are broken during catabolic chemical reactions, the energy released is used to form new compounds. The energy carried by ATP can thus be used in doing the body's work—the work of muscle contraction and movement, of active transport, and of biosynthesis (Figure 2-33, B).

Because ATP is the form of energy that cells generally use, it is an especially important organic molecule. ATP is a molecule that can pick up energy and give it to another chemical process; therefore, it is often called the *energy currency* of cells. A set of enzyme reactions releases the energy that is stored in ATP by splitting it into *adenosine diphosphate (ADP)* and an inorganic phosphate group. It

FIGURE 2-32

Transfer RNA. Flattened **(A)**, ribbon **(B)**, and space-filling **(C)** representations of a transfer RNA (tRNA) molecule show an attachment site at one end for a specific amino acid and a site at the other end for attachment of the anticodon to a codon of a copied gene. Gray areas in **A** represent slightly altered bases (a characteristic of tRNA). Areas of all three models are highlighted in *color* to show regions that may bind to other molecules.



is also possible to split ADP into *adenosine monophosphate (AMP)* and phosphate, with the release of energy. In this case the bond between the second and third phosphate groups is broken.

In prolonged or intense exercise, when ATP is in short supply, muscles turn to *creatine phosphate (CP)* for extra energy. Creatine phosphate is another high-energy molecule made up of an amino acid derivative and a phosphate connected with a high-energy bond. When CP releases its phosphate group, the energy can be used to add a phosphate to ADP, thus "recharging" ATP. In extreme cases, a cell may use ADP for energy by breaking another phosphate bond.

Chapters 4 and 30 discuss in detail the metabolic pathways that are involved in ATP synthesis and breakdown. A cell at rest has a relatively high ATP concentration, whereas an active cell has less ATP but is constantly rebuilding its stores. An exhausted cell has a high ADP concentration and very low levels of ATP. It must resynthesize needed ATP to sustain its activity over time. Fortunately, cells at rest can recycle ADP and ATP and then reverse the cycle, thus reusing small amounts of ATP on a continuing basis. Exercise physiologists estimate that the body can use up to 0.5 kilograms (1.1 pounds) of ATP per minute during very strenuous physical activity. If reuse was impossible, we would require about 40 kilograms (88 pounds) of ATP per day to remain active.

Other energy-transferring nucleotides such as nicotinamide adenine dinucleotide (NAD^+) and flavin adenine dinucleotide (FAD) are also used by cells to transfer energy among molecules (Figure 2-34, A). NAD^+ and FAD act as coenzymes (see Table 2-6) to shuttle energy-carrying particles (electrons) from one metabolic pathway to another during the many complicated steps of transferring energy from food molecules to ATP (Figure 2-34, B). The entire process of energy transfer, including the role of NAD^+ and FAD, is discussed in detail in Chapter 30.

Nucleotides are also sometimes used as a signal inside the cell. ATP is used throughout the body as a signal between cells. ATP can also break down to a one-phosphate molecule called *cAMP (cyclic*

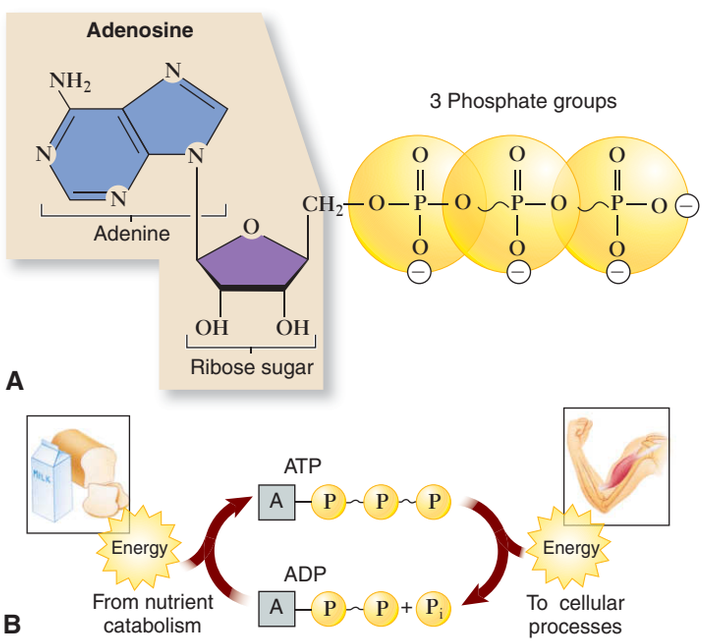


FIGURE 2-33

Adenosine triphosphate (ATP). A, Structure of ATP. A single adenosine group (A) has three attached phosphate groups (P). High-energy bonds between the phosphate groups can release chemical energy to do cellular work. **B,** General scheme of the ATP energy cycle. ATP stores energy in its last high-energy phosphate bond. When that bond is later broken, energy is transferred as important intermediate compounds are formed. The adenosine diphosphate (ADP) and phosphate groups that result can be resynthesized into ATP, thereby capturing additional energy from nutrient catabolism. Note that energy is transferred from nutrient catabolism to ADP, thus converting it to ATP, and energy is transferred *from* ATP to provide the energy required for anabolic reactions or cellular processes as it reverts back to ADP.

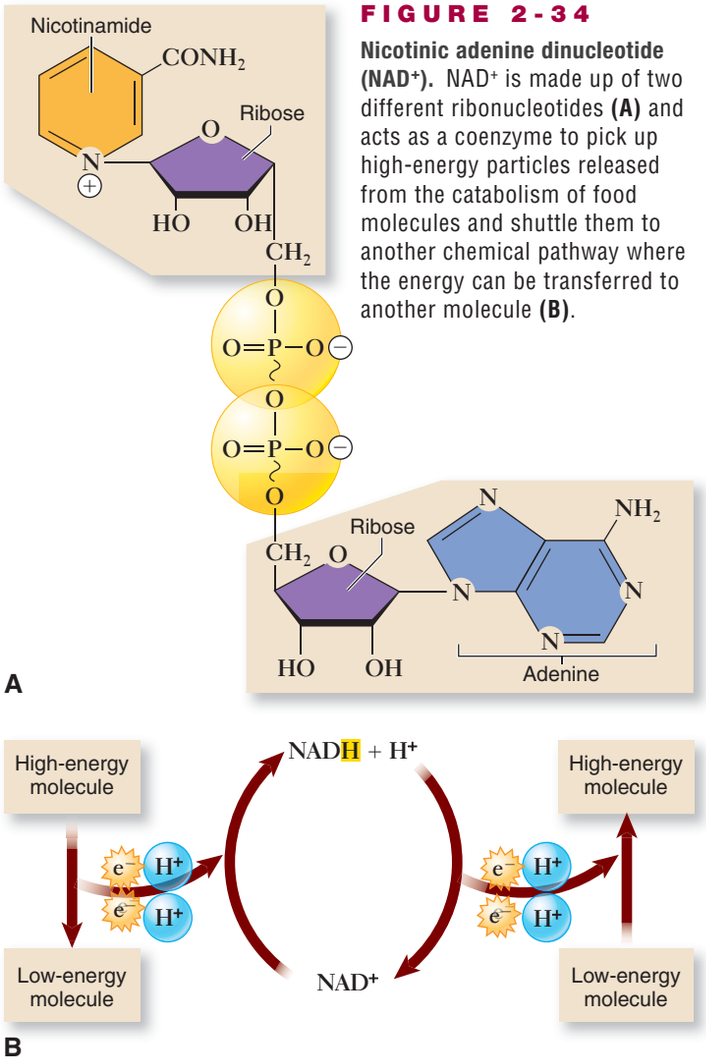


FIGURE 2-34

Nicotinic adenine dinucleotide (NAD^+). NAD^+ is made up of two different ribonucleotides **(A)** and acts as a coenzyme to pick up high-energy particles released from the catabolism of food molecules and shuttle them to another chemical pathway where the energy can be transferred to another molecule **(B)**.

adenosine monophosphate) that is used as an intracellular signal within cells. This role of cAMP is outlined in Chapters 13 and 18.

Combined Forms

You have already noticed that large molecules can be joined together to form even larger molecules. Sometimes, only a small addition or alteration is made. For example, in the case of adenosine triphosphate (ATP), two extra phosphate groups are added to an adenine-containing RNA nucleotide. This gives the nucleotide a completely different function. Instead of becoming involved in storing or transmitting genetic information, the ATP molecule transfers energy from one chemical pathway to another. We will learn much more about ATP later. The point now is that macromolecules can be joined to other molecules to make them even larger and to change their functions.

Table 2-3 lists some of the combined or altered macromolecules you will encounter in your study. Notice also the many different important functions performed by these molecules. The names of the combined molecules usually tell you what is in them. *Lipoproteins* contain lipid and protein groups combined into a single molecule. *Glycoproteins* contain carbohydrate (*glyco*, "sweet") and protein. Often, the base word (*protein* in this case) indicates which component is dominant. The prefix represents the component found in a lesser amount. Thus glycoproteins have more protein than they do carbohydrate. Review the examples of combined forms in Table 2-3 and their functions in the body.

| QUICK CHECK |

28. Name two important *nucleic acids.*
29. What is a *nucleotide*?
30. What is meant by the term *base pair?*
31. What are some roles of *nucleotides* in the body?

the BIG picture

The Chemical Basis of Life

The importance of the concept of organization at all levels of body structure and function was introduced in Chapter 1 and will be reinforced as you study the individual organ systems of the body in subsequent chapters of the text. Understanding the information in this chapter is a critical first step in connecting the chemistry of life with a real understanding of how the body functions and the relationships that exist between differing functions and body structures.

How the basic chemical building blocks of the body are organized and how they relate to one another are key determinants in understanding normal structure and function, as well as understanding pathological anatomy and disease.

As you learn about the structure and functioning of the various organ systems of the body, the information contained in this chapter will take on new meaning and practical significance. It will help you fully understand and answer many questions that require you to integrate otherwise isolated factual information to make anatomy and physiology emerge as living and dynamic topics of personal interest. Consider the following questions. Each one relates to the study of one or more organ systems covered in subsequent chapters. Your ability to answer these and many other questions correctly will require knowledge of basic chemistry.

- How do common antacids, such as Tums or Rolaids, work?
- Is an electrolyte-rich sports drink better than plain water in replacing fluids lost during prolonged, vigorous exercise?
- Why are high dietary levels of saturated fat considered inappropriate?
- How do we digest our food?
- Why must individuals with diabetes restrict their intake of sugars and other sweets?
- How do muscles contract or nerve impulses race from one body area to another?
- Why do some people inherit a particular disease and others do not?
- What food substances produce the most energy?
- Why does breathing oxygen at the end of a marathon run help an athlete recover more quickly?

These are the types of real-world, end-of-chapter questions that you will encounter throughout the text that require the application of basic chemistry. Refer often to the information in this chapter as you formulate your answers. Think of chemistry as an important part of the Big Picture in your study of anatomy and physiology.

MECHANISMS of DISEASE

CHEMICALS OUT OF BALANCE

As we have learned in this chapter, all the various classes of chemicals in the body each have their particular functions in maintaining the life of the body. If the balances among various groups of chemicals fluctuate too far from their set point values, the homeostatic balance of the body is threatened.

Let's examine just one common example of such an imbalance. The carbon dioxide (CO_2) concentration in the blood will climb too high, a condition called **hypercapnia,** when the respiratory system fails to remove it from the blood at the normal rate. Thus we have a CO_2 imbalance. This will have several effects. For one, the high CO_2 levels will inhibit cell metabolism and thus reduce the normal activity of the body. For another, because CO_2 tends to form an acid, the pH of the body's internal environment will drop to below the set point level—a condition called **acidosis.** Acidosis, in turn, may disrupt the shapes of proteins throughout the body and thus interfere with the normal structure and function of the body. Unless CO_2 balance is restored quickly, a person will die.

Various elements of the scenario we just described are touched on later in appropriate places in the book. However, this is just one of many examples of chemical imbalances that can serve as a mechanism of disease. Nutrient imbalances, ion imbalances, and so on, can all be life threatening.

Missing and Damaged Molecules

We all know that if we don't eat, we die. Of course, the process of digestion is the method by which we absorb new molecules into our internal environment. These nutrients are needed to replace molecules that have been lost or have been used up in the manufacture of molecules needed for body structure and function. Thus digestive and eating disorders are in fact disorders of "missing molecules."

We've learned in this chapter that the genes in DNA molecules serve as "recipes" for the structural and functional proteins of the body, which in turn make many other types of molecules in the body such as lipids and carbohydrates. If even one amino acid is missing or out of place, it may not fold correctly and thus the entire protein (and whatever molecule is made by the protein) will be ruined. Even if the protein has a normal sequence of amino acids, it may not fold correctly because of an improper pH or extreme body temperature. Although some types of molecules can be obtained from our food, others must be made in the body. If certain genes are damaged or missing, we cannot manufacture the chemicals needed for proper body function. For example, in "brittle bone disease" or *osteogenesis imperfecta*, the body fails to make normal *collagen*. Collagen is a structural protein needed to hold bones and other tissues together. Consequently, in a person with osteogenesis imperfecta, the body's bones are brittle and cannot bear much weight. Most genetic disorders are really disorders of "missing or damaged molecules."

Molecules in the body can also be damaged by physical agents such as radiation or other chemicals. For example, the ultraviolet radiation of the sun can sometimes damage the DNA in skin and cause skin cancer, or radiation from radioactive materials can cause a body-wide breakdown of molecules that results in **radiation sickness.**

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Check out ***Radioactivity*** online at ***A&P Connect*** for more on radiation and its adverse effect on health.

Some chemicals called **toxins** that enter the body can cause damage to our own molecules. Toxins, or poisons, cause their damage by destroying our molecules, combining with our molecules to render them useless, or otherwise disrupting the normal chemical balance and chemical activity of our bodies. For example, *carbon monoxide (CO)* is a gas that binds to hemoglobin in our blood so tightly that the hemoglobin can no longer carry the oxygen needed for life. Mercury (Hg), a toxic metal that was once used frequently in industry and health care, can enter cells and bind to sulfur-containing molecules in the organelles. Mercury can thus damage cell functions throughout the body.

Most diseases are ultimately chemical disorders—missing or malfunctioning molecules. Watch for these chemical problems as we explore mechanisms of disease in later chapters.

LANGUAGE OF SCIENCE *(continued from p. 33)*

enzyme
(EN-zime)
[*en-* **in,** *-zyme* **ferment]**

exchange reaction
[*ex-* **from,** *-change* **to change,** *re-* **again,** *-action* **action]**

functional group
(FUNK-shun-al groop)
[*function-* **to perform,** *-al* **relating to]**

functional protein
(FUNK-shun-al PRO-teen)
[*function-* **to perform,** *-al* **relating to,** *prote-* **primary,** *-in* **substance]**

high-energy bond
[*en-* **in,** *-erg* **work,** *-y* **state,** *bond* **band]**

hydrolysis
(hye-DROL-i-sis)
[*hydro-* **water,** *-lysis* **loosening]**

ion
(EYE-on)
[*ion* **to go]**

ionic bond
[*ion* **to go,** *bond* **band]**

isotope
(EYE-so-tope)
[*iso-* **equal,** *-tope* **place]**

lipid
(LIP-id)
[*lipi-* **fat,** *-id* **form]**

metabolism
(meh-TAB-o-lizem)
[*metabol-* **change,** *-ism* **condition]**

molecule
(MOL-eh-kyool)
[*mole-* **mass,** *-cule* **small]**

nonpolar
(non-PO-lar)
[*non-* **not,** *-pol-* **pole,** *-ar* **relating to]**

nucleic acid
(noo-KLAY-ik ASS-id)
[*nucle-* **nut kernel,** *-ic* **relating to,** *acid* **sour]**

nucleotide
(NOO-klee-oh-tide)
[*nucleo-* **nut or kernel,** *-ide* **chemical]**

octet rule
(ok-TET rool)
[*octet* **group of eight]**

peptide bond
(PEP-tyde bond)
[*pept-* **digest,** *-ide* **chemical]**

pH
(pee AYCH)
[abbreviation for *potenz* **power,** *hydrogen* **hydrogen]**

phospholipid
(fos-fo-LIP-id)
[*phospho-* **phosphorus,** *-lip-* **fat,** *-id* **form]**

polar
(PO-lar)
[*pol-* **pole,** *-ar* **relating to]**

prostaglandin
(pross-tah-GLAN-din)
[*pro-* **before,** *-sta-* **stand,** *-gland-* **acorn,** *-in* **substance]**

protein
(PRO-teen)
[*prote-* **primary,** *-in* **substance]**

radioactivity
(ray-dee-o-ak-TIV-it-ee)
[*radio* **send out rays]**

radioisotope
(ray-dee-oh-EYE-sotope)
[*radio-* **send out rays,** *-iso-* **equal,** *-tope* **place]**

reversible reaction
(ree-VER-si-bul ree-AK-shun)
[*re-* **again,** *-vers-* **turn,** *-ible* **able to,** *re-* **again,** *-action* **action]**

steroid
(STAYR-oid)
[*ster-* **sterol,** *-oid* **like]**

structural protein
(STRUK-cher-al PRO-teen)
[*structura-* **arrangement,** *-al* **relating to,** *prote-* **primary,** *-in* **substance]**

synthesis
(SIN-the-sis)
[*synthes-* **put together,** *-is* **process]**

triglyceride
(try-GLISS-er-yde)
[*tri-* **three,** *glycer-* **sweet (glycerine),** *-ide* **chemical]**

LANGUAGE OF MEDICINE

acidosis
(ass-i-DOE-sis)
[*acid-* **sour,** *-osis* **condition]**

hypercapnia
(hye-per-KAP-nee-ah)
[*hyper-* **above,** *-capn-* **vapor (CO_2),** *-ia* **condition]**

radiation sickness
(ray-dee-AY-shun SIK-ness)
[*radia-* **send out rays,** *-tion* **process]**

toxin
(TOK-sin)
[*tox-* **poison,** *-in* **substance]**

CASE study



This year, during her college's spring break, Calleigh is visiting Florida for the first time. On the first night of her vacation, she and her friends go out to dinner. Feeling rather adventurous, Calleigh eats raw oysters as an appetizer. Unfortunately, the oysters she ate had high concentrations of bacteria, and 24 hours later, Calleigh is experiencing the "adventure" of food poisoning. Among her symptoms are nausea, vomiting, abdominal pain, and diarrhea.

1. With continued vomiting, Calleigh keeps losing _____ from her stomach, which could make her entire body too _____.
   a. acid; acidic
   b. base; basic
   c. acid; basic
   d. base; acidic
2. When we talk about measuring the pH of a substance, we are measuring the concentration of what ions in that substance?
   a. Oxygen ions
   b. Carbon ions
   c. Phosphate ions
   d. Hydrogen ions

Finally, after another 24 hours, Calleigh is able to keep clear liquids down.

3. Why should she not drink just plain water?
   a. Water cannot replenish the electrolytes she has lost.
   b. Flavored liquids will more effectively stimulate her appetite.
   c. Water can irritate the stomach lining.
   d. Plain water is just fine; it will quickly replace her body's lost fluid.

When Calleigh feels well enough to try eating something, her first food items should provide energy but be easy to digest.

4. Which organic molecule best fits that description—high energy, easily digested?
   a. Protein
   b. Carbohydrates
   c. Triglycerides
   d. Nucleic acids

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

BASIC CHEMISTRY

A. Elements and compounds (Figure 2-1)
   1. Matter—anything that has mass and occupies space
   2. Element—simple form of matter, a substance that cannot be broken down into two or more different substances
      a. There are 26 elements in the human body
      b. There are 11 *major elements*, 4 of which (carbon, oxygen, hydrogen, and nitrogen) make up 96% of the human body (Figure 2-2)
      c. There are 15 *trace elements* that make up less than 2% of body weight
   3. Compound—atoms of two or more elements joined to form chemical combinations

B. Atoms (Figure 2-3)
   1. The concept of an atom was proposed by the English chemist John Dalton
   2. Atomic structure—atoms contain several different kinds of subatomic particles; the most important are:
      a. Protons (*p*)—positively charged subatomic particles found in the nucleus
      b. Neutrons (*n*)—neutral subatomic particles found in the nucleus
      c. Electrons (*e*)—negatively charged subatomic particles found in the electron cloud (Figure 2-4)
   3. Atomic number and mass number
      a. Atomic number (Table 2-1)
         (1) Number of protons in an atom's nucleus
         (2) Critically important; atomic number identifies the kind of element
      b. Mass number
         (1) Mass of a single atom
         (2) Equal to the number of protons plus the number of neutrons in the nucleus (p + n)
   4. Energy levels (Figures 2-5 and 2-6)
      a. Total number of electrons in an atom equals the number of protons in the nucleus (in a stable atom)
      b. Electrons form a "cloud" around the nucleus
      c. *Bohr model*—a model resembling planets revolving around the sun; useful in visualizing the structure of atoms
         (1) Exhibits electrons in concentric circles showing relative distances of the electrons from the nucleus
         (2) Each ring or shell represents a specific energy level and can hold only a certain number of electrons
         (3) Number and arrangement of electrons determine whether an atom is chemically stable
         (4) An atom with eight, or four pairs, of electrons in the outermost energy level is chemically stable
         (5) An atom without a full outermost energy level is chemically reactive
      d. *Octet rule*—atoms with fewer or more than eight electrons in the outer energy level will attempt to lose, gain, or share electrons with other atoms to achieve stability
   5. Isotopes (Figure 2-7)
      a. Isotopes of an element contain the same number of protons but different numbers of neutrons
      b. Isotopes have the same atomic number and therefore the same basic chemical properties as any other atom of the same element, but they have a different mass number
      c. Atomic weight—the average mass number of isotopes typically found among atoms in nature
      d. Radioactive isotope (radioisotope)—an unstable isotope that undergoes nuclear breakdown and emits nuclear particles and radiation

C. Attractions between atoms—chemical bonds
   1. Chemical reaction—interaction between two or more atoms that occurs as a result of activity between electrons in their outermost energy levels
   2. Molecule—two or more atoms covalently joined together
   3. Compound—consists of groupings of atoms of two or more elements
   4. Chemical bonds—two types unite atoms into groupings such as crystals and molecules
      a. Ionic, or electrovalent, bond (Figure 2-8)—formed by transfer of electrons; strong electrostatic force that binds positively and negatively charged ions together
      b. Covalent bond (Figure 2-9)—formed by sharing of electron pairs between atoms
   5. Hydrogen bond (Figures 2-10 and 2-11)
      a. Much weaker than ionic or covalent bonds
      b. Results from unequal charge distribution on molecules

D. Attractions between molecules
   1. Hydrogen bonds
      a. Form when electrons are unequally shared
         (1) Example: water molecule
         (2) Polar molecules have regions with partial electrical charges resulting from unequal sharing of electrons among atoms
      b. Areas of different partial charges attract one another and form hydrogen bonds
      c. Occur between a hydrogen bonded to an O, N, or F, and another hydrogen bonded to an O, N, or F
   2. Other weak attractions—molecules are attracted to each other through differences in electrical charge

E. Chemical reactions
   1. Involve the formation or breaking of chemical bonds
   2. Three basic types of chemical reactions are involved in physiology:
      a. Synthesis reaction—combining of two or more substances to form a more complex substance; formation of new chemical bonds: $A + B \longrightarrow AB$

b. Decomposition reaction—breaking down of a substance into two or more simpler substances; breaking of chemical bonds: AB ⟶ A + B
c. Exchange reaction—decomposition of two substances and, in exchange, synthesis of two new compounds from them: AB + CD ⟶ AD + CB
d. Reversible reactions—occur in both directions

METABOLISM

A. Metabolism—all of the chemical reactions that occur in body cells (Figure 2-12)
B. Catabolism
1. Chemical reactions that break down complex compounds into simpler ones and release energy; hydrolysis is a common catabolic reaction
2. Ultimately, the end products of catabolism are carbon dioxide, water, and other waste products
3. Some of the energy released is transferred to ATP, which is then used to do cellular work (Figure 2-33)
C. Anabolism
1. Chemical reactions that join simple molecules together to form more complex molecules
2. Chemical reaction responsible for anabolism is dehydration synthesis (condensation)

ORGANIC AND INORGANIC COMPOUNDS

A. Inorganic compounds—few have carbon atoms and none have C–C or C–H bonds
B. Organic molecules
1. Have at least one carbon atom and at least one C–C or C–H bond in each molecule
2. Often have functional groups attached to the carbon-containing core of the molecule (Figure 2-13)

INORGANIC MOLECULES

A. Water
1. Most abundant and important compound in the body
2. Properties of water (Table 2-2)
a. Polarity—allows water to act as an effective solvent in the body; ionizes substances in solution (Figure 2-10)
b. Solvent allows transportation of essential materials throughout the body (Figure 2-14)
c. High specific heat—water can lose and gain large amounts of heat with little change in its own temperature; enables the body to maintain a relatively constant temperature
d. High heat of vaporization—water requires the absorption of significant amounts of heat to change it from a liquid to a gas; allows the body to dissipate excess heat
B. Oxygen and carbon dioxide—closely related to cellular respiration
1. Oxygen—required to complete decomposition reactions necessary for the release of energy in the body
2. Carbon dioxide—produced as a waste product and also helps maintain the appropriate acid-base balance in the body
C. Electrolytes
1. Large group of inorganic compounds that includes acids, bases, and salts
2. Substances that dissociate in solution to form ions (the resulting ions are also sometimes called *electrolytes*)
3. Positively charged ions are cations; negatively charged ions are anions
4. Acids and bases—common and important chemical substances that are chemical opposites
a. Acids
(1) Any substance that releases a hydrogen ion (H^+) when in solution—*proton donor*
(2) Level of *acidity* depends on the number of hydrogen ions a particular acid will release
b. Bases
(1) Electrolytes that dissociate to yield hydroxide ions (OH^-) or other electrolytes that combine with hydrogen ions (H^+)
(2) Described as *proton acceptors*
c. pH scale—assigns a value to measures of acidity and alkalinity (Figure 2-15)
(1) pH indicates the degree of acidity or alkalinity of a solution
(2) pH of 7 indicates neutrality (equal amounts of H^+ and OH^-); a pH less than 7 indicates acidity; a pH higher than 7 indicates alkalinity
5. Buffers
a. Maintain the constancy of pH
b. Minimize changes in the concentrations of H^+ and OH^- ions
c. Act as a *reservoir* for hydrogen ions
6. Salts
a. Compound that results from chemical interaction of an acid and a base
b. Reaction between an acid and a base to form a salt and water is called a *neutralization reaction*

ORGANIC MOLECULES

A. *Organic* describes compounds that contain C–C or C–H bonds (Figure 2-16; Table 2-3)
B. Carbohydrates—organic compounds containing carbon, hydrogen, and oxygen (usual ratio 1:2:1); commonly called *sugars* and *starches*
1. Monosaccharides—simple sugars with short carbon chains; those with six carbons are hexoses (e.g., glucose), whereas those with five are pentoses (e.g., ribose, deoxyribose) (Figure 2-17)
2. Disaccharides and polysaccharides—two (di-) or more (poly-) simple sugars that are bonded together through a dehydration synthesis (condensation) reaction (Figure 2-18)
C. Lipids (Table 2-4)
1. Water-insoluble organic molecules that are critically important biological compounds
2. Major roles:
a. Energy source
b. Structural role
c. Integral parts of cell membranes

3. Triglycerides or fats (Figures 2-19 and 2-20)
   a. Most abundant lipids and most concentrated source of energy
   b. Building blocks of triglycerides are glycerol (the same for each fat molecule) and fatty acids (different for each fat and determine the chemical nature)
      (1) Types of fatty acids—saturated fatty acid (all available bonds are filled) and unsaturated fatty acid (has one or more double bonds)
      (2) Triglycerides are formed by a dehydration synthesis (condensation)
4. Phospholipids (Figure 2-21)
   a. Fat compounds similar to triglycerides
   b. One end of the phospholipid is water soluble (hydrophilic); the other end is fat soluble (hydrophobic)
   c. Phospholipids can join two different chemical environments
   d. Phospholipids may form double layers called *bilayers* that make up cell membranes (Figure 2-22)
5. Steroids (Figure 2-23)
   a. Main component is steroid nucleus
   b. Involved in many structural and functional roles
6. Prostaglandins (Figure 2-24)
   a. Commonly called *tissue hormones*; produced by cell membranes throughout the body
   b. Effects are many and varied; however, they are released in response to a specific stimulus and are then inactivated

D. Proteins (Table 2-5)
1. Most abundant organic compounds
2. Chainlike polymers of amino acids held together by peptide bonds to form a polypeptide
3. Amino acids—building blocks of proteins (Figures 2-25 to 2-27)
   a. Essential amino acids—eight amino acids that cannot be produced by the adult human body
   b. Nonessential amino acids—13 amino acids can be produced from molecules available in the adult human body
   c. Amino acids consist of a carbon atom, an amino group, a carboxyl group, a hydrogen atom, and a side group
4. Levels of protein structure (Figure 2-28)
   a. Protein molecules are highly organized and show a definite relationship between structure and function
   b. Four levels of protein organization
      (1) Primary structure—refers to the number, kind, and sequence of amino acids that make up the polypeptide chain held together by peptide bonds
      (2) Secondary structure—polypeptide is coiled or bent into helices (spirals) and pleated sheets stabilized by hydrogen bonds; may include recurring patterns of helices and/or sheets called motifs
      (3) Tertiary structure—a secondary structure can be further twisted and converted to a complex globular shape
         (a) The helices and pleated sheets touch in many places and are "welded" by covalent disulfide bonds, hydrogen bonds, and other attractive forces
         (b) May including regions called domains that act as functional units
      (4) Quaternary structure—highest level of organization occurring when protein contains more than one polypeptide chain
5. Importance of protein shape—shape of protein molecules determines their function (Figure 2-29)
   a. Final functional shape of the protein molecule is called its *native state*
   b. Structural proteins form the structures of the body
   c. Functional proteins cause chemical changes in the molecules
   d. Denatured proteins have lost their shape and therefore their function (Figure 2-30)
   e. Proteins can be denatured by changes in pH, temperature, radiation, and other chemicals
   f. If the chemical environment is restored, proteins may be renatured and function normally
   g. Proteins often have parts that move to perform their functions

E. Nucleic acids and related molecules
1. DNA (deoxyribonucleic acid)
   a. Composed of deoxyribonucleotides, that is, structural units composed of the pentose sugar (deoxyribose), phosphate group, and nitrogenous base (cytosine, thymine, guanine, or adenine)
   b. DNA molecule consists of two long chains of deoxyribonucleotides coiled into a double-helix shape (Figure 2-31)
   c. Alternating deoxyribose and phosphate units form the backbone of the chains
   d. Base pairs hold the two chains of DNA molecule together by hydrogen bonding
      (1) Adenine binds to thymine (two hydrogen bonds)
      (2) Cytosine binds to guanine (three hydrogen bonds)
   e. Specific sequence of more than 100 million base pairs constitutes one human DNA molecule; all DNA molecules in one individual are identical and different from those of all other individuals
   f. DNA functions as the molecule of heredity
2. RNA (ribonucleic acid) (Figure 2-32, Table 2-6)
   a. Composed of the pentose sugar (ribose), phosphate group, and a nitrogenous base
   b. Nitrogenous bases for RNA are adenine, uracil, guanine, or cytosine (uracil replaces thymine)
   c. Some RNA molecules are temporary copies of segments (genes) of the DNA code and are involved in synthesizing proteins
   d. Some RNA molecules are regulatory and act as enzymes (ribozymes) or silence gene expression (RNA interference)
3. Nucleotides
   a. Nucleotides have other important roles in the body
   b. ATP (Figure 2-33)
      (1) Composition
         (a) Adenosine
            i. Ribose—a pentose sugar
            ii. Adenine—a nitrogen-containing molecule
         (b) Three phosphate subunits
            i. High-energy bonds present between phosphate groups

ii. Cleavage of high-energy bonds releases energy during catabolic reactions
(2) Energy stored in ATP is used to do the body's work
(3) ATP often called the *energy currency* of cells
(4) ATP splits into adenosine diphosphate (ADP) and an inorganic phosphate group by special enzymes
(5) If ATP is depleted during prolonged exercise, creatine phosphate (CP) or ADP can be used for energy

c. NAD^+ and FAD (Figure 2-34)
(1) Used as coenzymes to transfer energy from one chemical pathway to another

d. cAMP (cyclic AMP)
(1) Made from ATP by removing two phosphate groups to form a monophosphate
(2) Used as an intracellular signal

F. Combined forms—large molecules can be joined together to form even larger molecules
1. Gives the molecules a completely different function
2. Names of combined molecules tell you what is in them
a. Base word tells which component is dominant
b. Prefix is the component found in a lesser amount
3. Examples
a. Adenosine triphosphate (ATP)—two extra phosphate groups to a nucleotide
b. Lipoproteins—lipid and protein groups combined into a single molecule
c. Glycoproteins—carbohydrate (*glyco*, "sweet") and protein
d. Examples of combined forms and their functions in the body listed in Table 2-3

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Define the following terms: element, compound, atom, molecule.
2. Compare early nineteenth century and present-day concepts of atomic structure.
3. Name and define three kinds of subatomic particles.
4. Are atoms electrically charged particles? Give the reason for your answer.
5. What four elements make up approximately 96% of the body's weight?
6. Define and contrast meanings of the terms *atomic number* and *mass number*.
7. Explain the general rule by which an atom can be listed as chemically stable and unable to react with another atom.
8. Define and give an example of an isotope.
9. Explain what the term *radioactivity* means.
10. How does radioactivity differ from chemical activity?
11. Define these terms: alpha particles, beta particles, and gamma rays.
12. Explain how radioactive atoms become transformed into atoms of a different element.
13. Explain what the term *chemical reaction* means.
14. Identify and differentiate between the three basic types of chemical reactions.
15. Define the term *inorganic*.
16. Explain why water is said to be polar and list at least four functions of water that are crucial to survival.
17. What are electrolytes and how are they formed?
18. What is a cation? an anion? an ion? Give an example of each.
19. Define the terms *acid*, *base*, *salt*, and *buffer*.
20. Explain how pH indicates the degree of acidity or alkalinity of a solution.
21. What are the structural units, or building blocks, of proteins? of carbohydrates? of triglycerides? of DNA?
22. Explain what a protein molecule's binding site is. What function does it serve in enzymes?
23. Describe some of the functions proteins perform.
24. Proteins, carbohydrates, lipids—which of these are insoluble in water? contain nitrogen? include prostaglandins? include phospholipids?
25. What groups make up a nucleotide?
26. What pentose sugar is present in a deoxyribonucleotide?
27. Describe the size, shape, and chemical structure of the DNA molecule.
28. What base is thymine always paired with in the DNA molecule? What other two bases are always paired?
29. What is the function of DNA?
30. What is catabolism? What function does it serve?
31. Compare catabolism, anabolism, and metabolism.

CRITICAL THINKING QUESTIONS

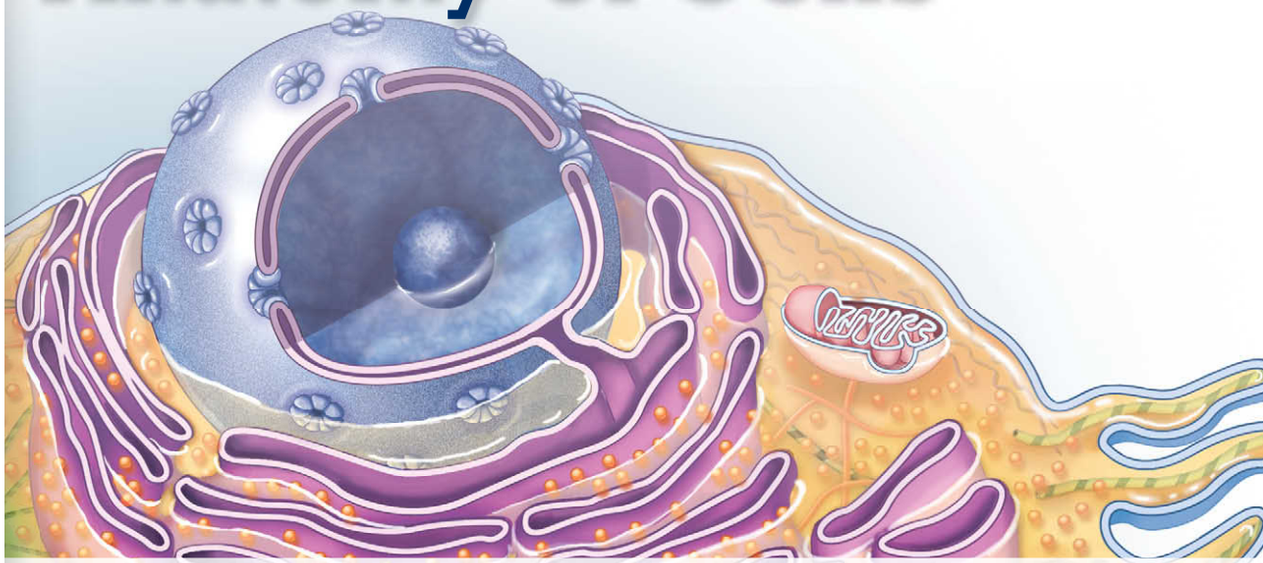


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Identify the specific areas of chemistry that would be of interest to a biochemist.
2. In modern blimps, the gas of choice used to inflate them is helium rather than hydrogen. Hydrogen would be lighter, but helium is safer. Compare and contrast the atomic structure of hydrogen and helium. What characteristics of the atomic structure of helium make it so much less reactive than hydrogen?
3. How would you contrast single covalent bonds, double covalent bonds, and ionic bonds?
4. If an adult has a body weight of 170 pounds, how much of that weight consists of water?
5. Amylase is an enzyme present in saliva that begins the breakdown of starch. As with all enzymes, amylase is specific to this particular chemical reaction. Explain how a change in the shape of this protein might affect this reaction.
6. Amino acids are the building blocks of proteins. Less than a dozen amino acids make up most of our proteins. Explain how so few amino acids are responsible for the billions of proteins that are used by the body.
7. How does ATP supply the cells with the energy they need to work? Outline the general scheme of the ATP energy cycle.

3

Anatomy of Cells



LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

aster
(AS-ter)
[*aster,* **star**]

centriole
(SEN-tree-ohl)
[*centr-* **center,** *-ole* **small**]

centrosome
(SEN-troh-sohm)
[*centr-* **center,** *-som-* **body**]

chromatin
(KROH-mah-tin)
[*chrom-* **color,** *-in* **substance**]

chromosome
(KROH-meh-sohm)
[*chrom-* **color,** *-som-* **body**]

chromosome territory (CT)
(KROH-meh-sohm TAIR-it-or-ee)
[*chrom-* **color,** *-som-* **body,** *terri-* **land,** *-ory* **place**]

cilium
(SIL-ee-um)
[*cili-* **eyelid**] *pl.*, cilia

composite cell
(kahm-PAH-zit sell)
[*composite* **to assemble,** *cell* **storeroom**]

crista
[*crista* **crest or fold**] *pl.*, cristae

cytoplasm
(SYE-toh-plaz-em)
[*cyto-* **cell,** *-plasm* **substance**]

cytoskeleton
(sye-toh-SKEL-e-ton)
[*cyto-* **cell,** *-skeleto-* **dried body**]

desmosome
(DES-mo-sohm)
[*desmos-* **band,** *-som-* **body**]

continued on p. 85

CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

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In the 1830s, two German scientists, Matthias Schleiden (SHLY-den) and Theodor Schwann, advanced one of the most important and unifying concepts in biology—the cell theory. *It states simply that the cell is the fundamental organizational unit of life. Although earlier scientists had seen cells, Schleiden and Schwann were the first to suggest that all living things are composed of cells. Some 100 trillion of them make up the human body. Actually, the study of cells has captivated the interest of countless scientists for over 300 years. However, these small structures have not yet yielded all their secrets, not even to the probing tools of present-day researchers.*

To introduce you to the world of cells, three brief chapters summarize the essential concepts of cell structure and function. This chapter begins the discussion by describing the functional anatomy of common cell structures. The term functional anatomy *refers to the study of structures as they relate to function. Chapter 4,* Physiology of Cells, *continues the discussion by outlining in more detail some important and representative cellular processes. Chapter 5 goes on to discuss the growth and reproduction of cells.*

| A&P CONNECT |

What *are* the probing tools available to today's cell scientists? Mostly, they are the tools used in various forms of **microscopy.** Check out ***Tools of Microscopic Anatomy*** online at ***A&P Connect*** to see explanations and examples of *light microscopy (LM), scanning* and *transmission electron microscopy (SEM and TEM),* and *atomic force microscopy (AFM)* that are used throughout this book.

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FUNCTIONAL ANATOMY OF CELLS

The principle of complementarity of structure and function was introduced in Chapter 1 and is evident in the relationships that exist between cell size, shape, and function. Almost all human cells are microscopic in size (Table 3-1). Their diameters range from 7.5 micrometers (μm) (example, red blood cells) to about 150 μm (example, female sex cell or ovum). The period at the end of this sentence measures about 100 μm—roughly 13 times as large as our smallest cells and two thirds the size of the human ovum. Like other anatomical structures, cells exhibit a particular size or form because they are intended to perform a certain activity. A nerve cell, for example, may have threadlike extensions over a meter in length! Such a cell is ideally suited to transmit nervous impulses from one area of the body to another. Muscle cells are adapted to contract, that is, to shorten or lengthen with pulling strength. Other types of cells may serve protective or secretory functions (Table 3-2).

| A&P CONNECT |

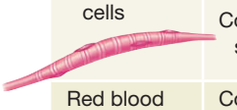
Are you a little confused by the metric size units used in science? Check out ***Metric Measurements and Their Equivalents*** online at ***A&P Connect.***

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TABLE 3-1 Units of Size

UNIT	SYMBOL	EQUAL TO	USED TO MEASURE
Centimeter	cm	1/100 meter	Objects visible to the eye
Millimeter	mm	1/1,000 meter (1/10 cm)	Very large cells; groups of cells
Micrometer (micron)	μm	1/1,000,000 meter (1/1000 mm)	Most cells; large organelles
Nanometer	nm	1/1,000,000,000 meter (1/1,000 μm)	Small organelles; large biomolecules
Angstrom	Å	1/10,000,000,000 meter (1/10 nm)	Molecules; atoms

TABLE 3-2 Example of Cell Types

TYPE	STRUCTURAL FEATURES	FUNCTIONS
Nerve cells 	Surface that is sensitive to stimuli Long extensions	Detect changes in internal or external environment Transmit nerve impulses from one part of the body to another
Muscle cells 	Elongated, threadlike Contain tiny fibers that slide together forcefully	Contract (shorten) to allow movement of body parts
Red blood cells 	Contain hemoglobin, a red pigment that attracts, then releases, oxygen	Transport oxygen in the bloodstream (from lungs to other parts of the body)
Gland cells 	Contain sacs that release a secretion to the outside of the cell	Release substances such as hormones, enzymes, mucus, and sweat
Immune cells 	Some have outer membranes able to engulf other cells Some have systems that manufacture antibodies Some are able to destroy other cells	Recognize and destroy "nonself" cells such as cancer cells and invading bacteria

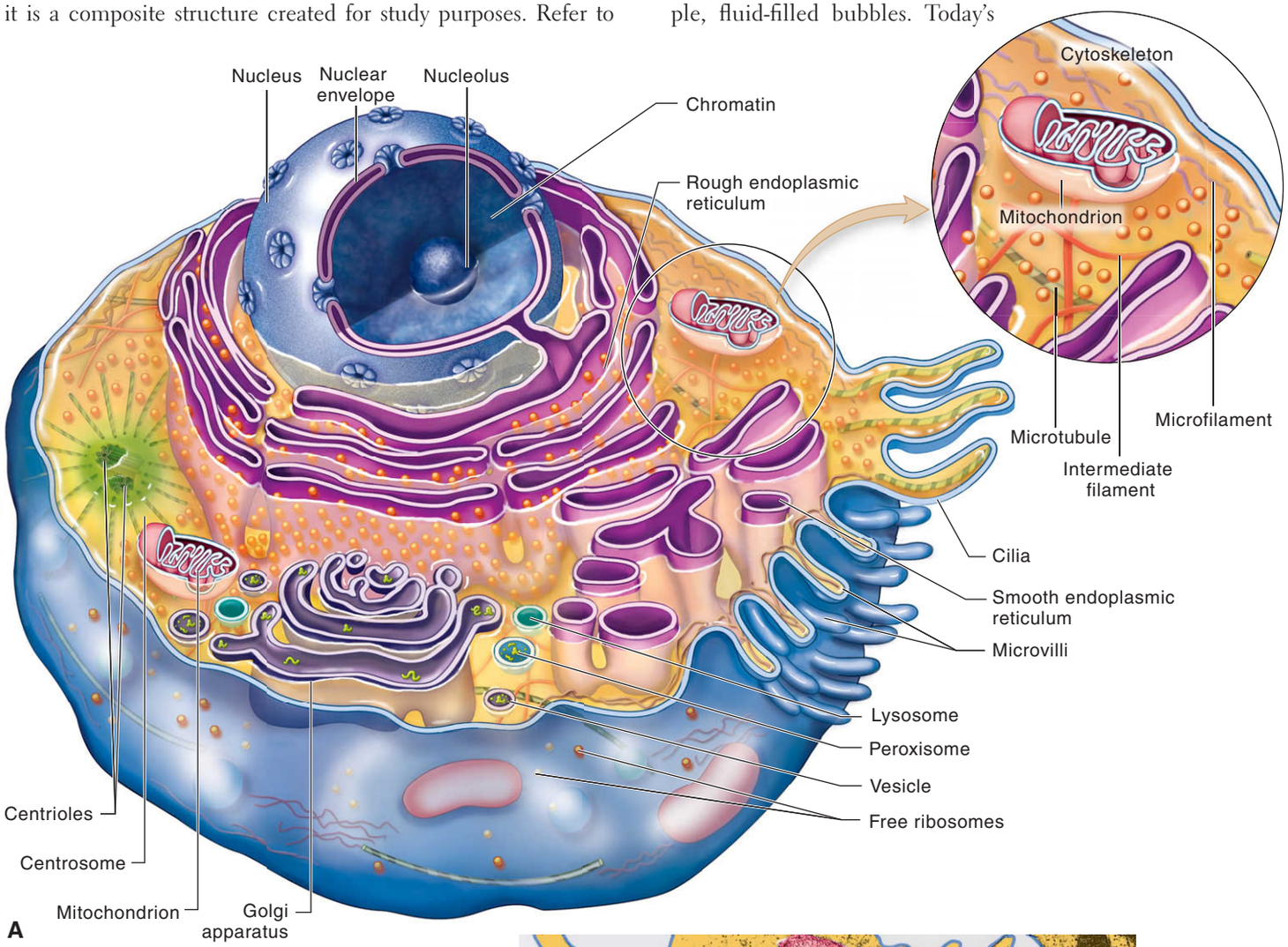
The Typical Cell

Despite their distinctive anatomical characteristics and specialized functions, the cells of your body have many similarities. There is no cell that truly represents or contains all of the various

components found in the many types of human body cells. As a result, students are often introduced to the anatomy of cells by studying a so-called *typical* or **composite cell**—one that exhibits the most important characteristics of many different human cell types. Such a generalized cell is illustrated in Figure 3-1. Keep in mind that no such "typical" cell actually exists in the body; it is a composite structure created for study purposes. Refer to Figure 3-1 and Table 3-3 often as you learn about the principal cell structures described in the paragraphs that follow.

Cell Structures

Ideas about cell structure have changed considerably over the years. Early biologists saw cells as simple, fluid-filled bubbles. Today's



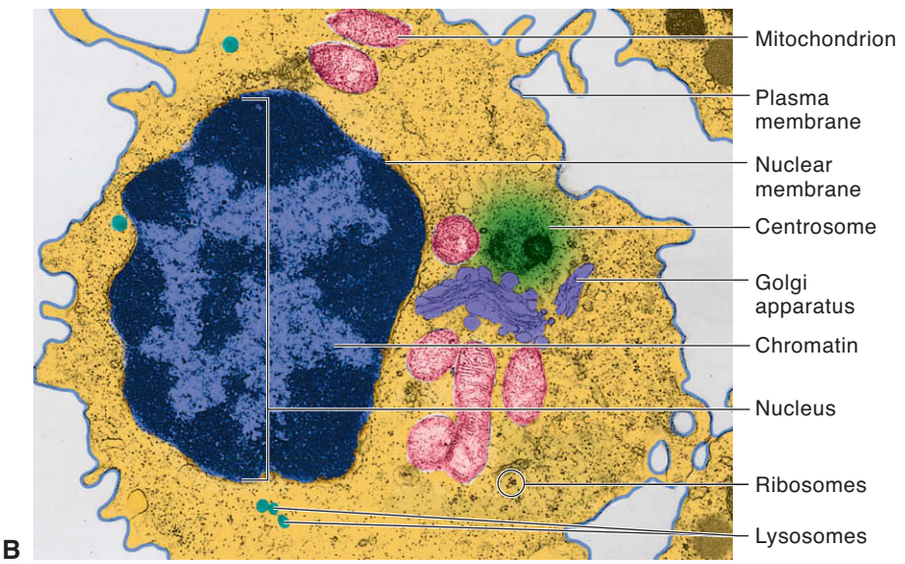


FIGURE 3-1

Typical, or composite, cell. A, Artist's interpretation of cell structure. **B,** Color-enhanced electron micrograph of a cell. Both show mitochondria, known as the "power plants of the cell." Note the innumerable dots bordering the endoplasmic reticulum. These are ribosomes, the cell's "protein factories."

TABLE 3-3 Some Major Cell Structures and Their Functions

CELL STRUCTURE	DESCRIPTION	FUNCTIONS
Membranous		
Plasma membrane	Phospholipid bilayer reinforced with cholesterol and embedded with proteins and other organic molecules	Serves as the boundary of the cell, maintains its integrity; protein molecules embedded in plasma membrane perform various functions; for example, they serve as markers that identify cells of each individual, as receptor molecules for certain hormones and other molecules, and as transport mechanisms
Endoplasmic reticulum (ER)	Network of canals and sacs extending from the nuclear envelope; may have ribosomes attached	Ribosomes attached to rough ER synthesize proteins that leave cells via the Golgi apparatus; smooth ER synthesizes lipids incorporated in cell membranes, steroid hormones, and certain carbohydrates used to form glycoproteins—also removes and stores Ca^{++} from the cell's interior
Golgi apparatus	Stack of flattened sacs (cisternae) surrounded by vesicles	Synthesizes carbohydrate, combines it with protein, and packages the product as globules of glycoprotein
Vesicles	Tiny membranous bags	Temporarily contain molecules for transport or later use
Lysosomes	Tiny membranous bags containing enzymes	Digestive enzymes break down defective cell parts and ingested particles; a cell's "digestive system"
Peroxisomes	Tiny membranous bags containing enzymes	Enzymes detoxify harmful substances in the cell
Mitochondria	Tiny membranous capsule surrounding an inner, highly folded membrane embedded with enzymes; has small, ringlike chromosome (DNA)	Catabolism; adenosine triphosphate (ATP) synthesis; a cell's "power plants"
Nucleus	A usually central, spherical double-membrane container of chromatin (DNA); has large pores	Houses the genetic code, which in turn dictates protein synthesis, thereby playing an essential role in other cell activities, namely, cell transport, metabolism, and growth
Nonmembranous		
Ribosomes	Small particles assembled from two tiny subunits of rRNA and protein	Site of protein synthesis; a cell's "protein factories"
Proteasomes	Hollow protein cylinders with embedded enzymes	Destroys misfolded or otherwise abnormal proteins manufactured by the cell; a "quality control" mechanism for protein synthesis
Cytoskeleton	Network of interconnecting flexible filaments, stiff tubules, and molecular motors within the cell	Supporting framework of the cell and its organelles; functions in cell movement (using molecular motors); forms cell extensions (microvilli, cilia, flagella)
Centrosome	Region of cytoskeleton that includes two cylindrical groupings of microtubules called centrioles	Acts as the microtubule-organizing center (MTOC) of the cell; centrioles assist in forming and organizing microtubules
Microvilli	Short, fingerlike extensions of plasma membrane; supported internally by microfilaments	Tiny, fingerlike extensions that increase a cell's absorptive surface area
Cilia and flagella	Moderate (cilia) to long (flagella) hairlike extensions of plasma membrane; supported internally by cylindrical formation of microtubules, sometimes with attached molecular motors	Cilia move substances over the cell surface or detect changes outside the cell; flagella propel sperm cells
Nucleolus	Dense area of chromatin and related molecules within nucleus	Site of formation of ribosome subunits

biologists know that cells are far more complex than this. Each cell is surrounded by a plasma membrane that separates the cell from its surrounding environment. The inside of the cell is composed largely of a gel-like substance called **cytoplasm** (literally, "cell substance"). The cytoplasm is made of various organelles and molecules suspended in a watery fluid called *cytosol*, or sometimes *intracellular fluid*. As Figure 3-2 shows, the cytoplasm is crowded with large and small molecules—and various organelles. This dense crowding of molecules and organelles actually helps improve the efficiency of chemical reactions in the cell.

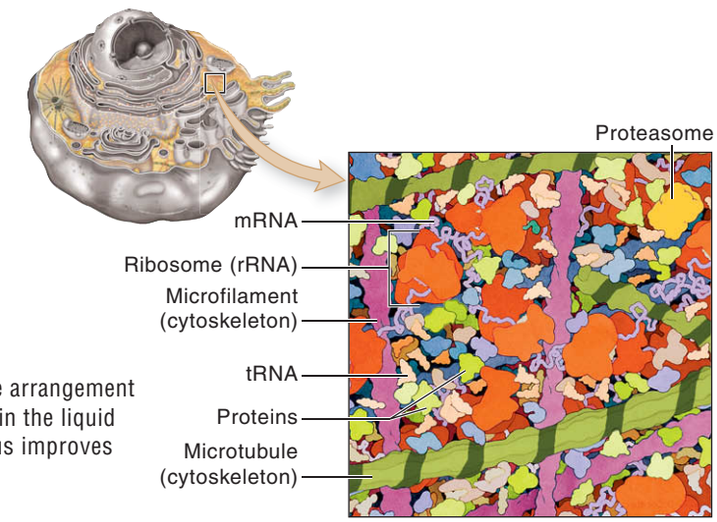


FIGURE 3-2

Cytoplasm. This drawing shows that the cytoplasm is made up of a dense arrangement of fibers, protein molecules, organelles, and other structures, suspended in the liquid cytosol. Such crowding helps molecules interact with one another and thus improves the efficiency of cellular metabolism.

The nucleus, which is not usually considered to be part of the cytoplasm, is generally at the center of the cell. Each different cell part is structurally suited to perform a specific function within the cell—much as each of your organs is suited to a specific function within your body. In short, the main cell structures are (1) the plasma membrane; (2) cytoplasm, including the organelles; and (3) the nucleus (see Figure 3-1).

| QUICK CHECK |

1. What important concept in biology was proposed by Schleiden and Schwann?
2. Give an example of how cell structure relates to its function.
3. List the three main structural components of a typical cell.

CELL MEMBRANES

Figure 3-1 shows that a typical cell contains a variety of membranes. The outer boundary of the cell, or **plasma membrane,** is just one of these membranes. Each cell also has various *membranous organelles.* Membranous organelles are sacs and canals made of the same type of membrane material as the plasma membrane. This membrane material is a very thin sheet—averaging only about 75 angstroms (Å) or 0.0000003 inch thick—made of lipid, protein, and other molecules (Table 3-1).

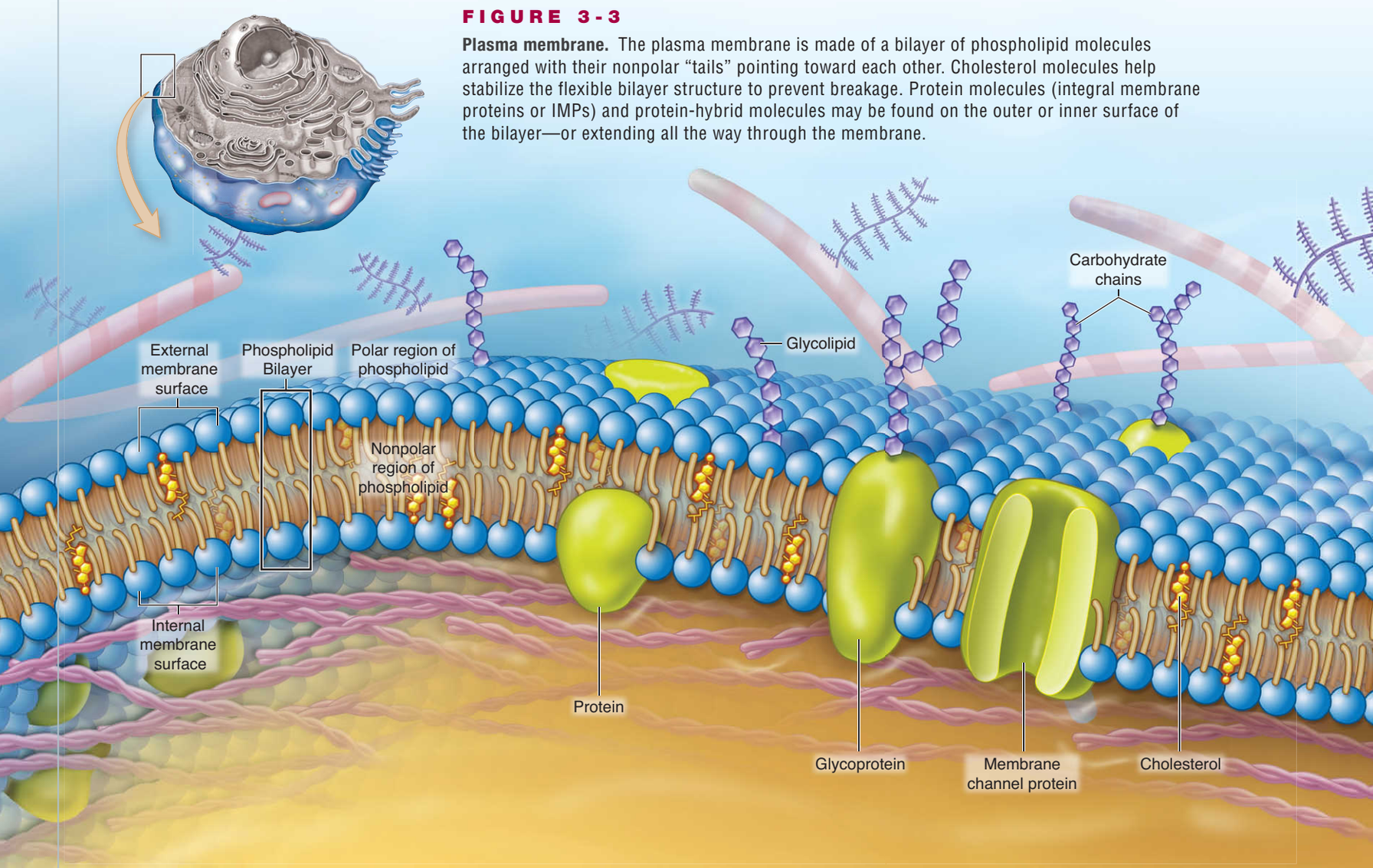
Membrane Structure

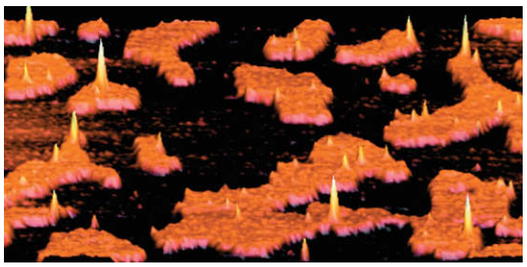
Figure 3-3 shows a simplified view of the evolving model of cell membrane structure. This concept of cell membranes is called the **fluid mosaic model.** Like the tiles in an art mosaic, the different molecules that make up a cell membrane are arranged in a sheet. Unlike art mosaics, however, this mosaic of molecules is *fluid;* that is, the molecules are able to slowly float around the membrane like icebergs in the ocean. The fluid mosaic model shows us that the molecules of a cell membrane are bound tightly enough to form a continuous sheet but loosely enough that the molecules can slip past one another.

What are the forces that hold a cell membrane together? The short answer to that question is chemical attractions. The primary structure of a cell membrane is a double layer of phospholipid molecules. Recall from Chapter 2 that phospholipid molecules have "heads" that are water soluble and double "tails" that are lipid soluble (see Figure 2-21 on p. 49). Because their heads are **hydrophilic** (water loving) and their tails are **hydrophobic** (water fearing), phospholipid molecules naturally arrange themselves into double layers, or *bilayers,* in water. This allows all the hydrophilic heads to face toward water and all the hydrophobic tails to face away from water (see Figure 2-22 on p. 50).

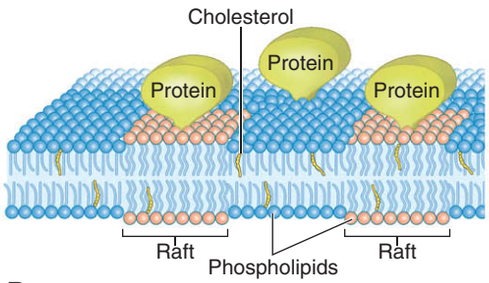
FIGURE 3-3

Plasma membrane. The plasma membrane is made of a bilayer of phospholipid molecules arranged with their nonpolar "tails" pointing toward each other. Cholesterol molecules help stabilize the flexible bilayer structure to prevent breakage. Protein molecules (integral membrane proteins or IMPs) and protein-hybrid molecules may be found on the outer or inner surface of the bilayer—or extending all the way through the membrane.





A



B

FIGURE 3-4

Rafts. A, Atomic force micrograph (AFM) in which an extremely fine-tipped needle drags over the surface of a cell membrane to reveal detailed surface features. Rafts are seen here as raised, orange areas surrounded by black areas of less rigid phospholipid structure. **B,** Diagram showing the basic structure of a membrane with rafts. The raft phospholipids have a richer supply of cholesterol than surrounding regions do and, along with attached integral membrane proteins, form rather rigid floating platforms in the surface of the membrane. Rafts help organize functions at the surfaces of cells and organelles.

Because the internal environment of the body is simply a water-based solution, phospholipid bilayers appear wherever phospholipid molecules are scattered among the water molecules. Cholesterol is a steroid lipid that mixes with phospholipid molecules to form a blend of lipids that stays just fluid enough to function properly at body temperature. Without cholesterol, cell membranes would break far too easily.

Each human cell manufactures various kinds of phospholipid and cholesterol molecules, which then arrange in a bilayer to form a natural "fencing" material of varying thickness that can be used throughout the cell. This "fence" allows many lipid-soluble molecules to pass through easily—just like a picket fence allows air and water to pass through easily. However, because most of the phospholipid bilayer is hydrophobic, cell membranes do not allow water or water-soluble molecules to pass through easily. This characteristic of cell membranes is ideal because most of the substances in the internal environment are water soluble. What good is a membrane boundary if it allows just about everything to pass through it?

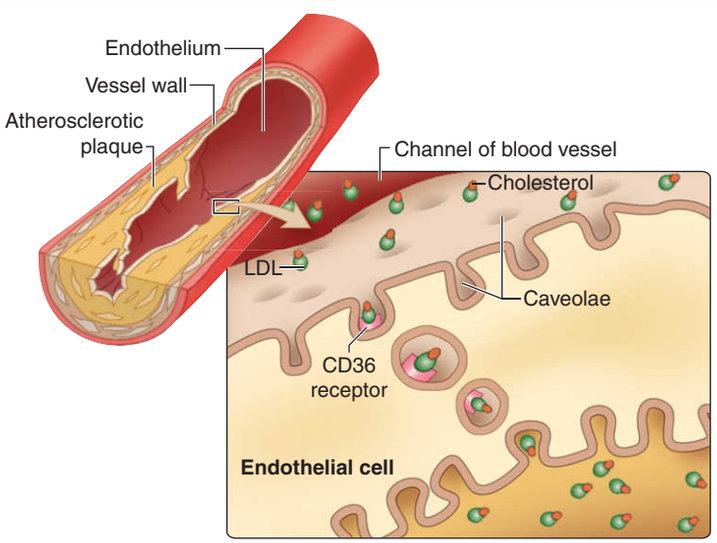
Just as there are different fencing materials for different kinds of fences, cells can make any of a variety of different phospholipids for different areas of a cell membrane. For example, some areas of a membrane are stiff and less fluid; others are somewhat flimsy. Many cell membranes are packed more densely with proteins than seen in Figure 3-3; other membranes have less protein.

Some membrane lipids combine with carbohydrates to form glycolipids, and some unite with protein to form lipoproteins easily. Recall from Chapter 2 that proteins are made up of many amino acids, some of which are polar, some nonpolar (see Figure 2-26, p. 53). By having different kinds of amino acids in specific locations, protein molecules may become anchored within the bilayer of phospholipid heads and tails or attached to one side or the other of the membrane.

The different molecular interactions within the membrane allow the formation of lipid **rafts,** which are stiff groupings of membrane molecules (often very rich in cholesterol) that travel together like a log raft on the surface of a lake (Figure 3-4). Rafts help organize the various components of a membrane. Rafts play an important role in the pinching of a parent cell into two daughter cells during cell division. Rafts may also sometimes allow the cell to form depressions that pouch inward and then pinch off as

Box 3-1 | Caveolae

The list of organelles inside human cells that have been identified with new techniques of cell imaging (see ***Tools of Microscopic Anatomy*** online at ***A&P Connect***) and biochemical analysis has continued to grow. Among the more recently discovered organelles are the "little caves," or *caveolae* (*singular,* caveola). Caveolae are tiny indentations of the plasma membrane that indeed resemble tiny caves (see the figure). Caveolae appear to form from rafts of lipid and protein molecules in the plasma membrane that pinch in and move inside the cell. Caveolae can capture extracellular material and shuttle it inside the cell or even all the way across the cell (see the figure). Although there is much yet to understand about the many functions of caveolae, one possible problem that they may cause has already been outlined. Some caveolae in the cells that line blood vessels may have CD36 cholesterol receptors that attract low-density lipoproteins (LDLs, which carry the so-called *bad cholesterol*). As the figure shows, once the LDLs attach to the receptor, the caveola closes and migrates to the other side of the cell. There, the LDL molecules are released to build up behind the lining of the blood vessel. As the LDLs accumulate, the blood vessel channel narrows and obstructs the flow of blood—a major cause of stroke and heart disease.



Researchers believe that other diseases, such as certain forms of diabetes, cancer, and muscular dystrophy, may also result from inappropriate actions taken by caveolae.

a means of carrying substances into the cell (Box 3-1). Human immunodeficiency virus (HIV), for example, enters cells by first connecting to a raft protein in the plasma membrane and then subsequently being pulled into the cell.

Membrane Function

Embedded within the phospholipid bilayer are a variety of **integral membrane proteins (IMPs).** As their name implies, they are integrated into structure of the membrane itself. Proteins that have some functional regions or *domains* that are hydrophilic and other domains that are hydrophobic can be integrated into a phospholipid bilayer and remain stable. IMPs have many different structural forms that allow them to serve various functions (see Table 3-3).

A cell can control what moves through any section of membrane by means of IMPs that act as transporters (see Figure 3-3). Many of these transporters have domains forming openings that, like gates in a fence, allow water-soluble molecules to pass through the membrane. Specific kinds of transporterss allow only certain kinds of molecules to pass through—and the cell can determine whether these "gates" are open or closed at any particular time. We consider this function of integral membrane proteins again in Chapter 4 when we study transport mechanisms in the cell.

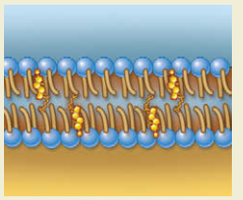
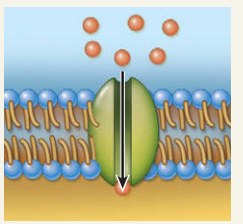
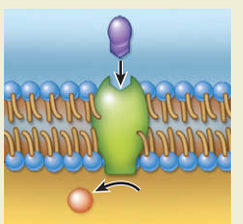
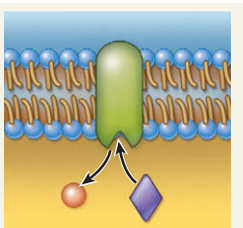
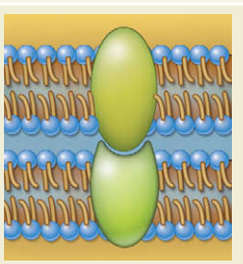
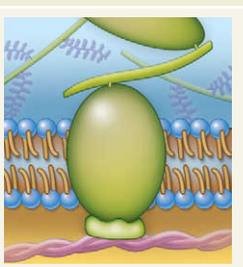
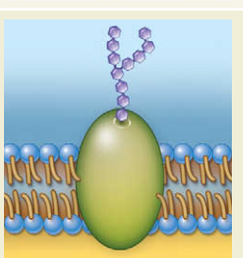
Some IMPs have carbohydrates attached to their outer surface—forming *glycoprotein* molecules—that act as identification markers. Such markers, which are recognized by other molecules, act as signs on a fence that identify the enclosed area. Cells and molecules of the immune system can thus distinguish between normal "self" cells and abnormal or "nonself" cells. Not only does this mechanism allow us to attack cancer or bacterial cells, it also prevents us from receiving blood donations from people who don't have cell markers similar to our own. Some membrane proteins are enzymes that catalyze cellular reactions. Some IMPs bind to other IMPs to form connections between cells or bind to support filaments within the cell to anchor them.

Other IMPs are **receptors** that can react to the presence of hormones or other regulatory chemicals and thereby trigger metabolic changes in the cell. The process by which cells translate the signal received by a membrane receptor into a specific chemical change in the cell is called **signal transduction.** The word *transduction* means "carry across," as a message being carried across a membrane. Recent discoveries continue to show the vital importance of signal transduction in the normal function of cells and therefore the whole body. Being one of the most active areas of biomedical research, the study of signal transduction has provided many answers to the causes of diseases, which in turn has led to effective treatments and cures. As you continue your study of human structure and function, try to find instances of signal transduction in cells that provide a vital link in important processes throughout the body. By doing so, you will better understand the "big picture" of human structure and function.

Some IMPs connect the cell membrane to another membrane, as when two cells join together to form a larger mass of tissue. Other IMPs connect a membrane to the framework of fibers inside the cell or to the mass of fibers and other molecules that make up the extracellular matrix (ECM).

Table 3-4 summarizes the functional anatomy of cell membranes.

TABLE 3-4 Functional Anatomy of Cell Membranes

	**Structure:** Sheet (bilayer) of phospholipids stabilized by cholesterol **Function:** Maintains boundary (integrity) of a cell or membranous organelle
	**Structure:** Integral membrane proteins that act as channels or carriers of molecules **Function:** Controlled transport of water-soluble molecules from one compartment to another
	**Structure:** Receptor molecules that trigger metabolic changes in membrane (or on other side of membrane) **Function:** Sensitivity to hormones and other regulatory chemicals; involved in signal transduction
	**Structure:** Enzyme molecules that catalyze specific chemical reactions **Function:** Regulation of metabolic reactions
	**Structure:** Integral membrane proteins that bind to molecules outside the cell **Function:** Form connections between one cell and another
	**Structure:** Integral membrane proteins that bind to support structures **Function:** Support and maintain the shape of a cell or membranous organelle; participate in cell movement; bind to fibers of the extracellular matrix (ECM)
	**Structure:** Glycoproteins or proteins in the membrane that act as markers **Function:** Recognition of cells or organelles

CYTOPLASM AND ORGANELLES

Cytoplasm is the gel-like internal substance of cells that contains many tiny suspended structures. Early cell scientists believed cytoplasm to be a rather uniform fluid filling the space between the plasma membrane and the nucleus. We now know that the cytoplasm of each cell is actually a watery solution called *cytosol* plus hundreds or even thousands of "little organs," or **organelles,** that thicken the cytoplasm and result in its gel-like consistency. Table 3-3 lists some of the major types of organelles that we will encounter in this book. Until relatively recently, when newer microscope technology became available, many of these organelles simply could not be seen. Those that could be seen were simply called *inclusions* because their roles as integral parts of the cell were not yet recognized. Undoubtedly, some of the cellular structures we now call inclusions will eventually be recognized as organelles and given specific names.

Many types of organelles have been identified in various cells of the body. To make it easier to study them, they have been classified into two major groups: *membranous organelles* and *nonmembranous organelles.* Membranous organelles are those that are described as sacs or canals made of cell membrane. Nonmembranous organelles are not made of membrane; they are made of microscopic filaments or other particles. As you read through the following sections, be sure to note whether the organelle being discussed is membranous or nonmembranous (see Table 3-3).

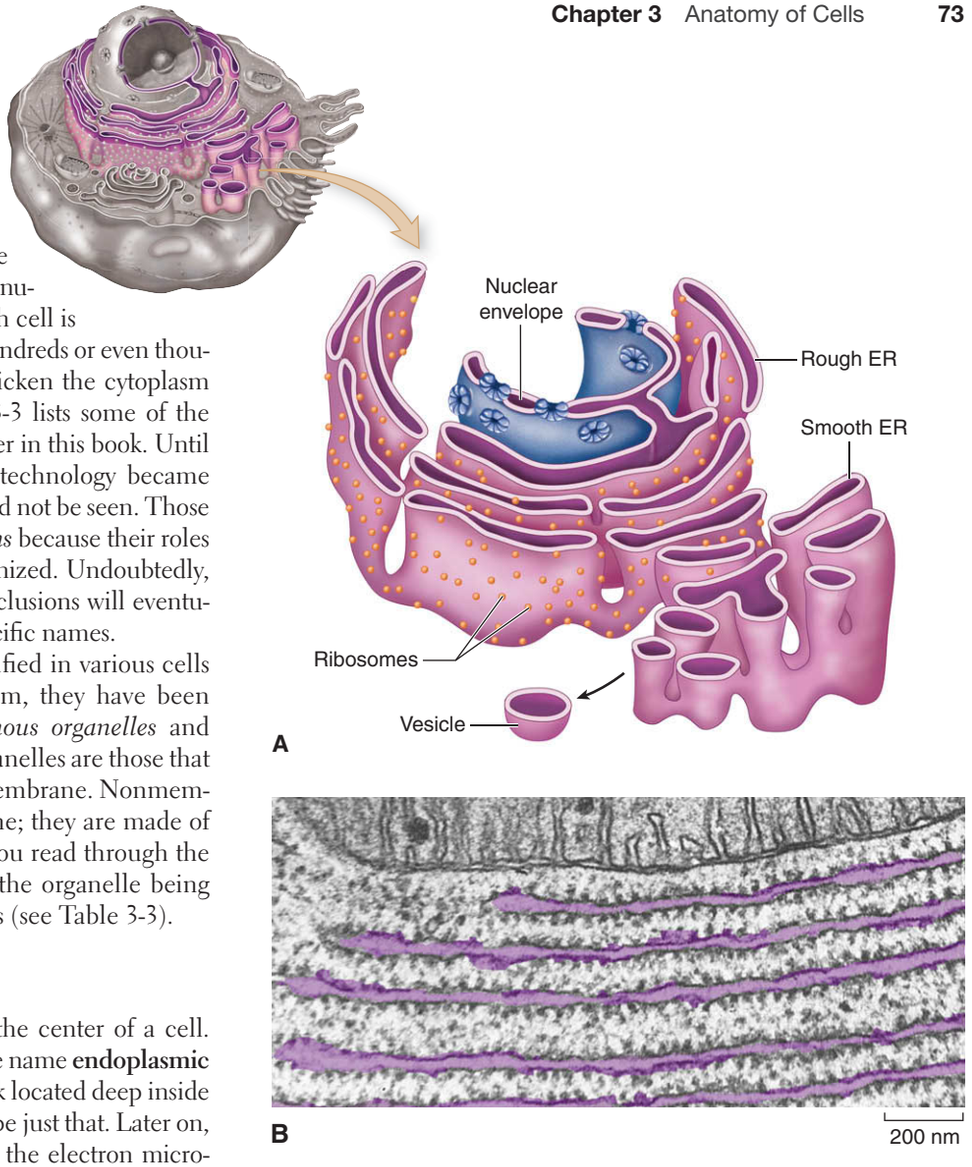


FIGURE 3-5

Endoplasmic reticulum (ER). In both the drawing **(A)** and the transmission electron micrograph **(B),** the rough ER (RER) is distinguished by the presence of tiny ribosomes dotting the boundary of flattened membrane sacs. The smooth ER (SER) is more tubular in structure and lacks ribosomes on its surface. Note also that the ER is continuous with the outer membrane of the nuclear envelope.

Endoplasmic Reticulum (ER)

Endoplasm is the cytoplasm located toward the center of a cell. *Reticulum* means small network. Therefore, the name **endoplasmic reticulum (ER)** means literally a small network located deep inside the cytoplasm. When first seen, it appeared to be just that. Later on, however, more highly magnified views under the electron microscope showed the ER to be distributed throughout the cytoplasm (see Figure 3-1). ER consists of membranous-walled canals and flat, curving sacs that are arranged in parallel rows.

The endoplasmic reticulum can serve a variety of functions in a cell. There are two types of ER: *rough ER (RER)* and *smooth ER (SER).*

ROUGH ER (RER)

Rough ER is made up of broad, flattened sacs that extend outward from the boundary of the nucleus. RER sacs are dotted with innumerable small granules called *ribosomes.* The granules give rough ER the "rough" appearance of sandpaper as you can see in Figure 3-5. Ribosomes are themselves distinct organelles for making proteins.

As new polypeptide strands are released from the ribosomes that "dock" at the RER surface, they enter the lumen (cavity) of the RER network. Once inside, the polypeptide strands fold and sometimes unite with other proteins to form larger molecules. The proteins made in the RER move through the lumen of the ER network, or become imbedded in the cell membrane (phospholipid bilayer) that forms the wall of each sac. Many of these molecules eventually move toward the Golgi apparatus, where they are processed further, and some of them eventually leave the cell.

SMOOTH ER (SER)

No ribosomes border the membranous wall of the smooth ER—hence its smooth appearance and its name. The SER part of the network is usually more tubular in structure than the flattened sacs of the RER, as you can see in Figure 3-5. The smooth ER contains enzymes and other molecules processed in the RER. Some of the enzymes synthesize certain lipids and carbohydrates. Included among these are the steroid hormones and some of the carbohydrates used to form glycoproteins. Lipids that form cell membranes are also synthesized here. As these membrane lipids are made, they simply become part of the smooth ER's wall. Bits of the ER break off from time to time and travel to other membranous organelles—even to the plasma membrane—and become

part of the membrane of those organelles. The smooth ER, then, is the organelle that makes membrane for use throughout the cell.

Smooth ER also transports calcium ions (Ca^{++}) from the cytosol into the sacs of the ER, thus helping maintain a low concentration of Ca^{++} in a cell's interior. Knowing that Ca^{++} is moved into the ER and stored there is a fact that will prove useful in helping you understand the information in later chapters.

Ribosomes

Every cell contains thousands of **ribosomes.** Many of them are attached to the rough endoplasmic reticulum, and many of them lie free, scattered throughout the cytoplasm. Find them in both locations in Figure 3-1. Because ribosomes are too small to be seen with a light microscope, no one knew they existed until the electron microscope revealed them in 1955. We now know that each ribosome is a nonmembranous structure made of two tiny, interlocking pieces. One piece is a *large subunit* and the other a *small subunit* (Figure 3-6).

Each subunit of the ribosome is composed of ribonucleic acid (RNA) bonded to protein. Ribosomal RNA is often abbreviated as rRNA. Other types of ribonucleic acid in the cell include messenger RNA (mRNA) and transfer RNA (tRNA), among others. Figure 3-6 shows a threadlike mRNA molecule moving through a ribosome, providing the "recipe" for a polypeptide strand. You can also see a tiny tRNA particle inside the cavity between the ribosomal subunits. tRNA's job is to bring (i.e., transfer) an amino acid to the correct location in the mRNA recipe sequence. The major types of RNA and their roles in the cell are discussed in more detail in Chapter 5.

The function of ribosomes is protein synthesis. Ribosomes are the molecular machines that translate the genetic code to make proteins, or to use a popular term, they are the cell's "protein factories." They make both its structural and its functional proteins (enzymes).

A ribosome is a temporary structure. The two ribosomal subunits link together only when there is an mRNA present and ready to direct the formation of a new polypeptide strand. When the polypeptide is finished, the subunits fall away from each other. The subunits may be used again in another round of protein synthesis.

Working ribosomes usually function in groups called *polyribosomes* or *polysomes.* Polyribosomes form when more than one ribosome begins translating the same long, threadlike mRNA molecule. Under the electron microscope, polyribosomes look like short strings of beads.

In Chapter 5, after you have learned a little more about cell structures, you will be ready to look at the details of how ribosomes carry out protein synthesis.

Golgi Apparatus

The **Golgi apparatus** is a membranous organelle consisting of separate tiny sacs, or *cisternae*, stacked on one another and located near the nucleus (Figure 3-7; see also Figure 3-1). Sometimes also called the *Golgi complex*, it was first noticed in the nineteenth century by the Italian biologist Camillo Golgi. Like the endoplasmic reticulum, the Golgi apparatus processes molecules within its membranes. The Golgi apparatus seems to be part of the same system that prepares protein molecules for export from the cell.

The role of the Golgi apparatus in processing and packaging protein molecules for export from the cell is summarized in Figure 3-8. First, proteins synthesized by ribosomes and transported to the end of

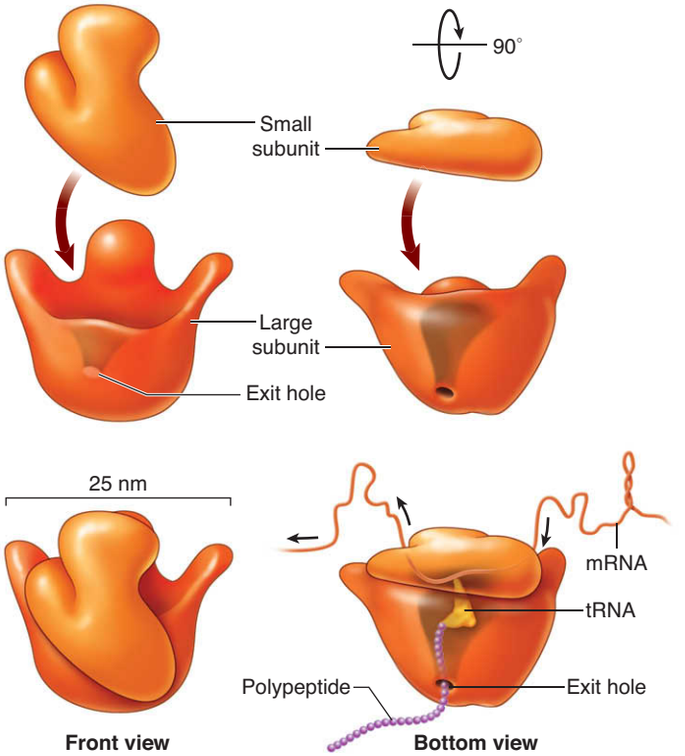


FIGURE 3-6

Ribosome. A ribosome is composed of a small subunit and a large subunit, shown here from two different perspectives. After the small subunit attaches to a messenger RNA (mRNA) strand containing the genetic "recipe" for a polypeptide strand, the subunits come together to form a complete ribosome. Transfer RNA (tRNA) brings amino acids into the cavity between subunits, where they are assembled into a strand according to the mRNA code. As the polypeptide strand elongates, it moves out through a tunnel and a tiny exit hole in the large subunit.

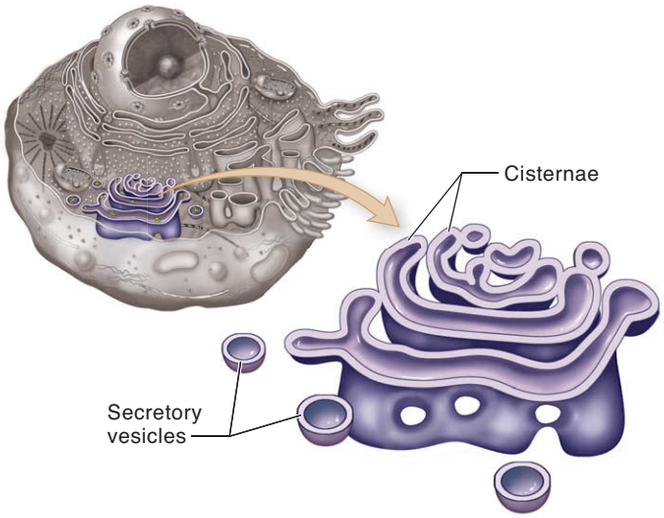
an endoplasmic reticulum canal are packaged into tiny membranous bubbles, or **vesicles,** that break away from the endoplasmic reticulum. The vesicles then move to the Golgi apparatus and fuse with the first cisterna. Protein molecules thus released into the cisterna are then chemically altered by enzymes present there. For example, the enzymes may attach carbohydrate molecules synthesized in the Golgi apparatus to form glycoproteins.

The processed and sorted molecules are then "pinched off" into another vesicle, which moves to the next cisterna for further processing. The proteins and glycoproteins eventually end up in the outermost cisterna, from which vesicles pinch off and move to another part of the cell. Often, the final destination is the plasma membrane.

At the plasma membrane, the vesicles release their contents outside the cell in a process called *secretion.* Other protein and glycoprotein molecules may instead be incorporated into the membrane of a Golgi vesicle. This means that these molecules eventually become part of the plasma membrane, as seen in Figure 3-3 and Table 3-2.

| A&P CONNECT |

Scientists are using their knowledge of the Golgi apparatus to mimic the cell's chemical-making functions in order to manufacture therapeutic treatments more efficiently. Check out ***Biomimicry*** online at ***A&P Connect.***



A



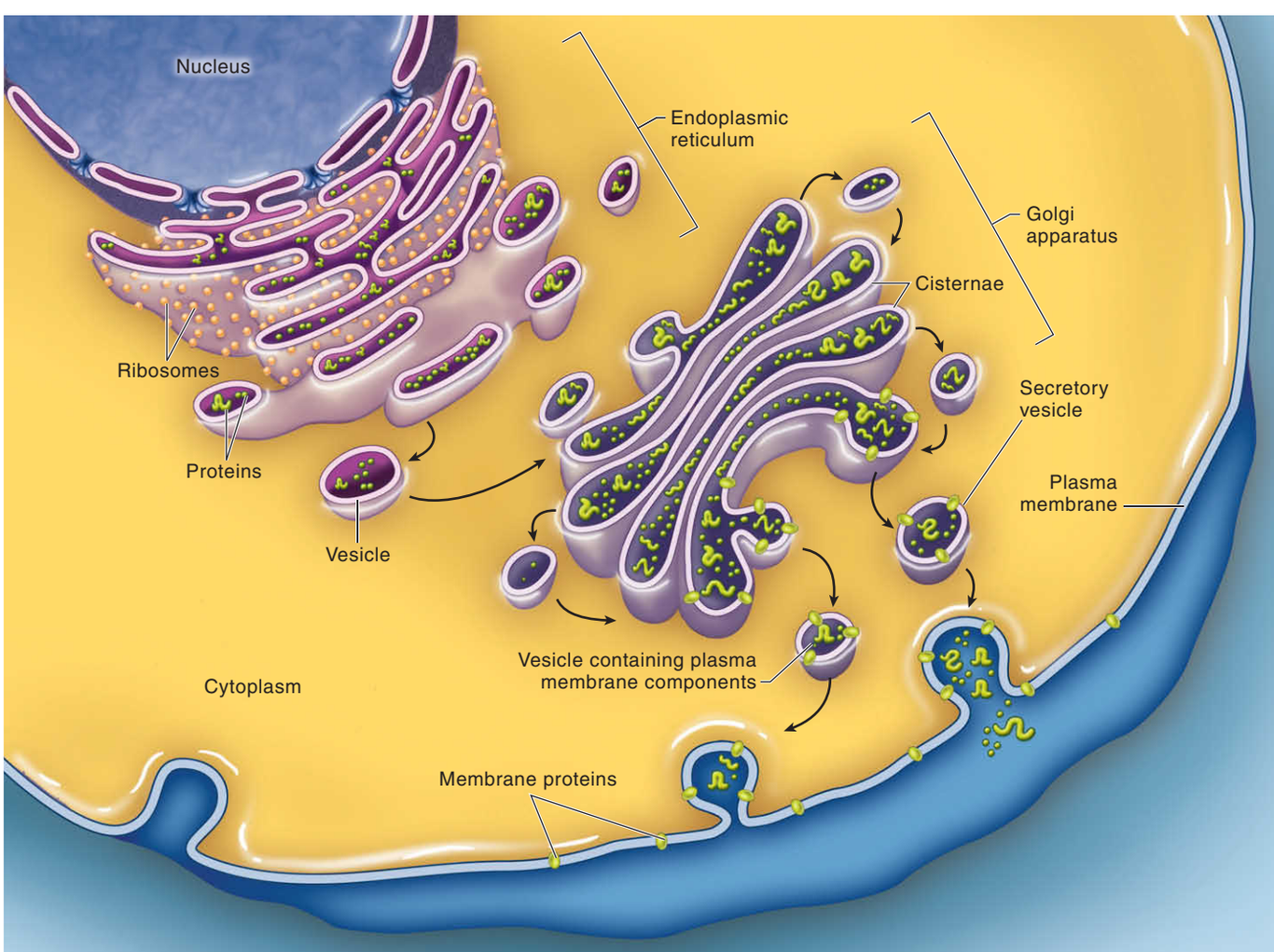
B

FIGURE 3-7

Golgi apparatus. A, Sketch of the structure of the Golgi apparatus showing a stack of flattened sacs, or *cisternae,* and numerous small membranous bubbles, or *secretory vesicles.* **B,** Transmission electron micrograph (TEM) showing the Golgi apparatus highlighted with color.

FIGURE 3-8

The cell's protein export system. The Golgi apparatus processes and packages protein molecules delivered from the endoplasmic reticulum by small vesicles. After entering the first cisterna of the Golgi apparatus, a protein molecule undergoes a series of chemical modifications, is sent (by means of a vesicle) to the next cisterna for further modification, and so on, until it is ready to exit the last cisterna. When it is ready to exit, a molecule is packaged in a membranous secretory vesicle that migrates to the surface of the cell and "pops open" to release its contents into the space outside the cell. The vesicle membrane, including any integral membrane proteins, then becomes part of the plasma membrane. Some vesicles remain inside the cell for some time and serve as storage vessels for the substance to be secreted.



Lysosomes

Like the endoplasmic reticulum and Golgi apparatus, **lysosomes** have membranous walls—indeed, they are vesicles that have pinched off from the Golgi apparatus. The size and shape of lysosomes change with the stage of their activity. In their earliest, inactive stage, they look like mere granules. Later, as they become active, they take on the appearance of small vesicles or sacs (see Figure 3-1). The interior of the lysosome contains various kinds of enzymes capable of breaking down all the protein components of cells.

Lysosomal enzymes have several important functions in cells. Chiefly, they help the cell break down proteins that are not needed to get them out of the way; the amino acids resulting from the breakdown process can be reused by the cell. In the process illustrated in Figure 3-9, defective organelles can be thus recycled. Integral membrane proteins from the plasma membrane can pinch off inside the cell and be recycled in the same manner. Likewise, cells may engulf bacteria or other extracellular particles and destroy them with lysosomal enzymes. Thus lysosomes deserve their nicknames of "digestive bags" and "cellular garbage disposals."

Proteasomes

The **proteasome** is another protein-destroying organelle in the cell. As Figure 3-10 shows, the proteasome is a hollow, cylindrical "drum" made up of protein subunits. Found throughout the cytoplasm, the proteasome is responsible for breaking down abnormal and misfolded proteins released from the ER, as well as destroying normal regulatory proteins in the cytoplasm that are no longer needed. But unlike the lysosome, which destroys large groups of protein molecules all at once, the proteasome destroys protein molecules one at a time.

Before a protein enters the hollow interior of the proteasome, it must be tagged with a chain of very small proteins called *ubiquitins*. The ubiquitin chain then enters the proteasome and subsequently "pulls" the rest of the protein in after it. As it passes through the cap of the proteasome, the protein is unfolded. Then active sites inside the central chamber break apart the peptide bonds. The resulting short peptide chains, 4 to 25 amino acids long, exit through the other end of the proteasome. The short peptides are easily broken down into their component amino acids for recycling by the cell.

Proper functioning of proteasomes is important in prevention of abnormal cell function and possibly severe disease. For example, in *Parkinson disease (PD)* the proteasome system fails, and consequently, the still intact improperly folded proteins kill nerve cells in the brain that are needed to regulate muscle tension.

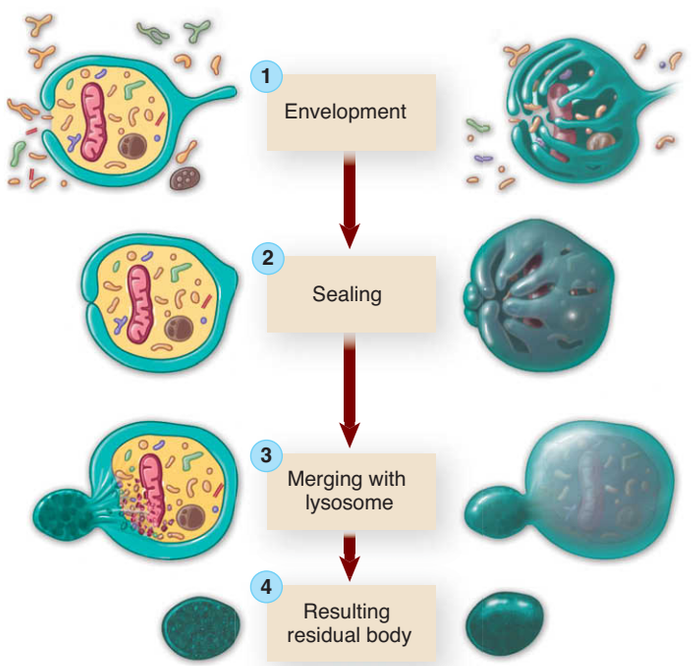


FIGURE 3-9

Lysosome. The process of destroying old cell parts follows these steps: (1) Membrane from the endoplasmic reticulum (ER) or Golgi apparatus encircles the material to be destroyed. (2) A membrane capsule completely traps the material. (3) A lysosome fuses with the membrane capsule, and digestive enzymes from the lysosome enter the capsule and destroy the contents. (4) Undigested material remains in a compact *residual body.*

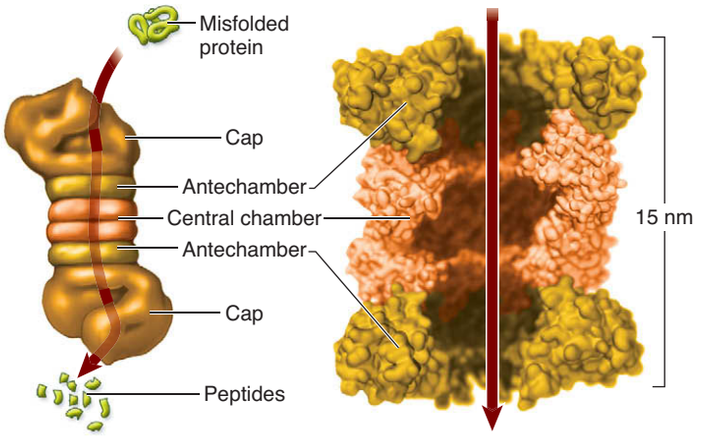


FIGURE 3-10

Proteasome. Made up of protein subunits, the proteasome is a hollow cylinder with regulatory end caps. Following the path shown by *arrows,* an ubiquitin-tagged protein molecule unfolds as it enters the cap and is then broken down into small peptide chains (4 to 25 amino acids), which leave through the other end of the proteasome. The peptides are subsequently broken down into amino acids, which are recycled by the cell. The proteasome is a little over half the size of a ribosome.

Peroxisomes

The **peroxisome** is another type of vesicle containing enzymes that is present in the cytoplasm of some cells. These organelles, which pinch off from the ER, detoxify harmful substances that may enter cells. They are often seen in kidney and liver cells and serve important detoxification functions in the body. Peroxisomes

contain the enzymes *peroxidase* and *catalase*, which are important in detoxification reactions involving hydrogen peroxide (H_2O_2). Hydrogen peroxide is the chemical that gives this organelle its name.

Mitochondria

Find the cell's little "power plants" called **mitochondria** shown in Figures 3-1 and 3-11. Magnified thousands of times, as they are there, they look like small, partitioned sausages—if you can imagine sausages only 1.5 µm (1500 nanometers [nm]) long and half as wide. (In case you are better at visualizing in inches than micrometers, 1.5 µm equals about 3/50,000 of an inch.) Yet, like all organelles, even as tiny as they are, mitochondria have a highly organized molecular structure.

Their membranous walls consist of not one but two delicate membranes. They form a sac within a sac. The inner membrane is contorted into folds called **cristae.** The large number and size of these folds gives the inner membrane a comparatively huge surface area for such a small organelle.

Embedded in the inner membrane are enzymes that are essential for assembling a chemical vital for life: *adenosine triphosphate (ATP)*. ATP was first introduced in Chapter 2 as the molecule that transfers energy from food to cellular processes. It is the job of each mitochondrion to extract energy from food molecules and use it to build ATP molecules. Then the ATP molecules leave the mitochondrion and break apart to release the energy in a variety of specific chemical reactions throughout the cell. Thus each mitochondrion acts as a tiny "power plant" that converts energy from a stored form to a more directly useable form (temporarily stored in ATP). Chapters 4 and 30 present more detailed information about this vital process that provides useable energy for the cell.

Both the inner and outer membranes of the mitochondrion have essentially the same molecular structure as the cell's plasma membrane. All evidence gathered so far indicates that the functional proteins in the membranes of the cristae are arranged precisely in the order of their functioning. This is another example, but surely an impressive one, of the principle stressed in Chapter 1—self-organization is a foundation stone and a vital characteristic of life.

The fact that mitochondria generate most of the power for cellular work suggests that the number of mitochondria in a cell might be directly related to its amount of activity. This principle does seem to hold true. In general, the more work a cell does, the more mitochondria its cytoplasm contains. Liver cells, for example, do more work and have more mitochondria than sperm cells do. A single liver cell contains 1000 or more mitochondria, whereas only about 25 mitochondria are present in a single sperm cell. The mitochondria in some cells multiply when energy consumption increases. For example, frequent aerobic exercise can increase the number of mitochondria inside skeletal muscle cells.

Each mitochondrion has its own DNA molecule, a very surprising discovery indeed! This enables each mitochondrion to make some of its own enzymes. Having its own DNA also enables each mitochondrion to divide and produce genetically identical daughter mitochondria. Scientists believe that mitochondria are bacteria that have become part of our cells—a concept that has several useful applications discussed more thoroughly in Chapter 37.

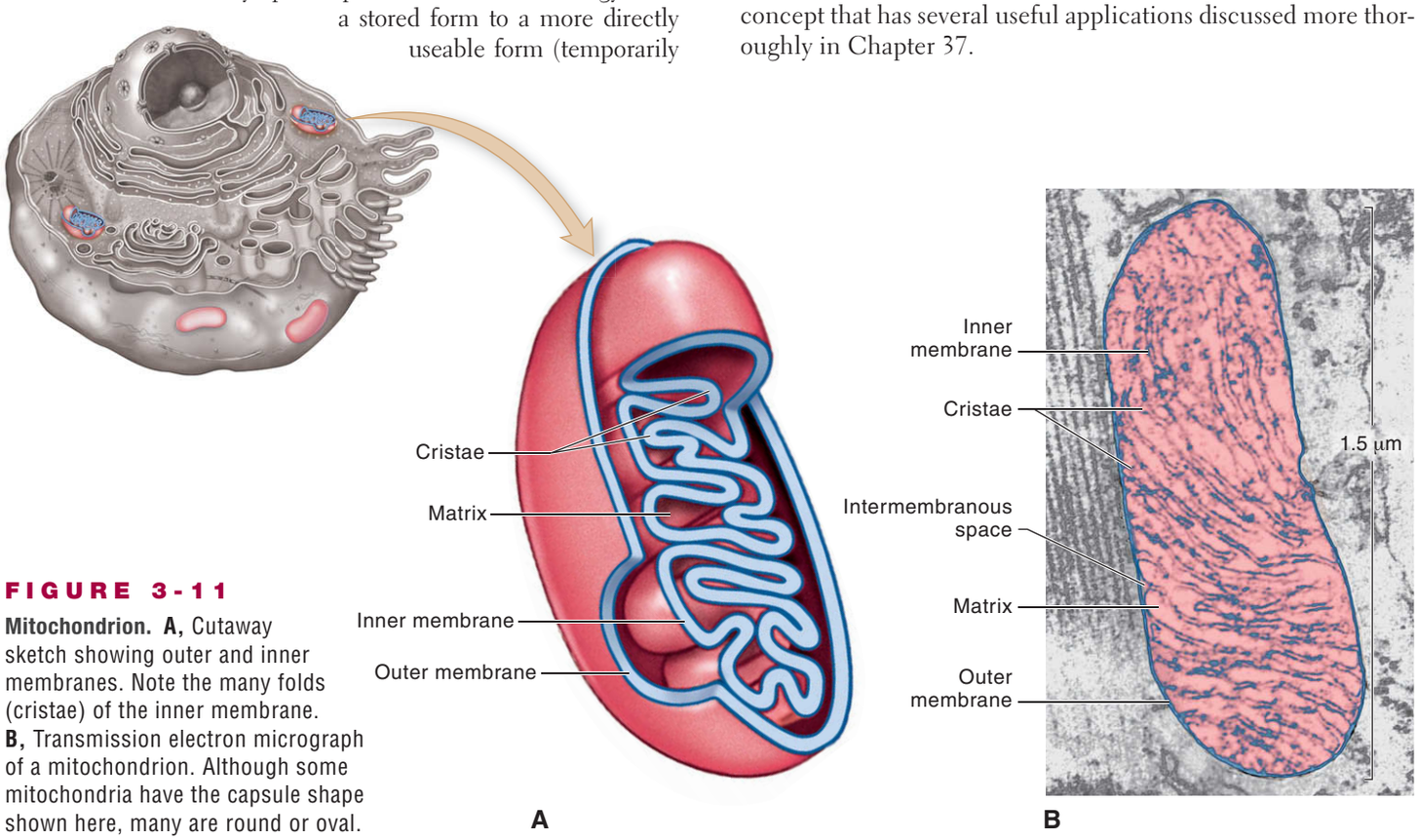


FIGURE 3-11

Mitochondrion. A, Cutaway sketch showing outer and inner membranes. Note the many folds (cristae) of the inner membrane. **B,** Transmission electron micrograph of a mitochondrion. Although some mitochondria have the capsule shape shown here, many are round or oval.

NUCLEUS

The **nucleus,** one of the largest cell structures (see Figure 3-1), usually occupies the central portion of the cell. The shape of the nucleus and the number of nuclei present in a cell vary. One spherical nucleus per cell, however, is common.

Electron micrographs show that two membranes perforated by openings, or pores, enclose the *nucleoplasm* (nuclear substance) (Figure 3-12). *Nuclear pores* are intricate structures often called *nuclear pore complexes* (NPCs) (Figure 3-13). Nuclear pore complexes act as gatekeepers and transport mechanisms that selectively permit molecules and other structures to enter or leave the nucleus. Organelles called *vaults* may also assist with such transport, as described in Box 3-2.

The two nuclear membranes, together called the *nuclear envelope,* have essentially the same type of structure as other cell membranes. The membranous walls of the endoplasmic reticulum extend outward from the membranes of the nuclear envelope.

Probably the most important fact to remember about the nucleus is that it contains DNA molecules, the well-known heredity molecules often referred to in news stories. In nondividing cells, the DNA molecules appear as tiny bunches of tangled threads sprinkled with granules. This material is named **chromatin.** Chromatin is from the Greek *chroma,* "color," so named because it readily takes the color of stains. These chromatin tufts are not randomly spread throughout the nucleus. They continually move like dancers into various positions within the nucleus as the DNA performs its functions.

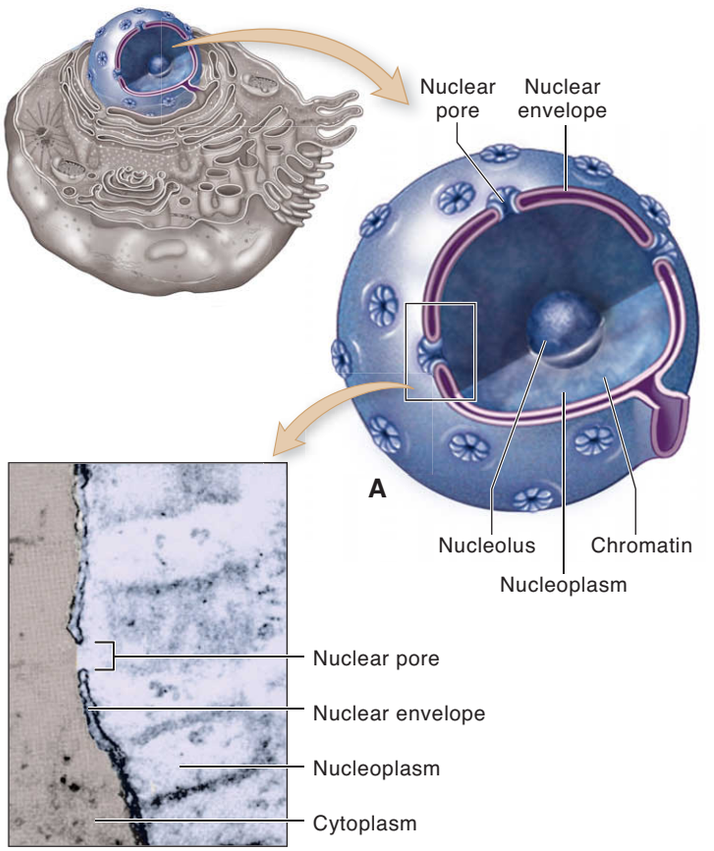


FIGURE 3-12

Nucleus. A, An artist's rendering and, **B,** an electron micrograph show that the nuclear envelope is composed of two separate membranes and is perforated by large openings, or nuclear pores.

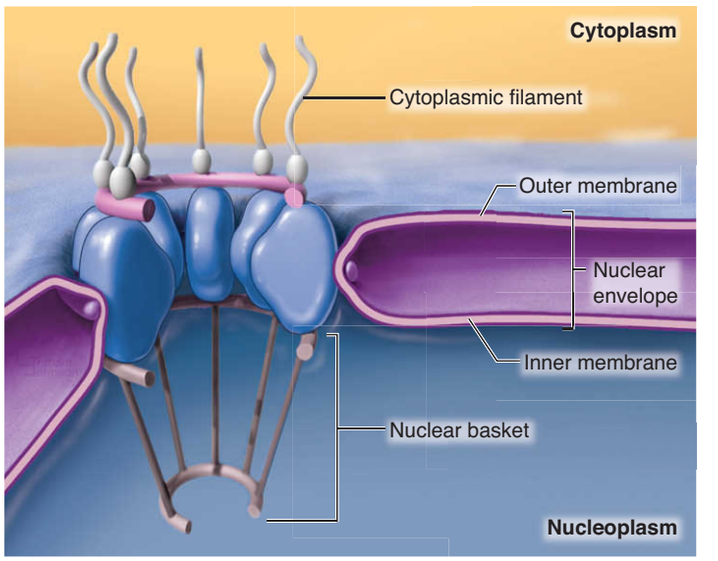


FIGURE 3-13

Nuclear pore complex (NPC). The elaborate structure of the nuclear pore complex hints at its many roles in regulating the movement of small particles between the inside and outside of the nucleus.

When the process of cell division begins, DNA molecules become more tightly coiled. They then become so compact that they look like short, rodlike structures and are then called **chromosomes.** All normal human cells (except mature sex cells) contain 46 chromosomes, and each chromosome consists of one DNA molecule plus some protein molecules.

The functions of the nucleus are primarily functions of DNA molecules. In brief, DNA molecules contain the master code for making all the RNA plus the many enzymes and other proteins of a cell. Therefore, DNA molecules ultimately dictate both the structure and the function of cells. Chapter 5 briefly discusses how a cell transcribes and translates the master code to synthesize specific proteins. DNA molecules are inherited, so DNA plays a pivotal role in the process of heredity—a concept we explore further in Chapter 37.

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In nondividing cells, chromosomes are found in the form of chromatin strands that occupy specific **chromosome territories (CTs)** within the nucleus. See an example of a CT map in ***Chromosome Territories*** online at ***A&P Connect.***

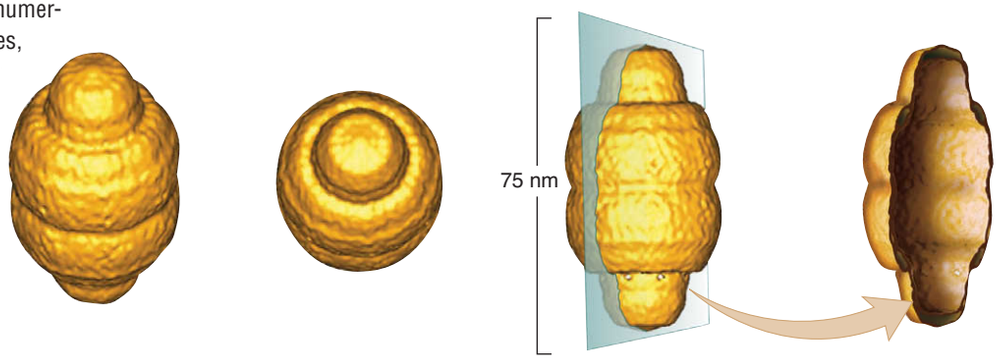
evolve

The most prominent structure visible in the nucleus is a small nonmembranous body that stains densely when studied in the laboratory setting and is called the **nucleolus** (Figure 3-12, A). Like chromosomes, it consists chiefly of a nucleic acid, but the nucleic acid is not DNA. It is RNA, or ribonucleic acid (see pp. 115–116).

The nucleolus functions to synthesize ribosomal RNA (rRNA) and combine it with protein to form the subunits that will later combine to form ribosomes, the protein factories of cells (see

Box 3-2 | Vaults

One cellular structure recently added to the list of organelles is a barrel-shaped structure called a *vault.* It is a very tiny capsule that, like the vaulted ceiling of a cathedral, is composed of a set of tapered pieces that fit together to form a rounded structure. They contain a small bit of RNA (*vault RNA* or *vRNA*) along with proteins. One proposed function for vaults, which are thought to be very numerous in each cell, is to fit into nuclear pores, where they open up one end to pick up or drop off small structures such as RNA molecules or ribosome subunits. The vaults may then connect to a microtubule and slide rapidly along to another part of the cell—acting like miniature railway cars. Besides shuttling molecules to and from the nucleus, vaults probably participate in a number of other transport roles in the cell.



Vaults. This computer reconstruction of electron microscopy (EM) data shows the shape of vaults. The right image reveals the thin wall and hollow interior of a vault, which may act as a tiny transport shuttle for small cellular structures.

Figure 3-6). You might guess, therefore, and correctly so, that the more protein a cell makes, the larger its nucleolus appears. Cells of the pancreas, to cite just one example, make large amounts of protein and have large nucleoli.

| QUICK CHECK |

4. List at least three functions of the plasma membrane.
5. Define the term *organelle.*
6. Identify three organelles by name and give one function of each.
7. Distinguish between membranous and nonmembranous organelles.

CYTOSKELETON

As its name implies, the **cytoskeleton** is the cell's internal supporting framework. Like the bony skeleton of the body, the cytoskeleton is made up of rather rigid, rodlike pieces that not only provide support but also allow movement. Like the body's musculoskeletal framework, the cytoskeleton has muscle-like groups of fibers and other mechanisms that move the cell, or parts of the cell, with great strength and mobility. In this section, we take a look at the basic characteristics of the cell's internal skeleton, as well as several organelles that are associated with it.

Cell Fibers

No one knew much about *cell fibers* until the development of two new research methods: one with fluorescent molecules and the other with stereomicroscopy, that is, three-dimensional pictures of whole, unsliced cells made with high-voltage electron microscopes. Using these techniques, investigators discovered intricate arrangements of fibers of varying widths. The smallest fibers seen have a width of about 3 to 6 nanometers (nm)—less than 1 millionth of an inch! Of particular interest is their arrangement. They form a three-dimensional, chaotic lattice, a kind of scaffolding in the cell. These fibers appear to support parts of the cell formerly thought to float free in the cytoplasm—the endoplasmic reticulum, mitochondria, and "free" ribosomes (Figure 3-14; see also

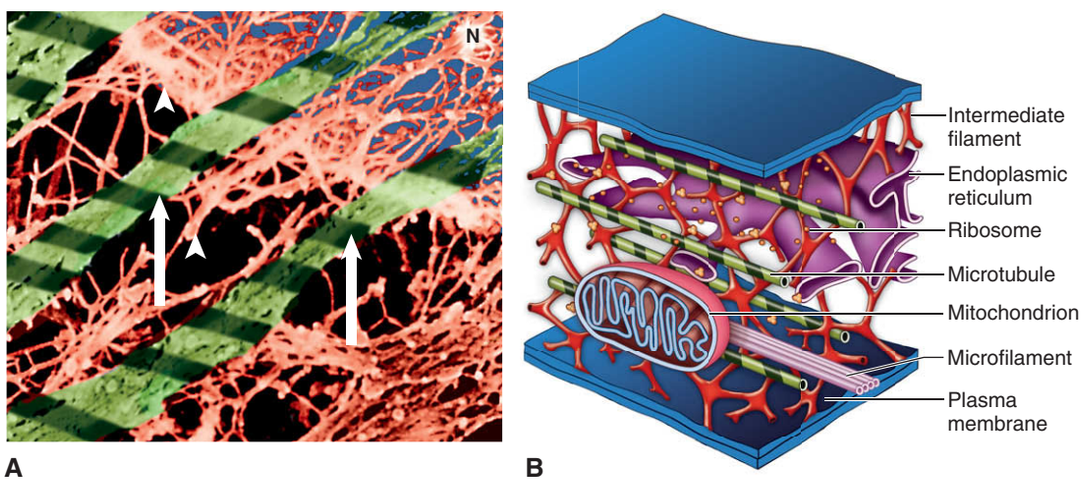


FIGURE 3-14

The cytoskeleton. A, Color-enhanced electron micrograph of a portion of the cell's internal framework. The letter *N* marks the nucleus, the *arrowheads* mark the intermediate filaments, and the *complete arrows* mark the microtubules. **B,** Artist's interpretation of the cell's internal framework. Notice that the "free" ribosomes and other organelles are not really freely floating in the cell.

Figures 3-1 and 3-2). Cytoskeletal fibers may even "fence in" regions of the plasma membrane to prevent free-floating movement of embedded proteins.

The smallest cell fibers are called **microfilaments.** Microfilaments often serve as part of our "cellular muscles." They are made of thin, twisted strands of protein molecules (Figure 3-15, A). In some microfilaments, the proteins can be pulled by little "motors" and slide past one another to cause shortening of the cell. The most obvious example of such shortening occurs in muscle cells, where many bundles of microfilaments are pulled together to shorten the cells with great force.

Cell fibers called **intermediate filaments** are twisted protein strands that are slightly thicker than microfilaments (Figure 3-15, B). Intermediate filaments are thought to form much of the supporting framework in many types of cells. They act as the tendons and ligaments of the cell, holding the cell together as it is pushed and pulled. For example, the protective cells in the outer layer of skin are filled with a dense arrangement of tough intermediate filaments.

The thickest of the cell fibers are tiny, hollow tubes called **microtubules.** As Figure 3-15, C, shows, microtubules are made of protein subunits arranged in a spiral fashion. Microtubules are sometimes called the "engines" of the cell because they often move things around in the cell—or even cause movement of the entire cell. For example, both the movement of vesicles within the cell and the movement of chromosomes during cell division are thought to be accomplished by microtubules.

Just as the body's musculoskeletal system helps us sense our body's position and environmental impacts, the cell's cytoskeleton can detect changes in the cell's position and impacts that affect the cell.

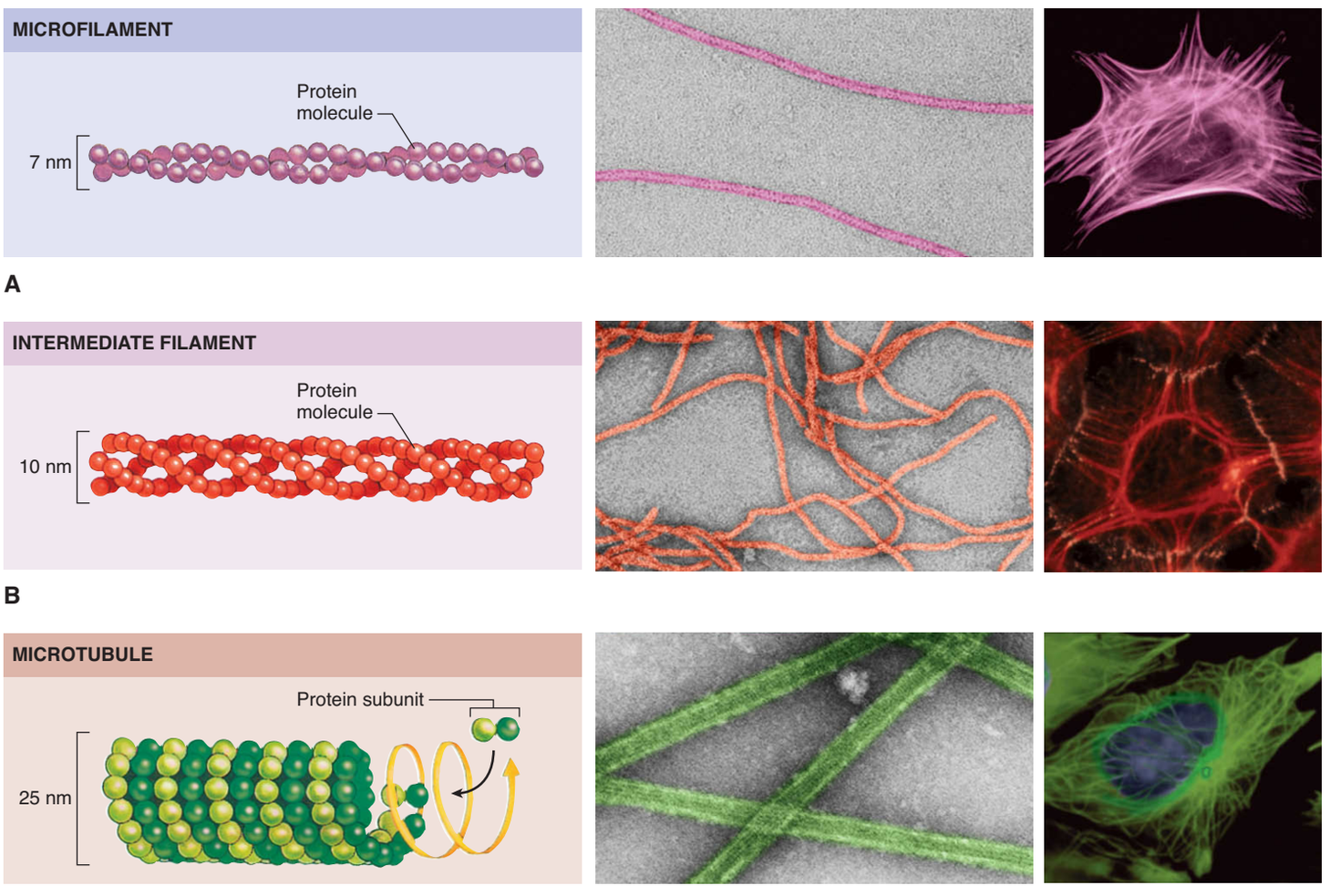


FIGURE 3-15

Cell fibers. The left panel of each part is a sketch, the middle panel is a transmission electron micrograph (TEM), and the right panel is a light micrograph using fluorescent stains to highlight specific molecules within each cell. **A,** *Microfilaments* are thin, twisted strands of protein molecules. **B,** *Intermediate filaments* are thicker, twisted protein strands. **C,** *Microtubules* are hollow fibers that consist of a spiral arrangement of protein subunits. Note the bright yellow-green microtubule-organizing center (centrosome) near the large purple nucleus in the bottomright panel.

In addition to the "bones" and "muscles" that make up the cytoskeleton, there are many types of functional proteins that allow the various parts to interact with one another. For example, receptor molecules help parts link to one another and may even permit signals to be sent between parts. Molecular motors, described later, move parts. Other functional proteins such as enzymes keep everything running smoothly, too.

Centrosome

An example of an area of the cytoskeleton that is very active and requires coordination by functional proteins is the **centrosome.** The centrosome is a region of the cytoplasm near the nucleus that coordinates the building and breaking apart of microtubules in the cell. For this reason, this nonmembranous structure is often called the *microtubule-organizing center (MTOC).*

Look for the tiny yellow-green centrosome in Figure 3-15, part C (right panel). You can see, radiating out from the centrosome in this micrograph, the green-stained microtubules organized around it.

The boundaries of the centrosome are rather indistinct because it lacks a membranous wall. However, the general location of the centrosome is easy to find because of a pair of cylindrical structures called **centrioles.**

Under the light microscope, centrioles appear as two dots located near the nucleus. The electron microscope, however, reveals them to be not mere dots but tiny cylinders (Figure 3-16). The walls of the cylinders consist of nine bundles of microtubules, with three tubules in each bundle. A curious fact about these two tubular-walled cylinders is that they are tethered by tiny fibers and sit at right angles to each other. This special arrangement occurs when the centrioles separate in preparation for cell division (see Table 5-5 on p. 123). Before separating, a daughter centriole is formed perpendicular to each member of the original pair (both become "mother" centrioles) so that a complete pair may be distributed to each new cell.

A cloudlike mass of material surrounding the centrioles is called the *pericentriolar material (PCM).* The PCM is active in starting the growth of new microtubules. The distal and subdistal appendages on the mother centriole that you can see in Figure 3-16, A, are anchor points for microtubules.

The microtubule organizing function of the centrosome plays an important role during cell division, when a special "spindle" of microtubules is constructed for the purpose of pulling chromosomes apart and toward each daughter cell. As this spindle forms, the centrosome is anchored by an **aster,** which is a formation of microtubules radiating outward from the centrioles.

In addition to their involvement in forming the spindle that appears during cell division and other key components of the cytoskeleton, the centrosome is involved in the formation of microtubular cell extensions (discussed in a later section).

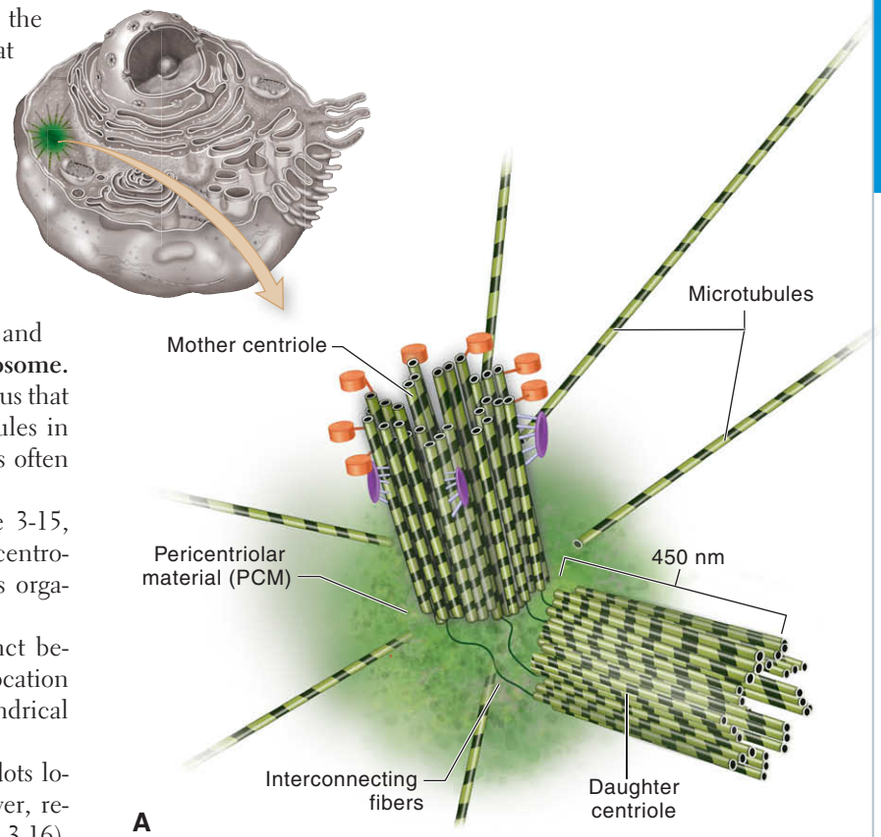


FIGURE 3-16

Centrosome. Sketch **(A)** and transmission electron micrograph (TEM) **(B)** showing the structure of the centrosome, which acts as a microtubule-organizing center for the cell's cytoskeleton.

Molecular Motors

Have you wondered as you read along how all the little vesicles, organelles, and molecules always seem to be able to move on their own power to where they need to go in a cell? Vesicles don't have feet! So how do they move from place to place in an organized way? The answer is surprising: cellular movement *does* rely on "foot" power! The cell's internal "feet" are actually little protein structures called **molecular motors.** As you can see in

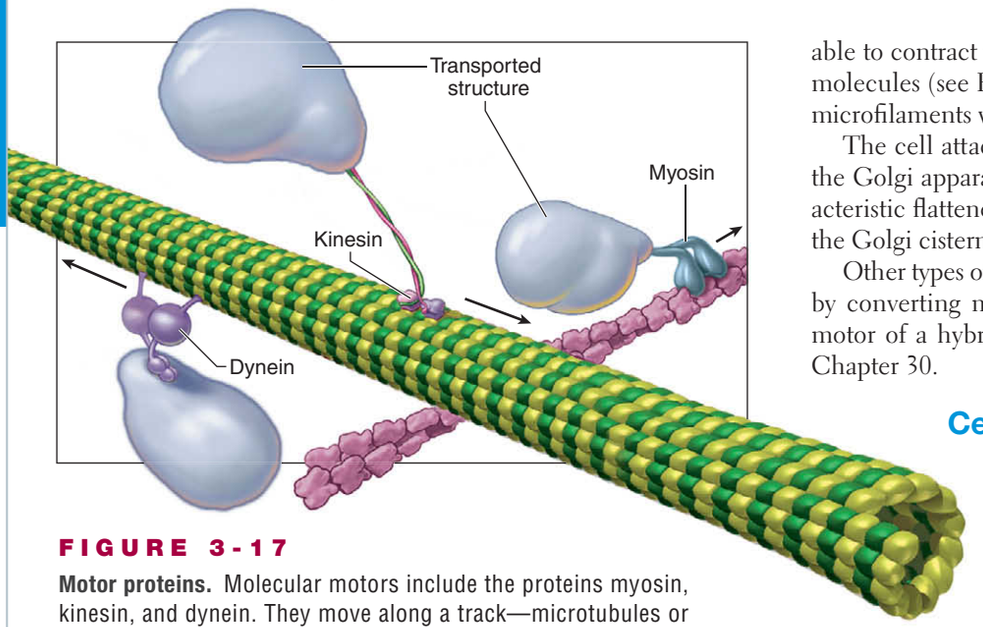


FIGURE 3-17

Motor proteins. Molecular motors include the proteins myosin, kinesin, and dynein. They move along a track—microtubules or microfilaments—and pull larger structures such as vesicles, fibers, or particles. Such movement can be used for intracellular transport or movement of the cell's entire framework.

Figure 3-17, these little motors are like tiny feet that pull huge loads along the microtubules and microfilaments of the cytoskeleton. The loads may be vesicles or other small organelles, fibers, or large molecules. The tiny *motor proteins* transport organelles along a microtubule or fiber as if they were railway cars being pulled along a track. This system provides rapid, orderly movement of structures and materials around the cell. It also allows the cell's framework to move with force, extending and contracting to create movements of the cell. In fact, muscles in your body are able to contract with force because of the action of many myosin molecules (see Figure 3-17) pulling together overlapping rows of microfilaments within each muscle cell, as mentioned earlier.

The cell attaches motor molecules to the ends of cisternae in the Golgi apparatus and pulls these sacs outward into their characteristic flattened shape. This action eventually pulls vesicles off the Golgi cisternae.

Other types of molecular motors can be used to generate power by converting mechanical energy to chemical energy, like the motor of a hybrid automobile—an example that we explore in Chapter 30.

Cell Extensions

In some cells the cytoskeleton forms projections that extend the plasma membrane outward to form tiny, fingerlike processes. These processes, *microvilli*, *cilia*, and *flagella*, are present only in certain types of cells—depending, of course, on a cell's particular functions.

Microvilli are found in epithelial cells that line the intestines and other areas where absorption is important (Figure 3-18, A). Like tiny fingers crowded against each other, microvilli cover part of the surface of a cell (see Figure 3-1). A single microvillus measures about 0.5 µm long and only 0.1 µm or less across. Inside each microvillus are microfilament bundles that provide both structural support and the ability to move. Because one cell has hundreds of these projections, the surface area of the cell is increased manyfold—a structural feature that enables the cell to perform its function of absorption at a faster rate.

Cilia and **flagella** are cell processes that have cylinders made of microtubules at their core. Each cylinder is composed of nine double microtubules arranged around two single microtubules in

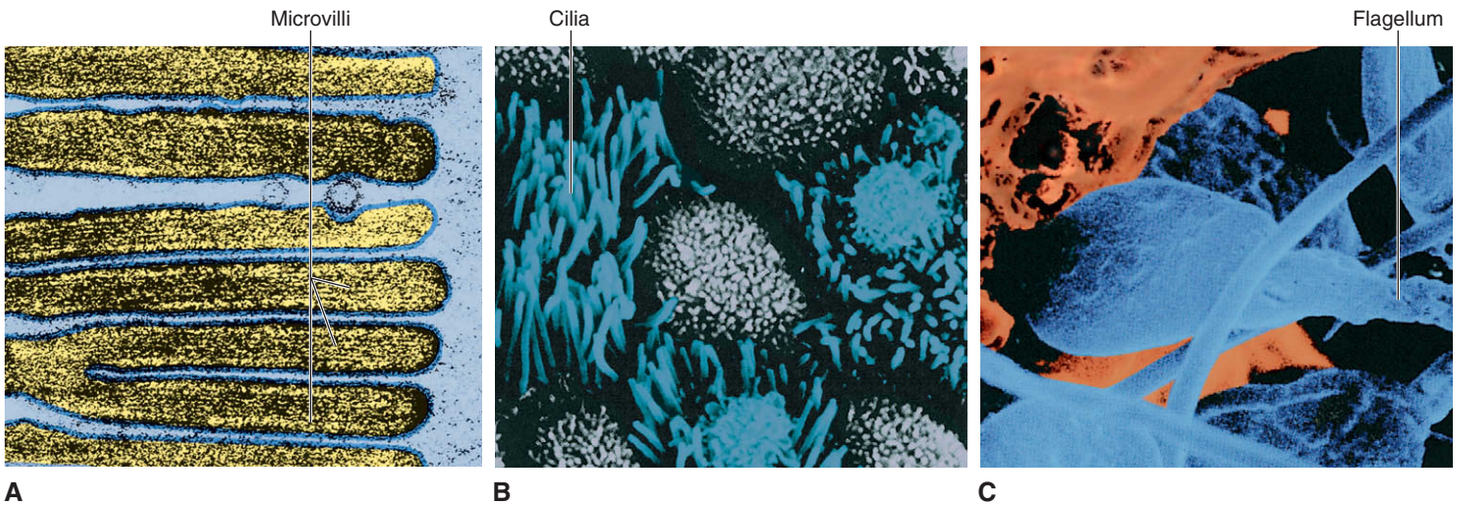
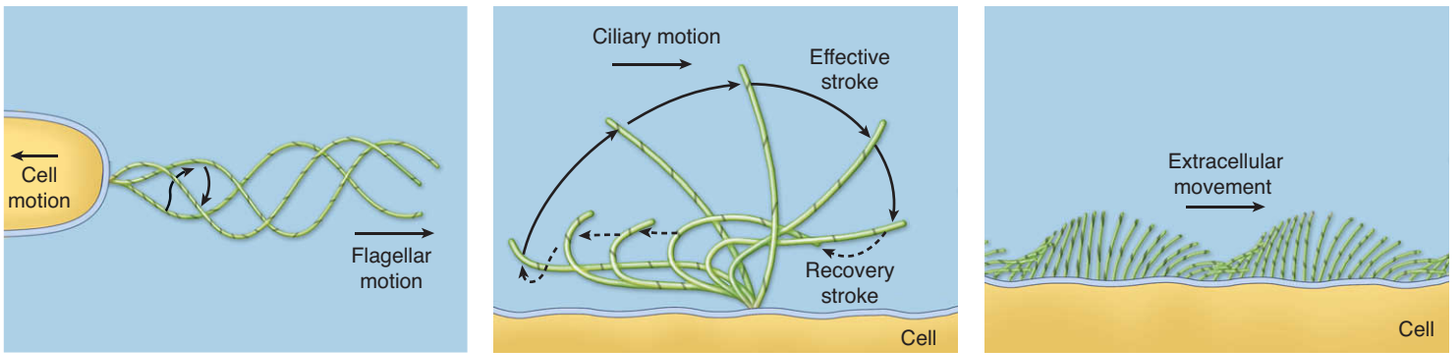


FIGURE 3-18

Cell processes. A, *Microvilli* are numerous, fingerlike projections that increase the surface area of absorptive cells. This electron micrograph shows a longitudinal section of microvilli from a cell lining the small intestine. Note the bundles of microfilaments that support the microvilli. **B,** *Cilia* are numerous, fine processes that transport fluid across the surface of the cell. This electron micrograph shows cilia (long projections) and microvilli (small bumps) on cells lining the lung airways. **C,** In humans, *flagella* are single, elongated processes on sperm cells that enable these cells to "swim."



Flagellum **Cilium** **Cilia**

FIGURE 3-19

Movement patterns. A flagellum (left) produces wavelike movements, which propels a sperm cell forward—like the tail of an eel. In humans, cilia (middle and right) found in groups on stationary cells beat in a coordinated oarlike pattern to push fluid and particles in the extracellular fluid along the outer cell surface.

the center—a slightly different arrangement than in centrioles. With the addition of molecular motors, this particular arrangement is suited to movement. Dynein, a type of motor protein (see Figure 3-17), moves the microtubule pairs so they slip back and forth past one another to produce a "wiggling" movement.

Among human cells, what distinguishes cilia from flagella are their size, number, and pattern of movement. Human cilia are shorter and more numerous than flagella (Figure 3-18, B). Under low magnification, cilia look like tiny hairs. The cilia often move in a rhythmic, coordinated way to push substances such as mucus along the cell surface, as explained in Figure 3-19. In the lining of the respiratory tract, the movement of cilia keeps contaminated mucus on cell surfaces moving toward the throat, where it can be swallowed. In the lining of the female reproductive tract, cilia keep the ovum moving toward the uterus. Cilia also have a sensory function, detecting changes in the mucus being moved.

Except for blood cells, most cell types have a single *primary cilium*. The primary cilium lacks the center pair of microtubules and certain motor molecules, such as dynein (see Figure 3-17). Therefore, the primary cilium cannot move like other types of cilia. However, they have other important functions. For example, primary cilia often act as sensory organelles that permit sensations such as vision, hearing, balance, and so on, as you will learn in Chapter 17. In the kidney, primary cilia monitor urine flow—and if damaged—can cause kidney failure. Primary cilia also play a critical role in centriole replication and regulation of cell reproduction (Chapter 5).

Flagella are single, long structures in the only type of human cell that has this feature: the human sperm cell (see Figure 3-18, C). A sperm cell's flagellum moves like the tail of an eel (as you can see in Figure 3-19) to allow the cell to "swim" toward the female sex cell (ovum).

Each year brings with it the discovery of new types of cytoskeletal components. As we tease out their functions, we find that the cytoskeleton is an amazingly rich network that is literally the "bones and muscles" of the cell. It provides a variety of many different types of cell movement, both internal and external, depending on the cell and the circumstances. It provides many different kinds of structural support for the cell and its parts—and even becomes involved in connections with other cells. Most amazing of all, the cytoskeleton has the ability to organize itself by means of a complex set of signals and reactions so that it can quickly respond to the needs of the cell.

CELL CONNECTIONS

The tissues and organs of the body must be held together, so they must, of course, be connected in some way. Many cells attach directly to the extracellular material, or *matrix*, that surrounds them. A group of integral membrane proteins called *integrins* helps hold cells in their place in a tissue. Some integrin molecules span the plasma membrane and often connect the fibers of the cytoskeleton inside the cell to the extracellular fibers of the matrix, thereby anchoring the cell in place. In this manner, also, some cells are held to one another indirectly by fibrous nets that surround groups of cells. Certain muscle cells are held together this way.

Cells may form direct connections with each other. Integrins are sometimes involved in direct cell connections, but other connecting proteins, such as *selectins*, *cadherins*, and *immunoglobulins*, help form most cell-to-cell connections. Not only do such connections hold the cells together, they sometimes also allow direct communication between the cells. The major types of direct cell connections are summarized in Figure 3-20.

Desmosomes sometimes have the appearance of small "spot welds" that hold adjacent cells together. Adjacent skin cells are held together this way. Notice in Figure 3-20 that fibers on the outer surface of each *spot desmosome* interlock with each other. This arrangement resembles Velcro, which holds things together tightly when tiny plastic hooks become interlocked with fabric loops. Notice also that the desmosomes are anchored internally by intermediate filaments of the cytoskeleton. Some cells have a belt-like version of the desmosome structure that completely encircles the cell. This form may be called a *belt desmosome* to distinguish it from a spot desmosome.

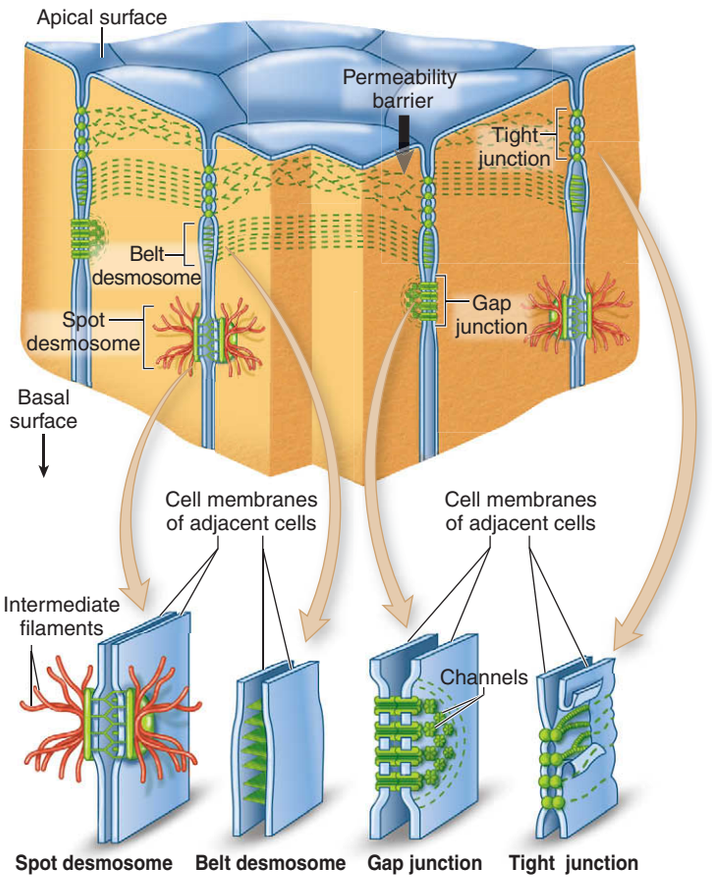


FIGURE 3-20

Cell connections. Spot and belt desmosomes, gap junction, and tight junction.

Gap junctions form when membrane channels of adjacent plasma membranes connect to each other. As Figure 3-20 shows, such junctions have the following two effects: (1) they form gaps or "tunnels" that join the cytoplasm of two cells, and (2) they fuse the two plasma membranes into a single structure. One advantage of this arrangement is that certain molecules can pass directly from one cell to another. Another advantage is that electrical impulses traveling along a membrane can travel over many cell membranes in a row without stopping in between separate membranes because they have "run out of membrane." Heart muscle cells are joined by gap junctions so that a single impulse can travel to, and thus stimulate, many cells at the same time.

Tight junctions occur in cells that are joined near their apical surfaces by "collars" of tightly fused membrane. As you can see in Figure 3-20, rows of integral membrane proteins that extend all the way around a cell fuse with similar integral membrane proteins in neighboring cells. An entire sheet of cells can be bound together the way soft drink cans are held in a six-pack by plastic collars—only more tightly. When tight junctions hold a sheet of cells together, molecules cannot easily *permeate*, or spread through, the cracks between the cells. Tight junctions occur in the lining of the intestines and other parts of the body, where it is important to control what gets past a sheet of cells. The only way for a molecule to get past the intestinal lining is through controlled channel, or carrier, molecules in the plasma membranes of the cells.

| QUICK CHECK |

8. Describe the three types of fibers in the cytoskeleton.
9. What is the function of the centrosome?
10. Name each of the three typical types of cell junctions and describe them.

the BIG picture

Cell Anatomy and the Whole Body

Probably one of the most difficult things to do when first exploring the microscopic world of the cell is to appreciate the structural significance a single cell has to the whole body. Where are these unseen cells? How does each relate to this big thing I call my body?

One useful way to approach the structural role of cells in the whole body is to think of a large, complicated building. For example, the building in which you take your anatomy and physiology course is made up of thousands, perhaps hundreds of thousands, of structural subunits. Bricks, blocks, metal or wood studs, boards, and so on are individual structures within the building that each have specific parts, or organelles, that somehow contribute to overall function. A brick often has sides of certain dimensions that allow it to fit easily with other bricks or with other building materials. Three or four surfaces are usually textured in an aesthetically pleasing manner, and holes in two of the brick surfaces lighten the weight of the brick, allow other materials such as wires or reinforcing rods to pass through, and permit mortar to form a stronger joint with the brick. The material from which each brick is made has been formulated with certain ratios of sand, clay, pigments, or other materials. Each structural feature of each brick has a functional role to play. Likewise, each brick and other structural subunits of the building have an important role to play in supporting the building and making it a pleasing, functional place to study.

Like the structural features of a brick, each organelle of each cell has a functional role to play within the cell. In fact, you can often guess a cell's function by the proportion and variety of different organelles it has. Each cell, like each brick in a building, has a role to play in providing its tiny portion of the overall support and function of the whole body. Where are these cells? In the same place you would find bricks and other structural subunits in a building—everywhere! Like bricks and mortar, everything in your body is made of cells and the extracellular material surrounding them. How do cells relate to the whole body? Like bricks that are held together to form a building, cells form the body.

Just as a brick building is made of many different materials, the human body includes many structural subunits, each with its own structural features or organelles that contribute to the function of the cell—and therefore to the whole body.

MECHANISMS of DISEASE

CELLULAR DISEASE

The more that we learn about the mechanisms of disease, the more apparent it becomes that most diseases known to medicine involve abnormalities of cells. Even a few abnormal cells can so disrupt the internal environment of the body that a person's health can be in immediate danger. The following paragraphs list several important categories of disease that are caused by cell abnormalities. Specific diseases belonging to these categories are discussed further in later chapters. The sampler here and in the next couple of chapters about cell function will start you off with a basic understanding of cellular mechanisms of disease.

Disorders Involving Cell Membranes

Disorders involving cell membrane receptors are being actively investigated by biologists. One such particularly common disorder is a form of **diabetes mellitus (DM)** called *type 2 diabetes*. This condition is often produced by a cellular response to obesity that triggers a reduction in the number of functioning membrane receptors for the hormone *insulin*. Cells throughout the body thus become less sensitive to insulin, the hormone that allows glucose molecules to enter the plasma membrane. Without sufficient stimulation by insulin, the cells literally starve for energy-rich glucose, even though it is available outside the cell.

Duchenne muscular dystrophy (DMD), a severe inherited condition, results from "leaky" membranes in muscle cells. *Dystrophin*, a protein that normally helps connect a muscle cell's cytoskeleton to the plasma membrane and to the surrounding extracellular matrix, is missing (Figure 3-21). Muscle contractions pull at the weakened connections to the plasma membrane and rip holes that allow calcium ions (Ca^{++}) to enter the cell. This flood of Ca^{++} triggers chemical reactions that destroy the muscle, causing life-threatening paralysis.

Disorders Involving Organelles

Any abnormality of any of the organelles is likely to produce disease. Knowing the functions of the organelles helps health professionals understand the nature and symptoms of these disorders.

Failure of mitochondria reduces the cell's ability to produce enough energy for normal function. Mitochondrial abnormalities resulting from chemical damage are known to be a factor in many significant degenerative diseases, such as **Parkinson disease (PD).** PD affects the areas of the brain that control muscles, progressively making effective movement more difficult. Mitochondrial dysfunction is also thought to be involved in the normal degeneration associated with aging.

Some degenerative diseases may also involve the breakdown of the microtubules of the cytoskeleton, which often happens in PD.

Failure of the protein-making system of the ribosomes, ER, and Golgi apparatus can produce many types of diseases that are caused by the absence of one or more proteins critical for body function. Failure of the quality control system provided by proteasomes has been implicated in the buildup of abnormal proteins that form the plaques that characterize **Alzheimer disease (AD)** and other degenerative disorders.

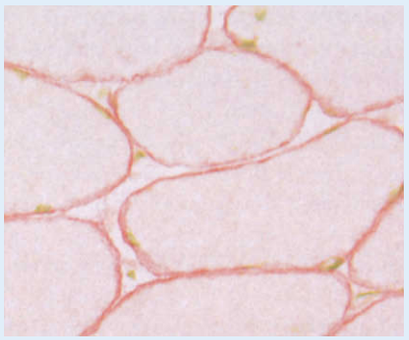


FIGURE 3-21

Dystrophin. This cross section of muscle fibers has been stained for the presence of dystrophin (seen along each cell's plasma membrane). In Duchenne muscular dystrophy (DMD), this protein would be completely absent, thus causing damage to the membranes of muscle fibers that results in destruction of muscle tissue.

LANGUAGE OF SCIENCE *(continued from p. 66)*

endoplasmic reticulum (ER)
(en-doh-PLAZ-mik reh-TIK-yoo-lum)
[*endo-* **inward or within,** *-plasm-* **substance,** *-ic* **relating to,** *ret-* **net,** *-ic-***relating to,** *-ul-* **little,** *-um* **thing**]
pl., endoplasmic reticula

flagellum
(flah-JEL-um)
[*flagellum* **whip**] *pl.*, flagella

fluid mosaic model
(FLOO-id mo-ZAY-ik MAHD-el)

gap junction
(gap JUNK-shen)

Golgi apparatus
(GOL-jee ap-ah-RA-tus)
[*Camillo Golgi* **Italian histologist**]

hydrophilic
(hye-dro-FIL-ik)
[*hydro-* **water,** *-phil-* **love,** *-ic* **relating to**]

hydrophobic
(hye-droh-FOH-bik)
[*hydro-* **water,** *-phob-* **fear,** *-ic* **relating to**]

integral membrane protein (IMP)
(IN-te-grel MEM-brayn PROH-teen)
[*integr-* **whole,** *-al* **relating to,** *membran-* **thin skin,** *prote-* **primary,** *-in* **substance**]

intermediate filament
(in-ter-MEE-dee-it FIL-ahment)
[*inter-* **between,** *-mediate* **to divide,** *fila-* **threadlike,** *–ment* **process**]

lysosome
(LYE-so-sohm)
[*lyso-* **dissolution,** *-som-* **body**]

microfilament
(my-kroh-FIL-ah-ment)
[*micro* **small,** *- fila-* **threadlike,** *-ment* **thing**]

LANGUAGE OF SCIENCE *(continued from p. 85)*

microscopy
(my-KRAH-skah-pee)
[*micro-* **small,** *-scop-* **see,** *-y* **activity**]

microtubule
(my-kroh-TOOB-yool)
[*micro-* **small,** *-tubule* **little tube**]

microvillus
(my-kroh-VIL-us)
[*micro-* **small,** *-villus* **shaggy hair**]
pl., microvilli

mitochondrion
(my-toh-KON-dree-on)
[*mito-* **thread,** *-chondrion-* **granule**]
pl., mitochondria

molecular motor
(mo-LEK-yoo-lar MO-ter)
[*mole-* **mass,** *-cul-* **small,** *-ar* **relating to,** *mot-***movement,** *-or* **agent**]

nucleolus
(noo-KLEE-oh-lus)
[*nucleo-* **nucleus (kernel),** *-olus* **little**] *pl.*, nucleoli

nucleus
(NOO-klee-us)
[*nucleus* **kernel**] *pl.*, nuclei

organelle
(org-an-EL)
[*organ-* **tool or organ,** *-elle* small]

peroxisome
(pe-ROKS-ih-sohm)
[*peroxi-* **hydrogen peroxide,** *-soma* **body**]

plasma membrane
(PLAZ-mah MEM-brayne)
[*plasma* **substance,** *membran-* **thin skin**]

proteasome
(PROH-tee-ah-sohm)
[*protea-* **protein,** *-som-* **body**]

raft

receptor
(ree-SEP-tor)
[*recept-* **receive,** *-or* **agent**]

ribosome
(RYE-boh-sohm)
[*ribo-* **ribose or RNA,** *-som-* **body**]

signal transduction
(SIG-nal tranz-DUK-shen)
[*trans-* **across,** *-duc-* **transfer,** *-tion* **process**]

tight junction
(tite JUNK-shen)

vesicle
(VES-i-kul)
[*vesic-* **blister,** *-cle* **little**]

LANGUAGE OF MEDICINE

Alzheimer disease (AD)
(AHLZ-hye-mer)
[*Alois Alzheimer* **German neurologist**]

diabetes mellitus (DM)
(dye-ah-BEE-teez mell-EYE-tus)
[*diabetes* **siphon,** *mellitus* **honey-sweet**]

Duchenne muscular dystrophy (DMD)
(doo-SHEN MUSS-kyoo-lar DISS-troh-fee)
[*Duchenne* **Guillaume B.A. Duchenne de Boulogne, French neurologist,** *muscul-* **little mouse (muscle)***–ar* **relating to,** *dys-* **bad,** *-troph-* **nourishment,** *-y* **state**]

Parkinson disease (PD)
(PAR-kin-son)
[*James Parkinson* **English physician**]

CASE study

Sunil had been looking forward to the Elementary Science Fair for weeks. His third-grade class had just finished a section on the biological cell, and he couldn't wait to walk through the greatly oversized cell model that was on display. His father seemed just as excited, maybe more, if that were possible. When they got to the cell model, their first challenge was figuring out how to get inside. The "membrane" of the cell had no holes in it. They walked around the cell and finally found a small doorway. A sign above the doorway identified this type of structure, through which they could crawl to enter the cell.

1. Which membrane structure could these hydrophilic molecules (people) pass through?
   a. A phospholipid
   b. A glycolipid
   c. A transmembrane cholesterol
   d. A channel protein

Farther into the cell, Sunil and his father entered what looked like a maze or a network of tunnels. Some of the transparent walls were studded on the outside with what looked like rocks, while other branching tunnels had smooth walls. They followed this maze until they came to another sign telling them they had arrived at the nucleus.

2. What organelle did the maze represent?
   a. Golgi apparatus
   b. Endoplasmic reticulum
   c. Mitochondrion
   d. Microtubules
3. What were the "rocks" stuck to the outside of the walls?
   a. Lysosomes
   b. Peroxisomes
   c. Ribosomes
   d. Mitochondria

After exploring the nucleus, Sunil and his father looked for a way to exit the cell. They had to work their way through a meshwork of plastic pipes, ropes, and yarn designed to represent the cell's cytoskeleton.

4. Which cell fiber type did the pipes (the thickest of the strands) represent?
   a. Microtubules
   b. Microfilaments
   c. Microvilli
   d. Intermediate filaments

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

FUNCTIONAL ANATOMY OF CELLS

A. The typical cell (Figure 3-1)
   1. Also called *composite cell*
   2. Vary in size; all are microscopic (Table 3-1)
   3. Vary in structure and function (Table 3-2)

B. Cell structures
   1. Plasma membrane—separates the cell from its surrounding environment
   2. Cytoplasm—thick gel-like substance inside the cell composed of numerous organelles suspended in watery cytosol; each type of organelle is suited to perform particular functions (Figure 3-2)
   3. Nucleus—large membranous structure near the center of the cell

CELL MEMBRANES

A. Each cell contains a variety of membranes
   1. Plasma membrane (Figure 3-3)—outer boundary of cell
   2. Membranous organelles—sacs and canals made of the same material as the plasma membrane

B. Fluid mosaic model—theory explaining how cell membranes are constructed
   1. Molecules of the cell membrane are arranged in a sheet
   2. The mosaic of molecules is fluid; that is, the molecules are able to float around slowly
   3. This model illustrates that the molecules of the cell membrane form a continuous sheet

C. Chemical attractions are the forces that hold membranes together

D. Groupings of membrane molecules form rafts that float as a unit in the membrane (Figure 3-4)
   1. Rafts may pinch inward to bring material into the cell or organelle
   2. Primary structure of a cell membrane is a double layer of phospholipid molecules
   3. Heads are hydrophilic (water loving)
   4. Tails are hydrophobic (water fearing)
   5. They arrange themselves in bilayers in water
   6. Cholesterol molecules are scattered among the phospholipids to allow the membrane to function properly at body temperature
   7. Most of the bilayer is hydrophobic; therefore water or water-soluble molecules do not pass through easily

E. Integral membrane proteins (IMPs) (Table 3-4)
   1. A cell controls what moves through the membrane by means of IMPs embedded in the phospholipid bilayer
   2. Some IMPs have carbohydrates attached to them and as a result form glycoproteins that act as identification markers
   3. Some IMPs are receptors that react to specific chemicals, sometimes permitting a process called *signal transduction*

CYTOPLASM AND ORGANELLES

A. Cytoplasm—gel-like internal substance of cells that includes many organelles suspended in watery intracellular fluid called *cytosol*

B. Two major groups of organelles (Table 3-3)
   1. Membranous organelles are sacs or canals made of cell membranes
   2. Nonmembranous organelles are made of microscopic filaments or other nonmembranous materials

C. Endoplasmic reticulum (Figure 3-5)
   1. Made of membranous-walled canals and flat, curving sacs arranged in parallel rows throughout the cytoplasm; extend from the plasma membrane to the nucleus
   2. Proteins move through the canals
   3. Two types of endoplasmic reticulum
      a. Rough endoplasmic reticulum
         (1) Ribosomes dot the outer surface of the membranous walls
         (2) Ribosomes synthesize proteins, which move toward the Golgi apparatus and then eventually leave the cell
         (3) Function in protein synthesis and intracellular transportation
      b. Smooth endoplasmic reticulum
         (1) No ribosomes border the membranous wall
         (2) Functions are less well established and probably more varied than for the rough endoplasmic reticulum
         (3) Synthesizes certain lipids and carbohydrates and creates membranes for use throughout the cell
         (4) Removes and stores Ca^{++} from the cell's interior

D. Ribosomes (Figure 3-6)
   1. Many are attached to the rough endoplasmic reticulum and many lie free, scattered throughout the cytoplasm
   2. Each ribosome is a nonmembranous structure made of two pieces, a large subunit and a small subunit; each subunit is composed of rRNA and protein
   3. Ribosomes in the endoplasmic reticulum make proteins for "export" or to be embedded in the plasma membrane; free ribosomes make proteins for the cell's domestic use

E. Golgi apparatus
   1. Membranous organelle consisting of cisternae stacked on one another and located near the nucleus (Figure 3-7)
   2. Processes protein molecules from the endoplasmic reticulum (Figure 3-8)
   3. Processed proteins leave the final cisterna in a vesicle; contents may then be secreted to outside the cell

F. Lysosomes (Figure 3-9)
   1. Made of microscopic membranous sacs that have "pinched off" from Golgi apparatus
   2. The cell's own digestive system; enzymes in lysosomes digest the protein structures of defective cell parts, including integral membrane proteins, and particles that have become trapped in the cell

G. Proteasomes (Figure 3-10)
   1. Hollow, protein cylinders found throughout the cytoplasm
   2. Break down abnormal/misfolded proteins and normal proteins no longer needed by the cell (and which may cause disease)
   3. Break down protein molecules one at a time by tagging each one with a chain of ubiquitin molecules, unfolding it as it enters the proteasome, and then breaking apart peptide bonds

H. Peroxisomes
   1. Small membranous sacs containing enzymes that detoxify harmful substances that enter the cells
   2. Often seen in kidney and liver cells

I. Mitochondria (Figure 3-11)
   1. Made up of microscopic sacs; wall composed of inner and outer membranes separated by fluid; thousands of particles make up enzyme molecules attached to both membranes
   2. The "power plants" of cells; mitochondrial enzymes catalyze series of oxidation reactions that provide nearly most of a cell's energy supply
   3. Each mitochondrion has a DNA molecule, which allows it to produce its own enzymes and replicate copies of itself

NUCLEUS

A. Definition—spherical body in center of cell; enclosed by an envelope with many pores

B. Structure (Figure 3-12)
   1. Consists of a nuclear envelope (composed of two membranes, each with essentially the same molecular structure as the plasma membrane) surrounding nucleoplasm
      a. Nuclear envelope has holes called *nuclear pores*
      b. Nuclear pore complexes (NPCs) are elaborate gateways into and out of the nucleus (Figure 3-13)
   2. Contains DNA (heredity molecules), which appear as:
      a. Chromatin threads or granules in nondividing cells
      b. Chromosomes in early stages of cell division

C. Functions of the nucleus are functions of DNA molecules; DNA determines both the structure and function of cells and heredity

CYTOSKELETON

A. The cell's internal supporting framework (Figure 3-14)
   1. Made up of tiny, flexible fibers and rigid, rodlike pieces
   2. Provides support for cell shape
   3. Can move the cell or its parts
   4. Detects changes inside and outside the cell

B. Cell fibers
   1. Intricately arranged fibers of varying length that form a three-dimensional, irregularly shaped lattice
   2. Fibers appear to support the endoplasmic reticulum, mitochondria, and "free" ribosomes
   3. Microfilaments (Figure 3-15)—smallest cell fibers
      a. Serve as "cellular muscles"
      b. Made of thin, twisted strands of protein molecules that lie parallel to the long axis of the cell
      c. Can slide past each other and cause shortening of the cell
   4. Intermediate filaments—twisted protein strands slightly thicker than microfilaments; form much of the supporting framework in many types of cells
   5. Microtubules—tiny, hollow tubes that are the thickest of the cell fibers
      a. Made of protein subunits arranged in a spiral fashion
      b. Their function is to move things around inside the cell

C. Centrosome (Figure 3-16)
   1. An area of the cytoplasm near the nucleus that coordinates the building and breaking apart of microtubules in the cell
   2. Nonmembranous structure also called the *microtubule organizing center (MTOC)*
   3. Plays an important role during cell division
   4. The general location of the centrosome is identified by the centrioles

D. Molecular motors
   1. Motor proteins (Figure 3-17) include dynein, myosin, and kinesin
   2. Molecular motors can pull larger structures along microtubules and microfilaments as if along a track—providing intracellular transport and movements of the entire cell

E. Cell extensions
   1. Cytoskeleton forms projections that extend the plasma membrane outward to form tiny, fingerlike processes
   2. There are three types of these processes; each has specific functions (Figure 3-18)
      a. Microvilli—found in epithelial cells that line the intestines and other areas where absorption is important; they help increase the surface area manyfold
      b. Cilia and flagella—cell processes that have cylinders made of microtubules and molecular motors at their core (Figure 3-19)
         (1) Cilia are shorter and more numerous than flagella; some cilia found in groups have coordinated oarlike movements that brush material past the cell's surface; all cilia have sensory functions
         (2) Flagella are found only on human sperm cells; flagella move with a tail-like movement that propels the sperm cell forward

CELL CONNECTIONS

A. Cells are held together by fibrous nets that surround groups of cells (e.g., muscle cells), or cells have direct connections to each other

B. Three types of direct cell connections (Figure 3-20)
   1. Desmosome
      a. Fibers on the outer surface of each desmosome interlock with each other; anchored internally by intermediate filaments of the cytoskeleton
      b. Spot desmosomes are like "spot welds" at various points connecting adjacent membranes
      c. Belt desmosomes encircle the entire cell

2. Gap junctions—membrane channels of adjacent plasma membranes adhere to each other; have two effects:
   a. Form gaps or "tunnels" that join the cytoplasm of two cells
   b. Fuse two plasma membranes into a single structure
3. Tight junctions
   a. Occur in cells that are joined by "collars" of tightly fused material
   b. Molecules cannot permeate the cracks of tight junctions
   c. Occur in the lining of the intestines and other parts of the body where it is important to control what gets through a sheet of cells

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. What is the range in human cell diameters?
2. List the three main cell structures.
3. Describe the location, molecular structure, and width of the plasma membrane.
4. Explain the communication function of the plasma membrane, its transportation function, and its identification function.
5. Briefly describe the structure and function of the following cellular structures/organelles: endoplasmic reticulum, ribosomes, Golgi apparatus, mitochondria, lysosomes, proteasomes, peroxisomes, cytoskeleton, cell fibers, centrosome, centrioles, and cell extensions.
6. Describe the three types of intercellular junctions. What are the special functional advantages of each?
7. Describe briefly the functions of the nucleus and the nucleoli.
8. Name three kinds of micrography used in this book to illustrate cell structures. What perspective does each give that the other two do not?

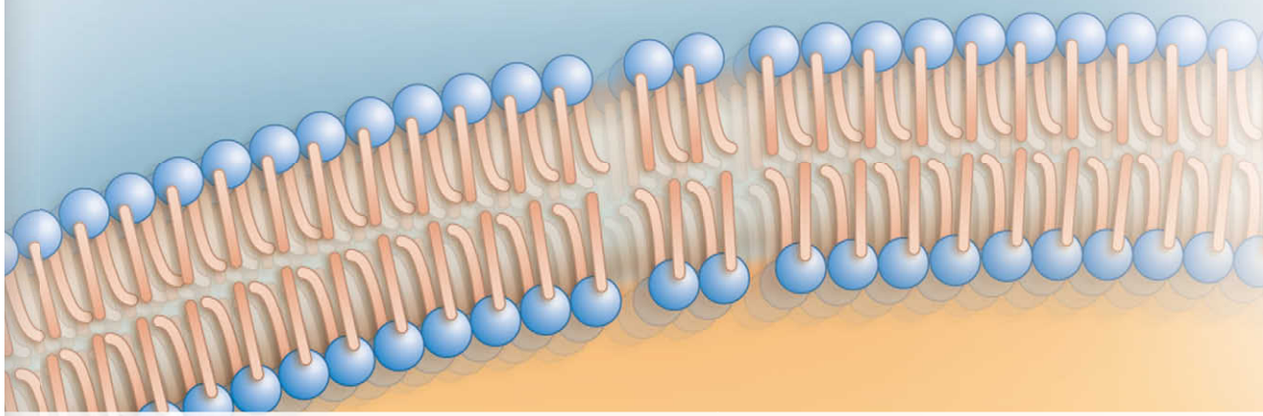
CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Using the complementarity principle that cell structure is related to its function, discuss how the shapes of the nerve cell and muscle cell are specific to their respective functions.
2. What is the relationship among ribosomes, endoplasmic reticulum, Golgi apparatus, and plasma membrane? How do they work together as a system?

4 Physiology of Cells



LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

active site
(AK-tiv site)

actual osmotic pressure
(actual os-MOT-ik PRESH-ur)
[*osmo-* **impulse**, *-ic* **relating to**]

aerobic
(air-OH-bik)
[*aer-* **air**, *-bi-* **life**, *-ic* **relating to**]

allosteric effector
(al-o-STEER-ik ee-FECKT-or)
[*allo-* **another**, *-ster-* **solid**, *-ic* **relating to**, *effect* **to accomplish**]

anabolism
(ah-NAB-o-liz-em)
[*anabol-* **to build up**, *-ism* **condition**]

anaerobic
(an-air-OH-bik)
[*an-* **without**, *-aer-* **air**, *-bi-* **life**, *-ic* **relating to**]

catabolism
(kah-TAB-oh-liz-em)
[*cata-* **against**, *-bol-* **to throw**, *-ism* **condition**]

catalyst
(KAT-ah-list)
[*cata-* **lower**, *-lys-* **loosen**, *-st* **actor**]

cellular respiration
(SELL-yoo-lar respih-RAY-shun)
[*cell* **storeroom**, *-ular* **relating to**, *respire-* **to breathe**, *-ation* **process**]

citric acid cycle
(SIT-rik ASS-id SYE-kul)
[*citr-* **lemony**, *-ic* **relating to**, *acid* **sour**, *cycle* **circle**]

coenzyme
(koh-EN-zyme)
[*co-* **together**, *-en-* **in**, *-zyme* **ferment**]

continued on p. 109

CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

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The cell is the basic functional unit of the body, so it is no wonder that a good understanding of human physiology begins with an overview of cell function. In Chapter 3, you were introduced to the basic structures of the cell. That discussion also included an introduction to some of the important functions of the cell. In this chapter, we take that a step further.

We begin with a brief study of cell membrane transport—a concept that is the foundation for understanding the function of muscles, nerves, glands, hormones, and most other concepts of human physiology. Then, an overview of cell metabolism will set the stage for understanding the "body chemistry" of the whole human organism. That will lead us into Chapter 5, where we explore concepts of cell growth and reproduction.

MOVEMENT OF SUBSTANCES THROUGH CELL MEMBRANES

If a cell is to survive, it must be able to move substances to where they are needed. We already know one way that cells move organelles within the cytoplasm: pushing or pulling performed by the cytoskeleton. A cell must also be able to move various molecules in and out through the plasma membrane, as well as from one membranous compartment to another within the cell. In this first part of the chapter, we explore some of the basic mechanisms a cell uses to move substances across its membranes.

Before beginning a discussion of individual processes, we must realize that membrane transport processes can be labeled as *passive* or *active*. Passive processes do not require any energy expenditure or "activity" of the cell membrane—the particles move by using energy that they already have. Active processes, on the other hand, do require the expenditure of metabolic energy by the cell. In active processes the transported particles are actively "pulled" across the membrane. Keep this distinction in mind as we explore the basic mechanisms of cell membrane transport.

Passive Transport Processes

DIFFUSION

Often, molecules simply spread or *diffuse* through the membranes. The term **diffusion** refers to a natural phenomenon caused by the tendency of small particles to spread out evenly within any given space. All molecules in a solution bounce around in short, chaotic paths. As they collide with one another, they tend to spread out, or diffuse. Think of the example of a lump of sugar dissolving in water (Figure 4-1). Right after the lump is placed in the water, the sugar molecules are very close to one another—the sugar concentration in the lump is very high. As the sugar molecules dissolve, they begin colliding with one another and thus push each other away. Given enough time, the sugar molecules eventually diffuse evenly throughout the water.

Notice that during diffusion, molecules move from an area of high concentration to an area of low concentration. It is not surprising, then, that molecules tend to move from the side of the membrane with high concentration to the side of the membrane with a lower concentration of that molecule. Another way of stating this principle is to say that diffusion occurs down a **concentration gradient.** A concentration gradient is simply a measurable difference in concentration from one area to another. Because molecules spread from the area of *high* concentration to the area of *low* concentration, they spread down the concentration gradient.

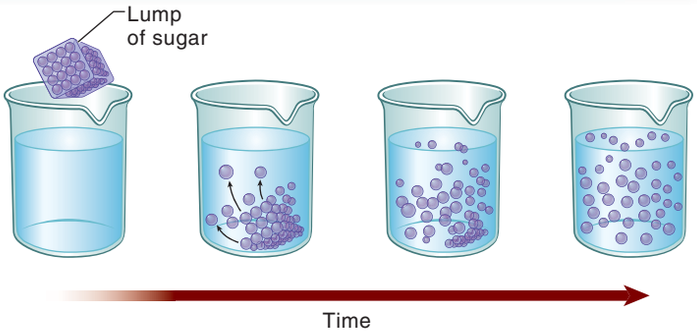


FIGURE 4-1

Diffusion. The molecules of a lump of sugar are very densely packed when they enter the water. As sugar molecules collide frequently in the area of high concentration, they gradually spread away from each other—toward the area of lower concentration. Eventually, the sugar molecules become evenly distributed.

Perhaps the best way to learn the principle of diffusion across a membrane is to look at the example illustrated in Figure 4-2. Here we have different mixtures of a *solute* (dissolved substance) in water. Suppose a 10% solute mixture is separated from a 20% solution by an artificial membrane. Suppose further that the membrane has pores in it that allow solute molecules to pass through, as well as pores that allow water molecules to pass. Solute particles and water molecules darting about the solution collide with each

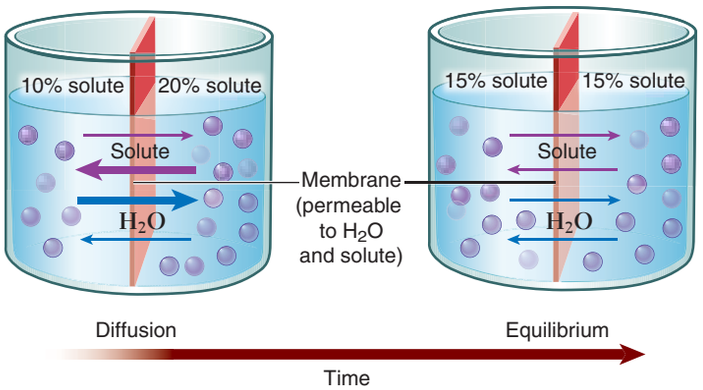


FIGURE 4-2

Diffusion through a membrane. Note that the membrane allows solute (a dissolved particle) and water to pass and that it separates a 10% solution from a 20% solution. The container on the left shows the two solutions separated by the membrane at the start of diffusion. The container on the right shows the result of diffusion after time.

other and with the membrane. Some inevitably hit the membrane pores from the 20% solute side, and some hit the membrane pores from the 10% side. Just as inevitably, some pass through the pores in both directions. For a while, more solute particles enter the pores from the 20% side simply because they are more numerous there than on the 10% side. More of these particles, therefore, move through the membrane from the 20% solute solution into the 10% solute solution than diffuse through it in the opposite direction. In other words, the overall direction of diffusion is from the side where the concentration is higher (20%) to the side where the concentration is lower (10%).

During the time that diffusion of solute particles is taking place, diffusion of water molecules is also going on. Remember, the direction of diffusion of any substance is always down that substance's concentration gradient. Water molecules are more concentrated on the 10% solute solution side because the solution is more dilute—or watery—on that side. Thus water molecules move from the 10% solute solution side to the 20% solute solution side. As Figure 4-2 shows, diffusion of both kinds of molecules eventually produces a dynamic form of equilibrium in which both solutions have equal concentrations. We say that *equilibration* has occurred.

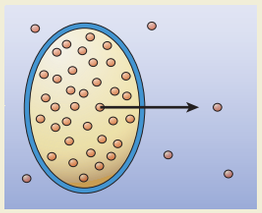
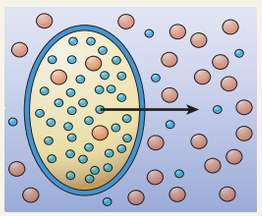
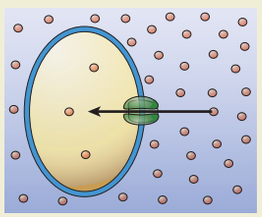
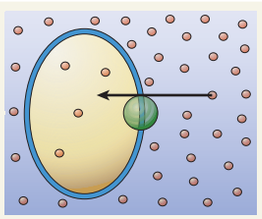
Dynamic equilibrium is not a static state with no movement of molecules across the membrane. Instead, it is a balanced state in which the number of molecules of a substance bouncing to one side of the membrane exactly equals the number of molecules of that substance that are bouncing to the other side. Once equilibration has occurred, overall diffusion may have stopped, but balanced diffusion of small numbers of molecules may continue.

SIMPLE DIFFUSION

Now that we know that concentration gradients drive diffusion, we can explore how the molecules actually find a way through a cell membrane (Table 4-1). Sometimes molecules diffuse directly through the bilayer of phospholipid molecules that forms most of a cell membrane. As discussed in Chapter 3, lipid-soluble molecules can pass through easily. As Figure 4-3 shows, small hydrophobic molecules such as oxygen (O_2) and carbon dioxide (CO_2) can diffuse directly through the phospholipid bilayer. Small, uncharged particles such as water (H_2O) and urea can diffuse only slightly. Such molecules simply dissolve in the phospholipid fluid, diffuse through this fluid, and then move into the water solution on the other side of the membrane. When molecules pass directly through the membrane, the process is called **simple diffusion.**

When molecules are allowed to cross a membrane, they are said to *permeate* the membrane. Thus a particular membrane is *permeable* to a particular molecule only if it can pass through that

TABLE 4-1 Passive Transport Processes

PROCESS		DESCRIPTION	EXAMPLES
Simple diffusion		Movement of particles through the phospholipid bilayer or through channels from an area of high concentration to an area of low concentration—that is, down the concentration gradient	Movement of carbon dioxide out of all cells
Osmosis		Diffusion of water through a selectively permeable membrane in the presence of at least one impermeant solute (often involves both simple and channel-mediated diffusion)	Diffusion of water molecules into and out of cells to correct imbalances in water concentration
Channel-mediated passive transport (facilitated diffusion)		Diffusion of particles through a membrane by means of channel structures in the membrane (particles move down their concentration gradient)	Diffusion of sodium ions into nerve cells during a nerve impulse
Carrier-mediated passive transport (facilitated diffusion)		Diffusion of particles through a membrane by means of carrier structures in the membrane (particles move down their concentration gradient)	Diffusion of glucose molecules into most cells

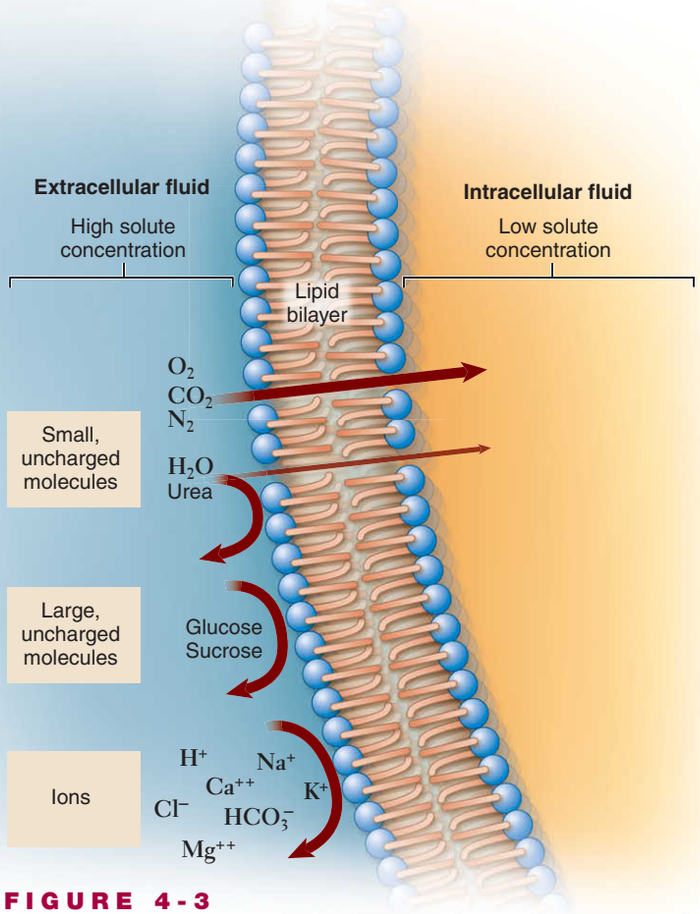


FIGURE 4-3

Simple diffusion through a phospholipid bilayer. Some small, uncharged molecules can easily pass through the phospholipid membrane, but water and urea (a waste product of protein catabolism) rarely get through the membrane. Larger uncharged molecules and ions (charged molecules) may not pass through the phospholipid membrane at all.

membrane. We say that a molecule is *permeant* if it is able to diffuse across a particular membrane. It is *impermeant* if it is unable to diffuse across the membrane.

Box 4-1 shows how the process of diffusion can be harnessed to "clean up" the blood after a person's kidneys fail.

OSMOSIS

A special case of diffusion is called **osmosis.** Osmosis is the diffusion of water through a selectively permeable membrane. Often, water is able to diffuse across a living membrane that does not allow diffusion of one or more other substances. Thus water is permeant and therefore can equilibrate its concentration on both sides of the membrane, but the impermeant solutes cannot.

But how can this be? If you look at Figure 4-3, you see that water barely passes through phospholipid membranes! In 1988 Peter Agre finally solved this mystery by proving the existence of small water channels in cell membranes called *aquaporins* (meaning "water pores"). It is the presence of aquaporins that make membranes permeable to water. We will see how such channels allow other substances to move easily across membranes later. For now, let us focus on osmosis—a very important type of diffusion in the body.

First, let us look at an example of osmosis. Imagine that you have a 10% albumin solution separated by a membrane from a 5% albumin solution (Figure 4-4). Assume that the membrane has water pores and is freely permeable to water but impermeable to albumin. The water molecules diffuse or *osmose* through the membrane from the area of high water concentration to the area of low water concentration. That is, the water moves from the more dilute 5% albumin solution to the less dilute 10% albumin solution. Although equilibrium is eventually reached, the albumin does not diffuse across the membrane. Only the water diffuses. Because of this osmosis, one solution loses volume and the other solution gains volume (see Figure 4-4).

Unlike the open container pictured in Figure 4-4, cells are closed containers. They are enclosed by their plasma membranes. Actually, most of the body is composed of closed compartments such as cells, blood vessels, tubes, and bladders. In closed compartments, such as a toy water balloon, changes in volume also mean changes in pressure. Adding volume to a cell by osmosis increases its pressure, just as adding volume to a water balloon increases its pressure. Water pressure that develops in a solution as a result of osmosis into that solution is called **osmotic pressure.** Taking this principle a step further, we can state that osmotic pressure develops in the solution that originally has the higher concentration of impermeant solute.

Potential osmotic pressure is the maximum osmotic pressure that *could develop* in a solution when it is separated from pure water by a selectively permeable membrane. **Actual osmotic pressure,** on the other hand, is pressure that *already has developed* in a solution by means of osmosis. Actual osmotic pressure is easy to measure because it is already there.

Because potential osmotic pressure is a *prediction* of what the actual osmotic pressure would be, it cannot be measured directly. What determines a solution's potential osmotic pressure? The answer, simply put, is the concentration of particles of impermeant

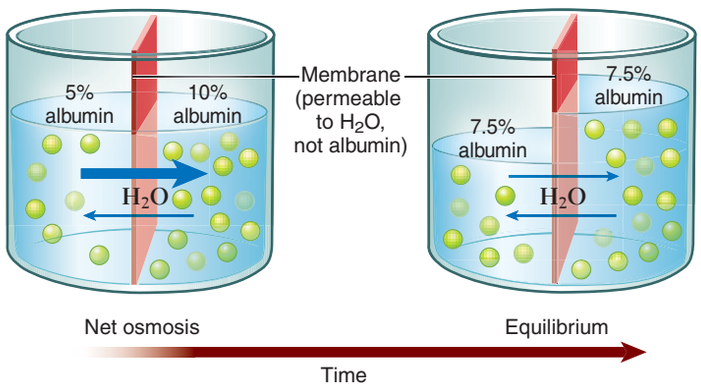


FIGURE 4-4

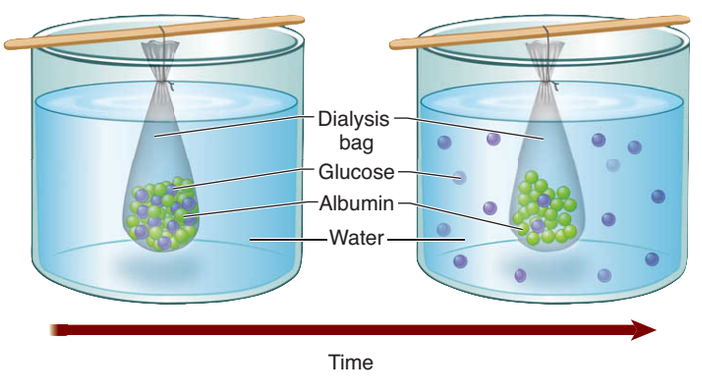
Osmosis. Osmosis is the diffusion of water through a selectively permeable membrane. The membrane shown in this diagram is permeable to water but not to albumin. Because there are relatively more water molecules in 5% albumin than 10% albumin, more water molecules osmose from the more dilute into the more concentrated solution (as indicated by the larger arrow in the left diagram) than osmose in the opposite direction. The overall direction of osmosis, in other words, is toward the more concentrated solution. Net osmosis produces the following changes in these solutions: (1) their concentrations equilibrate, (2) the volume and pressure of the originally more concentrated solution increase, and (3) the volume and pressure of the other solution decrease proportionately.

Box 4-1 | Dialysis

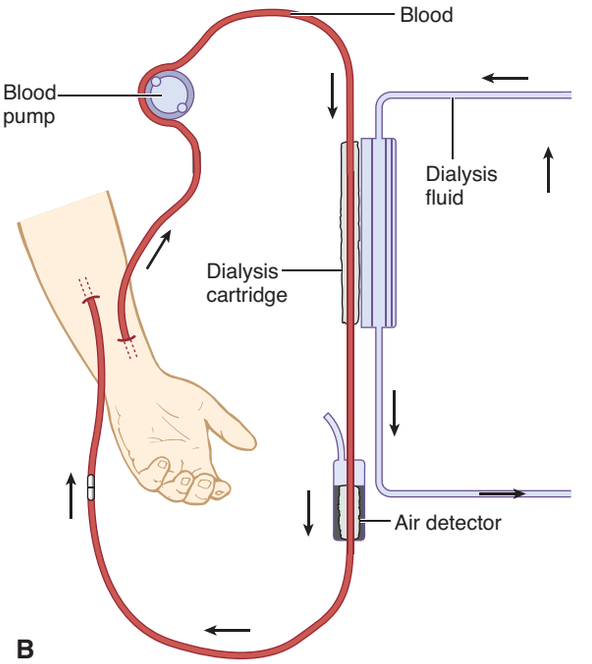
Under certain circumstances, a type of diffusion called **dialysis** may occur. Dialysis is a form of diffusion in which the selectively permeable nature of a membrane causes the separation of smaller solute particles from larger solute particles. *Solutes* are the particles dissolved in a *solvent* such as water. Together, the solutes and solvents form a mixture called a *solution.*

Part A of the figure illustrates the principle of dialysis. A bag made of dialysis membrane—material with microscopic pores—is filled with a solution containing glucose, water, and albumin (protein) molecules and immersed in a container of pure water. Both water and glucose molecules are small enough to pass through the pores in the dialysis membrane. Albumin molecules, like all protein molecules, are very large and do not pass through the membrane's pores. Because of differences in concentration, glucose molecules diffuse out of the bag as small water molecules diffuse into the bag. Despite a concentration gradient, the albumin molecules do not diffuse out of the bag. Why not? Because they simply will not fit through the tiny pores in the membrane. After some time has passed, the large solutes are still trapped within the bag, but most of the smaller solutes are outside of it.

The principle of dialysis can be used in medicine to treat patients with kidney failure. In **hemodialysis** (part B of the figure), blood pumped from a patient is exposed to a dialysis membrane that separates the blood from a clean, osmotically balanced dialysis fluid. Small solutes such as urea and various ions can diffuse through the membrane to reach an equilibrium, thus removing them from the blood. The larger plasma proteins (including albumin) and blood cells remain in the blood, which is returned to the patient's body. In hemodialysis, the process of dialysis is used to "clean up" the patient's blood because the kidneys have failed to perform this task.



A



B

A, Dialysis. A dialysis bag containing glucose, water, and albumin (protein) molecules is suspended in pure water. Over time, the smaller solute molecules (glucose) diffuse out of the bag. The larger solute molecules (albumin) remain trapped in the bag because the bag is impermeable to them. Thus dialysis is diffusion that results in separation of small and large solute particles. **B, Hemodialysis.** In hemodialysis, the patient's blood is pumped through a dialysis cartridge, which has a semipermeable membrane that separates the blood from the clean dialysis fluid. As dialysis occurs, some of the urea and other small solutes in the blood diffuse into the dialysis fluid whereas the larger solutes (plasma proteins) and blood cells remain in the blood.

solutes dissolved in the solution. Thus one can predict the direction of osmosis and the amount of pressure it will produce by knowing the concentrations of impermeant solutes in two solutions.

The concept of osmosis and osmotic pressure has very important practical consequences in human physiology and medicine. Homeostasis of volume and pressure is necessary to maintain the healthy functioning of human cells. The volume and pressure of body cells tend to remain fairly constant because intracellular fluid (fluid inside the cell) is maintained at about the same potential osmotic pressure as extracellular fluid (fluid outside the cell). A fluid that has the same potential osmotic pressure as a cell is said to be **isotonic** to the cell (Figure 4-5, B). Isotonic comes from the word parts *iso-*, meaning "same," and *-tonic*, referring to "pressure." The isotonic solution and cytosol have the same potential osmotic pressure because they have the same concentration of impermeant solutes.

A human cell placed in a concentrated solution of impermeant solutes will shrivel up. Look at the example of a red blood cell in Figure 4-5, C. The pictured cell is in a solution with a higher concentration of impermeant solutes than that found in the cell and, therefore, has a higher potential osmotic pressure. The extracellular solution is said to be **hypertonic** (higher pressure) to

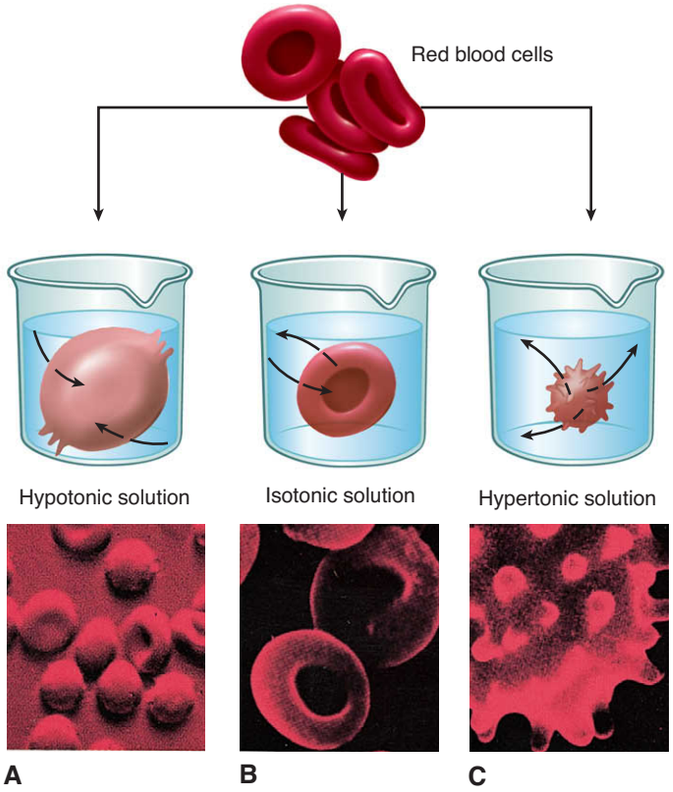


FIGURE 4-5

Effects of osmosis on cells. A, Normal red blood cells placed in a hypotonic solution may swell (as the scanning electron micrograph shows) or even burst (as the drawing shows). This change results from the inward diffusion of water (osmosis). **B,** Cells placed in an isotonic solution maintain constant volume and pressure because the potential osmotic pressure of the intracellular fluid matches that of the extracellular fluid. **C,** Cells placed in a solution that is hypertonic lose volume and pressure as water osmoses out of the cell into the hypertonic solution. The "spikes" seen in the scanning electron micrograph are rigid microtubules of the cytoskeleton. These supports become visible as the cell "deflates."

the intracellular solution (cytosol). Cells placed in solutions that are hypertonic to intracellular fluid always shrivel. If cells shrivel too much, they may become permanently damaged—or even die. Obviously, this fact is medically important. Large amounts of solutes cannot be introduced into the body without considering the effect they will have on the concentration of impermeant solutes in the extracellular fluid. If a treatment or procedure causes extracellular fluid to become hypertonic to the cells of the body, serious damage may occur.

If a human cell is placed in a very dilute solution, such as pure water, the cell may swell. If it expands enough, the cell may burst, or *lyse*. Look at the example of a red blood cell in Figure 4-5, A. This cell is placed in a solution that is **hypotonic** (lower pressure) to the intracellular fluid. Hypotonic solutions tend to lose pressure because they have a lower concentration of impermeant solutes, and thus a higher water concentration, than the opposite solution. Water always osmoses from the hypotonic solution to the cytosol.

In summary, we can make several generalizations about osmosis. First, osmosis is the diffusion of water across a membrane that limits the diffusion of at least some of the solute molecules. That is, at least one impermeant solute must be present. Second, osmosis results in the gain of volume (and thus pressure) on one side of the membrane and loss of volume (and pressure) on the other side of the membrane. Third, the direction of osmosis and the resulting changes in pressure can be predicted if you know the potential osmotic pressure or *tonicity* of the solution outside the plasma membrane.

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evolve

FACILITATED DIFFUSION

For a long time, biologists thought that simple diffusion was the only way that molecules could diffuse through a cell membrane. They found that water-soluble molecules such as sodium ions (Na^+) and glucose molecules could not pass through an artificial phospholipid bilayer easily (see Figure 4-3). However, they also found that indeed such small, water-soluble molecules could pass through living cell membranes quickly. Even water molecules, which pass through the thin phospholipid membrane only rarely, diffuse very rapidly through most living cell membranes. It was not until the presence of various transport proteins, such as membrane channels and membrane carriers, was discovered that we understood how these molecules diffuse across cell membranes. These membrane transporters enable a kind of mediated passive transport that is often called **facilitated diffusion.**

Channel-Mediated Passive Transport

As you already know, cell membranes possess protein "tunnels," better known as *membrane channels* (see Table 3-4, p. 72, and Figure 4-6). Membrane channels are pores through which water

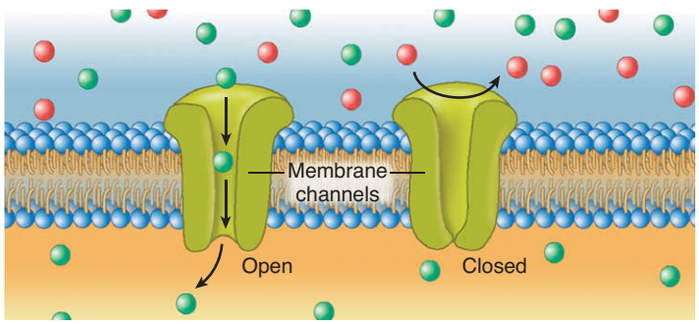


FIGURE 4-6

Membrane channels. Gated channel proteins form tunnels through which only specific molecules may pass—as long as the "gates" are open. Molecules that do not have a specific shape and charge are never permitted to pass through the channel. Notice that the transported molecules move from an area of high concentration to an area of low concentration. The cell membrane is said to be permeable to the type of molecule in question. Filtration, another type of passive transport process, is discussed in Box 4-2 on p. 97.

molecules, specific ions, or other small, water-soluble molecules can pass. For example, sodium ions (Na^+) pass only through *sodium channels* and chloride ions (Cl^-) pass only through *chloride channels*. Recall that water diffuses through aquaporins, which are water-specific channels, during osmosis. Membrane channels can exhibit such *specificity* because their molecular structure prevents molecules of the wrong shape and the wrong pattern of charges to pass through the channel. Thus living membranes can be permeable to some molecules but not to others, depending on the type of channels present.

As Figure 4-6 shows, the permeability of a membrane can also be affected by the opening and closing of membrane channels. Because channels can open or close, they are sometimes called *gated channels*. The active or "open" state can be almost immediately changed to the "closed" state, or changed from closed to open, by various triggering mechanisms. Some gated channels are triggered by electrical changes (voltage), others by light, and still others by mechanical or chemical stimuli. We will look at these various types of triggering mechanisms in later chapters. Open-gated channels may under certain conditions become inactive, stopping the flow of molecules and becoming insensitive to trigger stimuli, before actually closing and resuming sensitivity to stimuli.

Because a living cell membrane can limit the diffusion of some molecules by opening or closing channels in different situations, we say the membrane is *selectively permeable*. Membrane channel structure often permits diffusion in only one direction. So the cell can also determine whether to allow certain molecules to pass in either direction (depending on the concentration gradient, of course) or in only one direction (when the concentration gradient permits).

Aquaporins are among the more recently discovered types of membrane channels. As their name suggests, these channels permit water molecules to diffuse through a cell membrane much more rapidly than by simple diffusion. Aquaporins are thought to be responsible for the very rapid changes in blood cell volume during osmosis illustrated in Figure 4-5.

Because ions move down their concentration gradients as they pass through channels, this type of facilitated diffusion is passive and thus called *channel-mediated passive transport*.

Carrier-Mediated Passive Transport

Molecules may move down their concentration gradient by passing through a different type of membrane transporter called a *membrane carrier*. Thus the carrier may facilitate diffusion in a process called *carrier-mediated passive transport*.

As Figure 4-7 shows, the carrier structure attracts a solute to a binding site, changes its shape, and then releases the solute to the other side of the membrane. This mechanism differs from channel-mediated transport, which does not involve binding the solute molecule and changing shape to release the bound solute. Carrier reactions are reversible and may thus transport molecules in either direction, depending on the concentration gradient.

As in channel-mediated and simple diffusion, carrier-mediated diffusion also transports substances down a concentration gradient (that is, from high to low concentration). An example is the

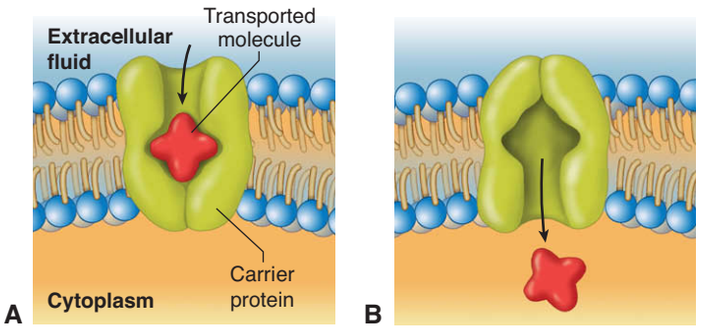


FIGURE 4-7

Membrane carrier. In carrier-mediated transport, a membrane-bound carrier protein attracts a solute molecule to a binding site **(A)** and changes shape in a manner that allows the solute to move to the other side of the membrane **(B)**. Passive carriers may transport molecules in either direction, depending on the concentration gradient.

ADP-ATP (adenosine diphosphate–adenosine triphosphate) carrier found in the membranes of the mitochondrion. This carrier moves ADP into the mitochondrion because the ADP concentration inside is kept low by constant conversion to ATP. Because ATP is thus kept constantly high inside the mitochondrion, ATP passes down its concentration gradient through the ADP-ATP carrier to the outside, where ATP is continually dropping (through use by cell processes).

ROLE OF PASSIVE TRANSPORT PROCESSES

Diffusion of any type is a passive process. In other words, the energy for transport through a membrane does not come from the membrane but from the energy of collision already possessed by the moving molecule. The only requirement of the cell is that it be permeable to the type of molecule in question. Because substances are moved down their concentration gradients, such passive transport tends to maintain an equilibrium of these substances.

We have explored many varieties of diffusion across a membrane, summarized in Table 4-1. Simple diffusion occurs when molecules dissolve directly through the phospholipid bilayer. Facilitated diffusion requires transport proteins in the membrane. The transporters could be channels, such as the water channels needed for osmosis or the ion channels needed to move sodium or potassium ions. The transporters could instead be carriers, such as those needed to move ADP and ATP into and out of the mitochondrion. Filtration, yet another type of passive transport process, is discussed in Box 4-2.

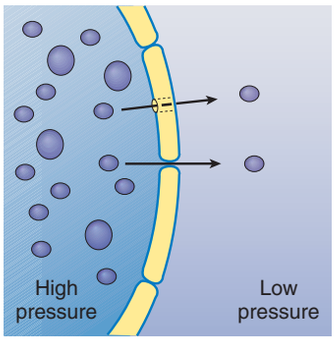
All of these passive transport mechanisms are needed to move critical substances into or out of cells and organelles to maintain an equilibrium. Considering the importance of homeostatic balance, you can see that passive transport is critical to human function. As you will discover in the last part of the chapter, many diseases and even death can result from malfunctions of these passive transport processes.

Box 4-2 | Filtration

Another important passive process for transport in the body is **filtration.** This form of transport involves the passing of water and permeable solutes through a membrane by the force of hydrostatic pressure. *Hydrostatic pressure* is the force, or weight, of a fluid pushing against a surface.

Filtration is movement of molecules through a membrane from an area of high hydrostatic pressure to an area of low hydrostatic pressure—that is, down a hydrostatic pressure gradient. Filtration most often transports substances through a sheet of cells. The force of pressure pushes the molecules through or between the cells that form the sheet. Because the filtration membrane does not allow larger particles through, filtration results in the separation of large and small particles, as you can see in the figure. This is similar to dialysis (Box 4-1, p. 94), except that dialysis is driven by a *concentration gradient.* Filtration is instead driven by a *hydrostatic pressure gradient.*

A simple model of filtration is found in many drip-type coffee makers. Ground coffee is placed in a porous paper filter cup in an upper container and boiling water is added. Gravity pulls downward on the mixture in the upper container, generating hydrostatic pressure against the bottom of the filter. The pores in the paper filter are large enough to let water molecules and other small particles pass through to a coffee pot below the filter. Most of the coffee grounds are too large to pass through the filter. The coffee in the pot below is called the *filtrate.*



Filtration. Particles small enough to fit through the pores in the filtration membrane move from the area of high hydrostatic pressure to the area of low hydrostatic pressure. This results in separation of small particles from larger particles.

How and where does filtration occur in the body? Most often, it occurs in tiny blood vessels called *capillaries,* which are found throughout the body. Hydrostatic pressure of the blood (blood pressure) generated by heart contractions, gravity, and other forces pushes water and small solutes out of the capillaries and into the interstitial spaces of a tissue. Blood cells and large blood proteins are too large to fit through pores in the capillary wall; therefore, they cannot be filtered out of the blood. Capillary filtration allows the blood vessels to supply tissues with water and other essential substances quickly and easily without losing its cells and blood proteins. Capillary filtration is also the first step used by the kidney to form urine.

Active Transport Processes

All the membrane transport processes that we have seen so far are passive processes. The force of movement comes from the concentration gradient—that is, from a physical force of nature. The driving force for active transport processes, on the other hand, comes from the cell itself. Energy of metabolism must be used by cells to force particles across a membrane that otherwise would not move across.

TRANSPORT BY PUMPS

Membrane transporters called *membrane pumps* carry out a transport process in which cellular energy is used to move molecules "uphill" through a cell membrane. By "uphill," we mean that the substance moves from an area of low concentration to an area of higher concentration. An actively transported substance moves *against* its concentration gradient. This is exactly the opposite of diffusion, in which a substance is transported *down* its concentration gradient—or "downhill." It is important to remember that molecules will not travel uphill on their own, anymore than a ball will roll uphill by itself. Molecules will travel uphill only when they are forced by pump mechanisms powered by cellular energy. Moving solutes in different directions is discussed in Box 4-3.

Active pumping is an extremely important process. It allows cells to move certain ions or other water-soluble particles to specific areas. For example, active *calcium pumps* in the membranes of muscle cells allow the cell to force nearly all of the intracellular calcium ions (Ca^{++}) into special compartments—or out of the cell entirely (Figure 4-8). This is important because a muscle cell cannot operate properly unless the intracellular Ca^{++} concentration

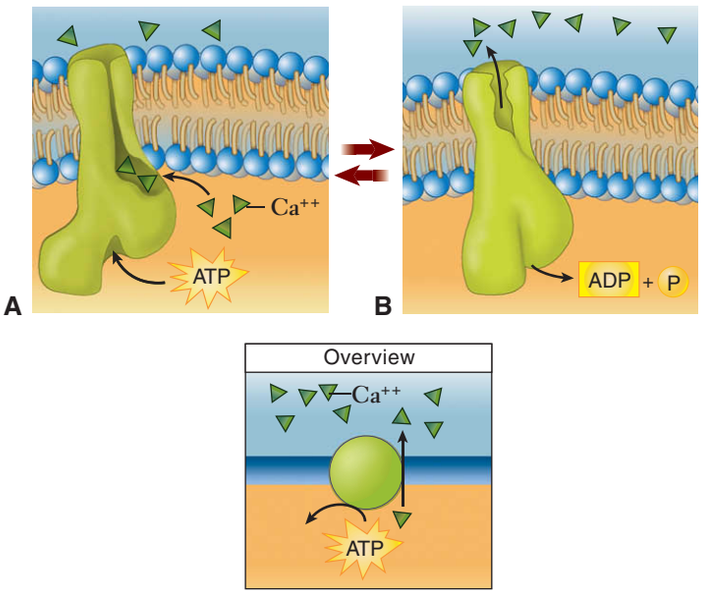


FIGURE 4-8

Calcium pump. A, Two calcium ions (Ca^{++}) enter the pump, and then adenosine triphosphate (ATP) associates with the activating center of the pump. **B,** As the energy released from ATP (forming adenosine diphosphate [ADP] + phosphate [P]) changes the shape of the pump, the Ca^{++} ions are released on the opposite side of the membrane. The small inset shows a simplified view of a calcium pump's action.

Box 4-3 | Transport of Different Solutes

In looking at different types of carriers and pumps in the body, we see that some transport only one type of molecule at a time. This type of transporter is often called a *uniporter.* For example, the GLUT uniporters in many cells passively move glucose from blood plasma into cells. *GLUT* is an acronym for *GLU*cose *T*ransporter. Figure 4-8 shows uniport of two Ca^{++} ions by a calcium pump.

Symporters instead move two or more types of molecule in the same direction through a membrane. For example, the SGLT1 symporter in the digestive tract transports sodium ions and glucose together into absorptive cells. *SGLT1* is the acronym for *S*odium-*GL*ucose *T*ransporter *1.* Symport can also be called **cotransport.**

Antiporters, on the other hand, are transporters that move two different types of molecule in opposite directions at the same time. For example, *Band 3* antiporters in red blood cells passively exchange bicarbonate ions (HCO_3^-) for chloride ions (Cl^-) in opposite directions at the same time. Na^+-K^+-ATPase (sodium-potassium pump) actively antiports sodium ions and potassium ions in all cells of the body. Antiport can also be called **countertransport.**

Sometimes, active transport of one type of solute creates a concentration gradient that drives the passive transport of another solute. For example, in part B of the figure the active transport of sodium ions creates a concentration gradient that drives the cotransport of glucose along with sodium by a symport mechanism. In this case, the movement of sodium is an example of *primary active transport.* The movement of glucose, which depends on the sodium concentration gradient created by primary active transport, is an example of *secondary active transport.* This particular example of secondary active transport is often referred to as *sodium cotransport of glucose.*

is kept low during rest. Other cells use active transport pumps for similar purposes—that is, to create a concentration gradient of a particular solute.

One type of active transport pump, the *sodium-potassium pump*, operates in the plasma membrane of all human cells (Figure 4-9). It is essential for healthy cell survival. As its name suggests, the sodium-potassium pump actively transports sodium ions (Na^+) and potassium ions (K^+)—but in opposite directions. It transports sodium ions *out* of cells and potassium ions *into* cells. By so doing, the sodium-potassium pump maintains a lower sodium concentration in intracellular fluid than in the surrounding extracellular fluid. At the same time, this pump maintains a higher potassium concentration in the intracellular fluid than in the surrounding extracellular fluid. Both ions bind to the same membrane transporter, a molecule known as *sodium-potassium adenosine triphosphatase (Na-K ATPase).* Figure 4-9 shows that three Na^+ ions bind to sodium-binding sites on the pump's inner face. At the same time, an energy-containing adenosine triphosphate (ATP) molecule produced by the cell's mitochondria binds to the pump. The ATP breaks apart, and its stored energy is transferred to the pump. The pump then changes shape, releases the three Na^+ ions to the outside of the cell, and attracts two K^+ ions to its potassium-binding sites. The pump then returns to its original shape and releases the two K^+ ions and the remnant of the ATP molecule to the inside of the cell.

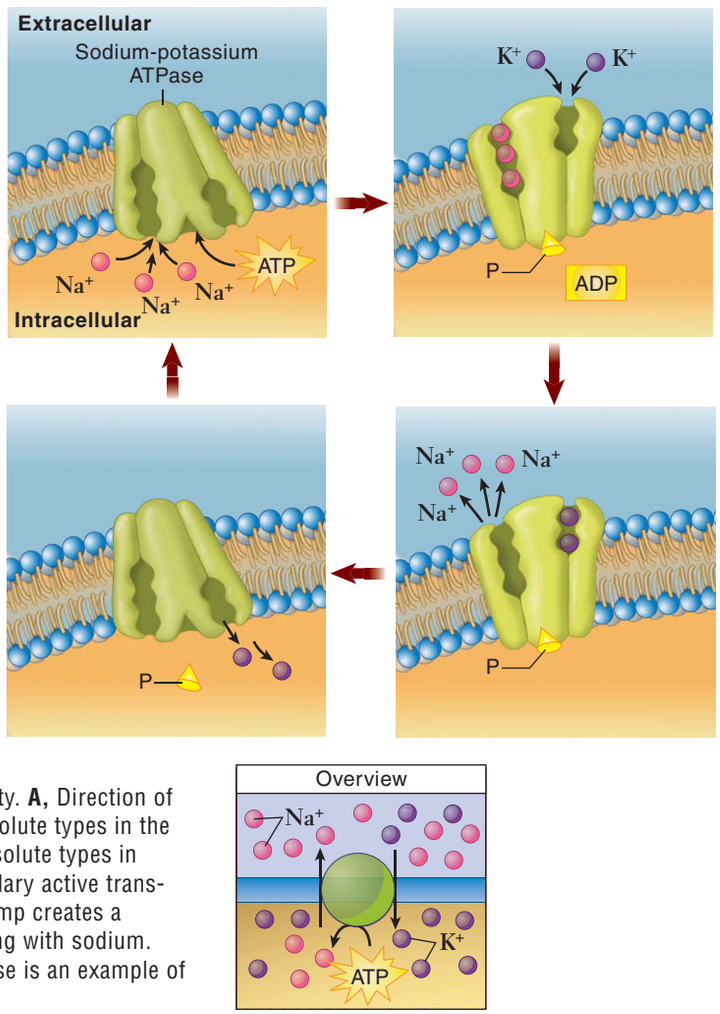
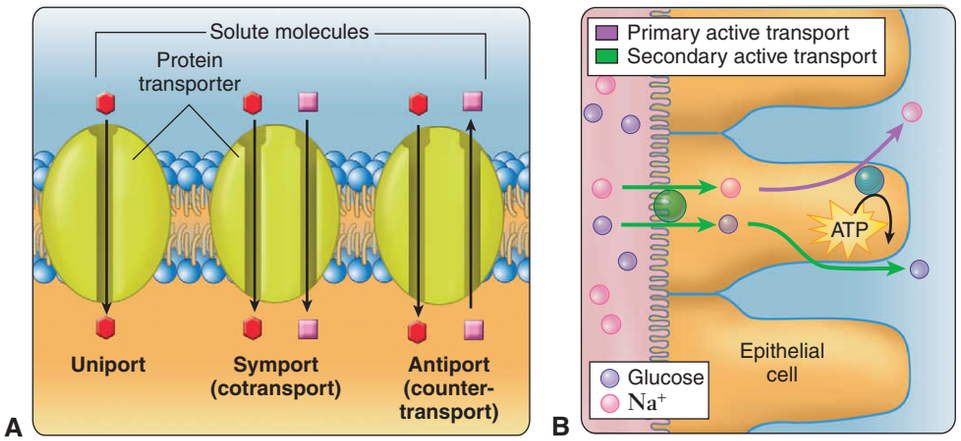


FIGURE 4-9

Sodium-potassium pump. Three sodium ions (Na^+) bind to sodium binding sites on the pump's inner face. At the same time, an energy-containing adenosine triphosphate (ATP) molecule produced by the cell's mitochondria binds to the pump. The ATP breaks apart, and its stored energy is transferred to the pump. The pump then changes shape, releases the three Na^+ ions to the outside of the cell, and attracts two potassium ions (K^+) to its potassium binding sites. The pump then returns to its original shape, and the two K^+ ions and the remnant of the ATP molecule are released to the inside of the cell. The pump is now ready for another pumping cycle. *ATPase,* Adenosine triphosphatase. The small inset is a simplified view of Na^+-K^+ pump activity. **A,** Direction of transport. Movement of one solute (uniport), movement of two or more solute types in the same direction (symport or cotransport), and movement of two or more solute types in opposite directions (antiport or countertransport). **B,** Primary and secondary active transport. In this example, primary active transport of sodium by a sodium pump creates a concentration gradient that drives the passive cotransport of glucose along with sodium. Because it depends on the sodium gradient, sodium cotransport of glucose is an example of secondary active transport. *ATP,* Adenosine triphosphate.



A, Direction of transport. Movement of one solute (uniport), movement of two or more solute types in the same direction (symport or cotransport), and movement of two or more solute types in opposite directions (antiport or countertransport). **B,** Primary and secondary active transport. In this example, primary active transport of sodium by a sodium pump creates a concentration gradient that drives the passive cotransport of glucose along with sodium. Because it depends on the sodium gradient, sodium cotransport of glucose is an example of secondary active transport. *ATP,* Adenosine triphosphate.

TRANSPORT BY VESICLES

Like active transport pumps, mechanisms that carry large groups of molecules into or out of the cell by means of vesicles require the expenditure of metabolic energy by the cell. Such bulk transport mechanisms differ from pump mechanisms in that they allow substances to enter or leave the interior of a cell without actually moving through its plasma membrane (Figure 4-10).

Endocytosis

In **endocytosis** the plasma membrane "traps" some extracellular material and brings it into the cell. The basic mechanism of endocytosis is summarized in Figure 4-10. In endocytosis, the cytoskeleton does all the work by pulling part of the plasma membrane inward, thereby forming a depression, while at the same time pushing the membrane at the edges to form a sort of trap for extracellular material. When the

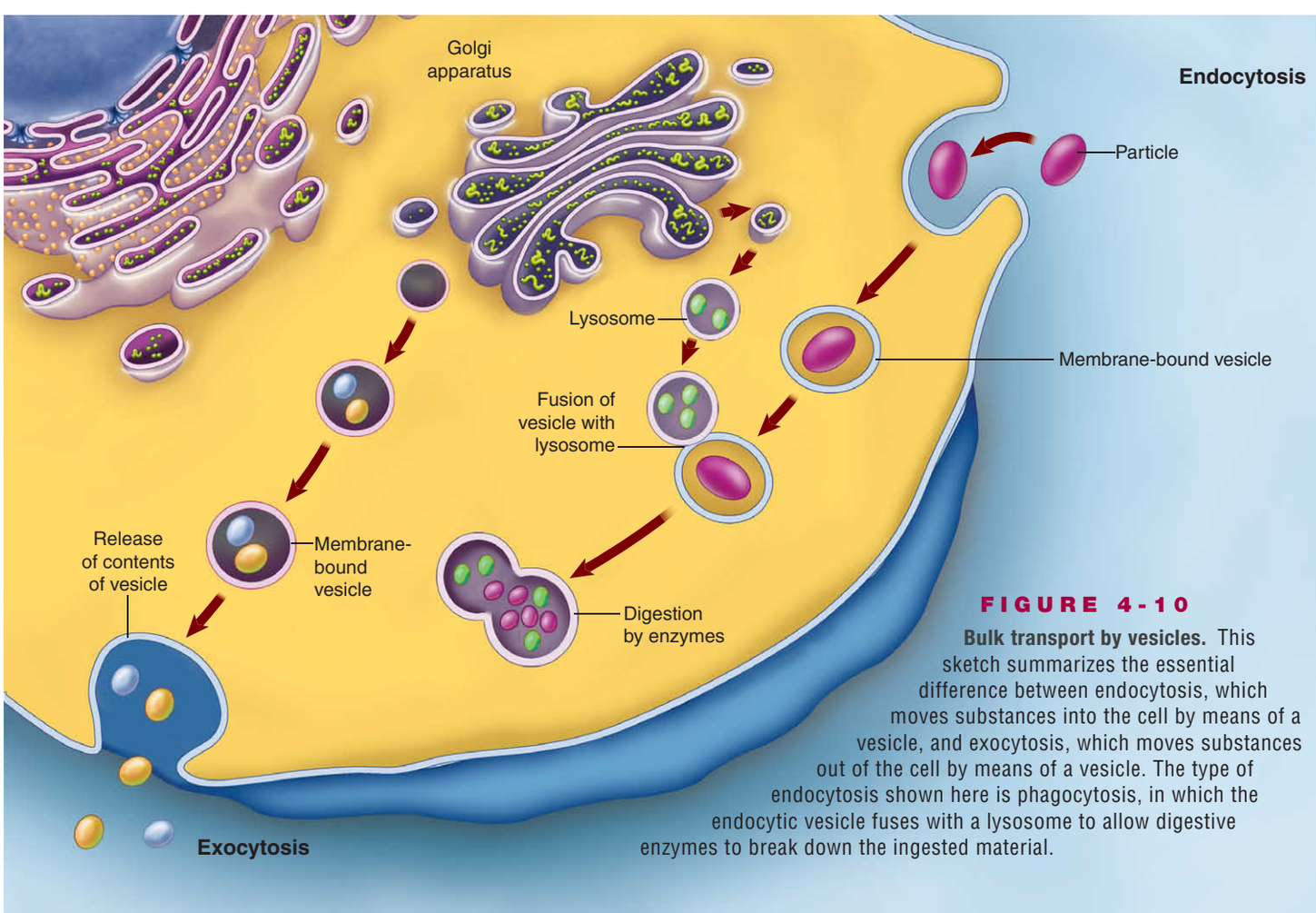


FIGURE 4-10

Bulk transport by vesicles. This sketch summarizes the essential difference between endocytosis, which moves substances into the cell by means of a vesicle, and exocytosis, which moves substances out of the cell by means of a vesicle. The type of endocytosis shown here is phagocytosis, in which the endocytic vesicle fuses with a lysosome to allow digestive enzymes to break down the ingested material.

extended edges of membrane fuse, a vesicle is formed. The cytoskeleton then pulls the vesicle containing extracellular material inward.

In a type of endocytosis called *receptor-mediated endocytosis*, receptors in the plasma membrane first bind to specific molecules in the extracellular fluid (Figure 4-11). This causes a portion of the plasma membrane to be pulled inward by the cytoskeleton and form a small pocket around the material to be moved into the cell. The edges of the membranous pocket extend and eventually fuse to form a vesicle. The vesicle is then pulled inward—away from the plasma membrane—by the cytoskeleton. Sometimes, endocytosis picks up various molecules and other particles along with receptor-bound molecules.

There are two basic forms of endocytosis: *phagocytosis* and *pinocytosis*. In **phagocytosis,** microorganisms or other large particles are engulfed by the plasma membrane and enter the cell in vesicles that have pinched off from the membrane. Once inside, they fuse with the membranous walls of lysosomes. Enzymes from the lysosomes then digest the particles into their component molecules. The products of digestion may subsequently diffuse through the membranous wall of the vesicle into the cytoplasm. The term *phagocytosis* means "condition of the cell eating" (from the word parts *phago-*, meaning "eat," *-cyto-*, meaning "cell," and *-osis*, meaning "condition").

Pinocytosis, or "condition of the cell drinking," is a similar process in which fluid and the substances dissolved in it enter a cell. Besides providing a way for a cell to bring fluids and solutes into the interior of the cell, pinocytosis also provides a way for the cell to remove material, including membrane receptors and transporters, from the plasma membrane. A cell can thus regulate the function of its plasma membrane (Table 4-2).

Exocytosis

Exocytosis is the process by which large molecules, notably proteins, can leave the cell even though they are too large to move out through the plasma membrane (see Figure 4-10 and Table 4-2). After first being enclosed in membranous vesicles by

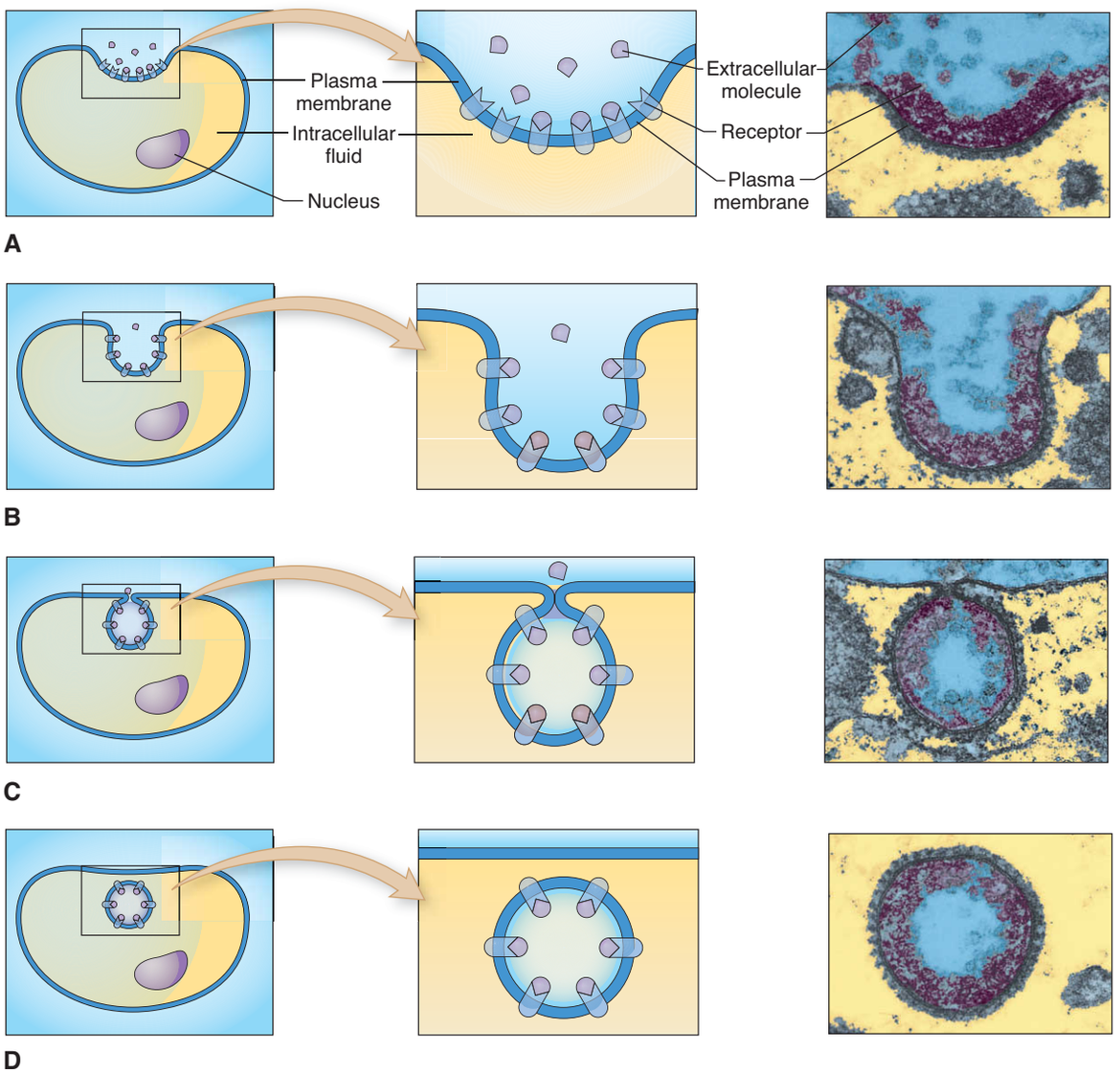
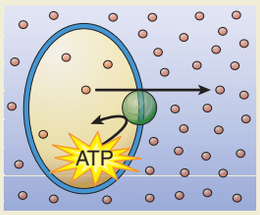
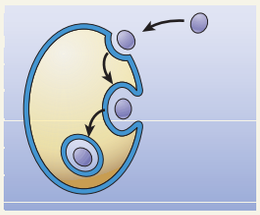
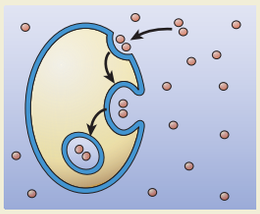
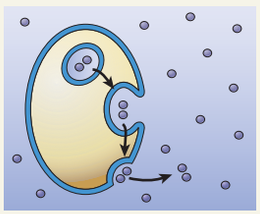


FIGURE 4-11

Receptor-mediated endocytosis. An artist's interpretation (left and center) and transmission electron micrographs (right) show the basic steps of receptor-mediated endocytosis. **A,** Membrane receptors bind to specific molecules in the extracellular fluid. **B,** A portion of the plasma membrane is pulled inward by the cytoskeleton and forms a small pocket around the material to be moved into the cell. **C,** The edges of the pocket eventually fuse and form a vesicle. **D,** The vesicle is then pulled inward—away from the plasma membrane—by the cytoskeleton. In this example, only the receptor-bound molecules enter the cell. In some cases, some free molecules or even entire cells may also be trapped within the vesicle and transported inward.

TABLE 4-2 Active Transport Processes

PROCESS		DESCRIPTION	EXAMPLES
Pumping		Movement of solute particles from an area of low concentration to an area of high concentration (up the concentration gradient) by means of an energy-consuming pump structure in the membrane	In muscle cells, pumping of nearly all calcium ions to special compartments—or out of the cell
Phagocytosis (endocytosis)		Movement of cells or other large particles into cell by trapping it in a section of plasma membrane that pinches off to form an intracellular vesicle; a type of *vesicle-mediated transport*	Trapping of bacterial cells by phagocytic white blood cells
Pinocytosis (endocytosis)		Movement of fluid and dissolved molecules into a cell by trapping them in a section of plasma membrane that pinches off to form an intracellular vesicle; a type of *vesicle-mediated transport*	Trapping of large protein molecules by some body cells
Exocytosis		Movement of proteins or other cell products out of the cell by fusing a secretory vesicle with the plasma membrane; a type of *vesicle-mediated transport*	Secretion of the hormone prolactin by pituitary cells

the Golgi apparatus, the vesicles are pulled out to the plasma membrane by the cytoskeleton. The vesicles then fuse with the plasma membrane and release their contents outside the cell. Some gland cells secrete their products by exocytosis. Besides providing a mechanism of transport, exocytosis also provides a way for new membrane material to be added to the plasma membrane.

ROLE OF ACTIVE TRANSPORT PROCESSES

Active transport processes include any mechanism that moves substances across a membrane using cellular energy—thus giving the membrane an active role in transport.

Major mechanisms of active transport in the body are ion pumps, which move ions against their concentration gradients and thus create a concentration of these ions on one side or the other. A cell can use ion pumps to keep a certain ion at an unusually high or low level, or concentrate them within an organelle. For example, the smooth ER (endoplasmic reticulum) membrane concentrates calcium ions inside the ER where they are stored for later use (as in muscle contraction).

Other active types of transport include endocytosis, exocytosis, and related vesicle-mediated processes within cells. Efforts of the cytoskeleton pull or push large volumes of material into or out of cells and organelles by wrapping them in (or unwrapping them from) bubbles of membrane (vesicles). In Chapter 3, we saw how these processes can be used to transport molecules from the ER to the Golgi apparatus, and eventually secreted out of the cell (see Figure 3-8). As you can imagine, this mechanism is used to secrete everything from hormones to neurotransmitters in the body.

| QUICK CHECK |

1. Name as many passive processes that transport substances across a cell membrane as you can. How are they alike? How are they different?
2. What causes osmotic pressure to develop in a cell?
3. Describe three different active processes that transport substances across a cell membrane. What distinguishes them from passive processes?

CELL METABOLISM

In Chapter 2 (pp. 33–65) we discovered the concept of **metabolism:** the chemical reactions that occur in the body. *Cell metabolism*, then, refers to the chemical reactions of the cell. This section of Chapter 4 picks up the important theme of human body chemistry and applies it to cell physiology. Later chapters also continue to bring up this theme because after all, body chemistry is the basis for all human functions.

Cell metabolism involves many different kinds of chemical reactions that often occur in a sequence of reactions called a **metabolic pathway.** A metabolic pathway can be described as being *catabolic* if its net effect is to break large molecules down into smaller ones. Recall that **catabolism** is the kind of metabolism that breaks down molecules, usually nutrient molecules, and thereby releases energy from the broken molecules. On the other hand, some metabolic pathways build larger molecules from smaller ones and are thus called *anabolic pathways.* Recall that **anabolism** is the kind of metabolism that builds large, complex molecules from smaller ones. Anabolic pathways usually require a net input of energy, whereas catabolic pathways usually produce a net output of energy.

Role of Enzymes

Enzymes, which are classified as *functional proteins*, were introduced on p. 61 in Chapter 2. We are now ready for a more comprehensive introduction to enzymes.

The series of chemical reactions that make up a metabolic pathway in a cell do not usually just happen on their own. At normal body temperatures, the *activation energy* needed to start a chemical reaction is too great for many molecules to react by themselves. What is needed to make essential chemical reactions happen is a **catalyst**—a chemical that reduces the amount of activation energy needed to start a chemical reaction (Figure 4-12). Catalysts participate in chemical reactions but are not themselves changed by the reaction. This is the role of enzymes in the cell—to act as chemical catalysts that allow metabolic reactions to occur. So important are they that life has been defined as the "orderly functioning of hundreds of enzymes" by one scientist.

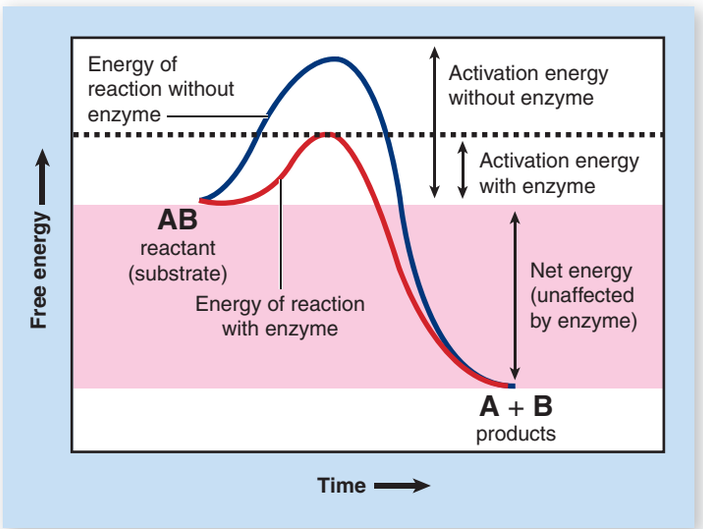


FIGURE 4-12

Enzymes as catalysts. A catalyst is a chemical that reduces the activation energy of a reaction—the energy needed to get a reaction started. Enzymes thus allow reactions to occur at the low level of free energy available at normal human body temperatures.

CHEMICAL STRUCTURE OF ENZYMES

Enzymes are proteins and have the chemical properties of proteins. Enzymes are usually tertiary or quaternary proteins of complex shape. Often, their molecules contain a nonprotein part called a *cofactor.* Inorganic ions or vitamins may make up part of a cofactor. If the cofactor is an organic nonprotein molecule, it is called a **coenzyme.**

A very important structural attribute of enzymes is the **active site.** The active site is the portion of the enzyme molecule that chemically "fits" the substrate molecule or molecules. Recall that a *substrate* is the molecule acted on by an enzyme molecule.

Since the enzyme acts on a substrate because the shape and electrochemical attractions of the active site complement some portion of the substrate or substrates, biochemists often use the **lock-and-key model** to describe the action of enzymes. As Figure 4-13 shows, the active site of an enzyme chemically fits a portion of the substrate just as a key fits into a lock. Like a key in a lock, the enzyme can

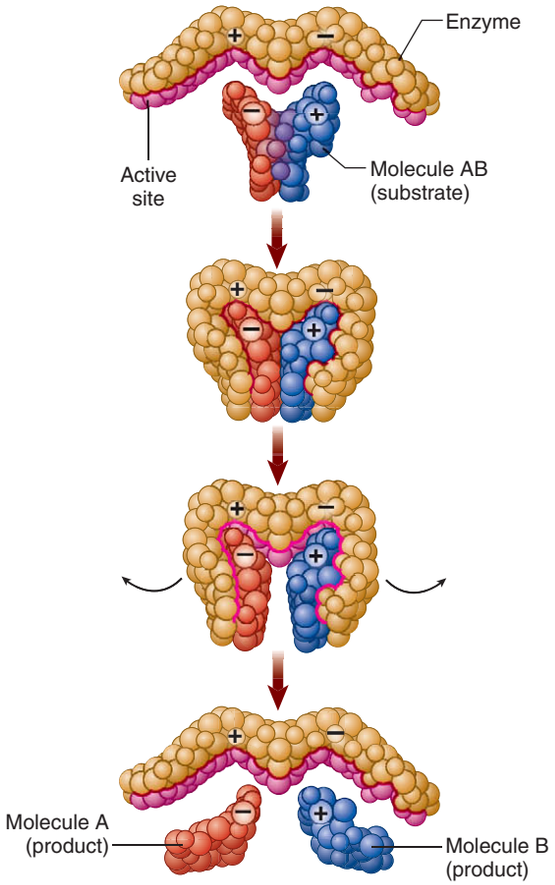


FIGURE 4-13

Model of enzyme action. Enzymes are functional proteins whose molecular shape allows them to catalyze chemical reactions. Substrate molecule AB is acted on by a digestive enzyme to yield simpler molecules A and B as products of the reaction. Notice how the active site of the enzyme chemically fits the substrate—the lock-and-key model of biochemical interaction. Notice also how the enzyme molecule bends its shape in performing its function.

bind substrates together ("locking" them together) or can unbind components of a substrate ("unlocking" them). And, as with a key, some movement of the enzyme shape is often required to "open the lock" or alter the substrate. As shown in Figure 4-13, such movements are critical to proper enzyme function.

CLASSIFICATION AND NAMING OF ENZYMES

Two systems used for naming enzymes are as follows: the suffix *-ase* is used with the root name of the substance whose chemical reaction is catalyzed (the substrate chemical, that is) or with the word that describes the kind of chemical reaction catalyzed. Thus, according to the first method, sucrase is an enzyme that catalyzes a chemical reaction in which sucrose takes part. According to the second method, sucrase might also be called a *hydrolase* because it catalyzes the hydrolysis of sucrose. Enzymes investigated before these methods of nomenclature were adopted are still called by older names, such as *pepsin* and *trypsin*.

Classified according to the kind of chemical reactions catalyzed, enzymes fall into several groups:

Oxidation-reduction enzymes. These are known as oxidases, hydrogenases, and dehydrogenases. Energy release for muscular contraction and all physiological work depends on these enzymes.

Hydrolyzing enzymes, or hydrolases. Digestive enzymes belong to this group. The hydrolyzing enzymes are named after the substrate acted on, for example, lipase, sucrase, and maltase.

Phosphorylating enzymes. These add or remove phosphate groups and are known as phosphorylases or phosphatases.

Enzymes that add or remove carbon dioxide. These are known as carboxylases or decarboxylases.

Enzymes that rearrange atoms within a molecule. These are known as mutases or isomerases.

Hydrases. These add water to a molecule without splitting it, as do hydrolases.

Enzymes are also classified as intracellular or extracellular, depending on whether they act within cells or outside them in the surrounding medium. Most enzymes act intracellularly in the body; an important exception is the digestive enzymes. All digestive enzymes are classified as hydrolases because they catalyze the hydrolysis of food molecules.

GENERAL FUNCTIONS OF ENZYMES

In general, enzymes regulate cell functions by regulating metabolic pathways (Figure 4-14). As stated earlier, each reaction of a metabolic pathway requires one or more types of enzymes to permit that reaction to occur. An entire metabolic pathway can be turned on or off by the activation or inactivation of any one of the enzymes that catalyze reactions in that particular pathway. A few general principles of enzyme function will help you understand their role in regulating cell metabolism more clearly.

Most enzymes are *specific in their action*; that is, they act only on a specific substrate. This is attributed to their "key-in-a-lock" kind of action, the configuration of the enzyme molecule fitting the configuration of some part of the substrate molecule (see Figure 4-13). This also means that every reaction that occurs in a metabolic pathway requires one or more specific enzymes—or else the reaction will not occur and the entire pathway will be disrupted.

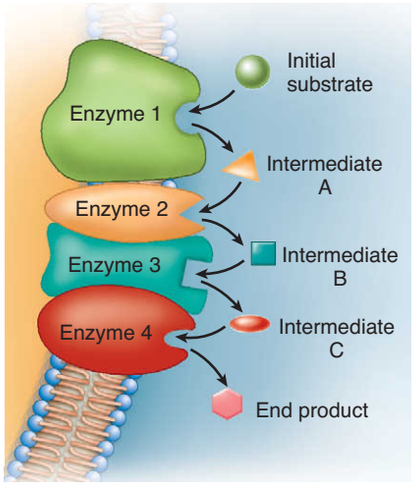


FIGURE 4-14

Enzyme regulation of a metabolic pathway. In a metabolic pathway, the product of one enzyme-regulated reaction becomes the substrate for the next reaction. Thus a whole series of enzymes is required to keep the pathway functioning. Notice that these enzymes are embedded in a cell membrane whereas other types of enzymes are mobile in the cytosol or extracellular in location.

Various physical and chemical agents activate or inhibit enzyme action by changing the shape of enzyme molecules. A molecule or other agent that alters enzyme function by changing its shape is called an **allosteric effector.** An *effector* is an agent that accomplishes something, and *allosteric* literally means "relating to a change in three-dimensional shape." Thus an allosteric effector is simply an agent that changes the shape of a molecule. Remember the principle you learned about the shape of proteins in Chapter 2: when the shape changes, so does the function. This certainly applies to enzymes. Some allosteric effectors are molecules that attach to an *allosteric site* on the enzyme molecule and thereby change the shape of the active site on a different part of the enzyme. As Figure 4-15 shows, allosteric effectors of this type may inhibit or

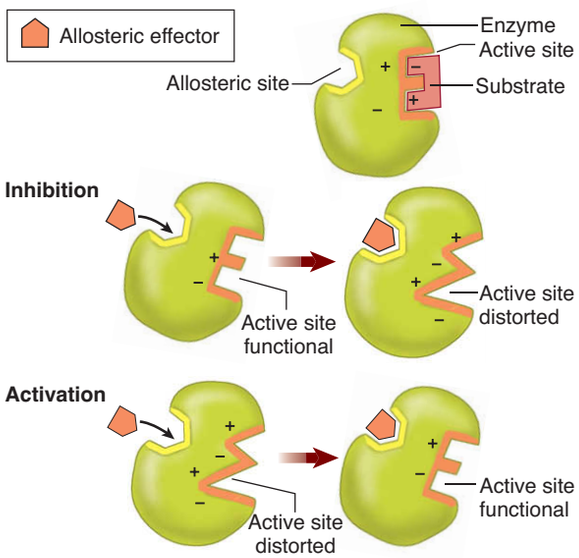
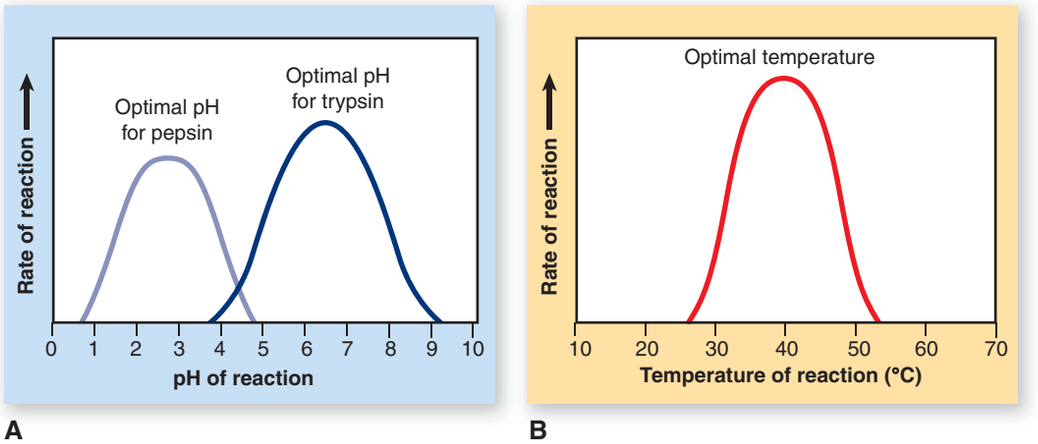


FIGURE 4-15

Allosteric effect. The allosteric effect occurs when some agent, in this case an allosteric effector molecule, binds to the enzyme at an allosteric site and thereby changes the shape of the enzyme's active site. Such an allosteric effect may inhibit enzyme action (by distorting the active site) or activate the enzyme (by giving the active site its functional shape).

FIGURE 4-16

Effects of pH and temperature on enzyme function. The rate of reactions catalyzed can be affected by the allosteric effects of the chemical or physical properties of the surrounding medium. **A,** Enzymes catalyze chemical reactions with greatest efficiency within a narrow range of pH. For example, pepsin (a protein-digesting enzyme in gastric juice) operates within a low pH range, whereas trypsin (a protein-digesting enzyme in pancreatic juice) operates within a higher pH range. **B,** Most enzymes in the human body work best within a narrow range of temperatures near 40° C.



activate enzymes by altering the shape of the active site. Other types of allosteric effectors include certain antibiotic drugs, changes in pH, or changes in temperature. The allosteric effect of pH is produced by the fact that changes in the concentration of hydrogen ions (H^+) influence the chemical attractions that hold molecules—including enzymes—in their complex, multidimensional shapes. Temperature has a similar allosteric, or shape-changing, effect on enzymes. As Figure 4-16 shows, changing the pH or temperature alters the shape of the active sites of enzyme molecules enough to affect their function. Cofactors, when they are added to or removed from an enzyme molecule, also have an allosteric effect.

In a process known as **end-product inhibition,** a chemical product at the end of a metabolic pathway binds to the allosteric site of one or more enzymes along the pathway that produced it and thereby inhibits the synthesis of more product (Figure 4-17). This is a type of automatic negative feedback mechanism in the cell that prevents the accumulation of an extreme amount of a metabolic product.

Most enzymes catalyze a chemical reaction in both directions, the direction and rate of the reaction being governed by the law of mass action. An accumulation of a product slows the reaction and tends to reverse it.

Enzymes are continually being destroyed and therefore have to be continually synthesized, even though they are not used up in the reactions they catalyze.

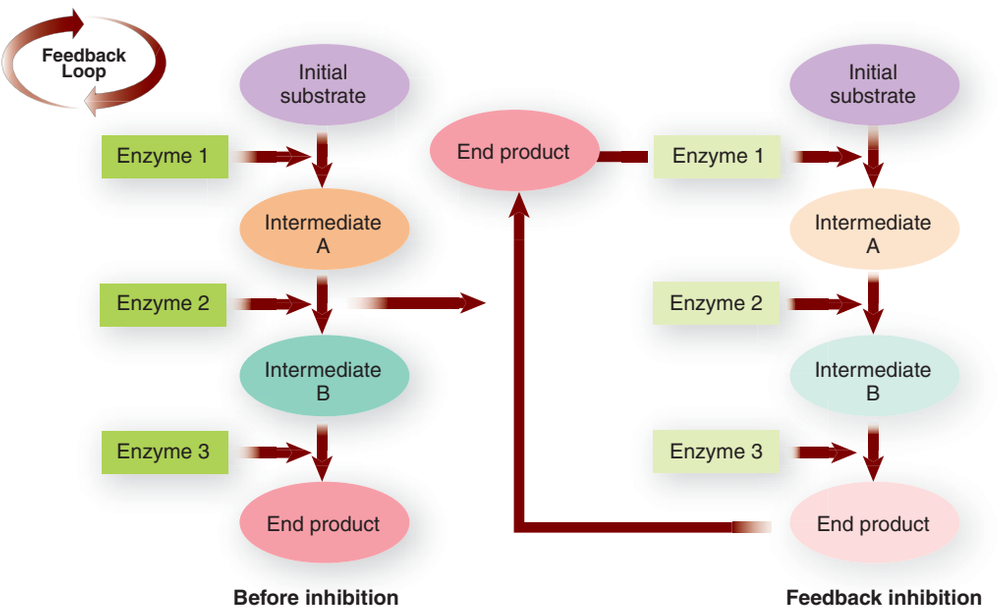
Many enzymes are synthesized as inactive **proenzymes.** Substances that convert proenzymes to active enzymes are often called **kinases.** Kinases usually do their job of activating enzymes by means of an allosteric effect (see Figure 4-15). For example, enterokinase changes inactive trypsinogen into active trypsin by changing the shape of the molecule. Within cells, a type of kinase called simply *kinase* A has been shown to activate enzymes that regulate certain pathways after a hormonal signal is received by the cell.

| QUICK CHECK |

4. Describe the structure of an enzyme. How does its structure determine its function?
5. What is an allosteric effector? Give examples.

FIGURE 4-17

Feedback inhibition of enzymes. Formation of an excessive amount of end product can be inhibited by a negative feedback mechanism. In this example, the end product itself inhibits the function of an enzyme needed early in the pathway. Thus the entire pathway is inhibited—as long as there is an excess of the end product.



Catabolism

There are many catabolic pathways that operate inside human cells. Perhaps the most important for a basic understanding of cell catabolism is the pathway known as **cellular respiration.** This section briefly outlines the basic concepts of the cellular respiratory pathway. Details of this pathway are further outlined in Chapter 30.

OVERVIEW OF CELLULAR RESPIRATION

Cellular respiration is the process by which cells break down glucose ($C_6H_{12}O_6$), or a nutrient that has been converted to glucose or one of its simpler products, into carbon dioxide (CO_2) and water (H_2O). As the molecule breaks down, the potential energy that had been stored in its bonds is released. Much of the released energy is converted into heat, but a portion of it is transferred to the high-energy bonds of adenosine triphosphate (ATP). Figure 2-33 on p. 58 shows how ATP is synthesized from adenosine diphosphate (ADP) and inorganic phosphate with energy obtained from cellular respiration.

Three smaller pathways are chemically linked together to form the larger catabolic pathway known as *cellular respiration:*

1. Glycolysis
2. Citric acid cycle
3. Electron transport system

The paragraphs that follow briefly introduce these three basic processes.

GLYCOLYSIS

Glycolysis is a catabolic pathway that begins with glucose, which contains six carbon atoms per molecule, and ends with pyruvic acid, which contains only three carbon atoms per molecule. As Figure 4-18 shows, each glucose molecule that enters this pathway is eventually broken in half. In fact, the name *glycolysis* literally means "breaking glucose."

Glycolysis occurs in the cytosol of cells, outside any particular organelle. The cytosol, then, must contain all the enzymes necessary to catalyze each of the reactions that make up the glycolysis pathway. Because the reactions of glycolysis require no oxygen, glycolysis is said to be **anaerobic.**

Glycolysis releases a small portion of the potential energy stored in the glucose molecule. Some of this energy is transferred to ATP, a molecule that can then transfer the energy to any of a large number of energy-consuming reactions in the cell. Some of the energy is transferred to another energy transfer molecule, a form of nicotinamide adenine dinucleotide, (NADH). NADH may eventually transfer its energy to ATP in the electron transport system, a later step of cellular respiration that is discussed shortly.

Once pyruvic acid is formed by glycolysis, there is a fork in the metabolic pathway. That is, the molecule could enter one of two pathways linked to glycolysis (see Figure 4-18). If oxygen is available, the pyruvic acid molecule will follow the *aerobic pathway* and enter the citric acid cycle. This type of respiration is called **aerobic** respiration because oxygen (O_2) is required for this sequence of reactions to occur. If oxygen is unavailable for a particular pyruvic acid molecule to enter the aerobic pathway, it will continue along an anaerobic pathway to form a molecule called

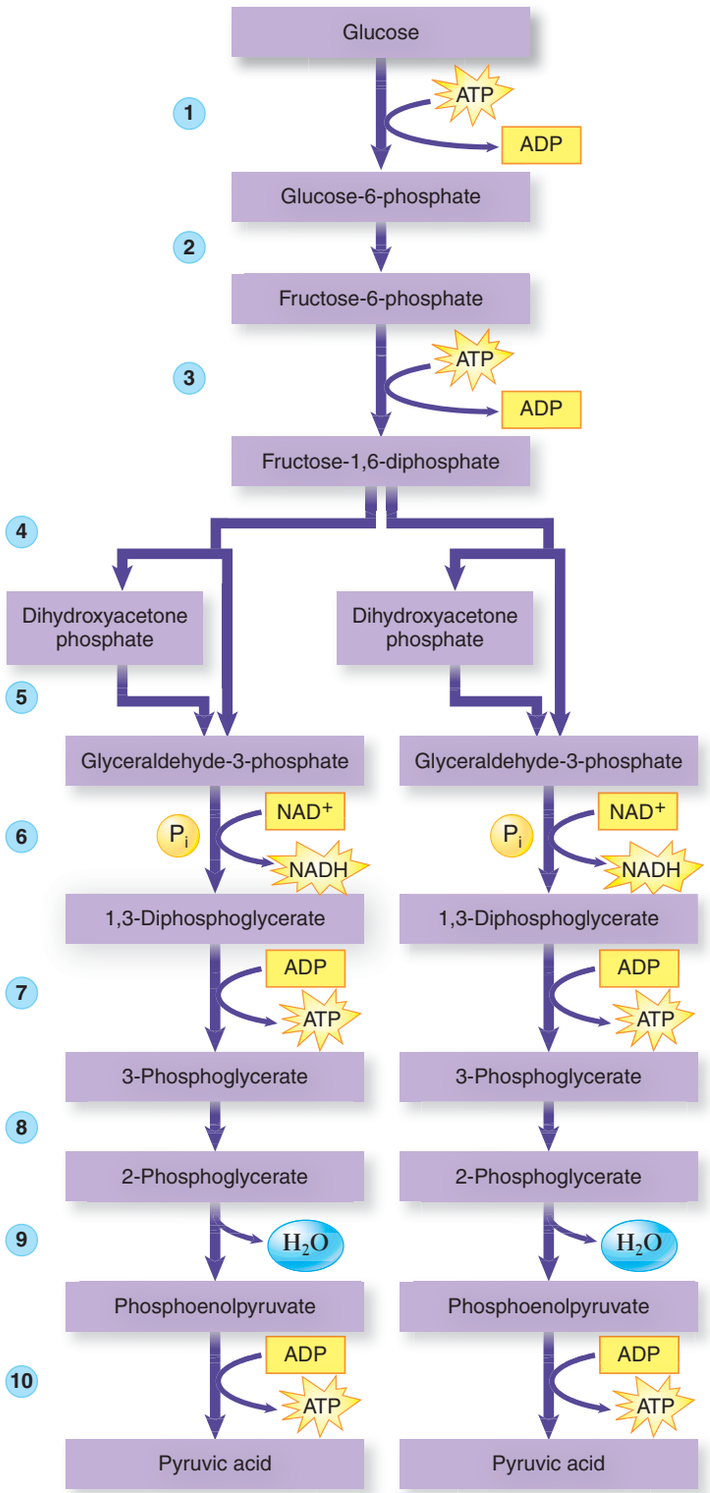


FIGURE 4-18

Glycolysis. This diagram of the reactions involved in glycolysis represents a classic example of a catabolic pathway. Note that each of the ten chemical reactions in this pathway cannot proceed until the previous step has occurred. Recall from our discussion that each step also requires the presence of one or more specific enzymes. *ADP,* Adenosine diphosphate; *ATP,* adenosine triphosphate; *NAD^+* and *NADH,* forms of nicotinamide adenine dinucleotide; *P_i,* inorganic phosphate.

lactic acid. Lactic acid is later converted back to pyruvic acid or glucose in an energy- and oxygen-requiring pathway.

When the anaerobic pathway is followed, a small amount of the total energy stored in glucose is made available to the cell. However, if enough oxygen is not available to maintain a set point level of ATP by means of the aerobic pathway, the anaerobic pathway can help maintain adequate ATP levels for cellular functions to continue. Because oxygen is later used to process the lactic acid formed by anaerobic processes, biochemists say that an *oxygen debt* has been incurred. Much of the lactic acid diffuses out of the cell that formed it and is later processed in liver cells, which are adapted to perform this function efficiently.

CITRIC ACID CYCLE

If oxygen is available, the pyruvic acid molecules formed by glycolysis are prepared to enter the next major phase of aerobic cellular respiration—the **citric acid cycle.** This cyclic (repeating) sequence of reactions is still sometimes called the *Krebs cycle* after Sir Hans Krebs, who discovered this pathway in the first part of the twentieth century. Figure 4-19 shows that pyruvic acid is converted to acetyl coenzyme A (CoA) and moves into the citric acid cycle. During this transition into the citric acid cycle, the molecule loses one of its carbons, along with some oxygen, producing waste carbon dioxide (CO_2). This cycle also produces some available energy that is transferred to NADH and then to the electron transport system, as explained later.

The citric acid cycle, like glycolysis, is a sequence of many chemical reactions (see Figure 4-19). As in glycolysis, each reaction of the citric acid cycle requires one or more specific enzymes. These enzymes are located in the inner chamber of the mitochondrion, so that is the cell location in which the citric acid cycle occurs.

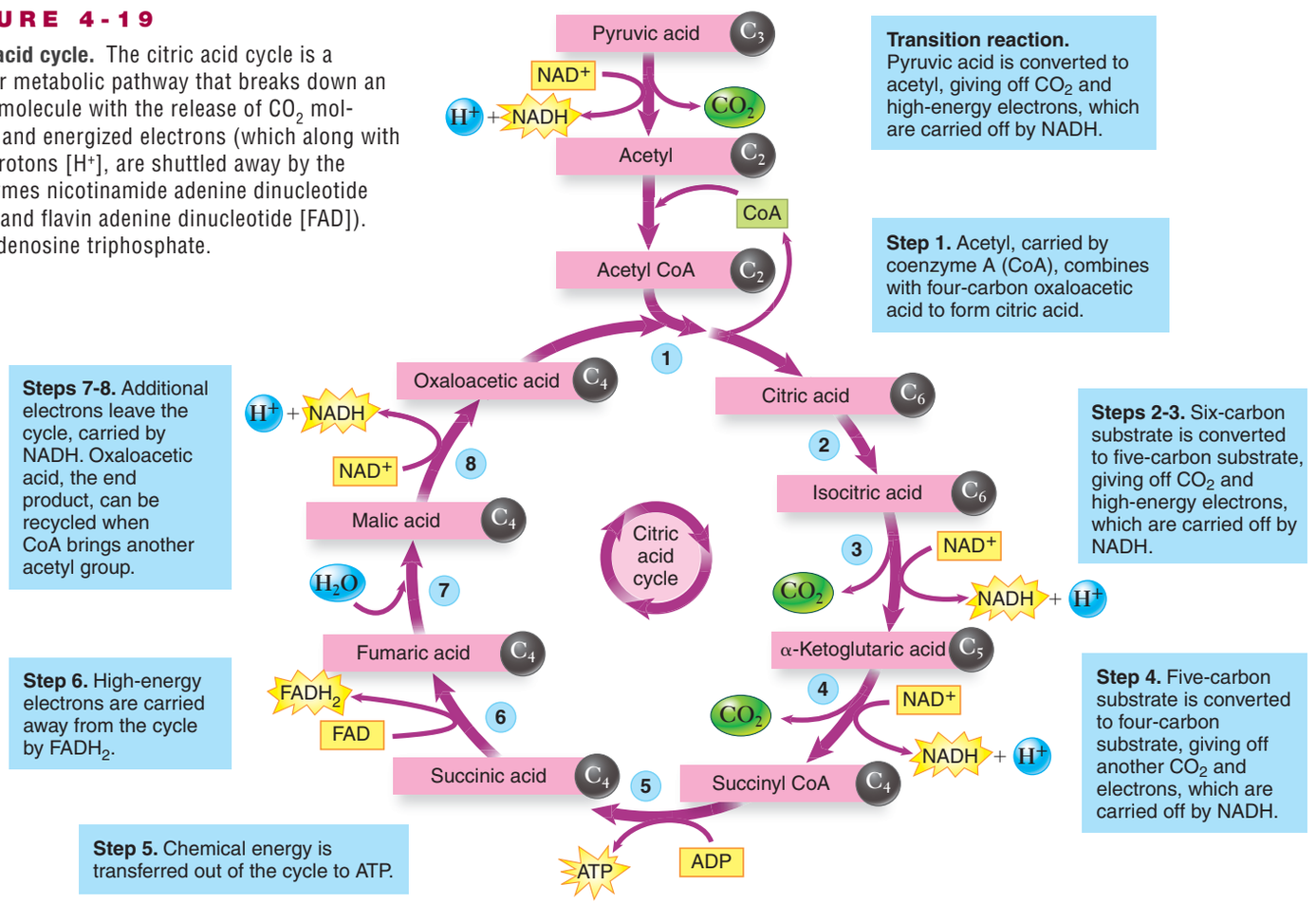
In the citric acid cycle, the two-carbon acetyl group that breaks away from its escort, CoA, is further broken down to yield its stored energy. A small amount of this energy is transferred directly to ATP molecules, but most of the available energy is transferred in the form of energized electrons (e^-) and their accompanying protons (H^+) to the coenzyme NAD or flavin adenine dinucleotide (FAD). NAD then becomes NADH and FAD becomes the reduced form of FAD ($FADH_2$). More information on how these coenzymes pick up energy released from a metabolic pathway is found in Chapter 30 on p. 933. The energized electrons (along with their protons) then move into the next phase of cellular respiration—the electron transport system.

ELECTRON TRANSPORT SYSTEM

As Figure 4-20 shows, NADH (and $FADH_2$) transfer the energized electrons to a set of special molecules embedded in the cristae of the inner mitochondrial membrane. These special electron-accepting molecules make up the **electron transport system (ETS).** As energized electrons leap from one of these molecules to the next, their energy is used to pump their accompanying protons (H^+) from the inner chamber of the mitochondrion to the outer chamber. As the

FIGURE 4-19

Citric acid cycle. The citric acid cycle is a circular metabolic pathway that breaks down an acetyl molecule with the release of CO_2 molecules and energized electrons (which along with their protons [H^+], are shuttled away by the coenzymes nicotinamide adenine dinucleotide [NAD] and flavin adenine dinucleotide [FAD]). *ATP,* Adenosine triphosphate.



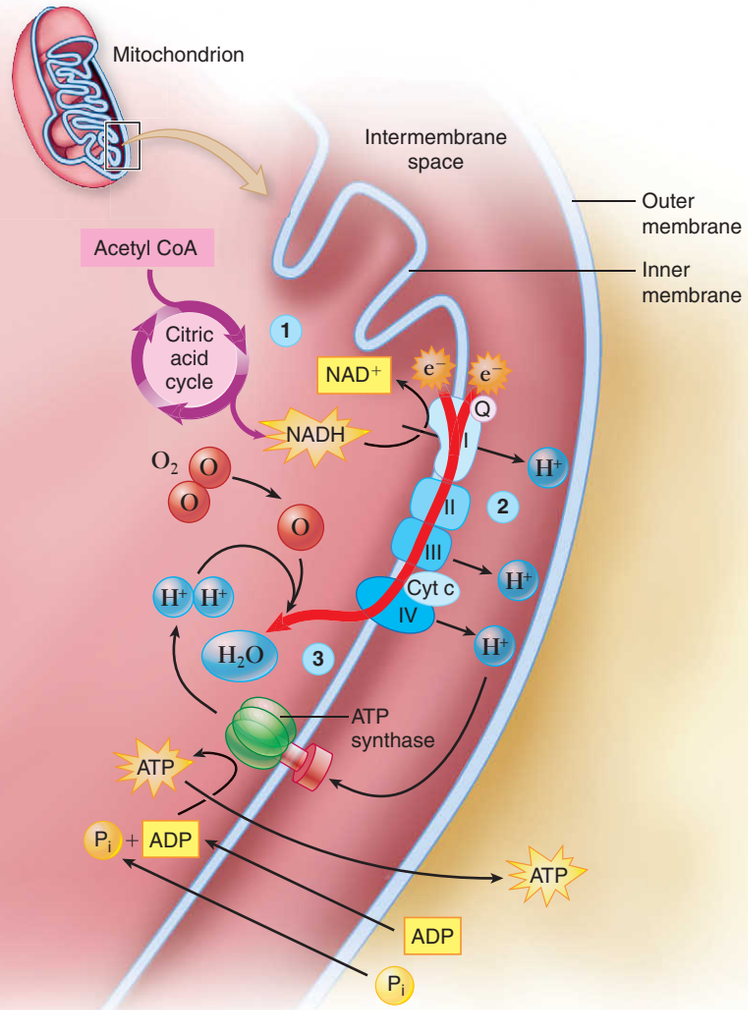


FIGURE 4-20

Electron transport system (ETS). 1, Pairs of high-energy electrons (e^-) and their protons (H^+) are shuttled from the citric acid cycle by coenzymes NAD and FAD to protein complexes (I, II, III, IV) embedded in the inner membrane of the mitochondrion. **2,** As the electrons are transported from molecule to molecule (*red path*), their energy is used to pump the protons (H^+) to the intermembrane space. **3,** As the proton gradient increases, passive movement of protons back across the membrane (through the ATP synthase carrier) provides the energy needed to "recharge" ADP and P to form ATP. Notice that oxygen (from O_2) is required as the final acceptor of the electrons and protons transported through the system, thus forming H_2O as a byproduct. *ADP,* Adenosine diphosphate; *ATP,* adenosine triphosphate; *FAD,* flavin adenine dinucleotide; *NAD,* nicotinamide adenine dinucleotide.

protons (H^+) build up in the outer chamber, a concentration gradient of protons develops. Protons then begin movement through the inner mitochondrial membrane into the inner chamber by way of "reverse pump" carriers (*ATP synthase*). These ATP synthase carriers convert the energy of proton flow into chemical energy, which is transferred to ATP molecules. In short, the energy transferred from the citric acid cycle is used to put protons behind a sort of dam, and then the energy of protons flowing back through "energy generators" from behind the dam is transferred to ATP. In most cells, aerobic respiration transfers enough energy from each glucose molecule to form 36 ATP molecules—2 directly from glycolysis and 34 from the rest of the pathway.

The deenergized electrons that come away from the electron transport system are accepted by oxygen molecules. This is why oxygen molecules are required for this metabolic pathway—to act as final electron acceptors. Once they combine with oxygen, the electrons are reunited with their accompanying protons (H^+) to form water (H_2O).

In summary, the aerobic respiratory pathway requires an input of glucose and oxygen and, by the action of specific enzymes, coenzymes, and other molecules, produces an output of carbon dioxide, water, and the real biochemical prize—energy in ATP. The major steps in cellular respiration are summarized in Figure 4-21. For an expanded discussion of cellular respiration, refer to Chapter 30, pp. 934–941.

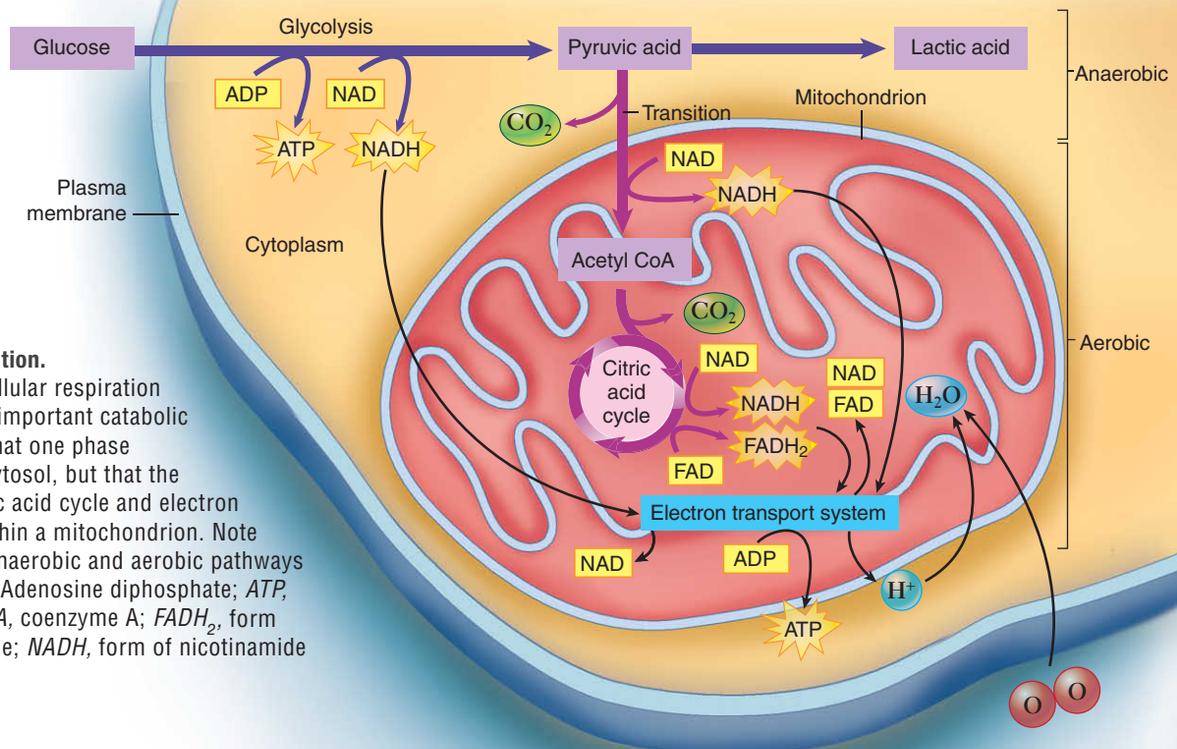


FIGURE 4-21

Summary of cellular respiration. This simplified outline of cellular respiration represents one of the most important catabolic pathways in the cell. Note that one phase (glycolysis) occurs in the cytosol, but that the two remaining phases (citric acid cycle and electron transport system) occur within a mitochondrion. Note also the divergence of the anaerobic and aerobic pathways of cellular respiration. *ADP,* Adenosine diphosphate; *ATP,* adenosine triphosphate; *CoA,* coenzyme A; *$FADH_2$,* form of flavin adenine dinucleotide; *NADH,* form of nicotinamide adenine dinucleotide.

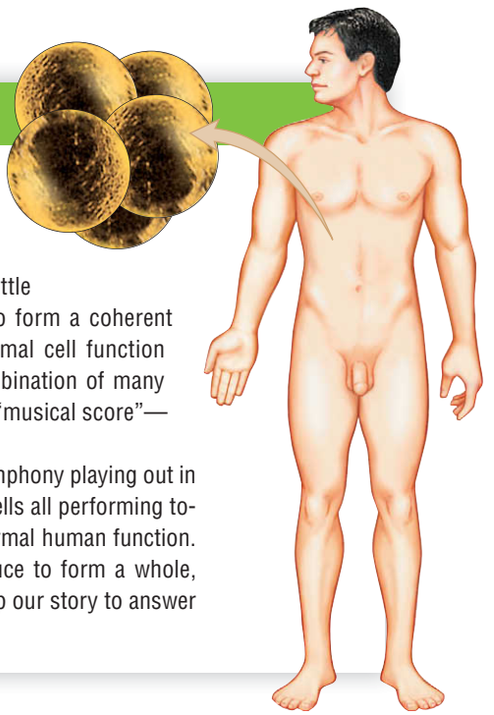
| QUICK CHECK |

6. What are the three catabolic pathways that together make up the process of cellular respiration?
7. Which extracts more energy for cell use, the aerobic or anaerobic pathway?
8. To what molecule must energy be transferred before it can be used by most cell processes?
9. Briefly outline each of the major steps of cellular respiration.

Anabolism

Many anabolic or "building" pathways occur in human cells. Perhaps the most important for the beginning student to understand is the process of protein synthesis. Why is protein synthesis considered the central anabolic process of the cell? How is protein synthesis accomplished? These questions are answered as the story of cell function continues in the next chapter.

the BIG picture



Cell Physiology and the Whole Body

When exploring the microscopic world of cells, it is easy to get caught up in the intricate mechanisms that operate in each specific organelle. Once you feel comfortable with these mechanisms, try to put them together into a bigger picture of cell function. For example, most of the processes that we explored in this chapter are going on at about the same time within each and every cell of your body. Each cell is transcribing genes and synthesizing polypeptides, which are then dumped into the ER and transported to the Golgi apparatus for processing and packaging before being sent off to become a lysosome or being secreted by exocytosis. At the same time, energy for this and other cell work is being transferred from nutrient molecules to ATP molecules, which act as energy storage batteries for the cell. The cytoskeleton and the cell membrane are transporting materials into, out of, and around the cytoplasm. Studying cell structure and function is like looking at the score of a symphony for the first time. All the individual parts look unrelated and somewhat confusing, but with a little effort you can combine them to form a coherent whole. The "symphony" of normal cell function results from a coordinated combination of many processes dictated by the cell's "musical score"—the genetic code.

However, there is a larger symphony playing out in the body. There are trillions of cells all performing together in concert to produce normal human function. How do cells grow and reproduce to form a whole, healthy body? Chapter 5 picks up our story to answer that question.

MECHANISMS of DISEASE

DISORDERS OF CELL TRANSPORT

Several very severe diseases result from damage to cell transport mechanisms. **Cystic fibrosis (CF),** for example, is an inherited condition in which chloride ion (Cl^-) channels in the plasma membrane called *CTFRs (cystic fibrosis transmembrane conductance regulators)* are defective. In the most common form of CF, this happens when abnormal CTFR channel proteins become misfolded in the ER and are thus not sent to the plasma membrane. Because Cl^- transport is altered, secretions such as sweat, mucus, and pancreatic juice are very salty—and often very thick. Abnormally thick mucus in the lungs impairs normal breathing and often leads to recurring lung infections. Thick pancreatic secretions can plug ducts that carry important enzymes to the digestive tract. Figure 4-22 shows a child with CF next to a healthy child of the same age. Because of the breathing, digestive, and other problems caused by the disease, the affected child has not developed normally.

Cholera (KAHL-er-ah) is a bacterial infection that causes cells lining the intestines to leak chloride ions (Cl^-). Water follows Cl^- out of the cells by osmosis, causing severe diarrhea and the resulting loss of water by the body. Death can occur in a few hours if

treatment is not received. Interestingly, carriers of the defective CTFR gene that produces CF are resistant to cholera infections. Having defective Cl^- transport mechanisms apparently protects a person from an infection that disrupts normal Cl^- transport. This is one of many examples where so-called "disease genes" have turned out to have beneficial effects.

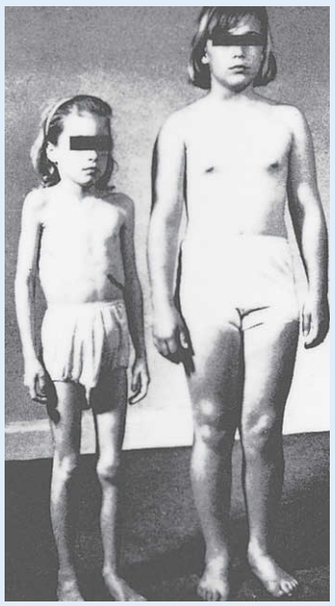


FIGURE 4-22

Cystic fibrosis (CF). The child on the left, who has CF, has failed to develop as normally as the child of the same age on the right.

LANGUAGE OF SCIENCE *(continued from p. 90)*

concentration gradient
(kahn-sen-TRAY-shun GRAY-dee-ent)
[*con-* **together**, *-centr-* **center**, *-ation* **process**, *gradi-***step**, *-ent* **state**]

cotransport
(koh-TRANZ-port)
[*co-* **together**, *-trans-* **across**, *-port* **carry**]

countertransport
[*counter-* **against**, *-trans-* **across**, *-port* **carry**]

dialysis
(dye-AL-i-sis)
[*dia-* **apart**, *-lysis* **loosening**]

diffusion
(dih-FYOO-shun)
[*diffus-* **spread out**, *-sion* **process**]

electron transport system (ETS)
(eh-LEK-tron TRANZ-port SIS-tem)
[*electro-* **electricity**, *-on* **subatomic particle**, *trans-* **across**, *-port* **carry**]

endocytosis
(en-doh-sye-TOH-sis)
[*endo-* **inward or within**, *-cyto-* **cell**, *-osis* **condition**]

end-product inhibition
(end-PROD-ukt in-hib-ISH-un)

enzyme
(EN-zyme)
[*en-* **in**, *-zyme* **ferment**]

exocytosis
(eks-o-sye-TOH-sis)
[*exo-* **outside or outward**, *-cyto* **cell**, *-osis* **condition**]

facilitated diffusion
(fah-SIL-i-tay-ted di-FYOO-shun)
[*facili-* **easy**, *-ate* **act of**, *diffuse-* spread **out**, *-sion* **process**]

filtration
(fil-TRAY-shun)
[*filtr-* **to strain**, *-ation* **process**]

hypertonic
(hye-per-TON-ik)
[*hyper-* **excessive**, *-ton-* **tension**, *-ic* **relating to**]

hypotonic
(hye-poh-TON-ik)
[*hypo-* **under or below**, *-ton-* **tension**, *-ic* **relating to**]

isotonic
(eye-soh-TON-ik)
[*iso-* **equal**, *-ton-* **tension**, *-ic* **relating to**]

kinase
(KYE-nayz)
[*kin-* **motion**, *-ase* **enzyme**]

lock-and-key model
(lok and kee MAHD-el)

metabolic pathway
(met-ah-BOL-ik PATH-way)
[*metabol-* **change**, *-ic* **relating to**]

metabolism
(meh-TAB-oh-liz-em)
[*metabol-* **change**, *-ism* **condition**]

osmosis
(os-MO-sis)
[*osmos-* **push**, *-osis* **condition**]

osmotic pressure
(os-MOT-ik PRESH-ur)
[*osmo-* **push**, *-ic* **relating to**]

phagocytosis
(fag-oh-sye-TOH-sis)
[*phago-* **eat**, *-cyto-* **cell**, *-osis* **condition**]

pinocytosis
(pin-oh-sye-TOE-sis)
[*pino-* **drink**, *-cyto-* **cell**, *-osis* **condition**]

potential osmotic pressure
(po-TEN-shal os-MOT-ik PRESH-ur)
[*potent-* **power**, *-ial* **relating to**, *osmo-* **push**, *-ic* **relating to**]

proenzyme
(pro-EN-zime)
[*pro-* **first**, *-en-* **in**, *-zyme* **ferment**]

simple diffusion
(simple di-FYOO-zhun)
[*diffus-* **spread out**, *-sion* **process**]

LANGUAGE OF MEDICINE

cholera
(KAHL-er-ah)
[*chole-* **bile**, *-a* **state**]

cystic fibrosis (CF)
(SIS-tik fye-BRO-sis)
[*cyst-* **sac**, *-ic* **relating to**, *fibro-* **fiber**, *-osis* **condition**]

hemodialysis
(he-mo-dye-AL-i-sis)
[*hemo-* **relating to blood**, *-dia-* **apart**, *-lysis* **loosening**]

CASE study

Tobie was visiting New York City for the first time. Being from a small town, he was fascinated by all the tall buildings and crowds of people. On his first day in the city, he took the subway across town. When the train finally arrived at its destination, Tobie was surprised to see a mob of people waiting on the subway platform; only a few people were already on the train. As the doors opened, the crowd surged forward through the doors and into the subway cars.

1. The movement of the crowd through the doors could be thought of as an example of what type of movement pertaining to a cell?
   a. Active transport by vesicles
   b. Facilitated diffusion
   c. Simple diffusion
   d. Active transport by pumps

With the crush of people flooding onto the train, Tobie found himself being pushed into the middle of the train car and was left with nothing to hold onto, making it difficult to keep his balance when the subway car was in motion. He kept shifting his weight from one leg to the other as the train sped along, rounding curves, lurching to a stop at one station, and then quickly accelerating on to the next. In order for Tobie to keep contracting the muscles in his legs, his muscle cells have to move sodium residing inside the cells back out of the cells—against their normal sodium concentration gradient.

2. The movement of sodium from a low concentration to a higher concentration is an example of _____.
   a. Active transport by vesicles
   b. Facilitated diffusion
   c. Simple diffusion
   d. Active transport by pumps

After rushing around most of the day on his whirlwind tour of the city, Tobie was so thirsty, he felt that he could drink gallons of water.

3. If he did indeed drink several gallons of water in a short time, what effect might that have on his blood?
   a. His blood would become hypertonic.
   b. His blood would become hypotonic.
   c. His blood would become isotonic.
   d. The water would have no effect on his blood.

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

MOVEMENT OF SUBSTANCES THROUGH CELL MEMBRANES

A. Passive transport processes—do not require any energy expenditure of the cell membrane (Table 4-1)
   1. Diffusion—a passive process (Figure 4-1)
      a. Molecules spread through the membranes
      b Molecules move from an area of high concentration to an area of low concentration, down a concentration gradient (Figure 4-2)
      c. As molecules diffuse, a state of equilibrium will occur
   2. Simple diffusion (Figure 4-3)
      a. Molecules cross through the phospholipid bilayer
      b Solutes permeate the membrane; therefore we call the membrane permeable
   3. Osmosis (Figure 4-4)
      a. Diffusion of water through a selectively permeable membrane; limits diffusion of at least some of the solute particles
      b. Water pressure that develops as a result of osmosis is called *osmotic pressure*
      c. Potential osmotic pressure is the maximum pressure that could develop in a solution when it is separated from pure water by a selectively permeable membrane; knowledge of potential osmotic pressure allows prediction of the direction of osmosis and the resulting change in pressure:
         (1) Isotonic—describes a fluid having the same potential osmotic pressure as cytosol (Figure 4-5)
         (2) Hypertonic—"higher pressure"; cells placed in solutions that are hypertonic always shrivel as water flows out of them; this has great medical importance: if medical treatment causes the extracellular fluid to become hypertonic, serious damage may occur
         (3) Hypotonic—"lower pressure"; cells placed in a hypotonic solution may swell as water flows into them; water always osmoses from the hypotonic solution into the cytosol
      d. Osmosis results in gain of volume on one side of the membrane and loss of volume on the other side of the membrane
   4. Facilitated diffusion (mediated passive transport)
      a. A special kind of diffusion in which movement of molecules is made more efficient by the action of transporters embedded in a cell membrane
      b. Transports substances down a concentration gradient
      c. Energy required comes from the collision energy of the solute

d. Channel-mediated passive transport (Figure 4-6)
(1) Channels are specific—allow only one type of solute to pass through
(2) Gated channels may be open or closed (or inactive)—may be triggered by any of a variety of stimuli
(3) Channels allow membranes to be selectively permeable
(4) Aquaporins are water channels that permit rapid osmosis
e. Carrier-mediated passive transport (Figure 4-7)
(1) Carriers attract and bind to the solute, change shape, and release the solute out the other side of the carrier
(2) Carriers are usually reversible, depending on the direction of the concentration gradient

5. Role of passive transport processes
a. Move substances down their concentration gradient, thus maintaining equilibrium—and homeostatic balance
b. Types of passive transport—simple and facilitated diffusion (channels and carriers); osmosis is a special example of channel-mediated passive transport of water

B. Active transport processes—require the expenditure of metabolic energy by the cell (Table 4-2)
1. Transport by pumps
a. Pumps are membrane transporters that move a substance against their concentration gradient—opposite of diffusion
b. Examples: calcium pumps (Figure 4-8) and sodium-potassium pumps (Figure 4-9)
2. Transport by vesicles—allow substances to enter or leave the interior of a cell without actually moving through its plasma membrane
a. Endocytosis—the plasma membrane "traps" some extracellular material and brings it into the cell in a vesicle
(1) Two basic types of endocytosis (Figure 4-10)
(a) Phagocytosis—"condition of cell eating"; large particles are engulfed by the plasma membrane and enter the cell in vesicles; the vesicles fuse with lysosomes, which digest the particles
(b) Pinocytosis—"condition of cell drinking"; fluid and the substances dissolved in it enter the cell
(2) Receptor-mediated endocytosis—membrane receptor molecules recognize substances to be brought into the cell (Figure 4-11)
b. Exocytosis
(1) Process by which large molecules, notably proteins, can leave the cell even though they are too large to move out through the plasma membrane
(2) Large molecules are enclosed in membranous vesicles and then pulled to the plasma membrane by the cytoskeleton, where the contents are released
(3) Exocytosis also provides a way for new material to be added to the plasma membrane

3. Role of active transport processes
a. Active transport requires energy use by the membrane
b. Pumps—concentrate substances on one side of membrane, as when storing an ion inside an organelle
c. Vesicle-mediated (endocytosis, exocytosis)—move large volumes of substances at once, as in secretion of hormones and neurotransmitters

CELL METABOLISM

A. Metabolism is the set of chemical reactions in a cell
1. Catabolism—breaks large molecules into smaller ones; usually releases energy
2. Anabolism—builds large molecules from smaller ones; usually consumes energy

B. Role of enzymes
1. Enzymes are chemical catalysts that reduce the activation energy needed for a reaction (Figure 4-12)
2. Enzymes regulate cell metabolism
3. Chemical structure of enzymes
a. Proteins of a complex shape
b. The active site is where the enzyme molecule fits the substrate molecule—the lock-and-key model (Figure 4-13)
4. Classification and naming of enzymes
a. Enzymes usually have an *–ase* ending, with the first part of the word signifying the substrate or the type of reaction catalyzed
b. Oxidation-reduction enzymes—known as oxidases, hydrogenases, and dehydrogenases; energy release depends on these enzymes
c. Hydrolyzing enzymes—hydrolases; digestive enzymes belong to this group
d. Phosphorylating enzymes—phosphorylases or phosphatases; add or remove phosphate groups
e. Enzymes that add or remove carbon dioxide—carboxylases or decarboxylases
f. Enzymes that rearrange atoms within a molecule—mutases or isomerases
g. Hydrases add water to a molecule without splitting it
5. General functions of enzymes
a. Enzymes regulate cell functions by regulating metabolic pathways (Figure 4-14)
b. Enzymes are specific in their actions
c. Various chemical and physical agents known as allosteric effectors affect enzyme action by changing the shape of the enzyme molecule; examples of allosteric effectors include (Figure 4-15):
(1) Temperature (Figure 4-16, B)
(2) Hydrogen ion (H^+) concentration (pH) (Figure 4-16, A)
(3) Ionizing radiation
(4) Cofactors
(5) End products of certain metabolic pathways (Figure 4-17)
d. Most enzymes catalyze a chemical reaction in both directions

e. Enzymes are continually being destroyed and continually being replaced
f. Many enzymes are first synthesized as inactive proenzymes

C. Catabolism
1. Cellular respiration, the pathway by which glucose is broken down to yield its stored energy, is an important example of cell catabolism; cellular respiration has three pathways that are chemically linked (Figure 4-21):
a. Glycolysis (Figure 4-18)
b. Citric acid cycle (Figure 4-19)
c. Electron transport system (ETS) (Figure 4-20)
2. Glycolysis (Figure 4-18)
a. Pathway in which glucose is broken apart into two pyruvic acid molecules to yield a small amount of energy (which is transferred to ATP and NADH)
b. Includes many chemical steps (reactions that follow one another), each regulated by specific enzymes
c. Is anaerobic (requires no oxygen)
d. Occurs within cytosol (outside the mitochondria)
3. Citric acid cycle (Krebs cycle) (Figure 4-19)
a. Pyruvic acid (from glycolysis) is converted into acetyl CoA and enters the citric acid cycle after losing CO_2 and transferring some energy to NADH
b. Citric acid cycle is a repeating (cyclic) sequence of reactions that occur inside the inner chamber of a mitochondrion; acetyl splits from CoA and is broken down to yield waste CO_2 and energy (in the form of energized electrons), which is transferred to ATP, NADH, and $FADH_2$
4. Electron transport system (ETS) (Figure 4-20)
a. Energized electrons are carried by NADH and $FADH_2$ from glycolysis and the citric acid cycle to electron acceptors embedded in the cristae of the mitochondrion
b. As electrons are shuttled along a chain of electron-accepting molecules in the cristae, their energy is used to pump accompanying protons (H^+) into the space between mitochondrial membranes
c. Protons flow back into the inner chamber through pump molecules in the cristae, and their energy of movement is transferred to ATP
d. Low-energy electrons coming off the ETS bind to oxygen and rejoin their protons to form water (H_2O)

D. Anabolism
1. Protein synthesis is a central anabolic pathway in cells, to be covered in more detail in Chapter 5

THE BIG PICTURE: CELL PHYSIOLOGY AND THE WHOLE BODY

A. Most cell processes are occurring at the same time in all of the cells throughout the body
B. Functions of individual cells are understood in the context of the trillions of cells of the body, to be explored further in Chapter 5

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Define the terms *diffusion*, *dialysis*, *facilitated diffusion*, *osmosis*, and *filtration*.
2. Explain how a concentration gradient relates to the process of diffusion.
3. Describe and give an example of a membrane channel.
4. Explain the terms *isotonic*, *hypotonic*, and *hypertonic*.
5. State the principle about a solution in which osmotic pressure develops, given appropriate conditions.
6. State the principle about the direction of active transport.
7. Name and describe the active transport pump that operates in the plasma membrane of all human cells.
8. Explain the processes of endocytosis and exocytosis.
9. Describe the classification of enzymes.
10. Discuss three general principles of enzyme function.
11. What is metabolism? Catabolism? Anabolism?
12. Describe briefly each of the three pathways that make up the process of cellular respiration.

CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. The process of peritoneal dialysis and the process of a white blood cell trapping bacteria by phagocytosis are both transport processes. Compare and contrast these processes and identify them as active or passive.
2. Which type of osmotic pressure can be more easily measured? Explain your answer.
3. Intravenous solutions can be isotonic to blood cells. Therefore, it is very important to know whether sugar, a nonelectrolyte, or salt (NaCl), an electrolyte, is being given in the solution so that the proper amount can be added. What would result if the tonicity of the solution is not isotonic to the blood cells?
4. White blood cells engulf bacteria and solutions that contain dissolved proteins. How would you summarize the processes that allow them to ingest both solids and liquids?
5. Explain how the shape of an enzyme determines its function. What would result if an allosteric effector changed the shape of the enzyme?
6. Compare and contrast aerobic and anaerobic pathways.
7. Why is the mitochondrion such an important organelle for survival of the cell? Explain why some cells, such as skeletal muscle cells, have more mitochondria than others do.

Cell Growth and Reproduction

5



CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

Protein Synthesis, 114
- Deoxyribonucleic Acid (DNA), 114
- Ribonucleic Acid (RNA), 115
- Transcription, 116
- Editing the Transcript, 116
- Translation, 117

Cell Growth, 121
- Production of Cytoplasm, 121
- DNA Replication, 122

Cell Reproduction, 123
- Mitosis, 123
- Meiosis, 124

Regulating the Cell Life Cycle, 125

Cycle of Life: Cells, 127

The Big Picture: Cell Growth, Reproduction, and the Whole Body, 127

Mechanisms of Disease, 127

LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

anaphase
(AN-ah-fayz)
[*ana-* **apart,** *-phase* **stage**]

apoptosis
(app-o-TOH-sis or app-op-TOH-sis)
[*apo-* **away,** *-ptosis* **falling**]

complementary pairing
(kom-pleh-MEN-tah-ree PAIR-ing)
[*comple-* **complete,** *-ment-* **process,** *-ary* **relating to**]

cytokinesis
(sye-toe-kin-EE-sis)
[*cyto-* **cell,** *-kinesis* **movement**]

deoxyribonucleic acid
(dee-ok-see-rye-boh-nooklay-ik ASS-id)
[*de-* **removed,** *-oxy-* **oxygen,** *-nucle-* **nucleus (kernel),** *-ic* **relating to,** *acid* **sour**]

differentiate
(dif-er-EN-shee-ayt)
[*different-* **difference,** *-iate* **act of**]

diploid
(DIP-loid)
[*diplo-* **double,** *-oid* **form**]

exon
(EKS-ahn)
[*exo-* **outside,** *-on* **unit**]

gamete
(GAM-eet)
[*gamet* **sexual union**]

haploid
(HAP-loid)
[*haplo-* **single,** *-oid* **form**]

interphase
(IN-ter-fayz)
[*inter-* **between,** *-phase* **stage**]

continued on p. 128

Cell growth and reproduction are the most fundamental of all living functions. These two processes together constitute the cell life cycle. *On these processes depend the continued survival of all organisms already living and the creation of all new organisms. Cell growth depends on using genetic information in DNA to make the structural and functional proteins needed for cell survival. Cell reproduction ensures that the genetic information is passed from one generation of cells to the next and from one generation of organisms to the next. Mistakes in these processes can cause lethal genetic disorders, cancer, and other conditions. Advances in our ability to manipulate the genetic code, and thus cell growth and reproduction, now present us with ethical implications more far-reaching than those accompanying the birth of the atomic age. All this makes the cell life cycle a worthy and fascinating topic of study.*

PROTEIN SYNTHESIS

As stated in the previous chapter, the most important anabolic pathway for the student beginning the study of anatomy and physiology to understand is the process of protein synthesis. Protein synthesis is important for several reasons. First of all, protein synthesis is required for cell growth and maintenance. Protein synthesis begins with reading of the genetic "master code" in the cell's DNA. The genetic code dictates the structure of each protein produced during the growth process of each cell. A basic understanding of how the genetic code is used by the cell is essential for understanding modern concepts of human biology, including the study of disease processes.

Protein synthesis is also an important process because it influences all cell structures and functions. Proteins synthesized by the cell either are structural elements themselves or are enzymes or other functional proteins that direct the synthesis of other structural and functional molecules such as carbohydrates, lipids, and nucleic acids. In short, protein synthesis is the central building process for cell growth and maintenance.

Deoxyribonucleic Acid (DNA)

In 1953, American scientist James Watson, and three British scientists, Francis Crick, Maurice Wilkins, and Rosalind Franklin, won the race to solve the puzzle of DNA's molecular structure (Figure 5-1). Nine years later, Watson, Crick, and Wilkins received the Nobel Prize for their brilliant and significant work—hailed as the greatest biological discovery of our time. (Franklin died before the Nobel Prize was awarded.)

Since the original discovery of DNA's structure, we have seen a new branch of biology called *molecular genetics* emerge from our rapidly growing knowledge of DNA and how it works. Indeed, we have seen a revolution in human biology as we witness the continuing application of molecular genetics transform every single aspect of anatomy, physiology, and medicine. We begin our outline of protein synthesis with a discussion of DNA because it truly is, as Watson called it, "the most golden of all molecules."

The **deoxyribonucleic acid** molecule is a giant among molecules. Its size and the complexity of its shape exceed those of most molecules. The importance of its function—in a word, information—surpasses that of any other molecule in the world. To visualize the shape of the DNA molecule, picture an extremely long, narrow ladder made of a pliable material (see Figure 5-1). Now see it twisting round and round on its axis and taking on the shape of a steep spiral staircase millions of turns long. This is the shape of the DNA molecule—a double spiral or *double helix*.

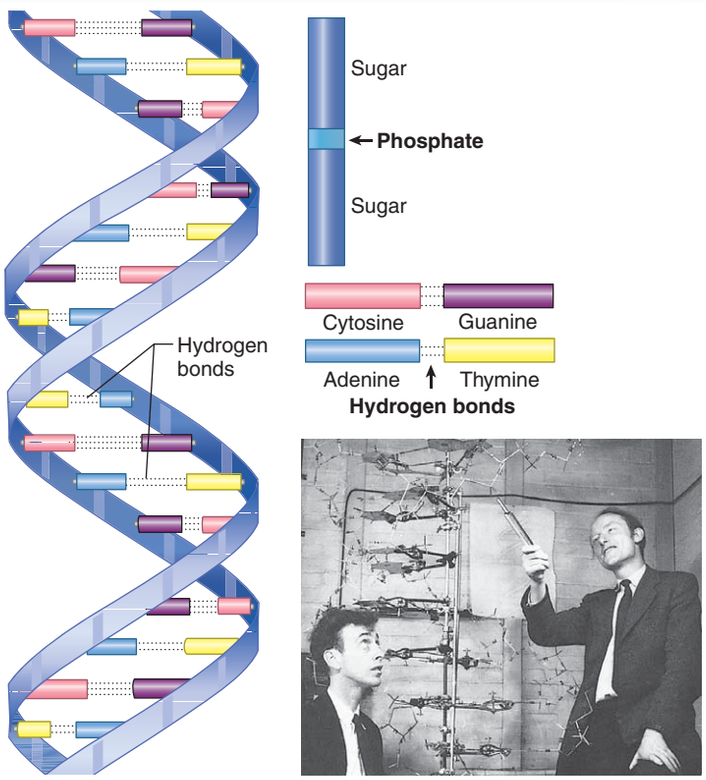


FIGURE 5-1

Watson-Crick model of the DNA molecule. The DNA structure illustrated here is based on that published by James Watson (photograph, left) and Francis Crick (photograph, right) in 1953. Note that each side of the DNA molecule consists of alternating sugar and phosphate groups. Each sugar group is united to the sugar group opposite it by a pair of nitrogenous bases (adenine-thymine or cytosine-guanine). The sequence of these pairs constitutes a genetic code that determines the structure and function of a cell.

The DNA molecule is a *polymer*, which means that it is a large molecule made up of many smaller molecules joined together in sequence. DNA is a polymer of millions of pairs of nucleotides. A nucleotide is a compound formed by combining phosphoric acid with a sugar and a nitrogenous base. The DNA molecule has four different kinds of nucleotides. Each consists of a phosphate group that attaches to the sugar deoxyribose, which attaches to one of four bases. Nucleotides differ, therefore, in their nitrogenous base component—containing either adenine or guanine (purine bases) or cytosine or thymine (pyrimidine bases). (Deoxyribose is a sugar that is not sweet and one whose molecules contain only five carbon atoms.) Notice what

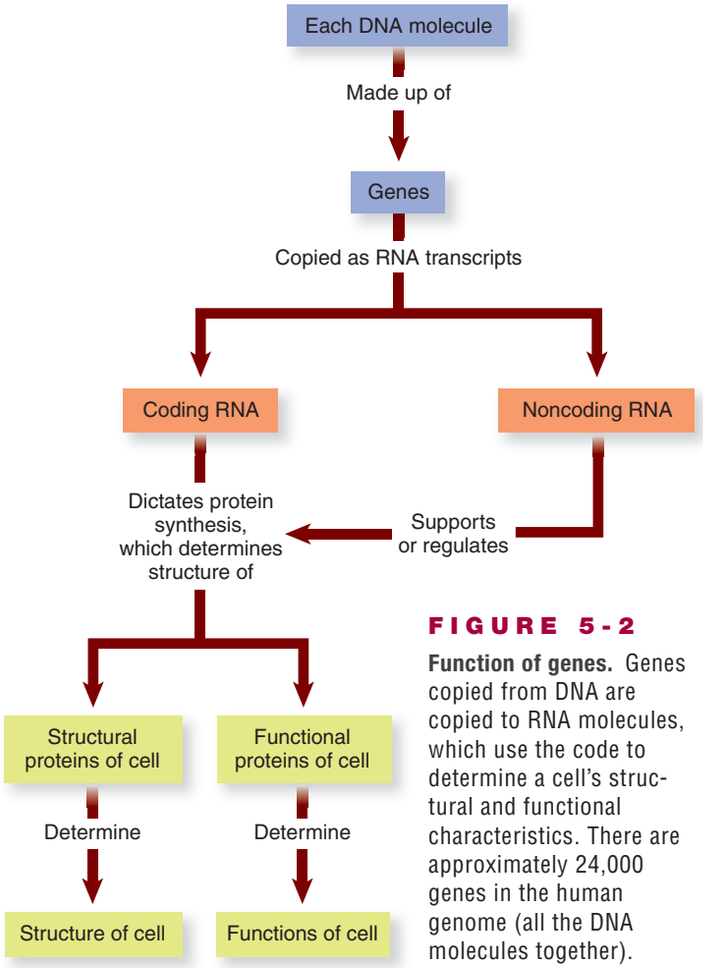


FIGURE 5-2

Function of genes. Genes copied from DNA are copied to RNA molecules, which use the code to determine a cell's structural and functional characteristics. There are approximately 24,000 genes in the human genome (all the DNA molecules together).

the name *deoxyribonucleic acid* tells you—that this compound contains deoxyribose, that it occurs in the nucleus, and that it is an acid.

Figure 5-1 reveals additional and highly significant facts about DNA's molecular structure. First, observe which compounds form the sides of the DNA spiral staircase—a long line of phosphate and deoxyribose units joined alternately one after the other. Look next at the stair steps. Notice two facts about them: two bases join (loosely bound by hydrogen bonds) to form each step, and only two combinations of bases occur. The same two bases invariably pair off with each other in a DNA molecule. Adenine always goes with thymine (or vice versa, thymine with adenine), and guanine always goes with cytosine (or vice versa). This aspect of DNA molecular structure is called **obligatory base pairing.** Pay particular attention to it, for it is the key to understanding how a DNA molecule is able to duplicate itself. DNA duplication, or *replication* as it is usually called, is one of the most important of all biological phenomena because it is an essential and crucial part of the mechanism of genetics.

Another aspect of DNA's molecular structure that has great functional importance is the sequence of its base pairs. Although the kinds of base pairs possible in all DNA molecules are the same, the *sequence* of these base pairs is not the same in all DNA molecules. For instance, the sequence of the base pairs composing the seventh, eighth, and ninth steps of one DNA molecule might be cytosine-guanine, adenine-thymine, and thymine-adenine. Such a sequence of three bases forms a code word or "triplet" called a *codon.* In another DNA molecule the coding sequence of the base pairs making up these same steps might be entirely different, perhaps thymine-adenine, guanine-cytosine, and cytosine-guanine. Perhaps these seem to be minor details, but nothing could be further from the truth, because it is the sequence of the base pairs in the nucleotides that make up the DNA molecules that identifies each gene. Therefore, it is the sequence of base pairs that determines all hereditary traits.

A human *gene* is a segment of a DNA molecule. One gene consists of a chain of approximately 1000 pairs of nucleotides joined one after the other in a precise sequence. Each gene in DNA is a code. As Figure 5-2 shows, a gene is the code for building a short strand of RNA (ribonucleic acid).

Ribonucleic Acid (RNA)

To make a protein, the gene code in DNA is first copied to a messenger ribonucleic acid (mRNA) molecule, or transcript. Each mRNA transcript of a gene may then be translated by the cell and used to build one polypeptide chain. Because it is a copy of a gene's code, we call mRNA *coding RNA.* A few RNA transcripts are instead used to support or regulate polypeptide production. We call such RNA molecules *noncoding RNAs.* Examples of noncoding RNAs are rRNA (ribosomal RNA) and tRNA (transfer RNA). Table 5-1 summarizes the major types of RNA.

TABLE 5-1 Major Types of RNA

ACRONYM	NAME	DESCRIPTION	ROLE IN CELL FUNCTION
RNA Involved in Protein Synthesis			
mRNA	Messenger RNA	Single, unfolded strand of nucleotides	Serves as working copy of one protein-coding gene
rRNA	Ribosomal RNA	Single, folded strand of nucleotides	Component of the ribosome (along with proteins); attaches to mRNA and participates in translation
tRNA	Transfer RNA	Single, folded strand of nucleotides; has an anticodon at one end and an amino acid–binding site at the other end	Carries a specific amino acid to a specific codon of mRNA at the ribosome during translation
snRNP	Small nuclear ribonucleo-protein	Single, folded strand of RNA (combined with polypeptide chains)	Component of the spliceosome (see Box 5-1); attaches to an mRNA transcript to facilitate editing (removal of introns; splicing of exons) into the final version of mRNA
RNA Involved in Gene Silencing (see Box 5-2)			
dsRNA	Double-strand RNA	Double strand of nucleotides (may be up to several hundred nucleotides long)	Involved in RNA interference; *see* siRNA, which is a type of dsRNA
siRNA	Short interfering RNA	Short segment of double-strand RNA (only 20-25 nucleotides long)	Forms part of the RNA-induced silencing complex (RISC) during RNA interference

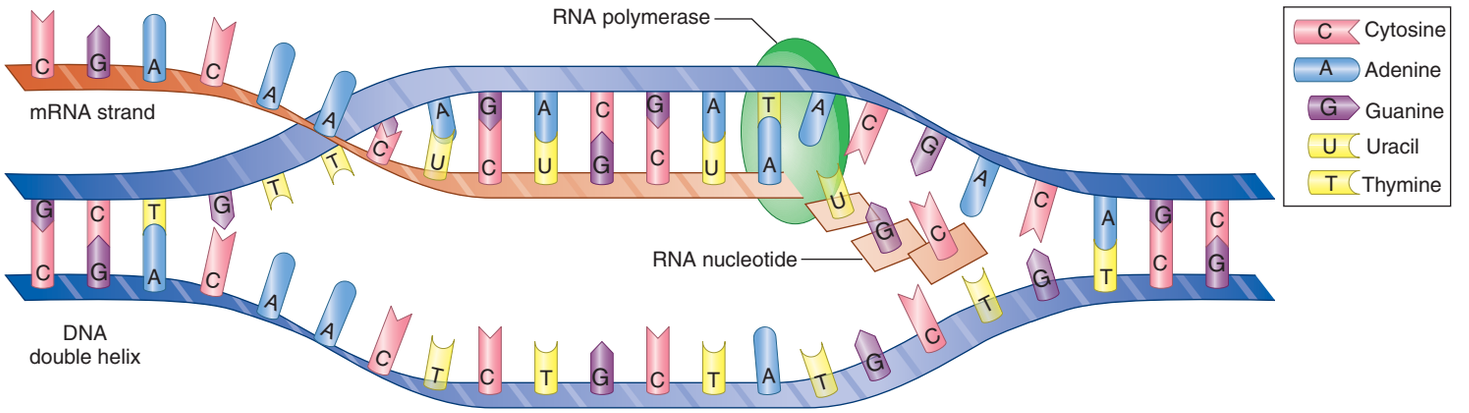


FIGURE 5-3

Transcription of messenger RNA (mRNA). A DNA molecule "unzips" in the region of the gene to be transcribed. RNA nucleotides already present in the nucleus temporarily attach themselves to exposed DNA bases along one strand of the unzipped DNA molecule according to the principle of complementary pairing. As the RNA nucleotides attach to the exposed DNA, they bind to each other and form a chainlike RNA strand called a *messenger RNA (mRNA)* molecule. Notice that the new mRNA strand is an exact copy of the base sequence on the opposite side of the DNA molecule. As in all metabolic processes, the formation of mRNA is controlled by an enzyme—in this case, the enzyme is called *RNA polymerase.*

One or more polypeptides made using RNA are used by the cell to make up each of a cell's structural proteins and the many functional proteins that regulate cellular processes. Therefore, as Figure 5-2 shows, the nearly 24,000 protein-coding genes that make up a cell's genome (DNA set) determine the cell's structure and its functions.

Transcription

Protein synthesis begins when a single strand of RNA (ribonucleic acid) forms along a segment of one strand of a DNA molecule. Figure 5-3 summarizes how this process happens. Recall from Chapter 2 that RNA differs from DNA in certain respects (see Table 2-6, p. 37). Its molecules are smaller than those of DNA, and RNA contains ribose instead of deoxyribose. In addition, one of the four bases in RNA is uracil instead of thymine. As a strand of RNA is forming along a strand of DNA, uracil attaches to adenine, and guanine attaches to cytosine. The process is known as **complementary pairing.** Thus a single-strand molecule of *messenger RNA (mRNA)* is formed.

The name "messenger RNA" describes its function. As soon as it is formed, it separates from the DNA strand, is edited, moves out of the nucleus, and carries a "message" to a ribosome in the cell's cytoplasm to direct the synthesis of a specific polypeptide. Synthesis of any RNA molecule is often called **transcription** because it actually copies or "transcribes" a portion of the DNA code—just like you "transcribe" your class notes when you make a copy of them.

Editing The Transcript

After the preliminary version of the mRNA molecule is formed, its message is "edited" into a final version before it reaches a ribosome (Figure 5-4). Just as you may edit your class notes by rearranging them for clarity after you transcribe them, the editing process allows the cell to arrange the code so that it will work in making a specific, needed polypeptide.

To begin editing, a modified guanine (G) nucleotide caps one end of the mRNA strand. At about the same time, a string of 50 to 200 adenine (A) nucleotides attaches to the opposite end of the mRNA strand. This string of A nucleotides is sometimes called the *poly A tail.* The cap and poly A tail both assist in the next step of mRNA editing. The cap and poly A tail also eventually help transport the mRNA strand out of the nucleus and assist in starting and stopping the translation process described in the next section.

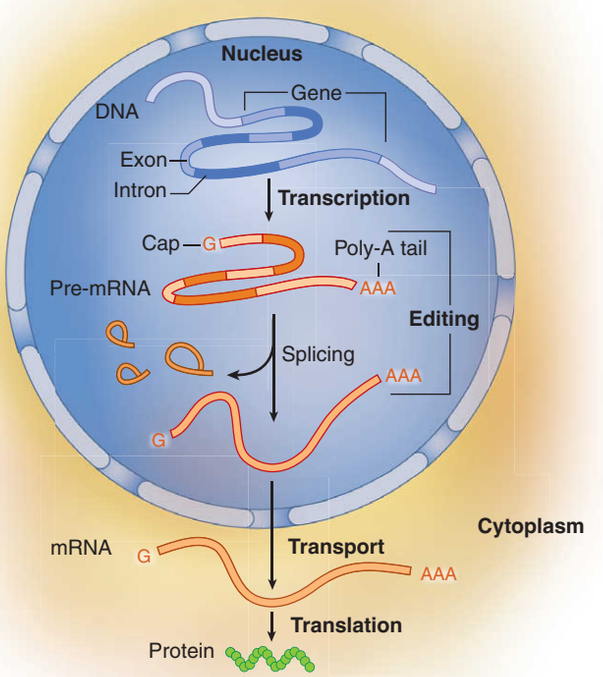


FIGURE 5-4

Editing of an mRNA transcript. After the preliminary mRNA strand is transcribed from a gene in DNA, it is capped with a modified G nucleotide at one end. At the same time, a poly A string is attached at the other end. The intron sections of the transcript are then removed and the remaining exons joined, or spliced, together to form the final version of mRNA. The edited mRNA transcript then moves out of the nucleus to participate in translation (see Figure 5-3).

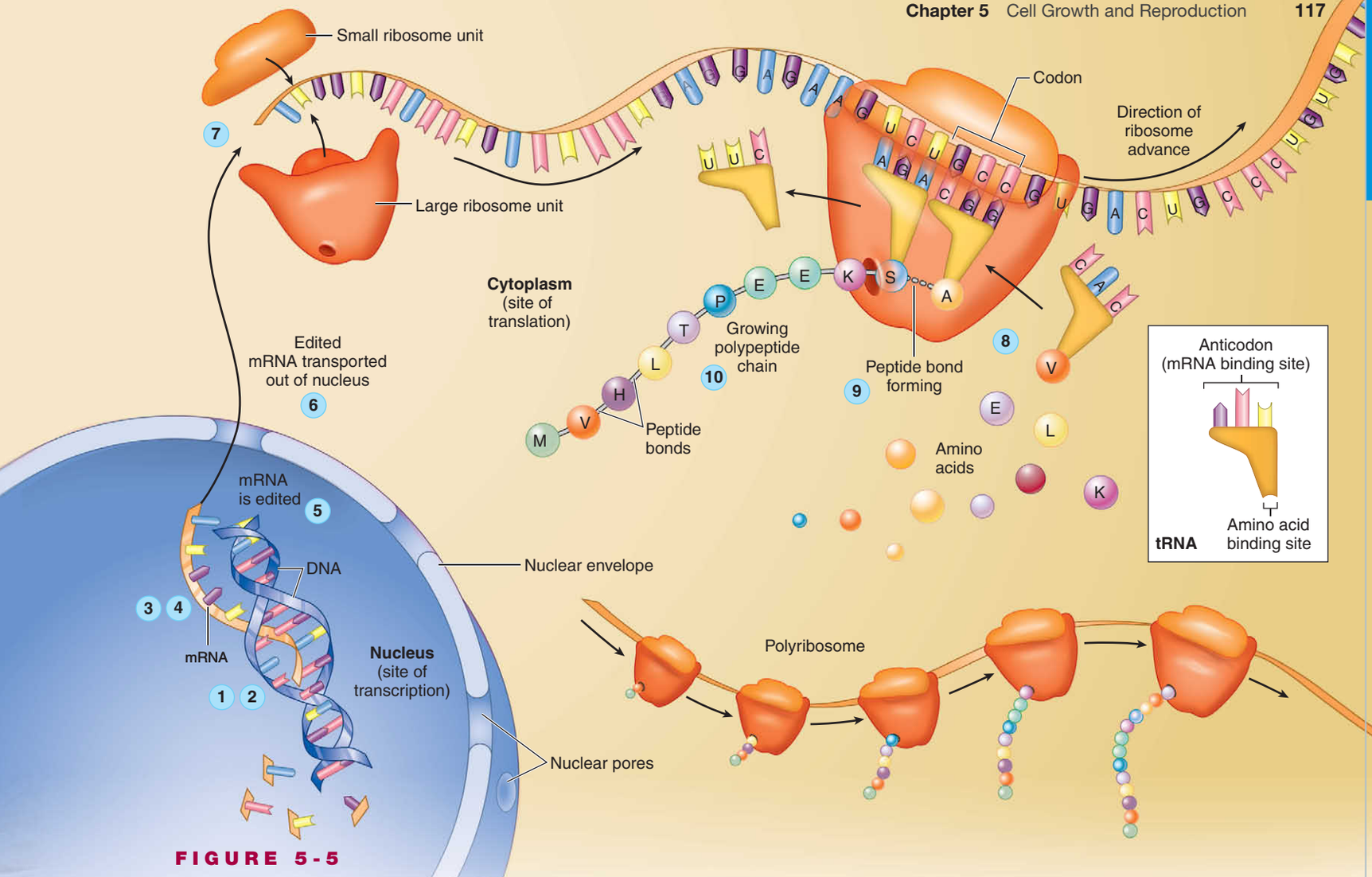


FIGURE 5-5

Protein synthesis. Each of the numbered steps in the figure is further summarized in Table 5-2. Protein synthesis begins with transcription, a process in which an mRNA molecule forms along one gene sequence of a DNA molecule within the cell's nucleus *(1-3)*. As it is formed, the mRNA molecule separates from the DNA molecule *(4)*, is edited *(5)*, and leaves the nucleus through the large nuclear pores *(6)*. Outside the nucleus, ribosome subunits attach to the beginning of the mRNA molecule and begin the process of translation *(7)*. In translation, transfer RNA (tRNA) molecules bring specific amino acids—encoded by each mRNA codon—into place at the ribosome site *(8)*. As the amino acids are brought into the proper sequence, they are joined together by peptide bonds *(9)* to form long strands called polypeptides *(10)*. Several polypeptide chains may be needed to make a complete protein molecule. Amino acids are identified by color codes and abbreviations (see Figure 2-26 on p. 55). See Table 5-2 for further clarification of protein synthesis.

Some segments of the RNA transcript represent noncoding parts of DNA called **introns.** These intron segments are removed by a complicated process involving small nuclear structures called *spliceosomes* (Box 5-1). This leaves behind segments that are copies of the DNA's **exons.** Many of these exons encode the functional domains within protein molecules. Only these exon copies will be used in the final recipe for the protein. All the RNA segments representing exons are then *spliced* (joined) together by enzymes to form the final edited form of mRNA. It is this edited version of RNA that leaves the nucleus and participates in the next step of protein synthesis.

Translation

In the cytoplasm, the edited mRNA molecule attracts first a small ribosome subunit and then a large subunit (see Figure 3-6). As the subunits come together, they form an "mRNA sandwich" with the mRNA molecule in the middle. Recall that the two subunits of the now-complete ribosome are composed largely of *ribosomal RNA* (rRNA). The cell is now ready to interpret or "translate" the genetic code and form a specific sequence of amino acids in a process called **translation.**

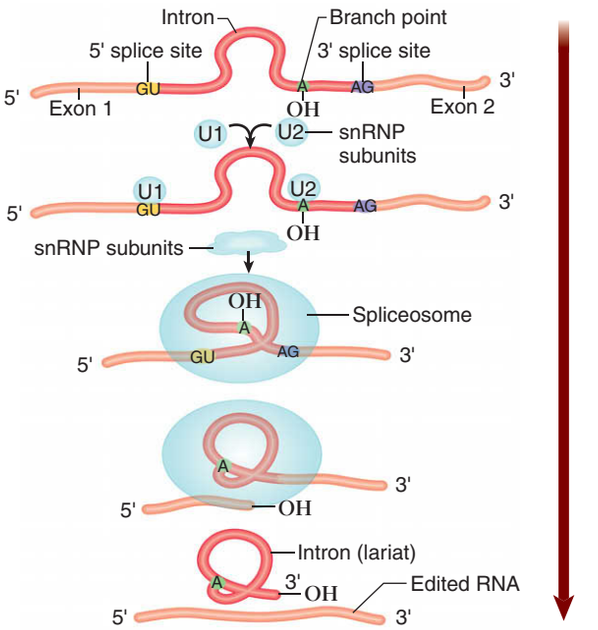
In translation, yet another type of RNA—*transfer RNA* (tRNA)—becomes involved in protein synthesis (Figure 5-5). As the name implies, tRNA molecules carry or "transfer" amino acids to the ribosome for placement in the prescribed sequence. This function is determined by a unique molecular structure: a binding site for a specific amino acid at one end and a binding site for a specific mRNA codon (base triplet) at the other end (see Figure 2-32 on p. 58). Because tRNA's binding site for mRNA contains the three bases that exactly complement one mRNA codon, this binding site is often called the *anticodon.*

Box 5-1 | Spliceosome

The noncoding *intron* segments of the mRNA initially transcribed from a DNA gene are removed by a complicated process involving small structures called **spliceosomes.** Found inside the nucleus, spliceosomes are about the size of a ribosome. Spliceosomes are made up of subunits consisting of *small nuclear ribonucleoprotein particles* (*snRNPs,* pronounced "snurps").

During mRNA editing, a snRNP subunit will attach at the beginning of an intron and another snRNP will attach at a spot in the intron called the "branch point." Eventually, several different subunits will all assemble on the intron in this manner to form a complete spliceosome. As the Figure shows, the assembled spliceosome then breaks the strand as it bends the intron into a loop called a *lariat.* The intron lariat breaks completely away from the strand, and the spliceosome splices the ends of the remaining coding *exon* segments together. Only the spliced exons remain in the final, edited version of mRNA, which is later translated into the polypeptide encoded by the gene.

The intron may later break down into individual nucleotides, which are then recycled by the cell and used again for transcription. The intron may instead be processed to form a noncoding RNA strand with regulatory functions (see Box 5-2). After splicing is accomplished, the snRNP subunits of the spliceosome are free to reassemble on another intron and repeat the process.



Editing of mRNA by the spliceosome. A simplified view of the complex splicing process.

After picking up its amino acid from a pool of different types of amino acids floating free in the cytoplasm, a tRNA molecule moves to the ribosome. There, its anticodon attaches to a complementary mRNA codon—the codon that signifies the specific amino acid carried by that tRNA molecule (Figure 5-6). After the next tRNA brings its amino acid into place, the two amino acids form a peptide bond. The ribosome then moves down the mRNA strand, making the next mRNA codon available for a complementary tRNA molecule bearing the appropriate amino acid. More tRNA molecules, one after the other in rapid sequence, bring more amino acids to the ribosome and fit them into their proper position in the growing chain of amino acids. As Figure 5-5 shows, the ribosome is all the while moving down the mRNA strand—until it reaches the end, where the ribosome subunits fall away.

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How many different amino acids can be used to make proteins? Is this the only function of amino acids in the human body? Find out in ***Amazing Amino Acids*** online at ***A&P Connect.***

evolve

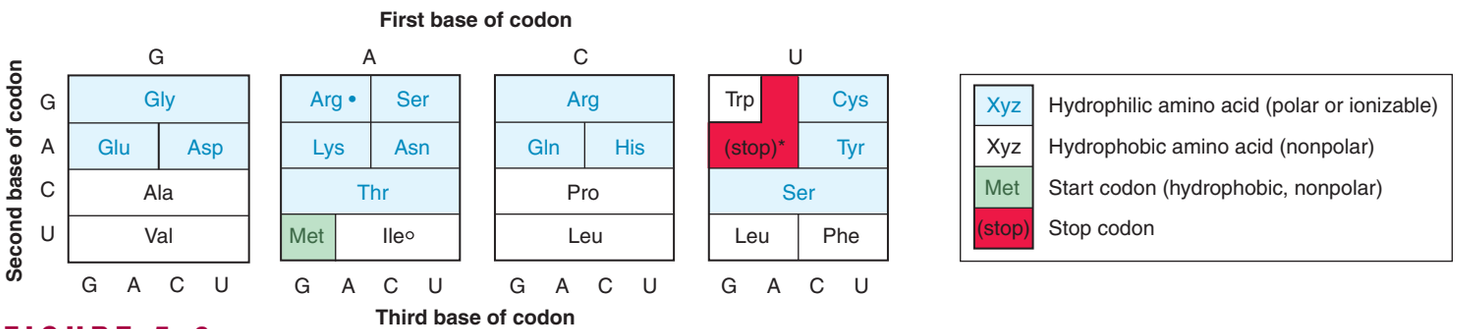


FIGURE 5-6

The genetic code. The first graphic "phrasebook" or "decoder" of the genetic language of the cell was developed in 1966 to summarize the amino acids encoded by various codons (three-base sequences of nucleotides) in RNA. To read this more recent decoder adapted for human biology, start with any codon (for example, CGA). Find the first base along the top of the decoder to find the correct box to use (*C* is the third box). The second base is found in each row of that box, labeled on the left (*G* is the first row). Then use the third base to find the correct column, labeled at the bottom of each box (*A* is the second column, showing that arginine [Arg] is the amino acid encoded by CGA; the bluish color tells us that arginine is a hydrophilic amino acid). •AGG, AGA act as stop codons in mitochondria ◦AUA codes for methionine (Met) in mitochondria * UGA, a stop codon, instead encodes selenocysteine (Sec) in the cytoplasm when a certain pattern appears in the surrounding codons; in mitochondria UGA instead encodes tryptophan.

Each of the tools needed for translation—mRNA, tRNA, and ribosome subunits—can be reused again and again to form copies of the same polypeptide. As a matter of fact, one ribosome can follow another along the same mRNA strand, each making its own polypeptide. Cell biologists often observe a whole train of ribosomes positioned along a single mRNA strand, each making an identical copy of the encoded polypeptide. Such a **polyribosome** is pictured in Figure 5-5.

Translation can be inhibited or prevented by a process called **RNA interference (RNAi).** Box 5-2 details the concept of silencing genes by interfering with the process of translating the genes. RNAi may be used by cells to protect against virus infections.

As specific polypeptides are formed, chaperone proteins and other enzymes in the endoplasmic reticulum (ER), Golgi apparatus, or cytosol assist them in folding and linking to form secondary, tertiary, and perhaps quaternary protein molecules (see Figure 3-8, p. 74). In some polypeptides, enzymes remove or insert additional amino acids or other chemical groups. Enzymes may also catalyze the formation of hybrid molecules such as lipoproteins or glycoproteins.

If any of the proteins formed during this process fail to fold or are misfolded, they will not function properly. Chaperone molecules may be able to refold them into the proper shape. But if not, then the cell risks serious problems. Recall from Chapter 3 that proteasomes break down unfolded and misfolded proteins, allowing the cell to recycle the amino acids and "start over again" (Figure 3-10, p. 76). If this "quality control" program fails to take care of all the defective proteins, they may clump together and form dense masses called *plaques* that could damage or kill the cell. Several degenerative diseases such as Alzheimer disease (AD) and Parkinson disease (PD) involve such a mechanism.

Protein anabolism is one of the major kinds of cellular work. One human cell is estimated to synthesize thousands of different enzymes! In addition to this staggering workload, the cell produces many different protein compounds that help form its own structures, and many cells also synthesize special functional proteins for use in other parts of the body. Liver cells are an example; they synthesize proteins such as prothrombin, fibrinogen, albumin, and globulin for blood plasma.

The complete set of proteins synthesized by a cell is called the **proteome** of the cell. The human proteome is the complete set of proteins synthesized by all the cells of the human body. The human proteome is much larger than the human genome (entire set of genes). How can that be, if genes are codes for the polypeptides that make up proteins? It is because each polypeptide may be used in a variety of different combinations with other polypeptides, enabling the production of a huge variety of different proteins.

For your convenience, Table 5-2 gives a detailed, step-by-step outline of this important process of protein synthesis.

TABLE 5-2 Summary of Protein Synthesis

STEP	LOCATION IN THE CELL	DESCRIPTION
Transcription		
1	Nucleus	One region, or gene, of a DNA molecule "unzips" to expose its bases
2	Nucleus	According to the principles of complementary base pairing, RNA nucleotides already present in the nucleoplasm temporarily attach themselves to the exposed bases along one side of the DNA molecule
3	Nucleus	As RNA nucleotides align themselves along the DNA strand, they bind to each other and thus form a chainlike strand called *messenger RNA* (mRNA) This binding of RNA nucleotides is controlled by the enzyme RNA polymerase
Preparation of mRNA		
4	Nucleus	As the preliminary mRNA strand is formed, it peels away from the DNA strand This mRNA strand is a copy, or *transcript,* of a gene
5	Nucleus	The spliceosome edits the mRNA molecule by removing noncoding portions of the strand (introns) and splicing the remaining pieces (exons)
6	Nuclear pores	The edited mRNA strand is transported out of the nucleus through pores in the nuclear envelope
Translation		
7	Cytoplasm	Two subunits sandwich the end of the mRNA molecule to form a ribosome
8	Cytoplasm	Specific transfer RNA (tRNA) molecules bring specific amino acids into place at the ribosome, which acts as a sort of "holder" for the mRNA strand and tRNA molecules The kind of tRNA (and thus the kind of amino acid) that moves into position is determined by complementary base pairing: each mRNA codon exposed at the ribosome site will permit only a tRNA with a complementary *anticodon* to attach
9	Cytoplasm	As each amino acid is brought into place at the ribosome, an enzyme in the ribosome binds it to the amino acid that arrived just before it The chemical bonds formed, called *peptide bonds,* link the amino acids together to form a long chain called a *polypeptide*
10	Cytoplasm	As the ribosome moves along the mRNA strand, more and more amino acids are added to the growing polypeptide chain in the sequence dictated by the mRNA codons (Each codon represents a specific amino acid to be placed in the polypeptide chain) When the ribosome reaches the end of the mRNA molecule, it drops off the end and separates into large and small subunits again; often, enzymes later link two or more polypeptides together to form a whole protein molecule

Box 5-2 | The RNA Revolution

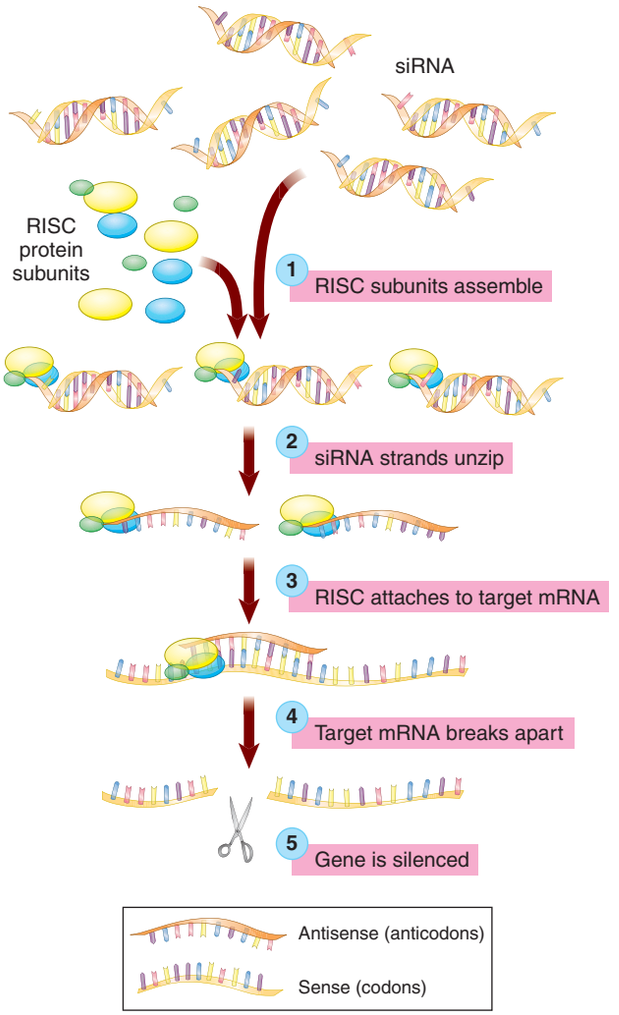
For nearly a half century after the discovery of DNA and its central role in heredity in 1953, scientific understanding of cellular physiology focused primarily on DNA—that "most golden of molecules." RNA was seen as the "go between" molecule, acting mainly as a temporary working copy of a segment of DNA code (gene). However, we soon learned that tRNA (transfer RNA) and rRNA (ribosomal RNA) play a functional role other than direct coding for proteins. This discovery sparked some interest in looking for possible additional regulatory or supportive roles of RNA. Soon, catalytic forms of *noncoding RNA* were shown to be involved in editing mRNA (messenger RNA) transcripts before translation (see Box 5-1). The dawn of the twenty-first century saw an explosion of new discoveries regarding additional roles of RNA in regulating the function of the genome—a scientific revolution that still continues.

One aspect of the RNA revolution involves the surprising treasure trove of noncoding RNA molecules transcribed from the roughly 98% of the DNA genome that does not code for proteins. This includes introns (noncoding segments) that are removed from transcribed (mRNA) protein-coding genes during the editing process before translation. Current scientific databases are chock full of thousands of such regulatory RNA sequences. To cell scientists, it is becoming clear that an extensive RNA regulatory system manages the human genome.

One of the more interesting and useful recent discoveries of the current RNA revolution involves a cellular process of "gene silencing" called **RNA interference (RNAi).** Stated simply, RNAi is a process in which certain genes are silenced and thus synthesis of a particular protein is halted. RNAi occurs naturally in every cell, and scientists are still working to discover the mechanisms that govern the process and the purposes it serves in the cell. In human cells, RNAi is thought to be part of a complex scheme of "fine-tuning" protein synthesis. RNAi plays a variety of roles in the normal regulation of gene expression—what proteins we make and when we make them. For example, the cell could use RNAi to inhibit replication of virus components within the cell during a viral infection—thus protecting the cell. When the RNAi systems fails, it may lead to disease.

How does RNAi work? A special form of RNA with two strands—double-strand RNA (dsRNA)—seems to be the key, as the Figure shows. A small segment of dsRNA, only about 20 or so nucleotides long, called *short interfering RNA (siRNA),* begins the process by combining with protein subunits to form an *RNA-induced silencing complex (RISC).* The siRNA within the RISC unwinds and exposes anticodons that allow the RISC to attach to a particular mRNA transcript. After the RISC attaches to its target mRNA, the mRNA breaks apart and therefore fails to translate its encoded protein. Of course, this effectively silences the gene encoded in the target mRNA. RNAi has also been shown to remodel chromatin, thus changing the "master code" in the DNA molecule!

Scientists are especially excited about using RNAi as a research tool. Researchers can synthesize a particular siRNA double strand and insert it into a cell that they want to study. The siRNA will induce the silencing of a particular gene so that researchers can see what happens to the cell. Knocking out the activity of just one gene at a time allows scientists to test hypotheses regarding how particular genes or particular proteins function in the cell.



RNA interference. 1, Short, double-stranded siRNA (short interfering RNA) segments combine with protein subunits to form an RNA-induced silencing complex (RISC). **2,** The siRNA within the RISC unwinds to expose anticodons. **3,** The activated RISC attaches to target mRNA possessing complementary codons. **4,** The RISC causes the mRNA molecule to break apart. **5,** The mRNA can no longer code for a polypeptide, and thus the gene is effectively silenced. Eventually, the mRNA is broken down into its component nucleotides, which can be reused by the cell to build other RNA molecules.

The therapeutic possibilities of RNAi are also very exciting. Work is already under way to find an effective means of using RNAi for creating antiviral creams containing siRNA to protect against HIV and other viruses. Some researchers are using RNAi to knock out genes that permit permanent tissue damage during heart attacks, kidney failure, and stroke. Researchers are also attempting to harness the power of RNAi to treat cancer and many types of infection.

| QUICK CHECK |

1. How does DNA act as a "master molecule" of a cell?
2. Where in the cell does transcription occur? Editing (splicing)? Translation?
3. What determines the primary sequence in which amino acids are assembled to form a specific polypeptide?

CELL GROWTH

As stated earlier, one of the two major phases of the cell life cycle is the growth phase (Figure 5-7 and Table 5-3). It is during this phase that a newly formed cell produces new molecules, from which it constructs the additional cell membrane, cell fibers, and other structures necessary for growth. And as just stated, all the structural proteins, plus the enzymes needed to make lipids, carbohydrates, and other substances, are made by the cell with information contained in the genes of DNA molecules. First, we will review a simplified account of how these proteins are made and how additional organelles are produced. Later, we explore how the cell replicates its DNA molecules in anticipation of reproduction.

Production of Cytoplasm

As a cell grows, it must produce additional cytoplasm and the plasma membrane necessary to contain it. One mechanism by which additional cytoplasm is produced is protein synthesis. Recall from the previous section that protein synthesis is an anabolic process, which means that small molecules are joined together to form large molecules. Amino acids are strung together in a specific sequence to form polypeptide chains. Two or more folded polypeptide chains may then be linked to form larger, more

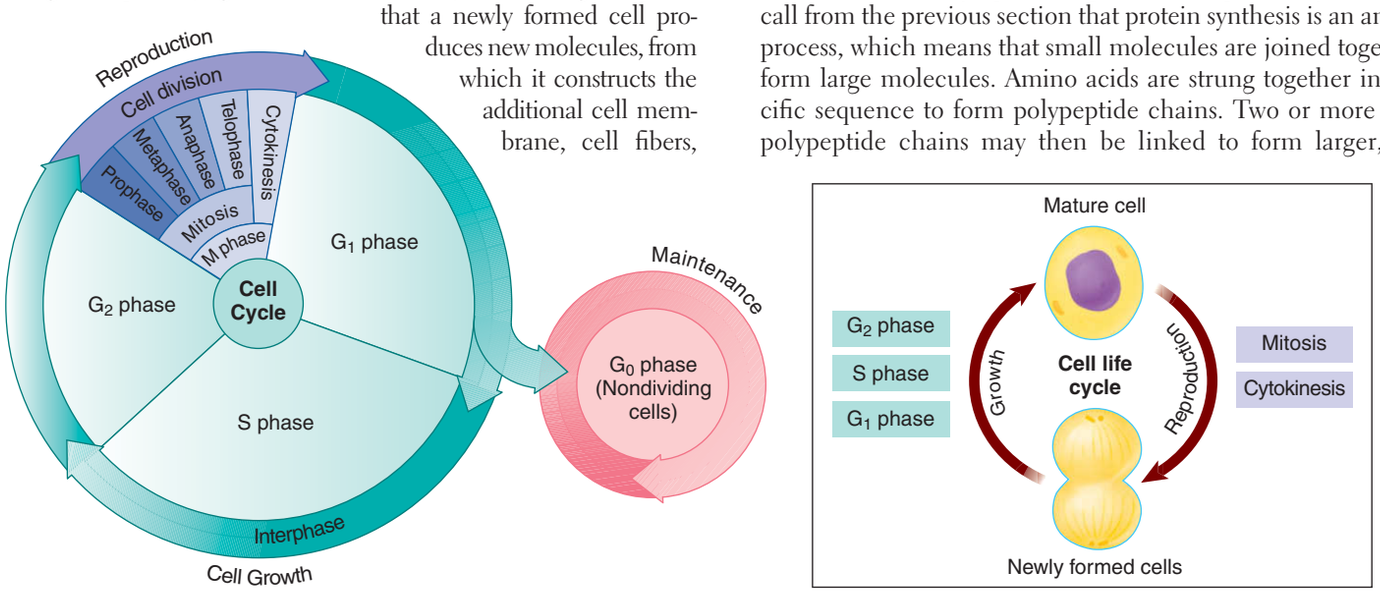


FIGURE 5-7

Life cycle of the cell. The processes of growth and reproduction of successive generations of cells exhibit a cyclic pattern. Newly formed cells grow to maturity by synthesizing new molecules and organelles (*G_1* and *G_2 phases*), including the replication of an extra set of DNA molecules (*S phase*) in anticipation of reproduction. Mature cells reproduce (*M phase*) by first distributing the two identical sets of DNA (produced during the S phase) in the orderly process of mitosis, then by splitting the plasma membrane, cytoplasm, and organelles of the parent cell into two distinct daughter cells (cytokinesis). Daughter cells that do not go on to reproduce are in a maintenance phase (*G_0*).

TABLE 5-3 Summary of the Cell Life Cycle

PHASE OF CELL LIFE CYCLE	DESCRIPTION
Cell Growth	***Interphase***
Protein synthesis	Proteins are manufactured according to the cell's genetic code; functional proteins, the enzymes, direct the synthesis of other molecules in the cells and thus the production of more and larger organelles and plasma membrane; sometimes called the *first growth phase* or *G_1 phase* of interphase
DNA replication	Nucleotides, influenced by newly synthesized enzymes, arrange themselves along the open sides of an "unzippered" DNA molecule, thereby creating two identical daughter DNA molecules; produces two identical sets of the cell's genetic code, which enables the cell to later split into two different cells, each with its own complete set of DNA; sometimes called the *(DNA) synthesis* stage or *S phase* of interphase
Protein synthesis	After DNA is replicated, the cell continues to grow by means of protein synthesis and the resulting synthesis of other molecules and various organelles; this *second growth phase* is also called the *G_2 phase*
Cell Reproduction	***M Phase***
Mitosis or meiosis	The parent cell's replicated set of DNA is divided into two sets and separated by an orderly process into distinct cell nuclei; mitosis is subdivided into at least four phases: *prophase, metaphase, anaphase,* and *telophase*
Cytokinesis	The plasma membrane of the parent cell "pinches in" and eventually separates the cytoplasm and two daughter nuclei into two genetically identical daughter cells

complex protein molecules. In the previous paragraphs, we briefly described how the cell "copies" information from genes and interprets it to form specific polypeptides. Refer again to Table 5-2 to review the process of protein synthesis.

Production of additional proteins means not only that more structural proteins are available to contribute to growth of the cytoplasm but also that more enzymes are available to catalyze the production of other organic compounds. Enzymes produced by protein synthesis are used to make additional carbohydrates, lipids, and nucleic acids—as well as more protein molecules.

Products of cell anabolism during the growth phase of the cell life cycle may be used in the production of additional organelles and plasma membrane. This is a good opportunity to go back to Chapter 3 and review the process by which the cell membrane—and thus membranous organelles and plasma membrane—is made by the ER and Golgi apparatus.

Most of the membranous organelles and plasma membrane increase in size or number (or both) by the membrane-producing processes referred to in Chapter 3. One notable exception is the mitochondrion. Each mitochondrion is capable of replicating itself in a process similar to that used by some one-celled organisms such as bacteria. Mitochondria often replicate themselves during the cell growth phase so that their total number is very large by the time the cell is ready to reproduce. Nonmembranous organelles grow by anabolic processes associated with the centrosome, or microtubule-organizing center, and other cell components, such as ribosomes, that manufacture elements of the cytoskeleton.

DNA Replication

As you may have noticed by now, nucleic acids such as RNA are synthesized directly on the DNA molecule with the help of enzymes. In Chapter 3, we discussed that rRNA is made and formed into ribosome subunits in the nucleolus. In a previous section, we described how mRNA molecules form during transcription by the complementary pairing of RNA bases with DNA bases. Transfer RNA is formed on DNA molecules in a similar fashion and then remains in the cytoplasm to be used over and over. As a cell becomes larger, mechanisms that are just now beginning to be understood trigger the synthesis of a complete copy of the nucleus' set of DNA molecules. Replication of the entire set of DNA molecules, or genome, prepares the cell for reproduction, when one set will go to one daughter cell and the other set to the other daughter cell. The mechanics of DNA replication resemble those of RNA synthesis—as we shall see.

In the first step of DNA replication, the tightly coiled DNA molecules uncoil except for small segments. (Because these remaining tight little coils are denser than the thin, elongated sections, they absorb more stain and appear as chromatin granules under the microscope. The thin, uncoiled sections, in contrast, are invisible because they absorb so little stain.) As the DNA molecule uncoils, its two strands come apart. Then, along each of the two separated strands of nucleotides, a complementary strand forms. Intracellular fluid contains many DNA nucleotides. By the mechanism of obligatory base pairing and with the work of specific enzymes, nucleotides become attached at their correct places along each DNA strand (Figure 5-8). This means that new thymine, that is, from the intracellular fluid, attaches to the "old" adenine in the original DNA strand. Conversely, new adenine attaches to old thymine. Also, new guanine joins old cytosine, and new cytosine joins old guanine.

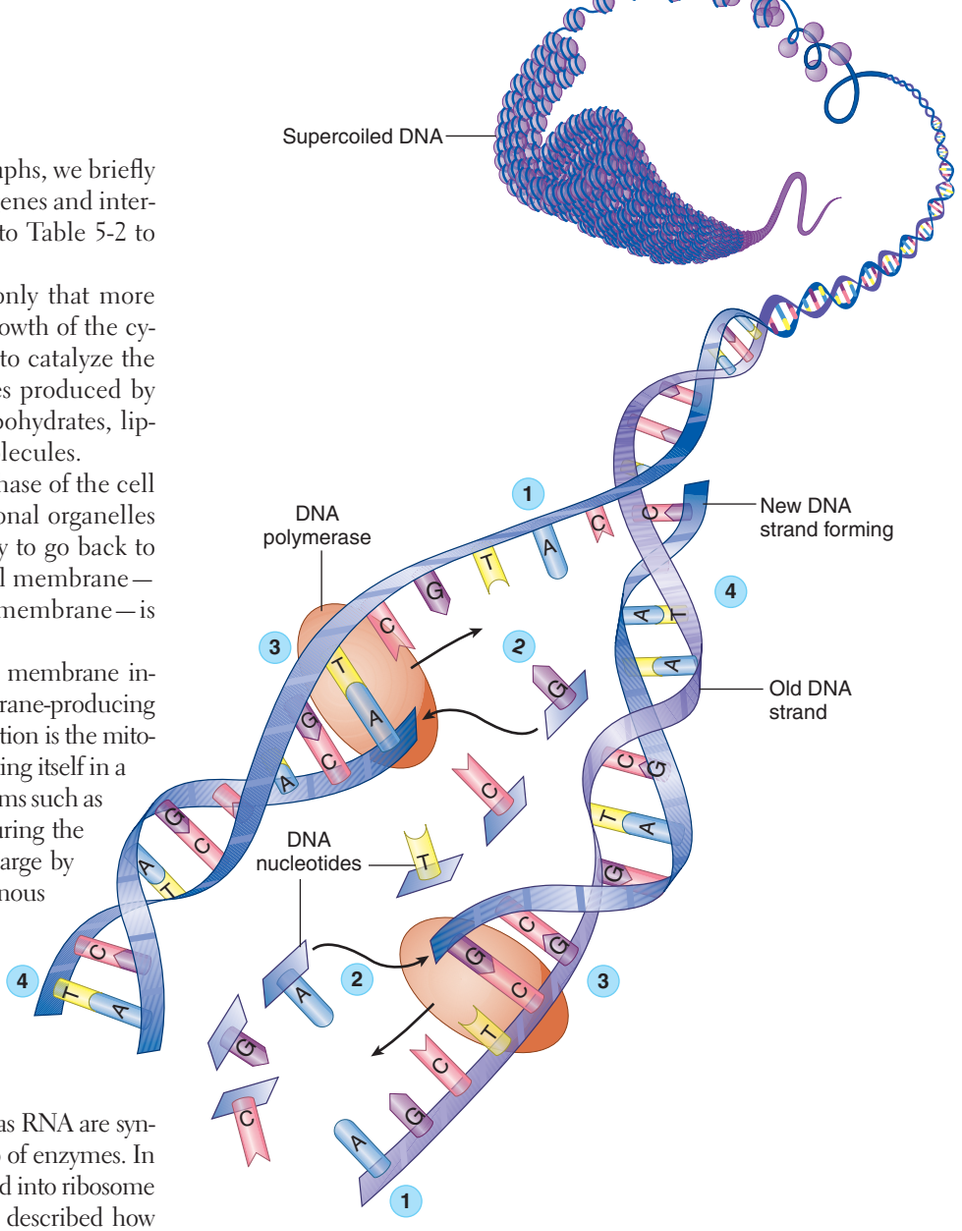


FIGURE 5-8

DNA replication When a DNA molecule makes a copy of itself, it "unzips" to expose its nucleotide bases. Through the mechanism of obligatory base pairing, coordinated by the enzyme DNA polymerase, new DNA nucleotides bind to the exposed bases (in an opposite direction on each strand). This forms a new "other half" to each half of the original molecule. After all the bases have new nucleotides bound to them, two identical DNA molecules will be ready for distribution to the two daughter cells. Numbers refer to steps described in Table 5-4.

Notice in Figure 5-8 that the DNA nucleotides are added in different directions in each of the two strands of the mother DNA molecule. This results in the end of one mother strand not being copied. The loss of useful code is prevented by the presence of **telomeres** (literally, "end roots"), which are strands of "extra" nucleotides that can be lost without affecting the coding part of the chromosome. As telomeres shorten, they eventually disappear unless rebuilt by the enzyme *telomerase*. Telomerase contains a bit of RNA that provides the code for rebuilding the telomere sequence.

TABLE 5-4 Summary of DNA Replication

STEP	DESCRIPTION
1	DNA molecules uncoil and "unzip" to expose their bases
2	Nucleotides already present in the intracellular fluid of the nucleus attach to the exposed bases according to the principle of obligatory base pairing
3	As nucleotides attach to complementary bases along each DNA strand, the enzyme *DNA polymerase* causes them to bind to each other
4	As new nucleotides fill in the spaces left open on each DNA strand, two identical *daughter molecules* are formed; as the parent DNA molecule completely unzips, the two daughter molecules coil to become distinct, but genetically identical, DNA double helices called *chromatids*

These steps are illustrated in Figure 5-8

By the end of this part of the growth phase, each of the two DNA strands of the original DNA molecule has a complete new complementary strand attached to it. Each half of the DNA molecule, or strand, in other words, has duplicated itself to create a whole new DNA molecule. Thus two new chromosomes now replace each original chromosome. However, at this stage (before cell reproduction has actually begun), they are called *chromatids* instead of chromosomes. The two chromatids formed from each original chromosome contain duplicate copies of DNA and, therefore, the same genes as the chromosome from which they were formed. Chromatids are present as attached pairs. Their point of attachment is called the *centromere*. Table 5-4 gives a detailed, step-by-step account of the process of DNA replication.

Because DNA replication is really the synthesis of new DNA, this part of a cell's growth phase is sometimes called the *synthesis phase* or, simply, the *S phase*. The portions of the growth phase before and after the S phase are simply called the *first growth* (G_1) *phase* and the *second growth* (G_2) *phase*. The first and second growth phases are characterized by a great deal of cytoplasm growth caused by a general increase in the anabolism of protein and other substances, as well as the production of new organelles and plasma membrane. The growth phases are also called *gap phases* because they represent a gap between major reproductive events.

CELL REPRODUCTION

Now that we have briefly looked at the growth phase, it is time to turn to the other major phase of the cell life cycle: cell reproduction (sometimes called the *M phase*). Simply put, cells reproduce by splitting themselves into two separate cells. One *parent cell* thus becomes two smaller *daughter cells*. Splitting of the plasma membrane and cytoplasm into two is called **cytokinesis** (meaning "cell movement"). This name is apt because the cell's cytoskeleton moves the plasma membrane and internal structures in a way that pinches it in half, thereby forming two equivalent daughter cells. Of course, each daughter cell must possess all the resources necessary for survival if the cycle of life is to remain unbroken. That means that besides sufficient cytoplasm, including mitochondria and other organelles, each cell must also have a complete set of genetic information (DNA) needed to run a cell properly. This aspect of cell reproduction or *cell division* is accomplished by a process called **mitosis.** During mitosis, the cell organizes replicated DNA into two identical sets and then distributes one complete set to each daughter cell.

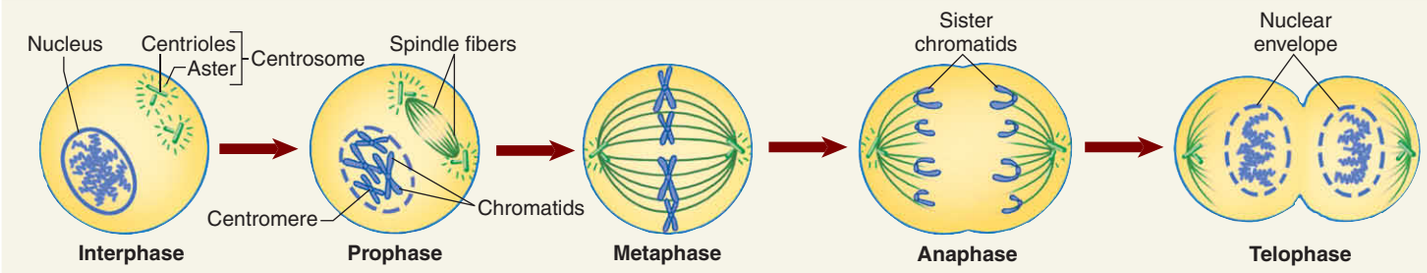
Mitosis

Mitosis, the process of organizing and distributing nuclear DNA during cell division, is a continuous process (Table 5-5) consisting of four distinct phases:

1. Prophase
2. Metaphase
3. Anaphase
4. Telophase

TABLE 5-5 The Major Events of Mitosis

PROPHASE	METAPHASE	ANAPHASE	TELOPHASE
1. Chromosomes shorten and thicken (from coiling of the DNA molecules that compose them); each chromosome consists of two chromatids attached at the centromere	1. Chromosomes align across the equator of the spindle fiber at its centromere	1. Each centromere splits, thereby detaching two chromatids that compose each chromosome from each other, elongating in the process (DNA molecules start uncoiling)	1. Changes occurring during telophase essentially reverse those taking place during prophase; new chromosomes start elongating (DNA molecules start uncoiling)
2. Centrosomes move to opposite poles of the cell; spindle fibers appear and begin to orient between opposing poles		2. Sister chromatids (now called *chromosomes*) move to opposite poles; there are now twice as many chromosomes as there were before mitosis started	2. A nuclear envelope forms again to enclose each new set of chromosomes
3. Nucleoli and the nuclear membrane disappear			3. Spindle fibers disappear



When the cell is not experiencing mitosis—during the growth phase between cell divisions—it is said to be in **interphase** (meaning "between phase"). A cell is not actively reproducing during interphase, but it is actively *preparing for* reproduction. Not just the DNA molecules replicate; the centrosomes replicate as well. The centriole pairs in the parent centrosome split, and each single centriole produces a daughter centriole to produce a new pair of centrioles surrounded by a starlike formation of microtubules called an *aster* radiating outward. Go back to p. 81 and look at Figure 3-16 to review the details of centrosome structure. Additional cytoplasm, membrane, and other cell structures are likewise being constructed in anticipation of cell division.

The cell enters **prophase** when it begins to divide, usually before cytokinesis, or "pinching in half," becomes apparent. During prophase, which literally means "before phase," the nuclear envelope falls apart as the paired chromatids coil up to form dense, compact *chromosomes* (Figure 5-9). By the end of prophase, each chromosome consists of a pair of short, thick bodies joined together at a centromere. At the same time that chromosomes are forming, the replicated centrosomes move away from each other and toward opposite ends, or "poles," of the parent cell. As the centrosomes move apart, a parallel arrangement of microtubules, or *spindle fibers*, is constructed between them. Aster fibers radiating from each centrosome anchor the spindle at each pole of the cell.

The term **metaphase** literally means "position-changing phase." This name is appropriate because during this phase the chromosomes, no longer trapped within a nucleus, are moved by the cytoskeleton into an orderly pattern. The chromosomes are aligned along a plane at the "equator" of the cell about midway between the centriole pairs at opposite poles of the cell (the *equatorial plate*). One chromatid of each chromosome faces one pole of the cell, and its identical sister chromatid faces the opposite pole. Each chromatid then attaches to a spindle fiber.

Anaphase, or the "apart phase," begins as soon as all the chromosomes have aligned along the cell's equator. During this phase of mitosis, the centromere of each chromosome splits to form two chromosomes, each consisting of a single DNA molecule. Each chromosome is pulled toward the nearest pole (that is, toward the nearest centrosome) by a spindle fiber. The effect of this movement is that one set of DNA molecules reaches one end of the cell and another set reaches the other end of the cell—forming two separate, but identical pools of genetic information. By the time a dividing cell has reached anaphase, cytokinesis has usually become apparent. The cell has not completely split yet, but cleavage along the equator may be visible.

Telophase is the "end phase," or "completion phase," of mitosis. It is during this phase that the DNA is returned to its original form and location within the cell. The cell rebuilds the nuclear envelope, and the DNA molecules are trapped within a membranous basket once again. At the same time, the chromosomes elongate back into the chromatin form. Recall that DNA cannot participate in protein synthesis unless at least some of its length is uncoiled. Spindle fibers, which are no longer needed, disappear during telophase. Cytokinesis is usually completed during or just after the telophase portion of mitosis. Each genetically identical daughter cell thus formed is now in interphase. It will grow and develop into a mature cell, perhaps becoming a parent itself.

A series of photographs summarizing the events of mitotic cell division (mitosis and cytokinesis) are shown in Figure 5-10.

| A&P CONNECT |

See an image of how chromosomes unwind during telophase to form specific areas of chromatin called *chromosome territories* in ***Chromosome Territories*** online at ***A&P Connect.***

evolve

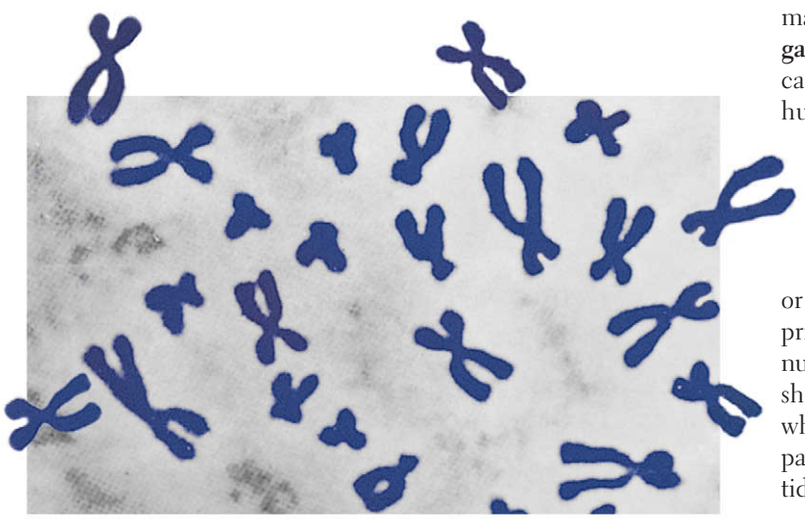


FIGURE 5-9

Chromosomes. Light micrograph showing chromosomes of a normal human cell before cell division is complete (metaphase). Additional detailed views of chromosome structure are found in Chapter 37.

Meiosis

Meiosis is the type of cell division that occurs only in primitive sex cells during the process of becoming mature sex cells. As a result of meiosis, the primitive sex cells (*spermatogonia* in the male and *oogonia* in the female) become mature sex cells called **gametes.** Male gametes are named *spermatozoa* but are usually called *sperm.* Female gametes are named *ova* (singular, *ovum*). In humans, all somatic cells contain 46 chromosomes. This total of 46 chromosomes per cell is known as the **diploid** number of chromosomes. *Diploid* comes from the Greek *diploos*, meaning "two" or "pair." In somatic cells the 46 chromosomes are present in 22 homologous pairs—the remaining 2 being the sex chromosomes XY (male) or XX (female). During meiosis, or *reduction division*, the diploid chromosome number (46) of the primitive spermatogonium or oogonium is reduced to the **haploid** number of 23 found in mature sex cells, or gametes. Figure 5-11 shows that meiotic division occurs in two steps: *meiosis I*, during which the number of chromosomes is halved but the chromatid pairs remain together, and *meiosis II*, during which the chromatids finally split apart.

The end result of fertilization is the fusion of two gametes, each containing the haploid number (23) of chromosomes. Fertilization results in formation of a zygote, which is a diploid cell having 46 chromosomes, 23 chromosomes being contributed by each parent. The zygote is the first cell of the human offspring. It will

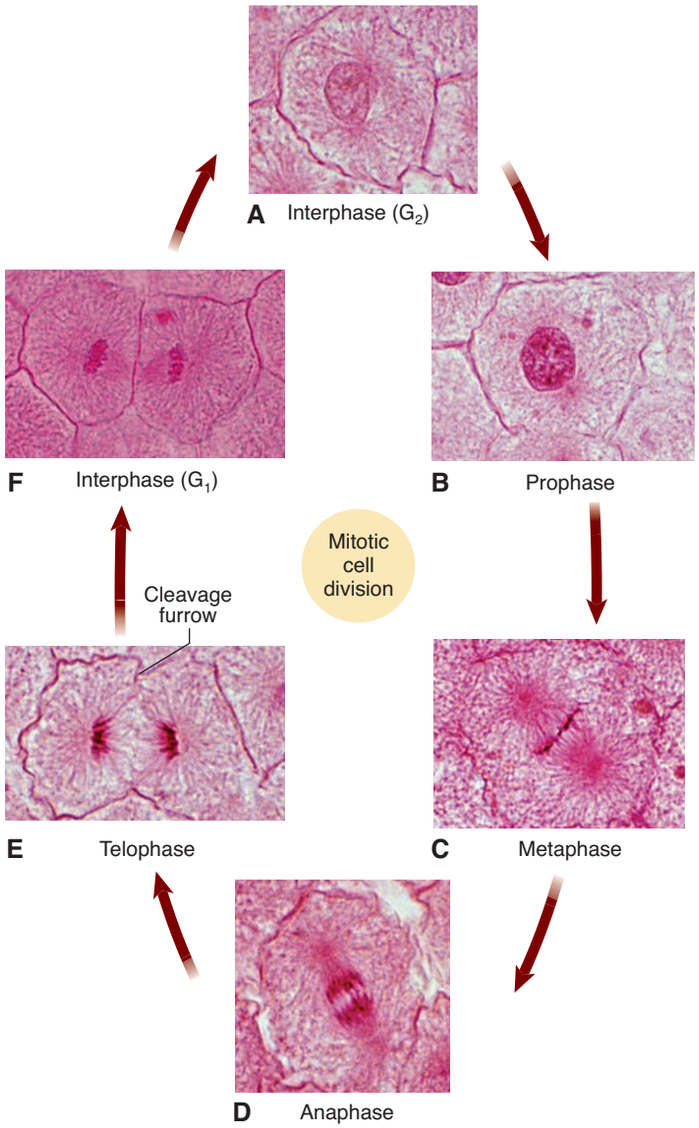


FIGURE 5-10

Mitotic cell division. Series of photomicrographs showing animal cells undergoing a cycle of mitotic cell division. **A,** Interphase—division begins at the end of interphase (G_2), after the cell has already replicated the DNA in its nucleus and increased its cytoplasm sufficiently for division. **B,** Prophase—chromosomes form from the nuclear chromatin material as the nuclear envelope disappears. **C,** Metaphase—chromosomes line up along the cell's equatorial plate, with spindle fibers distinctly visible on either side. **D,** Anaphase—spindle fibers pull each of the two chromatids (now called chromosomes) toward opposite poles of the cell. **E,** Telophase—chromosomes are now at opposite poles, nuclear envelopes begin forming around each group, and the cleavage furrow of cytokinesis becomes apparent. **F,** Interphase—after mitosis and cytokinesis are complete, the two daughter cells begin the first growth (G_1) of interphase. When they are ready, each daughter cell may continue the life cycle by undergoing mitotic division.

then undergo mitotic division to form 2 cells, then 4, and so on until 100 trillion cells are eventually formed.

During development, the new daughter cells will specialize, or **differentiate,** to become specific cell types, which in turn will form specific organs. In mature tissues, some cells may opt out of the cycle and remain in a growth and maintenance phase called the G_0 *phase*. We will have a little more to say about the development and maintenance of different tissue types in Chapter 6. More detailed information about meiosis and the formation of sex cells, fertilization, and development is explored in Chapters 34 through 37.

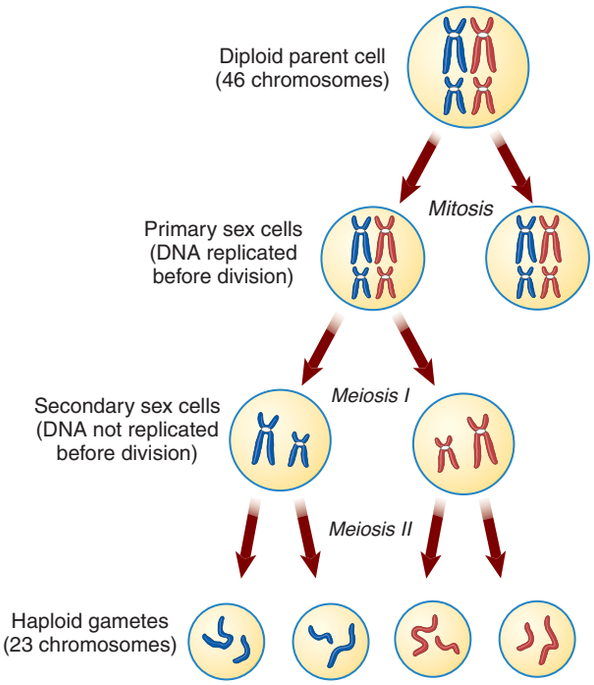


FIGURE 5-11

Meiosis. Meiotic cell division takes place in two steps: meiosis I and meiosis II. Meiosis I is called *reduction division* because the number of chromosomes is reduced by half (from the diploid number to the haploid number). A more detailed diagram of meiosis is presented in Figure 36-1 on p. 1098.

REGULATING THE CELL LIFE CYCLE

Table 5-3 summarizes the main phases of the cell life cycle, including the growth and reproductive phases. You may wonder what mechanisms control when and how a cell moves from one stage to another in its cycle of growth and reproduction. A series of independent experiments by Leland Hartwell, Tim Hunt, and Paul Nurse paved the way for understanding the molecular mechanisms that regulate the cell's life cycle. This achievement won the three scientists a Nobel Prize in 2001. Their experiments revealed the activity of regulatory proteins known as *cyclins* and *cyclin-dependent kinases* (CDKs) and the genes that produce them. The number of CDK enzyme molecules stays about the same throughout the cell's life cycle, but the number of cyclin molecules varies widely. Scientists often compare the CDK molecules with an engine that drives the cell forward through the phases of its life cycle. Cyclins act like a gear box that "shifts" the CDK into "drive" and thus moves the cell into the next phase of the cycle. Discoveries about how these molecules and their genes work have already helped us better understand the mechanisms of cancer and other cellular disorders (Box 5-3).

Box 5-3 | Changes in Cell Growth, Reproduction, and Survival

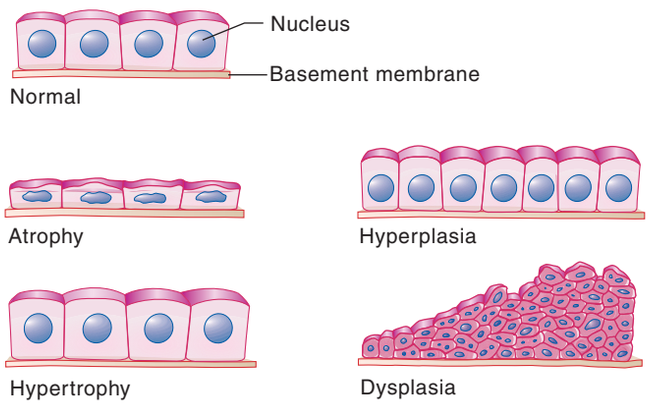
Cells have the ability to adapt to changing conditions. Cells may alter their size, reproductive rate, or other characteristics to adapt to changes in the internal environment. Such adaptations usually allow cells to work more efficiently. However, sometimes cells alter their characteristics abnormally—thereby decreasing their efficiency and threatening the health of the body. Common types of changes in cell growth and reproduction are summarized below.

Cells may respond to changes in function, hormone signals, or the availability of nutrients by increasing or decreasing in size. The term **hypertrophy** (hye-PER-tro-fee) refers to an increase in cell size, and the term **atrophy** (AT-ro-fee) refers to a decrease in cell size. Either type of adaptive change can occur easily in muscle tissue. When a person continually uses muscle cells to pull against heavy resistance, as in weight training, for example, the cells respond by increasing in size. Body builders thus increase the size of their muscles by hypertrophy—increasing the size of muscle cells. Atrophy often occurs in underused muscle cells. For example, when a broken arm is immobilized in a cast for a long period, muscles that move the arm often atrophy. Because the muscles are temporarily out of use, muscle cells decrease in size. Atrophy may also occur in tissues whose nutrient or oxygen supply is diminished. Sometimes cells respond to changes in the internal environment by increasing their rate of reproduction—a process called **hyperplasia** (hye-per-PLAY-zha). The ending *–plasia* comes from a Greek word that means "shape" or "formation"—referring to the formation of new cells. Because *hyper-* means "excessive," *hyperplasia* means excessive cell reproduction. Like hypertrophy, hyperplasia causes an increase in the size of a tissue or organ. However, hyperplasia is an increase in the *number of cells* rather than an increase in the size of each cell. A common example of hyperplasia occurs in the milk-producing glands of the female breast during pregnancy. In response to hormone signals, the glandular cells reproduce rapidly to prepare the breast for milk production and nursing.

If the body loses its ability to control mitosis normally, abnormal hyperplasia may occur. The new mass of cells thus formed is a tumor or **neoplasm** (NEE-o-plazm). Neoplasms may be relatively harmless growths called **benign** (be-NYNE) tumors. If tumor cells can break away and travel through the blood or lymphatic vessels to other parts of the body, the neoplasm is a **malignant tumor,** or cancer. Cells in malignant neoplasms often exhibit a characteristic called **anaplasia** (an-ah-PLAY-zha). Anaplasia is a condition in which cells fail to *differentiate* into a specialized cell type. **Dysplasia** (diss-PLAY-zha) is an abnormal change in shape, size, or organization of cells in a tissue and is often associated with neoplasms.

Part *A* of the Figure summarizes a few of the changes that can occur in cell growth and reproduction.

Cells also die sometimes. In **necrosis** (ne-KROH-sis), cells die because of an injury or pathological condition, often causing nearby cells to die and triggering an immune response called *inflammation,* which removes the debris if possible. Nonpathological cell death, often called **apoptosis** (ap-po-TOH-sis *or* ap-op-TOH-sis), occurs frequently in the cells of your body. Apoptosis is a type of programmed cell death in which organized biochemical steps within the cell lead to fragmentation of the cell and removal of the pieces by phagocytic cells. Apoptosis occurs when cells are no longer needed or when they have certain malfunctions that could lead to cancer or some other potential problem. Apoptosis is the normal process by which our tissues and other groups of cells remodel themselves throughout the life span. Although apoptosis is a normal cell function, it can be abnormally triggered in some conditions.



A, Alterations in cell growth and reproduction. **B,** Apoptosis. *1,* Early in apoptosis, the cell begins making the enzymes needed to break down the cell, but no structural changes yet occur. *2,* As apoptosis proceeds, surface features such as microvilli and cell junctions are lost, and nuclear DNA condenses and is broken into fragments. *3,* The cell then rapidly splits into apoptotic bodies. Notice that the nucleus has also fragmented. *4,* Apoptotic bodies may then be digested by adjacent cells, by extracellular enzymes, or (not shown) by nearby phagocytic cells.

| QUICK CHECK |

4. What are the two major phases of the cell life cycle? During which of these phases does mitosis occur?
5. How does the cytoplasm of a cell grow?
6. What is the difference between mitotic cell division and meiotic cell division?

Cycle of LIFE
Cells

Different types of cells have highly variable life cycles. The active life span of a single cell may vary from a few minutes to years, depending on its function and level of activity. Some cells may remain dormant or inactive for years. Then, when they are "activated" by some biological need and become functional, their life span may be shortened dramatically.

One example involves cells in the immune system that are programmed to produce antibodies against a specific disease. Other examples include the female sex cells, or ova, which are present from birth. They mature throughout the reproductive life span of the individual so that each month at least one cell will become fully developed and provide an opportunity for fertilization to occur.

Structure follows function at every level of organization in the body. Frequently, function decreases with advancing age, and resulting changes occur in cell numbers and their ability to function effectively. As a result, we lose functional capacity in every body organ system. Our muscles may atrophy, the skin will lose its elasticity, and our respiratory, cardiovascular, and skeletal systems will become affected because of cellular changes that accompany aging.

the BIG picture

Cell Growth, Reproduction, and the Whole Body

In previous chapters, we considered the cell as a whole living unit in which many dynamic processes keep an individual cell alive and functioning. Let's take another step back from our mental image of a cell. Picture a huge "society" of trillions of cells—the human body. We now understand more fully how we develop from a single cell to that huge society of cells. We have seen that the growth of cytoplasm, the accurate replication of the genetic code, and cell division are all necessary to the growth and maintenance of the entire human body.

Looking back on the last few chapters, we can now better appreciate that each cell contributes to the survival of its society (the body)—and itself—by specializing in functions that help maintain the relative constancy of the internal environment. When we think of that relative constancy, homeostasis, we should appreciate that it is all accomplished by the action of many individual cells. How are individual cells grouped together? How do they function as groups to promote homeostasis? These questions are answered, at least in part, in Chapter 6.

MECHANISMS of DISEASE

CELL GROWTH AND REPRODUCTION DISORDERS

Disorders Involving DNA and Protein Synthesis

Genetic disorders are pathological conditions caused by mistakes, or **mutations,** in a cell's genetic code. Abnormal genes cause the production of abnormal enzymes or other proteins. Abnormal proteins, in turn, cause abnormalities in cellular function—producing a specific disease. Many diseases are known to be caused by this mechanism, including some diseases such as infections or cancer that also involve other pathological mechanisms. Another example is **sickle cell anemia,** a blood disease caused by the production of abnormal hemoglobin (the protein in red blood cells that carries oxygen). Mistakes in enzyme production can cause a whole group of metabolic disorders called **inborn errors of metabolism.**

Disorders Involving Cell Reproduction

As mentioned earlier in this chapter (see p.126), abnormalities in mitotic division can cause tumors to arise. **Cancers** are tumors that tend to spread, often disrupting vital functions and eventually killing those with the disease. Even noncancerous tumors can cause significant health impairment—or death—depending on their size and location.

Infections

Bacteria and *viruses* can infect cells and thus damage them in ways that produce disease. Bacteria, tiny one-celled organisms, may parasitize cells directly and thus destroy them by stealing the cells' proteins and other substances needed for cell survival. The bacteria may produce toxins that damage cells

or interrupt cell functions. These toxins may also elicit violent reactions of the immune system. Viruses are microscopic particles that contain DNA or RNA. Viruses cause disease by taking over the genetic apparatus of a cell to force a cell to produce viral DNA or RNA and synthesize viral proteins. Thus, viral infections use the cell's resources to produce viral products—or even new viruses. If enough cells are damaged during a bacterial or viral infection to disrupt vital functions, death may result (Figure 5-12).

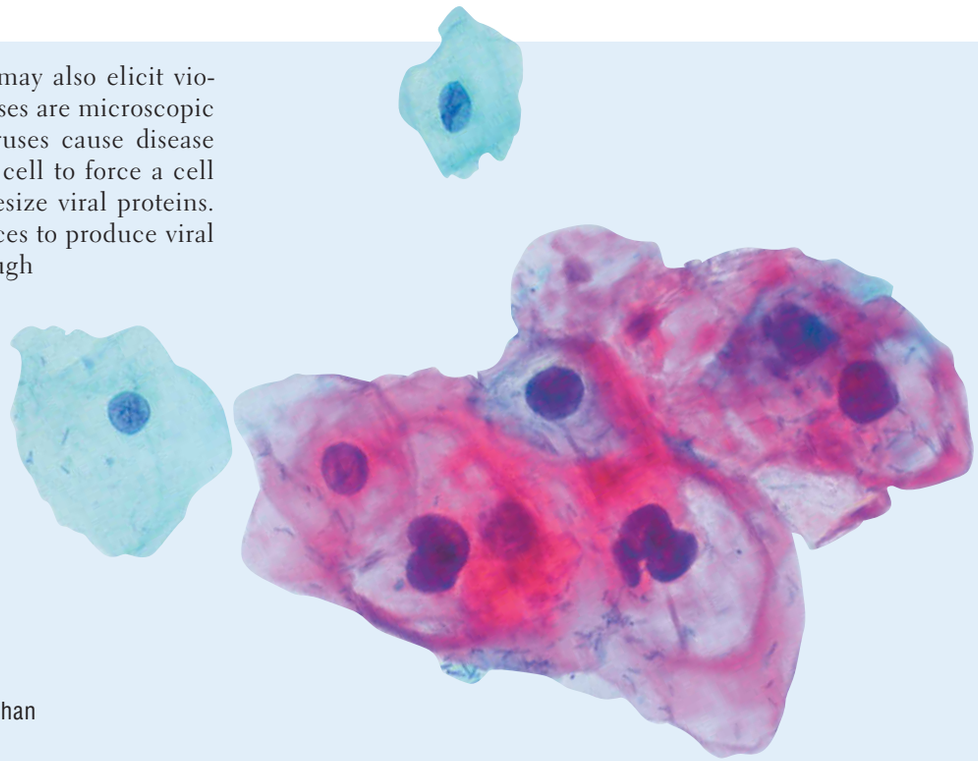


FIGURE 5-12

Viral infection. The pink cells have been infected by human papilloma virus (HPV) and show abnormal structure that is quite different than normal cells (blue).

LANGUAGE OF SCIENCE *(continued from p. 113)*

intron
(IN-trahn)
[*intra-* **within**, *-on* **unit**]

meiosis
(my-OH-sis)
[*meiosis* **becoming smaller**]

metaphase
(MET-ah-fayz)
[*meta-* **change**, *-phase* **stage**]

mitosis
(my-TOH-sis)
[*mitos-* **thread**, *-osis* **condition**]

obligatory base pairing
(oh-BLIG-ah-tor-ee base PAIR-ing)

polyribosome
(PAHL-ee-RYE-bo-sohm)
[*poly-* **many**, *-som-* **body**]

prophase
(PRO-fayz)
[*pro-* **first**, *-phase* **stage**]

proteome
(PRO-tee-ome)
[*prote-* **protein**, *-ome* **body (whole set)**]

RNA interference (RNAi)

spliceosome
(SPLISE-oh-sohm)
[*splice-* **cut rope and join remaining ends**, *-som-***body**]

telomere
(TEL-oh-meer)
[*telo-* **end**, *-mer-* **root**]

telophase
(TEL-oh-fayz)
[*telo-* **end**, *-phase* **stage**]

transcription
(trans-KRIP-shun)
[*trans-* **across**, *-script-* **write**, *-tion* **process**]

translation
(trans-LAY-shun)
[*translat-* **a bringing over**, *-tion* **process**]

LANGUAGE OF MEDICINE

anaplasia
(an-ah-PLAY-zha)
[*ana-* **without**, *-plasia* **shape**]

atrophy
(AT-ro-fee)
[*a-* **without**, *-trophy* **nourishment**]

benign
(be-NYNE)
[*benign* **kind**]

cancer
(KAN-ser)
[*cancer* **malignant tumor**]

dysplasia
(diss-PLAY-zha)
[*dys-* **disordered**, *-plasia* **substance**]

hyperplasia
(hye-per-PLAY-zha)
[*hyper-* **excessive**, *-plasia* **shape**]

hypertrophy
(hye-PER-tro-fee)
[*hyper-* **excessive**, *-troph-* **nourishment**, *-y* **state**]

inborn errors of metabolism

malignant tumor
(mah-LIG-nant TOO-mer)
[*malign* **bad**, *-ant* **state**, *tumor* **swelling**]

mutation
(myoo-TAY-shun)
[*mutat-* **change**, *-tion* **state**]

necrosis
(ne-KROH-sis)
[*necro-* **death**, *-osis* **condition**]

neoplasm
(NEE-o-plazm)
[*neo-* **new**, *-plasm* **tissue or substance**]

sickle cell anemia
(SIK-ul sell ah-NEE-mee-ah)
[*sickle* **crescent**, *cell* **storeroom**, *an* **without**, *-emia* **blood condition**]

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

GROWTH AND REPRODUCTION OF CELLS

A. Cell growth and reproduction of cells are the most fundamental of all living functions and together constitute the cell life cycle
   1. Cell growth—depends on using genetic information in DNA to make the structural and functional proteins needed for cell survival
   2. Cell reproduction—ensures that genetic information is passed from one generation to the next

PROTEIN SYNTHESIS

A. Protein synthesis is a central anabolic pathway in cells (Table 5-2)
B. Deoxyribonucleic acid (DNA)
   1. A double-helix polymer (composed of nucleotides) that functions to transfer information, encoded in genes, to direct the synthesis of proteins (Figure 5-1)
   2. Gene—a segment of a DNA molecule that consists of approximately 1000 pairs of nucleotides and contains the code for synthesizing one RNA molecule, which then may be translated into one polypeptide (Figure 5-2)
C. Ribonucleic acid (RNA) (Table 5-1)
   1. Coding RNA—mRNA, which is a transcript of a code for one polypeptide
   2. Noncoding RNA—rRNA and tRNA, which are each copies of a DNA gene but regulate processes rather than code for a polypeptide
D. Transcription—mRNA forms along a segment of one strand of DNA (Figure 5-3)
E. Editing the transcript (Figure 5-4)
   1. Noncoding introns are removed and the remaining exons are spliced together to form the final, edited version of the mRNA copy of the DNA segment
   2. Spliceosomes are ribosome-sized structures in the nucleus that splice mRNA transcripts (Box 5-1)
F. Translation (Figure 5-5)
   1. After leaving the nucleus and being edited, mRNA associates with a ribosome in the cytoplasm
   2. tRNA molecules bring specific amino acids to the mRNA at the ribosome; the type of amino acid is determined by the fit of a specific tRNA's anticodon with mRNA's codon (Figure 5-6)
   3. As amino acids are brought into place, peptide bonds join them—eventually producing an entire polypeptide chain
   4. Translation of genes can be inhibited by RNA interference (RNAi), which protects the cell against viral infection (Box 5-2)
G. Processing—chaperone molecules and other enzymes in the cytosol, ER, and Golgi apparatus help polypeptides fold and then possibly combine into larger protein molecules or hybrid molecules
H. Proteome
   a. All the proteins synthesized by a cell make up the cell's proteome
   b. All the proteins synthesized in the whole body is called the *human proteome*

CELL GROWTH

A. Newly formed cells produce a variety of molecules and other structures necessary for growth by using the information contained in the genes of DNA molecules; this stage is known as *interphase* (Figure 5-7)
B. Production of cytoplasm
   1. More cell material is made, a largely anabolic process
   2. Growth and/or replication of organelles and plasma membrane
   3. Replication of centrosomes and DNA in anticipation of cell division
C. DNA replication (Table 5-4)
   1. Replication of the genome prepares the cell for reproduction; the mechanics are similar to RNA synthesis
   2. DNA base pairing (Figure 5-8)
      a. The DNA strand uncoils and the strands come apart
      b. Along each separate strand, a complementary strand forms
         (1) Because the strands are rebuilt in opposite directions, one strand is not completely rebuilt
         (2) Telomeres are noncoding, protective segments of DNA at the ends of a chromosome; they are used up during DNA replication to prevent loss of needed DNA code; telomeres can be rebuilt by the enzyme telomerase
      c. The two new strands are called *chromatids* instead of chromosomes
      d. Chromatids are attached pairs; the point of attachment is called the centromere
D. The growth phase of the cell life cycle can be subdivided into the first growth phase (G_1), the [DNA] synthesis phase (S), and the second growth phase (G_2)

CELL REPRODUCTION

A. Cells reproduce by splitting themselves into two smaller daughter cells (Table 5-5)
B. Mitotic cell division—the process of organizing and distributing nuclear DNA during cell division has four distinct phases (Figure 5-10)
   1. Prophase—"before phase"
      a. After the cell has prepared for reproduction during interphase, the nuclear envelope falls apart as the chromatids coil up to form chromosomes that are joined at the centromere (Figure 5-9)
      b. As chromosomes form, centrosomes (centrioles/aster) move away from each other toward the poles of the

parent cell and spindle fibers are constructed between them
2. Metaphase—"position-changing phase"
   a. Chromosomes move so that one chromatid of each chromosome faces its respective pole
   b. Each chromatid attaches to a spindle fiber
3. Anaphase—"apart phase"
   a. The centromere of each chromosome splits to form two chromosomes, each consisting of a single DNA molecule
   b. Each chromosome is pulled toward the nearest pole to form two separate, but identical, pools of genetic information
4. Telophase—"end phase"
   a. DNA returns to its original form and location within the cell
   b. After completion of telophase, each daughter cell begins interphase to develop into a mature cell

C. Meiosis (Figure 5-11; see also Figure 36-1)

REGULATING THE CELL LIFE CYCLE

A. Cyclin-dependent kinases (CDKs) are activating enzymes that drive the cell through the phases of its life cycle
B. Cyclins are regulatory proteins that control the CDKs and "shift" them to start the next phase

CYCLE OF LIFE: CELLS

A. Different types of cells have different life cycles
B. Advancing age creates changes in cell numbers and in their ability to function effectively
   1. Examples of decreased functional ability include muscle atrophy, loss of elasticity of the skin, and changes in the cardiovascular, respiratory, and skeletal systems

THE BIG PICTURE: CELL PHYSIOLOGY AND THE WHOLE BODY

A. Most cell processes are occurring at the same time in all of the cells throughout the body
B. The processes of normal cell function result from the coordination dictated by the genetic code

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Describe the size and shape of a DNA molecule.
2. Where is DNA located?
3. Briefly outline the steps of protein synthesis.
4. As a cell grows, how is additional cell material added?
5. What are the steps involved in DNA replication and when does it occur?
6. Define mitosis.
7. Briefly describe the four distinct phases of mitosis.
8. Define meiosis and discuss its four distinct stages.
9. When does the reduction of chromosomes from the diploid to the haploid number take place?
10. Give examples of normal and abnormal hyperplasia.

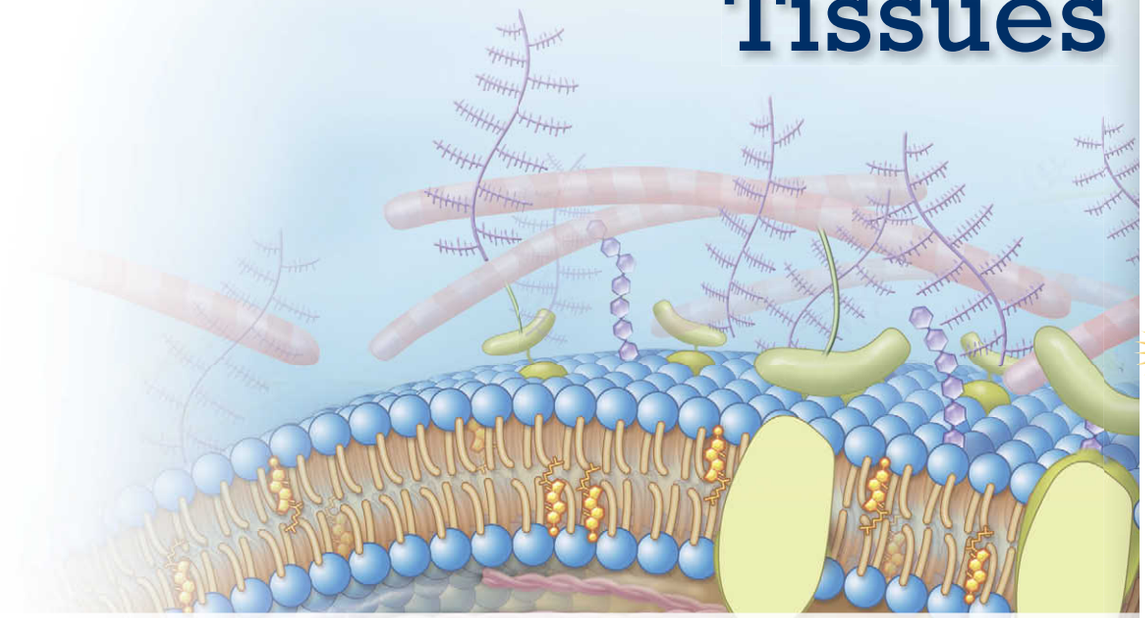
CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Certain antibiotics can damage ribosomes in normal human body cells. People taking these antibiotics need to be carefully monitored. Summarize the result of fewer ribosomes on the process of transcription and translation.
2. DNA is often called the "blueprint of life." However, DNA is composed of only four nitrogen bases as part of its nucleotide structure. Explain how these four nitrogen bases can influence the genetic makeup of an individual.
3. Watson called DNA "the most golden of all molecules" primarily because of its role in protein synthesis. How would you describe the importance of the process of protein synthesis in the functioning of a cell?
4. A cast is frequently used to immobilize a broken bone. When the cast is removed, the muscles on that limb are usually smaller and weaker than the muscles on the other limb. How would you explain the difference between the two limbs?
5. Compare and contrast hypertrophy and hyperplasia.
6. The nucleus has been called the "brain" or the "control center" of the cell. By applying what you have learned, describe how the nucleus can control growth, development, and day-to-day functions of a cell.

6 Tissues



CHAPTER OUTLINE

HINT *Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.*

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Extracellular Matrix, 134

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The Big Picture: Tissues, Membranes, and the Whole Body, 158

Mechanisms of Disease, 158

Case Study, 162

LANGUAGE OF SCIENCE

HINT *Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.*

absorption
(ab-SORP-shun)
[*absorp-* **swallow,** *-tion* **process**]

adipocyte
(AD-i-poh-syte)
[*adipo-* **fat,** *-cyte* **cell**]

adipose tissue
(AD-i-pohs)
[*adipo-* **fat,** *-ose* **full of,** *tissu-* **fabric**]

alveolar
(al-VEE-oh-lar)
[*alveo-* **hollow,** *-ola-* **little,** *-ar* **relating to**]

areolar
(ah-REE-oh-lar)
[*are-* **open space,** *-ola-* **little,** *-ar* **relating to**]

avascular
(ah-VAS-kyoo-lar)
[*a-* **without,** *-vas-* **vessel,** *-ula-* **little,** *-ar* **relating to**]

axon
(AK-son)
[*axon* **axle**]

basement membrane (BM)
[*base-* **base,** *-ment* **thing,** *membran-* **thin skin**]

body composition

canaliculus
(kan-ah-LIK-yoo-lus)
[*canal-* **channel,** *-iculi* **little**]
pl., canaliculi

cancellous bone tissue
(KAN-seh-lus)
[*cancel-* **lattice,** *-ous* **characterized by,** *tissu-* **fabric**]

cardiac muscle tissue
(KAR-dee-ak)
[*cardia-* **heart,** *-ac* **relating to,** *mus-* **mouse,** *-cle* **small,** *tissu-* **fabric**]

continued on p. 160

A tissue is a group of similar cells that perform a common function. Tissues can be thought of as the fabric of the body, which is "sewn together" to form the organs of the body and to hold all the organs together as a whole.

To understand the fabric of the body, we begin with an overview of the general organization and development of tissues. We then outline the chief characteristics of the various tissue types that you will encounter later in your study of human anatomy and physiology.

INTRODUCTION TO TISSUES

Each tissue specializes in performing at least one unique function that helps maintain homeostasis, ensuring the survival of the whole body. The arrangement of cells in one tissue may form a thin sheet only one cell deep, whereas the cells of another tissue may form huge masses containing millions of cells. Regardless of the size, shape, or arrangement of cells in a tissue, they all are surrounded by or embedded in a complex extracellular material that often is called simply **matrix.**

The four major types of human tissue that were introduced in Chapter 1 are described in more detail in this chapter. An understanding of the major tissue types will help you understand the next higher levels of organization in the body—organs and organ systems. Eventually, your knowledge of **histology** (the biology of tissues) will give you a better appreciation for the nature of the whole body.

| A&P CONNECT |

This brief introduction to histology involves many images made with microscopes of various types. Refer to ***Tools of Microscopic Anatomy*** online at ***A&P Connect*** for an overview of the types of microscopy used in this chapter.

evolve

PRINCIPAL TYPES OF TISSUE

Although a number of subtypes are present in the body, all tissues can be classified by their structure and function into four principal types:

1. **Epithelial tissue** covers and protects the body surface, lines body cavities, specializes in moving substances into and out of the body or particular organs (secretion, excretion, and absorption), and forms many glands. The cells in epithelial tissue are usually very close together, with very little extracellular matrix.
2. **Connective tissue** functions to support the body and its parts, connect and hold them together, transport substances through the body, and protect it from foreign invaders. The cells in connective tissue are often relatively far apart and separated by large quantities of matrix.
3. **Muscle tissue** produces movement; it moves the body and its parts. Muscle cells are adapted for contractility and produce movement by shortening or lengthening the contractile units found in cytoplasm. Muscle tissue also produces most of the heat of the body.
4. **Nervous tissue** may be the most complex tissue in the body. It specializes in communication between the various parts of the body and in integration of their activities. This tissue's major function is the generation of complex messages that coordinate the body functions.

The major tissue types are also summarized in Table 6-1.

The four major tissues of the body appear early in the embryonic period of development. Within the first 2 weeks after conception, cells of the offspring move and regroup in an orderly way into three **primary germ layers** called **endoderm, mesoderm,** and **ectoderm.** During this process the cells in each germ layer become increasingly more differentiated to form specific tissues—a process called **histogenesis** (Box 6-1). Remodeling themselves by a combination of new growth, differentiation, and apoptosis, these early layers eventually give rise to the various organs of the body.

| A&P CONNECT |

Embryonic development is discussed more thoroughly in Chapter 36. For now, take a look at a diagram illustrating the concept of primary germ layers in ***Embryonic Development of Tissues*** online at ***A&P Connect.***

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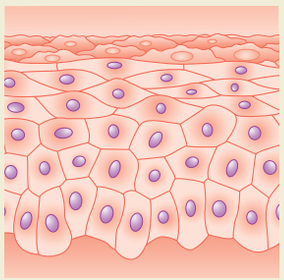
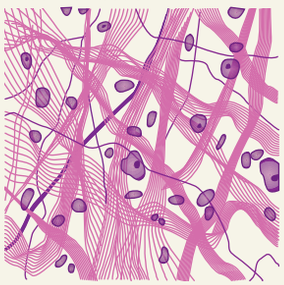
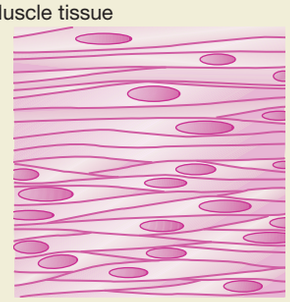
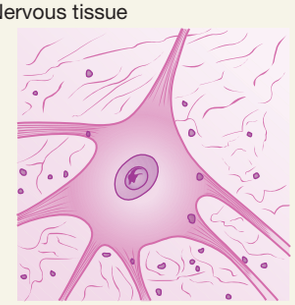
Box 6-1 | Stem Cells

During embryonic development, new kinds of cells can be formed from a special kind of undifferentiated cell called a **stem cell.**

Embryonic stem cells have the potential to reproduce many different kinds of daughter cells, including more stem cells—thus populating the body with all the different cells and tissues needed for body function. Sometimes controversial research is now under way to learn the secrets of embryonic stems cells and develop therapies in which embryonic stem cells might be used to repair or replace damaged tissue in adults.

Adult stem cells are undifferentiated cells found scattered within a differentiated, mature tissue. Many different tissues contain adult stem cells—we may soon find that all adult tissues have some stem cells. Adult stem cells can usually produce any of the specialized cell types within its particular tissue. However, recent research shows that some adult stem cells can be coaxed into producing a variety of different types of cells. For example, blood cell–producing stem cells from bone marrow have been used to help repair damaged muscle tissue in laboratory animals. Already, therapies for treating degenerative diseases of muscles, the heart, and the brain—even baldness—are being proposed by medical scientists.

TABLE 6-1 Major Tissues of the Body

TISSUE TYPE	STRUCTURE	FUNCTION	EXAMPLES IN THE BODY
Epithelial tissue 	One or more layers of densely arranged cells with very little extracellular matrix May form either sheets or glands	Covers and protects the body surface Lines body cavities Transport of substances (absorption, secretion, excretion) Glandular activity	Outer layer of skin Lining of the respiratory, digestive, urinary, reproductive tracts Glands of the body
Connective tissue 	Sparsely arranged cells surrounded by a large proportion of extracellular matrix often containing structural fibers (and sometimes mineral crystals)	Supports body structures Transports substances throughout the body	Bones Joint cartilage Tendons and ligaments Blood Fat
Muscle tissue 	Long fiberlike cells, sometimes branched, capable of pulling loads; extracellular fibers sometimes hold muscle fiber together	Produces body movements Produces movements of organs such as the stomach, heart Produces heat	Heart muscle Muscles of the head/neck, arms, legs, trunk Muscles in the walls of hollow organs such as the stomach, intestines
Nervous tissue 	Mixture of many cell types, including several types of neurons (conducting cells) and neuroglia (support cells)	Communication between body parts Integration/regulation of body functions	Tissue of brain and spinal cord Nerves of the body Sensory organs of the body

EXTRACELLULAR MATRIX

Tissues differ in the amount and kind of material between the cells—the **extracellular matrix (ECM).** Figure 6-1 hints at the complex nature of the ECM. The particular makeup of the extracellular matrix in bone and cartilage, for example, contributes to the strength and resiliency of the body. Some tissues have very little ECM. Other tissues are almost entirely extracellular matrix—with only a few cells present. Some types of ECM contain large numbers of structural protein fibers that make them flexible or elastic, some contain many mineral crystals that make them rigid, and others are very fluid.

It is only recently that scientists have discovered the complexities of the ECM and its important role in human biology. Besides water, the ECM is made up mostly of proteins and **proteoglycans** (Table 6-2).

Proteins in the extracellular matrix include various types of structural protein fibers such as *collagen* and *elastin*, both of which are discussed frequently throughout this book. The ECM also contains many *glycoproteins*, which are mainly protein molecules with attached carbohydrate subunits. For example, *fibronectin* and *laminin* both help connect collagen and proteoglycans to cells by attaching to *integrin* molecules embedded in the plasma membrane of cells (see Figure 6-1). This arrangement thus unites the cells and their surroundings into an integral structure. It also provides a communication mechanism between the ECM and the cell that allows coordination of cell and tissue development, as well as guidance of cell movement and shape changes.

Proteoglycans are hybrid molecules made up mostly of carbohydrates attached to a protein backbone, as you can see in Figure 6-1, B. Many of the sugars attached to the protein backbone of a proteoglycan molecule are *N-acetylglucosamine* (NAG). Examples of proteoglycans are *chondroitin sulfate*, *heparin*, and *hyaluronate* (see Table 6-2).

In some tissues, such as bone, there may also be calcium-containing mineral crystals that make the ECM rigid. Considering the makeup of ECM, it's no wonder that many dietary supplements that claim to improve the health of bones and joints include calcium, glucosamine, and/or chondroitin sulfate—all are important components of the ECM of cartilage and bone tissues.

In some tissues, it is the ECM that holds the tissue in a single mass. For example, in skeletal muscles, it is mostly a network of structural protein fibers in the ECM that holds skeletal muscle tissue together. In such cases, components of the ECM bind to the integrins in the outer membranes of the cells, and the integrins bind to components of the internal cytoskeleton.

In other tissues, it is primarily the intercellular junctions, such as the desmosomes and tight junctions described in a previous

FIGURE 6-1

Extracellular matrix (ECM). A, The extracellular matrix is made up of water, proteins/glycoproteins, and proteoglycans that often form large bundles or complexes that bind together and to the cells of the tissue. Although the makeup of ECM varies from tissue to tissue, it usually includes some connections to integrins in the plasma membranes, thereby allowing for structural integrity, as well as communication and coordination within the tissue. **B,** A detailed view of a proteoglycan complex shows many proteoglycans, each with a protein backbone and attached carbohydrate subunits—all held together by a polysaccharide chain. **C,** Detailed view of a collagen bundle showing the individual collagen fibers within it.

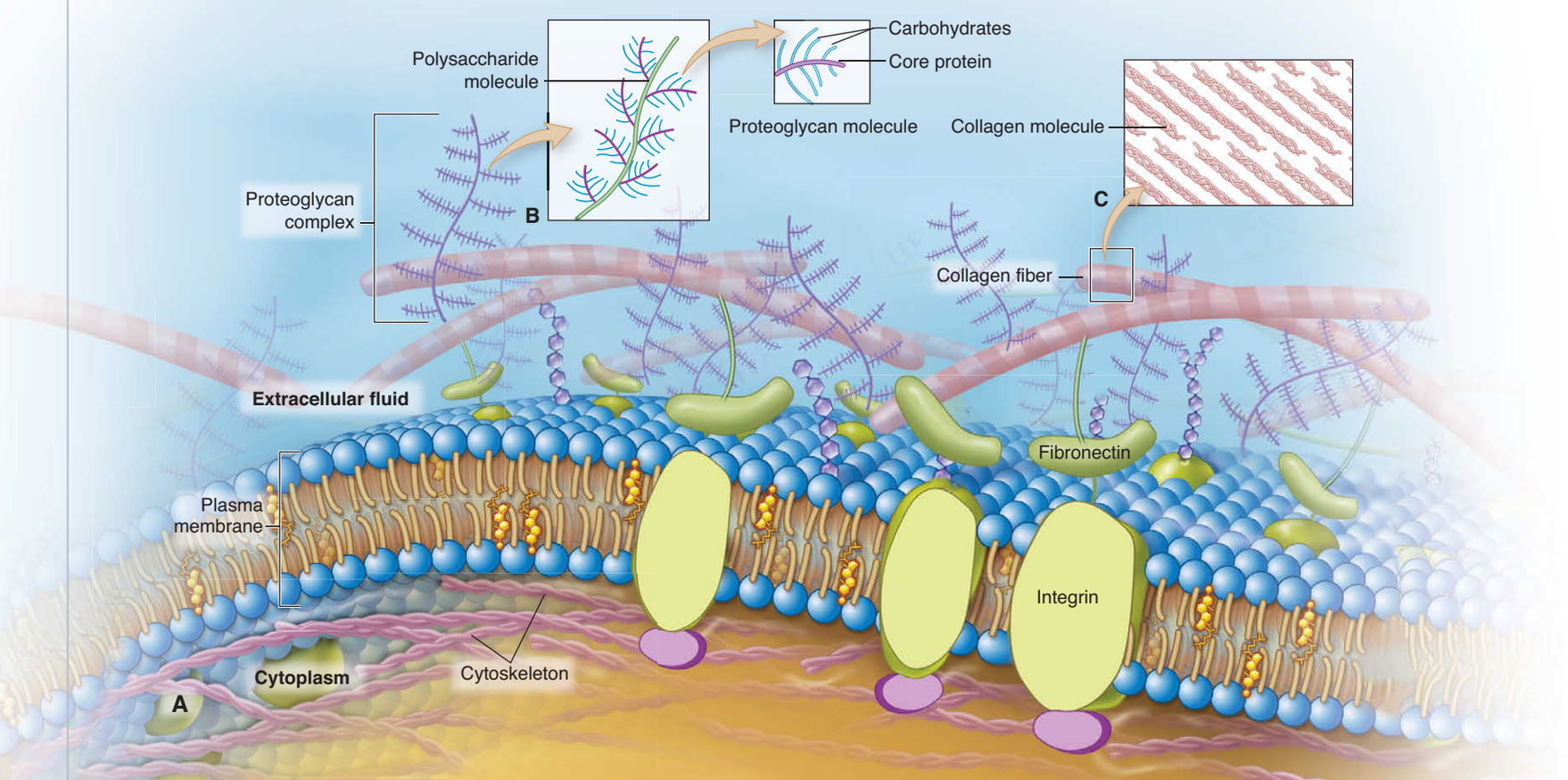


TABLE 6-2 Components of the Extracellular Matrix (ECM)*

COMPONENT	EXAMPLE	DESCRIPTION	FUNCTION	EXAMPLE OF LOCATION
Water		Water molecules along with a small number of ions (mostly Na^+ and Cl^-)	Solvent for dissolved ECM components; provides fluidity of ECM	All tissues of the body
Proteins and glycoproteins	Collagen	Strong, flexible structural protein fiber	Provides flexible strength to tissues	Tendons, ligaments, bones, cartilage, many tissues
	Elastin	Flexible, elastic structural protein fiber	Allows flexibility and elastic recoil of tissues	Skin, cartilage of ear, walls of arteries
	Fibronectin	Rodlike glycoprotein	Binds ECM to cells; communicates with cells through integrins	Many tissues of the body, for example, connective tissues
	Laminin	Glycoproteins arranged as a three-pronged fork	Binds ECM components together and to cells; communicates with cells through integrins	In basal lamina (basement membrane) of epithelial tissues
Proteoglycans	Various types	Protein backbone with attached chains of various polysaccharides:		
		Chondroitin sulfate	Shock absorber	Cartilage, bone, heart valves
		Heparin	Reduces blood clotting	Lining of some arteries
		Hyaluronate	Thickens fluid; lubricates	Loose fibrous connective tissue, joint fluids

*Not all components are present in all ECM; examples of only some of the many major ECM components are provided.

chapter (see Chapter 3, pp. 83–84), that hold groups of cells together to form tissues found in sheets or other continuous masses of cells. The tissue that forms the outer layer of skin is held together this way. In some tissues, the ECM does not bind to tissue cells. For example, the fluid nature of the blood's matrix (plasma) does not hold blood tissue in a solid mass at all.

| QUICK CHECK |

1. Name the four basic tissue types and give the major function of each.
2. What is the ECM? What is it made of?
3. What is a primary germ layer?

EPITHELIAL TISSUE

Types and Locations of Epithelial Tissue

Epithelial tissue, or **epithelium,** often is subdivided into two types: (1) **membranous** (covering or lining) epithelium and (2) **glandular** epithelium. Membranous epithelium covers the body and some of its parts and lines the serous cavities (pleural, pericardial, and peritoneal), the blood and lymphatic vessels, and the respiratory, digestive, and genitourinary tracts. Glandular epithelium is grouped in solid cords or hollow follicles that form the secretory units of endocrine and exocrine glands.

Functions of Epithelial Tissue

Epithelial tissues have a widespread distribution throughout the body and serve several important functions:

Protection. Generalized protection is the most important function of membranous epithelium. It is the relatively tough and impermeable epithelial covering of the skin that protects the body from mechanical and chemical injury and also from invading bacteria and other disease-causing microorganisms.

Sensory functions. Epithelial structures adapted for sensory functions are found in the skin, nose, eye, and ear.

Secretion. Glandular epithelium is adapted for secretory activity. Secretory products include hormones, mucus, digestive juices, and sweat.

Absorption. The lining epithelium of the gut and respiratory tract allows for the absorption of nutrients from the gut and the exchange of respiratory gases between air in the lungs and the blood.

Excretion. The unique epithelial lining of kidney tubules makes the excretion and concentration of excretory products in the urine possible.

Generalizations About Epithelial Tissue

Most epithelial tissues are characterized by extremely limited amounts of intercellular, or matrix, material. This explains their characteristic appearance, when viewed under a light microscope, of a continuous sheet of cells packed tightly together. With the electron microscope, however, narrow spaces—about 20 nanometers (one millionth of an inch) wide—can be seen around the cells. These spaces, like other intercellular spaces, contain **interstitial fluid (IF).**

Epithelial tissues generally renew themselves throughout life. The presence of stem cells in most epithelial tissues allows epithelium to continuously produce new cells of various types.

Sheets of epithelial cells compose the surface layer of skin and mucous and serous membranes. The epithelial tissue attaches to an underlying layer of connective tissue by means of a thin noncellular layer of adhesive, permeable material called the **basement membrane (BM)** (Figure 6-2). Both epithelial and

connective tissue cells synthesize the basement membrane, which is a highly complex structure made up partly of glycoprotein material secreted by the epithelial components and a fine mesh of fibers produced by the connective tissue cells. Histologists refer to the glycoprotein material secreted by epithelial cells as the *basal lamina* and to the connective tissue fibers as the *fibroreticular lamina*. The union of basal and fibroreticular lamina forms the basement membrane. *Integrins* embedded in each plasma membrane help bind the cytoskeletons of the epithelial cells to the fibers of the basement membrane so that a strong connection forms between them.

Epithelial tissues contain no blood vessels. As a result, epithelium is said to be **avascular** (*a*, "without"; *vascular*, "vessels"). Hence oxygen and nutrients must diffuse from capillaries in the underlying connective tissue through the permeable basement membrane to reach living epithelial cells.

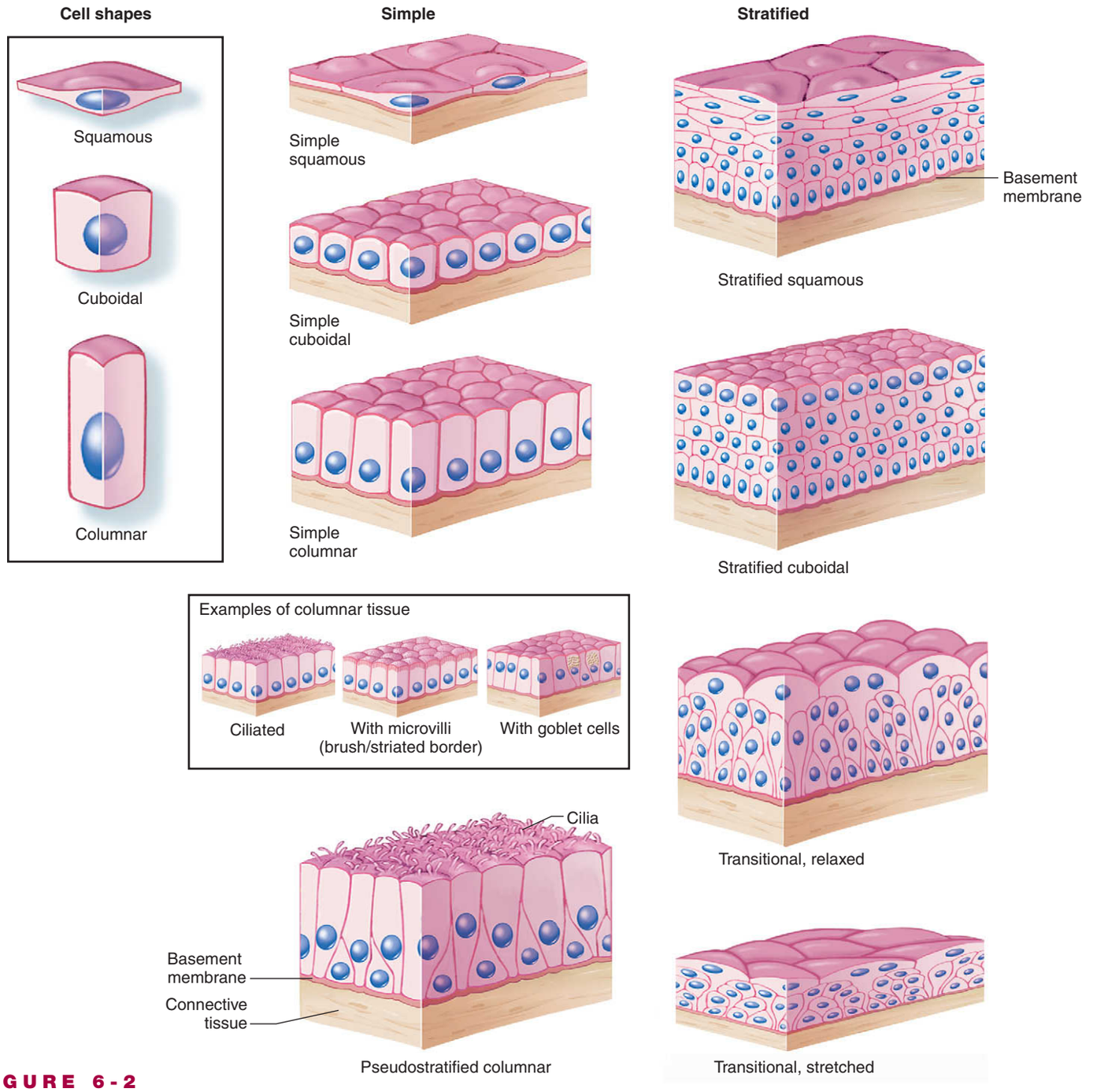
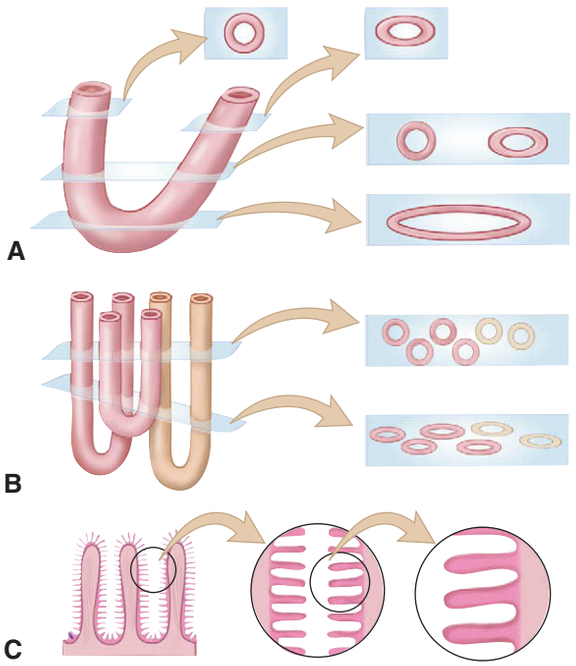


FIGURE 6-2

Classification of epithelial tissues. The tissues are classified according to the shape and arrangement of cells. The color scheme of these drawings is based on a common staining technique used by histologists called *hematoxylin and eosin (H&E)* staining. H&E staining usually renders the cytoplasm pink and the chromatin inside the nucleus a purplish color. The cellular membranes, including the plasma membrane and nuclear envelope, do not usually pick up any stain and thus may be transparent. (See Box 6-2 for information on cross sections of membranous tissues.)

Box 6-2 | Imagining Cross Sections

When you look at photomicrographs of epithelial tissues or other structures that are tubelike, saclike, or folded into complex shapes, it is sometimes hard to imagine what you are really looking at. As diagram A shows, when you cut a tube on a cross section, the slice looks like a ring (if cut at a right angle) or oval (if cut at an oblique, or slanted, angle). Diagram A also shows that if the tube is bent where the cut is made, it can also look like an oval on your slide. Diagram B shows what happens when you have many tubes next to one another—your slice has many round or oval rings (depending on the angle of the cut). Compare Diagram A to Figure 6-5. Can you imagine the type of tissue that produced this slice? Diagram C shows what can happen when a membrane such as the intestinal lining is folded into complex shapes. The slice may look like a sort of zigzag line of cells, or if it is at a high magnification, it may just look like a series of parallel rows. Look at Figure 6-6. Can you imagine what the original tissue must have looked like? Look ahead to Figures 28-9 through 28-21. Can you "see" the context or "situation" of the various tissue slices found in many of these figures? Try sketching out the "big picture" of the context of various tissue samples shown in the photomicrographs of this chapter, and then keep them in your notebook. By doing so, you'll be preparing yourself for later chapters (and later courses) by learning to identify the context of a tissue "on sight."



Cross sections.

At intervals between adjacent epithelial cells, their plasma membranes are modified to hold the cells together. These complex intercellular structures, such as **desmosomes** and **tight junctions,** are described in Chapter 3. Epithelial cells can reproduce themselves. They frequently go through the process of cell division. Because epithelial cells in many locations meet considerable wear and tear, this fact has practical importance. It means, for example, that new cells can replace old or destroyed epithelial cells in the skin or in the lining of the gut or respiratory tract.

Cross sections of epithelial tissues are described in Box 6-2.

Classification of Epithelial Tissue

MEMBRANOUS EPITHELIUM

Classification Based on Cell Shape

The shape of membranous epithelial cells may be used for classification purposes. Four cell shapes, called **squamous, cuboidal, columnar,** and **pseudostratified columnar,** are used in this classification scheme (see Figure 6-2). Squamous (Latin, "scaly") cells are flat and platelike. Cuboidal cells, as the name implies, are cube-shaped and have more cytoplasm than the scalelike squamous cells do. Columnar epithelial cells have more height than width and thus appear narrow and cylindrical. Pseudostratified columnar epithelium has only one layer of oddly shaped columnar cells. Although each cell touches the basement membrane, the tops of some pseudostratified cells do not fully extend to the surface of the membrane. Also, some nuclei are near the "top" of the cell and some near the "bottom" of the cell—rather than all nuclei being near the bottom. The result is a false *(pseudo)* appearance of layering, or stratification, when only a single layer of cells is present.

Classification Based on Layers of Cells

In most cases the location and function of membranous epithelium determine whether its cells will be stacked and layered or arranged in a sheet one cell layer thick. An arrangement of epithelial cells in a single layer is called **simple epithelium.** If epithelial cells are layered one on another, the tissue is called **stratified epithelium. Transitional epithelium** (described later) is a unique arrangement of differing cell shapes in a stratified, or layered, epithelial sheet.

If membranous or covering epithelium is classified by the shape and layering of its cells, the specific types listed in Table 6-3 are

TABLE 6-3 Classification Scheme for Membranous Epithelial Tissues

SHAPE OF CELLS*	TISSUE TYPE
One Layer	
Squamous	Simple squamous
Cuboidal	Simple cuboidal
Columnar	Simple columnar
Pseudostratified columnar	Pseudostratified columnar
Several Layers	
Squamous	Stratified squamous
Cuboidal	Stratified cuboidal
Columnar	Stratified columnar
(Varies)	Transitional

*In the top layer (if more than one layer is present in the tissue).

possible. Notice that stratified tissue types are named for the shape of cells in their top layer only. Each type is described in the paragraphs that follow, and selected examples are illustrated in Figures 6-3 to 6-10.

Simple Epithelium

Simple squamous epithelium consists of only one layer of flat, scalelike cells (Figure 6-3). Consequently, substances can readily diffuse or filter through this type of tissue. The microscopic air sacs (alveoli) of the lungs, for example, are composed of this kind of tissue, as are the linings of blood and lymphatic vessels and the surfaces of the pleura, pericardium, and peritoneum (Figure 6-4). (Blood and lymphatic vessel linings are called **endothelium,** and the surfaces of the pleura, pericardium, and peritoneum are called **mesothelium.** Some histologists classify these linings as connective tissue because of their embryological origin.)

Simple cuboidal epithelium is composed of one layer of cuboidal cells resting on a basement membrane (Figure 6-5). This type of epithelium is seen in many types of glands and their ducts. It is also found in the ducts and tubules of other organs, such as the kidney.

Simple columnar epithelium composes the surface of the mucous membrane that lines the stomach, intestine, uterus, uterine tubes, and parts of the respiratory tract (Figure 6-6). It consists of a single layer of cells, many of which have a modified structure. Three common modifications are goblet cells, cilia, and microvilli. Goblet cells have large, secretory vesicles that give them the appearance of a goblet. The vesicles contain mucus, which goblet cells produce in great quantity and secrete onto the surface of the epithelial membrane. Mucus is a solution of water, electrolytes, and proteoglycans. In the intestine, the plasma membranes of many columnar cells extend out in hundreds and hundreds of microscopic fingerlike projections called **microvilli.** By greatly increasing the surface area of the intestinal mucosa, microvilli make it especially well suited for absorbing nutrients and fluids from the intestine.

Pseudostratified columnar epithelium is found lining the air passages of the respiratory system and certain segments of the male reproductive system such as the urethra (Figure 6-7). Although appearing to be stratified, only a single layer of irregularly shaped columnar cells touches the basement membrane. The cells are of differing heights,

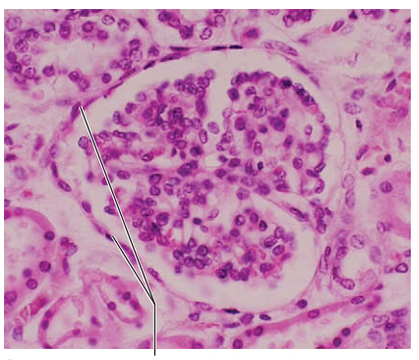


FIGURE 6-3

Simple squamous epithelium. Photomicrograph of the Bowman capsule of the kidney showing thin simple squamous epithelium. Notice how the H&E staining (see Figure 6-2) renders the cytoplasm of each cell pink and each nucleus a purplish color. The outlines of cellular membranes are transparent in the photomicrograph.



FIGURE 6-4

Simple squamous lining of the lung. The tiny air sacs of the lung, which are called *alveoli,* are lined with a thin layer of simple squamous epithelium. This thin epithelium, shown clearly in the scanning electron micrograph in the inset, allows for easy diffusion of oxygen and carbon dioxide across the walls of the alveoli. *Arrowheads* indicate pores that allow air to pass from one alveolus to another.

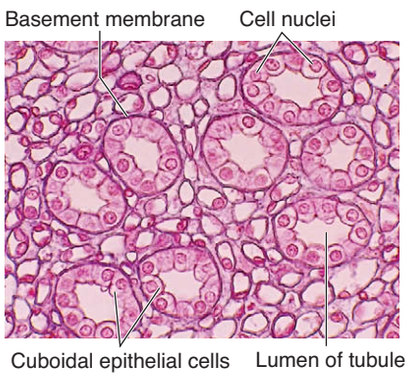


FIGURE 6-5

Simple cuboidal epithelium. Photomicrograph of kidney tubules showing the single layer of cuboidal cells touching a basement membrane. Note the cuboidal cells that enclose the tubule opening (lumen).

and many are not tall enough to reach the upper surface of the epithelial sheet. This fact, coupled with placement of cell nuclei at odd and irregular levels in the cells, gives a false (pseudo) impression of stratification. Mucus-secreting goblet cells are numerous and cilia are present. In the respiratory system air passages, uniform motion of the cilia causes a thin layer of tacky mucus to move in one direction only over the free surface of the epithelium. As a result, dust particles and other contaminants in the inspired air are trapped and moved toward the mouth and away from the delicate lung tissues.

Stratified Epithelium

Stratified squamous epithelium is characterized by multiple layers of cells with typically flattened squamous cells at the free, or outer, surface of the epithelial sheet (Figure 6-8).

In *keratinized* stratified squamous epithelium, the presence of tough keratin fibers in the squamous cells contributes to the protective qualities of skin covering the body surface. Details of the histology of this type of epithelium are presented in Chapter 7.

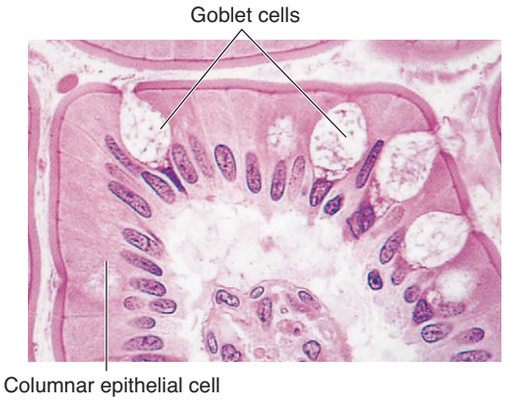


FIGURE 6-6

Simple columnar epithelium. Photomicrograph of simple columnar epithelium. Note the goblet, or mucus-producing, cells present.

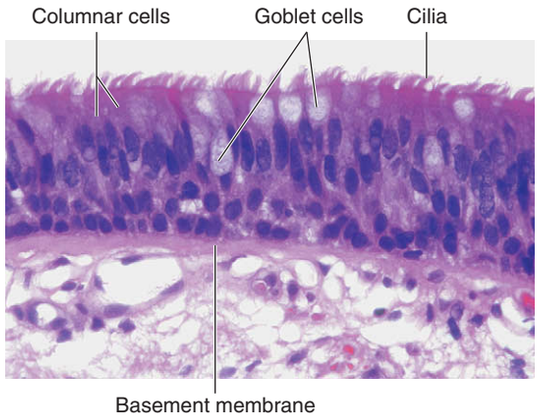


FIGURE 6-7

Pseudostratified columnar epithelium. This photomicrograph from the respiratory system shows that each irregularly shaped columnar cell touches the underlying basement membrane. Placement of cell nuclei at irregular levels in the cells gives a false (pseudo) impression of stratification. This tissue is ciliated—note the "fuzz" along the outer edge of the cells.

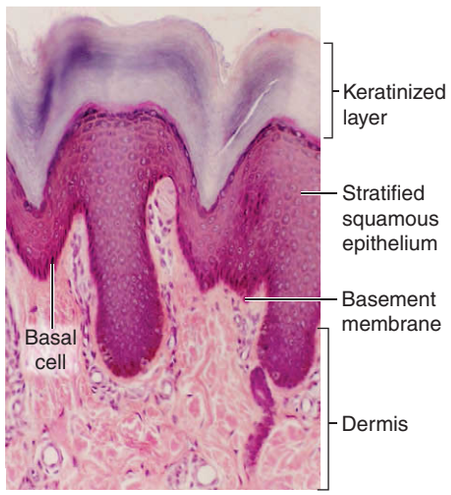


FIGURE 6-8

Keratinized stratified squamous epithelium. Photomicrograph of the thick skin showing cells becoming progressively flattened and scalelike as they approach the surface and are lost. The outer surface of this epithelial sheet contains many flattened cells that have lost their nuclei.

Nonkeratinized stratified squamous epithelium is found lining the vagina, mouth, and esophagus (Figure 6-9). Its free surface is moist, and the outer epithelial cells, unlike those found in the skin, do not contain keratin. This type of epithelium serves a protective function.

Stratified cuboidal epithelium also serves a protective function. Typically, two or more rows of low cuboidal cells are arranged randomly over a basement membrane. Stratified cuboidal epithelium can be located in the sweat gland ducts, in the pharynx, and over parts of the epiglottis.

Stratified columnar epithelium has multiple layers of columnar cells, with only the most superficial cells are truly columnar in appearance. It is a protective type of epithelium found in few places in the human body. It is located in segments of the male urethra and in the mucous layer near the anus.

Transitional epithelium is a stratified tissue typically found in body areas that are subjected to stress and tension changes, such as the wall of the urinary bladder (Figure 6-10). Because it lines part of the urinary

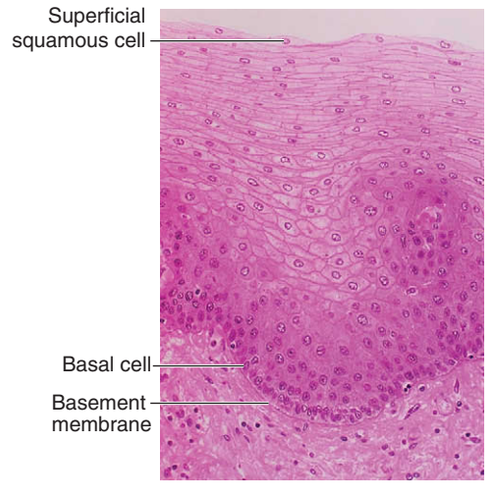


FIGURE 6-9

Nonkeratinized stratified squamous epithelium. Photomicrograph of the lining of the esophagus. Each cell in the layer is flattened near the surface and attached to the sheet. No flaking of dead cells from the surface occurs. All cells have nuclei. Compare with Figure 6-8.

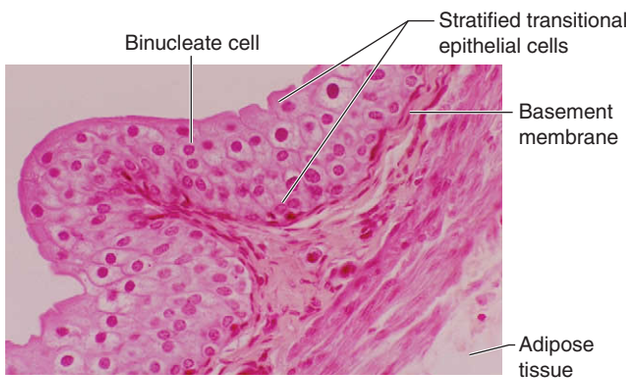
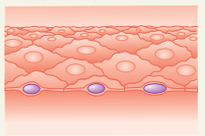
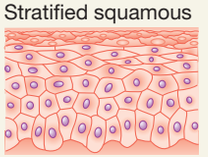
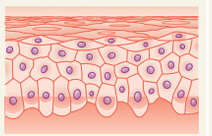
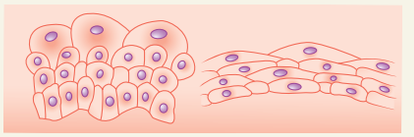
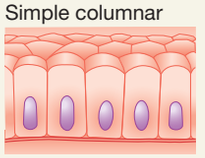
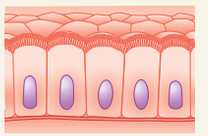
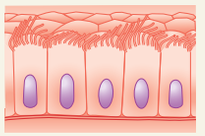
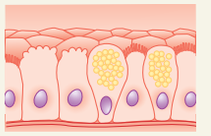
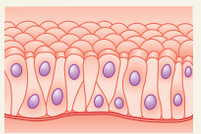
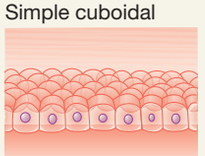
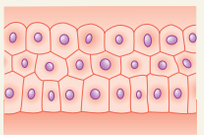
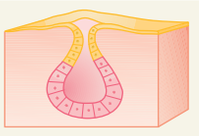


FIGURE 6-10

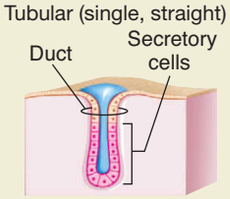
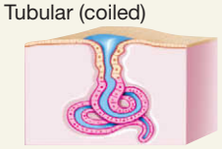
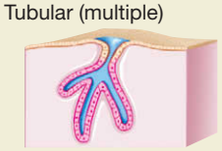
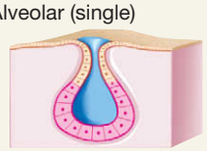
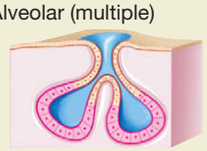
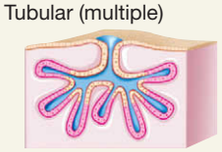
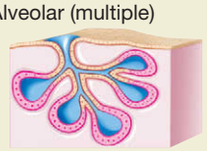
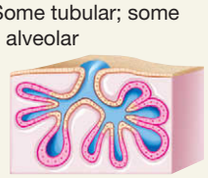
Transitional epithelium. Photomicrograph from the urethra showing that its cell shape is variable from cuboidal to squamous. Several layers of cells are present. Intermediate and surface cells do not touch the basement membrane.

TABLE 6-4 Epithelial Tissues

TISSUE	LOCATION	FUNCTION
Membranous		
Simple squamous 	Alveoli of lungs Lining of blood and lymphatic vessels (called endothelium; classified as connective tissue by some histologists) Surface layer of the pleura, pericardium, and peritoneum (called *mesothelium;* classified as connective tissue by some histologists)	Absorption by diffusion of respiratory gases between alveolar air and blood Absorption by diffusion, filtration, and osmosis Absorption by diffusion and osmosis; also, secretion
Stratified squamous  Nonkeratinized  Keratinized	Surface of the mucous membrane lining the mouth, esophagus, and vagina Surface of the skin (epidermis)	Protection Protection
Transitional  Relaxed Stretched	Surface of the mucous membrane lining the urinary bladder and ureters	Permits stretching Protection
Simple columnar  Without surface specialization  With microvilli (brush/striated border)  Ciliated  With goblet cells	Surface layer of the mucous lining of the stomach, intestines, and part of the respiratory tract	Protection Secretion Absorption Moving of mucus (by ciliated columnar epithelium)
Pseudostratified columnar 	Surface of the mucous membrane lining the trachea, large bronchi, nasal mucosa, and parts of the male reproductive tract (epididymis and vas deferens); lines the large ducts of some glands (e.g., parotid)	Protection
Simple cuboidal 	Ducts and tubules of many organs, including the exocrine glands and kidneys	Secretion Absorption
Stratified cuboidal/columnar 	Ducts of the sweat glands and mammary glands; lining of the pharynx; covering some of the epiglottis; lining portions of the male urethra	Protection
Glandular		
	Glands	Secretion

tract, it is also called *urothelium.* In many instances, 10 or more layers of cuboidal cells of varying shapes are present in the absence of stretching or tension. As tension increases, the epithelial sheet is expanded, the number of observable cell layers decreases, and cell shape changes from cuboidal to squamous in appearance. This ability of transitional epithelium to stretch protects the bladder wall and other distensible structures that it lines from tearing when stretched with great force.

TABLE 6-5 Structural Classification of Multicellular Exocrine Glands

SHAPE*	COMPLEXITY†	TYPE	EXAMPLE
Tubular (single, straight) 	Simple	Simple tubular	Intestinal glands
Tubular (coiled) 	Simple	Simple coiled tubular	Sweat glands
Tubular (multiple) 	Simple	Simple branched tubular	Gastric (stomach) glands
Alveolar (single) 	Simple	Simple alveolar	Sebaceous (skin oil) glands
Alveolar (multiple) 	Simple	Simple branched alveolar	Sebaceous glands
Tubular (multiple) 	Compound	Compound tubular	Mammary glands
Alveolar (multiple) 	Compound	Compound alveolar	Mammary glands
Some tubular; some alveolar 	Compound	Compound tubulo-alveolar	Salivary glands

*Shape of the distal secreting units of the gland.
†Number of ducts reaching the surface.

The major types of epithelium are summarized in Table 6-4.

GLANDULAR EPITHELIUM

Epithelium of the glandular type is adapted for secretory activity. Regardless of the secretory product produced, glandular activity depends on complex and highly regulated cellular activities requiring the expenditure of stored energy.

Unlike the single or layered cells of membranous epithelium typically found in protective coverings or linings, glandular epithelial cells may function singly as **unicellular glands,** or they may function in clusters, solid cords, or hollow follicles as **multicellular glands.** Glandular secretions may be discharged into ducts, into the lumen of hollow visceral structures, onto the body surface, or directly into the blood.

All **glands** in the body can be classified as either exocrine or endocrine glands. **Exocrine glands,** by definition, discharge their secretion products into ducts. The salivary glands are typical exocrine glands. The secretion product (saliva) is produced in the gland and then discharged into a duct that transports it to the mouth. **Endocrine glands** are often called *ductless glands* because they discharge their secretion products (hormones) directly into blood or interstitial fluid. The pituitary, thyroid, and adrenal glands are typical endocrine glands.

Structural Classification of Exocrine Glands

Multicellular exocrine glands are most often classified by structure, with the shape of their ducts and the complexity (branching) of their duct systems used as distinguishing characteristics. Shapes include **tubular** and **alveolar** (saclike). Simple exocrine glands have only one duct leading to the surface, and **compound** exocrine glands have two or more ducts. Table 6-5 describes some of the major structural types of exocrine glands. Figure 6-11 shows examples of exocrine glands in the lining of the stomach.

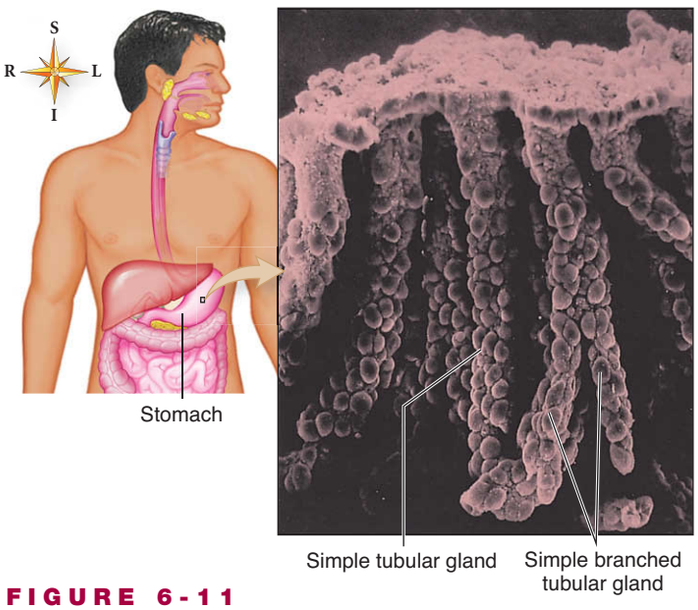


FIGURE 6-11

Exocrine glands in the stomach. The inset shows a scanning electron micrograph of exocrine glands, called *gastric glands,* in the lining of the stomach. These glands produce gastric juice—a mixture of water, mucus, enzymes, acid, and other substances.

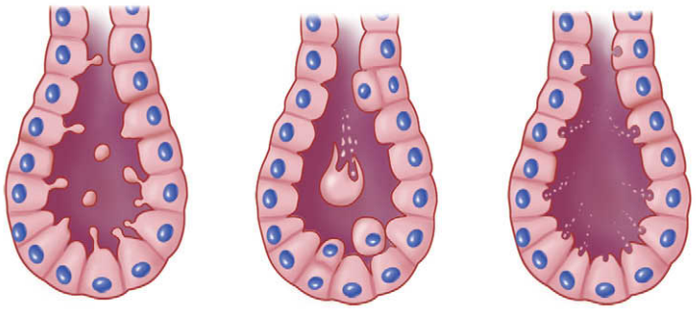


FIGURE 6-12

Three types of exocrine glands. Exocrine glands may be classified by the method of secretion.

Functional Classification of Exocrine Glands

In addition to structural differences, exocrine glands also differ in the method by which they discharge their secretion products from the cell. Using these functional criteria, three types of exocrine glands may be identified (Figure 6-12):

1. Apocrine
2. Holocrine
3. Merocrine

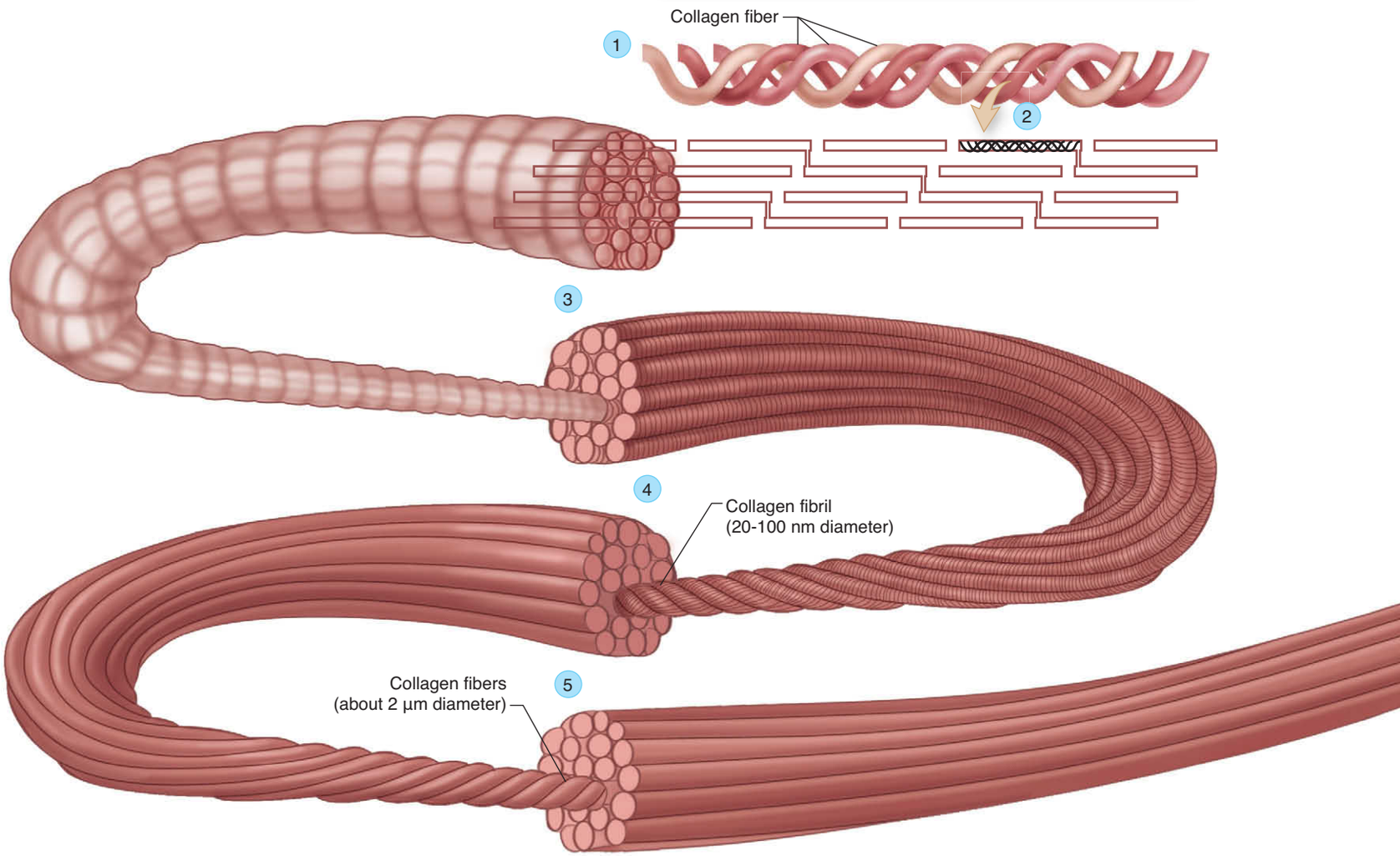
Apocrine glands collect their secretory products near the apex, or tip, of the cell and then release them into a duct by pinching off the distended end. This process results in some loss of cytoplasm and damage to the cell. Recovery and repair of cells are rapid, however, and continued secretion occurs. The milk-producing mammary glands are examples of apocrine-type glands.

Holocrine glands—such as the sebaceous glands that produce oil to lubricate the skin—collect their secretory product inside the cell and then rupture completely to release it. These cells literally self-destruct to complete their function.

Merocrine glands discharge their secretion product directly through the cell or plasma membrane. This discharge process is completed without injury to the plasma membrane and without loss of cytoplasm. Only the secretion product passes from the glandular cell into the duct. Most secretory cells are of this type. The salivary glands are examples of merocrine-type exocrine glands.

| QUICK CHECK |

4. List at least three functions of epithelial tissue.
5. What are the three basic shapes of epithelial cells?
6. Distinguish between a simple epithelial tissue and a stratified epithelial tissue.
7. How do exocrine glands secrete their products?



CONNECTIVE TISSUE

Connective tissue is one of the most widespread and diverse tissues in the body and is found in or around nearly every organ of the body. Connective tissue arises during embryonic development from stem cell tissue called *mesenchyme*, most of which originates in the mesoderm (primary germ layer). Connective tissue exists in more varied forms than the other three basic tissues do. Among the types that we will discuss are delicate tissue paper webs, tough resilient cords, rubbery elastic sheets, rigid bones, and a fluid (blood).

Functions of Connective Tissue

Connective tissue connects, supports, transports, and defends. It connects tissues to each other, for example. It also connects muscles to muscles, muscles to bones, and bones to bones. It forms a supporting framework for the body as a whole and for its organs individually. One kind of connective tissue—blood—transports a large array of substances between parts of the body. And finally, several kinds of connective tissue cells even defend us against microorganisms and other invaders.

Characteristics of Connective Tissue

Connective tissue consists predominantly of extracellular matrix. Embedded in the matrix are relatively few cells. The ECM of connective tissues is made up of varying numbers and kinds of fibers, fluid, and perhaps other material sometimes called *ground substance*. The qualities of the ECM's fibers and other components largely determine the structural characteristics of each type of connective tissue. The matrix of blood, for example, is a fluid (plasma). It contains numerous blood cells but no fibers, except when it coagulates. Some connective tissues have the consistency of a soft gel, some are firm but flexible, some hard and rigid, some tough, others delicate—and in each case it is their matrix and extracellular fibers that make them so.

A connective tissue's extracellular matrix contains one or more of the following kinds of fibers: collagenous (or white), reticular, or elastic (or yellow). Fibroblasts and some other cells produce these protein fibers. Collagenous fibers are tough and strong, reticular fibers are delicate, and elastic fibers are extensible and elastic.

Collagenous fibers are made of **collagen** and often occur in twisted bundles—an arrangement that provides great tensile strength (Figure 6-13). Because collagenous fibers look white in living tissue, they are sometimes called *white fibers*. However, they often appear pink in stained microscopic specimens.

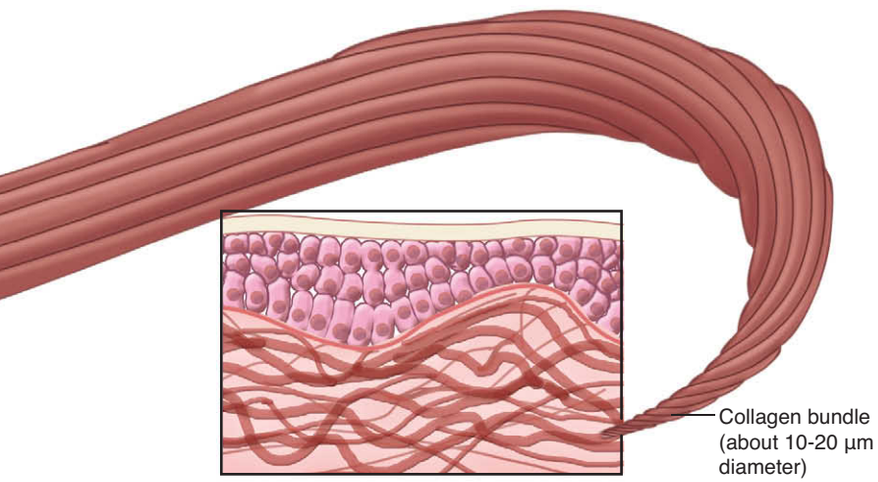
Of all the hundreds of different protein compounds in the body, collagen is the most abundant. Biologists estimate that it constitutes somewhat more than one fourth of all the protein in the body. And interestingly, one of the most basic factors in the aging process, according to some researchers, is the change in the molecular structure of collagen that occurs gradually with the passage of years. In its hydrated form, collagen is also known as *gelatin*. Perhaps you have eaten some flavored gelatin made from animal collagen.

Reticular fibers, in contrast to collagenous fibers, occur in networks and, although delicate, support small structures such as capillaries and nerve fibers. Reticular fibers are made of a special type of collagen called *reticulin*.

Elastic fibers are made of a protein called **elastin**, which returns to its original length after being stretched (Figure 6-14).

FIGURE 6-13

Collagen bundles. 1, Collagen forms when quaternary proteins made up of three tertiary protein chains twist into a fibrous molecule. **2,** Collagen molecules then assemble into a staggered strand of collagen. **3,** Bundles of collagen strands twist together to form collagen fibrils, which in turn twist together with additional fibrils (**4**) to form collagen fibers. **5,** The collagen fibers then twist together in groups to form rope-like collagen bundles having flexibility and great strength.



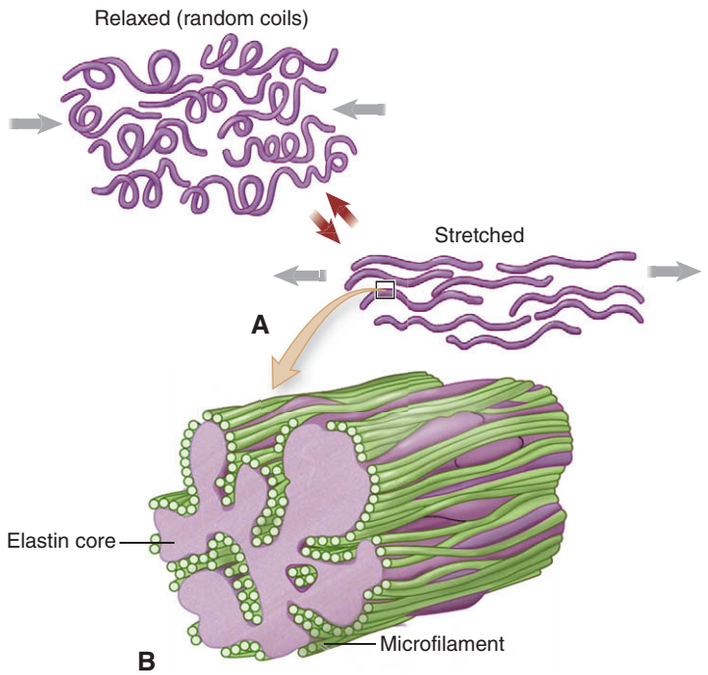


FIGURE 6-14

Elastin fibers. A, Elastin fibers form random coils within the extracellular matrix *(ECM)* that may easily be stretched. When released, the elastin fibers will recoil to a relaxed formation. **B,** Each elastin fiber is made of stretchy, formless elastin that is held in a fibrous shape by an arrangement of microfibrils.

Elastin is a rubbery substance that is held in a fibrous shape by long, thin microfilaments—as you can see in Figure 6-14, *B*. Elastic fibers are found in "stretchy" tissues, such as the cartilage of the external ear and the walls of arteries. Because elastin fibers look yellowish in living tissue, they are sometimes called *yellow fibers*.

In addition to protein fibers, the matrix of connective tissues contains a number of *proteoglycans* made up of polysaccharide chains often containing *glucosamine* and bound to a protein core (see Figure 6-1). These chemicals make the matrix fluid thick enough to be a barrier to bacteria and other microbes. They also form transparent lubricant and help hold the tissue together. Among the more notable of these compounds are *hyaluronic acid* and *chondroitin sulfate*.

Classification of Connective Tissue

Connective tissues have been classified by histologists in several different ways. Usually they are placed in different categories or types according to the structural characteristics of the intercellular material. The classification scheme we have adopted here is widely used and includes most of the major types:

1. Fibrous (connective tissue proper)
   a. Loose fibrous (areolar)
   b. Adipose
   c. Reticular
   d. Dense
      (1) Irregular
      (2) Regular
         (a) Collagenous
         (b) Elastic
2. Bone
   a. Compact
   b. Cancellous (spongy)
3. Cartilage
   a. Hyaline
   b. Fibrocartilage
   c. Elastic
4. Blood

Fibrous tissues, also called *connective tissue proper*, such as loose fibrous connective, adipose, reticular, and dense fibrous tissues have many fibers in the ECM as their predominant feature. The type and arrangement of extracellular fibers are what distinguish members of the group from each other. Bone is considered a separate category of connective tissue because it has fibers and a hard mineralized ECM. Cartilage is yet another category because besides fibers, it has a type of ECM that traps water to form a firm gel. Blood, the last category listed, is characterized by the lack of fibers in its matrix. These major types of connective tissues are described further in the following pages and in Table 6-6.

TABLE 6-6 Connective Tissues

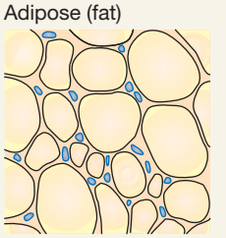
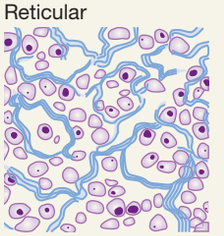
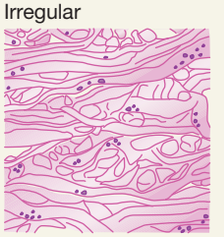
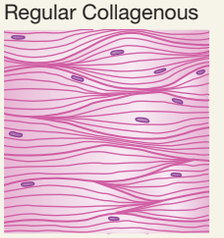
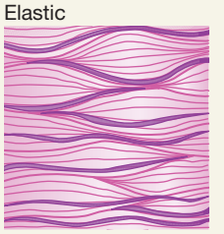
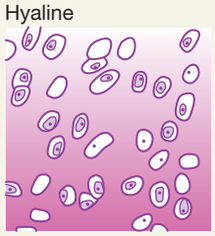
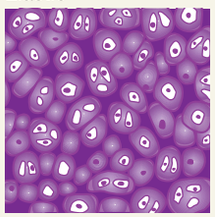
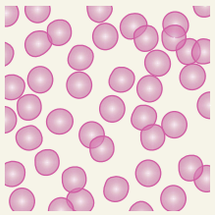
TISSUE	LOCATION	FUNCTION
Fibrous		
Loose fibrous (areolar) 	Between other tissues and organs Superficial fascia	Connection
Adipose (fat) 	Under skin Padding at various points	Protection Insulation Support Reserve food Regulation of other tissues
Reticular 	Inner framework of spleen, lymph nodes, bone marrow	Support Filtration Blood production Immunity
Dense Fibrous		
Irregular 	Deep fascia Dermis Scars Capsule of kidney, spleen, lymph nodes, etc.	Connection Support
Regular Collagenous 	Tendons Ligaments Aponeuroses	Flexible but strong connection
Elastic 	Walls of some arteries	Flexible, elastic support

TABLE 6-6 Connective Tissues *(continued)*

TISSUE	LOCATION	FUNCTION
Bone		
Compact bone 	Skeleton (outer shell of bones)	Support Protection Calcium reservoir
Cancellous (spongy) bone 	Skeleton (inside bones)	Support Provides framework for blood production
Cartilage		
Hyaline 	Part of nasal septum Covering articular surfaces of bones Larynx Rings in trachea and bronchi	Firm but flexible support; connection between structures
Fibrocartilage 	Disks between vertebrae Pubic symphysis	
Elastic 	External ear Eustachian or auditory tube	
Blood		
	In the blood vessels	Transportation Protection

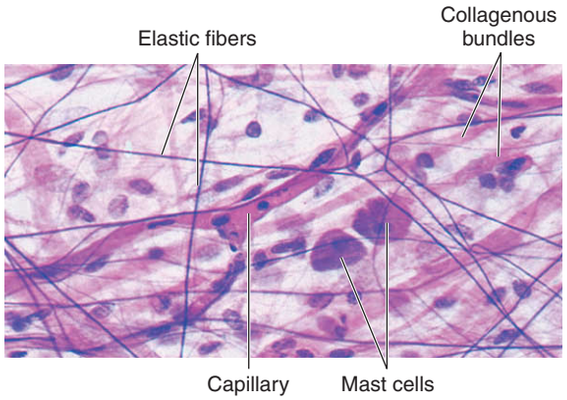


FIGURE 6-15

Loose fibrous (areolar) connective tissue. Notice how the H&E staining (see Figure 6-2) renders the bundles of collagen fibers a pinkish color and the elastin fibers and cell nuclei a darker, purplish color. Compare the loose arrangement of fibers here with fibers in Figures 6-20, 6-21, and 6-23.

Fibrous Connective Tissue

LOOSE FIBROUS CONNECTIVE TISSUE (AREOLAR)

Loose fibrous connective tissue, shown in Figure 6-15, is sometimes called *areolar tissue*. It is loose because it is stretchable and ordinary because it is one of the most widely distributed of all tissues. It is common and ordinary, not special like some kinds of connective tissue (e.g., bone and cartilage) that help form comparatively few structures. *Areolar* was the early name for the loose fibrous connective tissue that connects many adjacent structures of the body. It acts like a glue spread between them—but an elastic glue that permits movement. The word **areolar** means "like a small space" and refers to the bubbles that appear as areolar tissue is pulled apart during dissection. The matrix of loose fibrous connective tissue is a soft, thick gel mainly because it contains hyaluronic acid. An enzyme, hyaluronidase, can change the matrix from its thick gel state to a watery consistency. Physicians have made use of this knowledge for many years. They frequently inject a commercial preparation of hyaluronidase with drugs or fluids. By decreasing the viscosity (thickness) of intercellular material, the enzyme hastens diffusion and absorption of the injected material and lessens tissue tension and pain. Some bacteria, notably *pneumococci* and *streptococci*, spread through connective tissues by secreting hyaluronidase.

The matrix of loose fibrous connective tissue contains numerous fibers and cells, typically many interwoven collagenous and elastic fibers and about a half dozen kinds of cells

Box 6-3 | HEALTH matters

Hay Fever and Asthma

Mast cells in loose fibrous connective tissues are often involved in *allergy,* or *hypersensitivity,* reactions in local tissues. This is a type of inflammation (see ***A&P Connect: Inflammation*** online) in response to *allergens,* which are substances that trigger such allergic responses. For example, the inflammation that you experience after a bee sting or when your skin is exposed to poison ivy are both examples of allergic or hypersensitivity reactions. Such reactions are triggered when mast cells encounter an allergen and release any of a group of chemical mediators.

For example, in hay fever (allergies to grasses and other plants), mast cells release the chemical **histamine.** Histamine increases the permeability of blood vessels in the nasal membranes, which in turn causes swelling in the lining of the nose. This gives us a "stuffy feeling" because the swelling makes it difficult to breathe easily. Histamine can also cause itchiness of the nose and eyes (see figure). The stuffiness and itchy eyes of hay fever can be relieved by antihistamines such as diphenhydramine (Benadryl) and fexofenadine (Allegra), which block histamine's action.

On the other hand, a different mast cell product is responsible for the breathing difficulties in an asthma attack. In asthma, chemicals called *leukotrienes* trigger muscles in the walls of the respiratory tract to contract—thereby constricting the airways. Thus, leukotriene-blocking drugs such as montelukast (Singulair) and zileuton (Zyflo) are often used along with other drugs that prevent or reduce contraction of airway muscles.

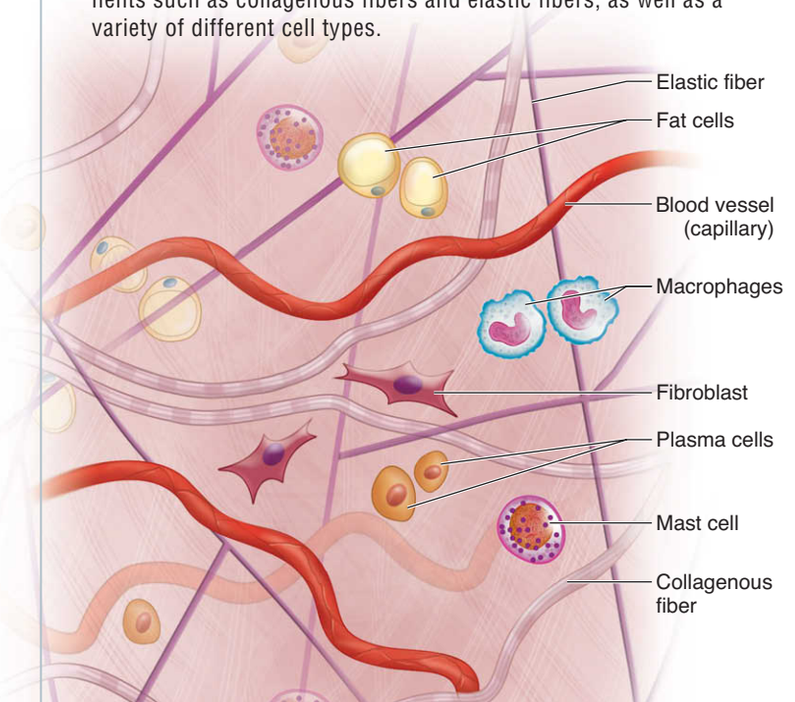


Allergic eyes. Some allergies cause itchiness and watering of the eyes, which may trigger frequent rubbing of the eyes, that produces these reddened features.

(Figure 6-16). **Fibroblasts** are usually present in the greatest numbers in loose fibrous connective tissue, and **macrophages** are second. Fibroblasts synthesize the gel-like ground substance and the fibers present in it. Macrophages carry on *phagocytosis,* hence their name, which means "large eater." Phagocytosis is part of the body's vital collection of defense mechanisms. **Mast cells,** also found in loose fibrous connective tissue, are capable of releasing a variety of molecules such as *histamine*, *heparin*, *leukotrienes*, and *prostaglandins*. These chemical mediators are released in response to exposure to substances from outside the body and produce a type of inflammation response (Box 6-3). Other kinds of cells found in loose fibrous connective tissue are various forms of white blood cells (leukocytes) and some fat cells.

FIGURE 6-16

Diagram of loose fibrous (areolar) connective tissue. This artist's sketch illustrates the fact that loose fibrous connective tissue includes a number of different extracellular matrix (ECM) components such as collagenous fibers and elastic fibers, as well as a variety of different cell types.



ADIPOSE TISSUE

Adipose tissue differs from loose fibrous connective tissue mainly in that it contains predominantly fat cells, also called **adipocytes,** and many fewer fibroblasts, macrophages, and mast cells (Figure 6-17). Each adipocyte typically has one large vesicle filled with stored triglycerides. This fat vesicle is so large that it pushes the cytoplasm of the cell outward against the plasma membrane as it stores more and more fat. This expands the entire cell to a

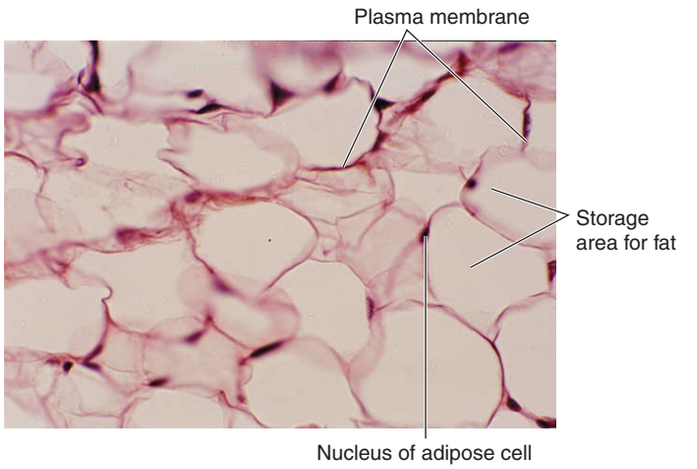


FIGURE 6-17

Adipose tissue. Note the large storage spaces for fat inside the adipose tissue cells.

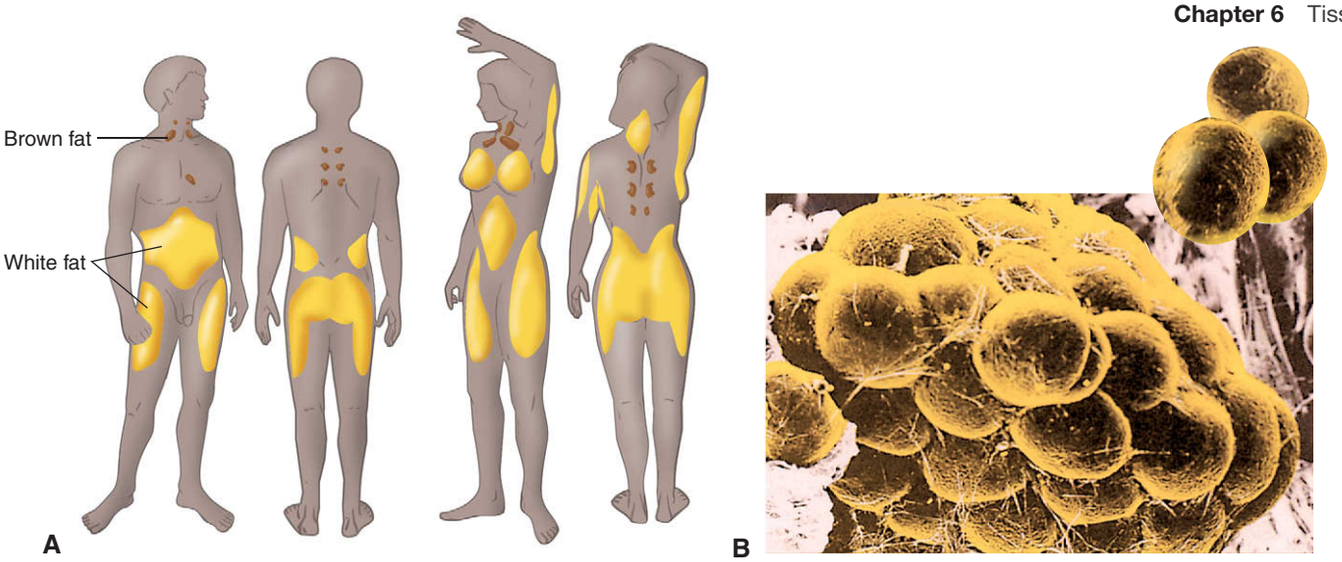


FIGURE 6-18

Fat distribution. A, The different distribution of fat in adult male and female bodies. **B,** Electron micrograph of a cluster of adipose cells in white fat held together by a network of fine reticular fibers (×150).

huge size. The hormone *leptin* is released from adipocytes as they expand, signaling the brain and other tissues regarding how much fat is stored and ready to use for energy. The role of leptin is described further in Chapters 19 and 30.

The predominant form of adipose tissue is *white fat*, which serves mainly as a storage depot for excess food. White fat also acts as an insulating material to conserve body heat. It also forms supporting, protective pads around the kidneys and various other structures.

Brown fat is a less abundant form of adipose tissue. Adipocytes in brown fat are able to use stored fat to generate heat with their numerous mitochondria. This function is vital to the survival of newborns, which do not have enough muscle to generate enough heat by shivering. In adults, this fat-burning function may help regulate overall fat content of the body.

Figure 6-18 shows the location of the main fat storage areas in adults and how fat distribution varies between males and females. Box 6-4 discusses body composition.

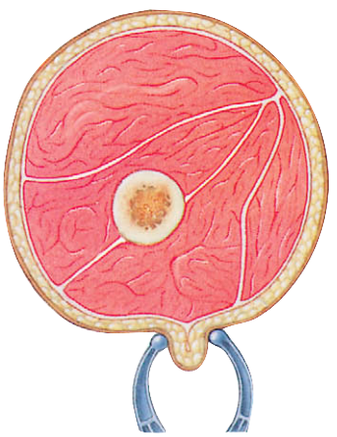
Box 6-4 | SPORTS and FITNESS

Tissues and Fitness

Achieving and maintaining ideal body weight is a health-conscious goal. However, a better indicator of health and fitness is **body composition.** Exercise physiologists assess body composition to identify the percentage of the body made of lean tissue and the percentage made of fat. Body fat percentage is often determined by using calipers to measure the thickness of skin folds at certain locations on the body (see figures). The thickness measurements, which reflect the volume of adipose tissue under the skin, are then used to estimate the percentage of fat in the entire body. A much more accurate method is to weigh a subject totally immersed in a tank of water. Fat has very low density and therefore increases the buoyancy of the body. When in water, a person's measured weight is relatively low if the body fat percentage is high and the measured weight is high if the body fat percentage is low.

A person with low body weight may still have a high ratio of fat to muscle, an unhealthy condition. In this case the individual is "underweight" but "overfat." In other words, fitness depends more on the percentage and ratio of specific tissue types than on the overall amount of tissue present. Therefore, one goal of a good fitness program is a desirable body fat percentage. For men, the ideal is 15% to 18%, and for women, the ideal is 20% to 22%.





Because fat contains stored energy (measured in calories), a low fat percentage means a low energy reserve. High body fat percentages are associated with several life-threatening conditions, including cardiovascular disease. A balanced diet and an exercise program ensure that the ratio of fat to muscle tissue stays at a level appropriate for maintaining homeostasis.

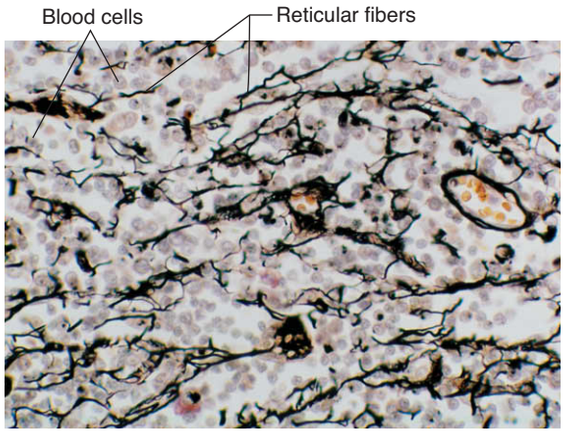


FIGURE 6-19

Reticular connective tissue. The supporting framework of reticular fibers are stained black in this section of lymph node.

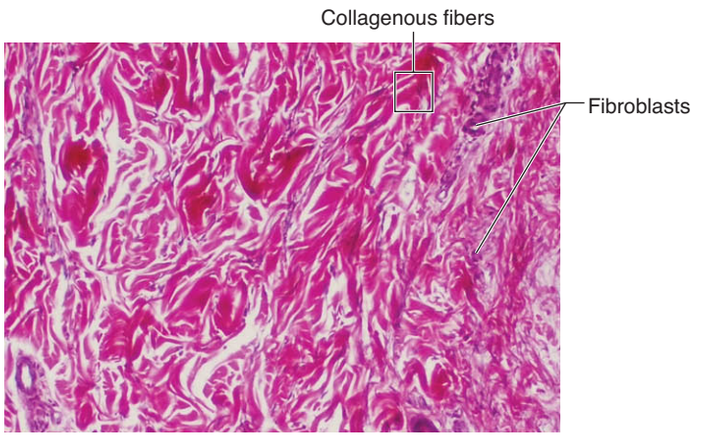


FIGURE 6-20

Dense irregular fibrous connective tissue. Section of skin (dermis) showing arrangements of collagenous fibers (pink) and purple-staining fibroblast cell nuclei.

RETICULAR TISSUE

A three-dimensional web, that is, a reticular network, identifies **reticular tissue** (Figure 6-19). The word *reticular* means "like a net." Slender, branching reticulin fibers with reticular cells overlying them compose the reticular meshwork. Branches of the cytoplasm of reticular cells follow the branching reticular fibers.

Reticular tissue forms the framework of the spleen, lymph nodes, and bone marrow. It is often called *marrow tissue* or *lymphoid tissue* in these locations. Reticular tissue functions as part of the body's complex mechanisms for producing blood cells and for defending itself against microorganisms and injurious substances. The reticular meshwork filters injurious substances out of the blood and lymph. Various types of reticular cells then phagocytose (engulf and destroy) the trapped substances. Another function of some reticular cells is to make reticular fibers.

DENSE FIBROUS TISSUE

Dense fibrous tissue consists mainly of fibers packed densely in the matrix. It contains relatively few fibroblast cells. Some dense fibrous tissues are designated as *regular* and others are designated as *irregular*, depending on the arrangement of fibers.

Dense Irregular Fibrous Tissue

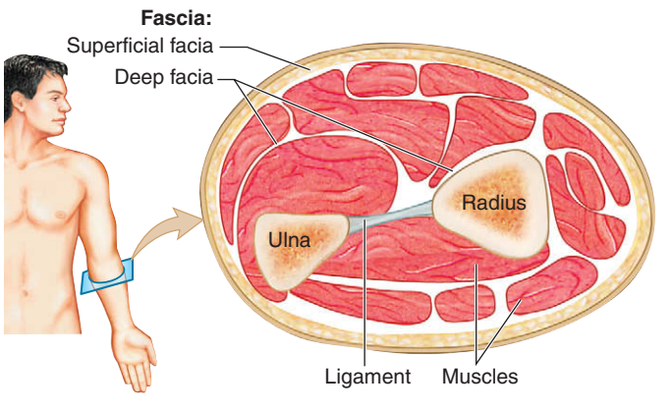
In dense irregular fibrous tissues, the bundles of collagenous fibers intertwine in irregular, swirling arrangements (Figure 6-20). This irregular pattern forms a thick mat of strong connective tissue that can withstand stresses applied from any direction. Dense irregular fibrous tissue forms the strong inner skin layer called the *dermis*. It also forms the outer capsule of such organs as the kidney and the spleen, as well as much of the fascia that surrounds muscles (Box 6-5).

Box 6-5 | Fascia

The term **fascia** (FASH-ee-ah) is a general name for the fibrous connective tissue masses that can be seen by the unaided eye in many locations throughout the body. The word *fascia* is Latin for "band." This literal translation is helpful because it summarizes the general structure and function of fascia: fibrous tissue that binds together the structures of the body.

Fascia is always some form of fibrous connective tissue and almost always features many collagenous fibers that are interwoven in an irregular arrangement. In some areas of the body, for example under the skin, fascia is mostly adipose tissue. In other areas, such as around some of the muscles, it is dense irregular fibrous tissue. Often, some of the fibers of fascia extend into the tissue of nearby organs, thus strongly binding to them.

For convenience, anatomists often distinguish between *superficial fascia,* which is just under the skin, and *deep fascia,* which extends well into the body and surrounds muscles, blood vessels, and other organs (see the figure).



Fascia. Horizontal section of the forearm showing the superficial fascia under the skin and deep fascia below that, extending to surround the individual muscles.

| A&P CONNECT |

Inflammation is an important defensive reaction in the body's tissues. Check out ***Inflammation*** online at ***A&P Connect*** for a brief overview of the inflammatory response and its effects on the tissues of your body.

evolve

Dense Regular Fibrous Tissue

In dense regular fibrous tissues, the bundles of fibers are arranged in regular, parallel rows. One form of dense regular fibrous tissue is predominantly bundles of collagenous fibers and may be called **collagenous dense regular fibrous tissue** (Figure 6-21). This type of fibrous tissue is flexible but possesses great tensile strength when pulled from either or both ends. These characteristics are desirable in structures that anchor muscle to bone, such as tendons (Figure 6-22). Ligaments (which connect bone to bone) instead have a predominance of elastic fibers. Hence ligaments exhibit some degree of elasticity.

Another form of dense (regular) fibrous tissue contains mostly elastic fibers and may be called **elastic dense regular fibrous tissue.** As you can see in Figure 6-23, elastic fibers in this type of tissue are in a parallel arrangement. In the walls of arteries, this arrangement permits the walls to be pushed out by blood pressure without breaking and then recoil to a smaller diameter when the blood pressure decreases.

Bone Tissue

Bone, or *osseous tissue*, is a rather unique form of very hard connective tissue. The mature cells of bone, **osteocytes,** are embedded in a unique matrix material containing both collagen fibers and mineral salt crystals. The inorganic mineral crystals make up about 66% of the total extracellular matrix. These mineral crystals are responsible for the hardness of bone.

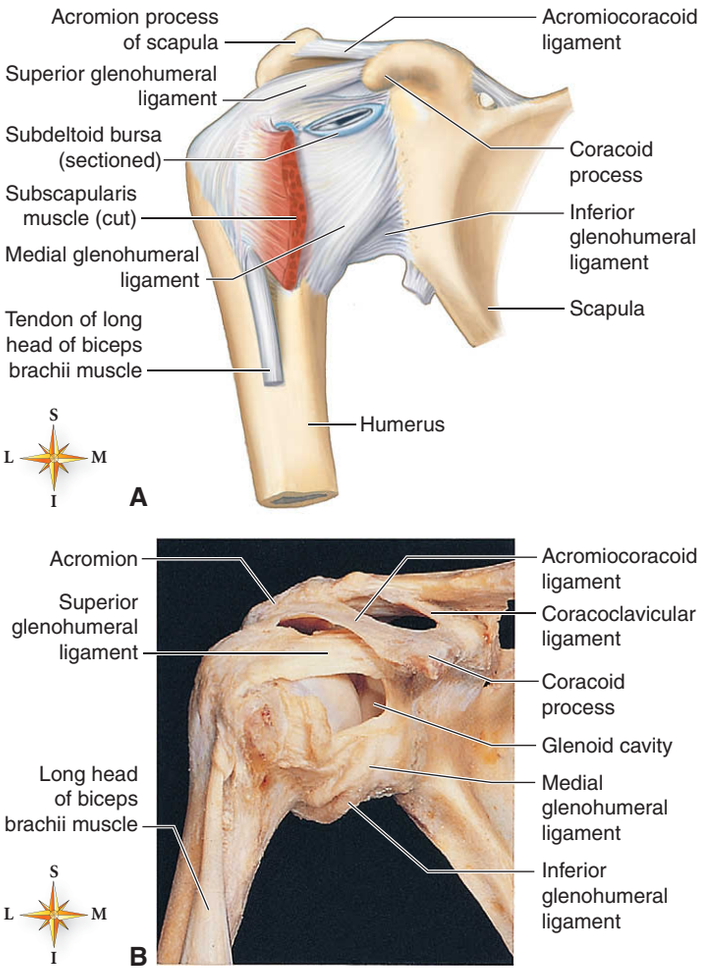


FIGURE 6-22

Tendons and ligaments. A, Tendons and ligaments of the shoulder are examples of dense fibrous connective tissue. **B,** Photo of cadaver dissection. Note the many strong connections needed to keep this important joint functioning properly.

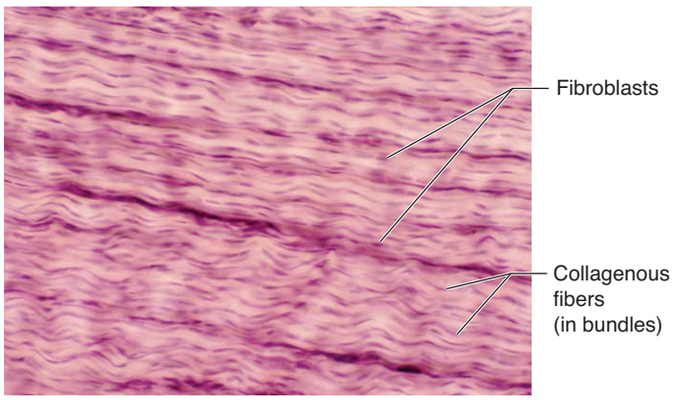


FIGURE 6-21

Collagenous dense regular fibrous connective tissue. Photomicrograph of tissue in a tendon. Note the multiple (regular) bundles of collagenous fibers arranged in parallel rows.

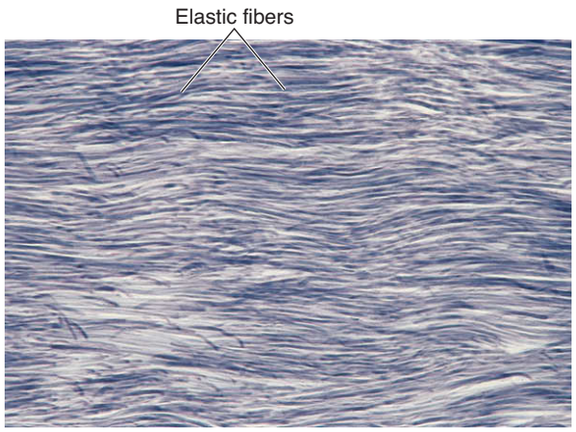


FIGURE 6-23

Elastic dense regular fibrous connective tissue. Note the roughly parallel arrangement of short, darkly stained elastic fibers.

Bones are the organs of the skeletal system. They provide support and protection for the body and serve as points of attachment for muscles. In addition, the calcified matrix of bones serves as a mineral reservoir for the body. A lattice made of bone also serves as the support for red bone marrow, which produces new blood cells.

Certain bones called **membrane bones** (e.g., flat bones of the skull) are formed within membranous tissue, whereas others (e.g., long bones such as the humerus) are formed indirectly through replacement of cartilage in a process called **endochondral ossification** (Figure 6-24). The details of bone formation are presented in Chapter 8.

COMPACT BONE TISSUE

The type of bone tissue that forms the hard shell of a bone is called **compact bone tissue** (Figure 6-25). The basic organizational or structural unit of compact bone is the microscopic **osteon,** or *Haversian system* (Figure 6-26). Osteocytes, or bone cells, are located in small spaces, or **lacunae,** which are arranged in concentric layers of bone matrix called **lamellae.** Small canals called **canaliculi** connect each lacuna and osteocyte with nutrient blood vessels found in the central, or Haversian, canal.

Mature osteocytes are actually trapped in hard bone matrix. At one time they were active, bone-forming cells called **osteoblasts.** However, as they surround themselves with bone, they become trapped and cease making new bone matrix. Another type of bone cell, the **osteoclast,** or bone-destroying cell, may dissolve the bone away from the mature osteocyte and release it to again become an active osteoblast. Mature bone can thus grow and be reshaped by the simultaneous activity of osteoclasts breaking down and removing existing bone tissue as osteoblasts lay down new bone.

CANCELLOUS (SPONGY) BONE TISSUE

Inside many bones is a lattice of thin beams of **cancellous bone tissue** (Figure 6-27). These thin beams, or **trabeculae,** form a framework that supports a softer tissue—*red bone marrow.* Red bone marrow is also called *myeloid tissue* (the term *myeloid* literally means "of marrow"). Myeloid tissue is a type of reticular tissue that contains the stem cells responsible for producing the various types of blood cells. It also contains fat-storing *adipocytes.*

The lattice of trabeculae also give internal support to the bone, much as the crisscrossing pattern of the roof trusses of a building help support the weight of a roof. Because cancellous bone looks somewhat like a sponge at first glance, it is sometimes called *spongy bone tissue.* This type of bone is also called *trabecular bone* because of its many trabeculae.

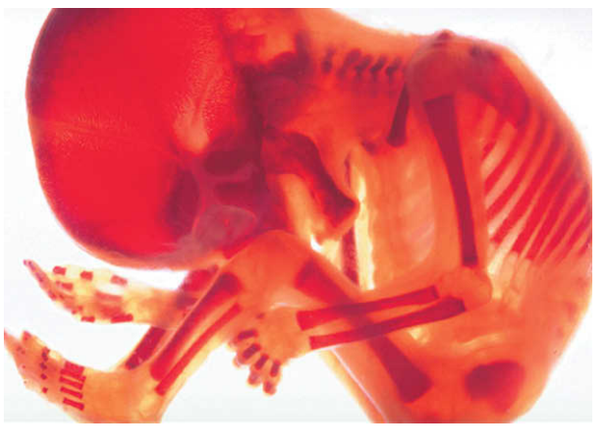


FIGURE 6-24

Ossification of the skeleton. The darkly stained areas of mineralization seen in this 14-week-old fetus show how the cartilage and membrane skeleton is beginning to develop into bone.

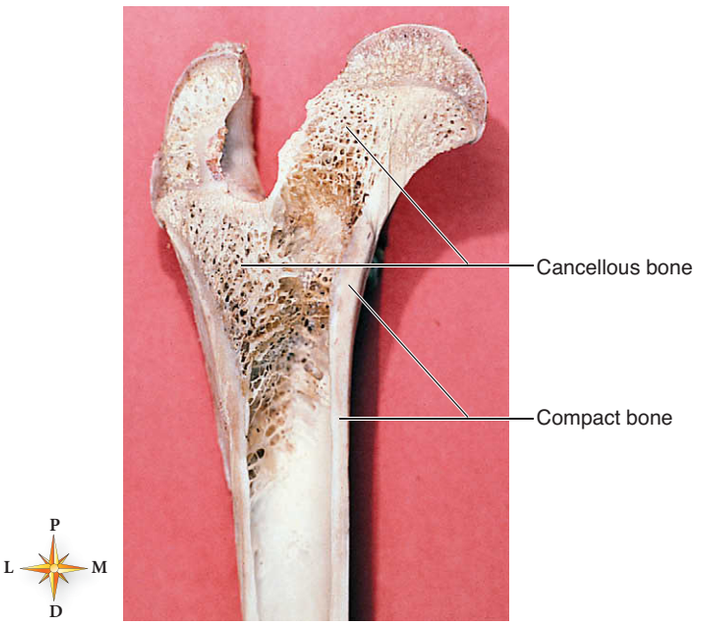


FIGURE 6-25

Types of bone tissue. Compact bone is found forming most of the hard shell of a bone. Cancellous (spongy) bone forms a network of hard beams of bone tissue inside many bones.

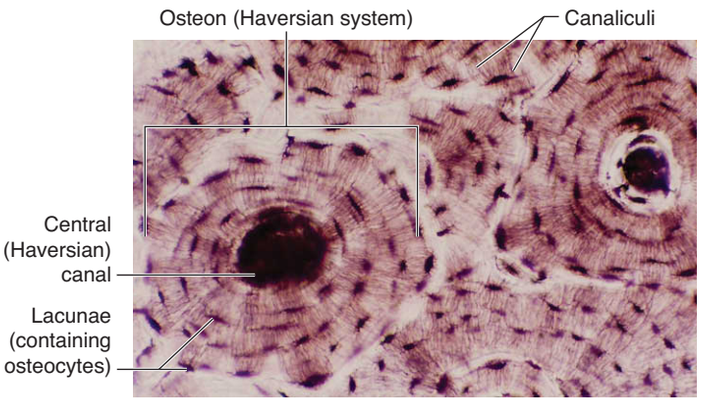


FIGURE 6-26

Compact bone tissue. Photomicrograph of ground compact bone. Many wheel-like structural units of bone, known as *osteons* or *Haversian systems,* are apparent in this section.

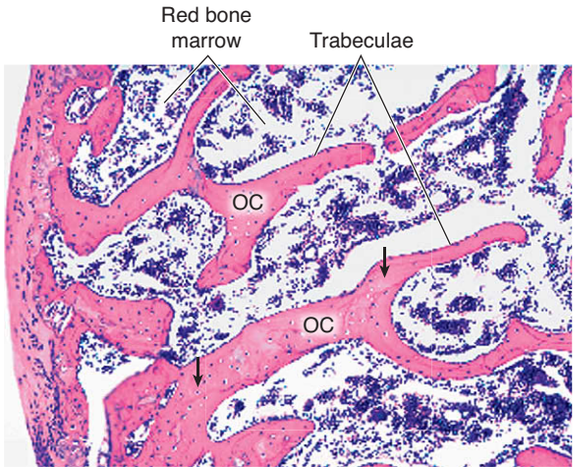


FIGURE 6-27

Cancellous bone tissue. Photomicrograph of cancellous (*spongy* or *trabecular*) bone. The pink-stained mineralized bone tissue forms a lattice of irregular beams, or *trabeculae,* that support the softer reticular tissue of the bone marrow. The darkly stained nuclei of osteocytes *(OC)* are visible, as well as the dark boundaries *(arrows)* of mineralized bone layers or lamellae.

Cartilage Tissue

Cartilage differs from other connective tissues in that only one cell type, the **chondrocyte,** is present. Chondrocytes produce the fibers and the tough, rubbery ground substance of cartilage. Chondrocytes, like bone cells, are found in small openings called *lacunae.* Cartilage is avascular (lacking blood vessels), so nutrients must reach the cells by diffusion. Movement is through the matrix from blood vessels located in a connective tissue membrane called the **perichondrium,** which surrounds the cartilage mass. Injuries to cartilage heal slowly, if at all, because of this inefficient method of nutrient delivery.

HYALINE CARTILAGE TISSUE

Hyaline cartilage takes its name from the Greek word *hyalos* or "glass." The name is appropriate because the low amount of collagen in the matrix gives hyaline cartilage a shiny and translucent appearance. This is the most prevalent type of cartilage and is found in the support rings of the respiratory tubes and covering the ends of bones that articulate at joints (Figure 6-28).

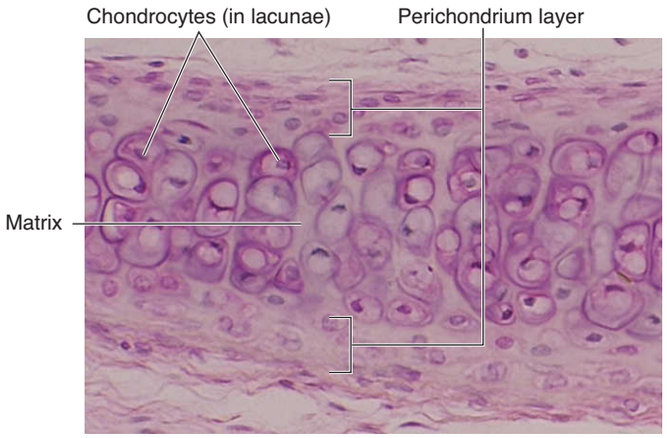


FIGURE 6-28

Hyaline cartilage. Photomicrograph of the trachea. Note the many spaces, or lacunae, in the gel-like matrix.

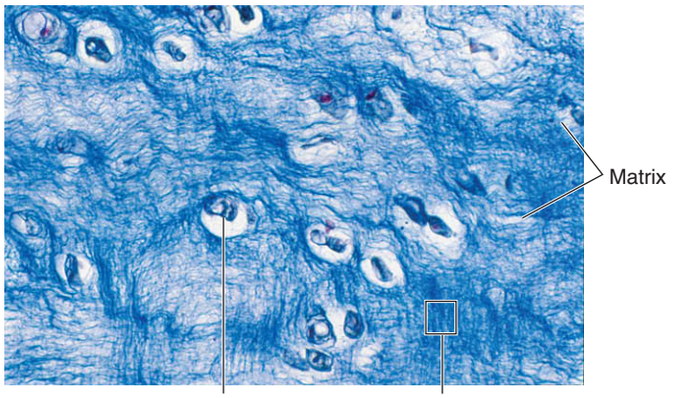


FIGURE 6-29

Fibrocartilage. Photomicrograph of the pubic symphysis joint. The strong dense fibers that fill the matrix convey shock-absorbing qualities.

FIBROCARTILAGE TISSUE

Fibrocartilage is the strongest and most durable type of cartilage (Figure 6-29). The matrix is rigid and filled with a dense packing of strong white collagen fibers. Fibrocartilage disks serve as shock absorbers between adjacent vertebrae (intervertebral disks) and in the knee joint. Damage to the fibrocartilage pads or joint menisci (curved pads) in the knee occurs frequently as a result of sports-related injuries.

ELASTIC CARTILAGE TISSUE

Elastic cartilage contains few collagen fibers, but large numbers of very fine elastic fibers that give the matrix material a high degree of flexibility (Figure 6-30). This type of cartilage is found in the external ear and in the voice box, or larynx.

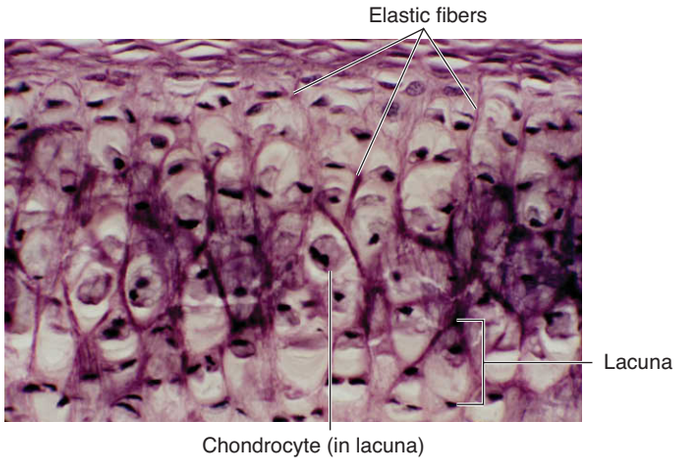


FIGURE 6-30

Elastic cartilage. Photomicrograph of the voice box (larynx). Note the cartilage cells in the lacunae surrounded by matrix and dark-staining elastic fibers.

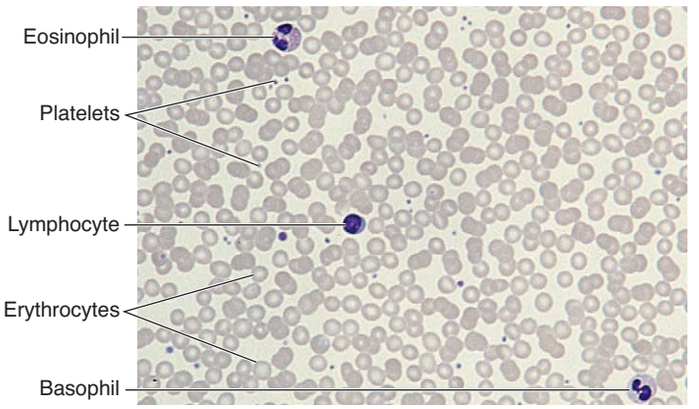


FIGURE 6-31

Blood. Photomicrograph of a human blood smear (×270) showing three white blood cells, or leukocytes, surrounded by numerous smaller red blood cells and platelets.

Blood Tissue

Blood is perhaps the most unusual connective tissue because it exists in a liquid state and contains neither ground substance nor fibers (Figure 6-31).

Whole blood is often divided into a matrix, or *liquid fraction*, called **plasma** and **formed elements,** or blood cells. Blood cells may be divided into three classes: red blood cells, or **erythrocytes;** white blood cells, or **leukocytes;** and **thrombocytes,** or platelets. The liquid fraction makes up about 55% of whole blood, and the formed elements compose about 45%.

Blood performs many body transport functions, including movement of respiratory gases (oxygen and carbon dioxide), nutrients, and waste products. In addition, blood plays a critical role in maintaining a constant body temperature and regulating the pH of body fluids. White blood cells function in destroying harmful microorganisms.

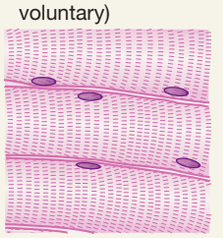
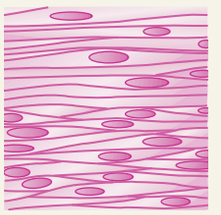
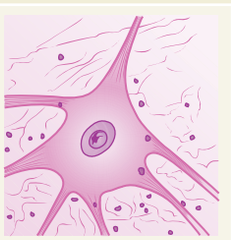
Circulating blood tissue is formed in the *red marrow* of bones and in other tissues by a process of differentiation called *hematopoiesis.* This blood-forming tissue is sometimes given the status of a separate connective tissue type: **hematopoietic tissue.**

Blood and its formation are described in detail in Chapter 20.

| QUICK CHECK |

8. Name three kinds of fibers that may be present in a connective tissue ECM. Of what are they made?
9. Name four types of fibrous connective tissue and briefly describe each.
10. What makes bone tissue hard?
11. What is unique about the matrix of blood tissue?

TABLE 6-7 Muscle and Nervous Tissues

TISSUE	LOCATION	FUNCTION
Muscle		
Skeletal (striated voluntary) 	Muscles that attach to bones Extrinsic eyeball muscles Upper third of the esophagus	Movement of bones Eye movements First part of swallowing
Smooth (nonstriated, involuntary, or visceral) 	In the walls of tubular viscera of the digestive, respiratory, and genitourinary tracts In the walls of blood vessels and large lymphatic vessels In the ducts of glands Intrinsic eye muscles (iris and ciliary body) Arrector muscles of hairs	Movement of substances along the respective tracts Change diameter of blood vessels, thereby aiding in regulation of blood pressure Movement of substances along ducts Change diameter of pupils and shape of the lens Erection of hairs (gooseflesh)
Cardiac (striated involuntary) 	Wall of the heart	Contraction of the heart
Nervous		
	Brain Spinal cord Nerves	Excitability Conduction

MUSCLE TISSUE

Three types of **muscle tissue** are present in the body—skeletal muscle, smooth muscle, and cardiac muscle (Table 6-7). Their names suggest their locations. **Skeletal muscle tissue** (Figure 6-32) makes up most of the muscles attached to bones; these are the organs that we think of as our muscles. **Smooth muscle tissue,** also sometimes called *visceral muscle tissue* (Figure 6-33), is found in the walls of the viscera (hollow internal organs, e.g., the stomach, intestines, and blood vessels; Figure 6-34). **Cardiac muscle tissue** makes up the wall of the heart (Figure 6-35).

Another name for skeletal muscle is *striated voluntary* muscle. The term *striated* refers to cross striations (stripes) visible on

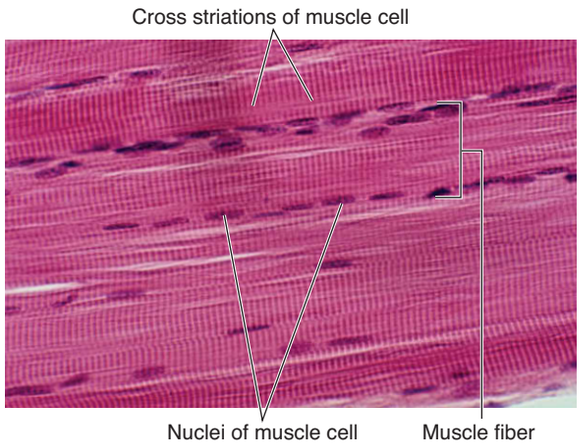


FIGURE 6-32

Skeletal muscle. Note the striations of the muscle cell fibers in longitudinal section.

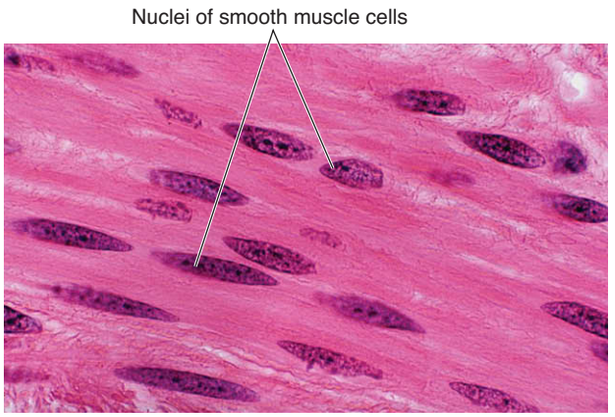
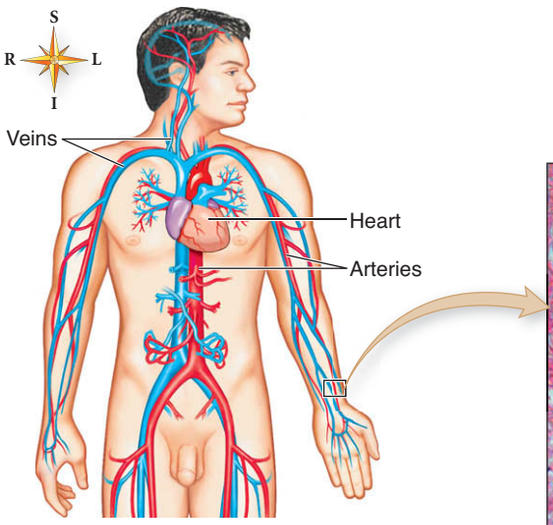


FIGURE 6-33

Smooth muscle. Photomicrograph, longitudinal section. Note the central placement of nuclei in the spindle-shaped smooth muscle fibers.



Cardiovascular system

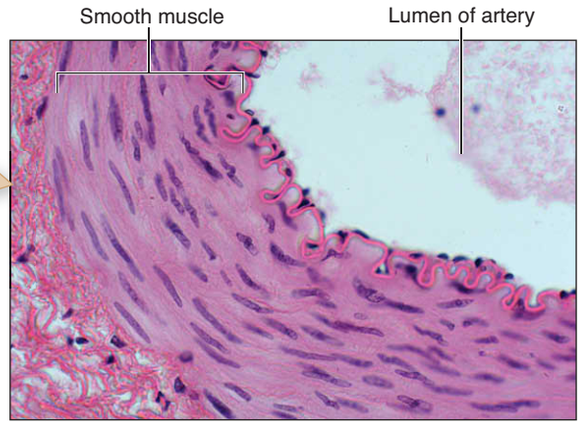


FIGURE 6-34

Location of smooth muscle. Smooth muscle is found in the walls of most internal hollow organs such as the stomach, intestines, and blood vessels. For example, the cross section of an artery shown in the inset reveals that the arterial wall has a thick layer of smooth muscle, which contracts or relaxes to control the diameter of the artery—thus controlling the flow of blood through this vessel.

microscopic slides of the tissue. The term *voluntary* indicates that voluntary or willed control of skeletal muscle contractions is possible. Another name for smooth muscle is *nonstriated involuntary*. Smooth muscle has no cross striations and cannot ordinarily be controlled by the will. Another name for cardiac muscle is *striated involuntary* muscle. Like skeletal muscle, cardiac muscle has cross striations, and like smooth muscle, its contractions cannot ordinarily be controlled by will.

Look now at Figure 6-32 and observe the following structural characteristics of skeletal muscle cells: many cross striations, many nuclei per cell, and long, narrow, threadlike shape of the cells. Skeletal muscle cells may have a length of more than 3.75 cm, but they have diameters of only 10 to 100 μm. Because this gives them a threadlike appearance, muscle cells are often called *muscle fibers*. Chapter 12 gives more detailed information about the structure of skeletal muscle tissue.

Smooth muscle cells are also long, narrow fibers, but not nearly as long as striated fibers. One can see the full length of a

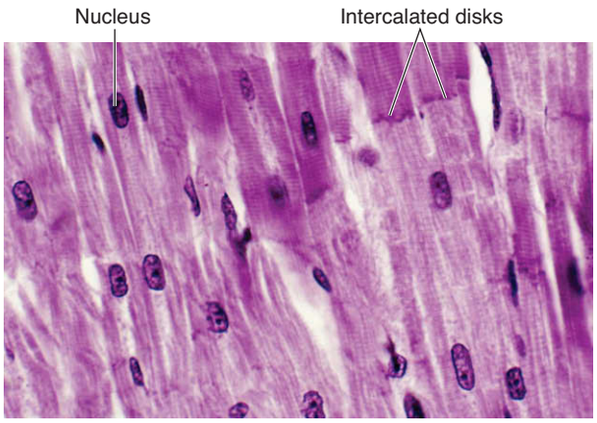


FIGURE 6-35

Cardiac muscle. The dark bands, called *intercalated disks,* which are characteristic of cardiac muscle, are easily identified in this tissue section.

smooth muscle fiber in a microscopic field, but only a small part of a striated fiber. According to one estimate, the longest smooth muscle fibers measure about 500 µm and the longest striated fibers about 40,000 µm. As Figure 6-33 shows, smooth muscle fibers have only one nucleus per fiber and are nonstriated or smooth in appearance. Smooth muscle fibers are shaped like a spindle—that is, they are cylinders that taper at both ends.

Under the light microscope, cardiac muscle fibers (see Figure 6-35) have cross striations and unique dark bands (intercalated disks) that join together the untapered ends of fibers. They also seem to be incomplete cells that branch into each other to form a big continuous mass of cytoplasm (a *syncytium*). The electron microscope, however, reveals that the intercalated disks are actually places where the plasma membranes of two cardiac fibers abut. Cardiac fibers branch in and out, but a complete plasma membrane encloses each cardiac fiber—around its end (at intercalated disks) and its sides.

Muscle cells are the movement specialists of the body. Because their cytoskeletons include bundles of microfilaments capable of movement, they have a higher degree of contractility (ability to shorten and lengthen with force) than cells of any other tissue.

NERVOUS TISSUE

The basic function of the nervous system is to rapidly regulate, and thereby integrate, the activities of the different parts of the body. Functionally, rapid communication is possible because **nervous tissue** has much more developed excitability and conductivity characteristics than any other type of tissue does.

The organs of the nervous system are the brain, the spinal cord, and the nerves. Actual nerve tissue is ectodermal in origin and consists of two basic kinds of cells: nerve cells, or **neurons,** which are the conducting units of the system, and special connecting, protective, and supporting cells called **neuroglia** (see Table 6-7 and Figure 6-36).

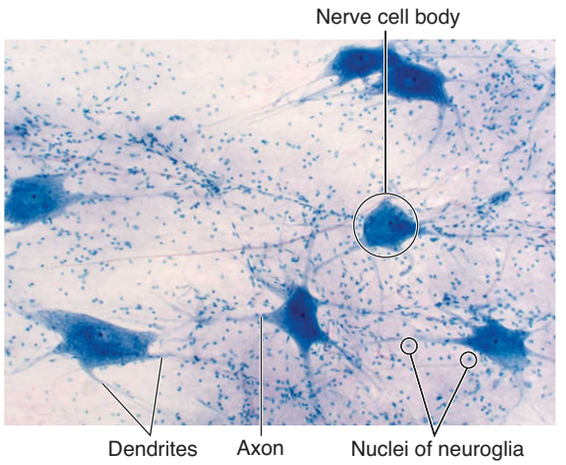


FIGURE 6-36

Nervous tissue. Photomicrograph showing multipolar neurons surrounded by smaller neuroglia in a smear of spinal cord tissue. All of the large neurons in this photomicrograph show characteristic soma, or cell bodies, and multiple cell processes.

All neurons are characterized by a cell body called the **soma** and, generally, at least two processes: one **axon,** which transmits nerve impulses away from the cell body, and one or more **dendrites,** which carry nerve signals toward the axon. Most neurons are located within the organs of the central nervous system.

There are many types of neuroglia, all with different structures and functions. For example, *astrocytes* form a blood-brain barrier that protects delicate brain tissue from potentially harmful substances in the blood. *Microglia* help destroy pathogens and damaged tissue cells in the brain. *Schwann cells* and *oligodendrocytes* electrically insulate axons to increase their speed of conduction. In addition to physically supporting neurons, neuroglia are known to have important coordinating roles in the nervous system—a concept that we explore further in Chapter 13.

The anatomy and physiology of the nervous system are presented in Chapters 13 through 17.

| QUICK CHECK |

12. Name the two types of involuntary muscle. Where is each found in the body?
13. What are the two principal types of cell in nervous tissue? What is the function of each?

TISSUE REPAIR

When damaged by mechanical or other injuries, tissues have varying capacity to repair themselves. Damaged tissue regenerates or is replaced by tissue we know as scars. Tissues usually repair themselves by allowing phagocytic cells to remove dead or injured cells and then filling in the gaps that are left. This growth of functional new tissue is called **regeneration.**

Epithelial and connective tissues have the greatest capacity to regenerate (Figure 6-37). When a break in an epithelial membrane occurs, as in a cut, cells quickly divide to form daughter cells that fill the wound. In connective tissues, cells that form collagen fibers become active after an injury and fill in a gap with an unusually dense mass of fibrous connective tissue. If this dense mass of fibrous tissue is small, it may be replaced by normal tissue later. If the mass is deep or large or if cell damage was extensive, it may remain as a dense fibrous mass, called a **scar.** An atypical and unusually thick scar that may develop in the lower layer of the skin, such as that shown in Figure 6-38, is called a **keloid.**

Muscle tissue, on the other hand, has a limited capacity to regenerate and thus heal itself. Scientists are just now learning about the abilities of muscle fibers to be replaced in adults. Damaged muscle is sometimes replaced with fibrous connective tissue instead of muscle tissue. When this happens, the organ involved loses some or all of its ability to function.

Like muscle tissue, nerve tissue also has a limited capacity to regenerate. Neurons can sometimes regenerate, but very slowly and only if certain neuroglia are present to "pave the way." In the normal adult brain and spinal cord, a few new neurons are regularly produced in certain regions. However, adult brain neurons do not often grow back when injured. Thus serious brain and spinal cord injuries often result in at least some permanent damage.

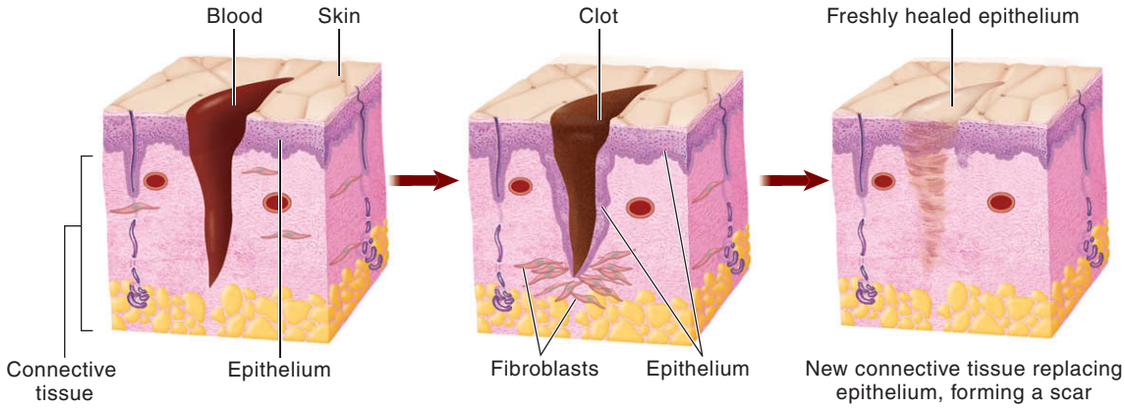


FIGURE 6-37

Healing of a minor wound. When a minor injury damages a layer of epithelium and the underlying connective tissue (as in a minor skin cut), the epithelial tissue and the connective tissue can self-repair.

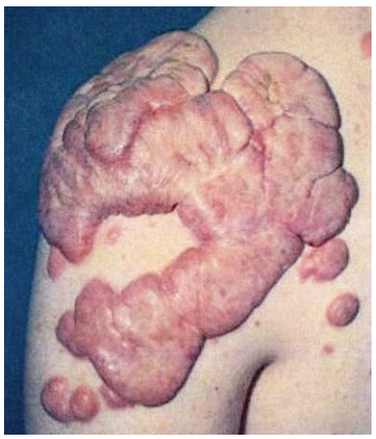


FIGURE 6-38

Keloid. Keloids are thick scars that form in the lower layer of the skin in predisposed individuals.

Fortunately, research on *nerve growth factors* produced by neuroglia offers the promise of treating brain damage. Research on adult stem cells present in both muscle and nerve tissue also holds hope for such therapies.

BODY MEMBRANES

The term **membrane** refers to a thin, sheetlike structure that may have many important functions in the body. Membranes cover and protect the body surface, line body cavities, and cover the inner surfaces of hollow organs such as the digestive, reproductive, and respiratory passageways. Some membranes anchor organs to each other or to bones, and others cover the internal organs. In certain areas of the body, membranes secrete lubricating fluids that reduce friction during organ movements such as beating of the heart or lung expansion and contraction. Membrane lubricants also decrease friction between bones and joints. Two major categories, or types, of body membranes exist (Figure 6-39):

1. **Epithelial membranes,** composed of epithelial tissue and an underlying layer of supportive connective tissue
2. **Connective tissue membranes,** composed exclusively of various types of connective tissue; no epithelial cells are present in this type of membrane

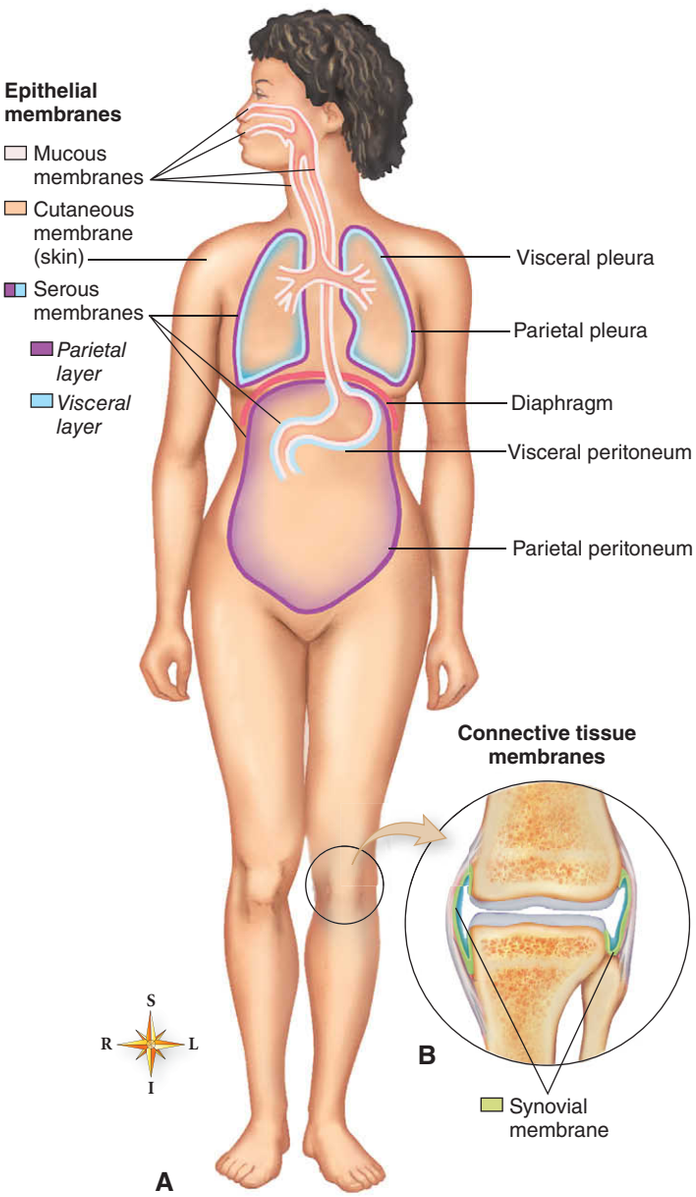


FIGURE 6-39

Types of body membranes. A, Epithelial membranes, including cutaneous membrane (skin), serous membranes (parietal and visceral pleura and peritoneum), and mucous membranes. **B,** Connective tissue membranes, including synovial membranes.

Epithelial Membranes

There are three types of epithelial tissue membranes in the body: (1) cutaneous membrane, (2) serous membranes, and (3) mucous membranes (Figure 6-40).

CUTANEOUS MEMBRANES

The **cutaneous membrane** covers body surfaces that are exposed to the external environment. The cutaneous membrane, or **skin,** is the primary organ of the integumentary system. It is one of the most important and certainly one of the largest and most visible organs of the body. In most individuals the skin composes approximately 16% of body weight. It fulfills the requirements necessary for an epithelial tissue membrane in that it has a superficial layer of epithelial cells and an underlying layer of supportive connective tissue. It also contains many sweat and oil glands that produce a *surface film* over the skin. The structure of the skin is uniquely suited to its many functions. The skin is discussed in depth in Chapter 7.

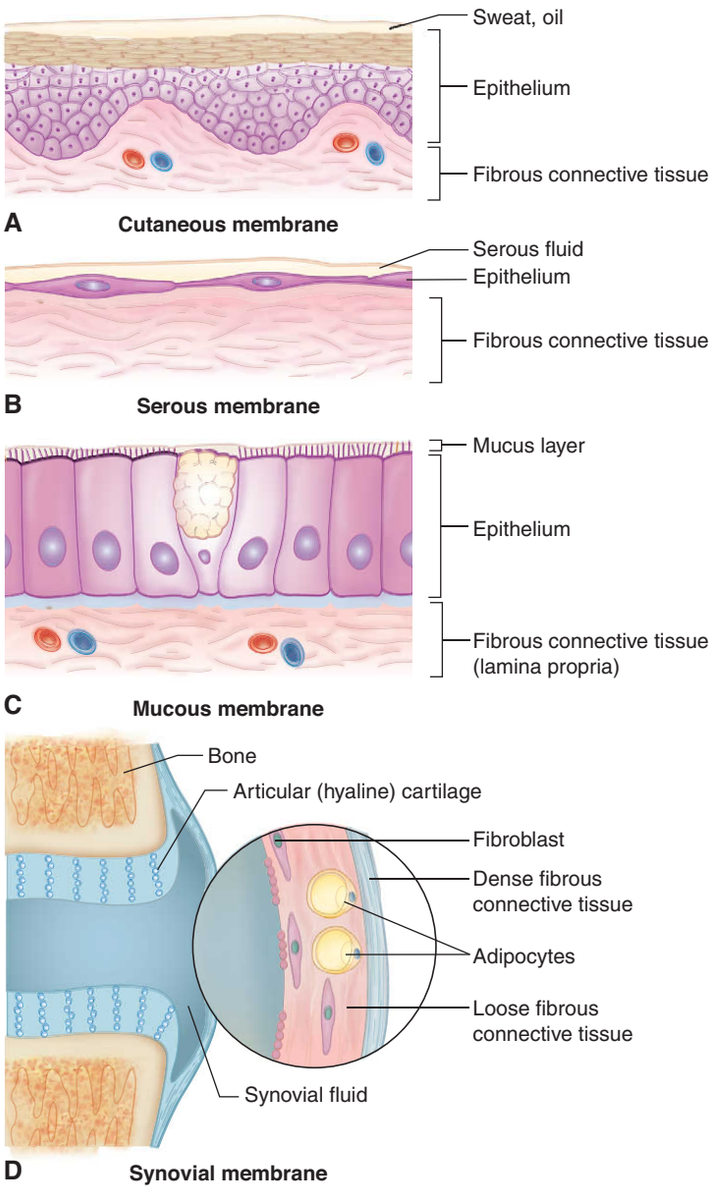


FIGURE 6-40
Structure of body membranes.

SEROUS MEMBRANES

Serous membrane lines cavities that are not open to the external environment and covers many of the organs inside these cavities. Serous membranes are sometimes called by their Latin name, *serosa*. Like all epithelial membranes, a serous membrane is composed of two distinct layers of tissue. One of the layers, the epithelial sheet, is a thin layer of simple squamous epithelium. The other layer, the connective tissue layer, forms a very thin sheet that holds and supports the epithelial cells.

The serous membrane that lines body cavities and covers the surfaces of organs in these cavities is in reality a single, continuous sheet covering two different surfaces. The *parietal membrane* is the portion that lines the wall of the cavity like wallpaper; the *visceral membrane* covers the surface of the viscera (organs within the cavity). Two important serous membranes are identified in Figure 6-39: the *pleura*, which surrounds a lung and lines the thoracic cavity, and the *peritoneum*, which covers the abdominal viscera and lines the abdominal cavity. Another example is the *pericardium*, which surrounds the heart (Box 6-6).

Serous membranes secrete a thin, watery fluid that lubricates organs as they rub against one another and against the walls of cavities.

MUCOUS MEMBRANES

Mucous membranes are epithelial membranes that line body surfaces opening directly to the exterior. Mucous membranes are sometimes called by their Latin name, *mucosa*. Examples of mucous membranes include those lining the respiratory, digestive, urinary, and reproductive tracts. The epithelial component of the mucous membrane varies, depending on its location and function. In the esophagus, for example, a tough, abrasion-resistant stratified squamous epithelium is found. A thin layer of simple columnar epithelium covers the walls of the lower segments of the digestive tract. The fibrous connective tissue underlying the epithelium in mucous membranes is called the **lamina propria.**

Box 6-6 | HEALTH matters

Inflammation of Serous Membranes

Pleurisy (PLOOR-i-see) (also called *pleuritis*) is a very painful pathological condition characterized by inflammation of the serous membranes (pleurae) that line the chest cavity and cover the lungs. Pain is caused by irritation and friction as the lungs rub against the walls of the chest cavity. In severe cases the inflamed surfaces of the pleura fuse, and permanent damage may develop. The term **peritonitis** (pair-i-toh-NYE-tis) is used to describe inflammation of the serous membranes in the abdominal cavity. Peritonitis is sometimes a serious complication of an infected appendix. See ***Inflammation*** online at ***A&P Connect*** for more about the inflammatory response.

Mucous membranes get their name from the fact that they produce a film of **mucus** that coats and protects the underlying cells. Besides protection, mucus also serves other purposes. For example, mucus acts as a lubricant for food as it moves along the digestive tract. In the respiratory tract, it serves as a sticky trap for contaminants.

Mucus is a watery secretion that contains a mixture of *mucins*, which are a group of about two dozen different proteoglycans. Different mucins are found in different locations in the body. Some mucins are attached directly to the plasma membranes of the epithelial cells to form a protective coat. Other mucins are released by goblet cells and form a protective, sometimes lubricating gel. Thus mucous membranes have two layers of protective coating.

The mucous membrane is clinically important because it is the place that our body will most likely interact with microorganisms from the external environment. In fact, a very active area of research is attempting to understand the microbial colonization of mucous membranes in the digestive tract, respiratory tract, urinary tract, and reproductive tract (Figure 6-41). As researchers learn more about how mucus defends our internal environment from attack, the better able they will be to develop new strategies to avoid life-threatening infections. Chapter 24 discusses the role of mucous membranes in immunity.

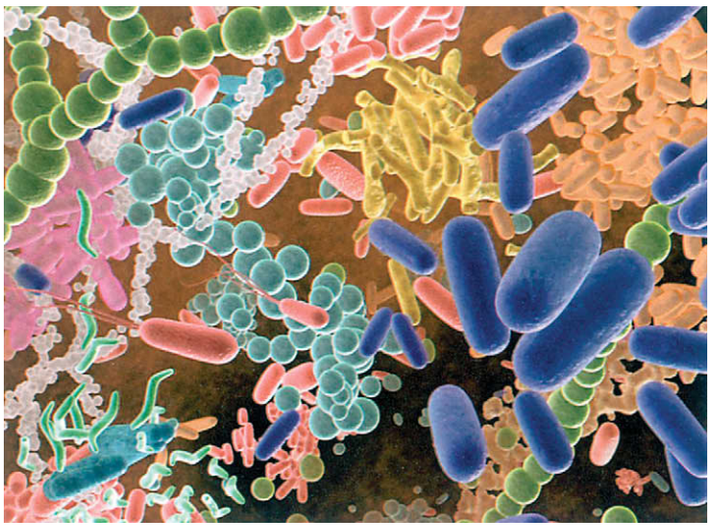


FIGURE 6-41

Colonization of mucous membranes by microbes. This colorized scanning electron micrograph shows many different types of bacteria that colonize the mucous membranes of the digestive tract and urinary tract within a short time after birth (*yellow,* bifidobacteria; *red,* coliform bacteria; *purple,* lactobacilli; *light blue,* streptococci; *green,* other coccal bacteria).

Connective Tissue Membranes

Unlike cutaneous, serous, and mucous membranes, connective tissue membranes do not contain epithelial components. The **synovial membranes** lining the spaces between bones and joints that move are classified as connective tissue membranes. These membranes are smooth and slick and secrete a thick and colorless lubricating fluid called **synovial fluid.** The membrane itself, with its specialized fluid, helps reduce friction between the opposing surfaces of bones in movable joints. Synovial membranes also line the small, cushionlike sacs called *bursae* found between some moving body parts.

Table 6-8 summarizes the main characteristics of the four major types of membranes in the body.

| QUICK CHECK |

14. Which two of the four major tissue types have the greatest capacity to regenerate after an injury?
15. Name the four principal types of body membranes. Which are epithelial membranes?

TABLE 6-8 Membranes of the Body

TYPE	SUPERFICIAL LAYER	DEEP LAYER	LOCATION	FLUID SECRETION	FUNCTION
Epithelial					
Cutaneous (skin)	Keratinized stratified squamous epithelium (epidermis)	Dense irregular fibrous connective tissue (dermis)	Directly exposed to external environment	Sweat; sebum (skin oil)	Protection, sensation, thermoregulation
Serous	Simple squamous epithelium	Fibrous connective tissue	Lines body cavities that are not open to the external environment	Serous fluid	Lubrication
Mucous	Various types of epithelium	Fibrous connective tissue (lamina propria)	Lines tracts that open to the external environment	Mucus	Protection, lubrication
Connective					
Synovial	Dense fibrous connective tissue	Loose fibrous connective tissue	Lines joint cavities (in movable joints)	Synovial fluid	Helps hold joint together, lubricates, cushions

the BIG picture

Tissues, Membranes, and the Whole Body

Tissues and body membranes are sometimes called "the fabric of the body." Like the pieces of fabric in a garment, tissues and body membranes are portions of a larger integrated structure. Just as each type of fabric in a complex garment has a different functional role determined by its structural characteristics, so does each type of tissue within the body. One of the ultimate functional goals of most tissues and membranes is maintenance of relative constancy in the body: homeostasis.

How do the major tissue types help maintain homeostasis? Epithelial tissues promote constancy of the body's internal environment in several ways. They form membranes that contain and protect the internal fluid environment, they absorb nutrients and other substances needed to maintain an optimum concentration in the body, and they secrete various products that regulate body functions involved in homeostasis. Connective tissues hold organs and systems together to form a whole, connected body. They also form structures that support the body and permit movement, such as the components of the skeleton.

Some connective tissues, such as blood, transport nutrients, wastes, and other substances within the internal environment. Some blood cells help protect the internal environment by participating in the body's immune system. Muscle tissues work in conjunction with connective tissues (bones, tendons, etc.) to permit movement (a function needed to avoid injury); to communicate; and to find food, shelter, and other requirements. Nervous tissue works with glandular epithelial tissue to regulate various body functions in a way that maintains homeostatic balance.

Now that you have a basic knowledge of the various types of body "fabric"—the tissues and body membranes—you are ready to study the structure and function of specific organs and systems. As you take this next step in your studies, pay close attention to the tissue types that make up each organ. If you do, you will find it easier to understand the characteristics of a particular organ, and you will also improve your understanding of the integrated nature of the whole body.

MECHANISMS of DISEASE

TUMORS AND CANCER

The concept of tumors and cancer was introduced in Chapter 1, then expanded in Box 5-3 on p. 126. Because tumors are tissue abnormalities, we resume our discussion here. Keep in mind that these and other tissue abnormalities continue to be important in later chapters as well.

Neoplasms

The term **neoplasm** literally means "new matter" and refers to any abnormal growth of cells: another name for a neoplasm is **tumor.** Neoplasms can be distinct lumps of abnormal cells or, in blood tissue, can be diffuse. Neoplasms are often classified as **benign** or **malignant.** Benign tumors are called that because they do not spread to other tissues and they usually grow very slowly. Their cells are often well differentiated, unlike the undifferentiated cells typical of malignant tumors. Cells in a benign tumor tend to stay together, and they are often surrounded by a capsule of dense tissue. Benign tumors are not usually life threatening, but can be if they disrupt the normal function of a vital organ. Malignant tumors, or **cancers,** on the other hand, are not encapsulated and tend to spread to other regions of the body. For example, cells from malignant breast tumors usually form new (secondary) tumors in bone, brain, and lung tissues. The cells migrate by way of lymphatic or blood vessels. This manner of spreading is called **metastasis.** Cells that do not metastasize can spread another way: they grow rapidly and extend the tumor into nearby tissues (Figure 6-42). Malignant tumors may replace part of a vital organ with abnormal, undifferentiated tissue—a life-threatening situation.

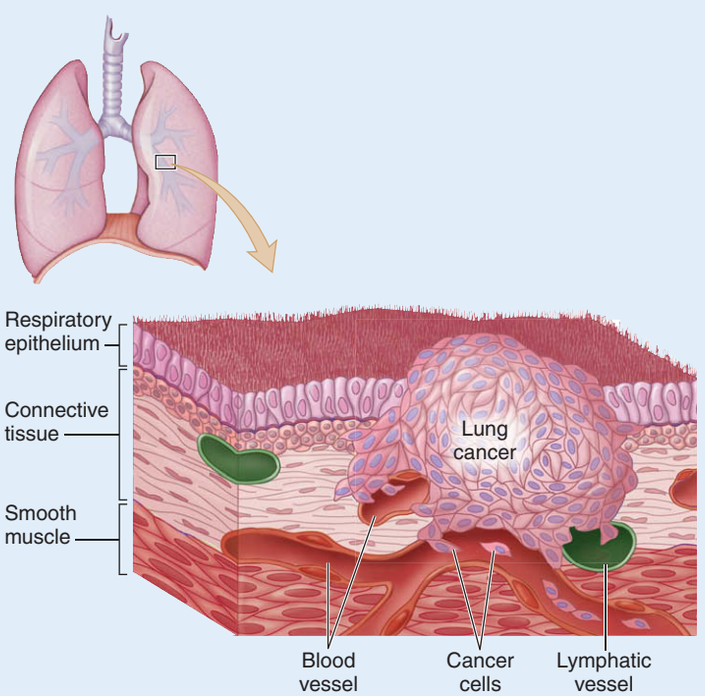


FIGURE 6-42

Cancer. This abnormal mass of proliferating cells in the lining of lung airways is a malignant tumor—lung cancer. Notice how some cancer cells are leaving the tumor and entering the blood and lymph vessels.

Neoplasms are classified further into subgroups, depending on the tissue in which they originate. Both benign and malignant tumors can be divided into three types: epithelial tumors, connective tissue tumors, and miscellaneous tumors. Benign tumor types that arise from epithelial tissues include *papilloma* (a finger-like projection), *adenoma* (glandular tumor), and *nevus* (small, pigmented skin tumors). Benign tumor types that arise from connective tissues include *lipoma* (adipose tumor), *osteoma* (bone tumor), and *chondroma* (cartilage tumor). Malignant tumors that arise from epithelial tissues are generally called **carcinomas.** Examples include *melanoma* (cancer of skin pigment cells) and *adenocarcinoma* (glandular cancer).

Malignant tumors that arise from connective tissues are generally called **sarcomas.** Examples include *lymphoma* (lymphatic cancer), *osteosarcoma* (bone cancer), and *fibrosarcoma* (cancer of fibrous connective tissue). Miscellaneous tumors are those that do not fit either of the previous categories. For example, an *adenofibroma* is a benign neoplasm formed by epithelial and connective tissues. Another example is *neuroblastoma*, a malignant tumor that arises from nerve tissue.

The etiologies (origins) of various forms of cancer puzzle medical science no less today than a hundred years ago. We do know that cancer involves uncontrolled cell division: **hyperplasia** (too many cells) and/or **anaplasia** (abnormal, undifferentiated cells). Thus the mechanism of all cancers is a mistake or problem in cell division. What we are uncertain of is the cause of the abnormal cell division. Currently, several factors are known to play a role.

Genetic Factors

Many forms of cancer are known to be inherited directly, perhaps involving abnormal "cancer genes" called **oncogenes.** Another type of gene, called a **tumor suppressor gene,** may fail to operate and thus allow cancer to develop. Exactly how these genes work is still being investigated. For example, a gene called *p53* springs into action at the first sign of cancer and initiates a chain reaction that causes the cell's death—before it can develop into full-blown cancer.

Presumably, many cancers involve a genetic predisposition (risk factor) coupled with other cancer-causing mechanisms. Cancers with known genetic risk factors include basal cell carcinoma (a type of skin cancer), breast cancer, and neuroblastoma (a cancer of nerve tissue).

Carcinogens

Carcinogens (cancer makers) are agents that affect genetic activity in some way and cause abnormal cell reproduction. Some carcinogens are **mutagens** (mutation makers) that cause changes or mutations in a cell's DNA structure. Although many industrial products are known to be carcinogens, various natural mineral, vegetable, and animal materials are also carcinogenic. Exposure to damaging types of radiation or other physical injuries can be carcinogenic. For example, sunburns or chronic exposure to sunlight can cause skin cancer. Even viruses have been known to cause cancer, perhaps by altering the genetic code of cells during an infection or by damaging the body's ability to suppress cancer. Papilloma (wart) viruses have been blamed for many cases of cervical cancer in women.

Age

Certain cancers are found primarily in young people (e.g., leukemia) and others primarily in older adults (e.g., colon cancer). The age factor may result from changes in the genetic activity of cells over time or from the accumulated effects of cell damage.

Detection and Treatment of Cancer

Signs of cancer are those one would expect of a malignant neoplasm: the appearance of abnormal, rapidly growing tissue. Cancer specialists, or *oncologists*, have stressed that early detection of cancer is important because it is in the early stages of development of primary tumors, before metastasis and the development of secondary tumors have begun, that cancer is most treatable. Some methods currently used to detect the presence of cancer include the following:

Self-examination for the early signs of cancer previously described is one method for detection of cancer. For example, women are encouraged to perform a monthly breast self-examination. Likewise, males are encouraged to perform a monthly testicular self-examination. If an abnormality is found, it can be further investigated with one of the following described methods.

Medical imaging techniques that visualize deep tissues for medical study are often used to detect cancers. Radiography (x-ray photography) often is used to detect the presence of tumors. *Mammography*, x-ray photography of a breast, is considered an important detection tool for this type of cancer. *Computed tomography (CT)* (x-ray scanning), *magnetic resonance imaging (MRI)* (electromagnetic scanning), and *ultrasonography* (ultrasound scanning) produce cross-sectional images of body regions suspected of having tumors.

| A&P CONNECT |

Check out ***Medical Imaging of the Body*** online at ***A&P Connect*** to see diagrams of medical imaging technology and examples of the images produced by them.



Blood tests to determine the concentration of ions, enzymes, or other blood components are useful in detecting cancer when the results show abnormalities associated with particular forms of cancer. Cancer cells may also produce or trigger the production of substances often referred to as *tumor markers*. For example, tests for a prostate cancer marker are now being used in conjunction with other diagnostic tests.

Biopsy is the removal and examination of living tissue. Microscopic examination of tumor tissue removed surgically or through a needle sometimes reveals whether it is malignant or benign.

The information gained from these techniques can be used to *stage* and *grade* malignant tumors. Staging involves classifying a tumor based on its size and the extent of its spread. Grading is an

assessment of what the tumor is likely to do based on the degree of abnormality of the cells—a useful basis for making a prognosis (statement of probable outcome).

Without treatment, cancer usually results in death. The progress of a particular type of cancer depends on the type of cancer and its location. Many cancer patients suffer from *cachexia*, a syndrome involving loss of appetite, weight loss, and general weakness. Various anatomical or functional abnormalities may arise as a result of damage to particular organs. The ultimate causes of death in cancer patients include secondary infection by pathogenic microorganisms, organ failure, hemorrhage (blood loss), and in some cases, undetermined factors.

Of course, once cancer has been identified, every effort is made to treat it and thus prevent or delay its development. Surgical removal of cancerous tumors is sometimes performed, but the probability that malignant cells have been left behind must be addressed. **Chemotherapy,** or "chemical therapy" with *cytotoxic* (cell-killing) compounds or antineoplastic drugs, can be used after surgery to destroy any remaining malignant cells. **Radiation therapy,** also called *radiotherapy*, involves the use of destructive x-ray or gamma radiation alone or with chemotherapy to destroy any remaining cancer cells. **Laser therapy,** in which an intense beam of light destroys a tumor, is also sometimes coupled with chemotherapy or radiation therapy. **Immunotherapy,** a newer type of cancer treatment, bolsters the body's own defenses against cancer cells. Because viruses cause some types of cancer, oncologists hope that vaccines against certain forms of cancer will greatly reduce cancer risk.

Perhaps the most promising research area in the battle against cancer is *molecular oncology*. This rapidly growing medical specialty attempts to use advances in molecular biology and genetics to develop so-called *rational drugs* that unlike conventional chemotherapy agents, target only those specific molecules, enzymes, receptors, or other features unique to cancer cells or tumor growth. Ideally, such treatments would affect only the cancer and spare normal cells and body functions, thus increasing efficiency and reducing side effects. Three of the most promising new classes of "rational" drugs used to treat various types of cancer include the following:

Monoclonal antibodies, for example, trastuzumab (Herceptin) for breast cancer and cetuximab (Erbitux) for colorectal cancer

Antiangiogenesis (anti–blood vessel formation) *agents*, for example, vascular endothelial growth factor (VEGF) for various solid tumors

Tyrosine kinase inhibitors (enzyme inhibitors), for example, imatinib mesylate (Gleevec) for chronic myeloid leukemia

Some oncologists believe that future advances in rational drug design could mean for cancer what antibiotics meant for infectious diseases.

LANGUAGE OF SCIENCE (continued from p. 131)

chondrocyte
(KON-droh-syte)
[*chondro-* **cartilage**, *-cyte* **cell**]

collagen
(KAHL-ah-jen)
[*colla-* **glue**, *-gen* **produce**]

collagenous dense fibrous tissue
(kah-LAJ-ehnus dense FYE-brus TISH-yoo)
[*colla-* **glue**, *-gen* **produce**, *dense* **thick**, *fibro-* **fiber**, *-ous* **relating to**, *tissu-* **fabric**]

columnar
(koh-LUM-nar)
[*column-* **column**, *-ar* **relating to**]

compact bone tissue
(kom-PAKT)
[*compact* **to put together**, *tissu-* **fabric**]

compound
[*compound* **put together**]

connective tissue
(koh-NEK-tiv TISH-yoo)
[*con-* **together**, *-nect-* **bind**, *-ive* **relating to**, *tissu-* **fabric**]

connective tissue membrane
(koh-NEK-tiv)
[*con-* **together**, *-nect-* **bind**, *-ive* **relating to**, *tissu-* **fabric**, *membran-* **thin skin**]

cuboidal
(KYOO-boyd-al)
[*cub-* **cube**, *-oid* **like**, *-al* **relating to**]

cutaneous membrane
(kyoo-TAYN-ee-us)
[*cut-* **skin**, *-aneous* **relating to**, *membran-* **thin skin**].

dendrite
(DEN-dryte)
[*dendr-* **tree**, *-ite* **part** (**branch**) **of**]

dense fibrous tissue
(dense FYE-brus TISH-yoo)
[*dense* **thick**, *fibro-* **fiber**, *-ous* **relating to**, *connect-* **bind**, *-ive* **relating to**, *tissu-* **fabric**]

desmosome
(DES-moh-sohms)
[*desmo-* **band**, *-som-* **body**]

ectoderm
(EK-toh-derm)
[*ecto-* **outside**, *-derm* **skin**]

elastic cartilage
(eh-LAS-tik KAR-ti-lij)
[*elast-* **to drive or beat out**, *-ic* **relating to**, *cartilag* **cartilage**]

elastic dense fibrous tissue
(eh-LAS-tik dense FYE-brus TISH-yoo)
[*elast-* **to drive or beat out**, *-ic* **relating to**, *dense* **thick**, *fibr* **fiber**, *tissu-* **fabric**]

elastin
(e-LAS-tin)
[*elast-* **drive or beat out**, *-in* **substance**]

endochondral ossification
(en-doh-KON-dral osi- fi-KAY-shun)
[*endo-* **inward or within**, *-chondr-* **cartilage**, *-al* **relating to**, *oss-* **bone**, *-fication* **to make**]

endocrine gland
(EN-doh-krin)
[*endo-* **inward or within**, *-crin-* **secrete**, *gland* **acorn**]

endoderm
(EN-doh-derm)
[*endo-* **inward or within**, *-derm* **skin**]

endothelium
(en-doh-THEE-lee-um)
[*endo-* **inward or within**, *-theli-* **nipple**, *-um* **thing**] *pl.*, endothelia

epithelial membrane
(ep-i-THEE-lee-al)
[*epi-* **on or upon**, *-theli* **nipple**, *-al* **relating to**, *membran-* **thin skin**]

epithelial tissue
(ep-i-THEE-lee-al)
[*epi-* **on or upon**, *-theli-* **nipple**, *-al* **relating to**, *tissu-***fabric**]

epithelium
(ep-i-THEE-lee-um)
[*epi-* **on or upon**, *theli-* **nipple**, *-um* **thing**] *pl.*, epithelia

erythrocyte
(eh-RITH-roh-syte)
[*erythro-* **red**, *-cyte* **cell**]

excretion
(eks-KREE-shun)
[*excret-* **to separate**, *-tion* **process**]

exocrine gland
(EK-soh-krin)
[*exo-* **outside or outward**, *-crin-* **secrete**, *gland* **acorn**]

extracellular matrix (ECM)
(eks-trah-SEL-yoolar MAY-triks) [*extra-* **beyond**, *-cell-* **storeroom**, *-ular* **relating to**, *matrix* **womb**] *pl.,* matrices]

fascia
(FASH-ee-ah) [*fascia* **band**]

fibroblast
(FYE-broh-blast) [*fibro-* **fiber**, *-blast* **bud**]

fibrocartilage
(fye-broh-KAR-ti-lij) [*fibro-* **fiber**, *-cartilage* **cartilage**]

formed element

gland
[*gland* **acorn**]

glandular
(GLAN-dyoo-lar) [*gland-* **acorn** (**gland**), *-ula-* **little**, *-ar* **relating to**]

hematopoietic tissue
(hee-mah-toh-poy-ET-ik) [*hema-* **blood**, *-poie-* **to make**, *-ic* **relating to**, *tissu-* **fabric**]

histamine
(HIS-tah-meen) [*hist-* **tissue**, *-amine* **ammonia compound**]

histogenesis
(his-toh-JEN-eh-sis) [*histo-* **tissue**, *-genesis* **origin**]

histology
(his-TOL-oh-jee) [*histo-* **tissue**, *-o-* **combining form**, *-log-* **words** (**study of**), *-y* **activity**]

hyaline cartilage
(HYE-ah-lin KAR-ti-lij) [*hyaline* **of glass**, *cartilage* **cartilage**]

interstitial fluid (IF)
(in-ter-STISH-al) [*inter-* **between**, *-stit-* **stand**, *-al* **relating to**]

lacuna
(lah-KOO-nay) [*lacuna* **pit**] *pl*,. **lacunae**

lamella
(lah-MEL-eye) [*lam-* **plate**, *-ella* **little**] *pl.,* lamellae

lamina propria
(LAM-in-ah PROH-pree-ah) [*lamina* **thin plate**, *propria* **proper**]

leukocyte
(LOO-koh-syte) [*leuko-* **white**, *-cyte* **cell**]

loose fibrous connective tissue
(LOOS FYE-brus koh-NEK-tiv TISH-yoo)

macrophage
(MAK-roh-fayj) [*macro-* **large**, *-phag-* **eat**]

mast cell
[*mast* **fattening**, *cell* **storeroom**]

matrix
(MAY-triks) [*matrix* **womb**] *pl.,* matrices

membrane
[*membran-* **thin skin**]

membrane bone
[*membran-* **thin skin**]

membranous
(MEM-brah-nus) [*membran-* **thin skin**, *-ous* **characterized by**]

mesoderm
(MEZ-oh-derm) [*meso-* **middle**, *-derm* **skin**]

mesothelium
(mez-oh-THEE-lee-um) [*meso-* **middle or median**, *-theli-* **nipple**, *-um* **thing**] *pl.,* mesothelia

microvillus
(my-kroh-VIL-us) [*micro-* **small**, *-villi* **shaggy hairs**] *pl.,* microvilli

mucus
(MYOO-kus) [*mucus* **slime**]

mucous membrane
(MYOO-kus) [*muc-* **slime**, *-ous* **characterized by**, *membran-* **thin skin**]

multicellular gland
[*multi-* **many**, *-cell-* **storeroom**, *-ular* **relating to**, *gland* **acorn**]

muscle tissue
(MUSS-el TISH-yoo) [*mus-* **mouse**, *-cle* **small**, *tissu-* **fabric**]

nervous tissue
[*nervous* **relating to nerves**, *tissu-* **fabric**]

neuroglia
(noo-ROG-lee-ah) [*neuro-* **nerve**, *-glia* **glue**] *sing.,* **neuroglial cell**

neuron
(NOO-ron) [*neuron* **string or nerve**]

osteoblast
(OS-tee-oh-blast) [*osteo-* **bone**, *-blast* **bud**]

osteoclast
(OS-tee-oh-klast) [*osteo-* **bone**, *-clast* **break**]

osteocyte
(OS-tee-oh-syte) [*osteo-* **bone**, *-cyte* **cell**]

osteon
(OS-tee-on) [*osteo-* **bone**, *-on* **unit**]

perichondrium
(pair-i-KON-dree-um) [*peri-* **around**, *-chondr-* **cartilage**, *-um* **thing**] *pl.,* perichondria

plasma
(PLAZ-mah) [*plasma* **substance**]

primary germ layer

proteoglycan
(PRO-tee-oh-GLYE-kan) [*proteo-* **protein**, *-glycan* **polysaccharide** (**from** *-glyc-* **sweet**)]

pseudostratified columnar epithelium
(SOOD-oh-STRAT-i-fyed koh-LUM-nar ep-i-THEE-lee-um) [*pseudo-* **false**, *-strati-* **layer**, *-fied* **to be made**, *column-* **column**, *-ar* **characterized by**] *pl.,* epithelia

regeneration
(ree-jen-er-AY-shun) [*re-* **again**, *generat-* **produce**, *-tion* **process**]

reticular tissue
(reh-TIK-yoo-lar) [*ret-* **net**, *-ic-* **relating to**, *-ul-* **little**, *-ar* **characterized by**, *tissu-* **fabric**]

secretion
(se-KREE-shun) [*secret-* **separate**, *-tion* **process**]

serous membrane
(SEE-rus) [*sero-* **watery body fluid**, *-ous* **characterized by**, *membran-* **thin skin**]

simple epithelium
(ep-i-THEE-lee-um) [*simple* **not mixed**, *epi-* **on**, *-theli-* **nipple**, *-um* **thing**] *pl.,* epithelia

skeletal muscle tissue
(SKEL-eh-tal) [*skeleto-* **dried body**, *-al* **relating to**, *mus-* **mouse**, *-cle* **small**, *tissu-* **fabric**]

skin

smooth muscle tissue
[*mus-* **mouse**, *-cle* **small**, *tissu-* **fabric**]

soma
(soh-mah) [*soma* **body**]

squamous
(SKWAY-muss) [*squam-* **scale**, *-ous* **characterized by**]

stratified epithelium
(STRAT-i-fyde ep-i-THEE-lee-um) [*strati-* **layer**, *epi-* **on**, *-theli-* **nipple**, *-um* **thing**] *pl.,* epithelia

synovial fluid
(si-NO-vee-all) [*syn-* **together**, *-ovi-* **egg (white)**, *-al* **relating to**, *fluid* **flow**]

ynovial membrane
(si-NO-vee-all) [*syn-* **together**, *-ovi-* **egg (white)**, *-al* **relating to**, *membran-* **thin skin**]

thrombocyte
(THROM-boh-syte) [*thrombo-* **clot**, *-cyte* **cell**]

tight junction

trabecula
(trah-BEK-yoo-la) [*trab-* **beam**, *-ula* **little**] *pl.,* trabeculae

transitional epithelium
(tran-ZISH-en-al ep-i-THEE-lee-um) [*trans-* **across**, *-tion* **process**, *epi-* on, *-theli-* **nipple**, *-um* **thing**] *pl.,* epithelium

tubular
(TOOB-yoo-lar) [*tub-* **tube**, *-ul-* **little**, *-ar* **relating to**]

unicellular gland
(yoon-ih-SEL-yoo-lar) [*uni-* **one**, *-cell-* **storeroom**, *-ular* **relating to**, *gland* **acorn**]

LANGUAGE OF MEDICINE *(continued from p. 161)*

anaplasia
(an-ah-PLAY-zee-ah)
[*ana-* **without,** *-plasia* **shape**]

benign
(bee-NYNE)
[*benign* **kind**]

biopsy
(BYE-op-see)
[*bio-* **life,** *-ops-* **view,** *-y* **act of**]

cancer
[*cancer* **crab or malignant tumor**]

carcinogen
(kar-SIN-oh-jen)
[*carcino-* **cancer,** *-gen* **produce**]

carcinoma
(kar-si-NO-mah)
[*carcin-* **cancer,** *-oma* **tumor**]

chemotherapy
(kee-moh-THAYR-ah-pee)
[*chemo-* **chemical,** *-therapy* **treatment**]

hyperplasia
(hye-per-PLAY-zee-ah)
[*hyper-* **excessive,** *-plasia* **shape**]

immunotherapy
(im-yoo-no-THAYR-ah-pee)
[*immuno-* **free,** *-therapy* **treatment**]

keloid
(KEE-loyd)
[*kel-* **claw,** *-oid* **like**]

laser therapy
(LAY-zer THAYR-ah-pee)
[*laser* **shortened "light amplification by stimulated emission of radiation"**]

malignant
(mah-LIG-nant)
[*malign* **bad**]

metastasis
(meh-TAS-tah-sis)
[*meta-* **change,** *-stasis* **standing**]

mutagen
(MYOO-tah-jen)
[*muta-* **change,** *-gen* **produce**]

neoplasm
(NEE-oh-plaz-em)
[*neo-* **new,** *-plasm* **formation**]

oncogene
(ON-koh-jeen)
[*onco-* **tumor,** *-gen-* **produce**]

peritonitis
(pair-i-toh-NYE-tis)
[*peri-* **around,** *-ton-* **to stretch,** *-itis* **inflammation**]

pleurisy
(PLOOR-i-see)
[*pleur-* **rib,** *-itis* **inflammation**]

radiation therapy
(ray-dee-AY-shun THAYR-ah-pee)
[*radiat-* **to emit rays,** *-tion* **process,** *therapy* **treatment**]

sarcoma
(SAR-koh-mah)
[*sarco-* **flesh,** *-oma* **tumor**]

scar

stem cell

tumor
(TOO-mer)
[*tumor* **swelling**]

tumor suppressor gene
(TOO-mer soo-PRESS-or jeen)
[*tumor* **swelling,** *suppress-* **press down,** *-or* **agent,** *gen-* **produce or generate**]

CASE study



Nathan had been mountain biking for about 2 hours, winding his way up and down the familiar trails with a devil-may-care attitude. Pedaling at a break-neck speed, he swerved around a fallen branch as he headed down the last steep incline, and suddenly he lost control and went flying off his bike. After rolling over a couple of times, he stopped hard, jamming his right foot against a boulder. His friends helped him limp the rest of the way down the hill and back to their car; then they drove him to the urgent care center (which was almost as familiar to Nathan as the trails).

The physician's assistant ordered an x-ray film of Nathan's leg to confirm no break in the bones. She came back soon with the results and told Nathan that there was no break, just "soft tissue damage" (i.e., a sprained ankle). By "soft tissue," she meant the tendons and ligaments that hold all of the bones of the foot and ankle together.

1. What specific tissue type did Nathan injure?
   a. Dense irregular connective tissue
   b. Skeletal muscle
   c. Dense regular connective tissue
   d. Reticular connective tissue

The bones in Nathan's ankle and foot are connected by joints (discussed in Chapter 10).

2. The tips of these bones are covered with what type of tissue?
   a. Fibrocartilage
   b. Transitional epithelium
   c. Stratified cuboidal epithelium
   d. Hyaline cartilage

In addition to spraining his ankle, Nathan cut his arm in the fall. He had a deep gash that required five stitches to close.

3. What type of membrane did the stitches go through?
   a. Cutaneous
   b. Serous
   c. Mucous
   d. Epidermal

4. In the membrane through which the stitches passed, which layer connects the epithelial layer to the connective tissue layer?
   a. Membrane glue
   b. Basement membrane
   c. Intercellular membrane
   d. Epithelial-connective lamina

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CAREER choices



Jean A. Proehl, RN, MN, CEN, CCRN

Emergency Clinical Nurse Specialist

As an emergency clinical nurse specialist at Dartmouth Hitchcock Medical Center in Lebanon, New Hampshire, my responsibilities involve the nursing care delivered to emergency patients. I teach classes, orient new nurses, evaluate supplies and equipment, troubleshoot patient care problems, set up systems to enhance care delivery, and help take care of patients.

I've wanted to be a nurse since I was 4 or 5 years old. I was drawn to the emergency care setting because I like action and variety. We see it all, cradle to grave, benign to life threatening. I've delivered babies in the parking lot; I've reassured parents that their child's "blue" hands are related to a new pair of jeans. I've seen teenagers with "lesions" that turned out to be pimples; I've held the hands of the dying as I administered blood to try to save their lives.

Change is a current trend in my field; new medications, new equipment, and new therapies are constantly being introduced. The reassuring thing about change in the twenty-first century is that it is more likely to be evidence based than in the past. In other words, we have scientific data to support doing things differently. We're questioning things we've always done and evaluating them in terms of their impact on the patient's outcome.

When I'm taking care of patients, the rewards are obvious: relief of pain and suffering (physical and emotional), saving lives, and helping people return to an optimum state of health. When I'm teaching other nurses, the reward is in promoting improved knowledge and skills so that the professional practice of the nurse is enhanced and the care that she or he delivers to patients is improved.

I use anatomy specifically for accurate and concise descriptions of my physical examination findings. Physiology is interwoven into the patient's overall care. In assessment, I relate the signs, symptoms, and laboratory results to potential underlying physiological causes. When implementing interventions such as medication administration or positioning, I must consider their intended effect on the patient and potential adverse affects. To evaluate the effectiveness of interventions, I rely on my understanding of physiology to gauge outcome. For example, if I am giving intravenous fluid to a patient in shock, I know that the glomerular filtration rate reflects perfusion to vital organs, so urine output is a valuable parameter to monitor.

One professor I had always emphasized that nurses needed to know anatomy because some day we might be the only one available who could identify something. I found an anatomy coloring book to be a great study aid. Mnemonics were also a lifesaver; I still recite "On Old Olympus' Tiny Tops A Friendly Viking Grew Vines And Hops" when naming cranial nerves.

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

INTRODUCTION

A. Tissue—group of similar cells that perform a common function
B. Matrix—nonliving intercellular material

PRINCIPAL TYPES OF TISSUE (TABLE 6-1)

A. Epithelial tissue
B. Connective tissue
C. Muscle tissue
D. Nervous tissue
E. Embryonic development of tissues
   1. Primary germ layers
      a. Endoderm
      b. Mesoderm
      c. Ectoderm
   2. Histogenesis—the process of the primary germ layers differentiating into different kinds of tissue

EXTRACELLULAR MATRIX (ECM)

A. Complex, nonliving material between cells in a tissue (Figure 6-1)
   1. Some tissues have a large amount of ECM; other tissues have hardly any ECM
   2. Different kinds of components give ECM in different tissues a variety of characteristics
B. Components (Table 6-2)
   1. Water
   2. Proteins
      a. Structural proteins
         (1) Collagen—strong, flexible protein fiber
         (2) Elastin—elastic fibers
      b. Includes glycoproteins—proteins with a few carbohydrate attachments
         (1) Fibronectin and laminin help connect the ECM components to cells by binding with integrins in plasma membranes
         (2) Glycoprotein attachments also allow local communication within a tissue

3. Proteoglycans
   a. Defined as hybrid molecules that are mostly carbohydrates attached to a protein backbone
   b. Examples: chondroitin sulfate, heparin, and hyaluronate
   c. Different proteoglycans give different characteristics to ECM, such as thickness, shock absorption (Table 6-2)

C. Functions
1. Help bind tissues together structurally
   a. ECM components bind to each other and to integrins in plasma membranes of cells
   b. In some tissues, it is primarily intercellular junctions that hold cells together
2. Allow local communication among ECM and various cells—through connection via integrins in plasma membranes

EPITHELIAL TISSUE

A. Types and locations
1. Epithelium is divided into two types:
   a. Membranous (covering or lining) epithelium
   b. Glandular epithelium
2. Locations
   a. Membranous epithelium—covers the body and some of its parts; lines the serous cavities, blood and lymphatic vessels, and respiratory, digestive, and genitourinary tracts
   b. Glandular epithelium—secretory units of endocrine and exocrine glands

B. Functions
1. Protection
2. Sensory functions
3. Secretion
4. Absorption
5. Excretion

C. Generalizations about epithelial tissue
1. Limited amount of matrix material
2. Membranous type attached to a basement membrane
3. Avascular
4. Cells are in close proximity, with many desmosomes and tight junctions
5. Capable of reproduction

D. Classification of epithelial tissue
1. Membranous (covering or lining) epithelium (Table 6-3)
   a. Classification based on cell shape (Figure 6-2)
      (1) Squamous
      (2) Cuboidal
      (3) Columnar
      (4) Pseudostratified columnar
   b. Classifications based on layers of cells (Table 6-4)
      (1) Simple epithelium
         (a) Simple squamous epithelium (Figures 6-3 and 6-4)
            (i) One-cell layer of flat cells
            (ii) Permeable to many substances
            (iii) Examples: endothelium—lines blood vessels; mesothelium—pleura
         (b) Simple cuboidal epithelium (Figure 6-5)
            (i) One-cell layer of cuboidal-shaped cells
            (ii) Found in many glands and ducts
         (c) Simple columnar epithelium (Figure 6-6)
            (i) Single layer of tall, column-shaped cells
            (ii) Cells often modified for certain functions such as goblet cells (secretion), cilia (movement), microvilli (absorption)
            (iii) Often lines hollow visceral structures
         (d) Pseudostratified columnar epithelium (Figure 6-7)
            (i) Columnar cells of differing heights
            (ii) All cells rest on basement membrane but may not reach the free surface above
            (iii) Cell nuclei at odd and irregular levels
            (iv) Line the air passages and segments of male reproductive system
            (v) Motile cilia and mucus are important modifications
      (2) Stratified epithelium
         (a) Keratinized stratified squamous epithelium
            (i) Multiple layers of flat, squamous cells (Figure 6-8)
            (ii) Cells filled with keratin
            (iii) Covering outer skin on body surface
         (b) Nonkeratinized stratified squamous epithelium (Figure 6-9)
            (i) Line the vagina, mouth, and esophagus
            (ii) Free surface is moist
            (iii) Primary function is protection
         (c) Stratified cuboidal epithelium
            (i) Two or more rows of cells are typical
            (ii) Basement membrane is indistinct
            (iii) Located in sweat gland ducts and pharynx
         (d) Stratified columnar epithelium
            (i) Multiple layers of columnar cells
            (ii) Only most superficial cells are typical in shape
            (iii) Rare
            (iv) Located in segments of male urethra and near anus
         (e) Transitional epithelium (Figure 6-10)
            (i) Located in lining of hollow viscera subjected to stress (e.g., urinary bladder)
            (ii) Stratified—often 10 or more layers thick
            (iii) Protects organ walls from tearing
2. Glandular epithelium
   a. Specialized for secretory activity
   b. Exocrine glands—discharge secretions into ducts
   c. Endocrine glands—"ductless" glands; discharge secretions directly into blood or interstitial fluid
   d. Structural classification of exocrine glands (Figure 6-11; Table 6-5)
      (1) Multicellular exocrine glands are classified by the shape of their ducts and the complexity of their duct system
      (2) Shapes include tubular and alveolar

(3) Simple exocrine glands—only one duct leads to the surface
(4) Compound exocrine glands—have two or more ducts
e. Functional classification of exocrine glands (Figure 6-12)
(1) Apocrine glands
(a) Secretory products collect near apex of cell and are secreted by pinching off the distended end
(b) Secretion process results in some damage to cell's plasma membrane and some loss of cytoplasm
(c) Mammary glands are good examples of this secretory type
(2) Holocrine glands
(a) Secretion products, when released, cause rupture and death of the cell
(b) Sebaceous glands are holocrine
(3) Merocrine glands
(a) Secrete directly through cell membrane
(b) Secretion proceeds with no damage to plasma membrane and no loss of cytoplasm
(c) Most numerous gland type

CONNECTIVE TISSUE

A. Functions, characteristics, and types
1. General function—connects, supports, transports, and protects
2. General structure
a. Extracellular matrix (ECM) predominates in most connective tissues and determines its physical characteristics; consists of fluid, gel, or solid matrix, with or without extracellular fibers (collagenous, reticular, and elastic) and proteoglycans or other compounds that thicken and hold together the tissue (Figures 6-1 and 6-15)
b. Collagenous fibers—twisted ropes that form strong, flexible bundles in many connective tissues (Figure 6-13)
c. Elastic fibers—stretchy fibers made of elastin that impart the ability to recoil in some connective tissues (Figure 6-14)
3. Four main types (Table 6-6)
a. Fibrous (connective tissue proper)
(1) Loose fibrous (areolar)
(2) Adipose
(3) Reticular
(4) Dense
(a) Irregular
(b) Regular (collagenous and elastic)
b. Bone
(1) Compact bone
(2) Cancellous bone
c. Cartilage
(1) Hyaline
(2) Fibrocartilage
(3) Elastic
d. Blood

B. Fibrous connective tissue
1. Loose fibrous (areolar) connective tissue (Figure 6-15)
a. One of the most widely distributed of all tissues
b. Intercellular substance is prominent and consists of collagenous and elastic fibers loosely interwoven and embedded in soft viscous ground substance
c. Several kinds of cells present, notably, fibroblasts and macrophages, also mast cells, plasma cells, fat cells, and some white blood cells (Figure 6-16)
d. Function—stretchy, flexible connection
2. Adipose tissue (Figures 6-17 and 6-18)
a. Similar to loose fibrous connective tissue but contains mainly fat cells
b. Functions
(1) Acts as food (energy) reserve, support, protection, insulation (white fat), and heat generation (brown fat)
(2) Produces the hormone leptin, which signals the brain how much fat is stored
3. Reticular tissue (Figure 6-19)
a. Forms framework of spleen, lymph nodes, and bone marrow
b. Consists of network of branching reticular fibers with reticular cells overlying them
c. Functions—defense against microorganisms and other injurious substances; reticular meshwork filters out injurious particles and reticular cells phagocytose them
4. Dense fibrous tissue
a. Matrix consists mainly of fibers packed densely and relatively few fibroblast cells
(1) Irregular—fibers intertwine irregularly to form a thick mat (Figure 6-20)
(2) Regular—bundles of fibers are arranged in regular parallel rows
(a) Collagenous—mostly collagenous fibers in ECM (Figures 6-21 and 6-22)
(b) Elastic—mostly elastic fibers in ECM (Figure 6-23)
b. Locations—composes structures that need great tensile strength, such as tendons and ligaments; also dermis and the outer capsule of the kidney and spleen
c. Function—furnishes flexible connections that are strong or stretchy

C. Bone tissue
1. Uniquely hard and strong connective tissue type
a. Cells—osteocytes—embedded in a calcified matrix
b. Inorganic component of matrix accounts for 65% of total bone tissue
2. Functions
a. Support
b. Protection
c. Point of attachment for muscles
d. Reservoir for minerals

e. Supports blood-forming tissue
3. Compact bone (Figures 6-25 and 6-26)
a. Osteon (Haversian system)
(1) Structural unity of bone
(2) Spaces for osteocytes called *lacunae*
(3) Matrix present in concentric rings called *lamellae*
(4) Canaliculi are canals that join lacunae with the central Haversian canal
b. Cell types
(1) Osteocyte—mature, inactive bone cell
(2) Osteoblast—active bone-forming cell
(3) Osteoclast—bone-destroying cell
c. Formation (ossification) (Figure 6-24)
(1) In membranes—e.g., flat bones of skull
(2) From cartilage (endochondral)—e.g., long bones, such as the humerus
4. Cancellous bone (Figures 6-25 and 6-27)
a. Trabeculae—thin beams of bone
b. Supports red bone marrow
(1) Myeloid tissue—a type of reticular tissue
(2) Produces blood cells
c. Called spongy bone because of its spongelike appearance

D. Cartilage
1. Chondrocyte is the only cell type present
2. Lacunae house cells as in bone
3. Avascular—therefore nutrition of cells depends on diffusion of nutrients through matrix
4. Heals slowly after injury because of slow nutrient transfer to cells
5. Perichondrium is membrane that surrounds cartilage
6. Types
a. Hyaline (Figure 6-28)
(1) Appearance is shiny and translucent
(2) Most prevalent type of cartilage
(3) Located on ends of articulating bones
b. Fibrocartilage (Figure 6-29)
(1) Strongest and most durable type of cartilage
(2) Matrix is semirigid and filled with strong white fibers
(3) Found in intervertebral disks and pubic symphysis
(4) Serves as shock-absorbing material between bones at the knee (menisci)
c. Elastic (Figure 6-30)
(1) Contains many fine elastic fibers
(2) Provides strength and flexibility
(3) Located in external ear and larynx

E. Blood
1. A liquid tissue (Figure 6-31)
2. Contains neither ground substance nor fibers
3. Composition of whole blood
a. Liquid fraction (plasma) is the matrix—55% of total blood volume
b. Formed elements contribute 45% of total blood volume
(1) Red blood cells, erythrocytes
(2) White blood cells, leukocytes
(3) Platelets, thrombocytes
4. Functions
a. Transportation
b. Regulation of body temperature
c. Regulation of body pH
d. White blood cells destroy bacteria
5. Circulating blood tissue is formed in the red bone marrow by a process called *hematopoiesis*; the blood-forming tissue is sometimes called *hematopoietic tissue*

MUSCLE TISSUE

A. Types (Table 6-7)
1. Skeletal, or striated voluntary (Figure 6-32)
2. Smooth, or nonstriated involuntary, or visceral (Figures 6-33 and 6-34)
3. Cardiac, or striated involuntary (Figure 6-35)

B. Microscopic characteristics
1. Skeletal muscle—threadlike cells with many cross striations and many nuclei per cell
2. Smooth muscle—elongated narrow cells, no cross striations, one nucleus per cell
3. Cardiac muscle—branching cells with intercalated disks (formed by abutment of plasma membranes of two cells)

NERVOUS TISSUE

A. Functions—rapid regulation and integration of body activities

B. Special characteristics
1. Excitability
2. Conductivity

C. Organs
1. Brain
2. Spinal cord
3. Nerves

D. Cell types (Table 6-7)
1. Neuron—conducting unit of system (Figure 6-36)
a. Cell body, or soma
b. Processes
(1) Axon (single process)—transmits nerve impulse away from the cell body
(2) Dendrite (one or more)—transmits nerve impulse toward the cell body and axon
2. Neuroglia—special connecting, supporting, coordinating cells that surround neurons

TISSUE REPAIR

A. Tissues have a varying capacity to repair themselves; damaged tissue regenerates or is replaced by scar tissue

B. Regeneration—growth of new tissue (Figure 6-37)

C. Scar—dense fibrous mass; unusually thick scar is a keloid (Figure 6-38)

D. Epithelial and connective tissues have the greatest ability to regenerate

E. Muscle and nervous tissues have limited capacity to regenerate

BODY MEMBRANES

A. Thin tissue layers that cover surfaces, line cavities, and divide spaces or organs (Figure 6-39, Table 6-8)
B. Epithelial membranes are most common type (Figure 6-40)
   1. Cutaneous membrane (skin)
      a. Primary organ of integumentary system
      b. One of the most important organs
      c. Composes approximately 16% of body weight
   2. Serous membrane (serosa)
   a. Parietal membranes—line closed body cavities
   b. Visceral membranes—cover visceral organs
   c. Pleura—surrounds a lung and lines the thoracic cavity
   d. Peritoneum—covers the abdominal viscera and lines the abdominal cavity
   3. Mucous membrane (mucosa)
      a. Lines and protects organs that open to the exterior of the body
      b. Found lining ducts and passageways of the respiratory, digestive, and other tracts
      c. Lamina propria—fibrous connective tissue underlying mucous epithelium
      d. Mucus is made up mostly of water and mucins—proteoglycans that form a double-layer protection against environmental microbes (Figure 6-41)
C. Connective tissue membranes
   1. Do not contain epithelial components
   2. Synovial membranes—line the spaces between bone in joints
   3. Have smooth and slick membranes that secrete synovial fluid
   4. Help reduce friction between opposing surfaces in a movable joint
   5. Synovial membranes also line bursae

THE BIG PICTURE: TISSUES, MEMBRANES, AND THE WHOLE BODY

A. Tissues and membranes maintain homeostasis
   1. Epithelial tissues
      a. Form membranes that contain and protect the internal fluid environment
      b. Absorb nutrients
      c. Secrete products that regulate functions involved in homeostasis
   2. Connective tissues
      a. Hold organs and systems together
      b. Form structures that support the body and permit movement
   3. Muscle tissues
      a. Work with connective tissues to permit movement
   4. Nervous tissues
      a. Work with glandular epithelial tissue to regulate body function

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Define the term *tissue* and identify the four principal tissue types.
2. What is the function of the primary germ layers? Name them.
3. What are the five most important functions of epithelial tissue?
4. Which of the following best describes the number of blood vessels in epithelial tissue: none, very few, very numerous?
5. Explain how the shape of epithelial cells is used for classification purposes. Identify the four types of epithelium described in this classification process.
6. Classify epithelium according to the layers of cells present.
7. List the types of simple and stratified epithelium and give examples of each.
8. What is glandular epithelium? Give examples.
9. Discuss the structural classification of exocrine glands. Give examples of each type.
10. Describe loose fibrous connective tissue.
11. How do the types of dense fibrous connective tissue differ from one another?
12. Discuss and compare the microscopic anatomy of bone and cartilage tissue.
13. Compare the structure of the three major types of cartilage tissue. Locate and give an example of each type.
14. List the components of whole blood and discuss the basic function of each fraction or cell type.
15. List the three major types of muscle tissue.
16. Identify the two basic types of cells in nervous tissue.
17. What are the four cardinal signs of inflammation? What causes each?
18. Describe the regenerative capacity of muscle and nerve tissues.
19. Name the two major categories or types of body membranes. Give examples of each.
20. What is a neoplasm?

CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. A baby was born with congenital problems in the skeleton and muscle systems. From what primary germ layers do these systems arise? What is the earliest possible developmental stage during which a problem could have affected just one primary germ layer? (Hint: Use ***A&P Connect.***)

2. Summarize the structural characteristics of epithelial tissues that enable them to perform their specific functions.
3. Does the production of saliva, milk, or oil cause the most damage to the cell that produces it? Explain.
4. Describe the role of the fiber types in the classification of connective tissue. What examples can you find of these various types?
5. Based on your knowledge of tissues, explain how sufficient dietary intake of calcium could ensure the normal development of bone.
6. Many athletes work to reduce their body fat to the lowest possible percentage. What would happen if too little body fat were present?
7. If a tendon is badly damaged, it may need to be replaced surgically. Based on what you know about the structural and functional differences, explain why a tendon rather than a ligament must replace it.
8. Develop a flowchart or other diagram to describe the process by which tissues respond to injury.
9. If a small, but deep cut involving skin and muscle occurs, predict which tissue will probably heal first and which will heal more completely. Explain your answer.
10. When a joint swells, sometimes it is necessary to remove a thick colorless liquid from the joint. What is it, where did it come from, and what is its normal function?

Unit Two

Support and Movement

The six chapters in Unit Two describe the outer covering of the body, as well as the bones, muscles, and articulations, or joints, of the body. The skin (and its appendages) is selected in Chapter 7 as the first organ system to be studied. Chapter 8—Skeletal Tissues—provides information on the types of skeletal tissues and how they are formed, grown, and repaired if injured and how they function. Skeletal tissues protect and support body structures and function as storage sites for important mineral elements vital to many body functions. Blood cell formation also occurs within the red marrow of bones.

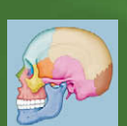
The organs of the skeletal system, bones, are described and organized into major subdivisions in Chapter 9. Movement between bones occurs at joints, or articulations, which are classified in Chapter 10 according to both structure and potential for movement.

Anatomy of the major muscle groups and the basic concepts of muscle physiology are discussed in Chapters 11 and 12. The microscopic and molecular structure of muscle cells and tissues is related to function, as is the gross structure of individual muscles and muscle groups. Movement and heat production constitute the two most important functions of muscle. Discussion of muscle groups in Chapter 11 focuses on how muscles function and on how they attach to bones, how they are named, and how they are integrated functionally with other body organ systems.

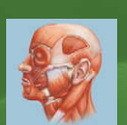
SEEING THE BIG PICTURE


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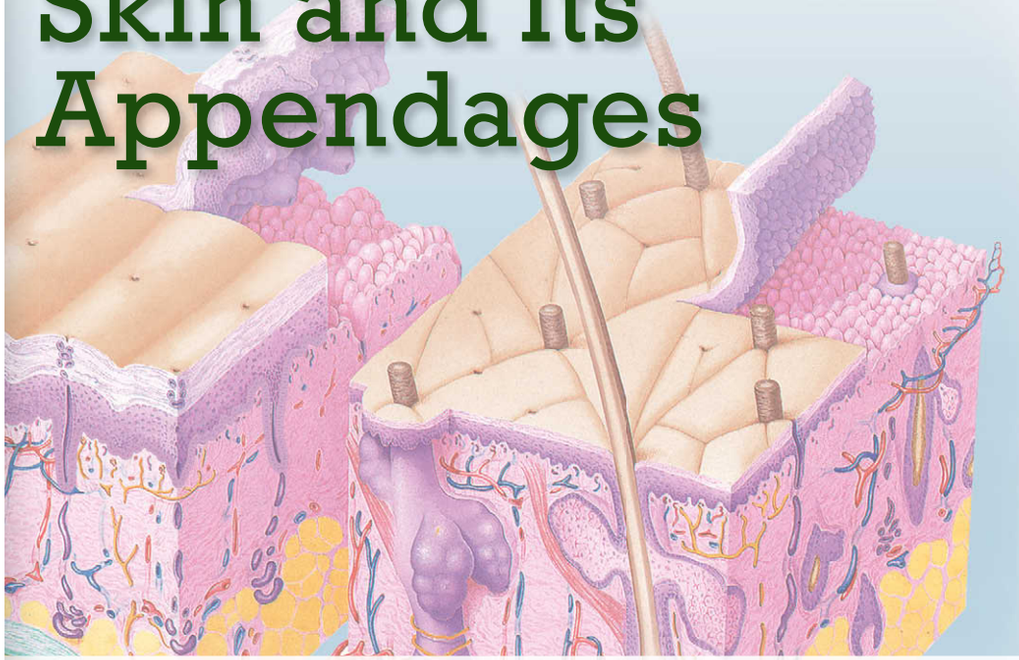

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7

Skin and Its Appendages



LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

albinism
(AL-bi-niz-em)
[*alba-* **white,** *-ism* **condition of**]

apocrine sweat gland
(AP-oh-krin)
[*apo-* **from,** *-crin-* **secrete,** *gland* **acorn**]

arrector pili muscle
(ah-REK-tor PYE-lye)
[*arrector* **raiser,** *pili* **of hair,** *mus-* **mouse,** *-cle* **small**]

callus
(KAL-us)
[*callus* **hard skin**]

cerumen
(seh-ROO-men)
[*cera* **wax**]

ceruminous gland
(seh-ROO-mi-nus)
[*cera-* **wax,** *-ous* **relating to,** *gland* **acorn**]

cleavage line
(KLEE-vij)

cortex
(KOHR-teks)
[*cortex* **bark**] *pl.,* cortices

cutaneous membrane
(kyoo-TAYN-ee-us)
[*cutis* **skin,** *-ous* **made of**]

cuticle
(KYOO-ti-kul)
[*cut-* **skin,** *-icle* **little**]

dendritic cell (DC)
(DEN-dri-tik)
[*dendrit-* **tree branch,** *-ic* **relating to,** *cell* **storeroom**]

dermal papilla
(DER-mal pah-PIL-ah)
[*derma-* **skin,** *-al* **relating to,** *papilla* **nipple**] *pl.,* **papillae**

continued on p. 193

CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

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Vital, diverse, complex, extensive—these adjectives describe the body's largest, thinnest, and one of its most important organs, the skin. It forms a self-repairing and protective boundary between the internal environment of the body and an often hostile external world.

The skin surface is as large as the body, an area in average-sized adults of roughly 1.6 to 1.9 m^2 (17 to 20 square feet). Its thickness varies from slightly less than 0.05 cm (1/50 inch) to slightly more than 0.3 cm (1/8 inch).

As you know, the body is characterized by a "nested," or hierarchical, type of organization. Complexity progresses from cells to tissues and then to organs and organ systems. This chapter discusses the skin and its appendages—hair, nails, and skin glands—as an organ system. Ideally, by studying the skin and its appendages before you proceed to the more complex organ systems in the chapters that follow, you will improve your understanding of how structure is related to function. Integument *is another name for the skin.* Integumentary system *is a term used to denote the skin and its appendages.*

STRUCTURE OF THE SKIN

The skin is a thin, relatively flat organ classified as a membrane—the **cutaneous membrane.** As Figure 7-1 shows, two primary layers compose the skin:

1. Epidermis—superficial, thinner layer
2. Dermis—the deep, thicker layer

| A&P CONNECT |

To briefly review the primary germ layers check out ***Embryonic Development of Tissues*** online at ***A&P Connect.***

evolve

The **epidermis** is an epithelial layer derived from the ectodermal germ layer of the embryo. By the seventeenth week of gestation, the epidermis of the developing baby has all the essential characteristics of the adult. The deeper dermis is derived from the mesoderm.

The **dermis** is a relatively dense and vascular connective tissue layer that may average more than 4 mm in thickness in some body areas. The area where the cells of the epidermis meet the connective tissue cells of the dermis is called the **dermoepidermal**

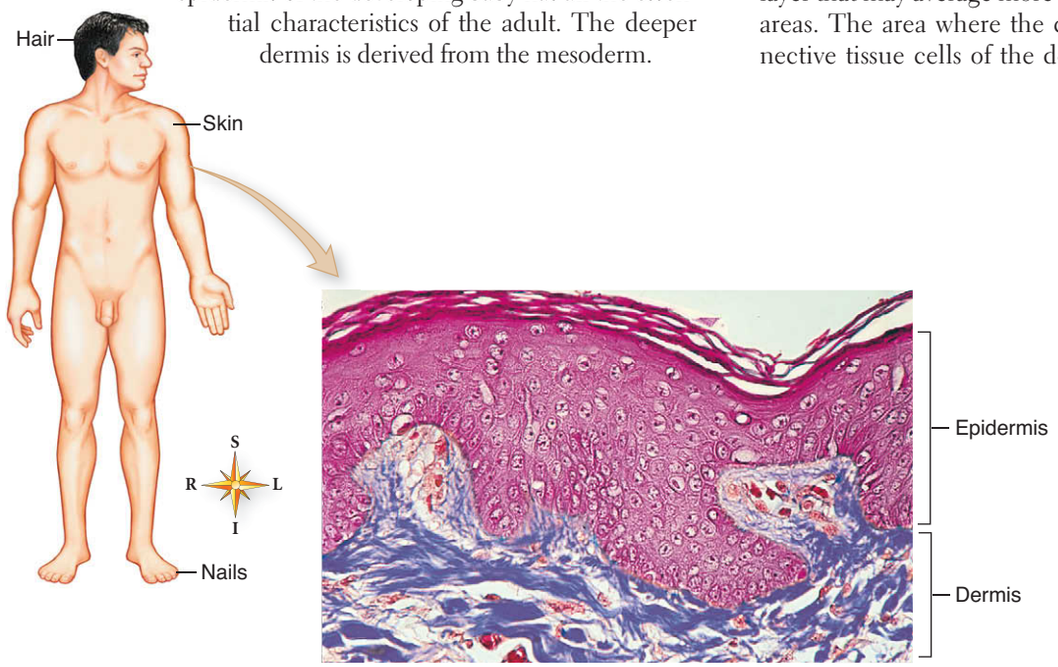


FIGURE 7-1

Photomicrograph of the skin. The staining of this cross section of skin clearly shows the red superficial epidermis and the bluish dermis below it. This photograph has been cropped; the dermis is actually quite thick in comparison to the epidermis.

junction (DEJ) (Figure 7-2). Beneath the dermis lies a loose **hypodermis** rich in fat and loose fibrous connective tissue.

Thin and Thick Skin

Most of the body surface is covered by skin that is classified as *thin skin*. The hairless skin covering the palms of the hands (and fingertips), soles of the feet, and other body areas subject to friction is classified as *thick skin*. These terms refer only to the epidermal layer and not to overall or total skin thickness, which includes the epidermis and dermis. Total skin thickness varies from 0.5 mm in areas such as the eyelids to more than 5 mm over the back, with most of the difference accounted for by variation in depth of the dermis.

In thick skin, each of the five strata, or layers, of the epidermis described below are present, and each stratum is generally several cell layers thick. The outermost stratum—the stratum corneum—is especially noticeable in thick skin and is generally composed of many cell layers. Hair is not found in thick skin.

Furthermore, in thick skin the underlying dermal papillae are raised in curving parallel *epidermal ridges*—or **friction ridges**—to form fingerprints or footprints that are visible on the overlying epidermis. As their name implies, friction ridges increase friction—similar to the function of the ridges of tire treads. These ridges help us pick up and manipulate small objects with the hands and provide slip resistance to the soles of the feet. The epidermal ridges also act as sensory organs, amplifying vibrations as we lightly swipe across a textured surface. The surface of thick skin is seen in Figure 7-3, A.

In thin skin, the number of cell layers in each epidermal stratum is less than in thick skin, and one or more strata may be absent entirely. Raised parallel ridges are not present in the dermis of thin skin (Figure 7-3, B). Instead, the dermal papillae project upward individually and therefore no "fingerprints" are formed on the more superficial epidermis above.

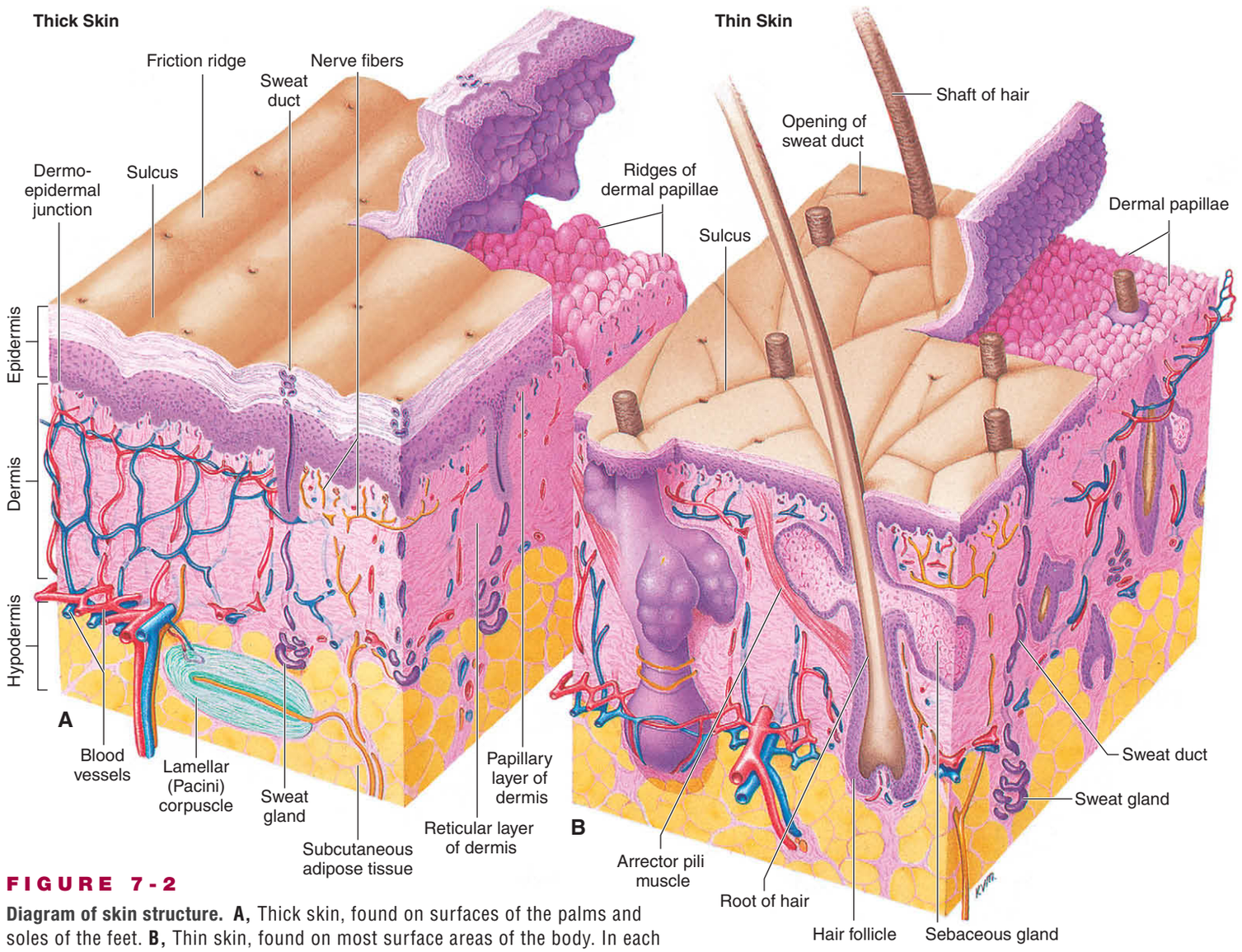
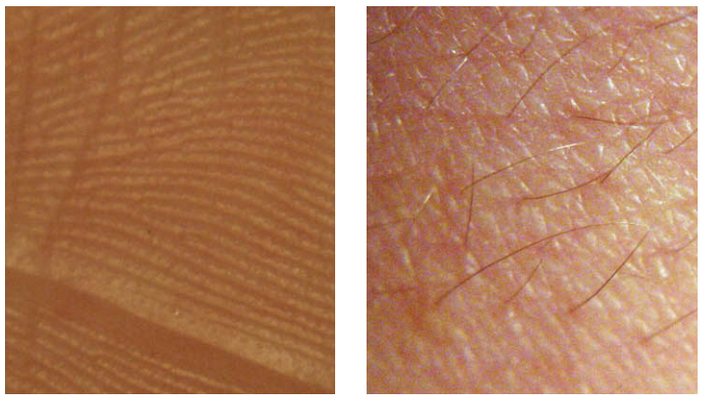


FIGURE 7-2

Diagram of skin structure. A, Thick skin, found on surfaces of the palms and soles of the feet. **B,** Thin skin, found on most surface areas of the body. In each diagram, the epidermis is raised at one corner to reveal the papillae of the dermis.



A B

FIGURE 7-3

Thick and thin skin. A, The surface of thick skin is hairless and features regular, deep sulci and friction ridges, which form the "prints" of the palmar and plantar surfaces of the hands and feet. **B,** The surface of thin skin features irregular sulci (grooves) and hairs.

Box 7-1 | HEALTH matters

Vitiligo

An acquired condition called **vitiligo** results in loss of pigment in certain areas of the skin. The patches of depigmented white skin that characterize this condition contain melanocytes, but for unknown reasons they no longer produce pigment.



Epidermis

CELL TYPES

The epidermis is composed of several types of epithelial cells (Figure 7-4).

Keratinocytes eventually become filled with a tough, fibrous protein called **keratin.** These cells, arranged in distinct *strata*, or layers, are by far the most important cells in the epidermis. They make up more than 90% of the epidermal cells and form the principal structural element of the outer skin. After they are dead and fully keratinized, the flattened keratinocytes are sometimes called *corneocytes.*

Melanocytes contribute colored pigments to the skin and serve to decrease the amount of ultraviolet (UV) light that can penetrate into the deeper layers of the skin. Although they often compose more than 5% of the epidermal cells, melanocytes may also be completely absent from the skin in certain nonlethal conditions (Box 7-1).

Epidermal **dendritic cells (DCs)** of the skin, also called *Langerhans cells*, are branched cells that play a role in immunity. As a type of *antigen-presenting cell (APC)*, each dendritic cell finds markers (antigens) on bacteria and other invaders and presents them to other immune system cells for recognition and destruction—an important defensive function. These cells originate in the bone marrow but migrate to the deep cell layers of the epidermis early in life. Dendritic cells and other APCs are discussed further in Chapter 24.

Tactile epithelial cells, also called *Merkel cells*, are located in the deepest layer of the epidermis. As Figure 7-4 shows, they connect to sensory nerve endings to form structures that serve as light touch receptors.

CELL LAYERS

The cells of the epidermis are found in up to five distinct layers, or **strata.** Each stratum (meaning "layer") is named for its structural

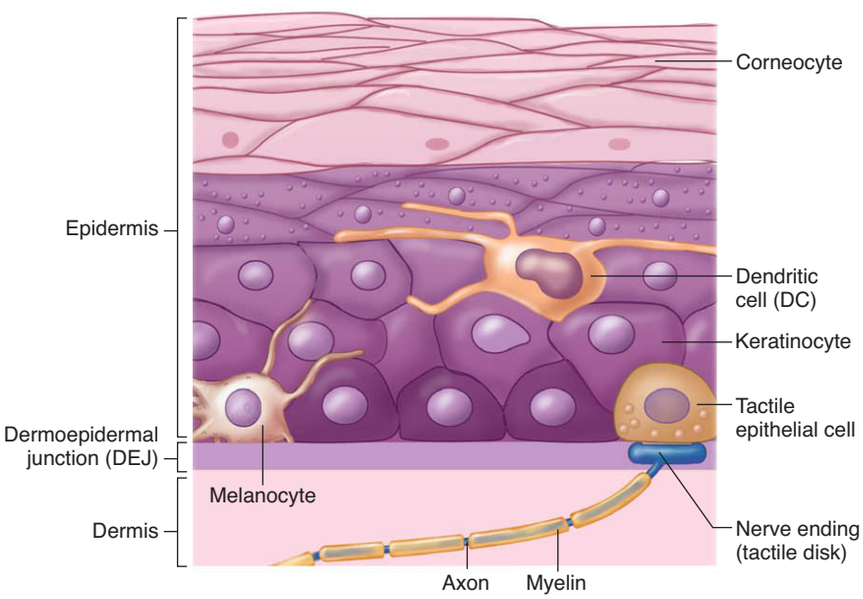


FIGURE 7-4

Epidermal cell types. Keratinocytes, most of the cells seen here, begin their life in the deepest layer of the epidermis and are pushed upward as more keratinocytes are formed. Melanocytes produce pigments. Epidermal dendritic cells *(DCs)* have a function in immunity. Tactile epithelial cells (Merkel cells) attach to sensory nerve endings to form "light touch" receptors.

or functional characteristics. The strata of the epidermis are listed here in order from deepest to most superficial.

1. **Stratum basale** (base layer). The stratum basale is a single layer of columnar cells. Only the cells in this deepest stratum of the epithelium undergo mitosis. As a result of this regenerative activity, cells transfer or migrate from the basal layer through the other layers until they are shed from the skin surface. The term *stratum germinativum* (growth layer) is often used to designate stratum basale (or sometimes, stratum basale and stratum spinosum together).
2. **Stratum spinosum** (spiny layer). The stratum spinosum layer of the epidermis is formed from 8 to 10 layers of irregularly shaped cells with very prominent intercellular bridges, or desmosomes. When viewed under a microscope, the desmosomes appear to pull points of the plasma membranes of adjoining cells toward one another. This gives cells of this layer a spiny or prickly appearance. Cells in this epidermal layer are rich in ribonucleic acid (RNA) and are therefore well equipped to initiate the protein synthesis required for the production of keratin.
3. **Stratum granulosum** (granular layer). The process of surface keratin formation begins in the stratum granulosum of the epidermis. Cells are arranged in a sheet two to four layers deep and are filled with intensely staining granules called **keratohyalin,** which is required for surface keratin formation. At this stage, the keratinocytes also form small bodies of *glycophospholipids* (part sugar, part phospholipid) built up in multiple layers. Even though there is some important biochemical activity at this stage, cells in the stratum granulosum have started to degenerate. As a result, high levels of lysosomal enzymes are present in the cytoplasm, and the nuclei are in the process of breaking down. In thin skin, not many cells at this stage are present, so this layer of the epidermis may not be visible.
4. **Stratum lucidum** (clear layer). The keratinocytes in the stratum lucidum are very flat, closely packed, and clear. Typically, nuclei are absent, and the cell outlines are now indistinct. These dying cells are filled with a substance called **eleidin,** which will eventually be transformed to keratin. This layer is absent in thin skin but is apparent in sections of thick skin from the soles of the feet and the palms of the hands.
5. **Stratum corneum** (horny layer). The stratum corneum is the most superficial layer of the epidermis. It is composed of very thin squamous (flat) cells, which at the skin surface are dead and continually being shed and replaced. Much of the cytoplasm in these cells has been replaced by a dense network of keratin fibers. The glycophospholipids from the multilayer bodies cement the keratin fibers into a strong, waterproof barrier. The desmosomes that hold adjacent keratinocytes together strengthen this layer even more and permit it to withstand considerable wear and tear. The process by which cells in this layer are formed from cells in deeper layers of the epidermis and then filled with keratin and moved to the surface is called **keratinization.**

   The stratum corneum is sometimes called the *barrier area* of the skin because it functions as a barrier to water loss and to many environmental threats ranging from microorganisms and harmful chemicals to physical trauma. Once this barrier layer is damaged, the effectiveness of the skin as a protective covering is greatly reduced, and most contaminants can easily pass through the lower layers of the cellular epidermis. If the glycophospholipid barrier is washed away by prolonged soaking in water (especially if the water contains lipid-dissolving detergents), the keratin may absorb water and make the skin appear puffy and wrinkled—most easily seen in thick skin because of its high water content. Certain diseases of the skin cause the stratum corneum layer of the epidermis to thicken far beyond normal limits—a condition called **hyperkeratosis.** The result is a thick, dry, scaly skin that is inelastic and subject to painful fissures.

Table 7-1 clearly shows each of these layers of the epidermis.

EPIDERMAL GROWTH AND REPAIR

The most important function of the integument—protection—largely depends on the special structural features of the epidermis and its ability to create and repair itself after injury or disease.

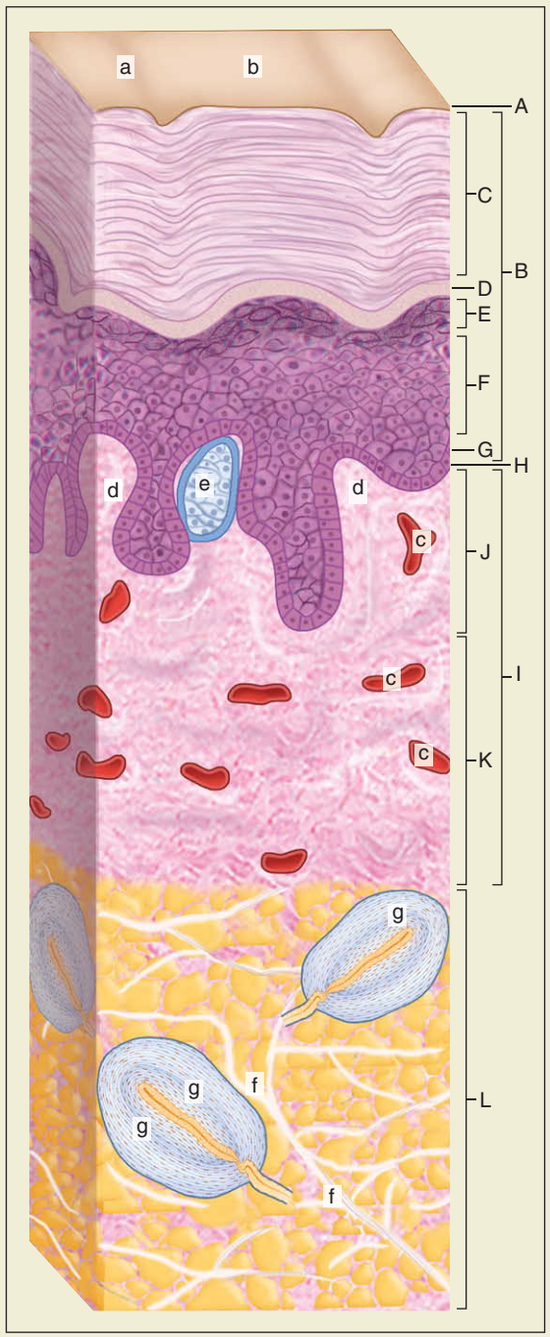
Turnover time and *regeneration* time are terms used to describe the period required for a population of cells to mature and reproduce. Obviously, as the surface cells of the stratum corneum are lost, replacement of keratinocytes by mitotic activity must occur. New cells must be formed at the same rate that old keratinized cells flake off from the stratum corneum to maintain a constant thickness of the epidermis. Cells push upward from the stratum basale into each successive layer, die, become keratinized, and eventually desquamate (fall away), as did their predecessors. This fact illustrates a physiological principle: while life continues, the body's work is never done. Even at rest it is producing millions upon millions of new cells to replace old ones.

A cell-signaling protein called *epidermal growth factor (EGF)* plays a role in regulating the regeneration and repair of the epidermis, as its name suggests. Discovery of EGF has led to its use as a therapy to stimulate skin repairs in diabetic and pressure ulcers and other conditions. EGF requires the hormone *insulin-like growth factor 1 (EGF-1)* to have its full effect in stimulating skin growth and repair. *Growth hormone (GH)* also has a growth-promoting effect on epidermal cells. The cooperative actions of hormones are explored further in Chapters 18 and 19.

Research suggests that the regeneration time required for completion of mitosis, differentiation, and movement of new keratinocytes from the stratum basale to the surface of the epidermis is about 35 days. The process can be accelerated by abrasion of the skin surface, which tends to peel off a few of the cell layers of the stratum corneum. The result is an intense stimulation of mitotic activity in the stratum basale and a shortened turnover period. If abrasion continues over a prolonged period, the increase in mitotic activity and shortened turnover time will result in an abnormally thick stratum corneum and the development of **calluses** at the point of friction or irritation. Although callus formation is a normal and protective response of the skin to friction, several skin diseases are also characterized by abnormally high mitotic activity in the epidermis. In such conditions, the thickness of the corneum is dramatically increased. As a result, scales accumulate and skin lesions often develop.

Normally, about 10% to 12% of all cells in the stratum basale enter mitosis each day. Cells migrating to the surface proceed

TABLE 7-1 Structure of the Skin



	STRUCTURE	DESCRIPTION
A	**Surface film**	Thin film coating the skin; made up of a mixture of sweat, sebum, desquamated cells/fragments, various chemicals; protects the skin
B	**Epidermis**	Superficial primary layer of the skin; made up entirely of keratinized stratified squamous epithelium; derived from the ectoderm; also includes hairs, sweat glands, sebaceous glands
C	Stratum corneum (horny layer)	Several layers of flakelike dead cells (or *corneocytes*) mostly made up of dense networks of *keratin* fibers cemented by *glycophospholipids* and forming a tough, waterproof barrier; the keratinized layer *a,* sulcus (groove) *b,* friction ridge
D	Stratum lucidum (clear layer)	A few layers of squamous cells filled with *eleidin*—a keratin precursor that gives this layer a translucent quality (not visible in thin skin)
E	Stratum granulosum (granular layer)	2-5 layers of dying, somewhat flattened cells filled with darkly staining keratohyalin granules and multilayered bodies of glycophospholipids; nuclei disappear in this layer
F	Stratum spinosum (spiny layer)	8-10 layers of cells pulled by desmosomes into a spiny appearance
G	Stratum basale (base layer)	Single layer of mostly columnar cells capable of mitotic cell division; it is from this layer that all cells of superficial layers are derived; includes keratinocytes and some melanocytes
H	**Dermoepidermal junction (DEJ)**	The basement membrane, a unique and complex arrangement of adhesive components that glue the epidermis and dermis together
I	**Dermis**	Deep primary layer of the skin; made up of fibrous tissue; also includes some blood vessels *(c),* muscles, and nerves; derived from mesoderm
J	Papillary layer	Loose fibrous tissue with collagenous and elastic fibers; forms nipplelike bumps (papillae, *d*); includes tactile corpuscles (touch receptors, *e*) and other sensory receptors
K	Reticular layer	Tough network (reticulum) of collagenous dense irregular fibrous tissue (with some elastic fibers); forms most of the dermis
L	**Hypodermis** (subcutaneous layer; superficial fascia)	Loose fibrous (areolar) connective tissue and adipose tissue; under the skin (not part of the skin); includes fibrous bands or *skin ligaments (f)* that connect the skin strongly to underlying structures; includes lamellar corpuscles (pressure receptors, *g*) and other sensory receptors

upward in vertical columns from discrete groups of 8 to 10 of these basal cells undergoing mitosis. Each group of active basal cells, together with its vertical columns of migrating keratinocytes, is called an *epidermal proliferating unit*, or EPU. Keratinization proceeds as the cells migrate toward the stratum corneum. As mitosis continues and new basal cells enter the column and migrate upward, fully keratinized "dead" cells are sloughed off at the skin surface. Numerous skin diseases are characterized by an abnormally high rate of keratinization.

| QUICK CHECK |

1. Identify the two main or primary layers of skin. What tissue type dominates each layer?
2. The terms *thin* and *thick* skin refer to which primary layer of skin? How do thin and thick skin differ?
3. Identify the two main cell types found in the epidermis.
4. List the five layers, or strata, of the epidermis.

Dermoepidermal Junction

Electron microscopy and histochemical studies have demonstrated the existence of a rather unique area between the epidermis and dermis called the *dermoepidermal junction (DEJ)*.

The DEJ is a unique kind of basement membrane (BM) that includes special fibrous elements and a unique polysaccharide gel that strongly cement the superficial epidermis to the dermis below. The junction "glues" the two layers together and provides mechanical support for the epidermis, which is attached to its upper surface. Box 7-2 shows what happens when this "skin glue" fails.

In addition, the DEJ serves as a partial barrier to the passage of some cells and large molecules. Certain dyes, for example, if injected into the dermis cannot passively diffuse upward into the epidermis unless the junctional barrier is damaged by heat, enzymes, or other chemicals that change its permeability characteristics. Although the junction is remarkably effective in preventing separation of the two skin layers, even when they are subjected to relatively high shear force, this barrier is thought to have only a limited role in preventing passage of harmful chemicals or disease-causing organisms through the skin from the external environment. Any widespread detachment of a large area of epidermis from the dermis is an extremely serious condition that may result in overwhelming infection and death.

Dermis

The dermis, or *corium*, is sometimes called the "true skin." It is composed of two layers—a thin **papillary** layer and a thicker **reticular** layer. The dermis is much thicker than the epidermis and may exceed 4 mm on the soles and palms. It is thinnest on the eyelids and penis, where it seldom exceeds 0.5 mm. As a rule of thumb, the dermis on the ventral surface of the body and over the appendages is generally thinner than on the dorsal surface. The mechanical strength of the skin is in the dermis. In addition to serving a protective function against mechanical injury and compression, this layer of the skin provides a reservoir storage area for water and important electrolytes. A widespread network of nerves and nerve endings in the dermis called *somatic sensory receptors* also process sensory information such as pain, pressure, touch, and temperature. Sensory receptors are discussed in detail in Chapter 17. At various levels of the dermis extend a variety of muscle fibers, hair follicles, sweat and sebaceous glands, and many blood vessels. It is the rich vascular supply of the dermis that plays a critical role in regulation of body temperature—a function described later in the chapter.

PAPILLARY LAYER

Note in Figure 7-2 that the thin superficial layer of the dermis forms bumps, called **dermal papillae,** that project into the epidermis. *Papilla* (plural, *papillae*) is the Latin word for "nipple" and is used often in anatomy to name any small, nipplelike bump. The papillary layer takes its name from the papillae on its surface. Between the sculptured surface of the papillary layer and the stratum basale lies the important dermoepidermal junction.

The papillary layer and its papillae are composed essentially of loose fibrous connective tissue elements and a fine network of thin collagenous and elastic fibers. The thin epidermal layer of the skin conforms tightly to the ridges of dermal papillae. As a result, the epidermis also has characteristic ridges on its surface. Epidermal ridges are especially well defined on the tips of the fingers and toes. In each of us they form a unique pattern—an anatomical fact made famous by the art of fingerprinting. These ridges perform a function that is very important to human survival: they allow us to grip surfaces well enough to walk upright on slippery surfaces and to grasp and use tools. For that reason, they are usually called *friction ridges*.

RETICULAR LAYER

The thick reticular layer of the dermis consists of a much more dense *reticulum*, or network of fibers, than is seen in the papillary

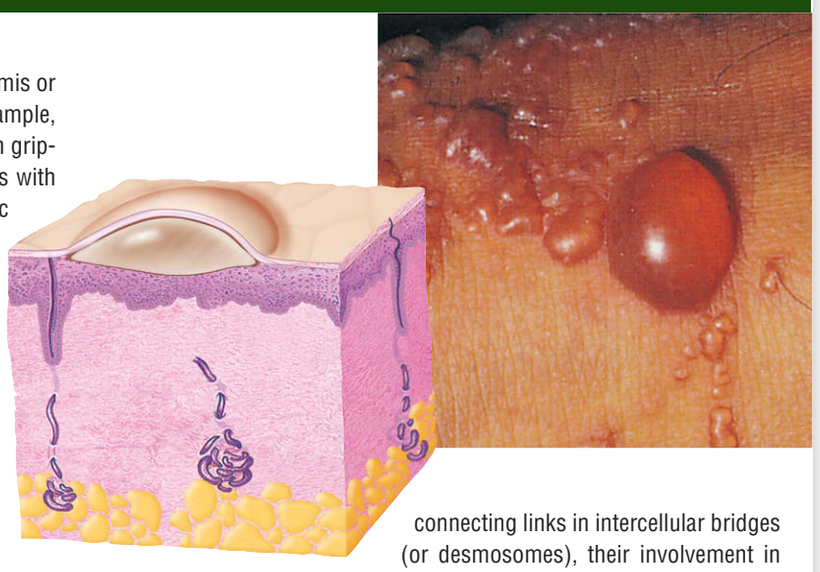
Box 7-2 | HEALTH matters

Blisters

Blisters (see figures) may result from injury to cells in the epidermis or from separation of the dermoepidermal junction (DEJ). For example, repeated rubbing of the skin against the inside of a shoe or when gripping a tool can pull cells or the DEJ and create a space that fills with interstitial fluid. Regardless of cause, blisters represent a basic reaction of skin to injury. Any irritant that damages the physical or chemical bonds that hold adjacent skin cells or layers together, such as poison ivy, initiates blister formation.

The cell-to-cell junctions (desmosomes) that hold adjacent cells in the epidermis together are essential for integrity of the skin. If these intercellular bridges, sometimes described as "spot welds" between adjacent cells, are weakened or destroyed, the skin literally falls apart and away from the body. Damage to the DEJ produces similar results.

Blister formation follows burns, friction injuries, exposure to primary irritants, or accumulation of toxic breakdown products after cell injury or death in the layers of the skin. Typically, chemical agents that break disulfide linkages or hydrogen bonds cause blisters. Because both types of these chemical bonds are the functional



connecting links in intercellular bridges (or desmosomes), their involvement in blister formation serves as a good example of the relationship between structure and function at the chemical level of organization.

layer above it. It is this dense layer of tough and interlacing white collagenous fibers that when commercially processed from animal skin, results in leather. Although most of the fibers in this layer are of the collagenous type, which gives toughness to the skin, elastic fibers are also present. These fibers make the skin stretchable and elastic (able to rebound).

The dermis serves as a point of attachment for numerous skeletal (voluntary) and smooth (involuntary) muscle fibers. Several skeletal muscles are located in the skin of the face and scalp. These muscles permit a variety of facial expressions and are also responsible for voluntary movement of the scalp. The distribution of smooth muscle fibers in the dermis is much more extensive than the skeletal variety. Each hair follicle has a small bundle of involuntary muscles attached to it. These are the **arrector pili muscles.** Contraction of these muscles makes the hair "stand on end"—as in extreme fright, for example, or from cold. As the hair is pulled into an upright position, shown in Figure 7-5, it raises the skin around it into what we commonly call "goose bumps." In the dermis of the skin of the scrotum and in the pigmented skin called the *areolae* surrounding the nipples, smooth muscle cells form a loose network. Contraction of these smooth muscle cells wrinkles the skin and causes elevation of the testes or erection of the nipples.

Millions of somatic sensory receptors are located in the dermis of all skin areas (Figure 7-6; see also Figure 7-2). They permit the skin to serve as a sense organ transmitting sensations of pain, pressure, touch, and temperature to the brain.

Hair follicles and various skin glands, made up of epithelial tissues that extend from the surface of the epidermis, have most of their structures within the reticular layer of the dermis.

DERMAL GROWTH AND REPAIR

Unlike the epidermis, the dermis does not continually shed and regenerate. It does maintain itself, but rapid regeneration of connective tissue in the dermis occurs only during unusual circumstances, as in the healing of wounds (see Figure 6-37, p. 155). In the healing of a wound such as a surgical incision, fibroblasts in the dermis quickly reproduce and begin forming an unusually dense mass of new connective tissue fibers. If this dense mass is not replaced by normal tissue, it remains as a *scar.*

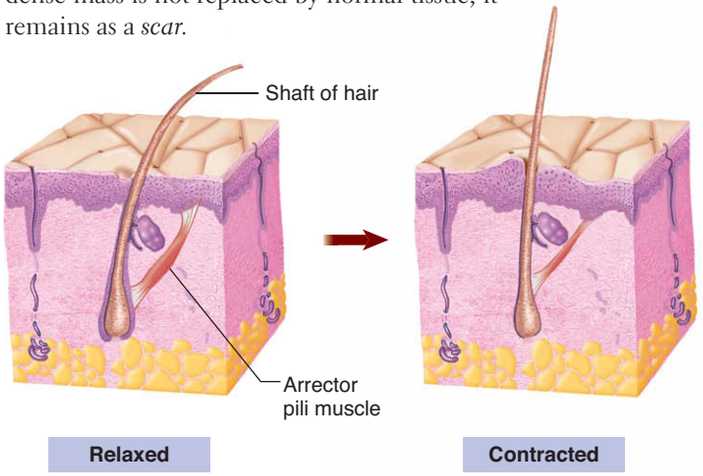


FIGURE 7-5

Arrector pili muscle. When the arrector pili muscle contracts, it pulls the follicle and hair into a more perpendicular position, thus "fluffing up" the hair. Notice how a "goose bump" is raised around the hair shaft.

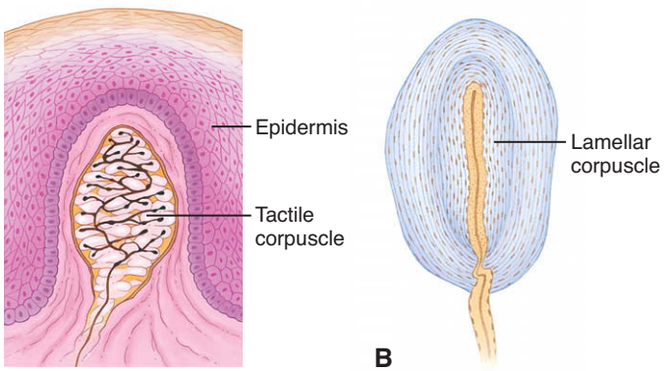


FIGURE 7-6

Skin receptors. Receptors are sensitive nerve endings that make it possible for the skin to act as a sense organ. **A,** This *tactile (Meissner) corpuscle* is capable of detecting light touch (slight pressure). **B,** Another skin receptor is the *lamellar corpuscle,* also called a *Pacini corpuscle,* which detects sensations of deep pressure.

The dense bundles of white collagenous fibers that characterize the reticular layer of the dermis tend to orient themselves in patterns that differ in appearance from one body area to another. The result is formation of patterns called **cleavage lines** (Figure 7-7). If surgical incisions are made parallel to the cleavage lines, or *Langer lines,* the resulting wound will have less tendency to gape open and will tend to heal with a thin and less noticeable scar.

If the elastic fibers in the dermis are stretched too much—for example, by a rapid increase in the size of the abdomen during pregnancy or as a result of great obesity—these fibers will weaken and tear. The initial result is the formation of pinkish or slightly bluish depressed furrows with jagged edges. These tiny linear markings *(stretch marks)* are really tiny tears. When they heal and lose their color, the *striae* (Latin, "furrows") that remain appear as glistening silver-white scar lines.

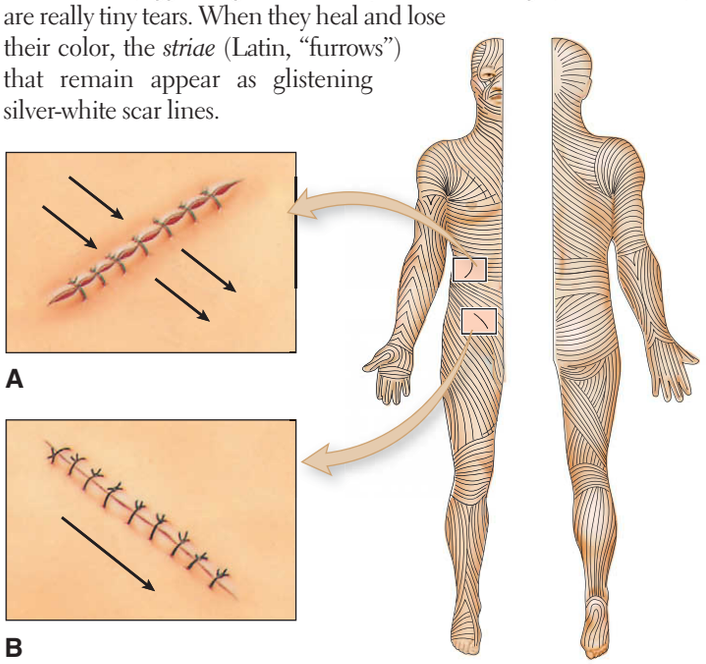


FIGURE 7-7

Cleavage lines. A, If an incision "cuts across" cleavage lines (Langer lines), stress tends to pull the cut edges apart and may retard healing. **B,** Surgical incisions parallel to cleavage lines are subjected to less stress and tend to heal more rapidly.

HYPODERMIS

The hypodermis is sometimes called the **subcutaneous layer,** or **superficial fascia** (see Box 6-5, p. 148). It is not part of the skin, but lies deep to the dermis and thus forms a connection between the skin and the underlying structures of the body. Thus the hypodermis is often discussed along with the skin because of the close structural and functional association of these two superficial body structures. Box 7-3 discusses one reason why it is important to know about the structure hypodermis.

The hypodermis is mostly loose fibrous and adipose tissue. The fat content of the hypodermis varies with the state of nutrition and in obese individuals may exceed 10 cm in thickness in certain areas. The density and arrangement of fat cells and collagen fibers in this area determine the relative mobility of the skin. Bands of fibers called *skin ligaments* running through the hypodermis help hold the skin to underlying structures such as deep fascia and muscles (Table 7-1, *f*). When skin is removed from an animal by blunt dissection, separation occurs in the "cleavage plane" that exists between the superficial fascia and the underlying structures.

| QUICK CHECK |

5. What is the name of the gluelike layer separating the dermis from the epidermis?
6. Which layer of the dermis forms the bumps that produce ridges on the palms and soles?
7. Which layer is vascular: the epidermis or dermis?
8. What is the main function of the hypodermis?

SKIN COLOR

Melanin

Human skin ranges widely in color. The main determinant of skin color is the quantity of **melanin** deposited in the cells of the epidermis by melanocytes. The number of pigment-producing melanocytes scattered throughout the stratum basale of the epidermis in most body areas is about the same in all humans. It is the amount and type of melanin pigment actually produced by these cells that account for the majority of skin color variations among families.

Two groups of melanin are made by the melanocytes of the body. One group of these pigments is called **eumelanin** (yoo-MEL-ah-nin) and the other group is called **pheomelanin** (fee-oh-MEL-ah-nin). The word *eumelanin* literally means "true black substance" because it is very dark brown, sometimes nearly black. *Pheomelanin* means "dusky black substance"—which hints at its lighter reddish or orange color. Dark-skinned and dark-haired people produce large quantities of eumelanin. On the other hand, people with very light skin with red-orange freckles and red hair produce pheomelanin—and little if any eumelanin—in the skin.

Of all body cells, only melanocytes have the ability to routinely convert the amino acid *tyrosine* into melanin pigments. The pigment granules are then released in tiny **melanosomes** and transferred to surrounding keratinocytes, where they form a sort of protective cap over the nucleus (Figure 7-8). The pigment-producing process is

Box 7-3 | HEALTH matters

Subcutaneous and Intradermal Injections

Although the hypodermis, or subcutaneous layer, is not part of the skin itself, it carries the major blood vessels and nerves to the skin above. The rich blood supply and loose spongy texture of this area make it an ideal site for the rapid and relatively pain-free absorption of injected material. Liquid medicines, such as insulin, and pelleted implant materials are often administered by *subcutaneous (SQ) injection* with a *hypodermic needle* into this spongy and porous layer beneath the skin. *Intradermal (ID) injections,* on the other hand, place the medication in the skin proper. ID injections, which are ideal for some vaccines, are hard to administer with a typical needle because it is so easy to punch through to the hypodermis. Therefore, this type of injection is sometimes given with special needle-free injectors.

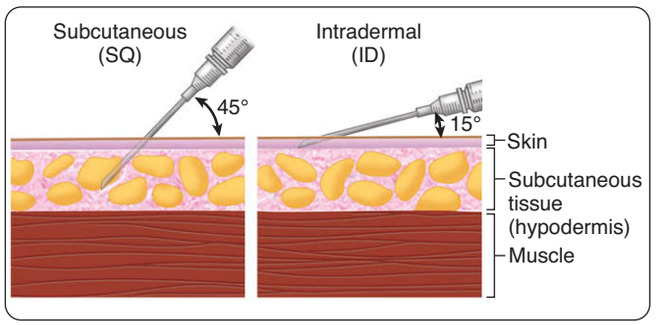
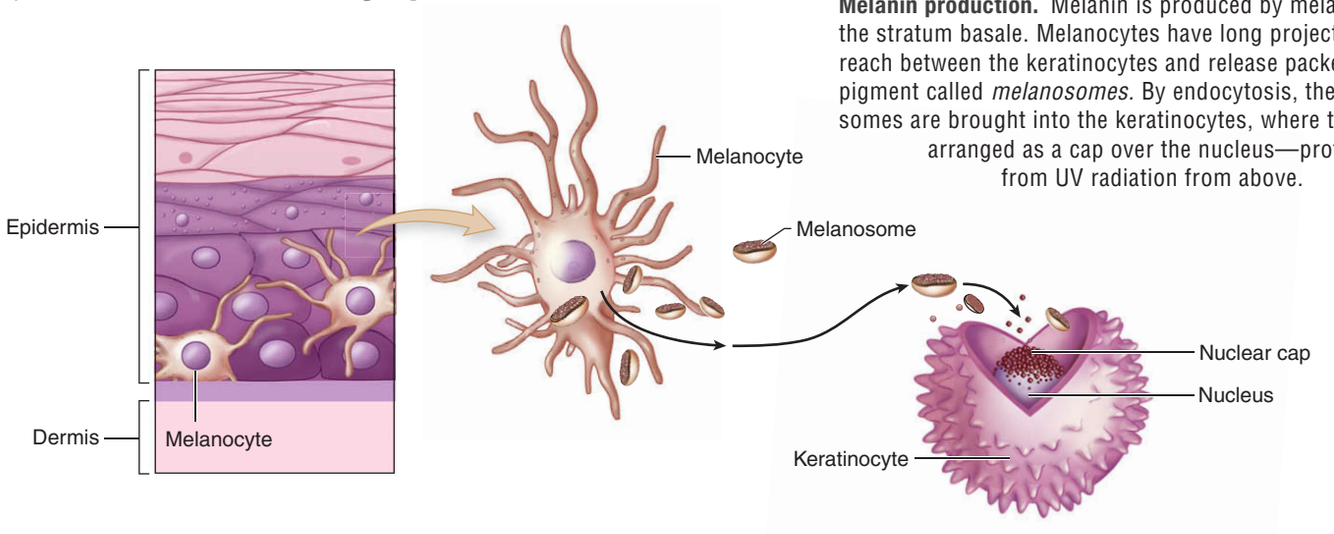


FIGURE 7-8

Melanin production. Melanin is produced by melanocytes in the stratum basale. Melanocytes have long projections that reach between the keratinocytes and release packets of pigment called *melanosomes.* By endocytosis, the melanosomes are brought into the keratinocytes, where they are arranged as a cap over the nucleus—protecting it from UV radiation from above.



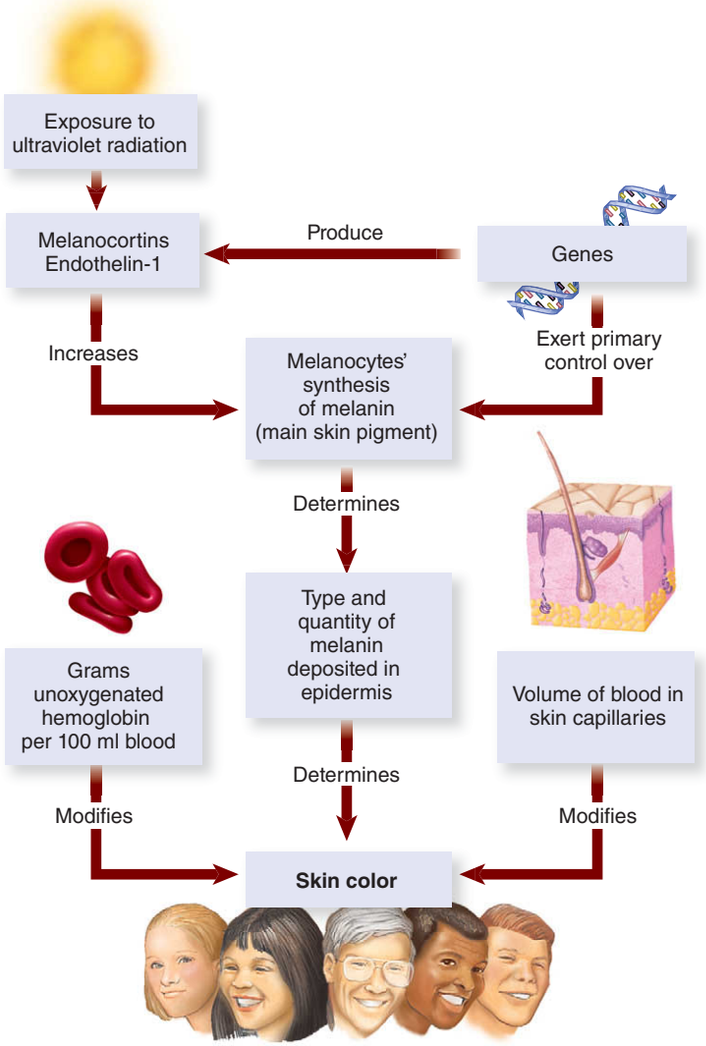


FIGURE 7-9

How genes affect skin color. Genes determine an individual's basic skin color by controlling the amount and type of melanin synthesized and deposited in the epidermis. However, as the diagram shows, other factors may modify the basic skin color.

regulated in the cell by the enzyme *tyrosinase*. But this conversion process depends on several factors (Figure 7-9).

Heredity is a major factor in melanin production. Geneticists tell us that several genes exert primary control over the amount of melanin formed by melanocytes. These genes may affect any part of the chemical pathway that produces the two types of melanin. For example, if the enzyme tyrosinase is absent from birth because of a genetic mutation, the melanocytes cannot form melanin and a condition called **albinism** results. Albino individuals have a characteristic absence of pigment in their hair, skin, and eyes. Thus heredity determines how dark or light one's skin color will be (see Chapter 37).

Other factors can influence the expression of the genes for melanin production. Sunlight is an obvious example. Prolonged exposure to the ultraviolet (UV) radiation in sunlight causes melanocytes to increase melanin production and darken skin color (Figure 7-10). Notice in Figure 7-8 that the melanosomes form a cap over the top of the nucleus in each keratinocyte. The melanin in this nuclear cap absorbs UV radiation before it can reach the DNA inside the nucleus, where it can cause severe damage that can lead to skin cancer and other problems. Unless the cells are protected by melanin, UV radiation can also break down other

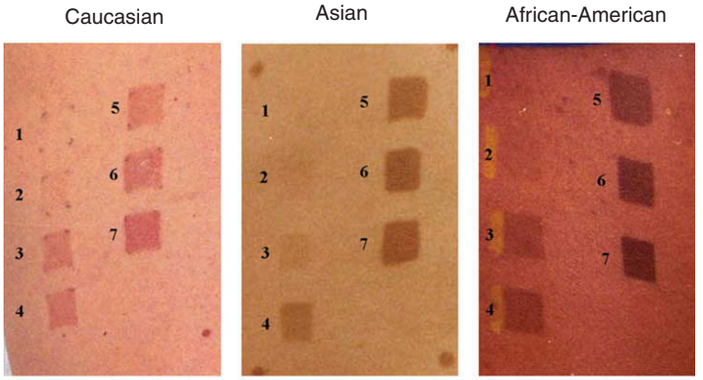


FIGURE 7-10

Tanning effects in skin. Photos showing skin effects of ultraviolet (UV) radiation on day 8 after exposure to increasing doses (1 through 7) in three skin types. Notice that the Caucasian skin involves more redness (from burning) than the darker skin types, which become even darker in response to higher doses of UV radiation.

important molecules, such as the vitamin *folic acid* (B_9). Eumelanin absorbs more UV radiation than pheomelanin does—which explains why very dark-skinned individuals have less risk of developing skin cancer than very light-skinned, reddish freckled individuals do.

Research shows that dark skin pigmentation also facilitates apoptosis (programmed cell death) of any cells that do suffer damage to their DNA structure. Removal of DNA-damaged cells prevents them from becoming cancerous.

Melanin production is stimulated when *melanocortin* receptors are triggered at the surface of a melanocyte. Melanocortins are a family of hormones produced from a single gene that codes for a large polypeptide that breaks into distinct hormones. One product of the gene is adrenocorticotropic hormone (ACTH), some of which breaks down further to form *alpha melanocyte-stimulating hormone* (*α-MSH*). Although tiny amounts of melanocortins are released by the anterior pituitary gland, they can also be made by keratinocytes in response to UV radiation—thus triggering nearby melanocytes to produce more melanin. Other local regulatory proteins, such as *endothelin-1 (ET-1)*, act with melanocortins to produce this "tanning" effect. Some people with light skin, red hair, and freckles inherit malfunctioning melanocyte receptors or melanocortin genes and thus fail to produce melanin in response to UV exposure.

Increasing age may also influence melanocyte activity. In many individuals, apoptosis of melanocyte stem cells in hair follicles produces the graying of the hair often associated with age. Cumulative exposure to UV radiation over the years can also trigger excess production of melanin. This may result in a collection of dark "age spots" on the skin (Figure 7-11).



FIGURE 7-11

Age spots. Hyperpigmentations from the cumulative effects of UV exposure over the years can produce a dark type of "age spots" that are also called "liver spots."

Other Pigments

In addition to melanin, other pigments such as the yellow pigment *beta-carotene (β-carotene)* found in many vegetables and roots (for example, carrots) also contribute to skin color. Because β-carotenes can be converted by the body into vitamin A—a critically important nutrient for skin growth—they are stored in skin tissue. Extremely high consumption of carrot juice or sweet potatoes, in infants especially, may cause an orange or yellow coloration of the skin. Yellowish discoloration can also be caused by jaundice (Box 7-4) or can be seen after a bruise begins to heal (see Figure 7-13).

As epidermal cells age and stop undergoing mitosis, they often accumulate a brown-yellow pigment called *lipofuscin*. Aged skin often shows a mottling of brown-yellow age spots as a result.

An individual's basic skin color can also change temporarily when the volume of blood flowing through skin capillaries increases or decreases. The reason is that blood contains the reddish pigment hemoglobin (Hb) that carries oxygen or carbon dioxide. If blood vessels in the skin dilate, as they do during blushing, the skin appears to be redder than usual because of additional hemoglobin flowing through the dermis. If skin blood vessels constrict, on the other hand, skin blood volume decreases, and the skin may turn paler (less red) than usual.

In general, the sparser the pigments in the epidermis, the more transparent the skin and therefore the more vivid the change in skin color with a change in skin blood volume. Conversely, the richer the pigmentation, the more opaque the skin and therefore the less the change in skin color with a change in skin blood volume.

In some abnormal conditions, skin color changes because of an excess amount of hemoglobin that is low in oxygen and high in carbon dioxide. If skin contains relatively little melanin, it will appear bluish, that is, *cyanotic*, when its blood has a high proportion of unoxygenated hemoglobin. The blue coloration results from the fact that hemoglobin changes from a bright red color to a deep maroon-red color when it loses oxygen and gains carbon dioxide. Light reflecting from the dark red hemoglobin and diffused by fibers in the skin may appear blue—as you can see in Figure 7-12. In general, the darker the skin pigmentation, the greater the amount of unoxygenated hemoglobin that must be present before **cyanosis** ("condition of blueness") becomes visible.



FIGURE 7-12

Cyanosis. The blue discoloration of the fingers of this light-skinned individual is caused by the diffusion of light reflected off dark, unoxygenated hemoglobin in the blood vessels of the skin. The fingertips have an especially high volume of blood and thus look bluer than other regions of the skin.

Bruising can cause a variety of different skin colors to appear in light-skinned individuals, as you can see in Figure 7-13. When damage to blood vessels in the skin permits the release of red blood cells, their reddish color begins to darken and produce the bluish colors described previously when hemoglobin loses oxygen and gains carbon dioxide. As the blood clots, it may begin to appear darker blue or even black. Macrophages remove the hemoglobin and break it down into iron-containing *hemosiderin* (a brownish pigment) and several iron-free *bile pigments* that are greenish and yellowish.

Pigments from cosmetics or from tattoos can also change the coloring of the skin. Most cosmetics simply add layers of pigment on top of the skin. Some temporary tattoos also add layers of pigment on top of the skin. Henna tattoos stain epidermal cells, which are later shed—making their brown color temporary. Permanent tattoos (see the photo in Box 7-4) are made by using

Box 7-4 | HEALTH matters

Jaundice

Yellowish discoloration of the skin and other tissues, such as the "white" or sclera of the eye, can be caused by bile pigments. Bile pigments are a natural breakdown product when old red blood cells are destroyed. Ordinarily, bile pigments are excreted from the liver into the digestive tract, where they become part of the feces and are eliminated by the body. However, in some cases the liver is unable to remove bile from the blood efficiently—thus allowing the bile to stain the tissues of the body. An example of a condition that can cause jaundice is a liver infection, as illustrated in the photograph.

Jaundice also often occurs just after birth. In about half of all full-term newborns, jaundice occurs when old red blood cells containing an immature fetal form of hemoglobin are rapidly replaced with red blood cells containing the mature form of hemoglobin. Often, a baby's liver is simply too immature to handle the removal of such a large amount of bile pigment all at once. This form of jaundice is temporary and usually disappears without treatment. UV light breaks down bile pigments in the skin and can help speed recovery in infants with moderate to severe cases of jaundice.



Jaundice. Yellowish discoloration of the skin and other tissues by bile pigments was, in the case seen here, caused by a liver infection. The patient was infected with hepatitis B by a contaminated tattoo needle. The yellow tinge of the skin can be best seen by comparing the patient's skin color with that of the physician's hand.



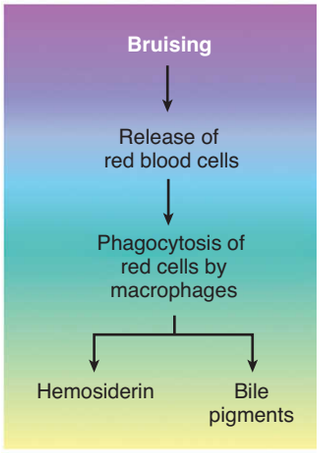


FIGURE 7-13

Color changes in a bruise. In this light-skinned individual, different colors appear in the skin as hemoglobin becomes unoxygenated and turns bluish (see Figure 7-12) and perhaps even black as the blood clots. As macrophages consume the hemoglobin, it is broken down into brownish, greenish, and yellowish pigments—sometimes producing a rainbow of skin colors.

a needle to insert pigments into the dermis of the skin. Because these pigments eventually diffuse to deeper layers of the dermis, such a tattoo may fade or become less distinct after several decades. Some permanent tattoos are made by cutting the skin and rubbing in pigments, producing colored scar tissue.

FUNCTIONS OF THE SKIN

Skin functions are crucial to maintenance of homeostasis and thus to survival itself. They are also diverse and include such different processes as protection, sensation, growth, synthesis of important chemicals and hormones (such as vitamin D), excretion, temperature regulation, and immunity. Because of its structural flexibility, the skin permits body growth and movement to occur without injury. We also know that certain substances can be absorbed through the skin, including the fat-soluble vitamins (A, D, E, and K), estrogens and other sex hormones, corticoid hormones, and certain drugs such as nicotine and nitroglycerin.

The skin also produces melanin—the pigment that serves as an extremely effective screen to potentially harmful ultraviolet light—and keratin—one of nature's most flexible, yet enduring protective proteins. Refer to Table 7-2 as you read about the seven functions of the skin described in the paragraphs that follow.

Protection

The keratinized stratified squamous epithelial cells that cover the epidermis makes the skin a formidable barrier. It protects underlying tissues against invasion by hordes of microorganisms, bars entry of most harmful chemicals, and minimizes mechanical injury to underlying structures that might otherwise be harmed by even the relatively minor types of trauma experienced on a regular basis.

In addition to protection from microbiological entry, chemical hazards, and mechanical trauma, the skin also protects us from dehydration caused by loss of internal body fluids and from unwanted entry of fluids from the external environment. The ability of the pigment melanin to protect us from the harmful effects of overexposure to ultraviolet light is yet another protective function of the skin.

SURFACE FILM

The ability of the skin to act as a protective barrier against an array of potentially damaging assaults from the environment begins with the proper functioning of a thin film of emulsified material spread over its surface. The **surface film** is produced by the mixing of residue and

TABLE 7-2 Functions of the Skin

FUNCTION	EXAMPLE	MECHANISM
Protection	Against microorganisms Against dehydration Against ultraviolet radiation Against mechanical trauma	Surface file/ mechanical barrier Keratin Melanin Tissue strength
Sensation	Pain Heat and cold Pressure Touch	Somatic sensory receptors
Permits movement and growth without injury	Body growth and change in body contours during movement	Elastic and recoil properties of skin and subcutaneous tissue
Endocrine	Vitamin D production	Activation of precursor compound in skin cells by ultraviolet light
Excretion	Water Urea Ammonia Uric acid	Regulation of sweat volume and content
Immunity	Destruction of microorganisms and interaction with immune system cells (helper T cells)	Phagocytic cells and epidermal dendritic cells
Temperature regulation	Heat loss or retention	Regulation of blood flow to the skin and evaporation of sweat

secretions from sweat and sebaceous glands with epithelial cells constantly being cast off from the epidermis. The shedding of epithelial elements from the skin surface is called **desquamation.** A variety of microbial cells are another important part of the mixture (Box 7-5).

Functions of surface film include the following:

- Antibacterial and antifungal activity
- Lubrication
- Hydration of the skin surface
- Buffering of caustic irritants
- Blockade of many toxic agents

The chemical composition of surface film includes (1) amino acids, sterols, and complex phospholipids from the breakdown of sloughed epithelial cells; (2) fatty acids, triglycerides, and waxes from sebum; and (3) water, ammonia, lactic acid, urea, and uric acid from sweat. The specific chemical composition of surface film is variable, and samples taken from skin covering one body area often have a different "mix" of chemical components than film covering skin in another area does. This difference helps explain the unique and localized distribution patterns of certain skin diseases and also explains why the skin covering a particular area of the body is sometimes more susceptible to attack by certain bacteria or fungi.

Sensation

The widespread placement of the millions of different somatic sensory receptors found in the skin enables it to function as a sophisticated sense organ covering the entire body surface (see Figures 7-1 and 7-3).The receptors serve as antennas that detect stimuli, which eventually produce the general, or somatic, senses, including pressure, touch, temperature, pain, and vibration. When these receptors are activated by their respective stimuli, they make it possible for the body to respond to changes occurring in both the external and internal environments. A full discussion of the anatomy and physiology of the somatic sense receptors is provided in Chapter 17.

Flexibility

Contraction of our muscles produces the purposeful movement that serves as one of the most easily observed "Characteristics of Life" discussed in Chapter 1. For movement of the body to occur without injury, the skin must be supple and elastic. It grows as we grow and exhibits stretch and recoil characteristics that permit changes in body contours to occur without tearing or laceration.

Excretion

By regulating the volume and chemical content of sweat, the body, through a function of the skin, can influence both its total fluid volume and the amounts of certain waste products, such as uric acid, ammonia, and urea that are excreted. In most circumstances the skin plays only a minor role in the overall excretion of body wastes. However, it can become a more important function in certain disease states or pathological conditions.

Hormone (Vitamin D) Production

The first step in the production of vitamin D in the body occurs when the skin is exposed to ultraviolet light. When this occurs, molecules of a chemical called *7-dehydrocholesterol*, which is normally found in skin cells, are converted into a precursor substance called *cholecalciferol* (Figure 7-14). This chemical is then transported in the blood to the liver and kidneys where it is converted into an active form of vitamin D—a compound that influences several important chemical reactions in the body. In this respect, vitamin D fulfills the requirements required for a substance to be classified as a *hormone*. In general, any chemical substance produced in one body area and then transported in the blood to another location where it has its effect is called a *hormone*. Hormones are critically important regulators of homeostasis and are discussed in detail in Chapters 18 and 19.

Box 7-5 | FYI

Microbes of the Skin

Surface film of the skin contains more than just the mixed secretions of various glands and the sloughed-off keratinized cells of stratum corneum. It is teaming with a variety of microbes—microscopic organisms such as bacteria and fungi (see Figure 6-41 on p. 157). There are up to ten times as many microbial cells on your body's skin and mucous membranes as there are human cells in your body! These microbes act as a set of interactive ecosystems—a microbiome.

There are always some pathogenic bacteria in the body's microbiome, but when you are healthy they are kept in check by a majority of nonpathogenic bacteria. If the healthy ecological balance is upset, however, the pathogenic bacteria can take over in local areas and cause disease. Scientists have been mapping out the widely varied microbial communities that inhabit different locations of our skin in hopes of preventing or curing skin disorders. They have already discovered that the microbiome of each person has unique characteristics. We may soon be able to identify individuals by their microbiome as easily as we do by using fingerprints!

Melanin in the skin must be dark enough to protect the skin from damage from UV radiation, destruction of folic acid, and other adverse health effects. However, if there is too much melanin, the body cannot synthesize enough vitamin D for normal function. In such a case, vitamin D from outside the body is necessary to compensate for the failure of skin to make enough vitamin D. Research shows that various ethnic groups often have just enough melanin to protect them from harm by the UV radiation levels in their native region—and not so much that it prevents vitamin D production.

Immunity

Important defensive cells that attach to and destroy pathogenic microorganisms are found in the skin and play an important role in immunity. In addition, epidermal dendritic cells function with helper T cells to trigger helpful immune reactions in certain diseases.

Homeostasis of Body Temperature

Despite sizable variations in environmental temperature, humans maintain a remarkably constant core body temperature. The functioning of the skin in homeostasis of body temperature is critical to survival and is examined in some detail.

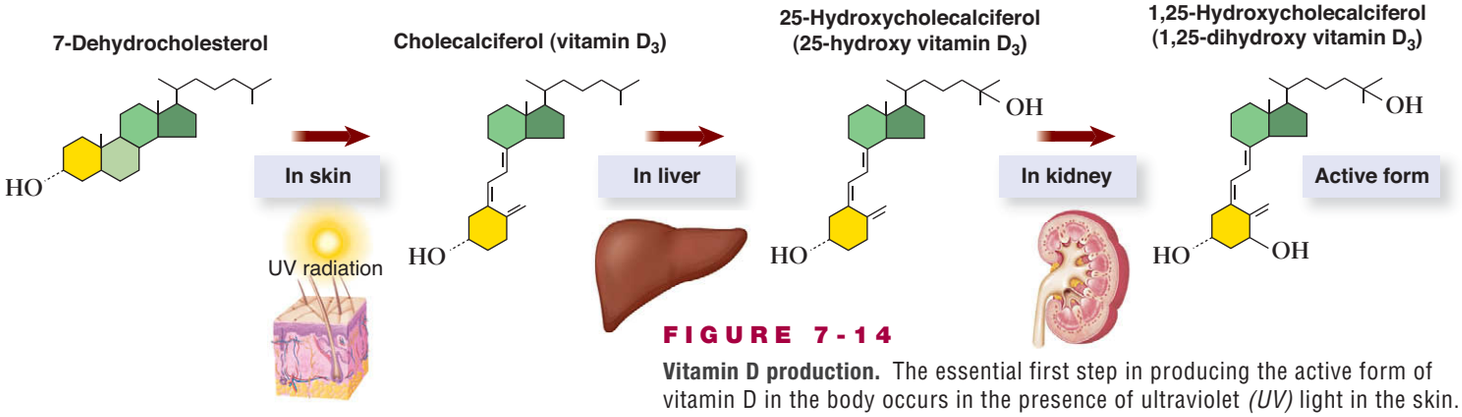


FIGURE 7-14

Vitamin D production. The essential first step in producing the active form of vitamin D in the body occurs in the presence of ultraviolet *(UV)* light in the skin.

In most people, body temperature moves up and down very little in the course of a day. It hovers close to a set point of about 37° C, perhaps increasing to 37.6° C by late afternoon and decreasing to around 36.2° C by early morning. This homeostasis of body temperature is of the utmost importance. Why? Because healthy survival depends on biochemical reactions taking place at certain rates—and these rates depend on normal enzyme functioning, which depends on body temperature staying within the narrow range of normal.

To maintain an even temperature, the body must balance the amount of heat it produces with the amount it loses. This means that if extra heat is produced in the body, this same amount of heat must be lost from it. Obviously, if this does not occur, if increased heat loss does not closely follow increased heat production, body temperature climbs steadily upward. If body temperature increases above normal for any reason, the skin plays a critical role in heat loss by the physical phenomena of evaporation, radiation, conduction, and convection.

HEAT PRODUCTION

Heat is produced by one means—metabolism of foods. Because the muscles and glands (especially the liver) are the most active tissues, they carry on more metabolism and therefore produce more heat than any of the other tissues. So the chief determinant of how much heat the body produces is the amount of muscular work it does. During exercise and shivering, for example, metabolism and heat production increase greatly. But during sleep, when very little muscular work is being done, metabolism and heat production decrease. The skin does not produce heat, but it plays a big role in retaining and dissipating heat to maintain homeostasis of body temperature.

HEAT LOSS

As already stated, one mechanism the body uses to maintain relative constancy of internal temperature is to regulate the amount of heat loss. Some 80% or more of this transfer of heat occurs through the skin; the remainder takes place in mucous membranes. As Figure 7-15 shows, heat loss can be regulated by altering the flow of blood in the skin. If heat must be conserved to maintain a constant body temperature, dermal blood vessels constrict (vasoconstriction) to keep most of the warm blood circulating deeper in the body. If heat loss must be increased to maintain a constant temperature, dermal blood vessels widen (vasodilation) to increase the skin's supply of warm blood from deeper tissues. Heat transferred from the warm blood to the epidermis can then be lost to the external environment through the physical processes of evaporation, radiation, conduction, and convection.

Evaporation

Heat energy must be expended to evaporate any fluid. Evaporation of water constitutes one method by which heat is lost from the body, especially from the skin. Evaporation is especially important in high environmental temperatures, when it is the only method by which heat can be lost from the skin. A humid atmosphere necessarily retards evaporation and therefore lessens the cooling effect derived from it—the explanation for the fact that the same degree of temperature seems hotter in humid climates than in dry ones. At moderate temperatures, evaporation accounts for about half as much heat loss as radiation does.

Radiation

Radiation is the transfer of heat from the surface of one object to that of another without actual contact between the two. Heat radiates from the body surface to nearby objects that are cooler than the skin and radiates to the skin from those that are warmer than the skin. This is the principle of heating and cooling systems. In cool environmental temperatures, radiation accounts for a greater percentage of heat loss from the skin than conduction and evaporation combined do. In hot environments, no heat is lost by radiation but may be gained by radiation from warmer surfaces to the skin.

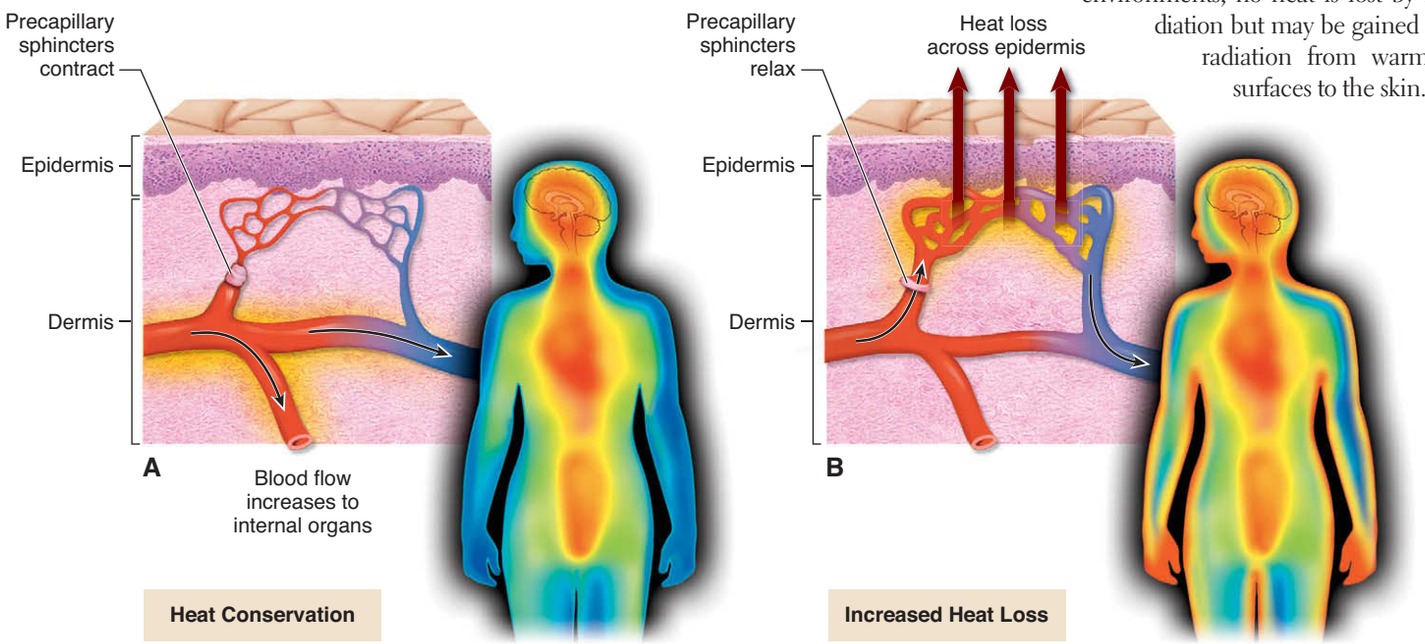
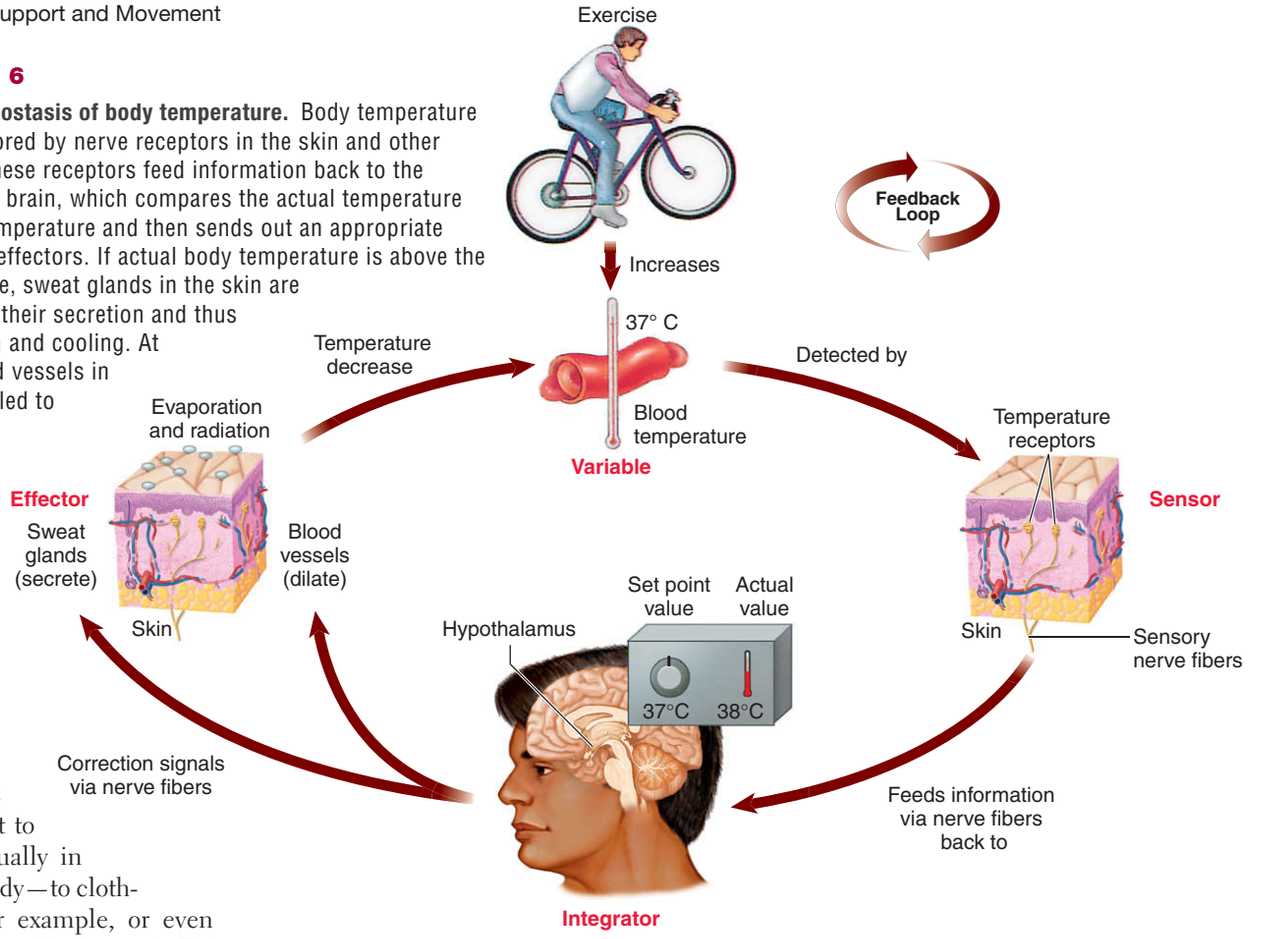


FIGURE 7-15

The skin as a thermoregulatory organ. When homeostasis requires that the body conserve heat, blood flow in the warm organs of the body's core increases. **A,** When heat must be lost to maintain stability of the internal environment, flow of warm blood to the skin increases. **B,** Heat can be lost from the blood and skin by means of radiation, conduction, convection, and evaporation. The head, hands, and feet are major areas of heat loss.

FIGURE 7-16

Role of skin in homeostasis of body temperature. Body temperature is continually monitored by nerve receptors in the skin and other parts of the body. These receptors feed information back to the hypothalamus of the brain, which compares the actual temperature with the set point temperature and then sends out an appropriate correction signal to effectors. If actual body temperature is above the set point temperature, sweat glands in the skin are signaled to increase their secretion and thus promote evaporation and cooling. At the same time, blood vessels in the dermis are signaled to dilate and thus promote radiation of heat away from the skin's surface.



Conduction

Conduction means the transfer of heat to any substance actually in contact with the body—to clothing or jewelry, for example, or even to cold foods or liquids ingested. This process accounts for a relatively small amount of heat loss.

Convection

Convection is the transfer of heat away from a surface by movement of heated air or fluid particles. Usually, convection causes very little heat loss from the body's surface. However, under certain conditions, it can account for considerable heat loss, as you know if you have ever stepped from your shower into even slightly moving air from an open window.

Box 7-6 | SPORTS and FITNESS

Exercise and the Skin

Excess heat produced by the skeletal muscles during exercise increases the core body temperature far beyond the normal range. Because blood in vessels near the skin's surface dissipates heat well, the body's control centers adjust blood flow so that more warm blood from the body's core is sent to the skin for cooling. During exercise, blood flow in the skin can be so high that the skin takes on a redder coloration.

To help dissipate even more heat, sweat production increases to as high as 3 L per hour during exercise. Although each sweat gland produces very little of this total, more than 3 million individual sweat glands are found throughout the skin. Sweat evaporation is essential to keeping body temperature in balance, but excessive sweating can lead to a dangerous loss of fluid. Because the usual intake of fluids may not replace the water lost through sweating, it is important to increase fluid consumption during and after any type of exercise to avoid *dehydration.*

HOMEOSTATIC REGULATION OF HEAT LOSS

The operation of the skin's blood vessels and sweat glands must be coordinated carefully and must take into account moment-by-moment fluctuations in body temperature. Like most homeostatic mechanisms, heat loss by the skin is controlled by a negative feedback loop (Figure 7-16). Temperature receptors in a part of the brain, called the *hypothalamus*, detect changes in the body's internal temperature. If some disturbance, such as exercise, increases body temperature above the set point value of 37° C, the hypothalamus acts as an integrator and sends a nervous signal to the sweat glands and blood vessels of the skin. The sweat glands and blood vessels (the effectors) respond to the signal by acting in ways that promote heat loss. That is, sweat glands increase their output of sweat (increasing heat loss by evaporation), and blood vessels increase their diameter (increasing heat loss by radiation and other means). This process continues until the homeostatic set point for normal body temperature is reached (Box 7-6).

| QUICK CHECK |

9. What is the one means of heat production in the body? In what type of organs does most heat production occur?
10. Name three of the four physical processes by which heat is lost from the body.

APPENDAGES OF THE SKIN

Appendages of the skin consist of *hair, nails,* and *skin glands.*

Hair

We have about 5 million hairs on the skin of our body. About 150,000 hairs are on our heads, with the rest scattered all over the skin. Only a few areas of the skin are hairless—notably the palms of the hands and the soles of the feet. Hair is also absent from the lips, nipples, and some areas of the genitals.

DEVELOPMENT OF HAIR

Many months before birth, tiny tubular pockets called **hair follicles** begin to develop in most parts of the skin. By about the sixth month of pregnancy the developing fetus is all but covered by an extremely fine and soft hair coat, called **lanugo.** Most of the lanugo hair is lost before birth. Soon after birth, any lanugo hair that remains is lost and then replaced by **vellus** hair, which is stronger, fine, and usually less pigmented (see Figure 7-3, B).

The replacement hair growth after birth first appears on the scalp, eyelids, and eyebrows, and the coarse pubic and axillary hair that develops at puberty is called **terminal hair.** In the adult male, terminal hair replaces 80% to 90% of the vellus hair on the chest and extremities and also makes up the beard. In the female, far less vellus hair is replaced with the more coarse terminal variety except in the pubic and axillary areas.

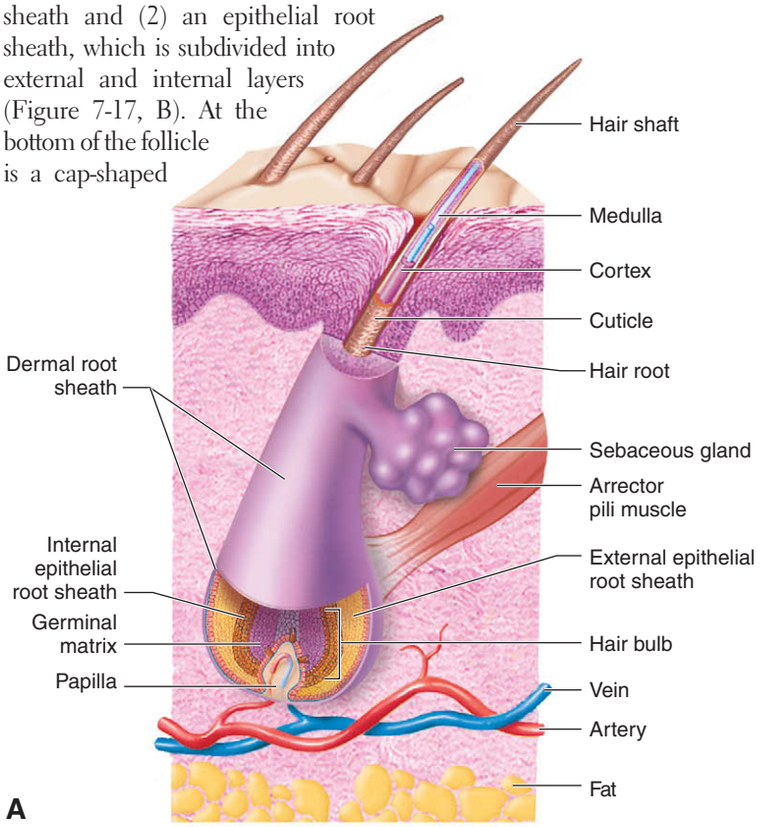
Hair growth begins at the base of the follicle (Figure 7-17). The follicle wall consists of two primary layers: (1) an outer dermal root sheath and (2) an epithelial root sheath, which is subdivided into external and internal layers (Figure 7-17, B). At the bottom of the follicle is a cap-shaped cluster of cells known as the **germinal matrix.** Protruding into the germinal matrix is a small mound of the dermis, called the **hair papilla,** which is an important structure because it contains the blood capillaries that nourish the germinal matrix (see Figure 7-17). Cells of the germinal matrix are responsible for forming hairs. They undergo repeated mitosis, push upward in the follicle, and become keratinized to form a hair. As long as cells of the germinal matrix remain alive, hair regenerates even though it is cut, plucked, or otherwise removed.

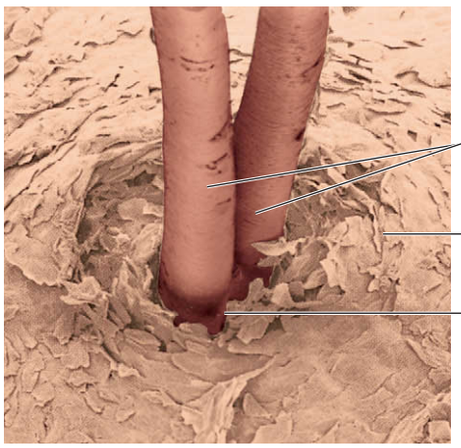
Part of the hair, namely, the root, lies hidden in the follicle. The visible part of a hair is called the **shaft.** The inner core of a hair is known as the **medulla,** the more superficial portion around it is called the **cortex,** and the covering layer is called the *cuticle.* If hair is plucked from the follicle, the internal epithelial root sheath will be torn free as well and appears as a whitish layer adherent to the hair cuticle. Layers of keratinized cells make up the cortex.

Besides being a structure to grow and support hair, the hair follicle wall also serves as a primary location of adult stem cells for various types of skin cells such as melanocytes and keratinocytes.

APPEARANCE OF HAIR

Deposited in the cells of the hair are varying amounts of melanins, the pigments responsible for hair color. Although reflections of light can affect hair color somewhat, it is largely the amount, type,





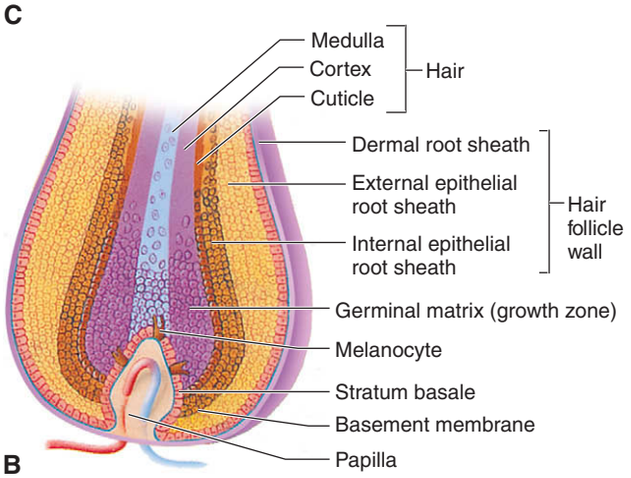


FIGURE 7-17

Hair follicle. A, Relationship of a hair follicle and related structures to the epidermal and dermal layers of the skin. **B,** Enlargement of a hair follicle wall and hair bulb. **C,** Scanning electron micrograph showing shafts of hair extending from their follicles.



FIGURE 7-18

Gray hair. Gray hair results from a scattered arrangement of both white (pigmentless) hairs and darker (pigmented) hairs.

and distribution of melanin that determine the color of hair. Varying amounts of eumelanins in the cortex and/or medulla can produce many shades of blonde and brunette hair. Pheomelanins give hair a reddish tint. Advancing age often produces an increasing smattering of white hairs—the proverbial "crown of glory." White hairs have no pigments at all but appear white because of the diffusion of light through the translucent hair shaft. White hair results from the accumulation of oxygen *free radicals*—highly reactive forms of oxygen that increase as we age. The free radicals damage stem cells in the hair follicle. We fail to maintain the production of new melanocytes and thus lose the ability to produce pigment in the hair. Gray hair, seen in Figure 7-18, is usually a "salt-and-pepper" mixed arrangement of white and dark hairs. Besides adding color, melanin also imparts strength to the hair shaft.

Whether hair is straight or wavy depends mainly on the shape of the shaft. Straight hair has a round, cylindrical shaft. Wavy hair, in contrast, has a flat shaft that is not as strong. As a result, it is more easily broken or damaged than is straight hair. Two or more small **sebaceous glands** secrete **sebum,** an oily substance, into each hair follicle (see Figure 7-17). The sebaceous gland secretions lubricate and condition the hair and surrounding skin to keep it from becoming dry, brittle, and easily damaged. Lipid-containing hair and skin conditioners can add to this damage-reducing effect.

Hair alternates between periods of growth and rest. On average, hair on the head grows a little less than 12 mm (1/2 inch) per month, or about 11 cm (5 inches) a year. Body hair grows more slowly. Head hairs reportedly live between 2 and 6 years, then die and are shed. Normally, however, new hairs replace those lost. But baldness, also called *alopecia*, can develop.

A common type of baldness occurs only when two requirements are met: genes for baldness must be inherited and the male sex hormones (*androgens*) must be present. When the right combination of these causative factors exist, *androgenic alopecia* or **male pattern baldness** (Figure 7-19) inevitably results. An available treatment that may slow or stop the development of male pattern baldness is the drug minoxidil (Rogaine). Unfortunately, the treatment is expensive, must be continued for life if new hair growth is to be retained, and does not always produce as dramatic an effect as hoped.



FIGURE 7-19

Male pattern baldness.

Contrary to what many people believe, hair growth is not stimulated by frequent cutting or shaving. In addition, stories about hair or beard growth continuing after death are also false. What may appear to be continuing beard growth after death is in reality only a more visible beard in a skin surface dehydrated by environmental conditions or the embalming process.

Nails

Heavily keratinized epidermal cells compose fingernails and toenails. The visible part of each nail is called the **nail body.** The rest of the nail, namely, the **root,** lies in a flat sinus hidden by a fold of skin bordered by the **cuticle.** The nail body nearest the root has a crescent-shaped white area known as the **lunula,** or "little moon." Under the nail lies a layer of epithelium called the **nail bed** (Figure 7-20). Because it contains abundant blood vessels, it normally appears pink through the translucent part of the nail bodies. Clinically, this is useful to know. Cyanosis (blueness) often appears under the nails first (see Figure 7-12), and thus nail beds are often monitored closely during surgery or other procedures in which oxygenation of the blood may suddenly drop. Sometimes, lightly pigmented streaks appear in the nail beds of dark-skinned individuals (Figure 7-21).

Nails grow by mitosis of cells in the stratum basale beneath the lunula. On average, nails grow about 0.5 mm a week. Fingernails, however, as you may have noticed, grow faster than toenails, and both grow faster in the summer than in the winter. Even minor trauma to long fingernails can sometimes result in loosening of the nail from the nail bed with a resulting separation that starts at the distal or free edge of the affected nail (Figure 7-22). The condition, called **onycholysis** (ahn-ik-oh-LYE-sis), is common.

Bruising under a nail can cause discoloration as the bruise forms, then heals. Fungal infections can also cause discoloration of nails, often turning them yellow or even black. Fungal

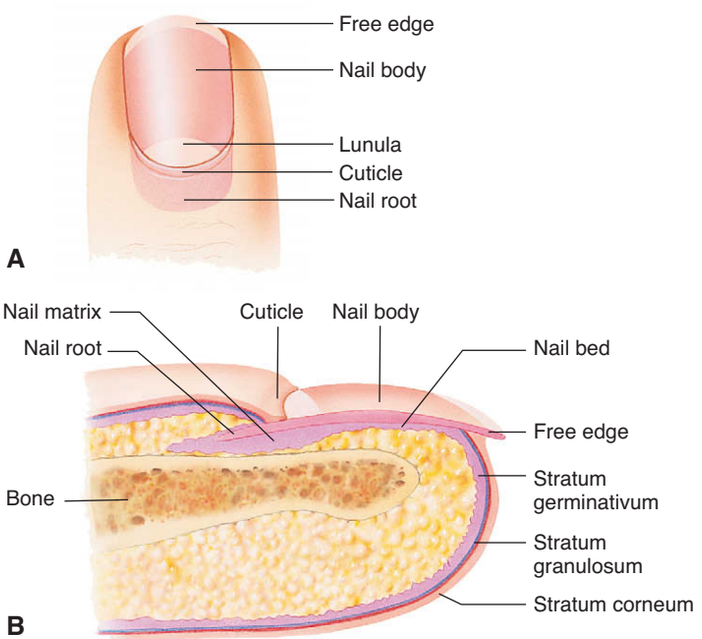


FIGURE 7-20

Structure of nails. A, Fingernail viewed from above. **B,** Sagittal section of a fingernail and associated structures.



FIGURE 7-21

Pigmented nails. In light-skinned individuals, the nail bed is usually free of pigmentation. In very dark-skinned individuals, yellowish or brown pigmented bands (seen in the photograph) are common.



FIGURE 7-22

Onycholysis. In the photo, note that separation of the nails from the nail bed begins at the free edge. Minor trauma to long fingernails is the most common cause.

infections also frequently weaken the nail structure, causing a nail to flake, split, or break more easily.

Artificial nails made of plastic can be used to help repair broken nails or simply to enhance the nails' appearance. However, health care workers are discouraged from using artificial nails because they tend to transmit bacterial infection more easily. In surgery patients, artificial nails obscure signs of cyanosis, which is a helpful clinical sign of oxygen deficiency.

| QUICK CHECK |

11. Identify the pigment that determines hair color.
12. List seven functions of the skin.
13. How does surface film contribute to the protective function of the skin?
14. List the appendages of the skin.

Skin Glands

The skin glands include three kinds of microscopic glands: sweat, sebaceous, and ceruminous (Figure 7-23).

SWEAT GLANDS

Sweat or **sudoriferous** (soo-doh-RIF-er-us) **glands** are the most numerous of the skin glands. They can be classified into two groups—*eccrine* and *apocrine*—based on the type of secretion, location, and nervous system connections.

Eccrine sweat glands are by far the most numerous, important, and widespread sweat glands in the body. They are small, with a secretory portion less than 0.4 mm in diameter, and are distributed over the total body surface with the exception of the lips, ear canal, glans penis, and nail beds. Eccrine sweat glands are a simple, coiled, tubular

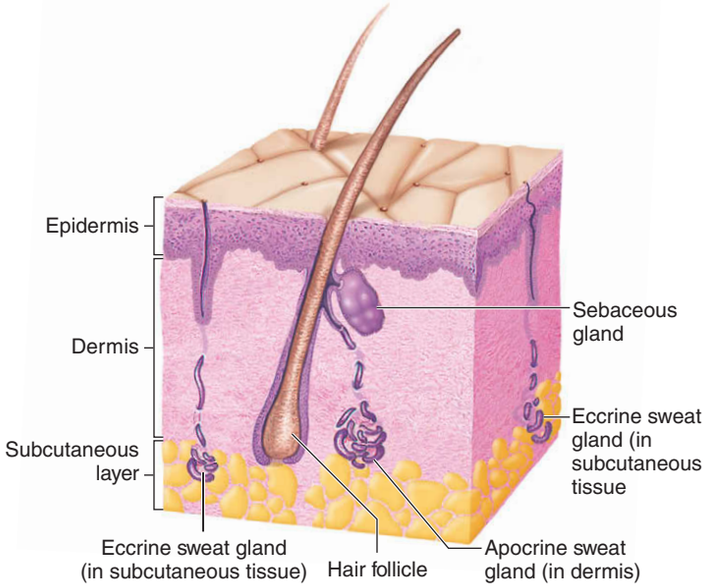


FIGURE 7-23

Skin glands. Several types of exocrine glands occur in the skin.

type of gland. They function throughout life to produce a transparent watery liquid (*perspiration*, or *sweat*) rich in salts, ammonia, uric acid, urea, and other wastes. In addition to elimination of waste, sweat plays a critical role in helping the body maintain a constant core temperature. Histologists estimate that a single square inch of skin on the palms of the hands contains about 3000 sweat glands. Eccrine sweat glands are also numerous on the soles of the feet, forehead, and upper part of the torso. With a good magnifying glass you can locate the openings of these sweat gland ducts on the skin ridges of the palms and on the skin of the palmar surfaces of the fingers. Although the ducts of eccrine glands travel through both the dermis and epidermis to open on the skin surface, the actual secretory portion is located in the subcutaneous tissue.

Apocrine sweat glands are located deep in the subcutaneous layer of the skin in the armpit (axilla), the areola of the breast, and the pigmented skin areas around the anus. They are much larger than eccrine glands and often have secretory units that reach 5 mm or more in diameter. They are connected to hair follicles and are classified as simple, branched tubular glands. Apocrine glands enlarge and begin to function at puberty; they produce a more viscous and colored secretion than eccrine glands do. In the female, apocrine gland secretions show cyclic changes linked to the menstrual cycle. The odor often associated with apocrine gland secretion is not caused by the secretion itself. Instead, it is caused by decomposition of the secretion by skin bacteria.

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Apocrine sweat contains a class of molecules called **pheromones,** which are signaling molecules detected by other individuals. They may be used as a territorial marker, but in humans they seem to serve mainly as social or sexual signals. Want to know more about these "sex molecules?" Check out ***Pheromones and the Vomeronasal Organ*** online at ***A&P Connect.***

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SEBACEOUS GLANDS

Sebaceous glands secrete oil for the hair and skin. Wherever hairs grow from the skin, there are sebaceous glands, at least two for each hair. The oil, or **sebum,** keeps the hair supple and the skin soft and pliant. It is nature's own protective skin cream that prevents excessive water loss from the epidermis. Because sebum is rich in chemicals that have an antifungal effect, such as triglycerides, waxes, fatty acids, and cholesterol, it also contributes to reducing fungal activity on the skin surface. This property of sebum increases the effectiveness of the skin's surface film and helps protect the skin from numerous types of fungal infections. Sebaceous glands are simple branched glands of varying size that are found in the dermis, except in the skin of the palms and soles. Although almost always associated with hair follicles, some sebaceous glands do open directly onto the skin surface in such areas as the glans penis, lips, and eyelids. Sebum secretion increases during adolescence because it is stimulated by increased blood levels of sex hormones. Frequently, sebum accumulates in and enlarges some of the ducts of the sebaceous glands, thereby forming white pimples. With oxidation, this accumulated sebum darkens and forms a **blackhead.**

CERUMINOUS GLANDS

Ceruminous glands are a special variety or modification of apocrine sweat glands. Histologically, they appear as simple coiled tubular glands with excretory ducts that open onto the free surface of the skin in the external ear canal or with sebaceous glands into the necks of hair follicles in this area. The mixed secretions of sebaceous and ceruminous glands form a brown waxy substance called **cerumen.** Although it serves a useful purpose in protecting the skin of the ear canal from dehydration, excess cerumen can harden and cause blockage in the ear, resulting in loss of hearing.

| QUICK CHECK |

15. What are the two types of sweat glands? How do they differ?
16. List two functions of sebum.
17. What substances make up the skin's surface film?

Cycle of LIFE

Skin

Everyone is aware of the dramatic changes in skin that each person experiences from birth through the mature years. Infants and young children have relatively smooth and unwrinkled skin characterized by the elasticity and flexibility associated with extreme youth. Because the skin tissues are in an active phase of new growth, healing of skin injuries is often rapid and efficient. Young children have fewer sweat glands than adults do, so their bodies rely more on increased blood flow to maintain normal body temperature. This explains why preschoolers often become "red-faced" while playing outdoors on a warm day.

As adulthood begins, at puberty, hormones stimulate the development and activation of sebaceous glands and sweat glands.

Box 7-7 | HEALTH matters

Acne



Common *acne,* or *acne vulgaris,* occurs most frequently in the adolescent years as a result of overactive secretion by the sebaceous glands, with blockage and inflammation of their ducts. The rate of sebum secretion increases more than fivefold between 10 and 19 years of age. As a result, sebaceous gland ducts may become plugged with sloughed skin cells and sebum contaminated with bacteria. The inflamed plug is called a *comedo* and is the most characteristic sign of acne. Pus-filled *pimples* or *pustules* result from secondary infections within or beneath the epidermis, often in a hair follicle or sweat pore.

After the sebaceous glands become active, especially during the initial years, they often overproduce sebum and thus give the skin an unusually oily appearance. Sebaceous ducts may become clogged or infected and form acne pimples or other blemishes on the skin (Box 7-7). Activation of apocrine sweat glands during puberty causes increased sweat production—an ability needed to maintain an adult body properly—and also the possibility of increased "body odor." Body odor is caused by wastes produced by bacteria that feed on the organic compounds found in apocrine sweat and on the surface of the skin.

As one continues past early adulthood, the sebaceous and sweat glands become less active. Although this can provide a welcome relief to those who suffer from acne or other problems associated with over-activity of these glands, it can affect normal function of the body. For example, the reduction of sebum production can cause the skin and hair to become less resilient and therefore more likely to wrinkle or crack. Wrinkling can also be caused by an overall degeneration in the skin's ability to maintain itself as efficiently as it did during the early years of development (Figure 7-24). Loss of function in sweat glands as adulthood advances adversely affects the body's ability to cool itself during exercise or when the external temperature is high. Thus elderly individuals are more likely to suffer severe problems during hot weather than are young adults. Figure 7-11 shows the hyperpigmented "age spots" seen in the elderly after years of sun exposure.



FIGURE 7-24

Aged skin. In late adulthood, wrinkles in the skin often develop—especially in areas of frequent movement such as on the hands, around the mouth, and around the eyelids.

the BIG picture

Skin and the Whole Body

The skin is one of the major components of the body's structural framework. It is continuous with the connective tissues that hold the body together, including the fascia, bones, tendons, and ligaments. The integumentary, skeletal, and muscular systems work together to protect and support the whole body.

As stated several times in this chapter, the skin is a barrier that separates the internal environment from the external environment. Put another way, the skin *defines* the internal environment of the body. The barrier formed by the skin is a formidable one indeed; the skin possesses numerous mechanisms for protecting internal structures from the sometimes harsh external environment. Without these protective mechanisms, the internal environment could not maintain a relative constancy that is independent of the external environment.

First, the dermis and epidermis work together to form a tough, waterproof envelope that protects us from drying out and from the dangers of chemical or microbial contamination. The sebaceous secretions of the skin, along with other components of the skin's surface film, enhance the skin's ability to protect the internal environment. Protection against mechanical injuries is provided by hair, calluses, and the layers of the skin itself. Pigmentation in the skin and our ability to regulate its concentration protect us from the harmful effects of solar radiation.

Although its primary functions are support and protection, the skin has other important roles in maintaining homeostasis. For example, the skin is also an important agent in the regulation of body temperature—it serves as a sort of "radiator" that can be activated or deactivated as needed. It helps maintain a constant level of calcium in the body by producing vitamin D, which is necessary for normal absorption of calcium in the digestive tract. Ridges on the palms and fingers allow us to make and use tools for getting food, building shelters, and conducting other survival tasks. The skin's flexibility and elasticity permit the free movement required to perform such tasks. Sensory nerve receptors in the dermis allow the skin to be a "window on the world." Information about the external environment is relayed from skin receptors to nervous control (integration) centers, where it is used to coordinate the function of other organs.

As you continue your study of the various organ systems of the body, keep in mind that none of them could operate properly without the structural and functional assistance of the integumentary system.

MECHANISMS of DISEASE

SKIN DISORDERS

Any disorder of the skin can be called a **dermatosis,** which means "skin condition." Many dermatoses involve inflammation of the skin, or **dermatitis.** Various disorders involving the skin have already been discussed in this chapter. A few more representative disorders are described here.

Skin Infections

The skin is the first line of defense against microorganisms that might invade the body's internal environment. It is no wonder that the skin is a common site of infection. In adults, the antimicrobial characteristics of sebum in the skin's surface film often inhibit skin infections. In children, the lack of sebum in surface film makes the skin less resistant to infection.

Many different viruses, bacteria, and fungi cause skin conditions. Here are a few examples of skin infections caused by different types of pathogenic (disease-causing) organisms:

1. **Impetigo.** This highly contagious bacterial condition results from *Staphylococcus* or *Streptococcus* infection and occurs most often in young children. Impetigo starts as a reddish discoloration, or *erythema*, but soon develops into vesicles (blisters) and yellowish crusts. Occasionally, the infection becomes systemic (bodywide) and thus is life threatening.
2. **Tinea.** Tinea is the general name for many different *mycoses* (fungal infections) of the skin. Ringworm, jock itch, and athlete's foot are all classified as tinea. Signs of tinea include erythema, scaling, and crusting. Occasionally, fissures, or cracks, in the epidermis develop at creases in the epidermis. Figure 7-25 shows a case of ringworm, a tinea infection that typically forms a round rash that heals in the center to form a ring. Antifungal agents usually stop the acute infection but

FIGURE 7-25

Tinea infection (ringworm). Note that the lesions heal in the center, with inflamed rings left on the skin's surface.



are unable to completely destroy the fungus. Recurrence of tinea can be avoided by keeping the skin dry because fungi require a moist environment to grow.

3. **Warts.** Caused by papillomaviruses, warts are nipplelike neoplasms of the skin. Although they are usually benign, some warts transform to become malignant. Transmission of warts generally occurs through direct contact with warts on the skin of an infected person. Warts can be removed by freezing, drying, laser therapy, or the application of chemicals.
4. **Boils.** Also called *furuncles*, boils are local *Staphylococcus* infections of hair follicles characterized by large, inflamed, pus-filled lesions. A group of untreated boils may fuse into even larger lesions called *carbuncles.*

Vascular and Inflammatory Skin Disorders

Everyone who might ever be called on to provide care to a bedridden or otherwise immobilized individual should be aware of the causes and nature of pressure sores, or **decubitus ulcers** (Figure 7-26). *Decubitus* means "lying down," a name that hints at a common cause of pressure sores: lying in one position for long periods. Also called *bedsores*, these lesions appear after blood flow to a local area of skin slows because of pressure on skin covering bony prominences such as the ankles. Ulcers form and infections develop as lack of blood flow causes tissue damage. Frequent changes in body position and soft support cushions help prevent decubitus ulcers.

A common type of skin disorder that involves blood vessels is **urticaria,** or *hives.* This condition is characterized by raised red lesions, called *wheals*, caused by leakage of fluid from the skin's blood vessels. Urticaria is often associated with severe itching. Hypersensitivity or allergic reactions, physical irritants, and systemic diseases are common causes.

Scleroderma is an autoimmune disease that affects the blood vessels and connective tissues of the skin. The name *scleroderma* comes from the word parts *sclera-*, which means "hard," and *derma*, which means "skin." Hard skin is a good description of the lesions characteristic of scleroderma. Scleroderma begins as a mild inflammation that later develops into a patch of yellowish, hardened skin. Scleroderma most commonly remains a mild, localized condition. Very rarely, localized scleroderma progresses to a systemic form that affects large areas of the skin and other organs. Persons with advanced systemic scleroderma seem to be wearing a mask because skin hardening prevents them from moving their mouths freely. Both forms of scleroderma occur more commonly in women than in men.



FIGURE 7-26

Decubitus ulcer. The skin forms crater-like lesions when the blood supply is diminished and skin tissue cannot be maintained in the area of reduced blood flow.



FIGURE 7-27

Psoriasis. Inflammation and scaling are characteristic of this skin disorder.

Psoriasis is a chronic inflammatory disorder of the skin thought to have a genetic basis. This common skin problem is characterized by cutaneous inflammation accompanied by silver-colored, scaly lesions that develop from an excessive rate of epithelial cell growth (Figure 7-27).

Eczema is the most common inflammatory disorder of the skin. This condition is characterized by inflammation often accompanied by papules (bumps), vesicles (blisters), and crusts. Eczema is not a distinct disease but rather a sign or symptom of an underlying condition. For example, an allergic reaction called *contact dermatitis* can progress to become eczematous. Poison ivy is a form of contact dermatitis—occurring on *contact* with chemicals produced by the poison ivy plant.

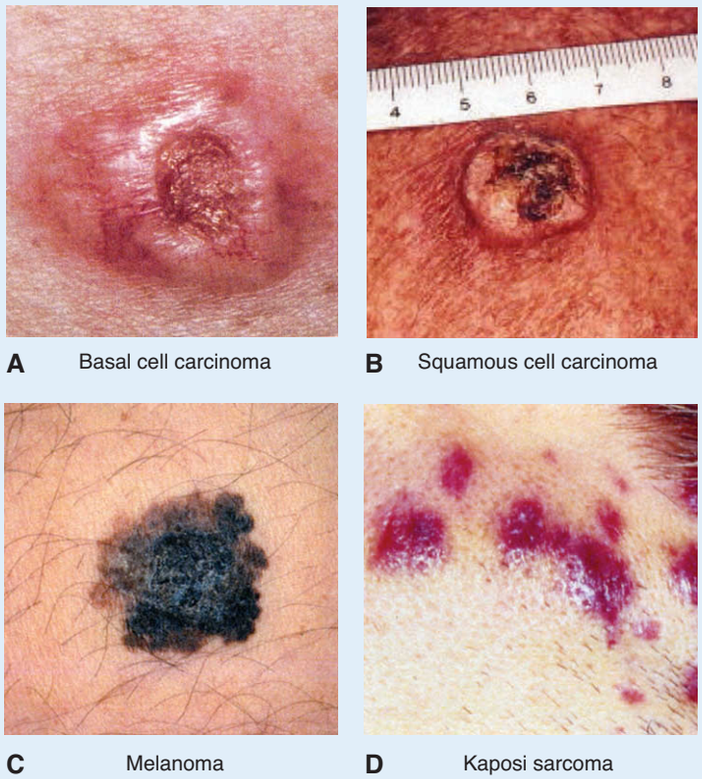
Skin Cancer

Each year in the United States more than 800,000 new cases of skin cancer are diagnosed. These *neoplasms*, or abnormal growths, result from cell changes in the epidermis and are the most common form of cancer in humans. They account for nearly 25% of all cancer in men and 14% of reported cases in women.

Two forms of the disease, called **basal cell carcinoma** and **squamous cell carcinoma,** account for more than 95% of all reported cases of skin cancer (Figure 7-28, *A* and *B*). Both types are very responsive to treatment and seldom *metastasize* (meh-TAS-tah-size), or spread to other body areas. However, if left untreated, these cancers can cause significant damage to adjacent tissues that results in disfigurement and loss of function.

A third type of skin cancer called **malignant melanoma** has a tendency to spread to other body areas and is a much more serious form of the disease than either the basal cell or squamous cell varieties (Figure 7-28, *C*). About 35,000 new cases of malignant melanoma are reported each year, and of that number more than 7000 die of the disease.

Kaposi (KAH-poh-see) **sarcoma** appears in immune deficiencies such as AIDS. It produces purple papules on the skin (Figure 7-28, *D*) and quickly spreads to the lymph nodes and internal organs.



A Basal cell carcinoma

B Squamous cell carcinoma

C Melanoma

D Kaposi sarcoma

FIGURE 7-28

Skin cancers.

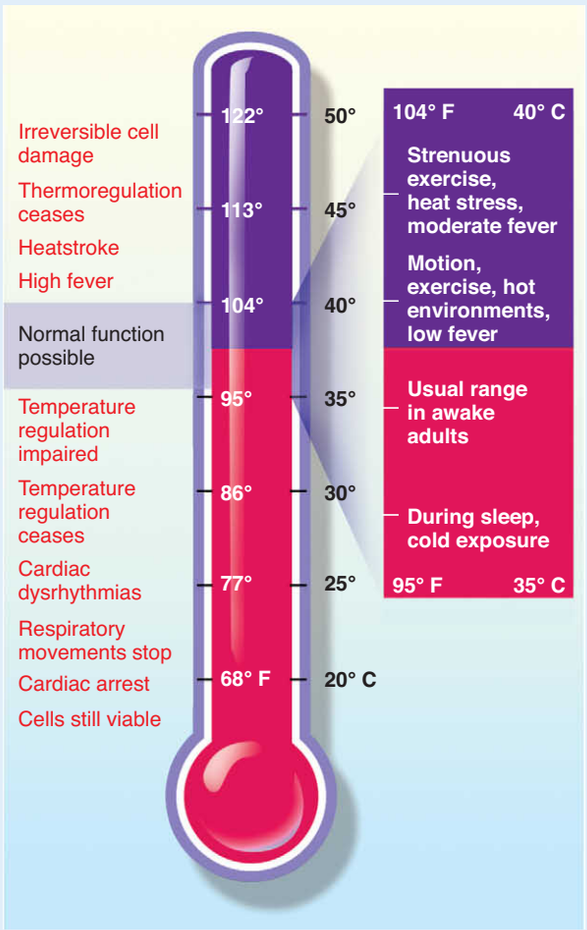


FIGURE 7-29

Body temperature. This diagram, modeled after a thermometer, shows some physiological consequences of abnormal body temperature. The inset shows a range of body temperatures at which normal function is possible. Ideally, body temperature should be near 37° C (98.6° F), but the body can operate normally within the range shown if conditions are not ideal.

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How can you tell the difference between a normal mole and skin cancer? Find out at ***Skin Cancer*** online at ***A&P Connect.***

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Abnormal Body Temperature

Maintenance of body temperature within a narrow range is necessary for normal functioning of the body. Figure 7-29 shows that straying too far out of the normal range of body temperatures can have very serious physiological consequences. A few important conditions related to body temperature follow:

1. **Fever,** or a *febrile* state, is an unusually high body temperature associated with a systemic inflammatory response. In the case of infections, chemicals called **pyrogens** (literally "fire makers") cause the thermostatic control centers of the hypothalamus to produce a fever. Because the body's "thermostat" is reset to a higher setting, a person feels a need to warm up to this new temperature and often experiences "chills" as the febrile state begins. The high body temperature associated with infectious fever is thought to enhance the body's immune responses to eliminate the pathogen. Strategies aimed at reducing the temperature of a febrile person are normally counteracted by the body's heat-generating mechanisms and have the effect of further weakening the infected person. Under ordinary circumstances, it is best to let the fever "break" on its own after the pathogen is destroyed.
2. **Malignant hyperthermia (MH),** an inherited condition, is characterized by abnormally increased body temperature (hyperthermia) and muscle rigidity when exposed to certain anesthetics or muscle relaxants (succinylcholine, for example). The drug *dantrolene (Dantrium)*, which inhibits heat-producing muscle contractions, has been used to prevent or relieve the effects of this condition.
3. **Heat exhaustion** occurs when the body loses a large amount of fluid from heat loss mechanisms. This usually happens when environmental temperatures are high. Although normal body temperature is maintained, the loss of water and electrolytes can cause weakness, dizziness, nausea, and possibly loss of consciousness. Heat exhaustion may also be accompanied by skeletal muscle cramps often called *heat cramps*. Heat exhaustion is treated with rest (in a cool environment) accompanied by fluid replacement.

4. **Heat stroke,** or *sunstroke,* is a severe, sometimes fatal condition resulting from the inability of the body to maintain normal temperature in an extremely warm environment. Such thermoregulatory failure may result from factors such as old age, disease, drugs that impair thermoregulation, or simply overwhelming elevated environmental temperatures. Heat stroke is characterized by body temperatures of 41° C (105° F) or higher, tachycardia (rapid heart rate), headache, and hot, dry skin. Confusion, convulsions, or loss of consciousness may occur. Unless the body is cooled and body fluids are replaced immediately, death may result.
5. **Hypothermia** is the inability to maintain normal body temperature in extremely cold environments. Hypothermia is characterized by body temperatures lower than 35° C (95° F), shallow and slow respirations, and a faint, slow pulse. Hypothermia is usually treated by slowly warming the affected person's body.
6. **Frostbite** is local damage to tissues caused by extremely low temperature. Damage to tissues results from the formation of ice crystals accompanied by a reduction in local blood flow. **Necrosis** (tissue death) and even **gangrene** (decay of dead tissue) can result from frostbite.

Burns

Typically we think of a burn as a thermal injury or lesion caused by contact of the skin with some hot object or fire. In addition, overexposure to ultraviolet light (sunburn) (Box 7-8) or contact with an electric current or corrosive chemicals causes injury or death to skin cells. The injuries that result can all be classified as *burns.*

| A&P CONNECT |

You recall from the article ***Radioactivity*** online at ***A&P Connect*** that ionizing radiation can also cause burns of the skin.

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Box 7-8 | HEALTH matters

Sunburn and Skin

Burns caused by exposure to harmful UV radiation in sunlight are commonly called *sunburns.* As with any burn, serious sunburns can cause tissue damage and lead to secondary infections and fluid loss. Cancer researchers have theorized that blistering (second-degree) sunburns during childhood may trigger the development of malignant melanoma later in life. Some epidemiological studies show that adults who had more than two blistering sunburns before the age of 20 years have a greater risk for melanoma than someone who experienced no such burns. If this theory is true, it could explain the dramatic increase in skin cancer rates in the United States in recent decades. Those who grew up as sunbathing and "suntans" became popular in the 1950s, 1960s and 1970s are now, as adults, exhibiting melanoma at a much higher rate than in previous generations.

Estimating Body Surface Area

When burns involve large areas of the skin, treatment and the prognosis for recovery depend in large part on the total area involved and the severity of the burn. The severity of a burn is determined by the depth and extent (percentage of body surface burned) of the lesion. There are several ways to estimate the extent of body surface area burned. One method is called the "**rule of palms**" and is based on the assumption that the palm size of a burn victim is about 1% of the total body surface area. Therefore, estimating the number of "palms" that are burned approximates the percentage of body surface area involved.

The "**rule of nines**" (Figure 7-30) is another and more accurate method of determining the extent of a burn injury. In this technique the body is divided into 11 areas of 9% each, with the area around the genitals, called the *perineum,* representing the additional 1% of body surface area. As Figure 7-30 shows, 9% of the skin covers the head and each upper extremity, including the front and back surfaces. Twice as much, or 18%, of the total skin area covers the front and back of the trunk and each lower extremity, including the front and back surfaces. The rule of nines works well with adults but does not reflect the differences in body surface area in small children. Special tables called *Lund-Browder charts,* which take the large surface area of certain body areas (such as the head) in a growing child into account, are used by physicians to estimate burn percentages in children.

The depth of a burn injury depends on the tissue layers of the skin that are involved (Figure 7-31). A **first-degree burn** (typical sunburn) causes minor discomfort and some reddening of the skin. Although the surface layers of the burned area may peel in

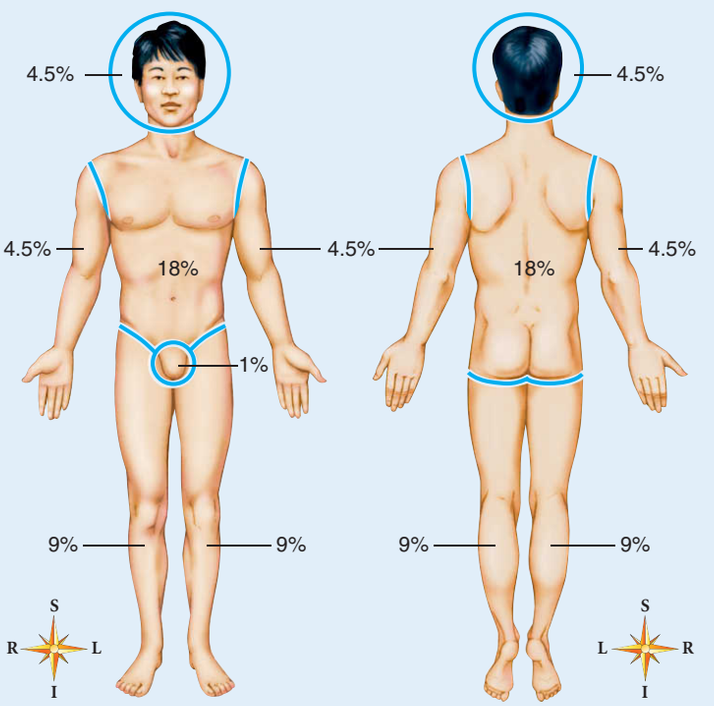


FIGURE 7-30

"Rule of nines." The "rule of nines" is one method used to estimate amount of skin surface burned in an adult.

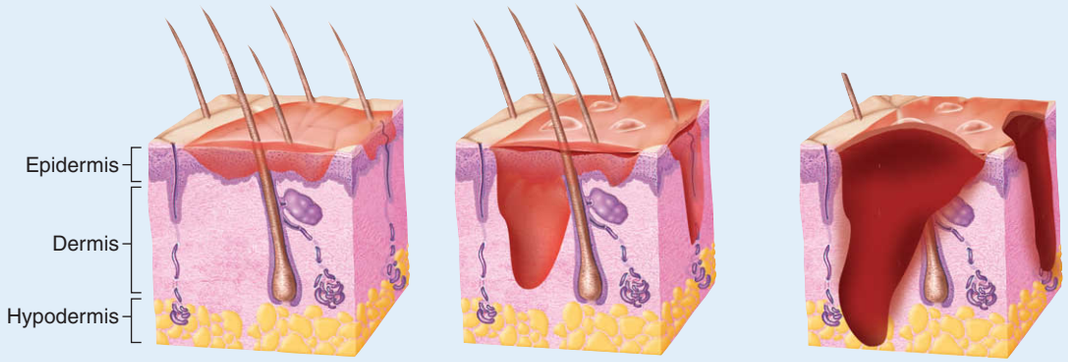


FIGURE 7-31
Classification of burns. Partial-thickness burns include first- and second-degree burns. Full-thickness burns include third-degree burns. Fourth-degree burns involve tissues under the skin, such as muscle or bone.

1 or 2 days, no blistering occurs and the actual tissue destruction is minimal. First- and second-degree burns are called **partial-thickness burns.**

Second-degree burns involve the deep epidermal layers and always cause injury to the upper layers of the dermis. In deep second-degree burns, damage to sweat glands, hair follicles, and sebaceous glands may occur, but tissue death is not complete. Blisters, severe pain, generalized swelling, and edema characterize this type of burn. Scarring is common.

Third-degree, or **full-thickness, burns** are characterized by destruction of both the epidermis and dermis. Tissue death extends below the hair follicles and sweat glands. If burning involves underlying muscles, fasciae, or bone, it may be called a **fourth-degree burn.** A distinction between second- and third- or fourth-degree burning is the fact that a third- or fourth-degree lesion is insensitive to pain immediately after injury because of the destruction of nerve endings. Scarring is a serious problem.

LANGUAGE OF SCIENCE *(continued from p. 170)*

dermis
(DER-mis)
[*derma* **skin**]

dermoepidermal junction (DEJ)
(DER-mo-EP-i-der-mal)
[*derm-* **skin**, *epi-* **on or upon**]

desquamation
(des-kwah-MAY-shun)
[*de-* **to remove**, *-squama-* **scale**, *-tion* **process**]

eccrine sweat gland
(EK-rin)
[*ec-* **out**, *-crin-* **secrete**, *gland* **acorn**]

eleidin
(eh-LEE-din)
[*elei-* **olive tree**, *-in* **substance**]

epidermis
(ep-i-DER-mis)
[*epi-* **on or upon**, *-dermis* **skin**]

eumelanin
(yoo-MEL-ah-nin)
[*eu-* **true**, *-melan-* **black**, *-in* **substance**]

friction ridge

germinal matrix
(JER-mi-nal MAY-triks)
[*germ* **sprout**, *-al* **relating to**, *matrix* **womb**] *pl.,* matrices

hair follicle
(FOHL-i-kul)
[*foll-* **bag**, *-icle* **little**]

hair papilla
(pah-PIL-ah)
[*papilla* **nipple**] *pl.,* **papillae**

hyperkeratosis
(hye-per-ker-ah-TOH-sis)
[*hyper* **excessive**, *-kera-* **horn**, *-osis* **condition**]

hypodermis
(hye-poh-DER-mis)
[*hypo-* **under or below**, *-dermis* **skin**]

integument
(in-TEG-yoo-ment)
[*integument* **covering**]

integumentary system
(in-teg-yoo-MEN-tar-ee)
[*integument* **covering**, *-ary* **relating to**]

keratin
(KER-ah-tin)
[*kera-* **horn**, *-in* **substance**]

keratinization
(ker-ah-tin-i-ZAY-shun)
[*kera* **horn**, *-in-* **substance**, *-iz-* **to cause**, *-ation* **process**]

keratinocyte
(keh-RAT-i-no-syte)
[*kera-* **horn**, *-in-* **substance**, *-cyte* **cell**]

keratohyalin
(ker-ah-toh-HYE-ah-lin)
[*kera-* **horn**, *-hyaline* **glass**]

lanugo
(lah-NOO-go)
[*lanugo* **down**]

lunula
(LOO-nyoo-lah)
[*luna-* **moon**, *-ula* **small**]

medulla
(meh-DUL-ah)
[*medulla* **middle**] *pl.* medullae or medullas

melanin
(MEL-ah-nin)
[*melan-* **black**, *-in* **substance**]

melanocyte
(MEL-ah-no-syte)
[*melan-* **black**, *-cyte* **cell**]

melanosome
(MEL-ah-no-sohm)
[*melan-* **black**, *-som-* **body**]

microbiome
(mye-kroh-BYE-ohm)
[*micro-* **small**, *-bio-* **life**, *-ome* **entire collection**]

nail bed

nail body

papillary
(PAP-i-lair-ee)
[*papilla-* **nipple**, *-ary* **relating to**]

pheomelanin
(fee-oh-MEL-ah-nin)
[*pheo-* **dusky**, *-melan-* **black**, *-in* **substance**]

pheromone
(fair-o-mohn)
[*pher-* **carry**, *-mone* **hormone (excite)**]

LANGUAGE OF SCIENCE *(continued from p. 193)*

reticular
(reh-TIK-yoo-lar)
[*ret-* **net**, *-ic-* **relating to**, *-ul-* **little**, *-ar* **relating to**]

root

sebaceous gland
(seh-BAY-shus)
[*seb-* **tallow (hard animal fat)**, *-ous* **relating to**, *gland* **acorn**]

sebum
(SEE-bum)
[*sebum* **tallow (hard animal fat)**]

shaft

stratum
(STRAH-tum)
[*stratum* **layer**] *pl.,* strata

stratum basale
(STRAH-tum bay-SAH-lee)
[*stratum* **layer**, *bas-* **base**, *-ale* **relating to**] *pl.,* strata

stratum corneum
(STRAH-tum KOR-nee-um)
[*stratum* **layer**, *corneum* **horn**] *pl.,* strata

stratum granulosum
(STRAH-tum gran-yoo-LOH-sum)
[*stratum* **layer**, *gran-* **grain**, *-ul-* **little**, *-osum* **thing**] *pl.,* strata

stratum lucidum
(STRAH-tum LOO-see-dum)
[*stratum* **layer**, *lucid-* **clear**, *-um* **thing**] *pl.,* strata

stratum spinosum
(STRAH-tum spi-NO-sum)
[*stratum* **layer**, *spino-* **spine**, *-um* **thing**] *pl.,* strata

subcutaneous layer
(sub-kyoo-TAY-nee-us)
[*sub-* **beneath**, *-cut-* **skin**, *-ous* **relating to**]

sudoriferous gland
(soo-doh-RIF-er-us)
[*sudo-* **sweat**, *-fer-* **bear or carry**, *-ous* **relating to**, *gland* **acorn**]

superficial fascia
(soo-per-FISH-all FAH-shah)
[*super-* **over or above**, *-fici-* **face**, *-al* **relating to**, *fascia* **band**]

surface film

sweat gland
[*gland* **acorn**]

terminal hair
(TUR-mih-nal)
[*termin-* **boundary**, *-al* **relating to**]

vellus
(VEL-us)
[*vellus* **wool**]

LANGUAGE OF MEDICINE

basal cell carcinoma
(BAY-sal cell kar-si-NOH-mah)
[*bas-* **base**, *-al* **relating to**, *cell* **storeroom**, *carcin-***cancer**, *-oma* **tumor**]

blackhead

boils
[**from** *bile*]

cyanosis
(sye-ah-NO-sis)
[*cyan-* **blue**, *-osis* **condition**]

decubitus ulcer
(deh-KYOO-bi-tus UL-ser)
[*decubitus* **a lying down position**, *ulcer* **sore**]

dermatitis
(der-mah-TYE-tis)
[*derma-* **skin**, *-itis* **inflammation**]

dermatosis
(der-mah-TOH-sis)
[*derma-* **skin**, *-osis* **condition**]

eczema
(EK-zeh-mah)
[*eczema* **to boil over**]

fever
(FEE-ver)

first-degree burn

fourth-degree burn

frostbite
(FROST-byte)

full-thickness burn

gangrene
(GANG-green)
[*gangrene* **gnawing sore**]

heat exhaustion
(ek-ZAWS-chun)

heat stroke

hypothermia
(hye-poh-THER-mee-ah)
[*hypo-* **under or below**, *-therm-* **heat**, *-ia* **abnormal condition**]

impetigo
(im-peh-TYE-go)
[*impetigo* **an attack**]

jaundice
(JAWN-dis)
[*jaun-* **yellow**, *-ice* **state**]

Kaposi sarcoma
(KAH-poh-see sar-KOH-mah)
[**Moritz K. Kaposi, Hungarian dermatologist**, *sarco-* **flesh**, *-oma* **tumor**]

male pattern baldness

malignant hyperthermia (MH)
(mah-LIG-nant hye-per-THERM-ee-ah)
[*malign-* **bad**, *-ant* **state**, *hyper-* **excessive**, *-therm-* **heat**, *-ia* **abnormal condition**]

malignant melanoma
(mah-LIG-nant mel-ah-NO-mah)
[*malign-* **bad**, *-ant* **state**, *melan-* **black**, *-oma* **tumor**]

necrosis
(neh-KROH-sis)
[*necro-* **death**, *-osis* **condition**]

onycholysis
(ahn-ik-oh-LYE-sis)
[*onycho-* **nail**, *-lysis* **loosen**]

partial-thickness burn

psoriasis
(so-RYE-ah-sis)
[*psor-* **itching**, *-iasis* **condition**]

pyrogen
(PYE-roh-jen)
[*pyro-* **heat**, *-gen* **produce**]

"rule of nines"

"rule of palms"

scleroderma
(skleer-oh-DER-mah)
[*sclero-* **hard**, *-derma* **skin**]

second-degree burn

squamous cell carcinoma
(SKWAY-muss sell kar-si-NO-mah)
[*squam-* **scale**, *-ous* **characterized by**, *cell* **storeroom**, *carcin-* **cancer**, *-oma* **tumor**]

third-degree burn

tinea
(TIN-ee-ah)
[*tinea* **worm**]

urticaria
(er-ti-KAIR-ee-ah)
[*urtica-* **nettle**, *-ia* **abnormal condition**]

vitiligo
(vit-i-LYE-go)
[*vitiligo* **blemish**]

wart

CASE study



One afternoon, Aidan (12 years old) was playing in his tree house. While running his fingers along the railing, he suddenly yelled, snatching his hand back off the rail. When he looked down, he saw a small sliver of wood sticking out of his middle finger. The splinter hurt, but his finger wasn't bleeding.

1. What primary layer or layers of the cutaneous membrane has the splinter gone through? (HINT: There's no bleeding.)
   a. Epidermis only
   b. Dermis only
   c. Both epidermis and dermis
   d. Stratum basale only
2. If the splinter went into Aidan's arm instead of his finger, which of these layers would the splinter NOT have pierced?
   a. Stratum corneum
   b. Stratum granulosum
   c. Stratum spinosum
   d. Stratum lucidum

This puncture has broken Aidan's intact skin barrier and now may allow bacteria or other pathogens to enter.

3. What cells will help identify these pathogens and mark them for destruction?
   a. Keratinocytes
   b. Melanocytes
   c. Dendritic cells (Langerhans cells)
   d. Lamellar (Pacinian) corpuscles

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

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HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

INTRODUCTION

A. Skin (integument) is body's largest organ
B. Skin measures approximately 1.6 to 1.9 m^2 in average-sized adult
C. Integumentary system describes the skin and its appendages—the hair, nails, and skin glands

STRUCTURE OF THE SKIN

A. Skin classified as a cutaneous membrane
B. Two primary layers—epidermis and dermis; joined by dermoepidermal junction (Figures 7-1 and 7-2)
C. Hypodermis lies beneath dermis
D. Thin and thick skin (Figure 7-3)
   1. "Thin skin"—covers most of body surface (1 to 3 mm thick); has hair and smooth surface
   2. "Thick skin"—soles and palms (4 to 5 mm thick); ridged surface with no hair
E. Epidermis
   1. Cell types (Figure 7-4)
      a. Keratinocytes—constitute over 90% of cells present; principal structural element of the outer skin; sometimes called *corneocytes* after they are fully keratinized
      b. Melanocytes—pigment-producing cells (5% of the total); contribute to skin color; filter ultraviolet light
      c. Epidermal dendritic cells—branched antigen-presenting cells (APCs); they play a role in immune response; also called *Langerhans cells*
      d. Tactile epithelial cells (Merkel cells)—attach to sensory nerve endings to form "light touch" receptors
   2. Cell layers
      a. Stratum basale (base layer)—single layer of columnar cells; only these cells undergo mitosis and then migrate through the other layers until they are shed; *stratum germinativum* (growth layer) is another name for stratum basale (or stratum spinosum and stratum basale together)
      b. Stratum spinosum (spiny layer)—cells arranged in 8 to 10 layers with desmosomes that pull cells into spiny shapes; cells rich in RNA
      c. Stratum granulosum (granular layer)—cells arranged in two to four layers and filled with keratohyalin granules; contain high levels of lysosomal enzymes
      d. Stratum lucidum (clear layer)—cells filled with keratin precursor called *eleidin*; absent in thin skin
      e. Stratum corneum (horny layer)—most superficial layer; dead cells filled with keratin (barrier area)
   3. Epidermal growth and repair
      a. Turnover or regeneration time refers to time required for epidermal cells to form in the stratum basale and migrate to the skin surface—about 35 days
      b. Several hormones support normal growth and repair of the epidermis: epidermal growth factor (EGF), insulin-like growth factor 1 (EGF-1), and growth hormone (GH)
      c. Shortened turnover time will increase the thickness of the stratum corneum and result in callus formation

d. Normally 10% to 12% of all cells in stratum basale enter mitosis daily
e. Each group of 8 to 10 basal cells in mitosis with their vertical columns of migrating keratinocytes is called an *epidermal proliferating unit*, or *EPU*

F. Dermoepidermal junction (DEJ)
1. A basement membrane, with unique fibrous elements, and a polysaccharide gel serve to "glue" the epidermis to the dermis below
2. The junction serves as a partial barrier to the passage of some cells and large molecules

G. Dermis
1. Sometimes called "true skin"—much thicker than the epidermis and lies beneath it
2. Gives strength to the skin
3. Serves as a reservoir storage area for water and electrolytes
4. Contains various structures
a. Arrector pili muscles and hair follicles (Figure 7-5)
b. Sensory receptors (Figure 7-6)
c. Sweat and sebaceous glands
d. Blood vessels
5. Rich vascular supply plays a critical role in temperature regulation
6. Layers of dermis
a. Papillary layer—composed of dermal papillae that project into the epidermis; contains fine collagenous and elastic fibers; contains the dermoepidermal junction; forms a unique pattern that gives individual fingerprints
b. Reticular layer—contains dense, interlacing white collagenous fibers and elastic fibers to make the skin tough yet stretchable; when processed from animal skin, produces leather
7. Dermal growth and repair
a. The dermis does not continually shed and regenerate itself as does the epidermis
b. During wound healing, fibroblasts begin forming an unusually dense mass of new connective fibers; if not replaced by normal tissue, this mass remains a scar
c. Cleavage lines (Figure 7-7)—patterns formed by the collagenous fibers of the reticular layer of the dermis; also called *Langer lines*

H. Hypodermis
1. Also called the *subcutaneous layer* or *superficial fascia*
2. Located deep to the dermis; forms connection between skin and other structures
3. Not part of the skin

SKIN COLOR

A. Melanin
1. Basic determinant is quantity, type, distribution of melanin
2. Types of melanin
a. Eumelanin—group of dark brown (almost black) melanins
b. Pheomelanin—group of reddish and orange melanins
3. Melanin formed from tyrosine by melanocytes (Figure 7-8)
a. Melanocytes release melanin in packets called *melanosomes*
b. Melanosomes are ingested by surrounding keratinocytes and form a cap over the nucleus
4. Albinism—congenital absence of melanin
5. Process regulated by tyrosinase, exposure to sunlight (UV radiation), and certain hormones, including melanocortins (ACTH, α-MSH) and ET-1 (Figures 7-9 and 7-10)
6. Cumulative effects of UV exposure may produce age spots (Figure 7-11)

B. Other pigments
1. Beta-carotene (group of yellowish pigments from food) can also contribute to skin color
2. Lipofuscin—accumulates in cells that have ceased mitosis in aging skin, producing brown-yellow age spots
3. Hemoglobin—color changes also occur as a result of changes in blood flow
a. Redder skin color when blood flow to skin increases
b. Cyanosis—bluish color caused by darkening of hemoglobin when it loses oxygen and gains carbon dioxide (Figure 7-12)
c. Bruising can cause a rainbow of different colors to appear in the skin (Figure 7-13)
4. Other pigments—from cosmetics, tattoos, bile pigments in jaundice (Box 7-4)

FUNCTIONS OF THE SKIN (TABLE 7-2)

A. Protection
1. Physical barrier to microorganisms
2. Barrier to chemical hazards
3. Reduces potential for mechanical trauma
4. Prevents dehydration
5. Protects against excess UV exposure (melanin function)

B. Surface film
1. Emulsified protective barrier formed by mixing of residue and secretions of sweat and sebaceous glands with sloughed epithelial cells from skin surface; shedding of epithelial elements is called *desquamation*
2. Functions
(1) Antibacterial, antifungal activity
(2) Lubrication
(3) Hydration of skin surface
(4) Buffer of caustic irritants
(5) Blockade of toxic agents
3. Chemical composition
(1) From epithelial elements—amino acids, sterols, and complex phospholipids
(2) From sebum—fatty acids, triglycerides, and waxes
(3) From sweat—water, ammonia, urea, and lactic and uric acid

C. Sensation
1. Skin acts as a sophisticated sense organ
2. Somatic sensory receptors detect stimuli that permit us to detect pressure, touch, temperature, pain, and other general senses

D. Flexibility
1. Skin is supple and elastic, thus permitting change in body contours without injury

E. Excretion
   1. Water
   2. Urea/ammonia/uric acid

F. Hormone (vitamin D) production (Figure 7-14)
   1. Exposure of skin to UV light converts 7-dehydrocholesterol to cholecalciferol—a precursor to vitamin D
   2. Blood transports precursor to liver and kidneys where vitamin D is produced

G. Immunity
   1. Phagocytic cells destroy bacteria
   2. Epidermal dendritic cells trigger helpful immune reaction working with "helper T cells"

H. Homeostasis of body temperature
   1. To maintain homeostasis of body temperature, heat production must equal heat loss; skin plays a critical role in this process
   2. Heat production
      a. By metabolism of foods in skeletal muscles and liver
      b. Chief determinant of heat production is the amount of muscular work being performed
   3. Heat loss—approximately 80% of heat loss occurs through the skin; remaining 20% occurs through the mucosa of the respiratory, digestive, and urinary tracts (Figure 7-15)
      a. Evaporation—to evaporate any fluid, heat energy must be expended; this method of heat loss is especially important at high environmental temperatures when it is the only method by which heat can be lost from the skin
      b. Radiation—transfer of heat from one object to another without actual contact; important method of heat loss in cool environmental temperatures
      c. Conduction—transfer of heat to any substance actually in contact with the body; accounts for relatively small amounts of heat loss
      d. Convection—transfer of heat away from a surface by movement of air; usually accounts for a small amount of heat loss
   4. Homeostatic regulation of heat loss (Figure 7-16)
      a. Heat loss by the skin is controlled by a negative feedback loop
      b. Receptors in the hypothalamus monitor the body's internal temperature
      c. If body temperature is increased, the hypothalamus sends a nervous signal to the sweat glands and blood vessels of the skin
      d. The hypothalamus continues to act until the body's temperature returns to normal

APPENDAGES OF THE SKIN

A. Hair (Figure 7-17)
   1. Development of hair
      a. Distribution—over entire body except palms of hands and soles of feet and a few other small areas
      b. Fine and soft hair coat existing before birth called *lanugo*
      c. Coarse pubic and axillary hair that develops at puberty called *terminal hair*
      d. Hair follicles and hair develop from epidermis; mitosis of cells of germinal matrix forms hairs
      e. Papilla—cluster of capillaries under germinal matrix
      f. Root—part of hair embedded in follicle in dermis
      g. Shaft—visible part of hair
      h. Medulla—inner core of hair; cortex—outer portion
   2. Appearance of hair
      a. Color—result of different amounts, distribution, types of melanin in cortex of hair (Figure 7-18)
      b. Growth—hair growth and rest periods alternate; hair on head averages 5 inches of growth per year
      c. Sebaceous glands—attach to and secrete sebum (skin oil) into follicle
      d. Male pattern baldness (androgenic alopecia) results from combination of genetic tendency and male sex hormones (Figure 7-19)

B. Nails (Figure 7-20)
   1. Consist of epidermal cells converted to hard keratin
   2. Nail body—visible part of each nail
   3. Root—part of nail in groove hidden by fold of skin, the cuticle
   4. Lunula—moon-shaped white area nearest root
   5. Nail bed—layer of epithelium under nail body; contains abundant blood vessels
      a. Appears pink under translucent nails
      b. Nails may have pigmented streaks (Figure 7-21)
      c. Separation of a nail from the nail bed is called *onycholysis* (Figure 7-22)
   6. Growth—nails grow by mitosis of cells in stratum basale beneath the lunula; average growth about 0.5 mm per week, or slightly over 1 inch per year

C. Skin glands (Figure 7-23)
   1. Two types of sweat glands
      a. Eccrine glands
         (1) Most numerous sweat glands; quite small
         (2) Distributed over total body surface with exception of a few small areas
         (3) Simple, coiled, tubular glands
         (4) Function throughout life
         (5) Secrete perspiration or sweat; eliminate wastes and help maintain a constant core temperature
      b. Apocrine glands
         (1) Located deep in subcutaneous layer
         (2) Limited distribution—axilla, areola of breast, and around anus
         (3) Large (often more than 5 mm in diameter)
         (4) Simple, branched, tubular glands
         (5) Begin to function at puberty
         (6) Secretion shows cyclic changes in female with menstrual cycle
   2. Sebaceous glands
      a. Secrete sebum—oily substance that keeps hair and skin soft and pliant; prevents excessive water loss from skin
      b. Lipid components have antifungal activity

c. Simple, branched glands
d. Found in dermis except in palms and soles
e. Secretion increases in adolescence; may lead to formation of pimples and blackheads

3. Ceruminous glands
a. Modified apocrine sweat glands
b. Simple, coiled, tubular glands
c. Empty contents into external ear canal alone or with sebaceous glands
d. Mixed secretions of sebaceous and ceruminous glands called *cerumen* (wax)
e. Function of cerumen to protect area from dehydration; excess secretion can cause blockage of ear canal and loss of hearing

CYCLE OF LIFE: SKIN

A. Children
1. Skin is smooth, unwrinkled, and characterized by elasticity and flexibility
2. Few sweat glands
3. Rapid healing

B. Adults
1. Development and activation of sebaceous and sweat glands
2. Increased sweat production; can result in body odor
3. Increased sebum production; can result in acne

C. Old age
1. Decreased sebaceous and sweat gland activity
a. Wrinkling (Figure 7-24)
b. Decrease in body's ability to cool itself

THE BIG PICTURE: SKIN AND THE WHOLE BODY

A. Skin is a major component of the body's structural framework
B. Skin defines the internal environment of the body
C. Primary functions are support and protection

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. List and briefly discuss several of the different functions of the skin.
2. List three cell types found in the epidermis.
3. List and describe the cell layers of the epidermis from superficial to deep.
4. What layer of the epidermis is sometimes called the *barrier area?*
5. Discuss the process of epidermal growth and repair.
6. What is keratin? Where is it found and how is it formed?
7. What part of the skin contains blood vessels?
8. Why is the process of blister formation a good example of the relationship between the skin's structure and function?
9. List the two layers of the dermis. Which layer helps make the skin stretchable and able to rebound?
10. What are arrector pili muscles?
11. List the appendages of the skin.
12. Identify each of the following: hair papilla, germinal matrix, hair root, hair shaft, follicle.
13. List the three primary types of skin glands.
14. What is the difference between eccrine and apocrine sweat glands?
15. Discuss the importance of the surface film of the skin.
16. How is the "rule of nines" used in determining the extent of a burn injury?
17. What are the differences between first-, second-, and third-degree burns?

CRITICAL THINKING QUESTIONS

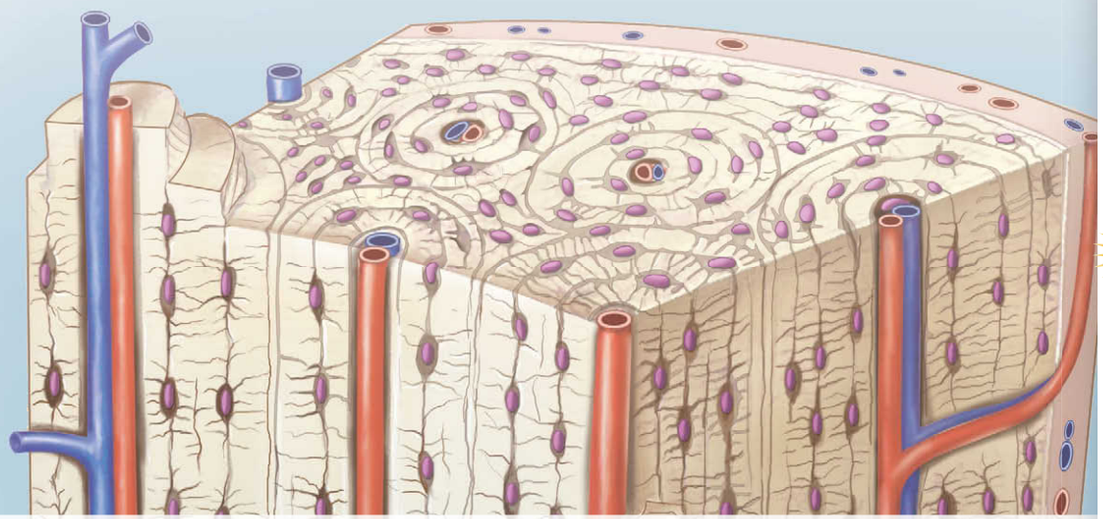


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. The stratum corneum, hair follicle, nails, sweat glands, oil glands, and stratum basale are all discussed in this chapter. Can you make a distinction regarding whether these structures are part of the integumentary system only or both the integumentary system and the integument?
2. Identify what affects the thickness of the skin (dermis and epidermis). What is the relationship between what affects the thickness of the skin and the thickness of the hypodermis?
3. What is the dermoepidermal junction (DEJ)? By analyzing its anatomical components, what inference can you make regarding how it functions?
4. In terms of leaving a less noticeable scar, why should an incision on the front of the thigh be made at a different angle than an incision on the back of the thigh?
5. Concern about skin cancer is causing people to reduce the amount of time they spend in the sun. If this caution is carried to the extreme, explain how it would impact skin function?
6. Explain why a light-skinned individual would be more susceptible to malignant melanoma?
7. An individual running a marathon expends a great deal of energy. Much of this energy generates heat, which increases core body temperature. What is the role of sweat glands in balancing body temperature during this strenuous exercise? With this loss of fluid, what suggestions do you have for avoiding dehydration?

Skeletal Tissues

8



CHAPTER OUTLINE

HINT *Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.*

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LANGUAGE OF SCIENCE

HINT *Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.*

appositional growth
(ap-oh-ZISH-un-al)
[*apposit-* **to put near,** *-ion* **process,** *-al* **relating to**]

articular cartilage
(ar-TIK-yoo-lar KAR-ti-lij)
[*artic-* **joint,** *-ul-* **little,** *-ar* **relating to,** *cartilag-* **cartilage**]

bone

bone matrix
(MAY-triks)
[*matrix* **womb**] *pl.,* matrices

cancellous bone
(KAN-seh-lus)
[*cancel-* **lattice,** *-ous* **characterized by**]

cartilage
(KAR-ti-lij)

central canal

chondrification center
(kon-dri-fi-KAY-shun)
[*chondr-* **cartilage,** *-fication* **to make**]

chondrocyte
(KON-droh-syte)
[*chondro-* **cartilage,** *-cyte* **cell**]

compact bone

diaphysis
(dye-AF-i-sis)
[*dia-* **through or apart,** *-physis* **growth**]
pl., diaphyses

diploe
(DIP-lo-EE)
[*diploe* **folded over (doubled)**]

elastic cartilage
(eh-LAS-tik KAR-ti-lij)
[*elast-* **to drive or beat out,** *-ic* **relating to,** *cartilag* **cartilage**]

endochondral ossification
(en-doh-KON-dral os-i- fi-KAY-shun)
[*endo-* **within,** *-chondr-* **cartilage,** *-al* **relating to,** *os-* **bone,** *-fication* **to make**]

continued on p. 218

*This is the first of three chapters on the skeletal system, or more simply, the skeleton (Figure 8-1). This chapter focuses mainly on two highly adapted types of connective tissues that make up the skeleton—*bone *and* cartilage. *We also briefly discuss the fibrous connective, blood, nervous, epithelial, lymphatic, marrow, and fatty tissues found in the skeleton.*

Chapter 9 then goes on to discuss the overall organization of the skeleton. Individual bones, which are considered separate, discrete organs, are also discussed in Chapter 9. Then Chapter 10 outlines the articulations, *or joints. Articulations are the points of contact between bones that either stabilize the parts of the skeleton or make movement possible.*

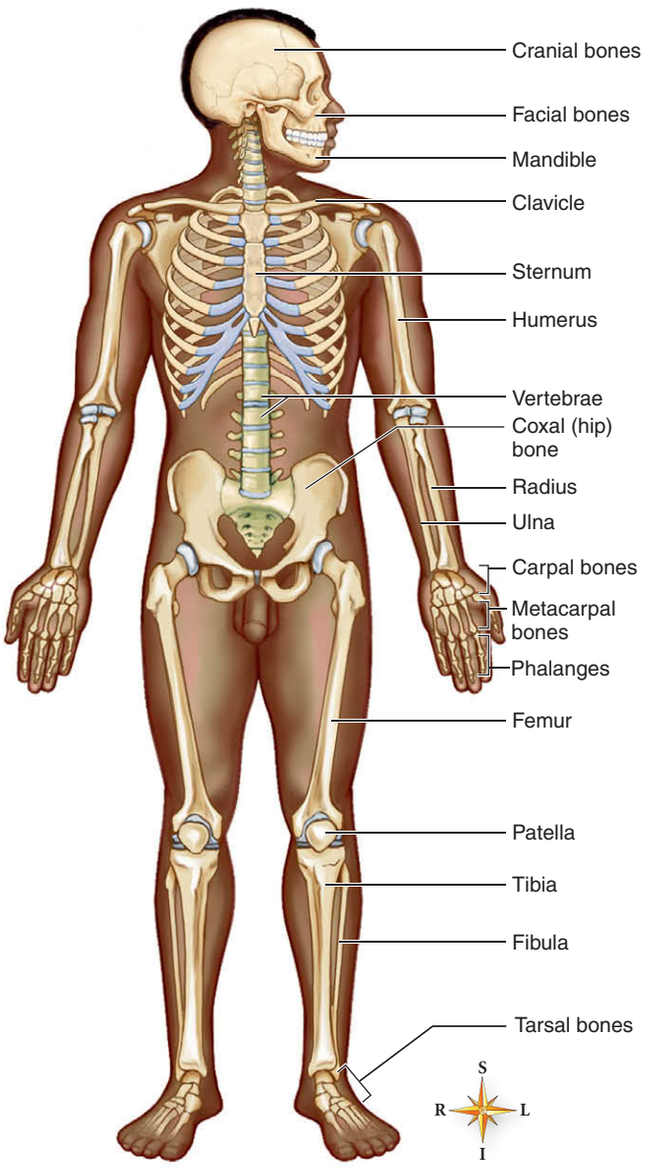


FIGURE 8-1
The skeleton.

FUNCTIONS OF BONE

A good place to begin a study of the skeletal system is with the overall functions of its organs, the bones and ligaments. **Ligaments** are fibrous bands that help hold the various bones together into an organized skeleton. **Bones** are rigid, mineralized structures that help perform five major roles in the body. Each is important for maintaining overall stability of the body's internal environment, or homeostasis.

1. **Support.** Bones serve as the supporting framework of the body, much as steel girders are the supporting framework of our modern buildings. They contribute to the shape, alignment, and positioning of the body parts. Bones are held in place by ligaments, muscles, and other structures.
2. **Protection.** Hard, bony "boxes" serve to protect the delicate structures they enclose. For example, the skull protects the brain, and the rib cage protects the lungs and heart. You can also use the bones of your arm to help defend against injuries to the face or abdomen.
3. **Movement.** Bones along with their joints constitute levers. Muscles are anchored firmly to bones. As muscles contract and shorten, they pull on bones, thereby producing movement at a joint. This process is discussed further in Chapter 10.
4. **Mineral storage.** Bones serve as the major reservoir for calcium, phosphorus, and certain other minerals. Homeostasis of the blood calcium concentration—essential for healthy survival—depends largely on changes in the rate of calcium movement between blood and bones. If, for example, the blood calcium concentration increases above normal, calcium moves more rapidly out of blood into bones and more slowly in the opposite direction. The result? Blood calcium concentration decreases—usually to its homeostatic level. Hormonal control of blood calcium is discussed further in Chapter 19.
5. **Hematopoiesis.** *Hematopoiesis*, or blood cell formation, is a vital process carried on by red bone marrow, or *myeloid tissue*. Myeloid tissue, in the adult, is located primarily in the ends, or epiphyses, of certain long bones, in the flat bones of the skull, in the pelvis, and in the sternum and ribs. The process of hematopoiesis is discussed further in Chapter 20.

TYPES OF BONES

Structurally, a simple way to categorize the 206 or more bones of the skeleton is by shape. Usually they are divided into five categories: long bones, short bones, flat bones, irregular bones, and sesamoid bones. Figure 8-2 shows an example of each type. The size,

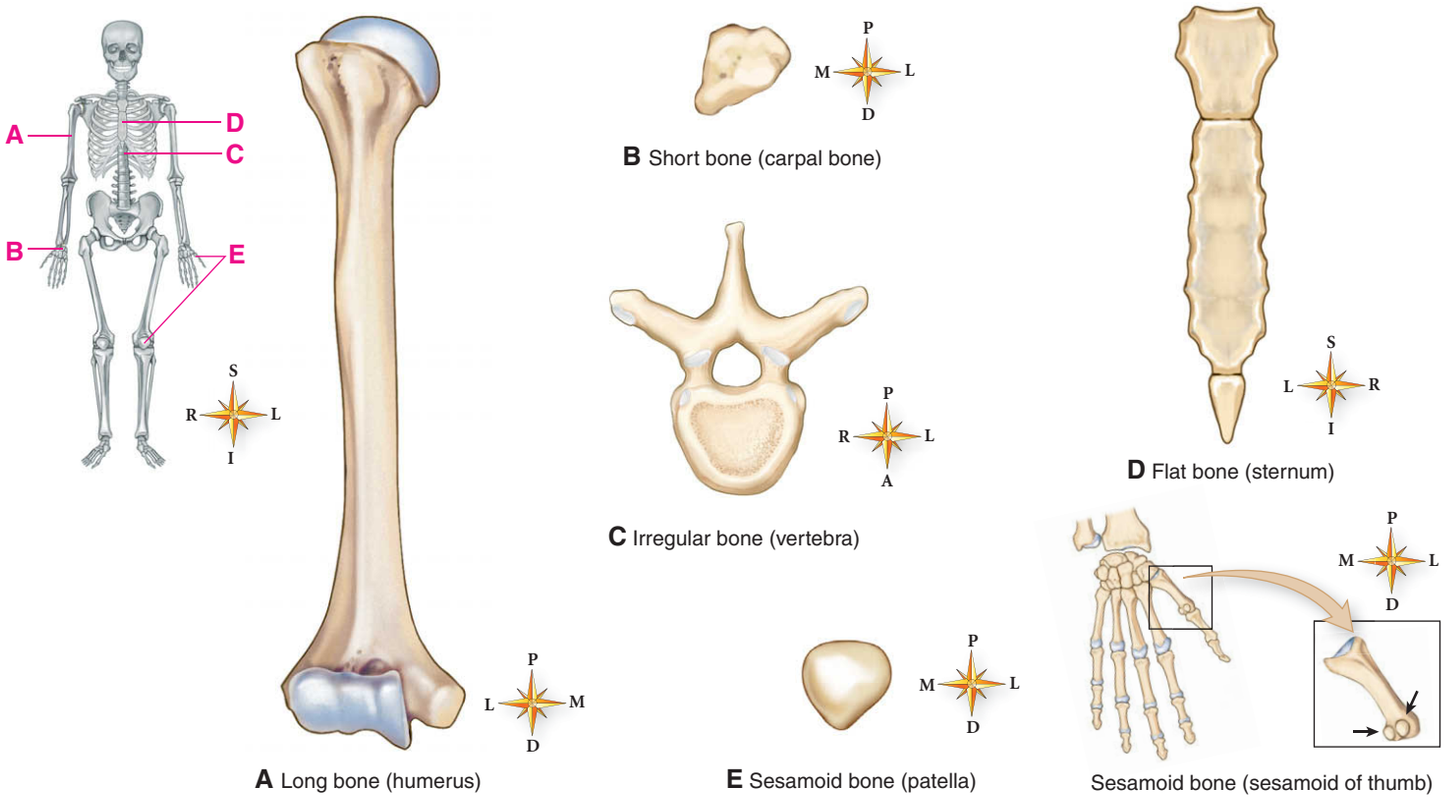


FIGURE 8-2

Types of bones. Examples of bone types include **A,** long bones (humerus); **B,** short bones (carpal bone); **C,** irregular bones (vertebra); **D,** flat bones (sternum); and **E,** sesamoid bones (patella and sesamoid of thumb).

shape, and appearance of bones vary according to the role of each bone in the skeleton. Some bones must bear great weight; others serve a protective function or serve as delicate support structures, such as for the fingers and toes.

Bones differ in size and shape and also in the amount and proportion of the two different types of bone tissue that compose them. **Compact bone** is dense and "solid" in appearance. **Cancellous bone,** on the other hand, is characterized by open space with a network of thin, branched crossbeams. Recall from Chapter 6 that cancellous bone is also called *spongy bone* or *trabecular bone*. Both compact and cancellous bone types are discussed when the microscopic structure of bone is described later in the chapter.

All five shape categories of bone discussed below have varying amounts of cancellous and compact bone in their structure.

Long bones are easily identified by their roughly cylindrical shape that is longer than it is wide. They also have enlarged and often uniquely shaped ends that articulate with other bones. The femur of the thigh and humerus of the arm are examples. Other examples include the radius, ulna, tibia, fibula, metacarpal bones, metatarsal bones, and phalanges.

Short bones are often described as cube- or box-shaped structures that are about as broad as they are long. Examples include each of the wrist (carpal) and ankle (tarsal) bones.

Flat bones are generally broad and thin with a flattened and often curved surface. Certain bones of the skull, the shoulder blades (scapulae), ribs, and breastbone (sternum) are typical flat bones.

Irregular bones are often clustered in groups and come in various sizes and shapes. The vertebral bones that form the spine and the facial bones of the skull are good examples.

Sesamoid bones, which are sometimes grouped with the irregular bones, often appear singly rather than in groups. The name comes from "sesame seed" because these bones often resemble sesame seeds in size and shape. The number of sesamoid bones in the body can be many or only a few—the number and size vary from one person to the next. Sesamoid bones usually develop in the tendons close to the joints. The patella (kneecap) is the largest sesamoid bone—one of the few that consistently appear in the human skeleton.

| QUICK CHECK |

1. Name the two major types of connective tissue found in the skeletal system.
2. Name the two different types of bone tissue.

Parts of a Long Bone

A long bone consists of the following structures visible to the naked eye: diaphysis, epiphyses, articular cartilage, periosteum, medullary (marrow) cavity, and endosteum. Identify each of these structures in the tibia shown in Figure 8-3, *A*. The tibia is the longer, stronger, and more medially located of the two leg bones.

1. **Diaphysis** (dye-AF-i-sis)—main shaftlike portion. Its hollow, cylindrical shape and the thick compact bone that composes it adapt the diaphysis well to its function of providing strong support without adding cumbersome weight.
2. **Epiphyses** (eh-PIF-i-seez)—the proximal and distal ends of a long bone. Epiphyses have a bulbous shape that provides generous space near joints for muscle attachments and also gives stability to joints. Look at Figure 8-3 to note the innumerable small spaces in the bone of the epiphysis. They make this kind of bone look a little like a sponge—hence its name spongy, or cancellous, bone. A soft connective tissue called *red marrow* fills the spaces within this spongy bone. Early in development, epiphyses are separated from the diaphysis by a layer of cartilage, the *epiphyseal plate*. The cartilage layer is eventually replaced by bone, forming an *epiphyseal line*. The region between the epiphyses and diaphysis (in a mature bone) or the epiphyseal plate region (in a growing bone) is called the *metaphysis* (meh-TAF-i-sis).
3. **Articular cartilage**—thin layer of hyaline cartilage that covers the articular or joint surfaces of epiphyses. The resiliency of this material cushions jolts and blows.
4. **Periosteum** (pair-ee-OS-tee-um)—dense, white fibrous membrane that covers bone except at joint surfaces, where articular cartilage forms the covering. Many of the periosteum fibers penetrate the underlying bone and weld these two structures to each other. In addition, muscle tendon fibers interlace with periosteal fibers, thereby anchoring muscles firmly to bone. The periosteum is a critically important membrane that, depending on its location, also contains

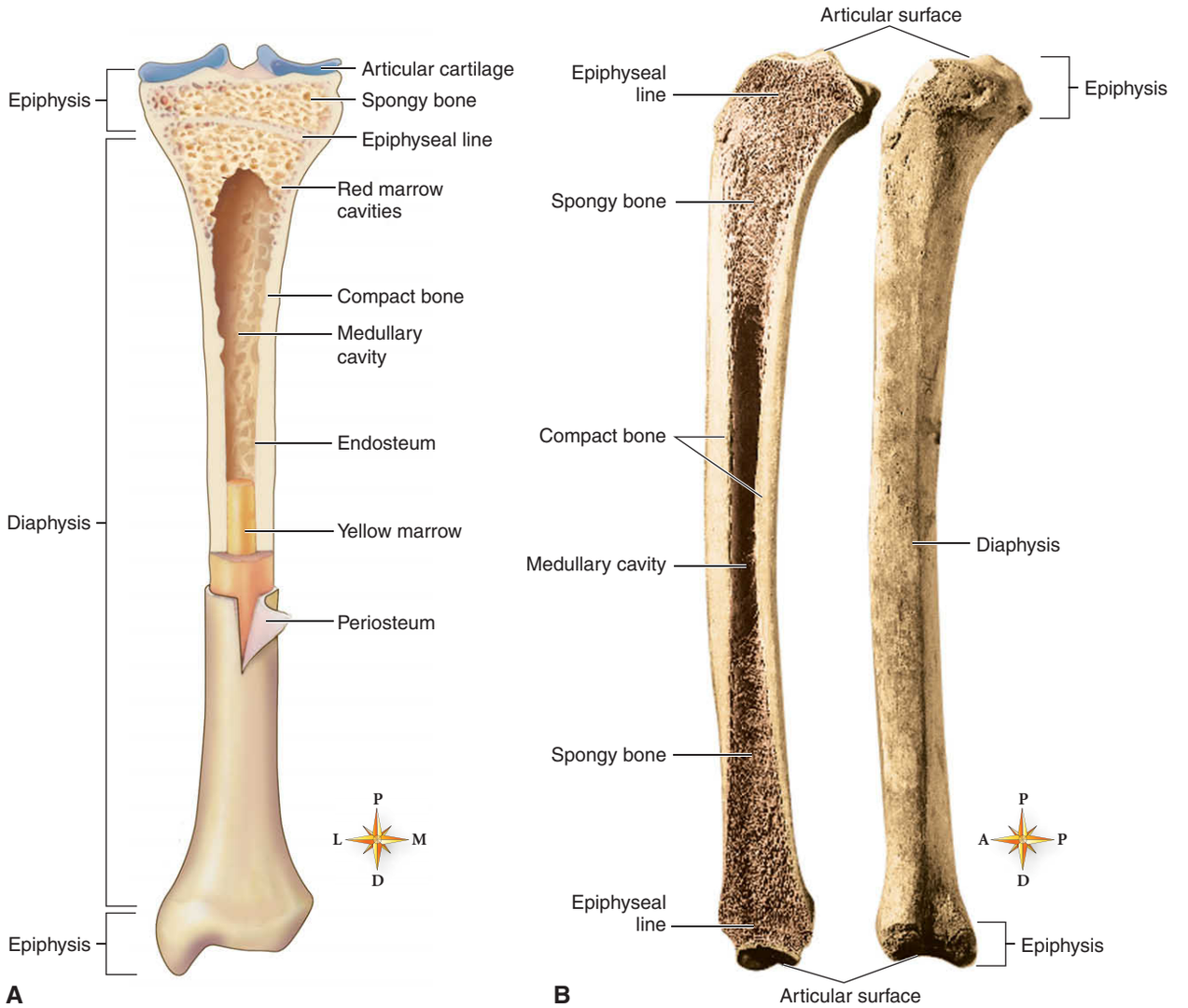


FIGURE 8-3

Long bone. A, Partial frontal section of a long bone (tibia) showing cancellous and compact bone. **B,** Sagittal section of a long bone with a whole long bone (tibia) in lateral view.

bone-forming and bone-destroying cells and blood vessels that become incorporated into bones during their initial growth or subsequent remodeling and repair. This important membrane is essential for bone cell survival and for bone formation, a process that continues throughout life.

5. **Medullary cavity**—a tubelike hollow space in the diaphysis of a long bone, also called a *marrow cavity*. In the adult the medullary cavity is filled with connective tissue rich in fat—a substance called *yellow marrow*.
6. **Endosteum** (en-DOS-tee-um)—a thin fibrous membrane that lines the medullary cavity of long bones. The endosteum lines the spaces of spongy bone as well. Like the periosteum, the endosteum has various types of bone cells and the stem cells that produce them.

Parts of Flat Bones and Other Bones

The structure of the flat bone is very similar to that of a long bone, but simpler. As you can see in Figure 8-4, a flat bone of the cranium has outer and inner walls made of compact bone. These hard walls are called the **internal table** and **external table.** Between is a region called the **diploe,** which is made up of cancellous bone. Other flat bones, such as the ribs and sternum, have a similar overall structure. Like long bones, flat bones are covered in a periosteum and the inner spaces are lined with endosteum.

Red marrow fills the spaces of the cancellous bone inside many flat bones. The sternum, which contains red marrow even in adulthood, is one example. To help in the diagnosis of leukemia and certain other diseases, a physician may decide to perform a needle puncture of one of these bones. In this type of diagnostic procedure, a needle is inserted through the skin and compact bone into the red marrow, and a small amount of the marrow is then aspirated and examined under the microscope for evidence of normal or abnormal blood cells. The procedure, called *aspiration biopsy cytology (ABC)*, is discussed on p. 619.

Short bones, irregular bones, and sesamoid bones all have features similar to those of flat bones.

BONE TISSUE

Bone tissue, sometimes called *osseous tissue*, is perhaps the most distinctive form of connective tissue in the body. It is typical of other connective tissues in that it consists of cells, fibers, and extracellular material, or *matrix*. However, its extracellular components are hard and *calcified*. In bone the extracellular material, or matrix, predominates. It is much more abundant than the bone cells, and it contains many fibers of collagen (the body's most abundant protein). The rigidity of bone enables it to serve supportive and protective functions.

As a tissue, bone is ideally suited to its functions. You can easily see the concept that structure and function are interrelated in bone tissue! It has a tensile strength nearly equal to that of cast iron but at less than one third the weight. Bone is organized so that its great strength and minimal weight result from the interrelationships of its structural components. The relationship of structure to function is seen all the way through the chemical, cellular, tissue, and organ levels of organization.

Composition of Bone Matrix

The extracellular matrix (ECM) of bone, or **bone matrix,** can be subdivided into two principal chemical components: *inorganic salts* and *organic matrix*. About two thirds of the matrix by dry weight analysis consists of inorganic salts and one third, organic material. You may find it helpful to review the section describing the unique characteristics of ECM in Chapter 6 on p. 134 and illustrated in Figure 6-1 on the same page.

INORGANIC SALTS

The calcified nature and thus the hardness of bone result from the deposition of rocklike crystals of calcium and phosphate. Chemists call them *hydroxyapatite* crystals. The process of forming these crystals within a softer tissue is called *calcification*. The tiny, needlelike hydroxyapatite crystals make up about 85% of

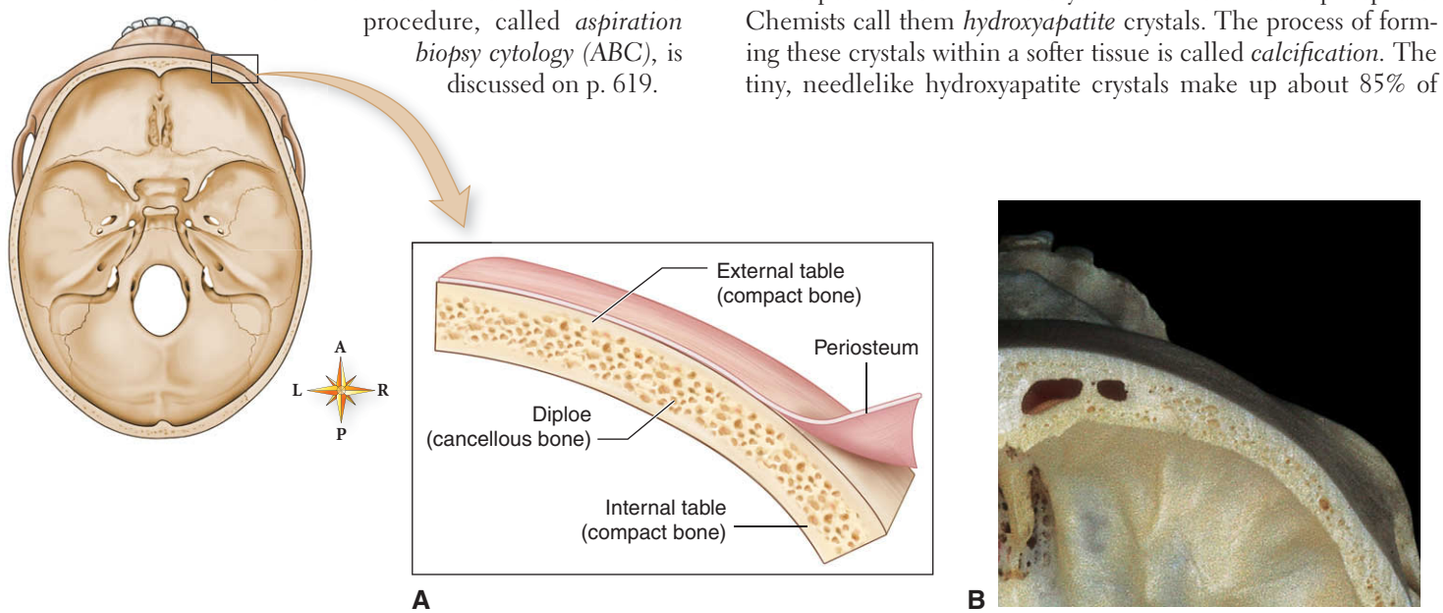


FIGURE 8-4

Flat bone. A, Horizontal section of a flat bone of the skull (frontal bone) showing cancellous and compact bone. **B,** Photograph of a frontal bone cut in horizontal section.

the total inorganic matrix and are found oriented in the microscopic spaces between collagen fibers so that they can most effectively resist stress and mechanical deformation. In addition to hydroxyapatite and about 10% calcium carbonate, other mineral constituents such as magnesium, sodium, sulfate, and fluoride are also found in bone. Unfortunately, harmful elements can become incorporated into bone matrix as well and result in loss of normal function or active disease. For example, radioactive elements such as radium, strontium-90, uranium, or plutonium can become concentrated in bone and continue to emit radiation, which can lead to various types of cancer and other serious disease.

| A&P CONNECT |

To learn more about the effects of radiation in the body and how it can be used in imaging bones, check out the articles ***Radioactivity*** and ***Bone Scans*** online at ***A&P Connection.***

evolve

ORGANIC MATRIX

The organic matrix of bone and other connective tissues is a composite of collagenous fibers and a mixture of protein and polysaccharides called *ground substance*. Connective tissue cells secrete the gel-like ground substance. The ground substance of bone provides support and adhesion between cellular and fibrous elements and also serves an active role in many cellular metabolic functions necessary for growth, repair, and remodeling.

Chondroitin sulfate and **glucosamine** are the names of chemical substances that many people recognize as components of over-the-counter dietary supplements. Taken alone or together they are widely thought to facilitate healing and reduce the "wear and tear" pain of osteoarthritis. However, research has yet to fully support that claim. Chondroitin sulfate and glucosamine are found naturally in the body and are important constituents of the ground substance in both bone and cartilage. Chemically, chondroitin sulfate is a large protein molecule that helps cartilage remain compressible and elastic and may slow its destruction. Glucosamine is an amino sugar important in cartilage formation, maintenance, and repair. Go back to Figure 6-1 (p. 134) to see how such molecules are incorporated into the ECM of a tissue.

Components of the organic matrix help cartilage maintain a smooth surface and springy consistency. They add to overall strength and also give bone some degree of plasticlike resilience so that applied stress—within reasonable limits—does not result in frequent crush or fracture injuries.

| QUICK CHECK |

3. List the six structural components of a typical long bone that are visible to the naked eye.
4. Identify the two principal chemical components of bone matrix.
5. Why is it important that cartilage in the skeleton have some "give" or spring to it?

MICROSCOPIC STRUCTURE OF BONE

The basic structural components and cell types of bone were described briefly in Chapter 6. In the paragraphs that follow, additional information about bone structure and cell types will serve as a basis for learning the functional characteristics of this important tissue. Understanding how a bone forms and grows, how it repairs itself after injury, and how it interacts with other tissues and organs in maintaining various important homeostatic mechanisms is based on a knowledge of its basic structure—a structure as unique as its chemical composition.

Compact Bone

Compact bone constitutes about 80% of the total bone mass in the adult human body. It contains many cylinder-shaped structural units called **osteons** (AHS-tee-onz), or *Haversian systems*. Note in Figure 8-5 that each osteon surrounds a **central canal** that runs lengthwise through the bone. Living bone cells in these units are literally cemented together to constitute the structural framework of compact bone. The unique structure of the osteon permits delivery of nutrients and removal of waste products from metabolically active, but imprisoned, bone cells.

Several simple structures make up each osteon: lamellae, lacunae, canaliculi, and a central canal. As you read the following descriptions, identify each structure in Figure 8-5.

Lamellae *(lah-MEL-ee)*. *Concentric lamellae* are cylinder-shaped layers of calcified matrix in the osteon. Lamellae (layers) of hard bone matrix are also present outside the osteon. *Interstitial lamellae* are layers of calcified matrix between osteons. They are the remnants of older osteons that have been altered by bone growth or remodeling. A few layers of bone matrix also run around the outer boundary of compact bone, encircling all the osteons. These layers that run along the inner circumference (along the endosteum) and outer circumference (along the periosteum) of a bone are called *circumferential lamellae*.

Lacunae *(lah-KOO-nay)*. These are small spaces in bone matrix that contain tissue fluid and in which bone cells lie imprisoned between the hard layers of the lamellae.

Canaliculi *(kan-ah-LIK-yoo-lye)*. These ultra-small canals radiate in all directions from the lacunae and connect them to each other and to a larger canal, the central canal.

Central canal. Also called an *osteonal canal* or *Haversian canal*, the central canal extends lengthwise through the center of each osteon. The central canal is lined with endosteum and contains blood vessels, lymphatic vessels, and nerves. Nutrients and oxygen move from the central canal through canaliculi to the lacunae and their bone cells—a short distance of about 0.1 mm or less.

Parallel central canals are connected to each other by **transverse canals** (*Volkmann canals*). These communicating canals contain nerves and vessels that carry blood and lymph from the exterior surface of the bone to the osteons.

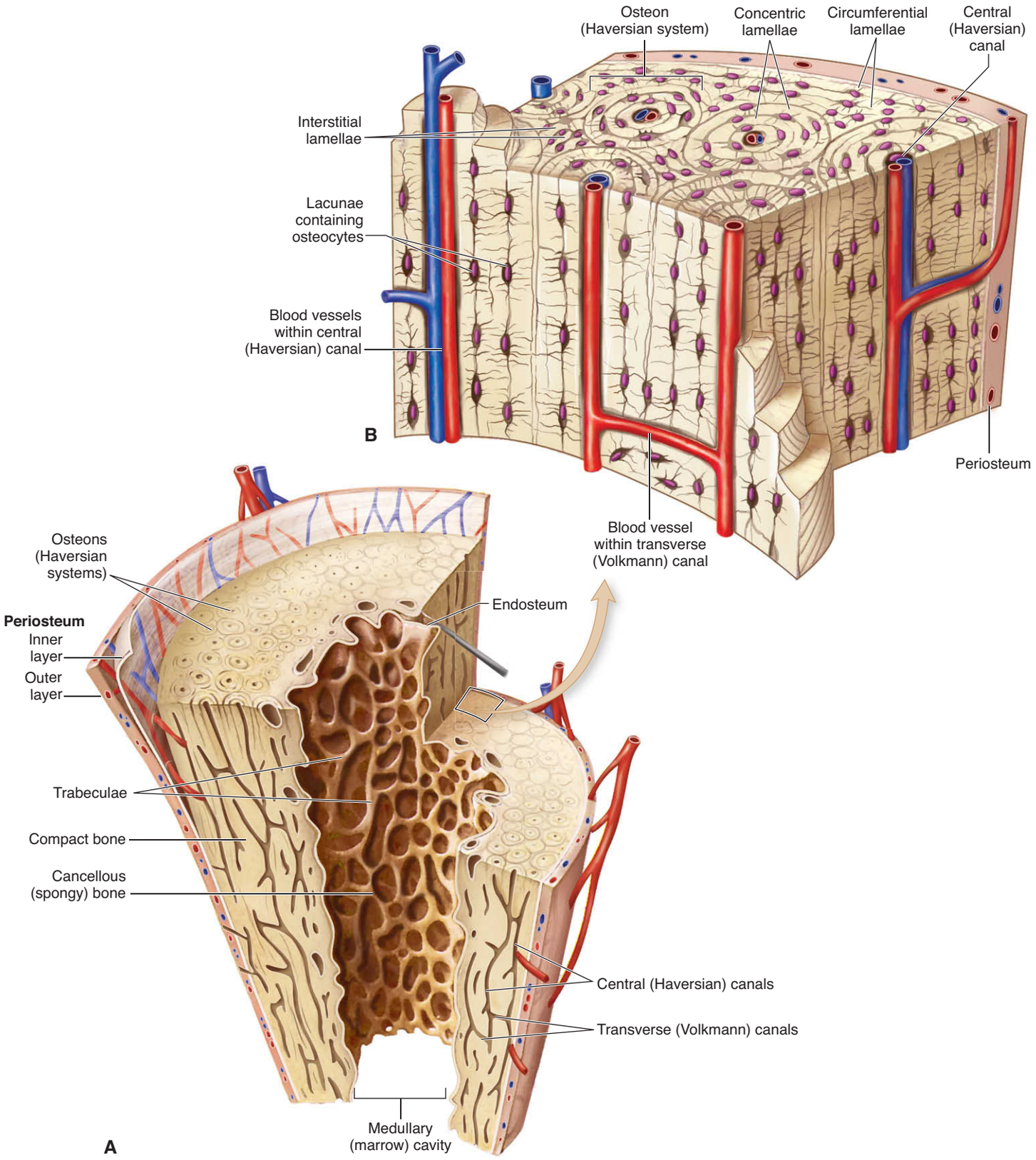


FIGURE 8-5

Compact and cancellous bone in a long bone. A, Longitudinal section of a long bone showing both cancellous and compact bone. **B,** Magnified view of compact bone.

Cancellous Bone

Cancellous, or spongy, bone constitutes about 20% of the total bone mass and differs in microscopic structure from compact bone. As you recall, the structural unit of compact bone is the highly organized osteon. There are no osteons in cancellous bone. Instead, it consists of crisscrossing bony branches called **trabeculae.** Bone cells are found within the trabeculae. Nutrients are delivered to the cells and waste products are removed by diffusion through tiny canaliculi that extend to the surface of the very thin bony branches. Cancellous bone is often called **trabecular bone.**

Note that the cancellous bone shown in Figure 8-6 lies between two layers of compact bone, much like the filling in a sandwich. Recall that the middle layer of spongy bone is called the *diploe*. This layered organization is typical of flat bones such as those found in the skull. Cancellous bone is also found inside short and irregular bones, as well as inside the epiphyses (see Figure 8-3) and lining the medullary cavities of long bones (see Figure 8-5, A).

The placement of trabeculae in spongy bone is not as random and unorganized as it might first appear. They are *fractal* in nature, meaning that they appear random, but there is really an underlying, complex organization to them. The bony branches are actually arranged along lines of stress, and their size and orientation will therefore differ between individual bones according to the nature and magnitude of the applied load (Figure 8-7). This feature greatly enhances a bone's strength and is yet another example of the relationship between structure and function.

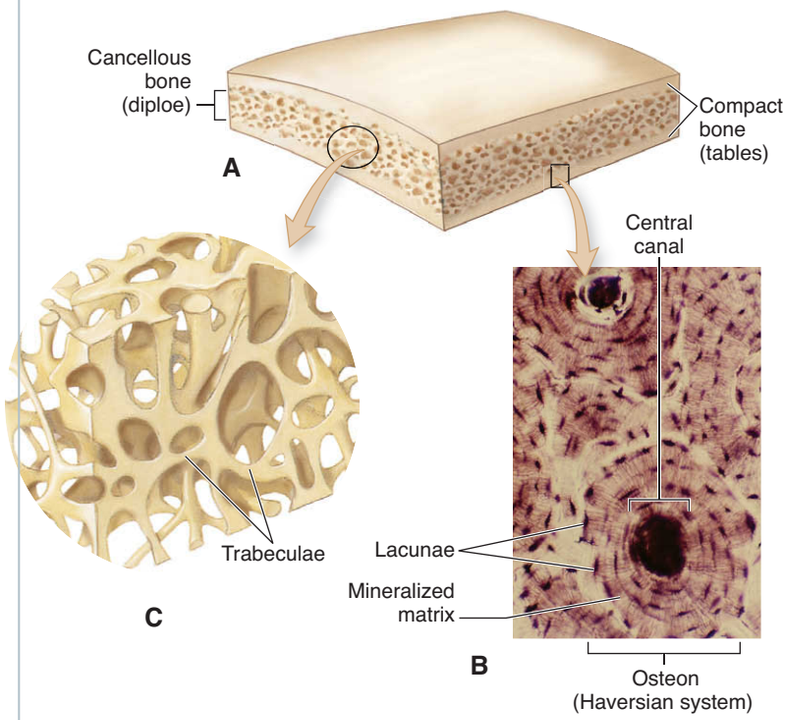


FIGURE 8-6

Compact and cancellous bone in a flat bone. A, Section of a flat bone. (See also Figure 8-4.) Outer layers of compact bone surround cancellous bone. Note the fine structure of compact **(B)** and cancellous **(C)** bone.

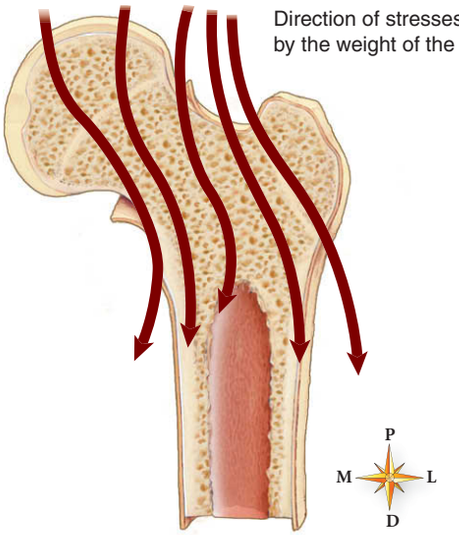


FIGURE 8-7

Orientation of trabeculae. Longitudinal section of a long bone showing trabeculae oriented along lines of stress.

Locked within a seemingly lifeless calcified matrix, bone cells are active metabolically. They must, like all living cells, continually receive food and oxygen and excrete their wastes, so blood supply to bone is both important and abundant. One or more arteries supply the bone marrow in the internal medullary cavity and provide nutrients to areas of cancellous bone. In addition, blood vessels from the periosteum, when they eventually become covered by new bone in the development process, become incorporated into the bone itself and then, by way of the transverse canals and by connections with other vessels in adjacent osteons, ultimately serve the nutrient needs of cells that, because of their own secretions, have become surrounded by calcified matrix in compact bone. The mechanism by which periosteal blood vessels become "imprisoned" by the deposition of new bone during growth and remodeling is described later in this chapter.

| QUICK CHECK |

6. Identify the main structures that form the osteon.
7. Name the canals that connect blood vessels between adjacent, parallel osteons.
8. Name the tiny branches of hard bone present in cancellous bone.

Types of Bone Cells

Three major types of cells are found in bone: *osteoblasts* (bone-forming cells), *osteoclasts* (bone-reabsorbing cells), and *osteocytes* (mature bone cells). All bone surfaces are covered with a continuous layer of cells that is critical to the survival of bone. This layer is composed of relatively large numbers of osteoblasts interspersed with a much smaller population of osteoclasts.

Osteoblasts (OS-tee-oh-blasts) are small cells that synthesize and secrete an organic matrix called *osteoid*. Collagen strands in the osteoid serve as a framework for the formation of hydroxyapatite

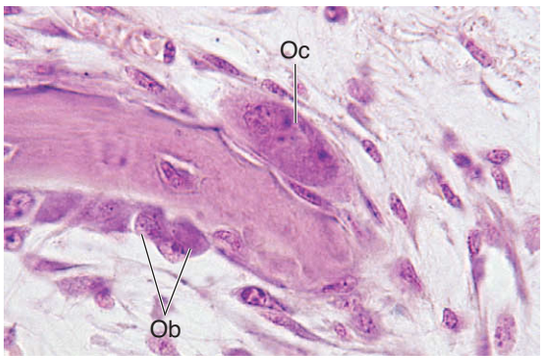


FIGURE 8-8

Bone-forming and bone-eroding cells. Note the large multinucleate osteoclast cell *(Oc)* dissolving bone on the upper surface of a developing branch of bone while smaller osteoblast cells *(Ob)* on the undersurface of the bone are secreting new osteoid.

crystals, which mineralizes the bone tissue. *Osteogenic* (os-tee-oh-JEN-ik) *stem cells*, found in the endosteum and lining the central canals, undergo cell division to form osteoblasts.

Osteoclasts (OS-tee-oh-klasts) are giant multinucleate cells (Figure 8-8) that are responsible for the active erosion of bone minerals. They are formed by the fusion of several precursor cells and contain large numbers of mitochondria and lysosomes. Each 24-hour period sees an alternation of primarily osteoblast, then osteoclast activity. Note in Figure 8-8 how a branchlike piece of bone is being "sculpted" by an osteoclast eroding existing bone mineral from its upper surface while osteoblasts are simultaneously depositing new osteoid on its under surface. As minerals are dissolved during bone erosion, they are reabsorbed back into the blood, their original source.

The process of bone formation and reabsorption characterizes bone as a dynamic tissue that undergoes continuous change and remodeling.

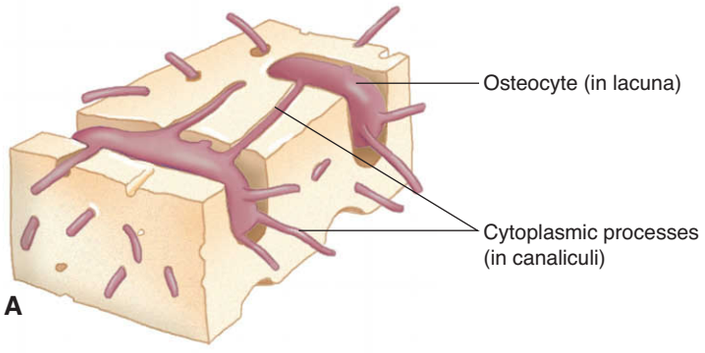
Osteocytes (OS-tee-oh-sytes) are mature, nondividing osteoblasts that have become surrounded by matrix and now lie within lacunae. Figure 8-9 includes an illustration and a scanning electron micrograph showing a mature osteocyte within a lacuna. Note that a cytoplasmic process from the cell is extending into a canaliculus below. Cytoplasmic processes from neighboring cells are connected by gap junctions, which allow the cells to share water and nutrients. Numerous collagen fibers are seen in the ground substance and mineralized bone surrounding the osteocyte.

The way in which these cell types work together to produce bone is described in detail when the development of bone is discussed later in this chapter.

BONE MARROW

Bone marrow is a type of soft, diffuse connective tissue called **myeloid tissue.** It serves as the site for production of blood cells and is found in the medullary cavities of certain long bones and in the spaces of spongy bone in some areas (Figure 8-10).

During the lifetime of an individual, two types of marrow exist. In an infant's or child's body, virtually all of the bones contain *red marrow*. This is named for its function in the production of red blood cells. As an individual ages, the red marrow is gradually replaced



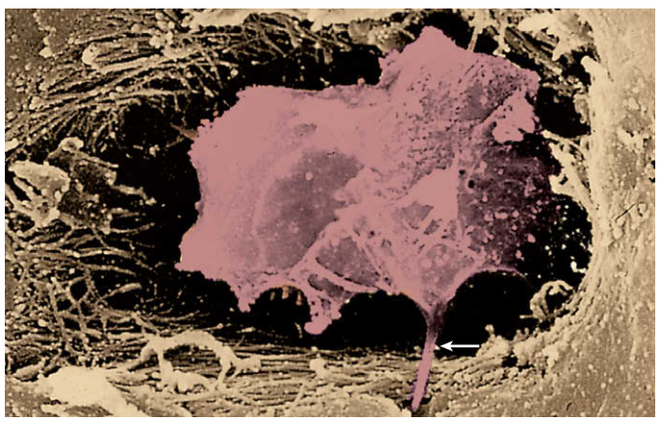


FIGURE 8-9

Osteocyte. A, Sketch showing osteocytes trapped inside hollow lacunae within hard bone matrix. **B,** Scanning electron micrograph showing an osteocyte within a lacuna. Note the cytoplasmic process *(arrow)* extending into a canaliculus below. The cell is surrounded by collagen fibers and mineralized bone.

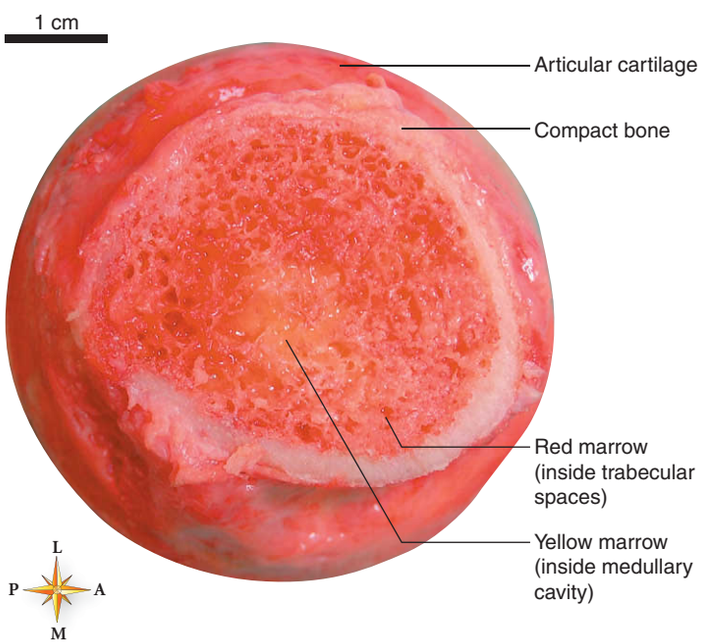


FIGURE 8-10

Bone marrow. Photograph of the head of the femur removed during a hip replacement surgery. A wedge has been removed from the bone to show the marrow spaces inside. Compare to Figure 8-3.

by *yellow marrow*. In yellow marrow, the increasing population of *adipocytes* (fat cells) begins to replace hemopoietic stem cells. The adipocytes also signal the remaining stem cells to reduce blood cell production. With advancing age, yellow marrow becomes almost rust-colored, less fatty, and more gelatinous in consistency.

The main bones in an adult that still contain red marrow include the ribs, bodies of the vertebrae, and ends of the humerus in the upper part of the arm, the pelvis, and the femur, or thigh bone. During times of decreased blood supply, yellow marrow in an adult can alter to become red marrow. Such a transition may occur during periods of prolonged anemia caused by chronic blood loss, exposure to radiation or toxic chemicals, and certain diseases.

If the bone marrow is severely diseased or damaged, a **bone marrow transplant** can be a lifesaving treatment. In this procedure, red marrow from a compatible donor is introduced into the recipient intravenously. If the recipient's immune system does not reject the new tissue, which is always a danger in tissue transplants, the donor cells may establish a colony of new, healthy tissue in the bone marrow.

REGULATION OF BLOOD CALCIUM LEVELS

The bones of the skeletal system serve as a storehouse for about 98% of the body calcium reserves. As the major reservoir for this physiologically important body mineral, bones play a key role in maintaining the constancy of blood calcium levels. To maintain homeostasis of blood calcium levels within a very narrow range, calcium is mobilized and moves into and out of blood during the continuous remodeling of bone. It is the balance between deposition of bone by osteoblasts and breakdown and reabsorption of bone matrix by osteoclasts that helps regulate blood calcium levels. During bone formation, osteoblasts serve to remove calcium from blood, thus lowering its circulating levels. However, when osteoclasts are active and breakdown of bone predominates, calcium is released into blood and circulating levels will increase.

Homeostasis of the calcium ion concentration is essential not only for bone formation, which is described below, but also for normal blood clotting, transmission of nerve impulses, and maintenance of skeletal and cardiac muscle contraction. The primary homeostatic mechanisms involved in the regulation of blood calcium levels involve the secretion of two hormones: (1) *parathyroid hormone (PTH)* by the parathyroid glands and (2) *calcitonin (CT)* by the thyroid gland.

Mechanisms of Calcium Homeostasis

PARATHYROID HORMONE

The actions of parathyroid hormone are fully discussed in Chapter 19. However, the importance of this hormone as the primary regulator of calcium homeostasis and its effect on bone remodeling call for a brief description here. When the level of calcium in blood passing through the parathyroid glands decreases below its normal homeostatic "set point" level, osteoclasts are stimulated to initiate increased breakdown of bone matrix, which results in the release of calcium into blood and the return of calcium levels to normal (Figure 8-11). In addition, parathyroid hormone also increases renal absorption of calcium from urine, thus reducing its loss from the body.

Another effect of parathyroid hormone is to stimulate vitamin D synthesis, which increases the efficiency of absorption of calcium from the intestine. If blood passing through the parathyroid glands has an elevated calcium level, osteoclast activity will be suppressed, thus reducing the breakdown of bone matrix and the level of calcium circulating in blood. The multiple effects of this type of hormonal control permit the body to precisely regulate a number of homeostatic mechanisms that have an effect both directly and indirectly on the blood levels of this important mineral.

Parathyroid hormone is the most critical factor in homeostasis of blood calcium levels. As a result of its actions and the ability of the body to regulate its formation and release, bones remain strong and calcium levels are maintained within normal limits during both bone formation and bone reabsorption.

CALCITONIN

Calcitonin, also discussed in Chapter 19, is a protein hormone produced by endocrine cells in the thyroid gland. It is produced in response to high blood calcium levels and functions to stimulate bone deposition by osteoblasts and inhibit osteoclast activity. As a result, calcium will move into the bones from the blood and circulating levels will decrease. Nasal spray containing calcitonin is available to treat postmenopausal osteoporosis.

Although calcitonin does play a role in the homeostasis of blood calcium levels, it is far less important than parathyroid hormone.

OTHER MECHANISMS

Additional regulatory mechanisms also play a role in calcium homeostasis by affecting mineral storage in the bone. For example, *growth hormone (GH)* secreted from the anterior pituitary gland stimulates the development of new bone and can thus reduce calcium in the blood. On the other hand, the neurotransmitter *serotonin* produced in the nerves of the gut may act as a

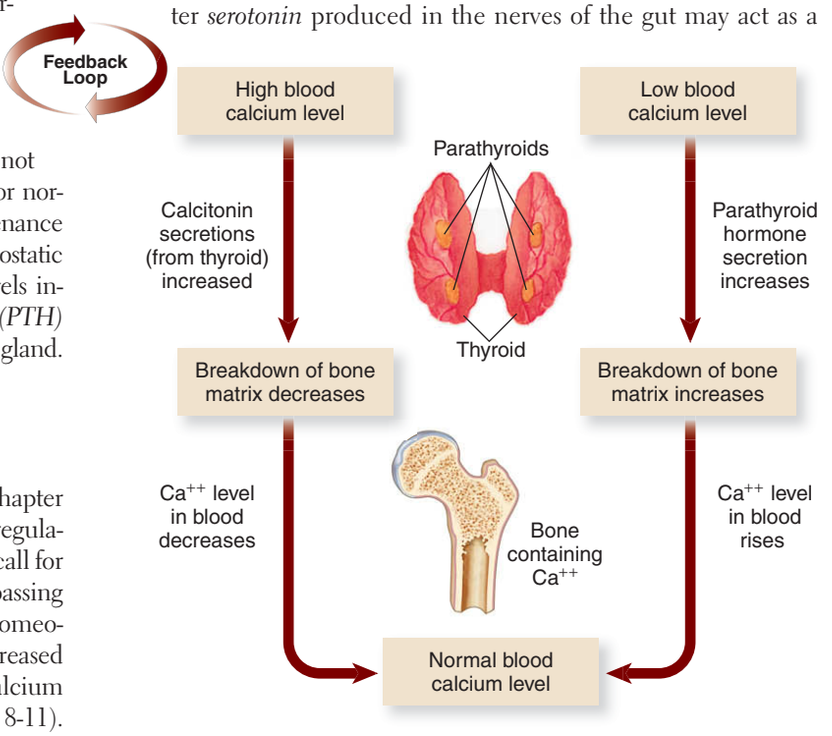


FIGURE 8-11

Calcium homeostasis. Calcitonin and parathyroid hormones have antagonistic (opposing) effects that help to maintain a homeostatic balance of calcium in the blood.

hormone to inhibit osteoblast activity and thus raise blood calcium level. Research also shows that osteoblasts themselves are able to monitor extracellular calcium levels and react to changes.

DEVELOPMENT OF BONE

When the skeleton begins to form in an infant before birth, it consists not of bones but of cartilage and fibrous structures shaped like bones. Gradually, these cartilage "models" become transformed into real bones when the cartilage is replaced with calcified bone matrix. This process of constantly "remodeling" a growing bone as it changes from a small cartilage model to the characteristic shape and proportion of the adult bone requires continuous activity by the bone-forming osteoblasts and bone-resorbing osteoclasts. The laying down of calcium salts in the gel-like matrix of the forming bones is an ongoing process. This calcification process is what makes bones as "hard as bone." The combined action of osteoblasts and osteoclasts sculpts bones into their adult shape. The term **osteogenesis** is used to describe this process.

"Sculpting" by the bone-forming and bone-resorbing cells allows bones to respond to stress or injury by changing size, shape, and density. The stress placed on certain bones during exercise increases the rate of bone deposition. For this reason, athletes or dancers may have denser, stronger bones than less active people.

Most bones of the body are formed from cartilage models in a process called **endochondral ossification,** meaning "bone formation in cartilage." A few flat bones are formed within fibrous membrane, rather than cartilage, in the process of **intramembranous ossification.** Figure 8-12 illustrates osseous development of an infant at birth.

| A&P CONNECT |

Patterns of bone-forming activity in the skeleton often can be visualized with a *bone scan.* To see a bone scan image and learn how it is produced, check out ***Bone Scans*** online at ***A&P Connect.***

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Intramembranous Ossification

Intramembranous ossification takes place, as its name implies, within a connective tissue membrane. The flat bones of the skull, for example, begin to take shape when groups of osteogenic stem cells within the membrane differentiate into osteoblasts. These clusters of osteoblasts are called **ossification centers.** They secrete matrix material and collagenous fibrils. The Golgi apparatus in an osteoblast specializes in synthesizing and secreting carbohydrate compounds of the type called *mucopolysaccharides,* and its endoplasmic reticulum makes and secretes collagen, a protein. In time, relatively large amounts of the mucopolysaccharide substance, or *ground substance,* accumulate around each osteoblast. Numerous bundles of collagenous fibers then become embedded in the ground substance. Together, the ground substance and collagenous fibers constitute the organic bone matrix. Calcification of the organic bone matrix occurs when complex calcium salts are deposited in it.

As calcification of bone matrix continues, the trabeculae appear and join in a network to form spongy bone (Figure 8-13).

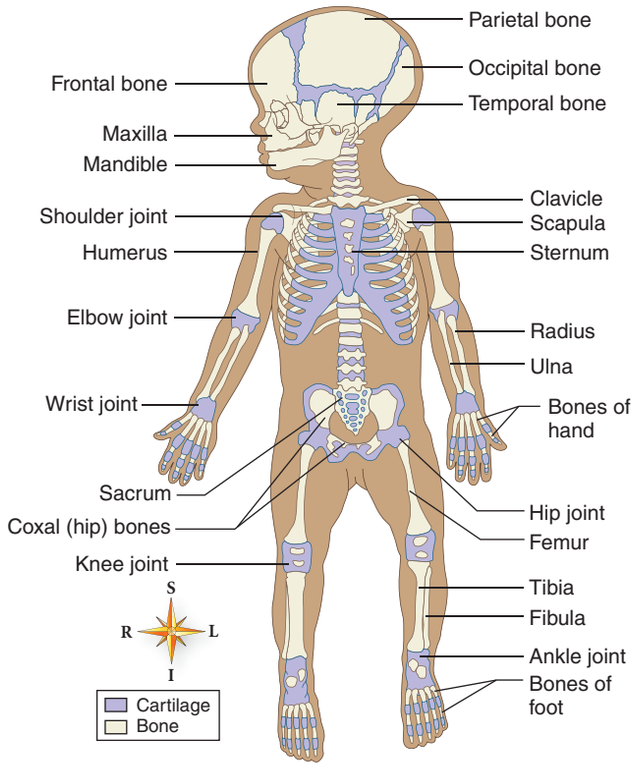


FIGURE 8-12

Bone development. Diagram showing osseous development at birth.

In time the core layer of spongy bone (diploe) will be covered on each side by plates of compact, or dense, bone. Once formed, a flat bone grows in size by the addition of osseous tissue to its outer surface. The process is called **appositional growth.** Flat bones cannot grow by interior expansion as is the case with endochondral bone growth described in the following section.

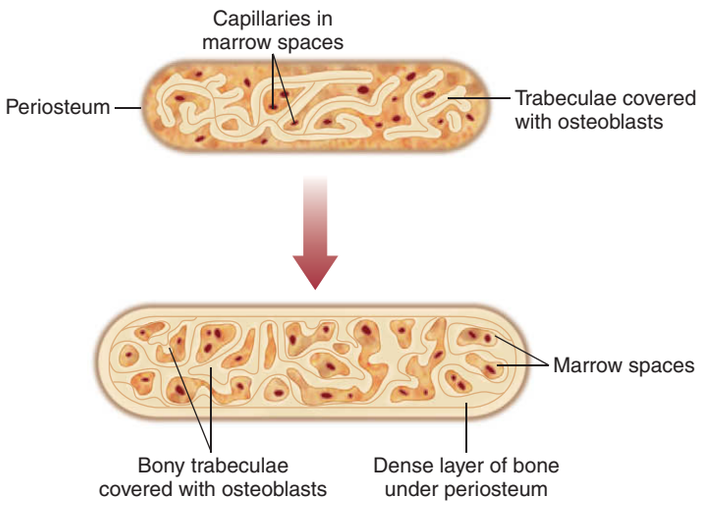


FIGURE 8-13

Intramembranous bone formation. Layers of bone matrix build up to form a lattice of branched trabeculae forming the diploe of a flat bone. Eventually, a layer of compact bone forms under the periosteum to form the tables of a flat bone. Compare to Figure 8-6.

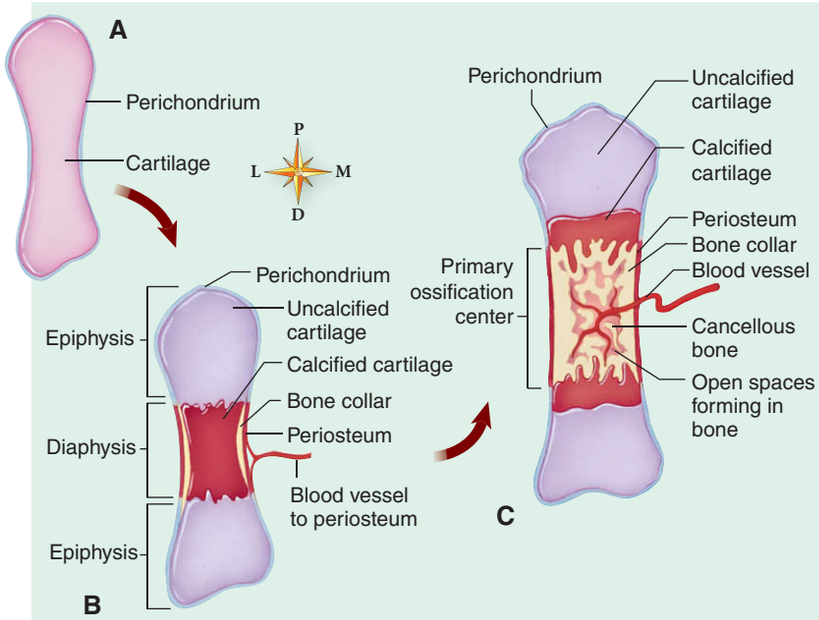


FIGURE 8-14

Endochondral bone formation. A, Cartilage model. **B,** Bone collar formation under the periosteum. **C,** Development of the primary ossification center and entrance of a blood vessel. **D,** Prominent medullary cavity with thickening and lengthening of the collar. **E,** Development of secondary ossification centers in epiphyseal cartilage. **F,** Enlargement of secondary ossification centers, with bone growth proceeding toward the diaphysis from each end. **G,** With cessation of bone growth, the lower, then upper epiphyseal plates disappear (only the epiphyseal lines remain).

Endochondral Ossification

Most bones of the body are formed from cartilage models, with bone formation spreading essentially from the center to the ends. The steps of endochondral ossification are illustrated in Figure 8-14. The cartilage model of a typical long bone, such as the tibia, can be identified early in embryonic life (Figure 8-14, *A*). The cartilage model then develops a periosteum (Figure 8-14, *B*) that soon enlarges and produces a ring, or collar, of bone. Bone is deposited by osteoblasts, which differentiate from cells on the inner surface of the covering periosteum. Soon after appearance of the ring of bone, the cartilage begins to calcify (Figure 8-14, *C*), and a **primary ossification center** forms when a blood vessel enters the rapidly changing cartilage model at the midpoint of the diaphysis. Endochondral ossification progresses from the diaphysis toward each epiphysis (Figure 8-14, *D*), and the bone grows in length. The process is called *interstitial growth.* Eventually, **secondary ossification centers** appear in the epiphyses (Figure 8-14, *E*), and bone growth proceeds toward the diaphysis from each end (Figure 8-14, *F*).

Until bone growth in length is complete, a layer of the cartilage, known as the **epiphyseal plate,** remains between each epiphysis and the diaphysis. During periods of growth, proliferation of epiphyseal cartilage cells brings about a thickening of this layer. Ossification of the additional cartilage nearest the diaphysis follows—that is, osteoblasts synthesize organic bone matrix, and the matrix undergoes calcification (Figure 8-15). As a result, the bone becomes longer (Figure 8-16). It is the epiphyseal plate that allows the diaphysis of a long bone to increase in length.

The epiphyseal plate shown in Figure 8-17 is composed of four layers of cells. The top layer of cells closest to the epiphysis is composed of "resting" cartilage cells. These cells are not proliferating or undergoing change. This layer serves as a point of attachment firmly joining the outer end, or epiphysis, of a bone to the shaft.

The second layer of cells shown in Figure 8-17 is called the *proliferating zone.* It is composed of cartilage cells that are undergoing active mitosis. As a result of mitotic division and increased cellular activity, the layer thickens and the plate as a whole increases in length (Figure 8-18).

The third layer of cells, called the *zone of hypertrophy*, is composed of older, enlarged cells that are undergoing degenerative changes associated with calcium deposition.

The layer closest to the diaphysis is a thin layer composed of dead or dying cartilage cells undergoing rapid calcification. As the process of calcification progresses, this layer becomes fragile and disintegrates. The resulting space is soon filled with new bone tissue, and the bone as a whole grows in length.

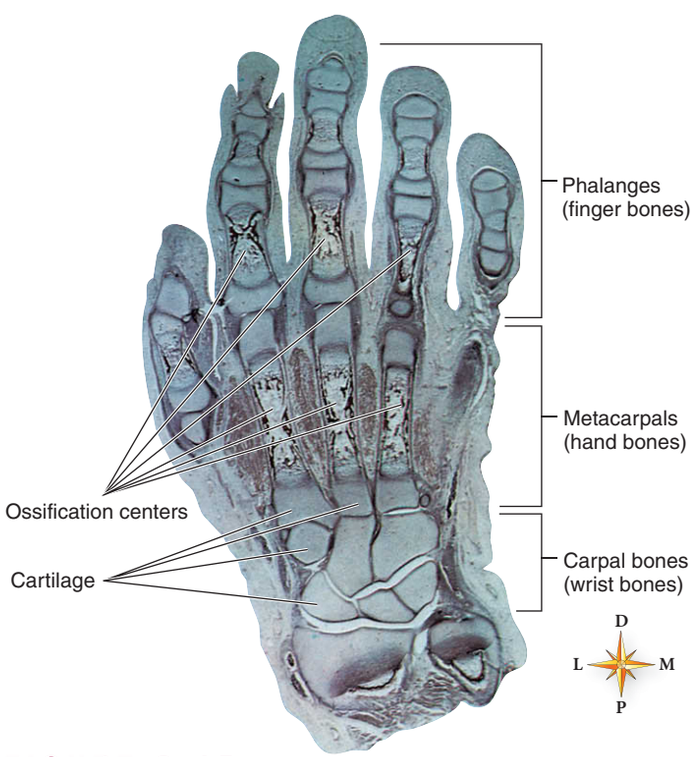
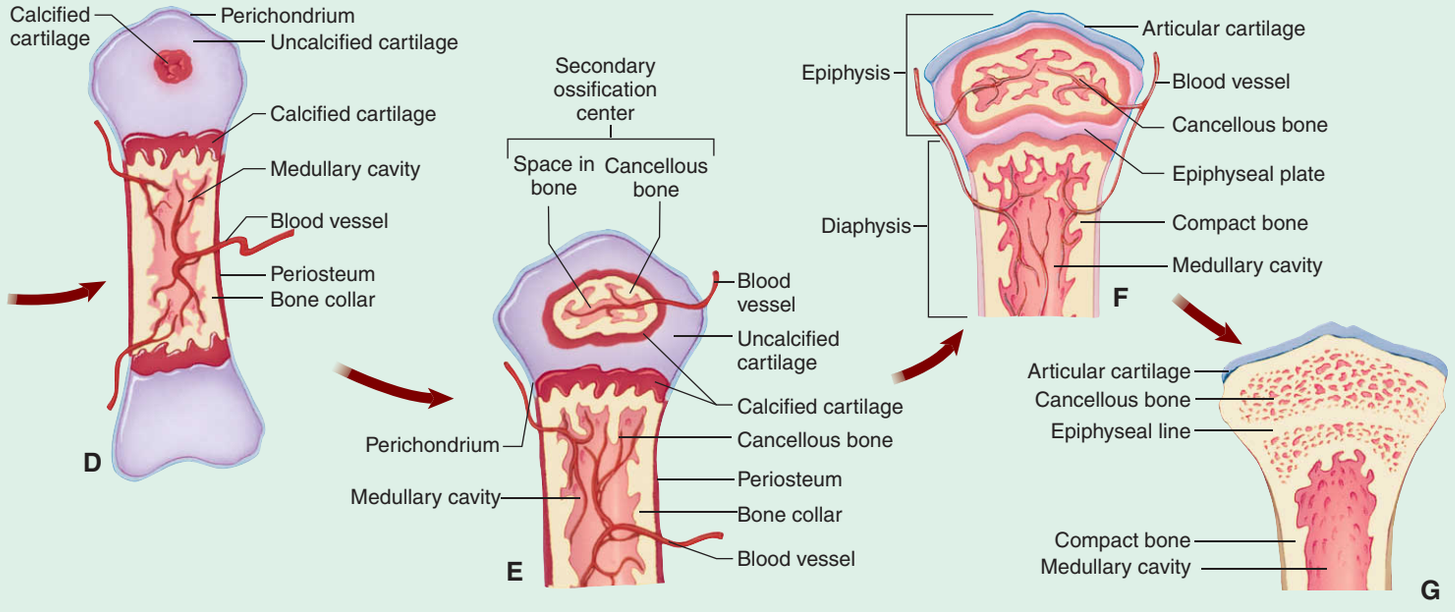


FIGURE 8-15

Fetal ossification centers. Photograph of a specially prepared fetal hand specimen showing primary ossification centers in the bones of the hand (metacarpal bones) and fingers (phalanges). Note that none of the wrist (carpal) bones show any evidence of ossification.



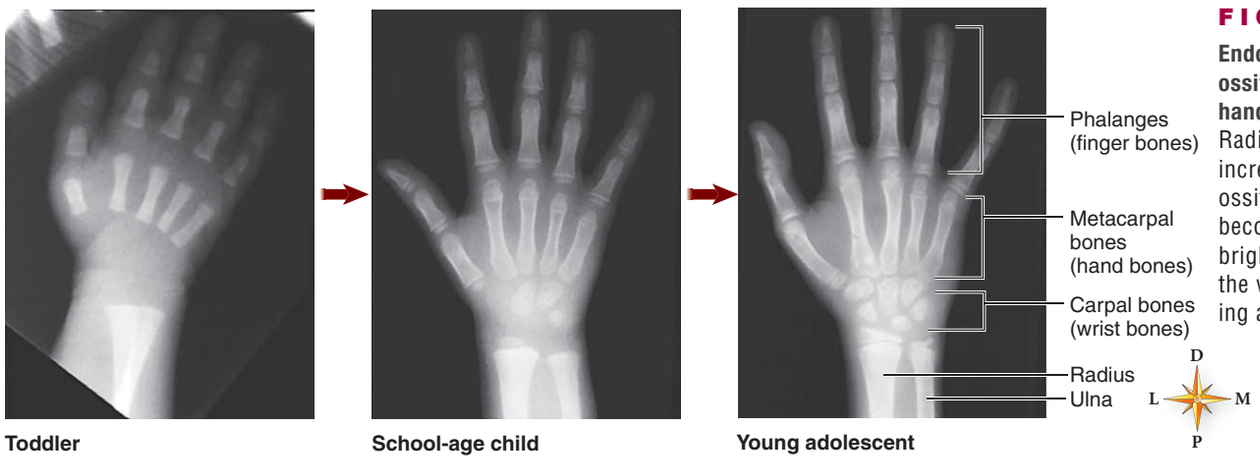


FIGURE 8-16

Endochondral ossification of the hand and wrist. Radiographs showing increasing numbers of ossification centers becoming visible as bright white areas in the wrist with increasing age.

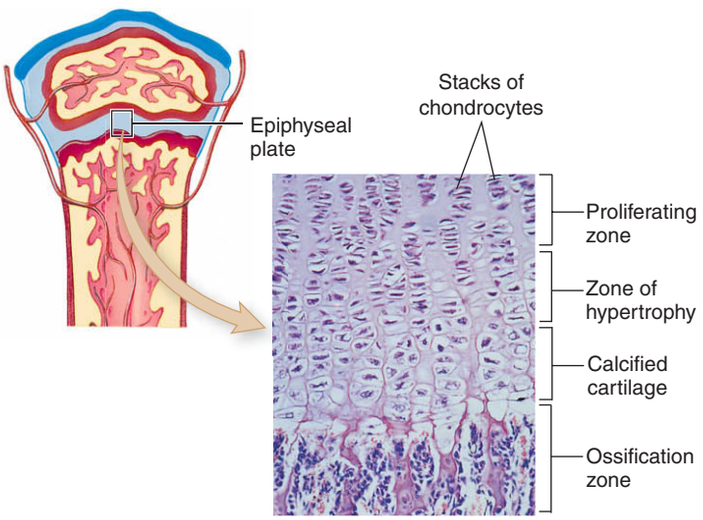


FIGURE 8-17

Epiphyseal plate structure. An epiphyseal plate between the epiphysis and diaphysis of a long bone. Photograph shows the zones of the epiphyseal plate.

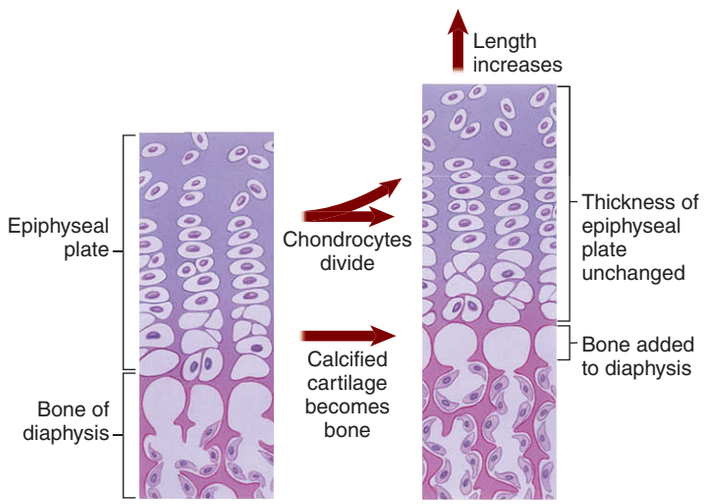


FIGURE 8-18

Growth of epiphyseal plate. Diagrams showing steps in ossification on either side of the epiphyseal plate.

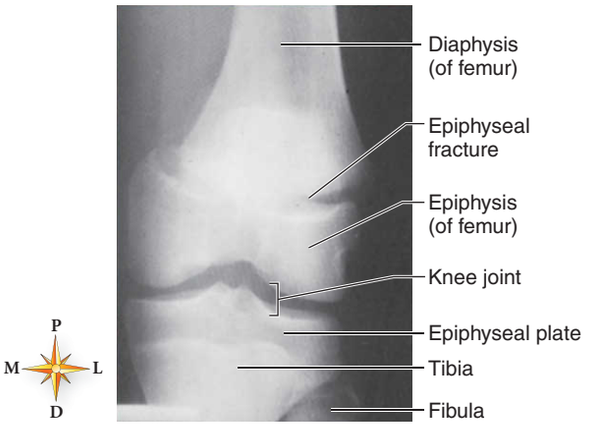


FIGURE 8-19

Epiphyseal fracture. Radiograph showing an epiphyseal fracture of the distal end of the femur in a young athlete. Note the separation of the diaphysis and epiphysis at the level of the growth plate.

When epiphyseal cartilage cells stop multiplying and the cartilage has become completely ossified, bone growth ends. Radiographs can reveal any epiphyseal cartilage still present. When bones have grown their full length, the epiphyseal cartilage disappears—bone has replaced it and is then continuous between epiphysis and diaphysis. The point of articulation between the epiphysis and diaphysis of a growing long bone, however, is susceptible to injury if overstressed—especially in a young child or preadolescent athlete. In these individuals the epiphyseal plate can be separated from the diaphysis or epiphysis and result in **epiphyseal fracture** (Figure 8-19). The relationship between interstitial growth (growth in length) and appositional growth (growth in diameter) during endochondral ossification of a long bone is shown in Figure 8-20.

| QUICK CHECK |

9. Name the three major types of bone cells.
10. Name the two types of bone marrow.
11. What are the five functions of bone?
12. Identify the two types of bone formation.

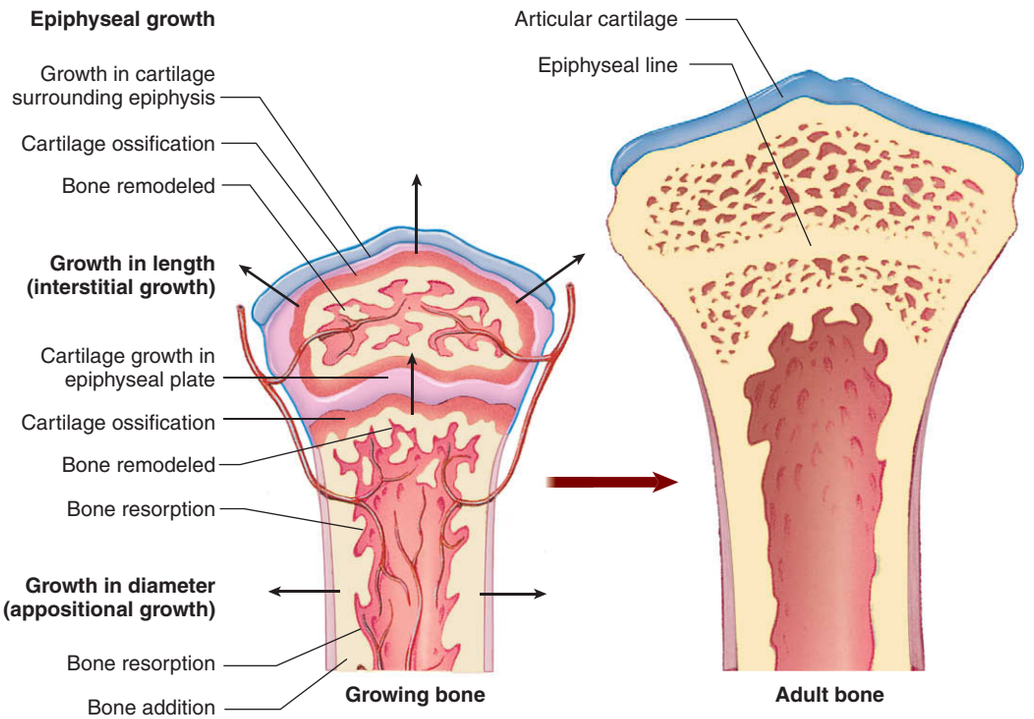
BONE REMODELING

In the early stages of ossification, bone tissue develops in a chaotic pattern of mineralized layers. Its crisscross appearance gives this new bone tissue the name *woven bone*. However, the woven bone is soon replaced by stronger, layered bone called *lamellar bone*, which is characterized by the presence of many osteons. The first osteons formed in lamellar bone are called *primary osteons*. To form a primary osteon, osteoclasts in the endosteum that surrounds a blood vessel first demineralize a cone or tube around a blood vessel. This leaves a cavelike hollow filled with collagenous fibers and lined with endosteum. Figure 8-21 shows how osteoblasts in the endosteum then form layer upon layer (lamellae) along the inside wall of the tube, trapping osteocytes between the lamellae. Eventually, the concentric lamella run out of space to mineralize—leaving only the central canal with its tightly packed blood vessels, nerves, and lymphatic vessels. As the bone develops, primary osteons are later replaced through the same process with *secondary osteons*.

Bones grow at their outer margins by the ossification of fibrous tissue by osteoblasts. Long bones grow in diameter by the combined action of osteoblasts and osteoclasts. Osteoclasts enlarge the diameter of the medullary cavity by eating away the bone of its walls. At the same time, osteoblasts from the periosteum build new bone around the outside of the bone. By this dual process, a bone with a larger diameter and larger medullary cavity is produced from a smaller bone with a smaller medullary cavity.

FIGURE 8-20

Bone remodeling. Bone formation on the outside of the shaft coupled with bone reabsorption on the inside increases the bone's diameter. Endochondral growth during bone remodeling increases the length of the diaphyses and causes the epiphysis to enlarge.



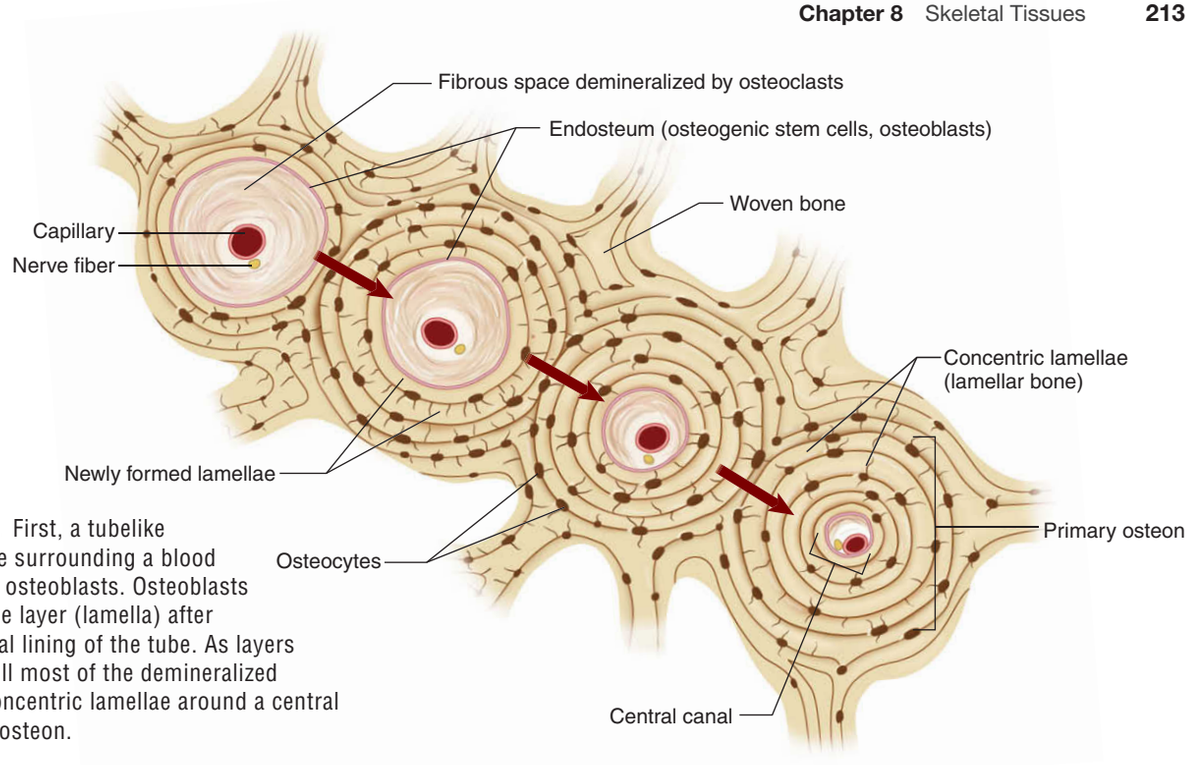


FIGURE 8-21

Primary osteon formation. First, a tubelike passage in the woven bone surrounding a blood vessel is demineralized by osteoblasts. Osteoblasts then begin laying down one layer (lamella) after another along the endosteal lining of the tube. As layers build up, they eventually fill most of the demineralized tube—thus forming the concentric lamellae around a central canal that characterize an osteon.

The remodeling activity of osteoclasts (removal of old bone) and osteoblasts (deposition of new bone) is important in homeostasis of blood calcium levels. It also permits bones to grow in length and diameter and to change their overall shape and the size of the marrow cavity (see Figure 8-20).

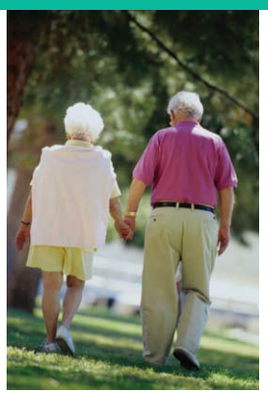
The formation of bone tissue continues long after bones have stopped growing. Throughout life, bone formation (ossification) and bone destruction (reabsorption) proceed concurrently. These opposing processes balance each other during the early to middle years of adulthood. The rate of bone formation equals the rate of bone destruction. Bones, therefore, neither grow nor shrink. They stay constant in size. Not so in the earlier years. During childhood and adolescence, ossification occurs at a faster rate than bone reabsorption does. Bone gain outstrips bone loss, and bones grow larger. But between the ages of 35 and 40 years, the process reverses, and from that time on, bone loss exceeds bone gain. Bone gain occurs slowly at the outer, or periosteal, surfaces of bones. Bone loss, on the other hand, occurs at the inner, or endosteal, surfaces and takes place at a somewhat faster pace. More bone is lost on the inside than gained on the outside, and inevitably bones become remodeled as the years go by.

Recall that under mechanical stress cancellous bone remodels its trabecula in different directions and thicker diameters to better withstand the stress (see Figure 8-7). Remodeling in compact bone involves the formation of new (secondary) osteons when bones are stressed. The higher the mechanical load on a bone, the narrower the tube hollowed out by osteoclasts as they prepare for the new osteon. Thus bones that bear the greatest weight have the narrowest osteons. These narrower osteons also have denser mineralization. The dense mineralization along with more numerous, narrower osteons gives the bone great strength to resist the stress. It is clear then why physical activity, which increases the various loads on bones throughout the body, tends to increase the density and strength of the skeleton (Box 8-1).

Box 8-1 | SPORTS and FITNESS

Exercise and Bone Density

Walking, jogging, and other forms of exercise subject bones to stress. They respond by laying down more collagen fibers and mineral salts in the bone matrix. This, in turn, makes bones stronger. But inactivity and lack of exercise tend to weaken bones because of decreased collagen formation and excessive calcium withdrawal. To prevent these changes, as well as many others, astronauts regularly perform special exercises in space because of the lack of gravity. Regular weight-bearing exercise is also an important part of the prevention and treatment of osteoporosis.



Physical activity increases bone density.

REPAIR OF BONE FRACTURES

The term *fracture* is defined as a break in the continuity of a bone. *Fracture healing* is the process that results in bone repair. The complex bone tissue repair process that follows a fracture is apparently initiated by bone death or by damage to periosteal and osteon blood vessels.

A bone fracture invariably tears and destroys blood vessels that carry nutrients to osteocytes. It is this vascular damage that initiates the highly regulated and generally very successful repair

process described below. When uncomplicated fractures occur in healthy children and young adults, the healing process often results in a repair that is all but impossible to detect 6 months after injury. Healing thus becomes a simple matter of adjusting normal bone remodeling processes to repair the injury. However, especially in older age groups, fracture repair may be complicated by underlying disease or other health problems, such as osteoporosis, diabetes, infection, or diminished blood supply to the injured area. In these cases, delayed healing, instability, deformity, or even nonunion of the fractured bone can result in very serious medical complications.

The process of fracture healing is shown in Figure 8-22, A to D. Vascular damage occurring immediately after a fracture results in hemorrhage and the pooling of blood at the point of injury. The resulting blood clot is called a *fracture hematoma* (Figure 8-22, *B*). The fracture hematoma quickly becomes "organized," develops a fibrin mesh, and transforms into a soft mass of *granulation tissue* containing inflammatory cells, fibroblasts, bone- and cartilage-forming cells, and new capillaries. Soon, islands of cartilaginous tissue called *procallus* form, and although they offer no structural rigidity for weight bearing, they help anchor the ends of the fractured bone more firmly. Growing numbers of osteoblasts continue the healing process with the formation of bony *callus* tissue. It serves to bind the broken ends of the fracture on both the outside surface and along the marrow cavity internally. The rapidly growing callus tissue effectively "collars" or "splints" the broken ends and stabilizes the fracture so that healing can proceed (Figure 8-22, C). If the fracture is properly aligned and immobilized and if complications do not develop, callus tissue will be actively "modeled" and eventually replaced with normal bone as the injury heals completely (Figure 8-22, D).

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What are the types of bone fractures? How are they treated? Learn more about bone fractures in Chapter 9, p. 264, and in ***Bone Fractures*** online at ***A&P Connect.***

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CARTILAGE

Types of Cartilage

Cartilage is classified as connective tissue and is classified into three types called **hyaline** (HYE-ah-lin) **cartilage, elastic cartilage,** and **fibrocartilage.** As a tissue, cartilage resembles bone in some ways but differs from bone in other ways. Innumerable collagenous fibers reinforce the matrix of both tissues, and as with bone, cartilage consists more of extracellular substance than cells. However, in cartilage the fibers are embedded in a firm gel instead of a calcified cement substance. Hence cartilage has the flexibility of a firm plastic material, whereas bone has the rigidity of cast iron. Another difference is that no canal system and no blood vessels penetrate the cartilage matrix. Cartilage is avascular and bone is abundantly vascular. Nevertheless, cartilage cells, as with bone cells, lie in lacunae. However, because no canals and blood vessels interlace cartilage matrix, nutrients and oxygen can reach the scattered, isolated **chondrocytes** (cartilage cells) only by diffusion. They diffuse through the matrix gel from capillaries in the fibrous covering of the cartilage—the **perichondrium**—or from synovial fluid in the case of articular cartilage.

The three cartilage types differ from one another largely by the relative amounts of elastic and collagenous fibers that are embedded in the matrix material. *Hyaline* is the most abundant type, and both elastic cartilage and fibrocartilage are considered modifications of the hyaline type. Collagenous fibers are present in all three types, but are most numerous in *fibrocartilage.* Hence it has the greatest tensile strength. *Elastic cartilage* matrix contains elastic fibers, as well as collagenous fibers, and thus has elasticity, as well as firmness.

Cartilage is an excellent skeletal support tissue in the developing embryo. It forms rapidly and yet retains a significant degree of rigidity, or stiffness. A majority of the bones that eventually form the axial and the appendicular skeleton described in Chapter 9 first appear as cartilage models. Skeletal maturation involves replacement of the cartilage models with bone.

After birth there is a decrease in the total amount of cartilage tissue present in the body. However, it continues to play an important role in the growth of long bones until skeletal maturity and is found throughout life as the material that covers the articular surfaces of bones in joints. The three types of cartilage also serve other important functions throughout the body.

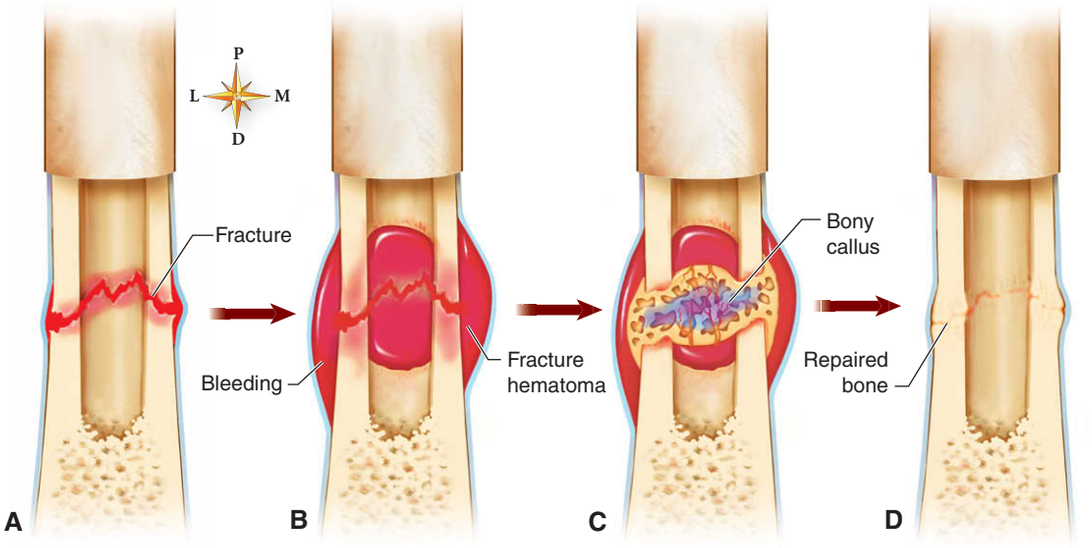


FIGURE 8-22

Bone fracture healing. A, Fracture of the femur. **B,** Formation of a fracture hematoma. **C,** Formation of internal and external bony callus. **D,** Bone remodeling complete.

HYALINE CARTILAGE

Hyaline, in addition to being the most common type of cartilage, serves many functions. It resembles milk glass in appearance (Figure 8-23, A). In fact, its name is derived from the Greek word meaning "glassy." Sometimes called *gristle*, it is semitransparent and often has a bluish, opalescent cast.

In the embryo, hyaline cartilage forms from differentiation of mesenchymal cells that become crowded together in so-called **chondrification centers.** As the cells enlarge, they secrete matrix material that surrounds the delicate collagen fibrils. Eventually, the continued production of matrix separates and isolates the cells, or chondrocytes, into compartments, which as in bone, are called *lacunae*. Like bone, the organic matrix of hyaline cartilage is a mixture of ground substance and collagenous fibers. The ground substance is rich in both chondroitin sulfate and a unique gel-like polysaccharide. Both substances are secreted from chondrocytes in much the same way protein and carbohydrates are secreted from glandular cells.

In addition to covering the articular surfaces of bones, hyaline cartilage forms the costal cartilages that connect the anterior ends of the ribs with the sternum, or breastbone. It also forms the cartilage rings in the trachea, bronchi of the lungs, and tip of the nose.

ELASTIC CARTILAGE

Elastic cartilage gives form to the external ear, the epiglottis that covers the opening of the respiratory tract when swallowing, and the eustachian, or auditory, tubes that connect the middle ear and nasal cavity. The collagenous fibers of hyaline cartilage are also present—but in fewer numbers—in elastic cartilage. Large numbers of darkly stained elastic fibers confer the elasticity and resiliency typical of this form of cartilage (Figure 8-23, B).

FIBROCARTILAGE

Fibrocartilage—or *fibrous cartilage*—is characterized by abundant fibrous elements within the matrix (Figure 8-23, C). It is strong, rigid, and most often associated with regions of dense connective tissue in the body. It occurs in the pubic symphysis, in intervertebral disks, and near the points of attachment of some large tendons to bones.

Function of Cartilage

The tough, rubberlike nature of cartilage permits it to sustain great weight when covering the articulating surfaces of bones. It also may serve as a shock-absorbing pad between articulating bones in the spine. In other areas, such as the external ear, nose, or respiratory passages, cartilage provides a strong, yet pliable support structure that resists deformation or collapse of tubular passageways. Cartilage permits growth in the length of long bones and is largely responsible for their adult shape and size.

Growth of Cartilage

Growth of cartilage occurs in two ways:

1. Interstitial growth
2. Appositional growth

During interstitial growth, cartilage cells within the substance of the tissue mass divide and begin to secrete additional matrix. Internal division of chondrocytes is possible because of the soft, pliable nature of cartilage tissue. This form of growth is most often seen during childhood and early adolescence, when a majority of cartilage is still soft and capable of expansion from within. Interstitial growth may be referred to as *endogenous growth* because it occurs *within* the cartilage tissue.

Appositional growth occurs when chondrocytes in the deep layer of the perichondrium begin to divide and secrete additional matrix. The new matrix is then deposited on the surface of the cartilage, which causes it to increase in size. Appositional growth is unusual in early childhood but, once initiated, continues beyond adolescence and throughout an individual's life. Appositional growth may be referred to as *exogenous growth* because it occurs on the *outer* surfaces of cartilage tissue.

| QUICK CHECK |

13. Name three major types of cartilage.
14. Identify the primary type of cartilage cell.
15. List the two mechanisms of cartilage growth.

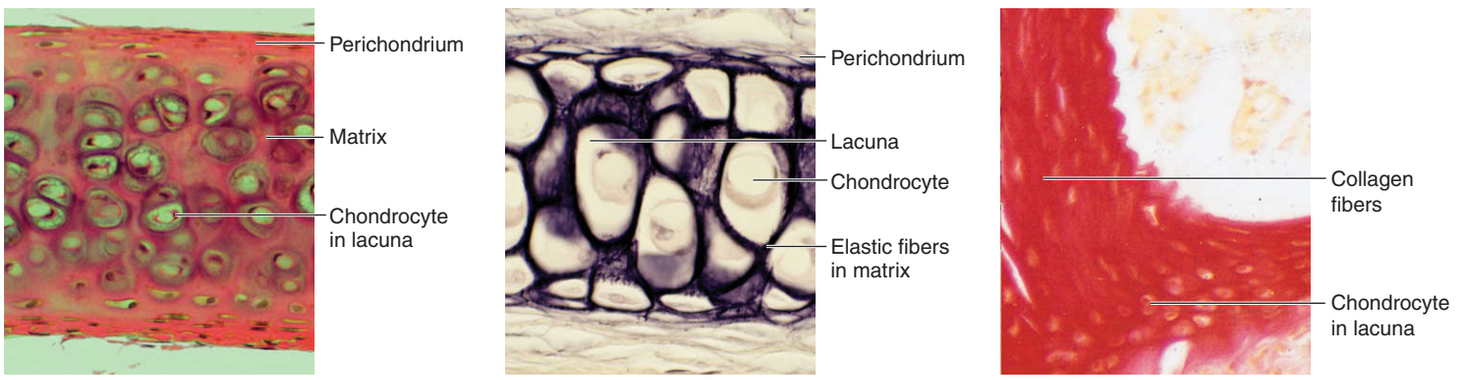


FIGURE 8-23

Types of cartilage. A, Hyaline cartilage of the trachea. **B,** Elastic cartilage of the epiglottis. Note the black elastic fibers in the cartilage matrix and the perichondrium layers on both surfaces. **C,** Fibrocartilage of an intervertebral disk.

Cycle of LIFE

Skeletal Tissues

This chapter focused on the changes that occur in bone and cartilage tissue from the time before birth to advanced old age. For instance, we have outlined in some detail the process by which the soft cartilage and membranous skeleton become ossified over a period of years. By the time a person is a young adult in the mid-twenties, the skeleton has become fully ossified. A few areas of soft tissue—the cartilaginous areas of the nose and ears, for example—may continue to grow and ossify very slowly throughout adulthood so that by advanced old age, some structural changes are apparent.

Changes in skeletal tissue that occur during adulthood usually result from specific conditions. For example, the mechanical stress of weight-bearing exercise can trigger dramatic increases in the density and strength of bone tissue. Pregnancy, nutritional deficiencies, and illness can all cause loss of bone density accompanied by loss of structural strength.

In advanced adulthood, degeneration of bone and cartilage tissue becomes apparent. Replacement of hard bone matrix by softer connective tissue results in a loss of strength that increases susceptibility to injury. This is especially true in older women who suffer from osteoporosis. Fortunately, even very light exercise by elderly individuals can counteract some of the skeletal tissue degeneration associated with old age.

the BIG picture

Skeletal Tissues

Skeletal tissues influence many important body functions that are crucial to the "big picture" of overall health and survival of the individual. The pervasive importance of the protective and support functions of skeletal tissues is immediately apparent. Bone and cartilage tissues are organized and grouped to protect the body and its internal organs from injury. In addition to providing a supporting and protective framework, these tissues also contribute to the shape, alignment, and positioning of the body and its myriad parts. Also, because of the organization of skeletal tissues into bones and the articulation of these bones in joints, we are able to engage in purposeful and coordinated movement. Bone remodeling permits ongoing change to occur in both structure and related functions throughout the cycle of life.

The homeostatic function of skeletal tissues is beautifully illustrated by the role they play in mineral storage and release. For example, regulation of blood calcium levels is important in such diverse areas as nerve transmission, muscle contraction, and normal clotting of blood. Because they contain red marrow, the bones also serve in the important role of hematopoiesis, or blood cell formation. This function ties skeletal tissues to such diverse homeostatic functions as regulation of body pH and the transport of respiratory gases and vital nutrients. By viewing skeletal tissues in such a broad and interrelated functional context, you can more readily sense the "connectedness" that unites these otherwise seemingly isolated body structures to the "big picture" of overall health and survival.

MECHANISMS of DISEASE

DISEASES OF SKELETAL TISSUES

Malignant Tumors of Bone and Cartilage

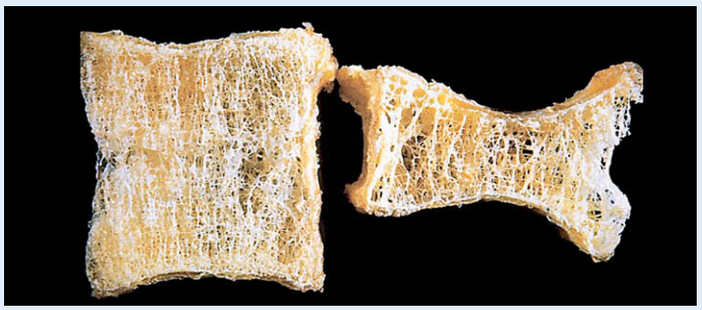
Osteosarcoma (osteogenic sarcoma) is the most common primary malignant tumor of skeletal tissue and is often the most fatal. It appears more frequently in males, with a peak age of incidence between 10 and 25 years. Common sites of involvement are the tibia, femur, and humerus. Roughly 10% of patients experience metastases to the lungs, and if left untreated, the course can involve widespread metastases and death within 1 year. Therapy commonly involves surgery followed by chemotherapy.

Chondrosarcoma is a malignant tumor of hyaline cartilage that arises from chondroblasts. It is a large, bulky, slow-growing tumor occurring most frequently in middle-aged persons. Common sites of involvement include the humerus, femur, spine, pelvis, ribs, and scapula. Large excisions or amputation of the affected extremity can improve survival rates. Chemotherapy has not been proven to be effective.

Metabolic Bone Diseases

Metabolic bone diseases are disorders of bone remodeling.

As a serious and very common bone disease, especially in older age groups, **osteoporosis** (os-tee-oh-poh-ROH-sis) has been the subject of intense scientific research and widespread public interest and concern. Characterized by increased bone porosity and reduced mineral density and mass, osteoporotic bones fracture easily. Some bones, such as the vertebral bodies in the spinal column, are particularly susceptible to damage. These bones have a large percentage of cancellous bone with trabeculae that become less numerous and weak in osteoporosis. The result is extensive and progressive microfracture of many of the remaining trabeculae and eventual vertebral collapse (Figure 8-24). Over time, increasing numbers of vertebral compression fractures result in a shortened stature and cause an abnormal backward curvature of the spine called "dowager's hump." The condition is, unfortunately, a common sign of long-standing



A



B



C

FIGURE 8-24

Osteoporosis. A, Compare the normal vertebral body (left) with the osteoporotic specimen (right). Note that the osteoporotic vertebral body has been shortened by compression fractures. **B,** Scanning electron micrograph (SEM) of normal bone. **C,** SEM of osteoporotic bone. Note the loss of trabeculae and appearance of enlarged pores caused by osteoporosis.

osteoporosis in many untreated older women. Although osteoporosis can occur in both men and women, one of every two women who survive 40 years after menopause will suffer an osteoporosis-related fracture, in contrast to one in 40 men of similar age.

In most women, a majority of the bone loss characteristic of osteoporosis occurs during the decade after menopause and beyond. However, significant loss can occur much earlier—even during adolescence. Therefore, health care providers are suggesting earlier screening for the disease and lifestyle changes that include weight-bearing exercise and a diet adequate in calcium and vitamin D.

| A&P CONNECT |

How can you tell if you have osteoporosis? View ***Measuring Bone Mineral Density*** at your ***A&P Connect*** to learn how bone density is measured.

evolve

Rickets and Osteomalacia

Rickets in young children and **osteomalacia** (os-tee-oh-mah-LAY-shah) in adults are metabolic skeletal diseases that affect significant numbers of individuals worldwide. Both diseases are characterized by demineralization or loss of minerals from bone related to vitamin D deficiency. The loss of minerals is coupled with increased production of unmineralized matrix. Rickets involves demineralization of developing bones in infants and young children before skeletal maturity. In osteomalacia, mineral content is lost from bones that have already matured. In rickets, the lack of rigidity caused by the demineralization of developing bones results in gross skeletal changes, including the classic "bowing of the legs" symptom (Figure 8-25). The demineralization of bones in osteomalacia does not generally affect overall skeletal contours but does result in increased susceptibility to fractures, especially in the vertebral bodies and femoral necks. Box 8-2 discusses how nutritional deficiencies affect cartilage as well as bone tissue.



FIGURE 8-25

Rickets. Bowing of legs in this toddler is due to poorly mineralized bones from rickets.

Box 8-2 | HEALTH matters

Cartilage and Nutritional Deficiencies

Certain nutritional deficiencies and other metabolic disturbances have an immediate and very visible effect on cartilage. It is for this reason that changes in cartilage often serve as indicators of inadequate vitamin, mineral, or protein intake. Vitamin A and protein deficiency, for example, will decrease the thickness of epiphyseal plates in the growing long bones of young children—an effect immediately apparent on x-ray examination. The opposite effect occurs in vitamin D deficiencies. As the epiphyseal cartilage increases in thickness but fails to calcify, the growing bones become deformed and bend under weight bearing. The bent long bones are a sign of rickets (see Figure 8-25).

Osteitis deformans, also known as *Paget disease*, is a disorder affecting older adults. It is characterized by proliferation of osteoclasts and compensatory increased osteoblastic activity. The result is rapid and disorganized bone remodeling. The bones formed are poorly constructed and weakened. It commonly affects the skull, humerus, femur, vertebra, and pelvic bones. Clinical manifestations may include bone pain, tenderness, and fractures. However, the majority of patients experience minimal changes and never know they have the disease. No treatment is recommended in an asymptomatic patient.

Osteomyelitis is a bacterial infection of the bone and marrow tissue. Infections of bone are often more difficult to treat than soft tissue infections because of the decreased blood supply and density of the bone. Bacteria, viruses, fungi, and other pathogens may cause osteomyelitis. *Staphylococcus* bacteria are the most common pathogens. Osteomyelitis is associated with extension of another infection (e.g., bacteremia, urinary tract infection, vascular ulcer) or direct bone contamination (e.g., gunshot wound, open fracture). Patients who are elderly, poorly nourished, or diabetic are also at risk. Thrombosis of blood vessels in osteomyelitis often results in ischemia and bone necrosis. As a result, infection can extend under the periosteum and spread to adjacent soft tissues and joints. Signs and symptoms may include an area swollen, warm, tender to touch, and painful. Early recognition of infection and aggressive antimicrobial management are required. Sometimes patients may require many weeks of antibiotic therapy.

LANGUAGE OF SCIENCE *(continued from p. 199)*

endosteum
(en-DOS-tee-um)
[*end-* **within**, *-osteum* **bone**]

epiphyseal plate
(ep-i-FEEZ-ee-al)
[*epi-* **on**, *-phys-* **growth**, *-al* **relating to**, *plate* **flat**]

epiphysis
(eh-PIF-i-sis)
[*epi-* **on**, *-physis* **growth**]
pl., epiphyses

external table
[*extern-* **outside**, *-al* **relating to**]

fibrocartilage
(fye-broh-KAR-ti-lij)
[*fibro-* **fiber**, *-cartilag* **cartilage**]

hyaline cartilage
(HYE-ah-lin KAR-ti-lij)
[*hyaline* **glass**, *cartilag* **cartilage**]

internal table
[*intern-* **inside**, *-al* **relating to**]

intramembranous ossification
(in-trah-MEM-brah-nus os-i-fi-KAY-shun)
[*intra-* **within**, *-membran-* **thin skin**, *-ous* **characterized by**, *os-* **bone**, *-fication* **to make**]

ligament
(LIG-ah-ment)
[*liga-* **bind**, *-ment* **result of action**]

medullary cavity
(MED-oo-lair-ee)
[*medulla* **middle**, *-ary* **relating to**, *cav-* **hollow**, *-ity* **state**]

myeloid tissue
(MY-eh-loyd)
[*myel-* **marrow**, *-oid* **of or like**, *tissu-* **fabric**]

ossification center
(os-i- fi-KAY-shun SEN-ter)
[*os-* **bone**, *-fication* **to make**]

osteoblast
(OS-tee-oh-blast)
[*osteo-* **bone**, *-blast* **bud**]

osteoclast
(OS-tee-oh-klast)
[*osteo-* **bone**, *-clast* **break**]

osteocyte
(OS-tee-oh-syte)
[*osteo-* **bone**, *-cyte* **cell**]

osteon
(AHS-tee-on)
[*osteo-* **bone**, *-on* **unit**]

perichondrium
(pair-i-KON-dree-um)
[*peri-* **around**, *-chondr-* **cartilage**, *-um* **thing**] *pl.,* perichondria

periosteum
(pair-ee-OS-tee-um)
[*peri-* **around**, *-osteum* **bone**]

primary ossification center
(os-i-fi-KAY-shun)
[*primary* **first order**, *os-* **bone**, *-fication* **to make**]

secondary ossification center
(SEK-on-dair-ee os-i-fih-KAY-shun)
[*secondary* **second order**, *os-* **bone**, *-fication* **to make**]

sesamoid bone
(SES-ah-moyd)
[*sesam-* **sesame seed**, *-oid* **like**]

trabecula
(trah-BEK-yoo-la)
[*trab-* **beam**, *-ula* **little**] *pl.,* trabeculae

trabecular bone
(trah-BEK-yoo-lar)
[*trab-* **beam**, *-ula-* **little**, *-ar* **relating to**]

transverse canal
(tranz-vers kah-NAL)
[*trans-* **across**, *-vers-* **turn**]

LANGUAGE OF MEDICINE

bone marrow transplant
(MAIR-oh TRANS-plant)

chondroitin sulfate
(kon-DROY-tin SUHL-fayt)
[*chondr-* **cartilage**, *-oid* **of or like**, *-in* **substance**, *sulf-* **sulfur**, *-ate* **oxygen**]

epiphyseal fracture
(ep-i-FEEZ-ee-al)
[*epi-* **on**, *-phys-* **growth**, *-al* **relating to**, *fracture* **to break**]

glucosamine
(gloo-KOHS-ah-meen)
[*glucos-* **sweetness or glucose**, *-amine* **ammonia compound**]

osteogenesis
(os-tee-oh-JEN-eh-sis)
[*osteo-* **bone**, *-genesis* **origin**]

osteomalacia
(os-tee-oh-mah-LAY-shah)
[*osteo-* **bone**, *-malacia* **softening**]

osteoporosis
(os-tee-oh-poh-ROH-sis)
[*osteo-* **bone**, *-poro-* **pore**, *-osis* **condition**]

rickets
(RIK-ets)
[**unknown origin**]

CASE study

Eleanor stepped off the curb by her mailbox, just as she had done thousands of times before. But this time, her hip gave way, and she suddenly found herself on the ground, unable to get back up. An x-ray film at the hospital showed a fracture in the neck of her femur. Eleanor wondered how she could have broken a bone by simply stepping off a curb. The doctor was talking about surgery and a 6-month recovery time. She would definitely have to reschedule the cruise she had booked to celebrate retirement.

1. Which of the following conditions likely caused Eleanor's broken hip?
   a. Osteosarcoma
   b. Rickets
   c. Osteoporosis
   d. Osteomyelitis
2. What type of bone did Eleanor fracture?
   a. Long bone
   b. Short bone
   c. Flat bone
   d. Irregular bone
3. What type of cartilage would you find covering the ends of that bone?
   a. Elastic cartilage
   b. Hylophil cartilage
   c. Fibrocartilage
   d. Hyaline cartilage

After her surgery, Eleanor gets a prescription from her doctor for calcitonin nasal spray.

4. What is the primary effect of that medication?
   a. Stimulates osteoclasts
   b. Stimulates osteoblasts
   c. Stimulates osteocytes
   d. All of the above

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

FUNCTIONS OF BONE

A. Support—bones form the framework of the body and contribute to the shape, alignment, and positioning of body parts; ligaments help hold bones together (Figure 8-1)
B. Protection—bony "boxes" protect the delicate structures they enclose
C. Movement—bones with their joints constitute levers that move as muscles contract
D. Mineral storage—bones are the major reservoir for calcium, phosphorus, and other minerals
E. Hematopoiesis—blood cell formation is carried out by myeloid tissue

TYPES OF BONES

A. Structurally, there are five major types of bones (Figure 8-2)
   1. Long bones—cylindrical
   2. Short bones—boxlike
   3. Flat bones—broad, sheetlike
   4. Irregular bones—various shapes
   5. Sesamoid bones—seedlike

B. Size, shape, and appearance of bones vary to meet the various needs served
C. Bones vary in the proportion of compact and cancellous (spongy) bone
   1. Compact bone—dense and solid in appearance
   2. Cancellous bone—characterized by open space partially filled with a lattice of thin branched structures supporting soft tissue
D. Parts of a long bone (Figure 8-3)
   1. Diaphysis
      a. Main shaft of a long bone
      b. Hollow, cylindrical shape and thick compact bone
      c. Function—to provide strong support without cumbersome weight
   2. Epiphyses
      a. Both ends of a long bone; made of cancellous bone filled with marrow
      b. Bulbous shape
      c. Function—to provide attachments for muscles and give stability to joints
   3. Articular cartilage
      a. Layer of hyaline cartilage that covers the articular surface of epiphyses
      b. Function—to cushion jolts and blows
   4. Periosteum
      a. Dense, white fibrous membrane that covers bone
      b. Attaches tendons firmly to bones
      c. Contains cells that form and destroy bone
      d. Contains blood vessels important in growth and repair

e. Contains blood vessels that send branches into bone
f. Essential for bone cell survival and bone formation

5. Medullary (or marrow) cavity
   a. Tubelike, hollow space in the diaphysis
   b. Filled with yellow marrow in adults
6. Endosteum—thin fibrous membrane that lines the medullary cavity

E. Parts of a flat bone
1. Inner portion is cancellous bone covered on the outside with compact bone
   a. Cranial flat bones have an internal and external table of compact bone and an inner cancellous region called the *diploe* (Figure 8-4)
   b. Bones are covered with periosteum and lined with endosteum, as in a long bone
   c. Other flat bones, short bones, and irregular bones have features similar to the cranial bones
2. Spaces inside the cancellous bone of short, flat, irregular and sesamoid bones are filled with red marrow

BONE TISSUE

A. Most distinctive form of connective tissue
B. Extracellular components are hard and calcified
C. Rigidity of bone allows it to serve its supportive and protective functions
D. Tensile strength nearly equal to that of cast iron at less than one third the weight
E. Composition of bone matrix
1. Inorganic salts
   a. Hydroxyapatite—crystals of calcium and phosphate contribute to bone hardness
   b. Slender needlelike crystals are oriented to most effectively resist stress and mechanical deformation
   c. Magnesium, sodium, sulfate, and fluoride are also found in bone
2. Organic matrix
   a. Composite of collagenous fibers and an amorphous mixture of protein and polysaccharides called *ground substance*
   b. Ground substance—secreted by connective tissue cells
   c. Adds to overall strength of bone and gives some degree of resilience to bone

MICROSCOPIC STRUCTURE OF BONE

A. Compact bone (Figure 8-5)
1. Contains many cylinder-shaped structural units called *osteons*, or *Haversian systems* (Figure 8-6)
2. Osteons surround central (osteonal or Haversian) canals that run lengthwise through bone and are connected by transverse (Volkmann) canals
   a. Living bone cells located in these units
   b. Constitute the structural framework of compact bone
3. Osteons permit delivery of nutrients and removal of waste products
4. Structures make up each osteon
   a. Lamellae
      (1) Concentric—cylinder-shaped layers of calcified matrix around the central canal
      (2) Interstitial—layers of bone matrix *between* the osteons; leftover from previous osteons
      (3) Circumferential—few layers of bone matrix that surround all the osteons; run along the outer circumference of a bone and inner circumference (boundary of medullary cavity) of a bone
   b. Lacunae—small spaces containing tissue fluid in which bone cells are located between hard layers of the lamella
   c. Canaliculi—ultra-small canals radiating in all directions from the lacunae and connecting them to each other and to the central canal
   d. Central (osteonal or Haversian) canal—extends lengthwise through the center of each osteon and contains blood vessels and lymphatic vessels

B. Cancellous bone—also called *spongy bone* or *trabecular bone* (Figure 8-6)
1. No osteons in cancellous bone; instead, it has trabeculae
2. Nutrients are delivered and waste products removed by diffusion through tiny canaliculi
3. Lattice of bony branches (trabeculae) are arranged along lines of stress to enhance the bone's strength (Figure 8-7)
4. Blood supply
   a. Bone cells receive blood supply from the bone marrow in the internal medullary cavity of cancellous bone
   b. Blood vessels from the periosteum become incorporated into the bone and serve nutrient needs of cells by way of transverse (Volkmann) canals, connected with vessels in the central canals of osteons

C. Types of bone cells
1. Osteoblasts (Figure 8-8)
   a. Bone-forming cells found in all bone surfaces
   b. Small cells synthesize and secrete osteoid, an important part of the ground substance
   c. Collagen fibrils line up in osteoid and serve as a framework for the deposition of calcium and phosphate
2. Osteoclasts (Figure 8-8)
   a. Giant multinucleated cells
   b. Responsible for the active erosion of bone minerals
   c. Contain large numbers of mitochondria and lysosomes
3. Osteocytes—mature, nondividing osteoblasts surrounded by matrix and lying within lacunae (Figure 8-9)

BONE MARROW

A. Type of soft, diffuse connective tissue; called *myeloid tissue*
B. Site for the production of blood cells
C. Found in the medullary cavities of long bones and in the spaces of spongy bone
D. Two types of marrow occur during a person's lifetime (Figure 8-10)
1. Red marrow
   a. Found in virtually all bones in an infant's or child's body
   b. Functions to produce red blood cells
2. Yellow marrow
   a. As an individual ages, red marrow is replaced by yellow marrow

b. Marrow cells become saturated with fat and are no longer active in blood cell production

E. Main bones in an adult that still contain red marrow include the ribs, bodies of the vertebrae, humerus, pelvis, and femur

F. Yellow marrow can change to red marrow during times of decreased blood supply, such as anemia, exposure to radiation, and certain diseases

REGULATION OF BLOOD CALCIUM LEVELS

A. Skeletal system serves as a storehouse for about 98% of body calcium reserves
   1. Helps maintain constancy of blood calcium levels
      a. Calcium is mobilized and moves into and out of blood during bone remodeling
      b. During bone formation, osteoblasts remove calcium from blood and lower circulating levels
      c. During breakdown of bone, osteoclasts release calcium into blood and increase circulating levels
   2. Homeostasis of calcium ion concentration essential for the following:
      a. Bone formation, remodeling, and repair
      b. Blood clotting
      c. Transmission of nerve impulses
      d. Maintenance of skeletal and cardiac muscle contraction

B. Mechanisms of calcium homeostasis (Figure 8-11)
   1. Parathyroid hormone
      a. Primary regulator of calcium homeostasis
      b. Stimulates osteoclasts to initiate breakdown of bone matrix and increase blood calcium levels
      c. Increases renal absorption of calcium from urine
      d. Stimulates vitamin D synthesis
   2. Calcitonin
      a. Protein hormone produced in the thyroid gland
      b. Produced in response to high blood calcium levels
      c. Stimulates bone deposition by osteoblasts
      d. Inhibits osteoclast activity
      e. Far less important in homeostasis of blood calcium levels than is parathyroid hormone
   3. Other mechanisms
      a. Growth hormone (GH)—increases bone growth, thus reducing blood calcium
      b. Serotonin—inhibits osteoblast activity, thus increases blood calcium

DEVELOPMENT OF BONE

A. Osteogenesis—development of bone from small cartilage or membrane model to adult bone

B. Intramembranous ossification (Figure 8-13)
   1. Occurs within a connective tissue membrane
   2. Flat bones begin when groups of cells differentiate into osteoblasts
   3. Osteoblasts are clustered together in ossification center
   4. Osteoblasts secrete matrix material and collagenous fibrils
   5. Large amounts of ground substance accumulate around each osteoblast
   6. Collagenous fibers become embedded in the ground substance and constitute the bone matrix
   7. Bone matrix calcifies when calcium salts are deposited
   8. Trabeculae appear and join in a network to form spongy bone
   9. Appositional growth occurs by adding osseous tissue

C. Endochondral ossification (Figure 8-14)
   1. Most bones begin as a cartilage model with bone formation spreading essentially from the center to the ends
   2. Periosteum develops and enlarges to produce a collar of bone
   3. Primary ossification center forms (Figure 8-15)
   4. Blood vessel enters the cartilage model at the midpoint of the diaphysis
   5. Bone grows in length as endochondral ossification progresses from the diaphysis toward each epiphysis (Figure 8-16)
   6. Secondary ossification centers appear in the epiphysis, and bone growth proceeds toward the diaphysis
   7. Epiphyseal plate remains between the diaphysis and each epiphysis until bone growth in length is complete
   8. Epiphyseal plate is composed of four layers (Figures 8-17 and 8-18)
      a. "Resting" cartilage cells—point of attachment joining the epiphysis to the shaft
      b. Zone of proliferation—cartilage cells undergoing active mitosis, which causes the layer to thicken and the plate to increase in length
      c. Zone of hypertrophy—older, enlarged cells undergoing degenerative changes associated with calcium deposition
      d. Zone of calcification—dead or dying cartilage cells undergoing rapid calcification
   9. Epiphyseal plate can be a site for bone fractures in young people (Figure 8-19)
   10. Long bones grow in both length and diameter (Figure 8-20)

BONE REMODELING

A. Primary osteons develop within early woven bone (Figure 8-21)
   1. Conelike or tubelike space is hollowed out by osteoclasts
   2. Osteoblasts in the endosteum that lines the tube begin forming layers (lamellae) that trap osteocytes between layers.
   3. A central canal is left for the blood and lymphatic vessels and nerves
   4. Primary osteons can be replaced later by secondary osteons in a similar manner

B. Bones grow in length and diameter by the combined action of osteoclasts and osteoblasts
   1. Osteoclasts enlarge the diameter of the medullary cavity
   2. Osteoblasts from the periosteum build new bone around the outside of the bone

C. Mechanical stress, as from physical activity, strengthens bone

REPAIR OF BONE FRACTURES

A. Fracture—break in the continuity of a bone

B. Fracture healing (Figure 8-22)
   1. Fracture tears and destroys blood vessels that carry nutrients to osteocytes
   2. Vascular damage initiates repair sequence
   3. Callus—special repair tissue that binds the broken ends of the fracture together
   4. Fracture hematoma—blood clot occurring immediately after the fracture, which is then resorbed and replaced by callus

CARTILAGE

A. Characteristics
   1. Avascular connective tissue
   2. Fibers of cartilage are embedded in a firm gel
   3. Has the flexibility of firm plastic
   4. No canal system or blood vessels
   5. Chondrocytes receive oxygen and nutrients by diffusion
   6. Perichondrium—fibrous covering of the cartilage
   7. Cartilage types differ because of the amount of matrix present and the amounts of elastic and collagenous fibers

B. Types of cartilage (Figure 8-23)
   1. Hyaline cartilage
      a. Most common type
      b. Covers the articular surfaces of bones
      c. Forms the costal cartilages, cartilage rings in the trachea, bronchi of the lungs, and the tip of the nose
      d. Forms from special cells in chondrification centers, which secrete matrix material
      e. Chondrocytes are isolated into lacunae
   2. Elastic cartilage
      a. Forms external ear, epiglottis, and eustachian tubes
      b. Large number of elastic fibers confers elasticity and resiliency
   3. Fibrocartilage (fibrous cartilage)
      a. Occurs in pubic symphysis and intervertebral disks
      b. Small quantities of matrix and abundant fibrous elements
      c. Strong and rigid

C. Function of cartilage
   1. Tough, rubberlike nature permits cartilage to sustain great weight or serve as a shock absorber
   2. Strong yet pliable support structure
   3. Permits growth in length of long bones

D. Growth of cartilage
   1. Interstitial or endogenous growth
      a. Cartilage cells divide and secrete additional matrix
      b. Seen during childhood and early adolescence while cartilage is still soft and capable of expansion from within
   2. Appositional or exogenous growth
      a. Chondrocytes in the deep layer of the perichondrium divide and secrete matrix
      b. New matrix is deposited on the surface, thereby increasing its size
      c. Unusual in early childhood, but once initiated, continues throughout life

CYCLE OF LIFE: SKELETAL TISSUES

A. Skeleton fully ossified by mid-twenties
   1. Soft tissue may continue to grow—ossifies more slowly

B. Adults—changes occur from specific conditions
   1. Increased density and strength from exercise
   2. Decreased density and strength from pregnancy, nutritional deficiencies, and illness

C. Advanced adulthood—apparent degeneration
   1. Hard bone matrix replaced by softer connective tissue
   2. Exercise can counteract degeneration

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Describe the microscopic structure of bone and cartilage.
2. Describe the structure of a long bone.
3. Explain the functions of the periosteum.
4. Describe the two principal chemical components of extracellular bone.
5. List and discuss each of the major anatomical components that together constitute an osteon.
6. Compare and contrast the three major types of cells found in bone.
7. Discuss and discriminate between the sequence of steps characteristic of fracture healing.
8. Compare and contrast the basic structural elements of bone and cartilage.
9. Compare the structure and function of the three types of cartilage.

CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Cancer treatment may precipitate the need for a bone marrow transplant. Osteoporosis is a condition characterized by an excessive loss of calcium in bone. These two conditions are disruptions or failures of two bone functions. Identify these two functions and explain what their normal functioning should be.
2. Compare and contrast bone formation in intramembranous and endochondral ossification.
3. Can you make a distinction between the growth processes of cartilage and bone? Explain.
4. Explain why a bone fracture along the epiphyseal plate may have serious implications in children and young adults.
5. During the aging process, adults face the issue of a changing skeletal framework. Describe these changes and explain how these skeletal framework changes affect the health of older adults.

Skeletal System



9

UNIT 2

CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

Divisions of the Skeleton, 224

Axial Skeleton, 226
- Skull, 226
  - Cranial Bones, 238
  - Facial Bones, 240
  - Eye Orbits, 240
  - Fetal Skull, 242
- Hyoid Bone, 243
- Vertebral Column, 245
- Sternum, 248
- Ribs, 248

Appendicular Skeleton, 250
- Upper Extremity, 250
- Lower Extremity, 255

Skeletal Differences Between Men and Women, 261

Cycle of Life: Skeletal System, 262

The Big Picture: Skeletal System, 263

Mechanisms of Disease, 263

Case Study, 267

LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

appendicular skeleton
(ah-pen-DIK-yoo-lar SKEL-eh-ton)
[*append-* **hang upon**, *-ic-* **relating to**, *-ul-* **little**, *-ar* **relating to**]

axial skeleton
(AK-see-all SKEL-eh-ton)
[*axi-* **axis**, *-al* **relating to**]

carpal bone
(KAR-pul bohn)
[*carp-* **wrist**, *-al* **relating to**]

cervical vertebra
(SER-vi-kal VER-teh-bra)
[*cervi-* **neck**, *-al* **relating to**, *vertebra* **that which turns**] *pl.,* vertebrae

clavicle
(KLAV-i-kul)
[*clavi-* **key**, *-cle* **little**]

coxal bone
(KOK-sal)
[*coxa-* **hip**, *-al* **relating to**]

cranium
(KRAY-nee-um)
[*cranium* **skull**]

cribriform plate
(KRIB-ri-form)
[*cribri-* **sieve**, *-form* **shape**]

ethmoid
(ETH-moyd)
[*ethmo-* **sieve**, *-oid* **like**]

face

false pelvis
(PEL-vis)
[*pelvis* **basin**]

femur
(FEE-mur)
[*femur* **thigh**]

fibula
(FIB-yoo-lah)
[*fibula* **clasp**] *pl.,* fibulae or fibulas

continued on p. 266

Just as skeletal tissues are organized to form bones, the bones are organized or grouped to form the skeletal system. The rigid bones lie buried within soft tissues, providing support and shape to the body. Understanding the relationship of bones to each other and to other body structures provides a basis for understanding the function of many other organ systems. Coordinated movement, for example, is possible only because of the way bones are joined in joints and the way muscles are attached to those bones.

The adult skeleton is composed of 206 named bones. Variations in the total number of bones in the body occur as a result of certain anomalies, such as extra ribs, or from failure of certain small bones to fuse in the course of development.

In Chapter 8 the basic types of skeletal tissue, including bone and cartilage, were discussed providing the background for study in this chapter of individual bones and their interrelationships in the skeleton. Chapter 10 explores articulations—that is, how the bones form joints.

DIVISIONS OF THE SKELETON

The human skeleton consists of two main divisions—the axial skeleton and the appendicular skeleton (Figure 9-1). Eighty bones make up the **axial skeleton.** This includes 74 bones that form the upright axis of the body and 6 tiny middle ear bones. The **appendicular skeleton** consists of 126 bones—more than half again as many as in the axial skeleton. Bones of the appendicular skeleton form the appendages to the axial skeleton: the shoulder girdles, arms, wrists, and hands and the hip girdles, legs, ankles, and feet.

One of the first things you should do in studying the skeleton is to familiarize yourself with the names of the individual bones listed in Table 9-1. Next, look at Table 9-2, which lists some terms often used to name or describe bone markings—specific features on an individual bone. After this preparation, begin a step-by-step exploration of the skeletal system by studying the illustrations, text, and tables that constitute the rest of this chapter. To help you learn to distinguish between the names of bones and the names of their markings, the bone names are highlighted in a boldface font and the markings are shown in a normal font in illustrations and tables throughout this chapter.

A picture is worth a thousand words. The illustrations and tables contained in this chapter were carefully selected and compiled to assist you in visualizing and organizing the material discussed. If in addition to your textbook, you have access to individual bones or an articulated skeleton in a laboratory setting, frequent reference to chapter illustrations and tabular material will prove immensely helpful in your study efforts.

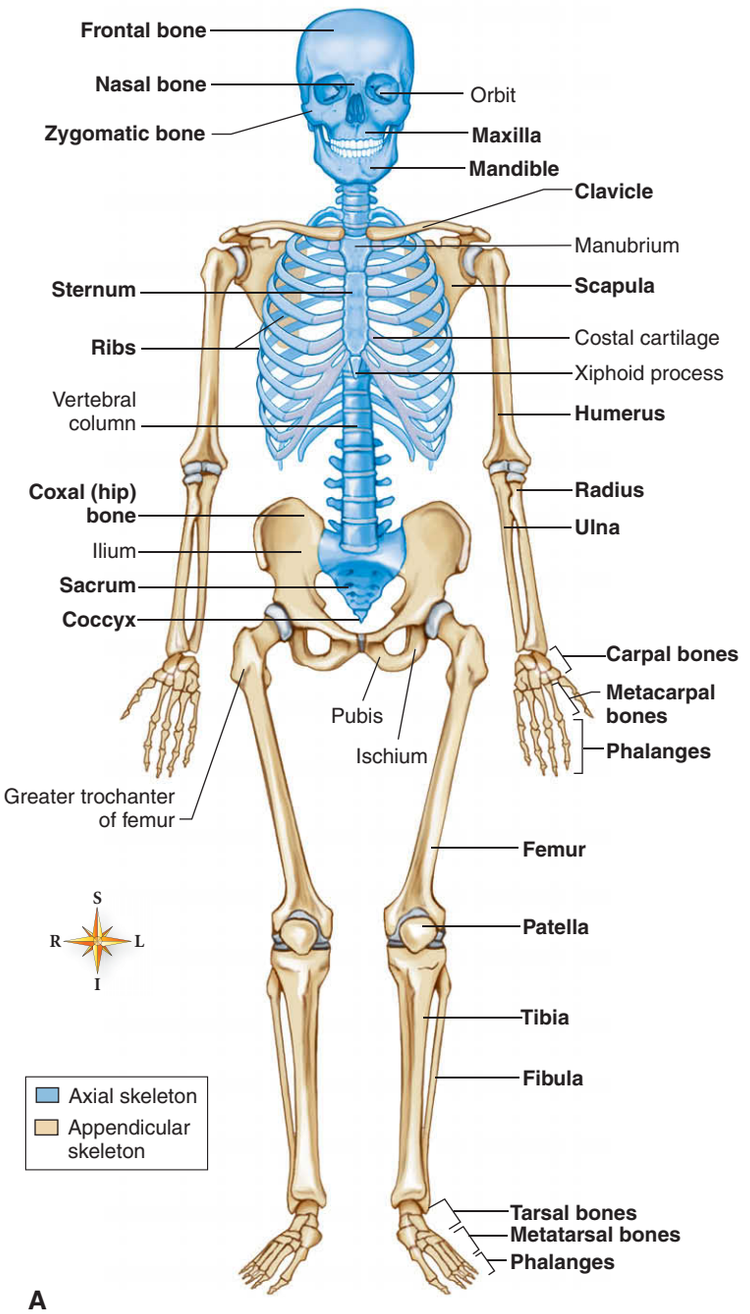
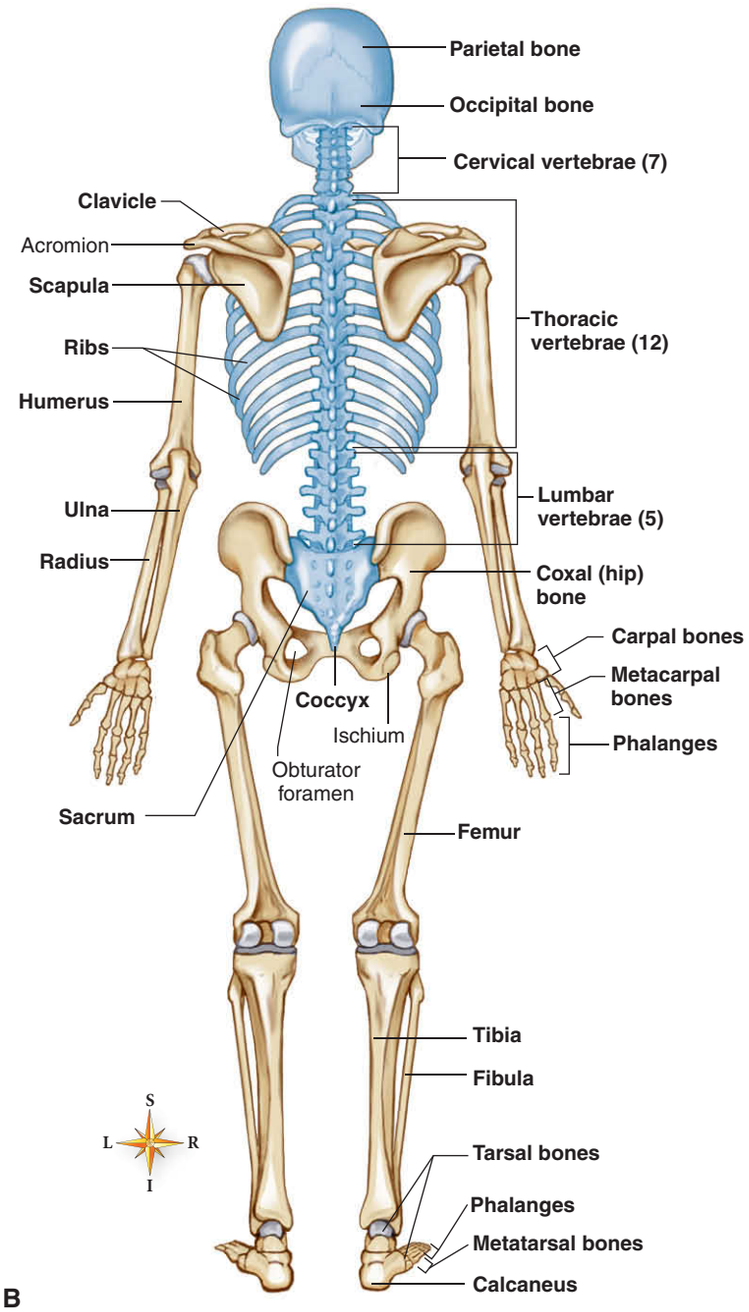
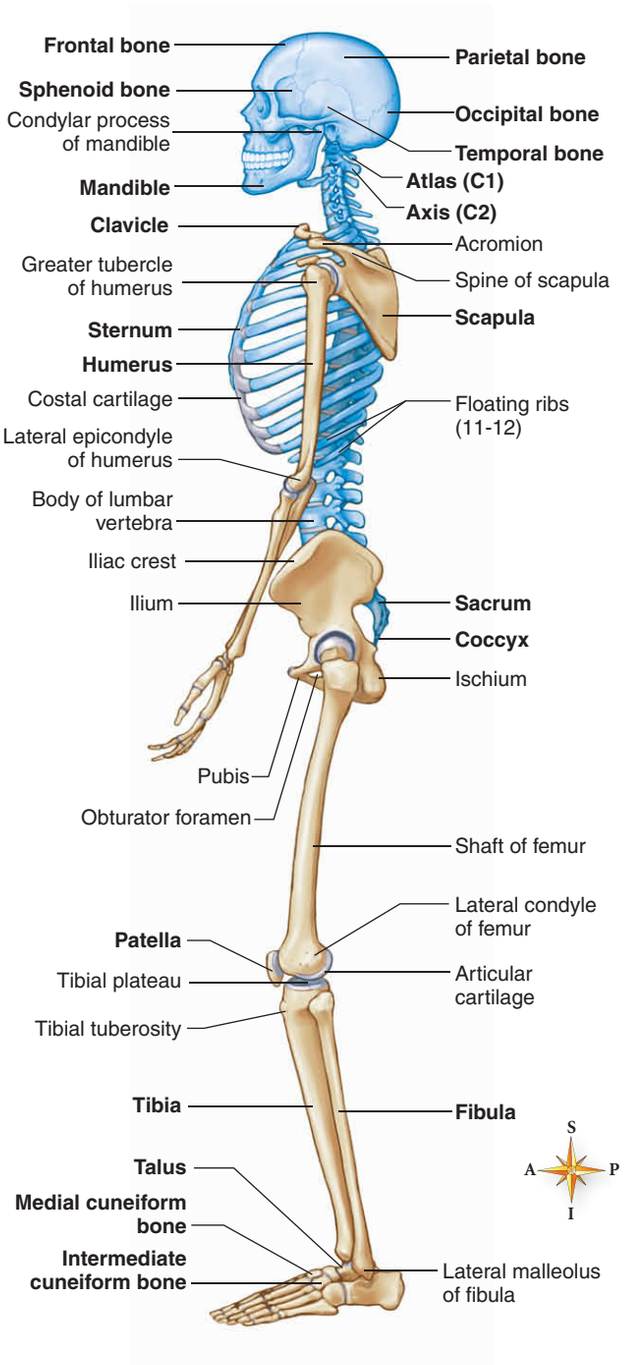


FIGURE 9-1

Skeleton. A, Anterior view. **B,** Posterior view. **C,** Lateral view.


Parietal bone
Occipital bone
Cervical vertebrae (7)
Clavicle
Acromion
Scapula
Ribs
Humerus
Thoracic vertebrae (12)
Ulna
Radius
Lumbar vertebrae (5)
Coxal (hip) bone
Carpal bones
Metacarpal bones
Coccyx
Ischium
Obturator foramen
Phalanges
Sacrum
Femur
Tibia
Fibula
Tarsal bones
Phalanges
Metatarsal bones
Calcaneus
S
L
R
I

B


Frontal bone
Parietal bone
Sphenoid bone
Occipital bone
Condylar process of mandible
Temporal bone
Atlas (C1)
Mandible
Axis (C2)
Clavicle
Acromion
Greater tubercle of humerus
Spine of scapula
Scapula
Sternum
Humerus
Costal cartilage
Floating ribs (11-12)
Lateral epicondyle of humerus
Body of lumbar vertebra
Iliac crest
Ilium
Sacrum
Coccyx
Ischium
Pubis
Obturator foramen
Shaft of femur
Lateral condyle of femur
Patella
Articular cartilage
Tibial plateau
Tibial tuberosity
Tibia
Fibula
S
A
P
I
Talus
Medial cuneiform bone
Intermediate cuneiform bone
Lateral malleolus of fibula

C

TABLE 9-1 Bones of the Skeleton (206 Total)*

PART OF BODY	NAME OF BONE
Axial Skeleton (80 Bones Total)	
Skull (28 bones total)	
Cranium (8 bones)	Frontal (1) Parietal (2) Temporal (2) Occipital (1) Sphenoid (1) Ethmoid (1)
Face (14 bones)	Nasal (2) Maxillary (2) Zygomatic (malar) (2) Mandible (1) Lacrimal (2) Palatine (2) Inferior nasal conchae (turbinates) (2) Vomer (1)
Ear bones (6 bones)	Malleus (hammer) (2) Incus (anvil) (2) Stapes (stirrup) (2)
Hyoid bone (1)	
Spinal column (26 bones)	Cervical vertebrae (7) Thoracic vertebrae (12) Lumbar vertebrae (5) Sacrum (1) Coccyx (1)
Sternum and ribs (25 bones)	Sternum (1) True ribs (14) False ribs (10)
Appendicular Skeleton (126 Bones Total)	
Upper extremities (including shoulder girdle) (64 bones)	Clavicle (2) Scapula (2) Humerus (2) Radius (2) Ulna (2) Carpal bones (16) Metacarpal bones (10) Phalanges (28)
Lower extremities (including hip girdle) (62 bones)	Innominate (2) Fibula (2) Femur (2) Patella (2) Tibia (2) Tarsal bones (14) Metatarsal bones (10) Phalanges (28)

*An inconstant number of small, flat, round bones known as *sesamoid bones* (because of their resemblance to sesame seeds) are found in various tendons in which considerable pressure develops. Because the number of these bones varies greatly between individuals, only two of them, the patellae, have been counted among the 206 bones of the body. Generally, two of them can be found in each thumb (in the flexor tendon near the metacarpophalangeal and interphalangeal joints) and great toe, plus several others in the upper and lower extremities. *Sutural bones (wormian bones),* the small islets of bone frequently found in some of the cranial sutures, have not been counted in this list of 206 bones because of their variable occurrence.
The numeral following each bone name is the typical number of bones found in the adult skeleton.

TABLE 9-2 Terms Used to Describe Bone Markings

TERM	MEANING
Angle	A corner
Body	The main portion of a bone
Border	Edge of a bone
Condyle	Rounded bump; usually fits into a fossa on another bone to form a joint
Crest	Moderately raised ridge; generally a site for muscle attachment
Epicondyle	Bump near a condyle; often gives the appearance of a "bump on a bump"; for muscle attachment
Facet	Flat surface that forms a joint with another facet or flat bone
Fissure	Long, cracklike hole for blood vessels and nerves
Foramen	Round hole for vessels and nerves (*pl.,* foramina)
Fossa	Depression; often receives an articulating bone (*pl.,* fossae)
Head	Distinct epiphysis on a long bone, separated from the shaft by a narrowed portion (or neck)
Line	Similar to a crest but not raised as much (is often rather faint)
Margin	Edge of a flat bone or flat portion of the edge of a flat area
Meatus	Tubelike opening or channel (*pl.,* meatus or meatuses)
Neck	A narrowed portion, usually at the base of a head
Notch	A V-like depression in the margin or edge of a flat area
Process	A raised area or projection
Ramus	Curved portion of a bone, like a ram's horn (*pl.,* rami)
Sinus	Cavity within a bone
Spine	Similar to a crest but raised more; a sharp, pointed process; for muscle attachment
Sulcus	Groove or elongated depression (*pl.,* sulci)
Trochanter	Large bump for muscle attachment (larger than a tubercle or tuberosity)
Tuberosity	Oblong, raised bump, usually for muscle attachment; also called a *tuber*; a small tuberosity is called a *tubercle*

AXIAL SKELETON

Skull

Twenty-eight irregularly shaped bones form the skull (Figures 9-2 to 9-8). Figures 9-2 through 9-7 show the articulated bones of the skull in full or sectioned views.

Figure 9-8 is a multipart series highlighting the individual bones and shows their relationship to the skull as a whole. As you study the skull, refer often to the illustrations and the descriptive information contained in Tables 9-3 to 9-5.

The skull consists of two major divisions: the **cranium,** or brain case, and the **face.** The cranium is formed by eight bones, namely, the frontal, two parietal, two temporal, the occipital, the sphenoid,

(continued on page 232)

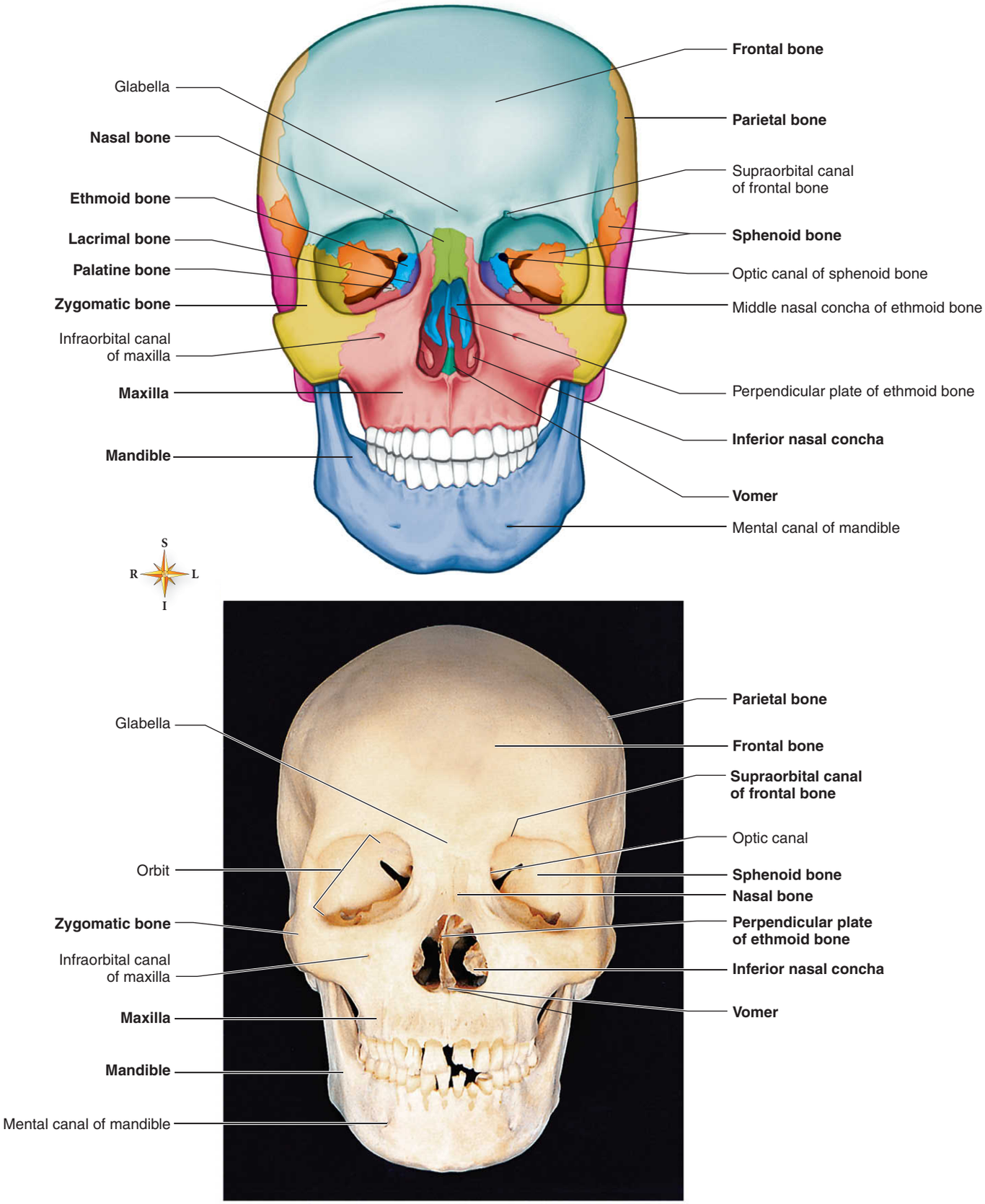
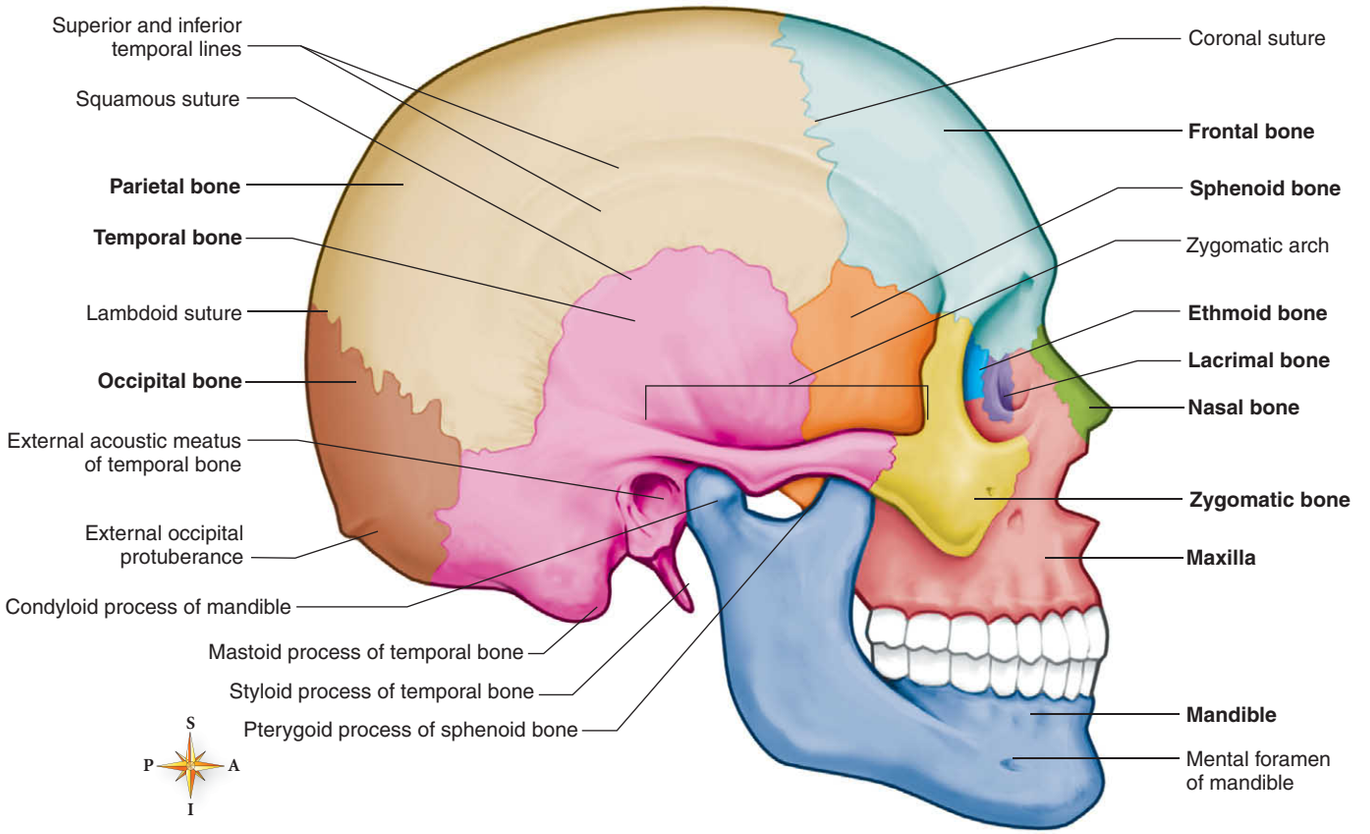


FIGURE 9-2

Anterior view of the skull.



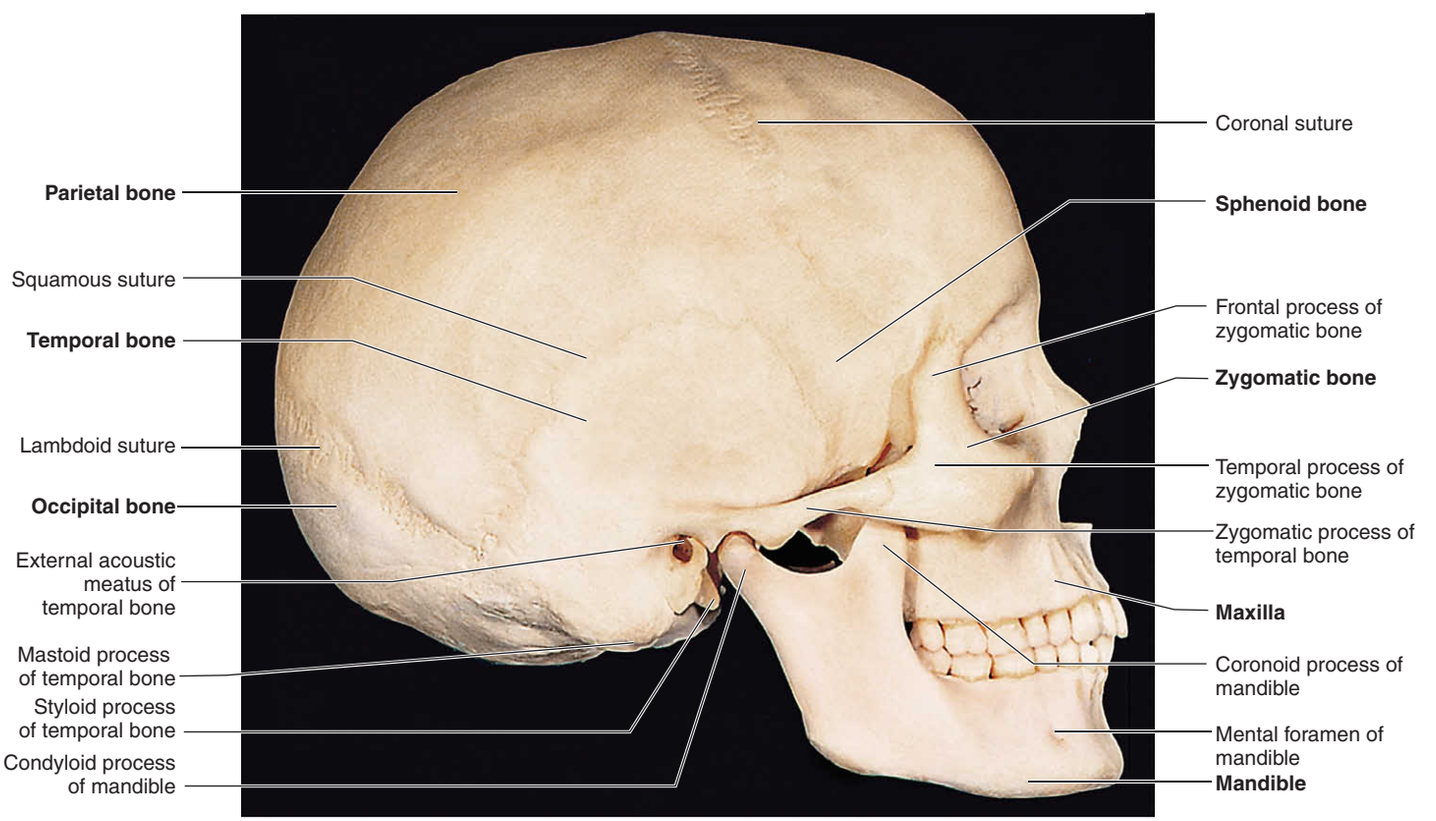


FIGURE 9-3

Skull viewed from the right side.

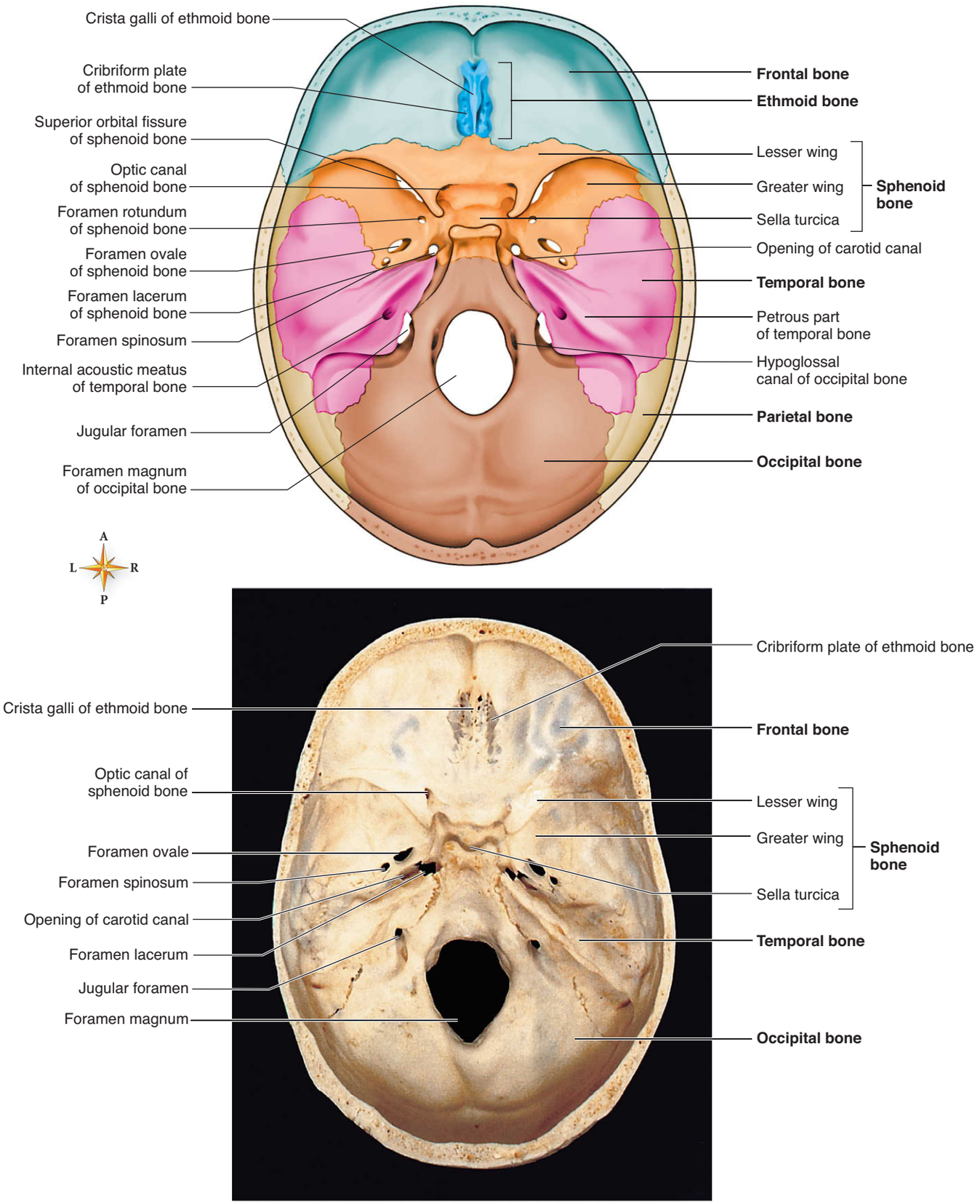


FIGURE 9-4

Floor of the cranial cavity viewed from above.

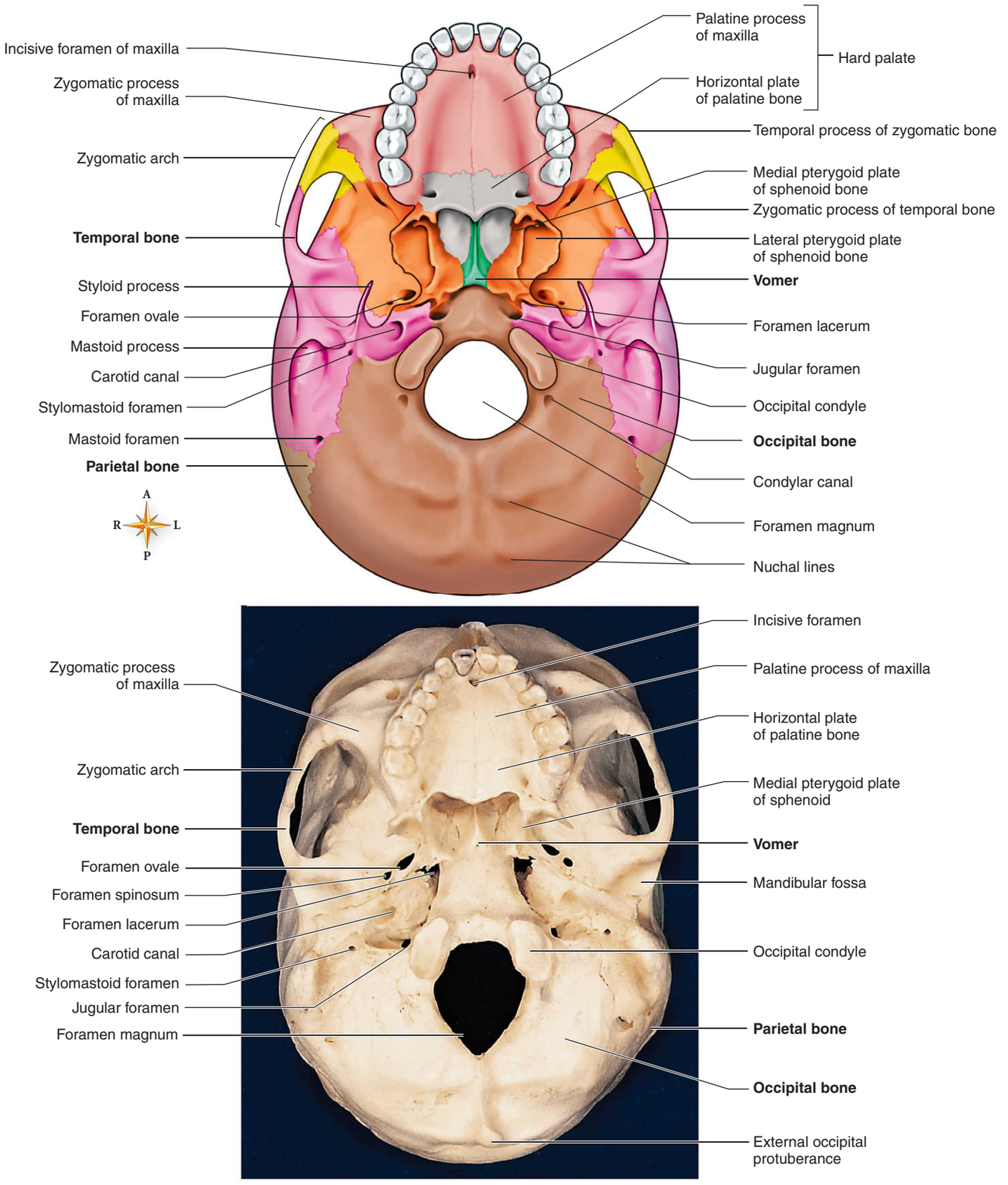


FIGURE 9-5

Skull viewed from below.

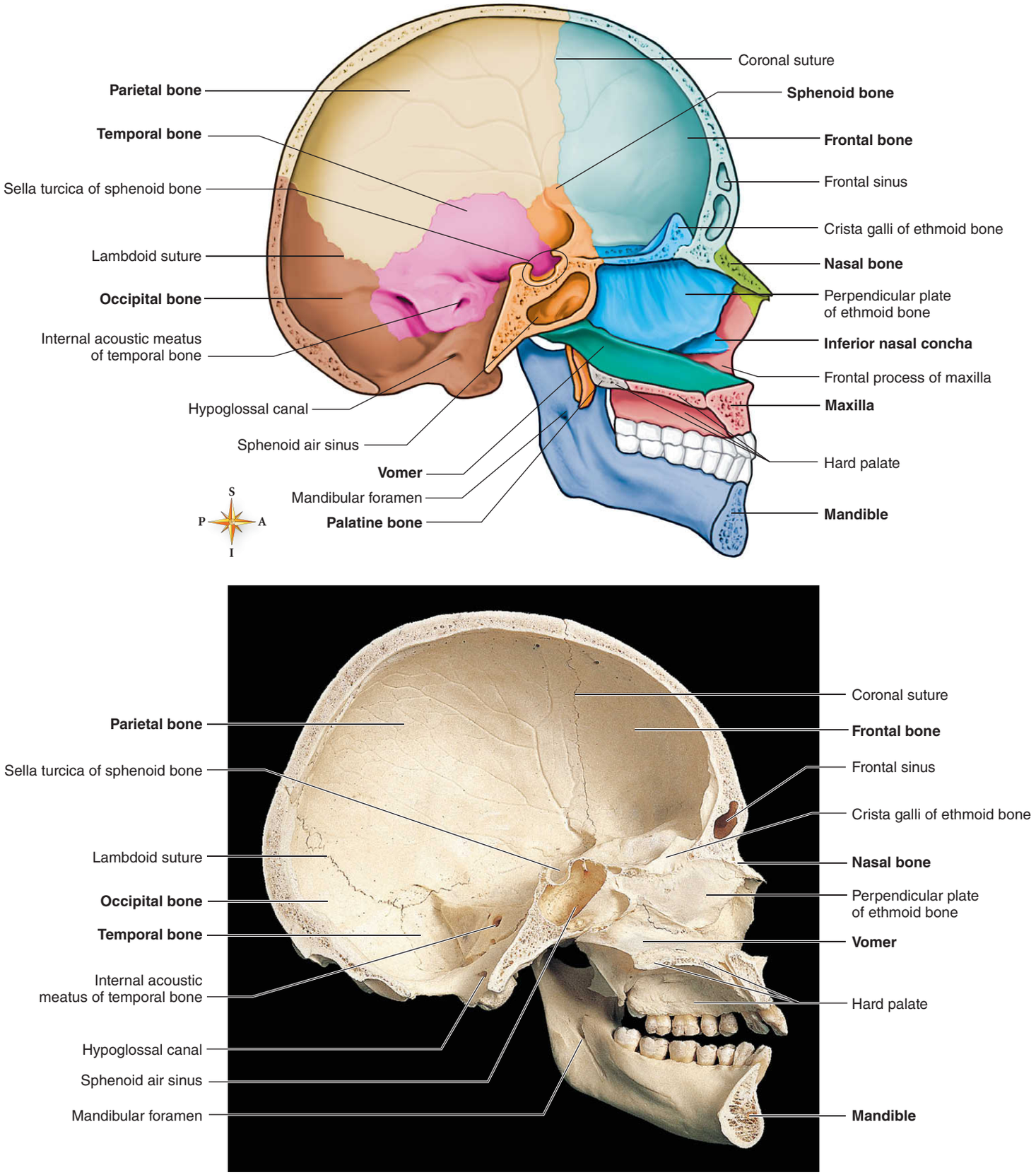


FIGURE 9-6

Left half of the skull viewed from within.

and the ethmoid (Table 9-3). The 14 bones that form the face are the two maxillae, two zygomatic (malar), two nasal, the mandible, two lacrimal, two palatine, two inferior nasal conchae (turbinates), and the vomer (Table 9-4). Note that all the facial bones are paired except for the mandible and vomer. All the cranial bones, on the other hand, are single (unpaired) except for the parietal and temporal bones, which are paired. The frontal and ethmoid bones of the skull help shape the face but are not numbered among the facial bones.

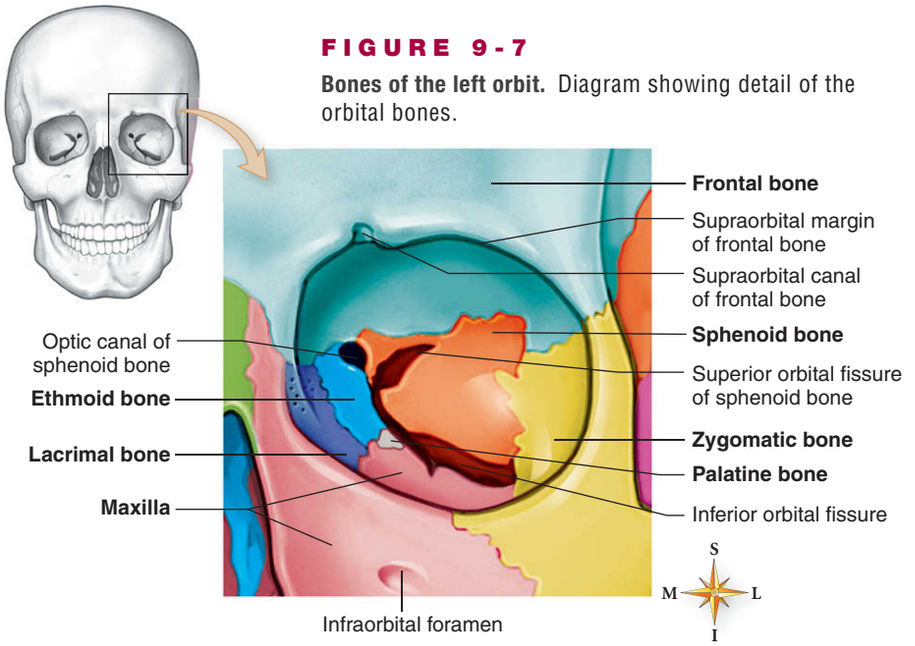


FIGURE 9-7

Bones of the left orbit. Diagram showing detail of the orbital bones.

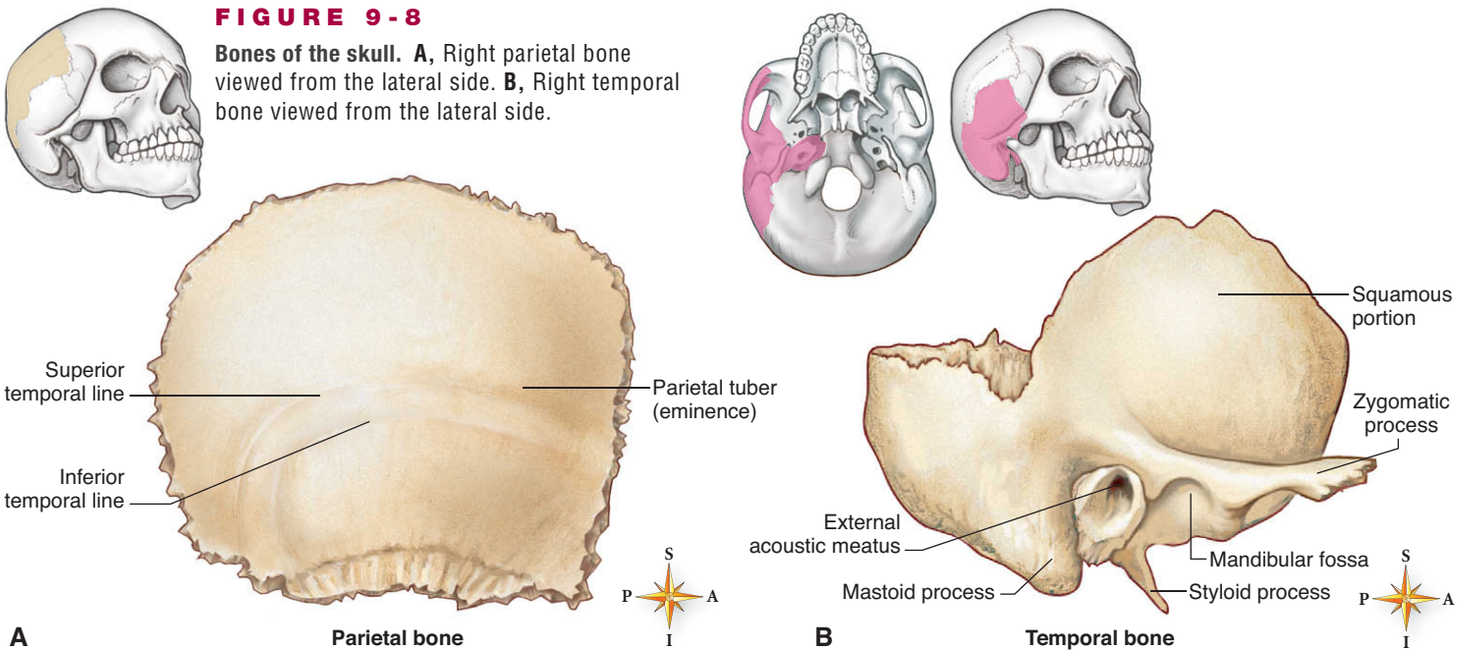


FIGURE 9-8

Bones of the skull. A, Right parietal bone viewed from the lateral side. **B,** Right temporal bone viewed from the lateral side.

TABLE 9-3 Cranial Bones and Their Markings

BONES AND MARKINGS	DESCRIPTION
Parietal	Prominent, bulging bones behind the frontal bone; forms the top sides of the cranial cavity
Temporal	Form the lower sides of the cranium and part of the cranial floor; contain the middle and inner ear structures
Squamous portion	Thin, flaring upper part of the bone
Mastoid portion	Rough-surfaced lower part of the bone posterior to the external acoustic meatus
Petrous portion	Wedge-shaped process that forms part of the center section of the cranial floor between the sphenoid and occipital bones; name derived from the Greek word for stone because of the extreme hardness of this process; houses the middle and inner ear structures
Mastoid process	Protuberance just behind the ear
Mastoid air cells	Mucosa-lined, air-filled spaces within the mastoid process
External acoustic meatus (or canal)	Tube extending into the temporal bone from the external ear opening to the tympanic membrane

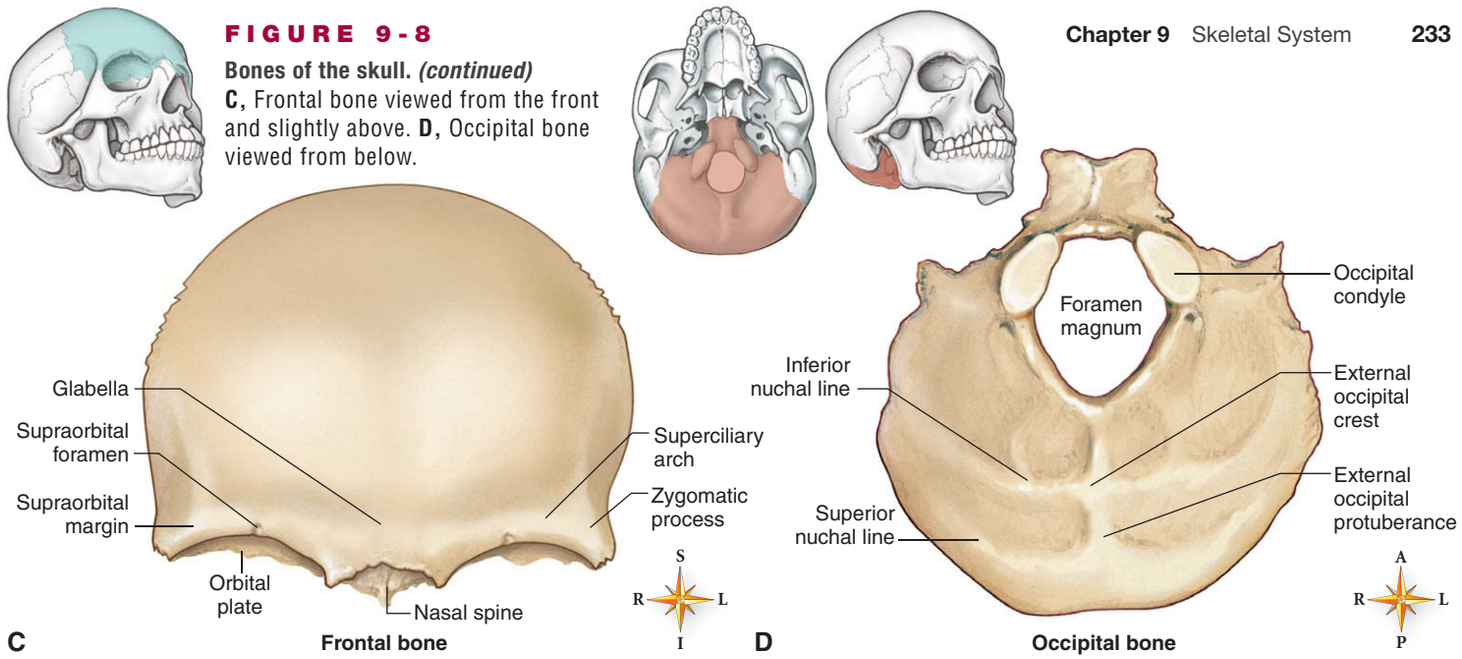


FIGURE 9-8

Bones of the skull. ***(continued)***
C, Frontal bone viewed from the front and slightly above. **D**, Occipital bone viewed from below.

(continued)

TABLE 9-3 Cranial Bones and Their Markings *(continued)*

BONES AND MARKINGS	DESCRIPTION
Zygomatic process	Projection that articulates with the zygomatic (or malar) bone
Internal acoustic meatus	Fairly large opening on the posterior surface of the petrous part of the bone; transmits the eighth cranial nerve to the inner ear and the seventh cranial nerve on its way to the facial structures
Mandibular fossa	Oval-shaped depression anterior to the external acoustic meatus; forms the socket for the condyle of the mandible
Styloid process	Slender spike of bone extending downward and forward from the undersurface of the bone anterior to the mastoid process; often broken off in a dry skull; several neck muscles and ligaments attach to the styloid process
Stylomastoid foramen	Opening between the styloid and mastoid processes where the facial nerve emerges from the cranial cavity
Jugular fossa	Depression on the undersurface of the petrous part; dilated beginning of the internal jugular vein lodged here
Jugular foramen	Opening in the suture between the petrous part and occipital bone; transmits the lateral sinus and ninth, tenth, and eleventh cranial nerves
Carotid canal (or foramen)	Channel in the petrous part; best seen from the undersurface of the skull; transmits the internal carotid artery
Frontal	Forehead bone; also forms most of the roof of the orbits (eye sockets) and the anterior part of the cranial floor
Supraorbital margin	Arched ridge just below eyebrow; forms the upper edge of the orbit
Frontal sinuses	Cavities inside the bone just above supraorbital margin; lined with mucosa; contain air
Frontal tuberosities (tubers or eminences)	Bulge above each orbit; most prominent part of forehead
Superciliary arches (ridges)	Curved ridges caused by projection of the frontal sinuses; eyebrows lie superficial to these ridges
Supraorbital foramen (sometimes notch)	Foramen or notch in the supraorbital margin slightly medial to its midpoint; transmits supraorbital nerve and blood vessels
Glabella	Smooth area between the superciliary ridges and above the nose
Occipital	Forms the posterior part of the cranial floor and walls
Foramen magnum	Hole through which the spinal cord enters the cranial cavity
Occipital condyles	Convex, oval processes on either side of the foramen magnum; articulate with depressions on the first cervical vertebra
External occipital protuberance	Prominent projection on the posterior surface in the midline a short distance above the foramen magnum; can be felt as a definite bump
Superior nuchal line	Curved ridge extending laterally from the external occipital protuberance
Inferior nuchal line	Less well defined ridge paralleling the superior nuchal line a short distance below it
Internal occipital protuberance	Projection in the midline on the inner surface of the bone; grooves for the lateral sinuses extend laterally from this process and one for sagittal sinus extends upward from it

(continued)

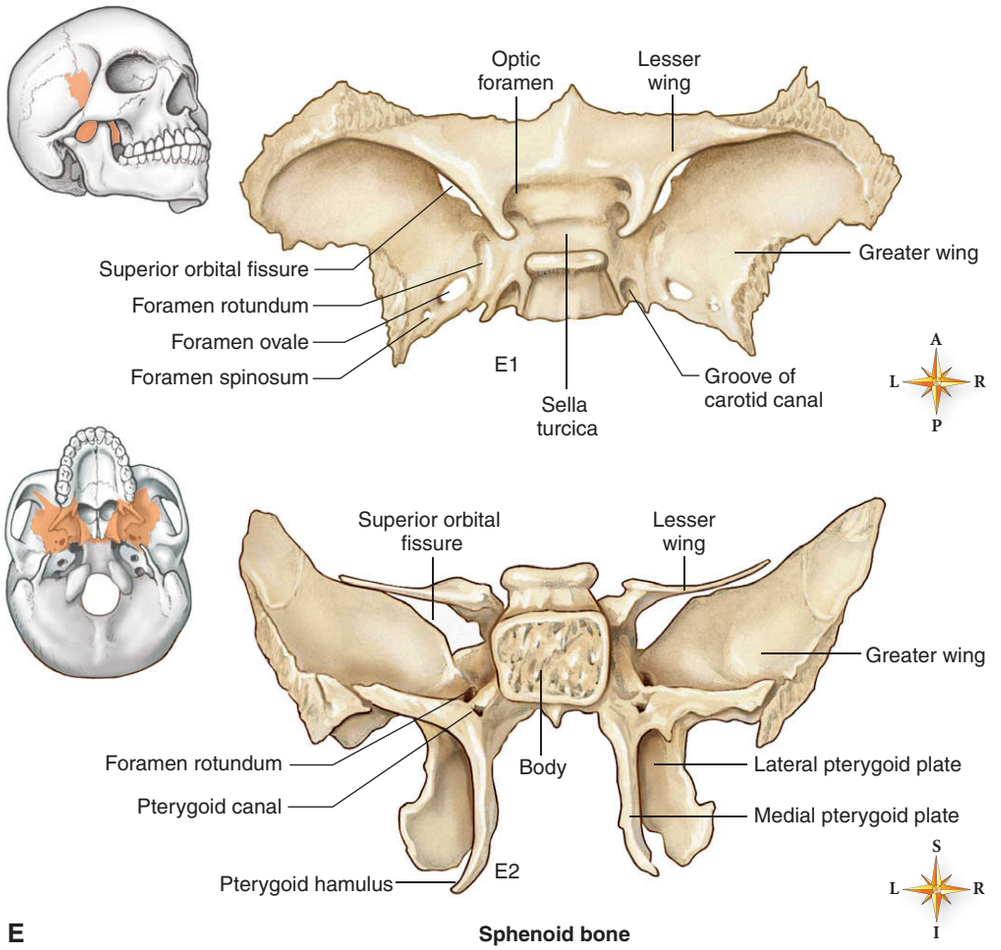


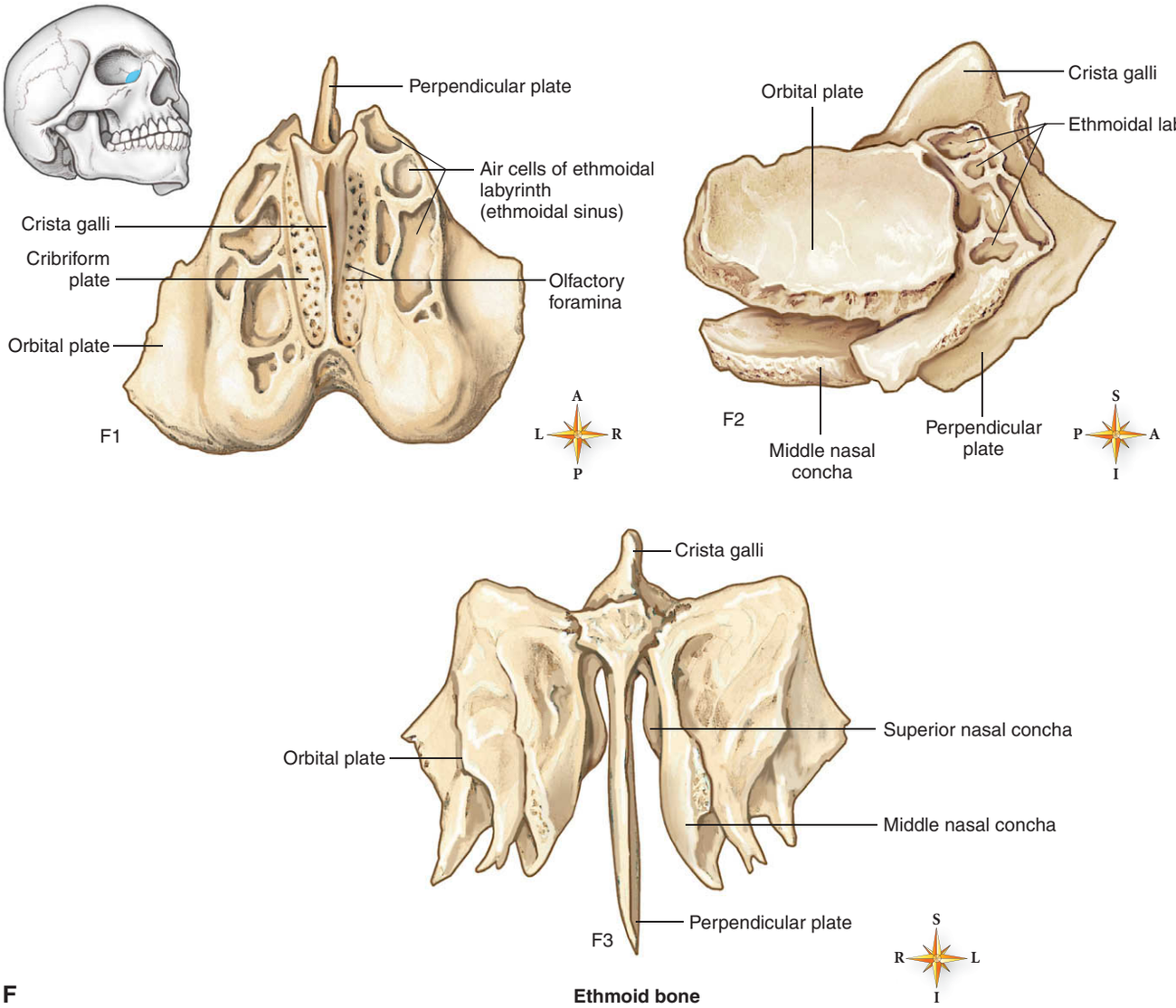
FIGURE 9-8

Bones of the skull. ***(continued)***
E, Sphenoid bone. **E1**, Superior view; **E2,** posterior view.

TABLE 9-3 **Cranial Bones and Their Markings** ***(continued)***

BONES AND MARKINGS	DESCRIPTION
Sphenoid	Keystone of the cranial floor; forms its midportion; resembles a bat with wings outstretched and legs extended downward posteriorly; lies behind and slightly above the nose and throat; forms part of the floor and sidewalls of the orbit
Body	Hollow, cubelike central portion
Greater wings	Lateral projections from the body; form part of the outer wall of the orbit
Lesser wings	Thin, triangular projections from the upper part of the sphenoid body; form the posterior part of the roof of the orbit
Sella turcica	Saddle-shaped depression on the upper surface of the sphenoid body; contains the pituitary gland; literally "Turkish saddle"
Sphenoid sinuses	Irregular mucosa-lined, air-filled spaces within the central part of the sphenoid
Pterygoid processes	Downward projections on either side where the body and greater wing unite; comparable to the extended legs of a bat if the entire bone is likened to this animal; form part of the lateral nasal wall
Optic canal	Opening into the orbit at the root of the lesser wing; transmits the optic nerve
Superior orbital fissure	Slitlike opening into the orbit; lateral to the optic foramen; transmits the third, fourth, and part of the fifth cranial nerves
Foramen rotundum	Opening in the greater wing that transmits the maxillary division of the fifth cranial nerve
Foramen ovale	Opening in the greater wing that transmits the mandibular division of the fifth cranial nerve
Foramen lacerum	Opening at the junction of the sphenoid, temporal, and occipital bones; transmits a branch of the ascending pharyngeal artery
Foramen spinosum	Opening in the greater wing that transmits the middle meningeal artery to supply the meninges

(continued)



F **Ethmoid bone**

FIGURE 9-8

Bones of the skull. ***(continued)*** **F,** Ethmoid bone. **F1,** Superior view; **F2,** lateral view; **F3,** anterior view.

(continued)

TABLE 9-3 Cranial Bones and Their Markings *(continued)*

BONES AND MARKINGS	DESCRIPTION
Ethmoid	Complex irregular bone that helps make up the anterior portion of the cranial floor, medial wall of the orbits, upper parts of the nasal septum, and sidewalls and part of the nasal roof; lies anterior to the sphenoid and posterior to the nasal bones
Cribriform plate	Olfactory nerves pass through numerous holes in this horizontal plate
Crista galli	Meninges (membranes around the brain) attach to this process
Perpendicular plate	Forms the upper part of the nasal septum
Ethmoid sinuses	Honeycombed, mucosa-lined air spaces within the lateral masses of the bone
Superior and middle nasal conchae (turbinates)	Help form the lateral walls of the nose
Ethmoidal labyrinth	Hollow lateral masses of the ethmoid; contain many air spaces (ethmoid cells or sinuses); the inner surface forms the superior and middle conchae

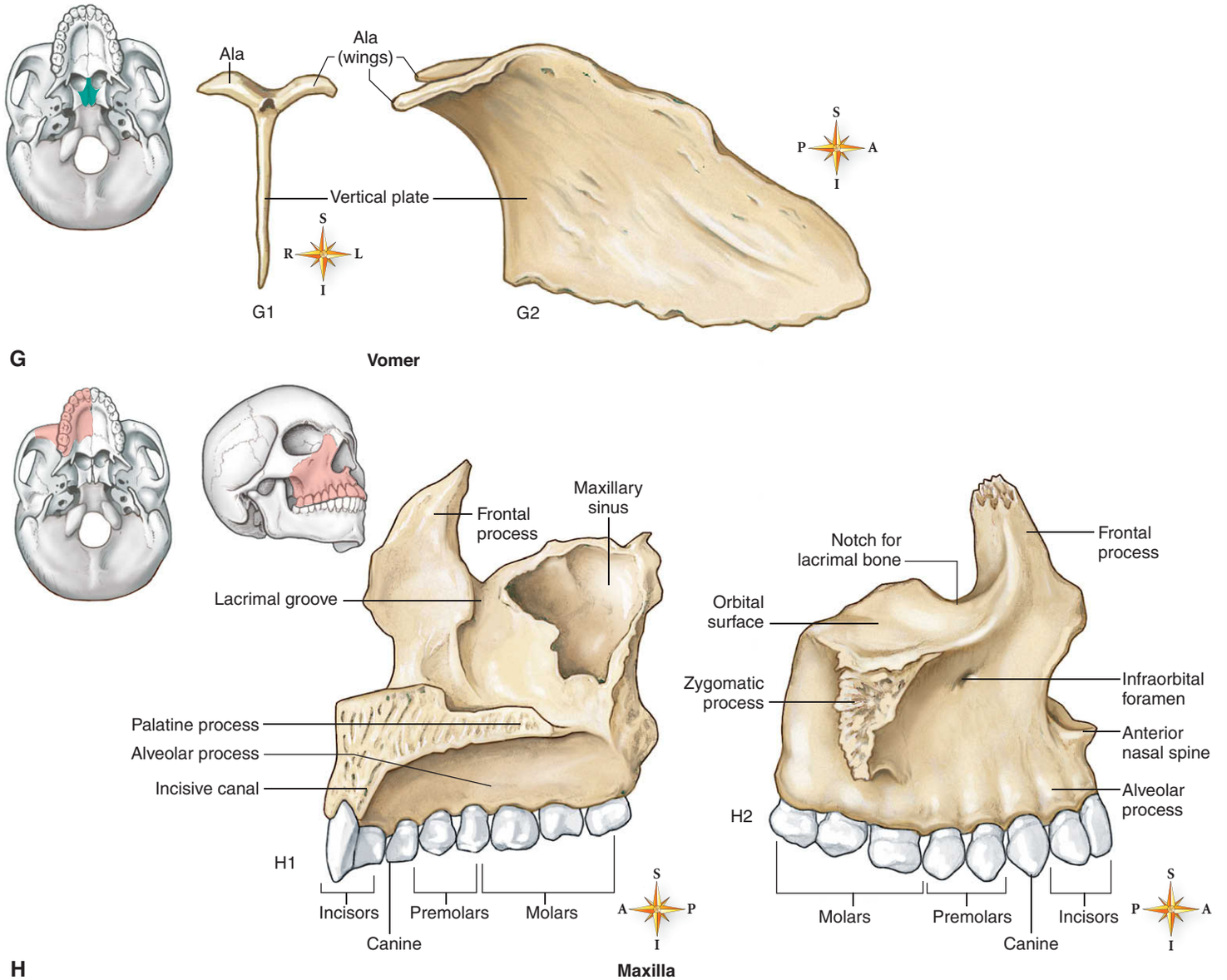


FIGURE 9-8

Bones of the skull. ***(continued)*** **G,** Vomer. **G1,** Anterior view; **G2,** lateral view. **H,** Right maxilla. **H1,** Medial view; **H2,** lateral view.

TABLE 9-4 Facial Bones and Their Markings

BONES AND MARKINGS	DESCRIPTION
Vomer	Forms lower and posterior part of nasal septum; shaped like the blade of a plough
Maxilla	Upper jaw bones; form part of the floor of the orbit, anterior part of the roof of the mouth, and floor of the nose and part of the sidewalls of the nose
Alveolar process	Archlike process that holds the tooth sockets
Maxillary sinus	Large, air-filled cavity within body of maxilla; lined with mucous membrane; largest of paranasal sinuses
Palatine process	Horizontal plate that projects inward from the alveolar process; forms anterior and larger part of hard palate
Infraorbital foramen	Hole on external surface orbit; transmits vessels and nerves
Lacrimal groove	Groove on inner surface; joined by similar groove on lacrimal bone to form bony space for the nasolacrimal duct

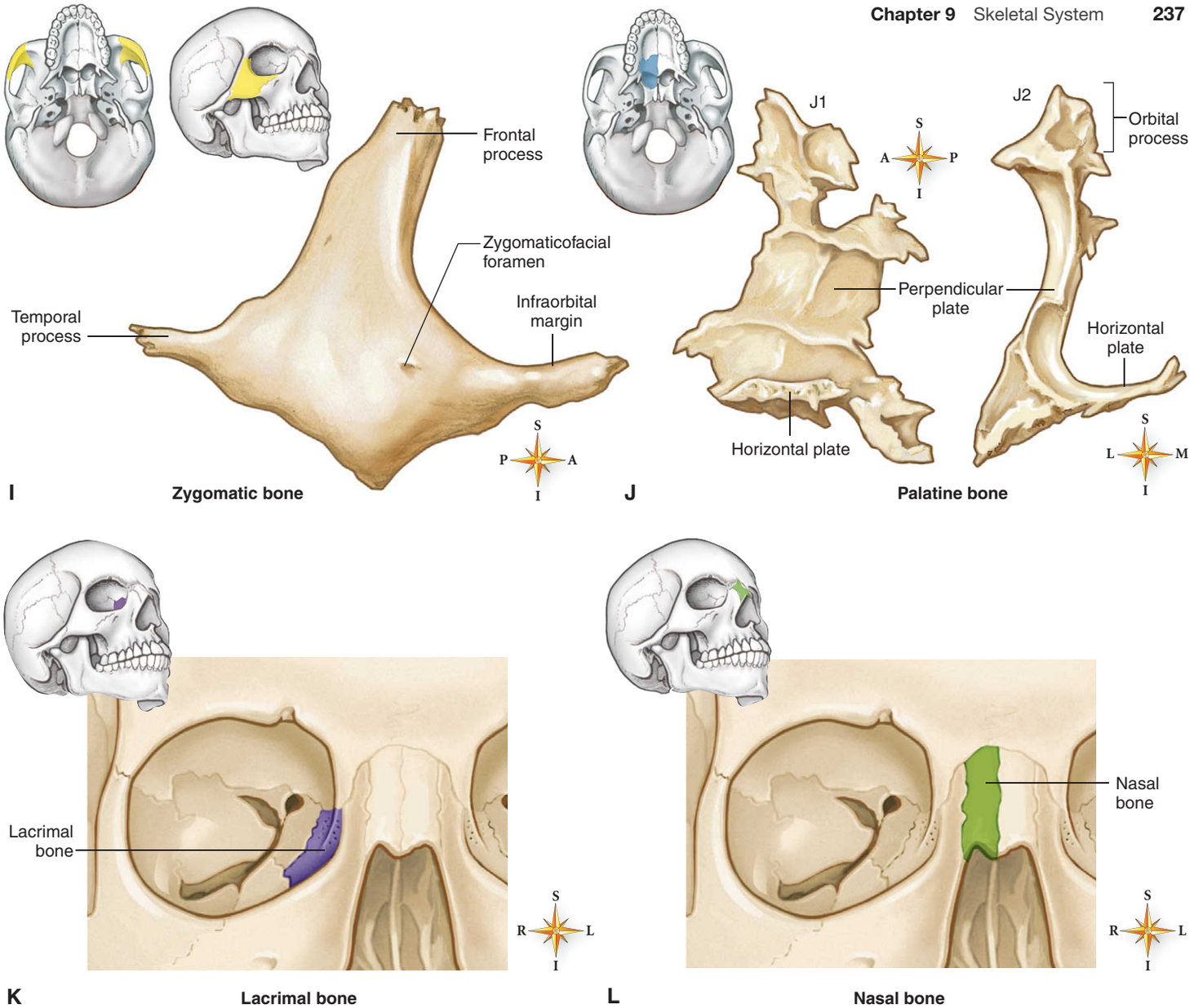


FIGURE 9-8

Bones of the skull. ***(continued)*** **I,** Right zygomatic bone viewed from the lateral side. **J,** Right palatine bone. **J1,** Medial view; **J2,** anterior view. **K,** Right lacrimal bone viewed from the lateral side. **L,** Right nasal bone viewed from the lateral side.

(continued)

TABLE 9-4 Facial Bones and Their Markings *(continued)*

BONES AND MARKINGS	DESCRIPTION
Zygomatic	Cheekbones; form part of floor and sidewall of eye orbit
Palatine	Form the posterior part of the hard palate, floor, and part of the sidewalls of the nasal cavity and floor of orbit
Horizontal plate	Joined to the palatine processes of the maxillae to complete part of the hard palate
Lacrimal	Thin platelike bones; posterior and lateral to nasal bones in medial wall of eye orbit; help form sidewall of nasal cavity (often missing in dry skull specimen)
Nasal	Pair of small bones that form the upper part of bridge of nose
Inferior nasal conchae (turbinates)	Thin scroll of bone forming shelf along inner surface of sidewall of nasal cavity; lies above roof of mouth

(continued)

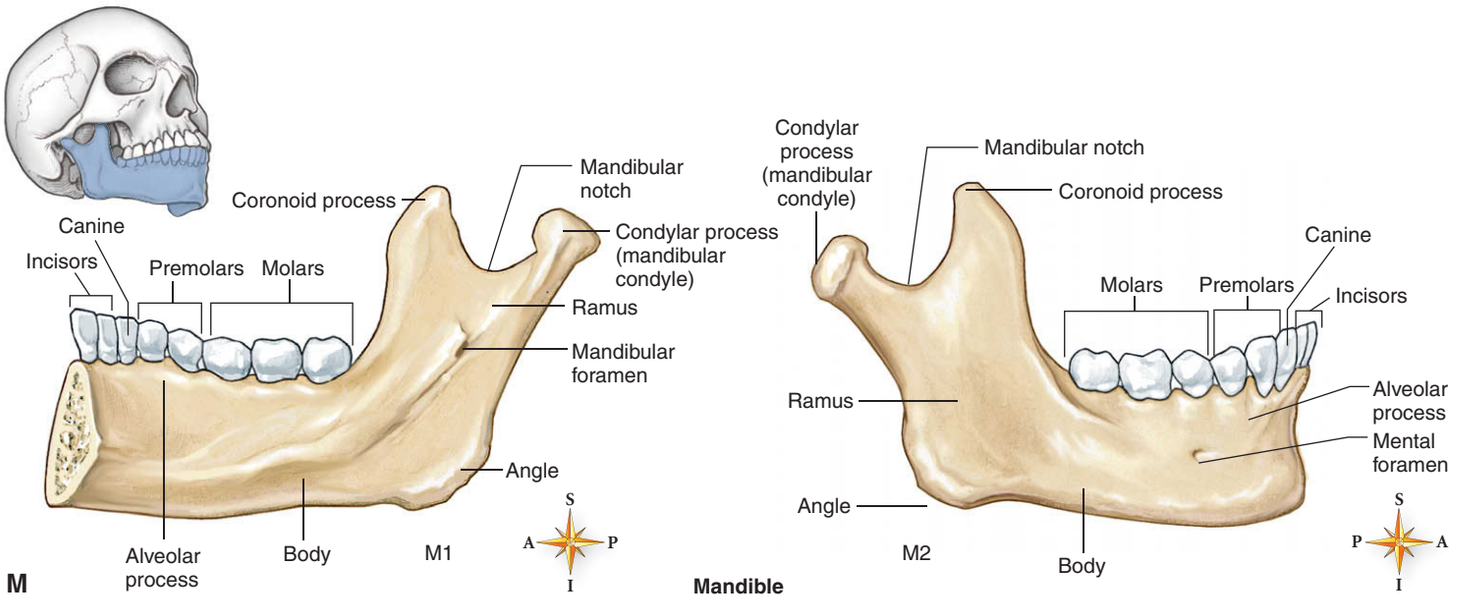


FIGURE 9-8

Bones of the skull. ***(continued)*** **M,** Right half of the mandible. **M1,** Medial view; **M2,** lateral view.

TABLE 9-4 Facial Bones and Their Markings *(continued)*

BONES AND MARKINGS	DESCRIPTION
Mandible	Lower jawbone; largest, strongest bone of the face
Body	Main part of the bone; forms the chin
Ramus	Process, one on either side, that projects upward from the posterior part of the body
Condylar process	Part of each ramus that articulates with the mandibular fossa of the temporal bone
Neck	Constricted part just below the condyles
Alveolar process	Teeth set into this arch
Mandibular foramen	Opening on the inner surface of the ramus; transmits nerves and vessels to the lower teeth
Mental foramen	Opening on the outer surface below the space between the two bicuspids; transmits the terminal branches of the nerves and vessels that enter the bone through the mandibular foramen; dentists inject anesthetics through these foramina
Coronoid process	Projection upward from the anterior part of each ramus; the temporal muscle inserts here
Angle	Juncture of posterior and inferior margins of ramus

CRANIAL BONES

The **frontal bone** forms the forehead and the anterior part of the calvaria or top of the cranium (see Figure 9-8, *C*). It contains mucosa-lined, air-filled spaces, or **sinuses**—the *frontal sinuses.* The frontal sinuses, with similar sinuses in the sphenoid, ethmoid, and maxillae, are often called *paranasal sinuses* because they have narrow channels that open into the nasal cavity (Figure 9-9). The paranasal sinuses are also discussed in Chapter 26, p.802. A portion of the frontal bone forms the upper part of the orbits. It unites with the two parietal bones posteriorly in an immovable joint, or **suture**—the *coronal suture.* Several of the more prominent frontal bone markings are described in Table 9-3.

The two **parietal bones** give shape to the bulging topside of the cranium (see Figure 9-8, *A*). They form immovable joints with several bones: the *lambdoid suture* with the occipital bone, the *squamous suture* with the temporal bone and part of the sphenoid, and the *coronal suture* with the frontal bone.

The lower sides of the cranium and part of its floor are fashioned from two **temporal bones** (see Figure 9-8, *B*). They house the middle and inner ear structures and contain the *mastoid sinuses,* notable because of the occurrence of *mastoiditis,* an inflammation of the mucous lining of these spaces (see Mechanisms of Disease, pp. 264–265). For a description of several other temporal bone markings, see Table 9-3.

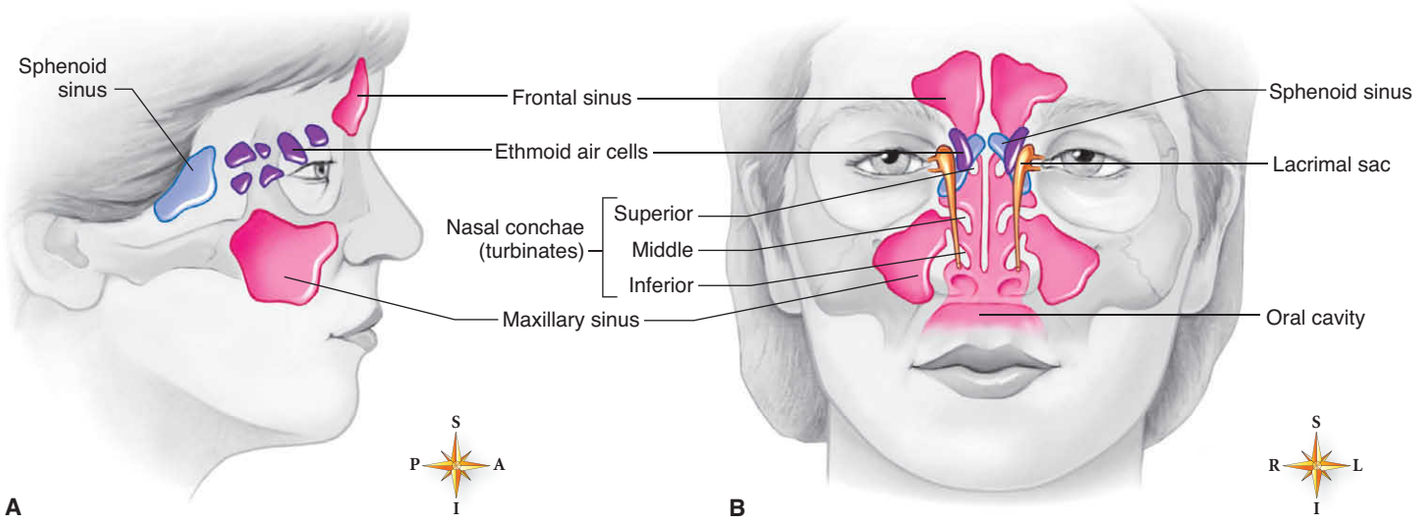


FIGURE 9-9

The paranasal sinuses. A, Lateral view. **B,** Frontal view.

The **occipital bone** creates the framework of the lower, posterior part of the skull (see Figure 9-8, *D*). It forms immovable joints with three other cranial bones—the parietal, temporal, and sphenoid—and a movable joint with the first cervical vertebra. Table 9-3 lists a description of some of its markings.

The shape of the **sphenoid bone** resembles a bat with its wings outstretched and legs extended down and back. Note in Figures 9-4 and 9-8, *E*, the location of the sphenoid bone in the central portion of the cranial floor. Here it serves as the keystone in the architecture of the cranium and anchors the frontal, parietal, occipital, and ethmoid bones. The sphenoid bone also forms part of the lateral wall of the cranium and part of the floor of each orbit (see Figures 9-2 and 9-3). The sphenoid bone contains fairly large mucosa-lined, air-filled spaces—the sphenoid sinuses (see Figure 9-6). Several prominent sphenoid markings are described in Table 9-3.

The **ethmoid,** a complex, irregular bone, lies anterior to the sphenoid but posterior to the nasal bones. It helps fashion the anterior part of the cranial floor (see Figures 9-4 and 9-8, *F*), the medial walls of the orbits (see Figures 9-2 and 9-7), the upper parts of the nasal septum (see Figure 9-2) and the sidewalls of the nasal cavity (Figure 9-10), and the part of the nasal roof (the cribriform plate) perforated by small foramina through which olfactory nerve branches reach the

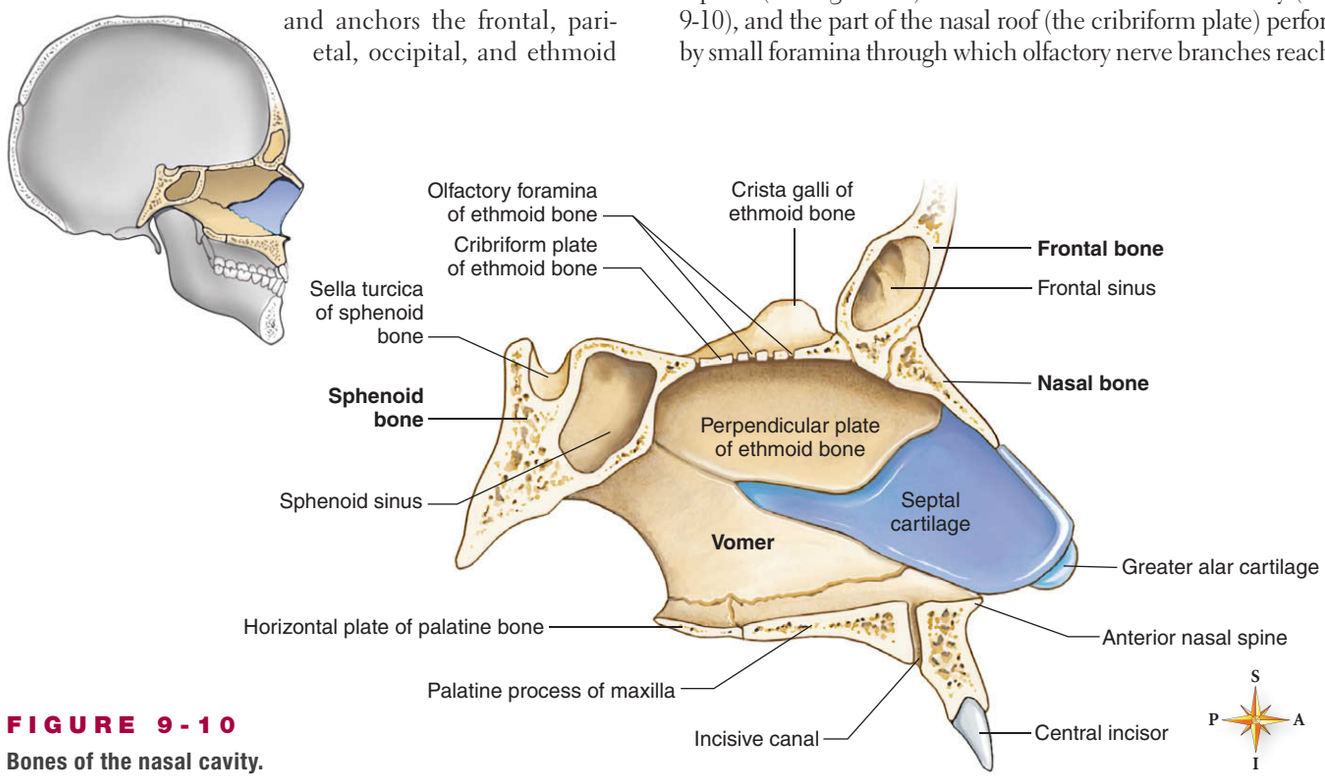


FIGURE 9-10

Bones of the nasal cavity.

brain (Box 9-1). The lateral masses of the ethmoid bone are honeycombed with sinus spaces called *ethmoid air cells* (see Figure 9-9). For more ethmoid bone markings, see Table 9-3.

FACIAL BONES

The two **maxillae** serve as the keystone in the architecture of the face, just as the sphenoid bone acts as the keystone of the cranium. Each maxilla articulates with the other maxilla and also with a nasal, a zygomatic, an inferior concha, and a palatine bone (see Figure 9-8, *H*). Of all the facial bones, only the mandible does not articulate with the maxillae. The maxillae form part of the floor of the orbits, part of the roof of the mouth, and part of the floor and sidewalls of the nose. Each maxilla contains a mucosa-lined space, the *maxillary sinus* (see Figure 9-9). This sinus is the largest of the paranasal sinuses, that is, sinuses connected by channels to the nasal cavity. For other markings of the maxillae, see Table 9-4.

Unlike the upper jaw, which is formed by the articulation of the two maxillae, the lower jaw, because of fusion of its halves during infancy, consists of a single bone, the **mandible** (see Figure 9-8, *M*). It is the largest, strongest bone of the face. It articulates with the temporal bone in the only movable joint of the skull. Its major markings are identified in Table 9-4.

The cheek is shaped by the underlying **zygomatic,** or malar, **bone** (see Figure 9-8, *I*). This bone also forms the outer margin of the orbit and, with the zygomatic process of the temporal bone, makes the zygomatic arch. It articulates with four other facial bones: the maxillary, temporal, frontal, and sphenoid bones.

Shape is given to the nose by the two **nasal bones,** which form the upper part of the bridge of the nose (see Figure 9-8, *L*), and by the *septal cartilage*, which forms the lower part (see Figure 9-10). Although small, the nasal bones enter into several articulations: with the perpendicular plate of the ethmoid bone, the cartilaginous part of the nasal septum, the frontal bone, the maxillae, and each other.

Box 9-1 | HEALTH matters

The Cribriform Plate

Separation of the nasal and cranial cavities by the cribriform plate of the ethmoid bone has great clinical significance. The cribriform plate is perforated by many small openings that permit branches of the olfactory nerve responsible for the special sense of smell to enter the cranial cavity and reach the brain. Separation of these two cavities by a thin, perforated plate of bone presents real hazards. If the cribriform plate is damaged as a result of trauma to the nose, it is possible for potentially infectious material to pass directly from the nasal cavity into the cranial fossa. If fragments of a fractured nasal bone are pushed through the cribriform plate, they may tear the coverings of the brain or enter the substance of the brain itself.

An almost paper-thin bone, shaped and sized about like a fingernail, lies just posterior and lateral to each nasal bone. It helps form the sidewall of the nasal cavity and the medial wall of the orbit. Because it contains a groove for the nasolacrimal (tear) duct, this bone is called the **lacrimal bone** (see Figure 9-8, *K*). It joins the maxilla, frontal bone, and ethmoid bone.

| A&P CONNECT |

The sinuses of the skull are often visible in x-ray images and other radiographs, as you can see in ***Skeletal Radiography*** online at ***A&P Connect.***

The two **palatine bones** join to each other in the midline like two L's facing each other. Their united horizontal portions form the posterior part of the hard palate (see Figure 9-8, *J*). The vertical portion of each palatine bone forms the lateral wall of the posterior part of each nasal cavity. The tip of the vertical portion is the *orbital process*, which forms part of the eye orbit (see Figure 9-7). The palatine bones articulate with the maxillae and the sphenoid bone.

There are two **inferior nasal conchae** (turbinates). Each concha is scroll shaped and forms a kind of ledge projecting into the nasal cavity from its lateral wall. Each nasal cavity has three such ledges. The superior and middle conchae (which are projections of the ethmoid bone) form the upper and middle ledges. The inferior concha (which is a separate bone) forms the lower ledge. They are covered by mucosa and divide each nasal cavity into three narrow, irregular channels, the nasal meatus. The inferior nasal conchae form immovable joints with the ethmoid, lacrimal, maxilla, and palatine bones.

Two structures that are involved in the formation of the nasal septum have already been mentioned—the perpendicular plate of the ethmoid bone and the septal cartilage. One other structure, the **vomer bone,** completes the septum posteriorly (see Figures 9-8, *G*, and 9-10 and Table 9-5). It forms immovable joints with four bones: the sphenoid, ethmoid, palatine, and maxillae.

EYE ORBITS

The right and left orbital cavities of the skull contain not only the eyes and associated muscles but also the lacrimal apparatus and important blood vessels and nerves. These structures are separated from the cranial cavity, nose, paranasal sinuses, and mouth by the often very thin and fragile orbital walls (see Figures 9-2 and 9-7).

| A&P CONNECT |

The fragile bones of the eye orbit can fracture easily, causing a dramatic condition called ***raccoon eyes.*** See for yourself in ***Bone Fractures*** online at ***A&P Connect.***

TABLE 9-5 Special Features of the Skull

FEATURE	DESCRIPTION
Sutures	Immovable joints between skull bones
Squamous	Line of articulation along the top curved edge of the temporal bone
Coronal	Joint between the parietal bones and frontal bone
Lambdoid	Joint between the parietal bones and occipital bone
Sagittal	Joint between the right and left parietal bones
Fontanels	"Soft spots" where ossification is incomplete at birth; allow some compression of the skull during birth; also important in determining the position of the head before delivery; six such areas located at angles of the parietal bones
Anterior (or frontal)	At the intersection of the sagittal and coronal sutures (juncture of the parietal bones and frontal bone); diamond shaped; largest of the fontanels; usually closed by 11.2 years of age
Posterior (or occipital)	At the intersection of the sagittal and lambdoid sutures (juncture of the parietal bones and occipital bone); triangular; usually closed by the second month
Sphenoid (or anterolateral)	At the juncture of the frontal, parietal, temporal, and sphenoid bones
Mastoid (or posterolateral)	At the juncture of the parietal, occipital, and temporal bones; usually closed by the second year
Air sinuses	Spaces, or cavities, within bones; those that communicate with the nose are called *paranasal sinuses* (frontal, sphenoidal, ethmoidal, and maxillary); mastoid cells communicate with the middle ear rather than the nose, so not included among the paranasal sinuses
Orbits formed by	
Frontal bone	Roof of the orbit
Ethmoid bone	Medial wall
Lacrimal bone	Medial wall
Sphenoid bone	Lateral wall
Zygomatic bone	Lateral wall
Maxilla	Floor
Palatine bone	Floor
Nasal septum formed by	Partition in the midline of the nasal cavity; separates the cavity into right and left halves
Perpendicular plate of the ethmoid bone	Forms the upper part of the septum
Vomer	Forms the lower, posterior part of the septum
Cartilage	Forms the anterior part of the septum
Sutural (wormian) bones	Small islets of bone in sutures; vary greatly from person to person
Malleus, incus, stapes	Tiny bones, referred to as *auditory ossicles,* in the middle ear cavity in the temporal bones; resemble, respectively, a miniature hammer, anvil, and stirrup

FETAL SKULL

The skulls of both a fetus and a newborn infant have unique anatomical features not seen in an adult. For example, placement of the cranial bones in the fetal skull allows it to change shape during the birth process. During infancy and childhood, differential growth and development of certain areas of the skull produce changing proportions of the cranium and face. As you will learn in Chapter 36, the face at birth forms a relatively smaller proportion of the cranium (about one eighth) than in the adult (about one half). Also, whereas an infant's head is approximately one fourth the total height of the body, an adult's head is only about one eighth the total height (see Figure 36-22 on p. 1116).

The **fontanels,** visible in Figure 9-11 and described in Table 9-5, are perhaps the best known of the unique features

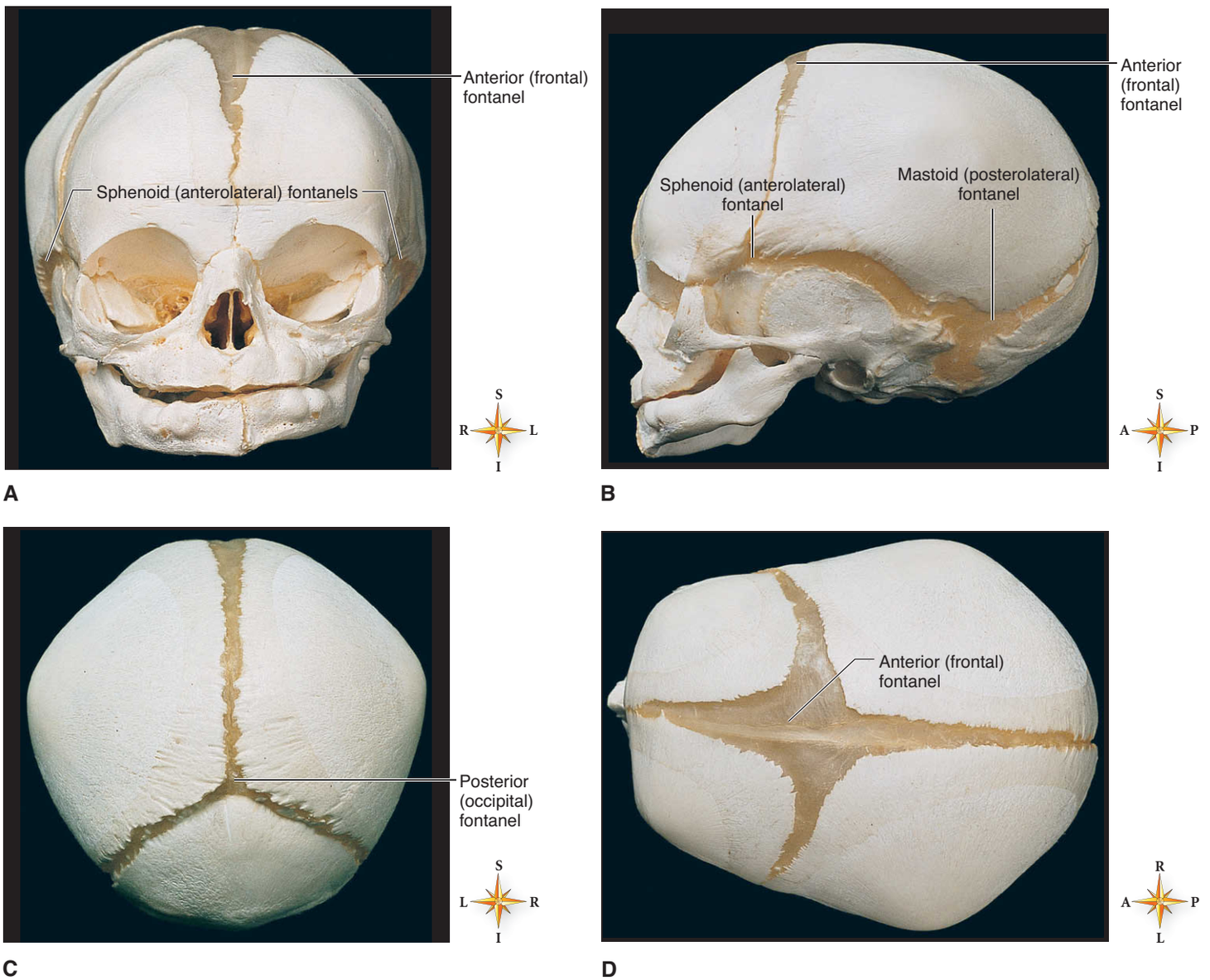


FIGURE 9-11

Skull at birth. A, Viewed from the front. **B,** Viewed from the left and slightly below. **C,** Viewed from behind. **D,** Viewed from above.

in the infant skull. Without the additional space between skull bones provided by the fontanels, molding of head shape as the baby passes through the birth canal could result in fracture of one or more cranial bones. Fontanels also allow rapid brain growth to occur in infancy without causing damaging increases in intracranial pressure. When the fontanels close and the cranial bones grow together as they reach adult size and shape, they fuse together and form the adult suture lines that remain visible throughout life (see Table 9-5).

Numerous other changes occur as the skull of the newborn undergoes skeletal aging processes that prepare it for adult functions. For example, the paranasal sinuses, shown in Figure 9-6 and described in detail in Chapter 26, undergo dramatic changes in size and placement during the time between birth and skeletal maturity. They are listed as special features of the skull in Table 9-5. In Figure 9-11, elevations that cover the developing deciduous, or baby, teeth can be seen in the body of the mandible. Over time these teeth will erupt and eventually be replaced by the adult dentition. These and other anatomical changes in the skull are possible because of the orderly sequence of aging processes that occur between fetal life and skeletal maturity.

Special features of the skull including the eye orbits, nasal septum, sutures, fontanels, sutural (wormian) bones, and the auditory ossicles, are briefly described in Table 9-5.

| A&P CONNECT |

The skull changes quite a bit over the life span, a fact that helps anthropologists and forensic scientists determine the age of a person simply by examining the skeleton or skeletal remains. You can see examples of these changes in ***Skeletal Variations*** online at ***A&P Connect.***

evolve

Hyoid Bone

The hyoid bone is a single bone in the neck—a part of the axial skeleton (Table 9-6). Its U shape may be felt just above the larynx (voice box) and below the mandible, where it is suspended from the styloid processes of the temporal bones (Figure 9-12). Several muscles attach to the hyoid bone. Among them are an extrinsic tongue muscle and certain muscles of the floor of the mouth. The hyoid claims the distinction of being the only bone in the body that articulates with no other bones.

| QUICK CHECK |

1. Name the eight bones of the cranium and describe how they fit together.
2. Name the 14 bones of the face and describe how they fit together.
3. Which bone is the only bone that normally does not form a joint with any other bone of the skeleton?

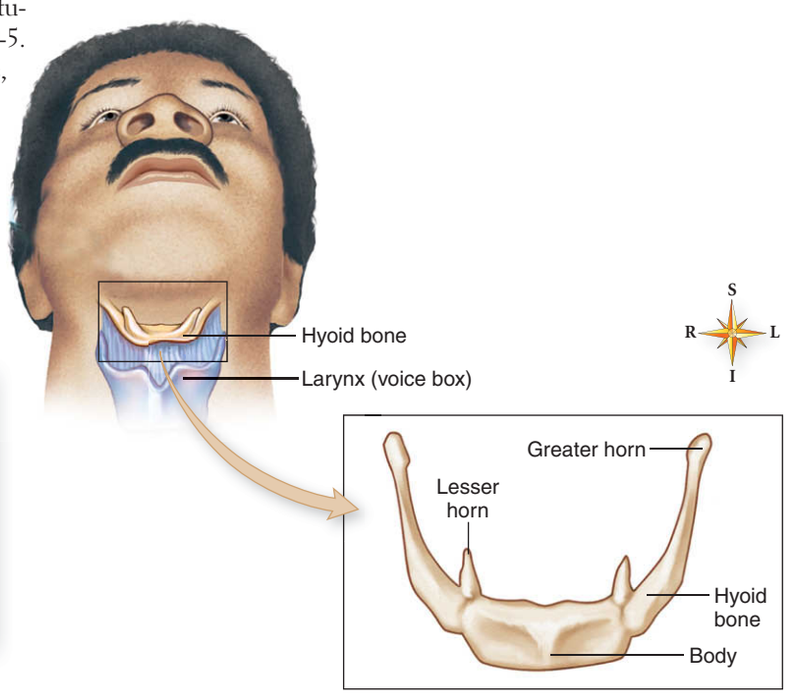


FIGURE 9-12

Hyoid bone. The insert shows the relationship of the hyoid bone in the neck below the skull and above the voice box (larynx). Note that the hyoid does not articulate with any other bony structure.

TABLE 9-6 Hyoid, Vertebrae, and Thoracic Bones and Their Markings

BONES AND MARKINGS	DESCRIPTION
Hyoid	U-shaped bone in the neck between the mandible and upper part of the larynx; distinctive as the only bone in the body not forming a joint with any other bone; suspended by ligaments from the styloid processes of the temporal bones

(continued)

TABLE 9-6 Hyoid, Vertebrae, and Thoracic Bones and Their Markings *(continued)*

BONES AND MARKINGS	DESCRIPTION
Vertebral column	Not actually a column, but a flexible, segmented curved rod; forms the axis of the body; head balanced above, ribs and viscera suspended in front, and lower extremities attached below; encloses the spinal cord *General features:* Anterior part of each vertebra (except the first two cervical) consists of the body; posterior part of the vertebrae consists of the neural arch, which in turn consists of two pedicles, two laminae, and seven processes projecting from the laminae
Body	Main part; flat, round mass located anteriorly; supporting or weight-bearing part of the vertebra
Pedicles	Short projections extending posteriorly from the body
Lamina	Posterior part of the vertebra to which pedicles join and from which processes project
Neural arch	Formed by the pedicles and laminae; protects the spinal cord posteriorly; congenital absence of one or more neural arches is known as *spina bifida* (the cord may protrude right through the skin)
Spinous process	Sharp process projecting inferiorly from laminae in the midline
Transverse processes	Right and left lateral projections from laminae
Superior articulating processes	Project upward from laminae; have smooth *superior articular facets*
Inferior articulating processes	Project downward from laminae; articulate with the superior articulating processes of vertebrae below; have smooth *inferior articular facets*
Spinal foramen	Hole in the center of the vertebra formed by union of the body, pedicles, and laminae; spinal foramina, when vertebrae are superimposed on one another, form the spinal cavity that houses the spinal cord
Intervertebral foramina	Opening between the vertebrae through which the spinal nerves emerge
Cervical vertebrae	First or upper seven vertebrae; the foramen in each transverse process for transmission of the vertebral artery, vein, and plexus of nerves; short bifurcated spinous processes except on the seventh vertebra, where it is extra long and may be felt as a protrusion when head is bent forward; the bodies of these vertebrae are small, whereas spinal foramina are large and triangular
Atlas	First cervical vertebra; lacks a body and spinous process; superior articulating processes are concave ovals that act as rockerlike cradles for the condyles of the occipital bone; named *atlas* because it supports the head as Atlas supports the world in Greek mythology
Axis (epistropheus)	Second cervical vertebra, so named because the atlas rotates about this bone in rotating movements of the head; the *dens,* or odontoid process, is a peglike projection extending upward from the body of the axis that forms a pivot for rotation of the atlas
Thoracic vertebrae	Next 12 vertebrae; 12 pairs of ribs attached to these vertebrae; stronger, with more massive bodies than the cervical vertebrae; no transverse foramina; two sets of facets for articulations with the corresponding rib: one on the body, the second on the transverse process; the upper thoracic vertebrae have elongated spinous processes
Lumbar vertebrae	Next five vertebrae; strong, massive; superior articulating processes directed medially instead of upward; inferior articulating processes, laterally instead of downward; short, blunt spinous processes
Sacrum	Five separate vertebrae until about 25 years of age; then fused to form one wedge-shaped bone
Sacral promontory	Protuberance from the anterior, upper border of the sacrum into the pelvis; of obstetrical importance because its size limits the anteroposterior diameter of the pelvic inlet
Coccyx	Four or five separate vertebrae in a child but fused into one in an adult
Curves	Curves have great structural importance because they increase the carrying strength of the vertebral column, make balance possible in an upright position (if the column was straight, the weight of the viscera would pull the body forward), absorb jolts from walking (a straight column would transmit jolts straight to the head), and protect the column from fracture
Primary curves Thoracic curve Sacral curve	Column curves at birth from the head to the sacrum with the convexity posteriorly; after the child stands, the convexity persists only in the *thoracic* and *sacral* regions, which are therefore called *primary curves*
Secondary curves Cervical curve Lumbar curve	Concavities in the *cervical* and *lumbar* regions; the cervical concavity results from the infant's attempts to hold the head erect (2 to 4 months); the lumbar concavity, from balancing efforts in learning to walk (10 to 18 months)

(continued on page 248)

Vertebral Column

The vertebral, or spinal, column forms the longitudinal axis of the skeleton. It is a flexible rather than a rigid column because it is segmented. As Figure 9-13 shows, the vertebral column consists of 24 **vertebrae** plus the sacrum and coccyx. Joints between the vertebrae permit forward, backward, and sideways movement of the column. Consider too these additional facts about the vertebral column. The head is balanced on top, the ribs are suspended in front, the lower extremities are attached below, and the spinal cord is enclosed within. It is indeed the "backbone" of the body.

The seven **cervical vertebrae** constitute the skeletal framework of the neck (see Figure 9-13). The next 12 vertebrae are called **thoracic vertebrae** because of their location in the posterior part of the chest, or the thoracic region. The next five, the **lumbar vertebrae,** support the small of the back. Below the lumbar vertebrae lie the sacrum and coccyx. In an adult the sacrum is a single bone that has formed from the fusion of five separate vertebrae, and the coccyx is a single bone that has formed from the fusion of four or five vertebrae.

All the vertebrae resemble each other in certain features and differ in others. For example, all except the first cervical vertebra have a flat, rounded body placed anteriorly and centrally, plus a sharp or blunt *spinous process* projecting inferiorly in the posterior midline and two transverse processes projecting laterally (Figure 9-14). All but the sacrum and coccyx have a central opening, the *vertebral foramen*. An upward projection (the *dens*) from the body of the second cervical vertebra furnishes an axis for rotating the head. A long, blunt spinous process, which can be felt at the back of the base of the neck, characterizes the seventh cervical vertebra. Each thoracic vertebra has articular facets for the ribs. More detailed descriptions of separate vertebrae are given in Table 9-6. The vertebral column, as a whole, articulates with the head, ribs, and iliac bones. Individual vertebrae articulate with each other in joints between their bodies and between their articular processes.

To increase the carrying strength of the vertebral column and to make balance possible in the upright position, the vertebral column is curved. At birth there is a continuous posterior convexity from the head to the coccyx. Later, as the child learns to sit and stand, secondary posterior concavities necessary for balance develop in the cervical and lumbar regions (see Figures 36-23 and 36-24, p. 1117).

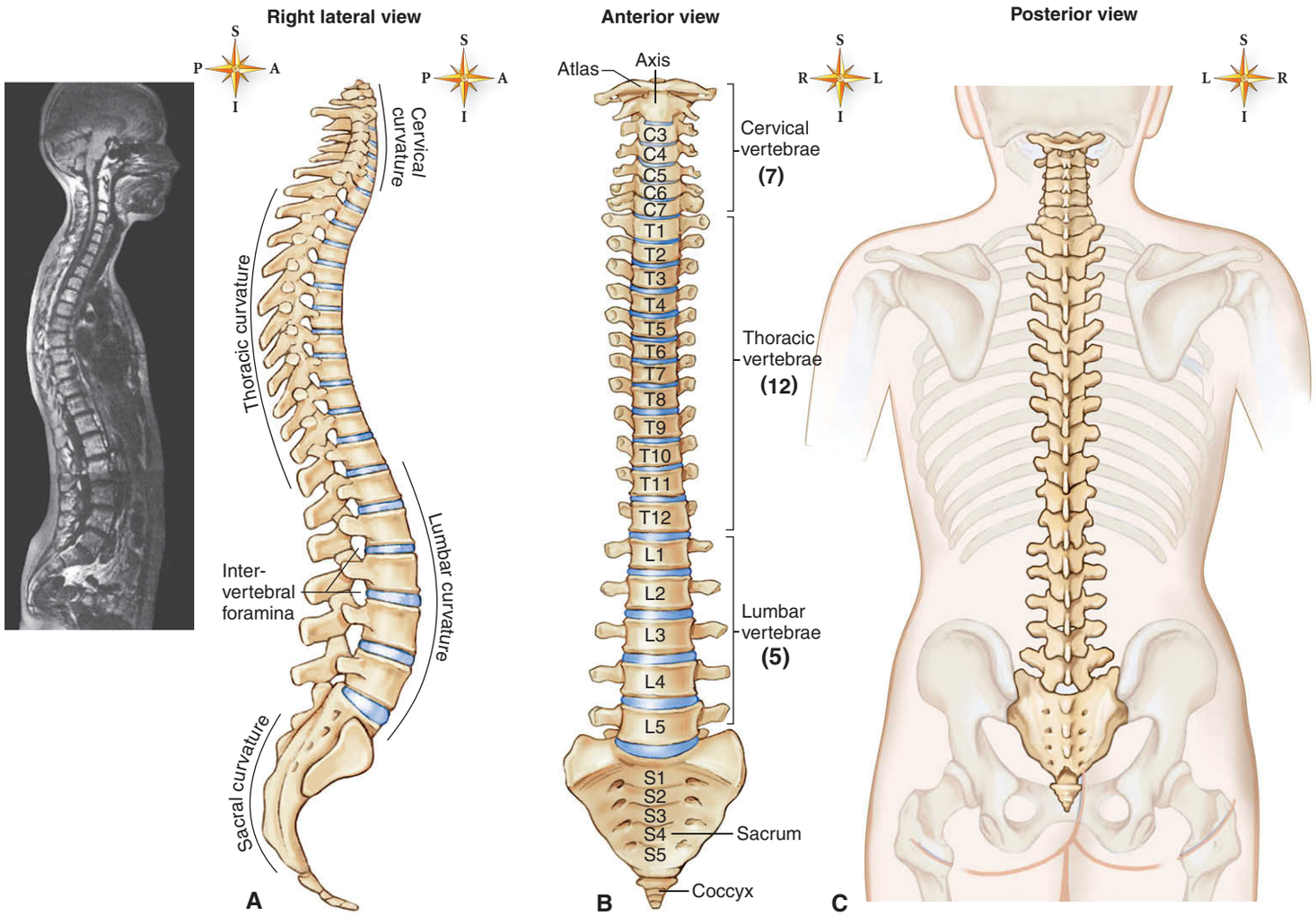


FIGURE 9-13

The vertebral column. A, Right lateral view. **B,** Anterior view. **C,** Posterior view. The photo inset shows a midline sagittal magnetic resonance image (MRI) of the vertebral column.

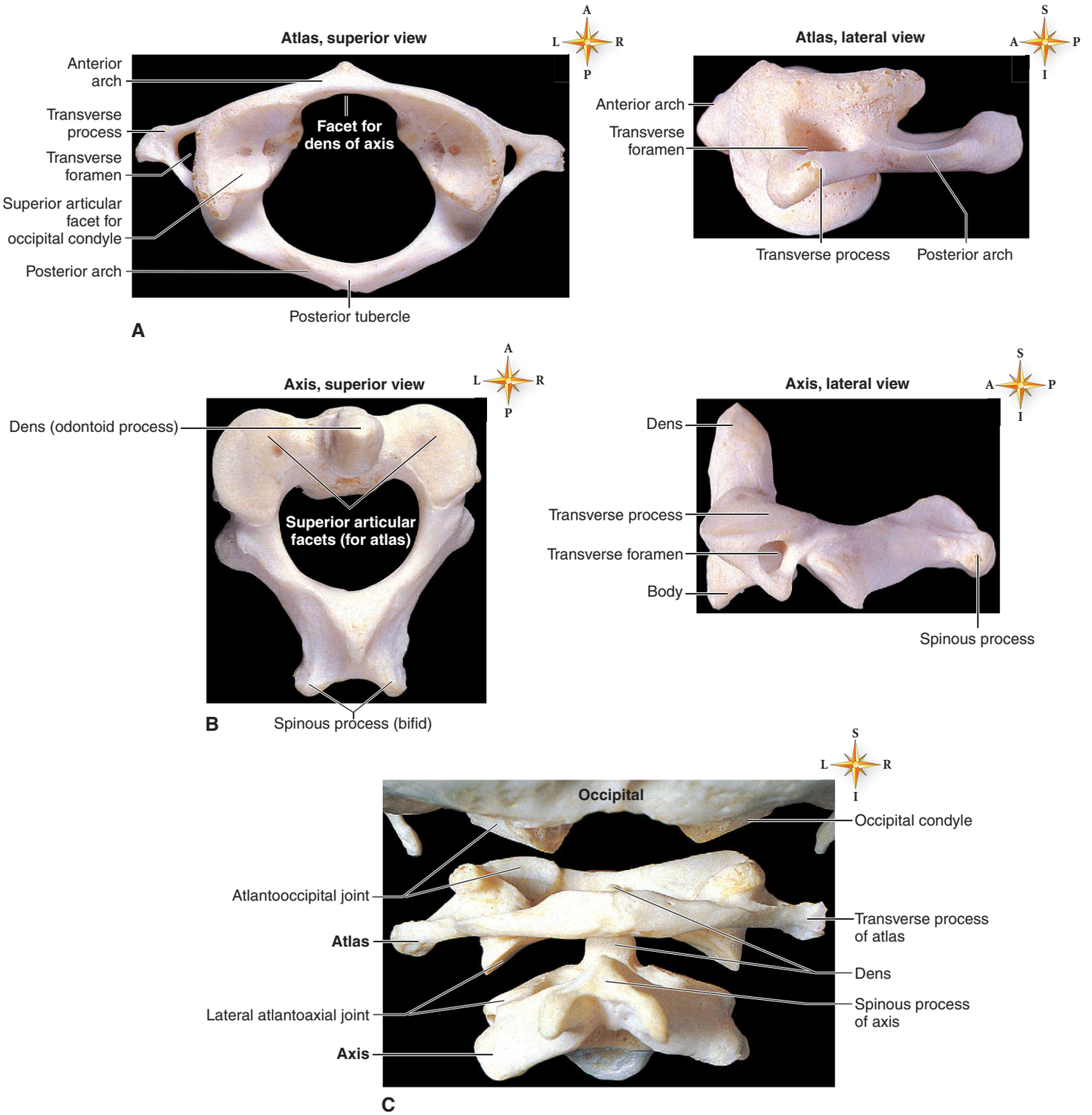
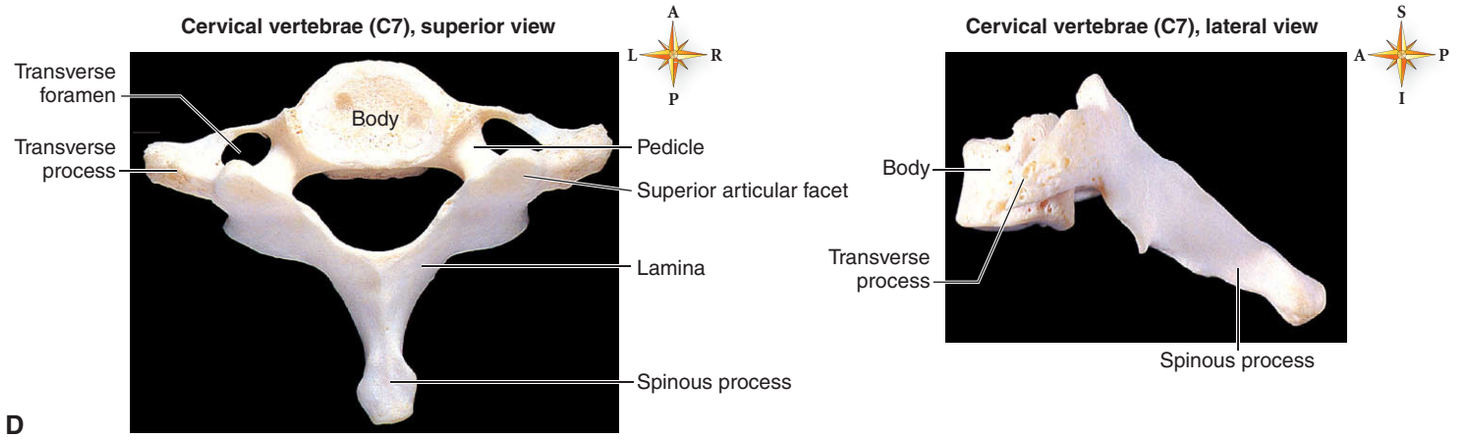
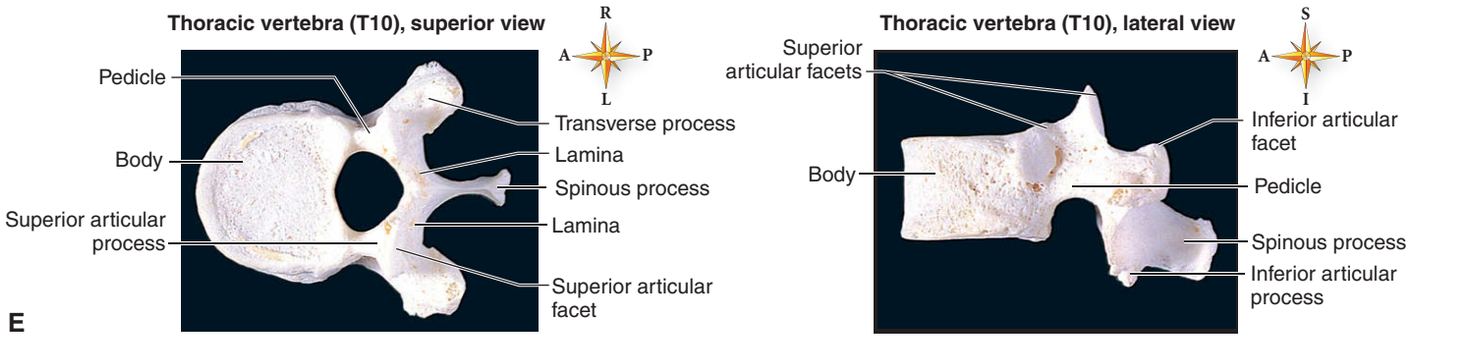


FIGURE 9-14

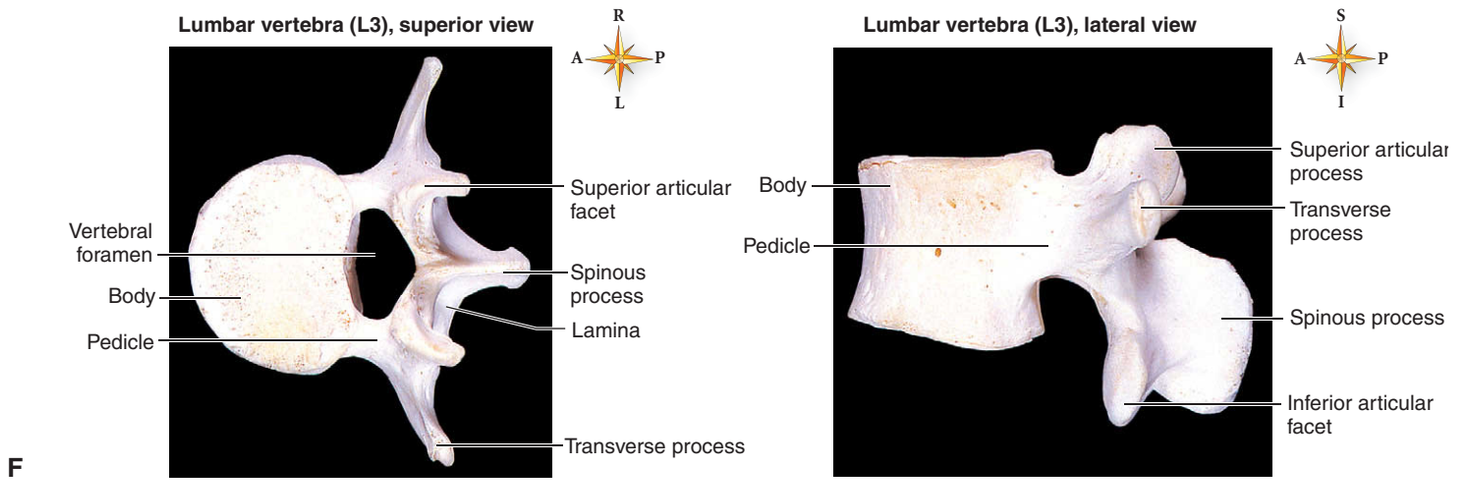
Vertebrae. A, Lateral and superior views of C1, the *atlas*. **B,** Lateral and superior views of C2, the axis. **C,** Base of the skull showing C1 (atlas) and C2 (axis) in posterior view. **D,** Lateral and superior views of a cervical vertebra, C7 (note the prominent spinous process). **E,** Lateral and superior views of a thoracic vertebra, T10. **F,** Lateral and superior views of a lumbar vertebra, L3. **G,** Lumbar vertebra L5 and the upper portion of the sacrum in an expanded anterior view. **H,** Oblique view of the sacrum and coccyx, showing the right coxal (hip) bone for reference.


Cervical vertebrae (C7), superior view
Transverse foramen
Transverse process
Body
Pedicle
Superior articular facet
Lamina
Spinous process
A
L
R
P
Cervical vertebrae (C7), lateral view
Body
Transverse process
Spinous process
S
A
P
I

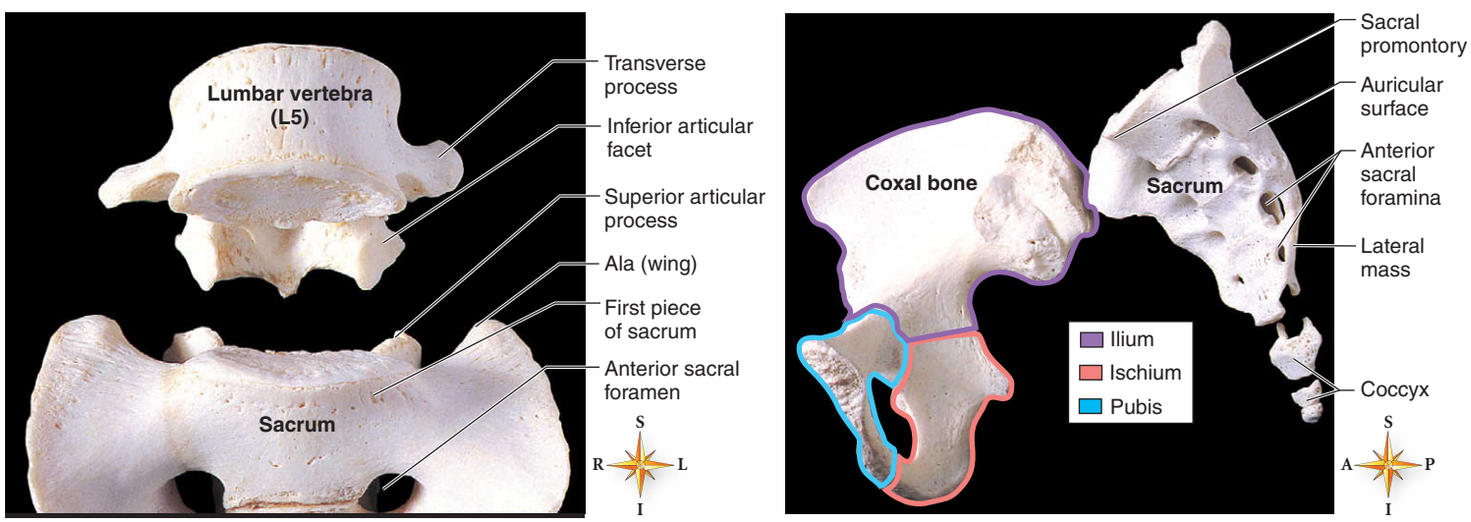
D


Thoracic vertebra (T10), superior view
Pedicle
Body
Superior articular process
Transverse process
Lamina
Spinous process
Lamina
Superior articular facet
R
A
P
L
Thoracic vertebra (T10), lateral view
Superior articular facets
Body
Inferior articular facet
Pedicle
Spinous process
Inferior articular process
S
A
P
I

E


Lumbar vertebra (L3), superior view
Vertebral foramen
Body
Pedicle
Superior articular facet
Spinous process
Lamina
Transverse process
R
A
P
L
Lumbar vertebra (L3), lateral view
Body
Pedicle
Superior articular process
Transverse process
Spinous process
Inferior articular facet
S
A
P
I

F


Lumbar vertebra (L5)
Sacrum
Transverse process
Inferior articular facet
Superior articular process
Ala (wing)
First piece of sacrum
Anterior sacral foramen
S
R
L
I
Coxal bone
Sacrum
Ilium
Ischium
Pubis
Sacral promontory
Auricular surface
Anterior sacral foramina
Lateral mass
Coccyx
S
A
P
I

G H

Sternum

The medial part of the anterior chest wall is supported by the **sternum,** a somewhat dagger-shaped bone consisting of three parts: the upper handle part, the *manubrium*; the middle blade part, the *body*; and a blunt cartilaginous lower tip, the *xiphoid process*. The last ossifies during adult life. The manubrium articulates with the clavicle and first rib, whereas the next nine ribs join the body of the sternum, either directly or indirectly, by means of the *costal cartilages* (Figure 9-15).

Ribs

Twelve pairs of ribs, together with the vertebral column and sternum, form the bony cage known as the *thoracic cage* or, simply, the **thorax.** Each rib articulates with both the body and the transverse process of its corresponding thoracic vertebra. The head of each rib articulates with the body of the corresponding thoracic vertebra, and the tubercle of each rib articulates with the vertebra's transverse process (Figure 9-16). In addition, the second through ninth ribs articulate with the body of the vertebra above. From its vertebral attachment, each rib curves outward, then forward and downward (see Figures 9-1 and 9-16), a mechanical fact important for breathing.

Anteriorly, each rib of the first seven pairs joins a costal cartilage that attaches to the sternum. For this reason, these ribs are often called the *true ribs*. Ribs of the remaining five pairs, the *false ribs*, do not attach directly to the sternum. Instead, each costal cartilage of pairs 8, 9, and 10 attaches to the costal cartilage of the rib above it—indirectly attaching it to the sternum. Ribs of the last two pairs of false ribs are designated *floating ribs* because they do not attach even indirectly to the sternum (see Figure 9-15).

| QUICK CHECK |

4. Name the three types of vertebrae and how many of each type are found in the vertebral column.
5. What bones make up the bony cage known as the thorax? How do these bones fit together to form this structure?
6. What is a floating rib?

TABLE 9-6 Hyoid, Vertebrae, and Thoracic Bones and Their Markings *(continued)*

BONES AND MARKINGS	DESCRIPTION
Sternum	Breastbone; flat dagger-shaped bone; the sternum, ribs, and thoracic vertebrae together form a bony cage known as the *thorax*
Body	Main central part of the bone
Manubrium	Flaring, upper part
Xiphoid process	Projection of cartilage at the lower border of the bone
Ribs	
Types	
True ribs	Upper seven pairs; fasten to the sternum by costal cartilages
False ribs	False ribs do not attach to the sternum directly; the upper three pairs of false ribs attach by means of the costal cartilage of the seventh ribs
Floating ribs	The last two pairs of false ribs do not attach to the sternum at all and are therefore called "floating" ribs
Parts	
Head	Projection at the posterior end of a rib; articulates with the corresponding thoracic vertebra and one above, except the last three pairs, which join the corresponding vertebrae only
Neck	Constricted portion just below the head
Tubercle	Small knob just below the neck; articulates with the transverse process of the corresponding thoracic vertebra; missing in the lowest three ribs
Body or shaft	Main part of a rib
Costal cartilage	Cartilage at the sternal end of true ribs; attaches ribs (except floating ribs) to the sternum

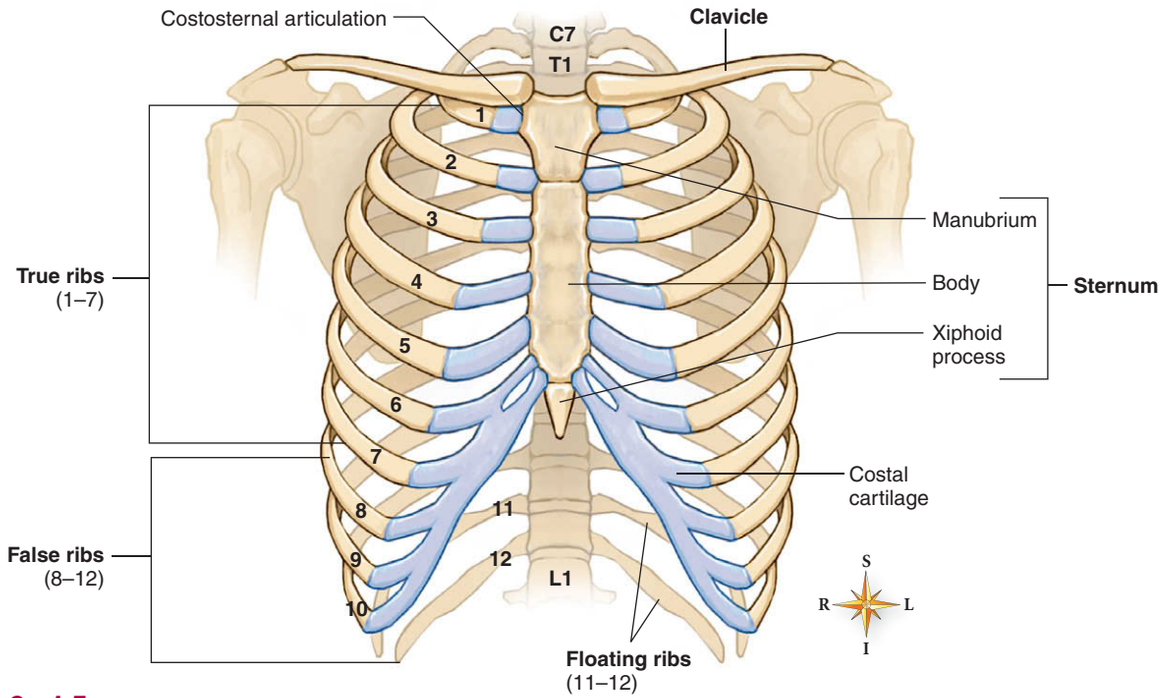


FIGURE 9-15

Thoracic cage. Note the costal cartilages and their articulations with the body of the sternum.

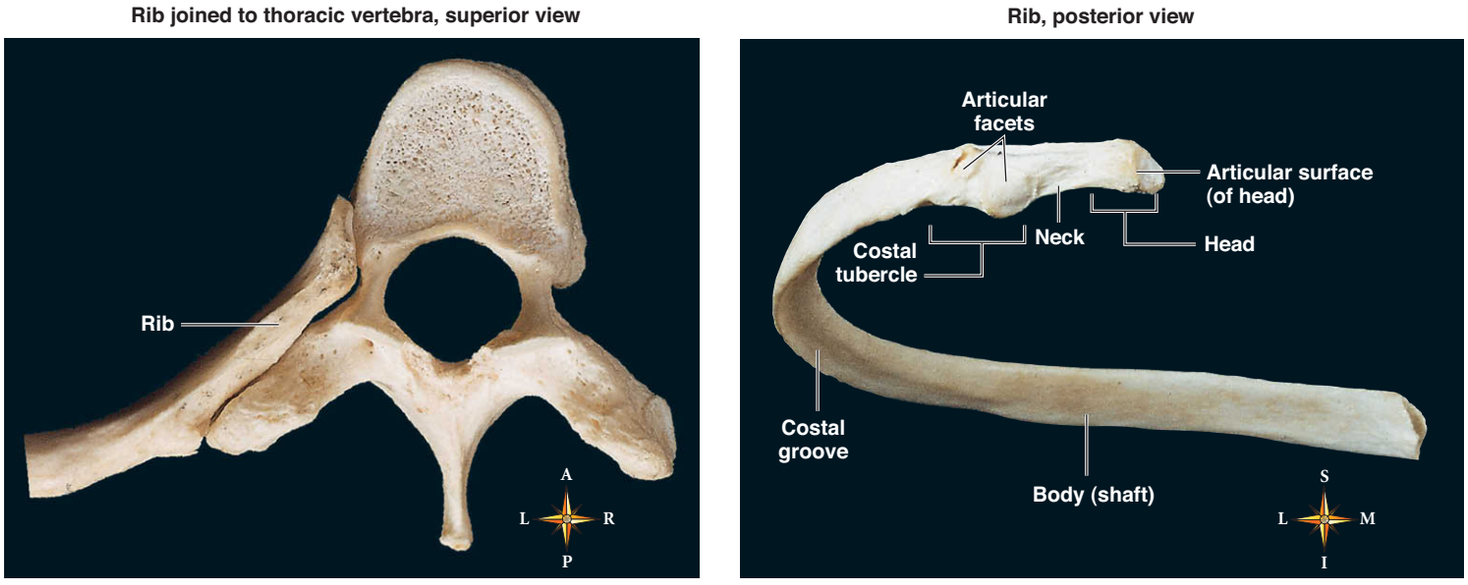


FIGURE 9-16

Articulation of a rib and vertebra. A, Note the head of the rib articulating with the vertebral body and the tubercle of the rib articulating with the transverse process of the vertebra. **B,** Anatomical components of a typical rib (fifth rib) viewed from behind.

APPENDICULAR SKELETON

Upper Extremity

The upper extremity consists of the bones of the shoulder girdle, upper part of the arm, forearm, wrist, and hand. Two bones, the **clavicle** and **scapula,** compose the **shoulder girdle** or *pectoral girdle.* Contrary to appearances, this belt or girdle of bone forms only one bony joint with the trunk: the sternoclavicular joint between the sternum and clavicle. At its outer end, the clavicle articulates with the scapula, which attaches to the ribs by muscles and tendons, not by a joint. All shoulder movements therefore

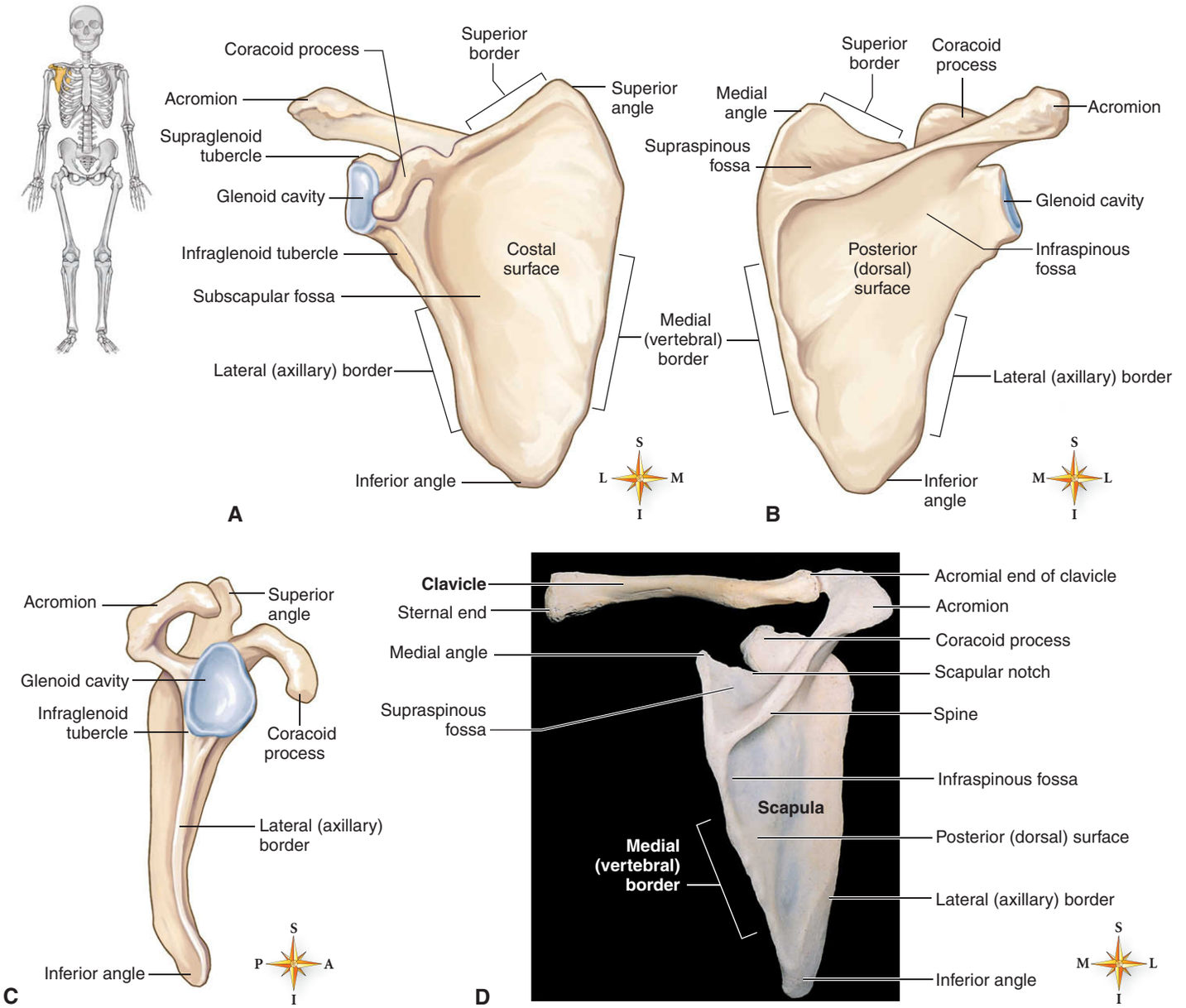


FIGURE 9-17

Right scapula. A, Anterior view. **B,** Posterior view. **C,** Lateral view. **D,** Posterior view showing articulation of the right scapula with the clavicle. (The skeleton inset shows the relative position of the right scapula within the entire skeleton.)

TABLE 9-7 Upper Extremity Bones and Their Markings

BONES AND MARKINGS	DESCRIPTION
Clavicle	Collar bones; the shoulder girdle is joined to the axial skeleton by articulation of the clavicles with the sternum (the scapula does not form a joint with the axial skeleton)
Scapula	Shoulder blades; the scapulae and clavicles together make up the shoulder girdle
Borders	
Superior	Upper margin
Medial (vertebral)	Margin toward the vertebral column
Lateral (axillary)	Lateral margin, toward axilla
Spine	Sharp ridge running diagonally across the posterior surface of the shoulder blade
Acromion	Slightly flaring projection at the lateral end of the scapular spine; may be felt at the tip of the shoulder; articulates with the clavicle
Coracoid process	Projection on the anterior surface from the upper border of the bone; may be felt in the groove between the deltoid and pectoralis major muscles, about 1 inch below the clavicle
Glenoid cavity	Arm socket

(continued)

involve the sternoclavicular joint. Various markings of the scapula are described in Table 9-7 (see also Figure 9-17).

The **humerus,** or arm bone, like other long bones, consists of a shaft, or diaphysis, and two ends, or epiphyses (Figures 9-18 and 9-19). The upper epiphysis bears several identifying structures: the head, anatomical neck, greater and lesser tubercles, intertubercular groove, and surgical neck. On the diaphysis are found the deltoid tuberosity and the radial groove. The distal epiphysis has four projections—the medial and lateral epicondyles, the capitulum, and the trochlea—and two depressions—the olecranon and coronoid fossae. For descriptions of all of these markings, see Table 9-7. The humerus articulates proximally with the scapula and distally with the radius and the ulna.

Two bones form the framework for the forearm: the **radius** on the thumb side and the **ulna** on the little finger side. At the proximal end of the ulna, the olecranon projects posteriorly and the coronoid process projects anteriorly. There are also two depressions: the semilunar notch on the anterior surface and the radial notch on the lateral surface. The distal end has two projections: a rounded head and a sharper styloid process. For more detailed identification of these markings, see Table 9-7. The ulna articulates proximally with the humerus and radius and distally with a fibrocartilaginous disk, but not with any of the carpal bones.

The radius has three projections: two at its proximal end, the head and radial tuberosity, and one at its distal end, the styloid process (see Figures 9-18 and 9-19). There are two proximal articulations: one with the capitulum of the humerus and the other with the radial notch of the ulna. The three distal articulations are with the scaphoid and lunate carpal bones and with the head of the ulna.

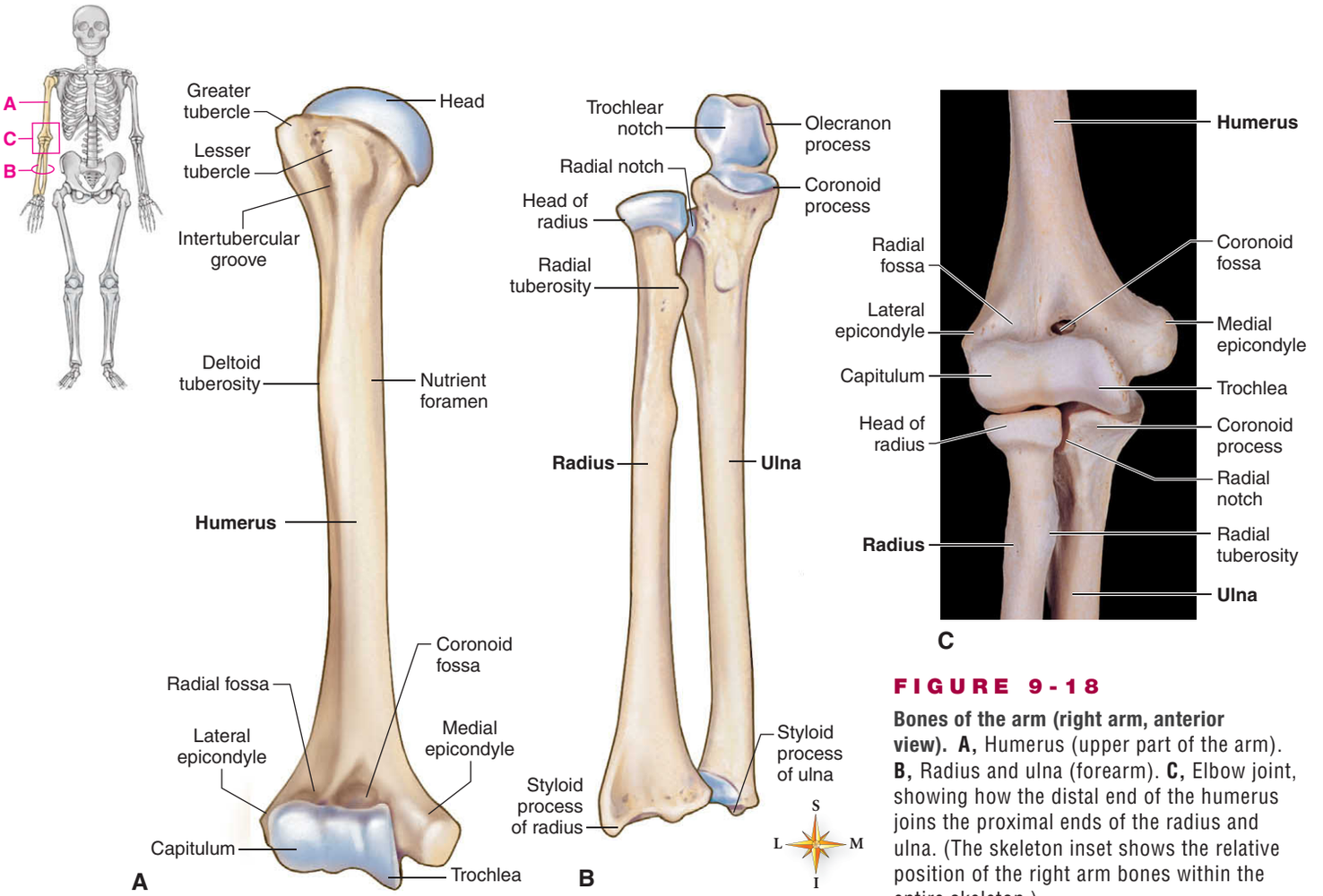


FIGURE 9-18

Bones of the arm (right arm, anterior view). A, Humerus (upper part of the arm). **B,** Radius and ulna (forearm). **C,** Elbow joint, showing how the distal end of the humerus joins the proximal ends of the radius and ulna. (The skeleton inset shows the relative position of the right arm bones within the entire skeleton.)

TABLE 9-7 Upper Extremity Bones and Their Markings *(continued)*

BONES AND MARKINGS	DESCRIPTION
Humerus	Long bone of the arm
Head	Smooth, hemispherical enlargement at the proximal end of the humerus
Anatomical neck	Oblique groove just below the head
Greater tubercle	Rounded projection lateral to the head on the anterior surface
Lesser tubercle	Prominent projection on the anterior surface just below the anatomical neck
Intertubercular groove	Deep groove between the greater and lesser tubercles; the long tendon of the biceps muscle lodges here
Surgical neck	Region just below the tubercles; so named because of its liability to fracture
Deltoid tuberosity	V-shaped, rough area about midway down the shaft where the deltoid muscle inserts
Radial groove	Groove running obliquely downward from the deltoid tuberosity; lodges the radial nerve
Epicondyles (medial and lateral)	Rough projections at both sides of the distal end
Capitulum	Rounded knob below the lateral epicondyle; articulates with the radius; sometimes called the *radial* head of the humerus
Trochlea	Projection with a deep depression through the center similar to the shape of a pulley; articulates with the ulna
Olecranon fossa	Depression on the posterior surface just above the trochlea; receives the olecranon of the ulna when the forearm extends
Coronoid fossa	Depression on the anterior surface above the trochlea; receives the coronoid process of the ulna in flexion of the forearm

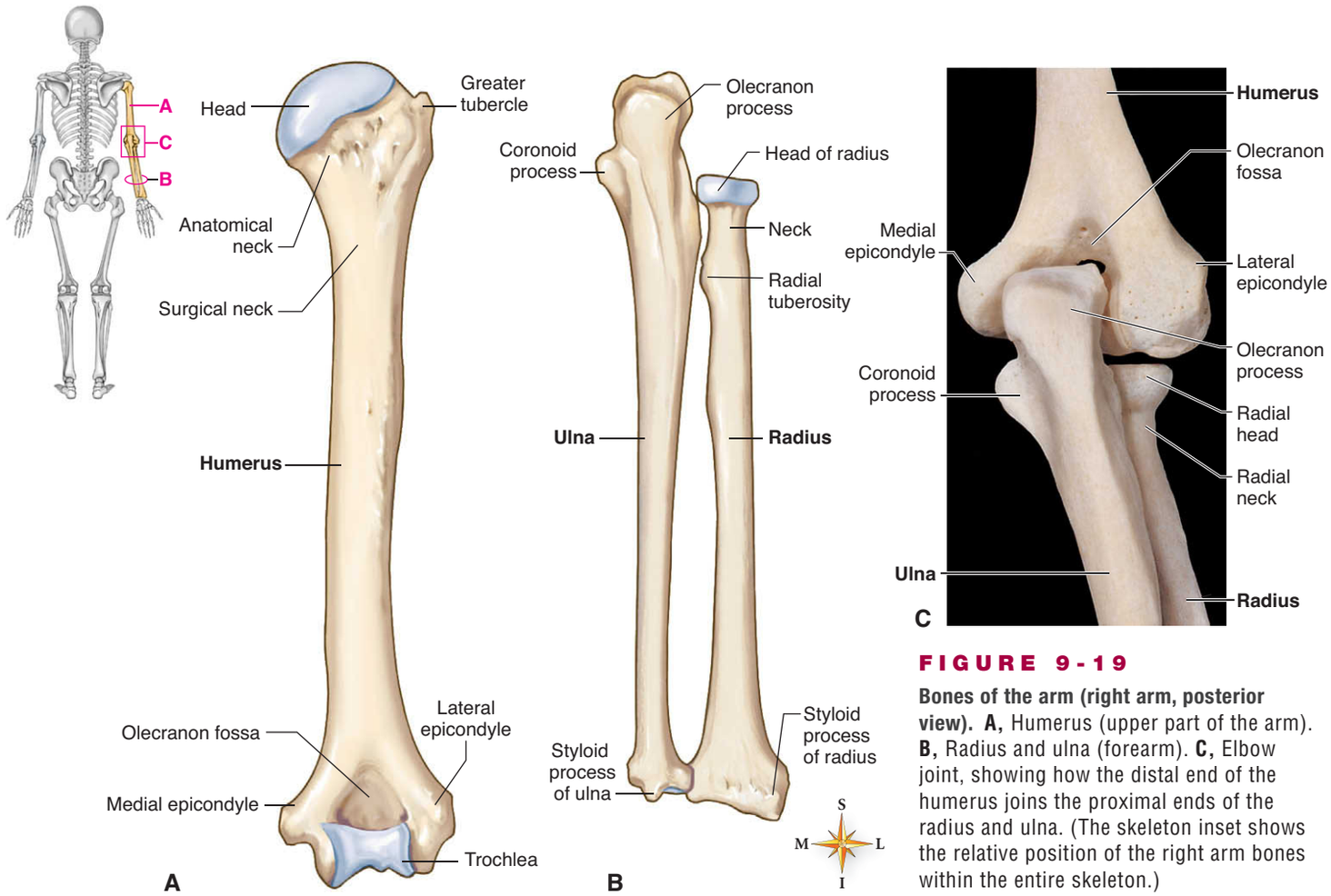


FIGURE 9-19

Bones of the arm (right arm, posterior view). A, Humerus (upper part of the arm). **B,** Radius and ulna (forearm). **C,** Elbow joint, showing how the distal end of the humerus joins the proximal ends of the radius and ulna. (The skeleton inset shows the relative position of the right arm bones within the entire skeleton.)

TABLE 9-7 Upper Extremity Bones and Their Markings *(continued)*

BONES AND MARKINGS	DESCRIPTION
Radius	Bone of the thumb side of the forearm
Head	Disk-shaped process forming the proximal end of the radius; articulates with the capitulum of the humerus and with the radial notch of the ulna
Radial tuberosity	Roughened projection on the ulnar side, a short distance below the head; the biceps muscle inserts here
Styloid process	Protuberance at the distal end on the lateral surface (with the forearm in the anatomical position)
Ulna	Bone of the little finger side of the forearm; longer than the radius
Olecranon	Scooplike process that joins the trochlea of the humerus at the elbow
Coronoid process	Projection on the anterior surface of the proximal end of the ulna; the trochlea of the humerus fits snugly between the olecranon and coronoid processes
Trochlear notch	Curved notch between the olecranon and coronoid process into which the trochlea fits; also called *semilunar notch*
Radial notch	Curved notch lateral and inferior to the semilunar notch; the head of the radius fits into this concavity
Head	Rounded process at the distal end; does not articulate with the wrist bones but with the fibrocartilaginous disk
Styloid process	Sharp protuberance at the distal end; can be seen from outside on the posterior surface
Carpal bones	Wrist bones; arranged in two rows at the proximal end of the hand; proximal row (from the little finger toward the thumb)—*pisiform, triquetrum, lunate,* and *scaphoid;* distal row—*hamate, capitate, trapezoid,* and *trapezium*
Metacarpal bones	Long bones forming the framework of the palm of the hand; numbered (from medial side) I, II, III, IV, V
Phalanges	Miniature long bones of the fingers, three (proximal, middle, distal) in each finger, two (proximal, distal) in each thumb; numbered (from medial side) I (except first middle), II, III, IV, V

The eight **carpal bones** (Figure 9-20) form what most people think of as the upper part of the hand but what, anatomically speaking, is the wrist. Only one of these bones is evident from the outside, the pisiform bone, which projects posteriorly on the little finger side as a small rounded elevation. The pisiform bone is an example of a sesamoid bone. Ligaments bind the carpal bones closely and firmly together in two rows of four each: proximal row (from the little finger toward the thumb)—pisiform, triquetrum, lunate, and scaphoid bones; distal row—hamate, capitate, trapezoid, and trapezium bones. The joints between the carpal bones and radius permit wrist and hand movements.

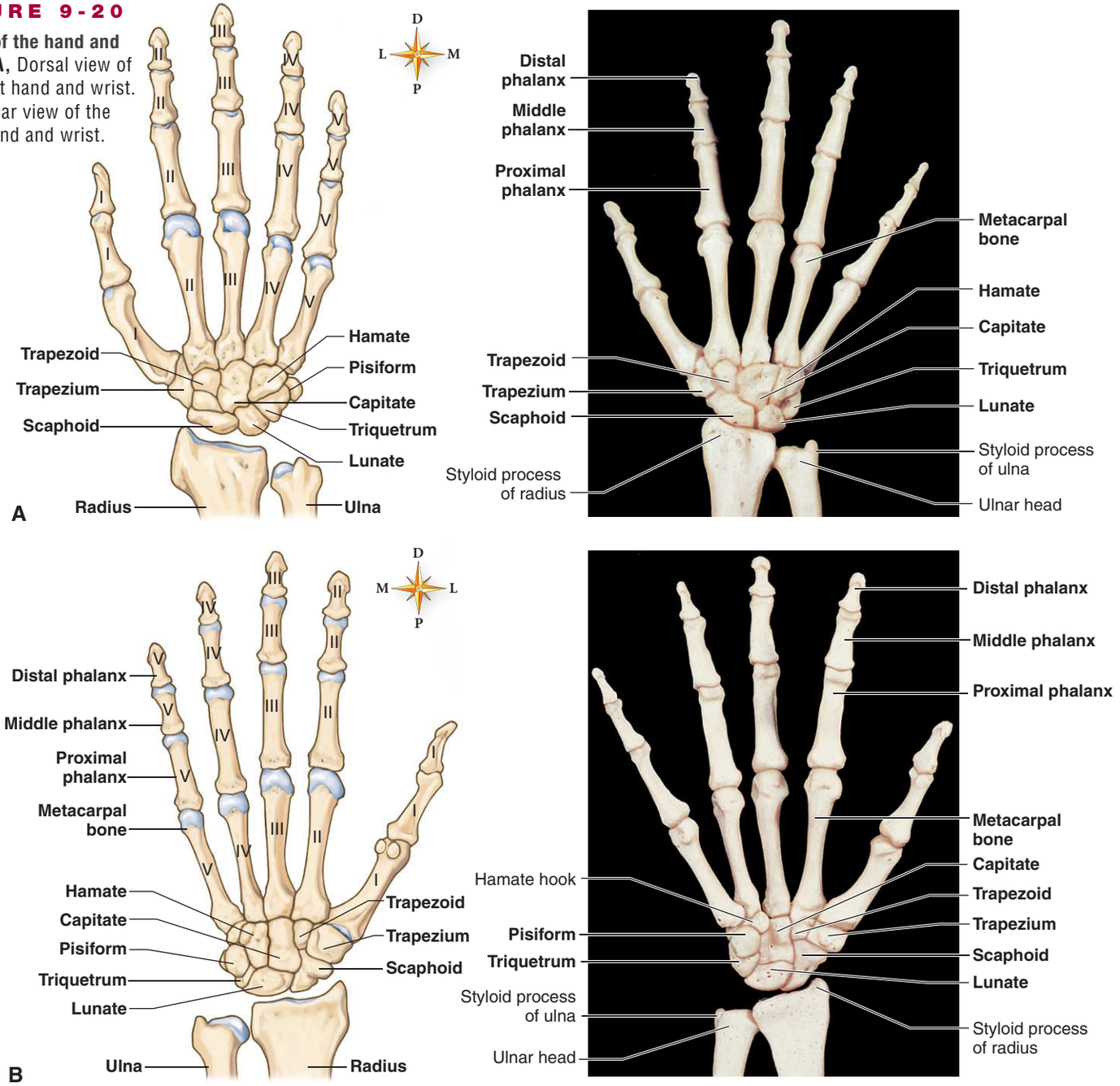
Of the five **metacarpal bones** that form the framework of the hand, the thumb metacarpal forms the most freely movable joint with the carpal bones. This fact has great significance. Because of the wide range of movement possible between the thumb metacarpal and the trapezium, particularly the ability to oppose the thumb to the fingers, the human hand has much greater dexterity than the forepaw of any animal, which has enabled humans to manipulate even small objects in their environment effectively. The heads of the metacarpal bones, prominent as the proximal knuckles of the hand, articulate with the phalanges.

| QUICK CHECK |

7. What bones make up the shoulder girdle? Where does the shoulder girdle form a joint with the axial skeleton?
8. What are the two bones of the forearm? In the anatomical position, which one is lateral?
9. Name the bones of the hand and wrist.

FIGURE 9-20

Bones of the hand and wrist. A, Dorsal view of the right hand and wrist. **B,** Palmar view of the right hand and wrist.



Lower Extremity

Bones of the hip, thigh, leg, ankle, and foot constitute the lower extremity (Table 9-8). Strong ligaments bind each **coxal bone** (*pelvic* or *hip bone*) to the sacrum posteriorly and to each other anteriorly to form the **pelvic girdle** (see Figures 9-21 and 9-26). The pelvic girdle serves as a stable, circular base that supports the trunk and attaches the lower extremities to it. In early life, each coxal bone is made up of three separate bones. Later, they fuse into a single, massive irregular bone that is broader than any other bone in the body. The largest and uppermost of the three bones is the **ilium,** the strongest and lowermost is the **ischium,** and the most anteriorly placed is the **pubis.** Numerous markings are present on the three bones (see Table 9-8 and Figures 9-21 and 9-22). (The coxal bone was formerly called the os coxae or innominate bone.)

The pelvis can be divided into two parts by an imaginary plane called the *pelvic inlet*. The edge of this plane, outlined in Figure 9-21, is called the *pelvic brim*, or *brim of the true pelvis*. The structure above the pelvic inlet, termed the **false pelvis,** is bordered by muscle in the front and by bone along the sides and back. The structure below the pelvic inlet, the so-called *true pelvis*, creates the boundary of another imaginary plane called the *pelvic outlet*. It is through the pelvic outlet that the digestive tract empties. The female reproductive tract also passes through the pelvic outlet; this is a fact of great importance in childbirth. The pelvic outlet is just large enough for the passage of a baby during delivery; however, careful positioning of the baby's head is required. Measurements such as those shown in Figure 9-21 are routinely made by obstetricians to ensure successful delivery.

Despite its apparent rigidity, the joint between the pubic portions of each coxal bone, the *pubic symphysis*, softens before delivery. This softening allows the pelvic outlet to expand to accommodate the newborn's head as it passes out of the birth canal. The tiny coccyx bone, which protrudes into the pelvic outlet, sometimes breaks when the force of labor contractions pushes the newborn's head against it.

The two thigh bones, or **femurs,** have the distinction of being the longest and heaviest bones in the body. Several prominent markings characterize them. For example, three projections are

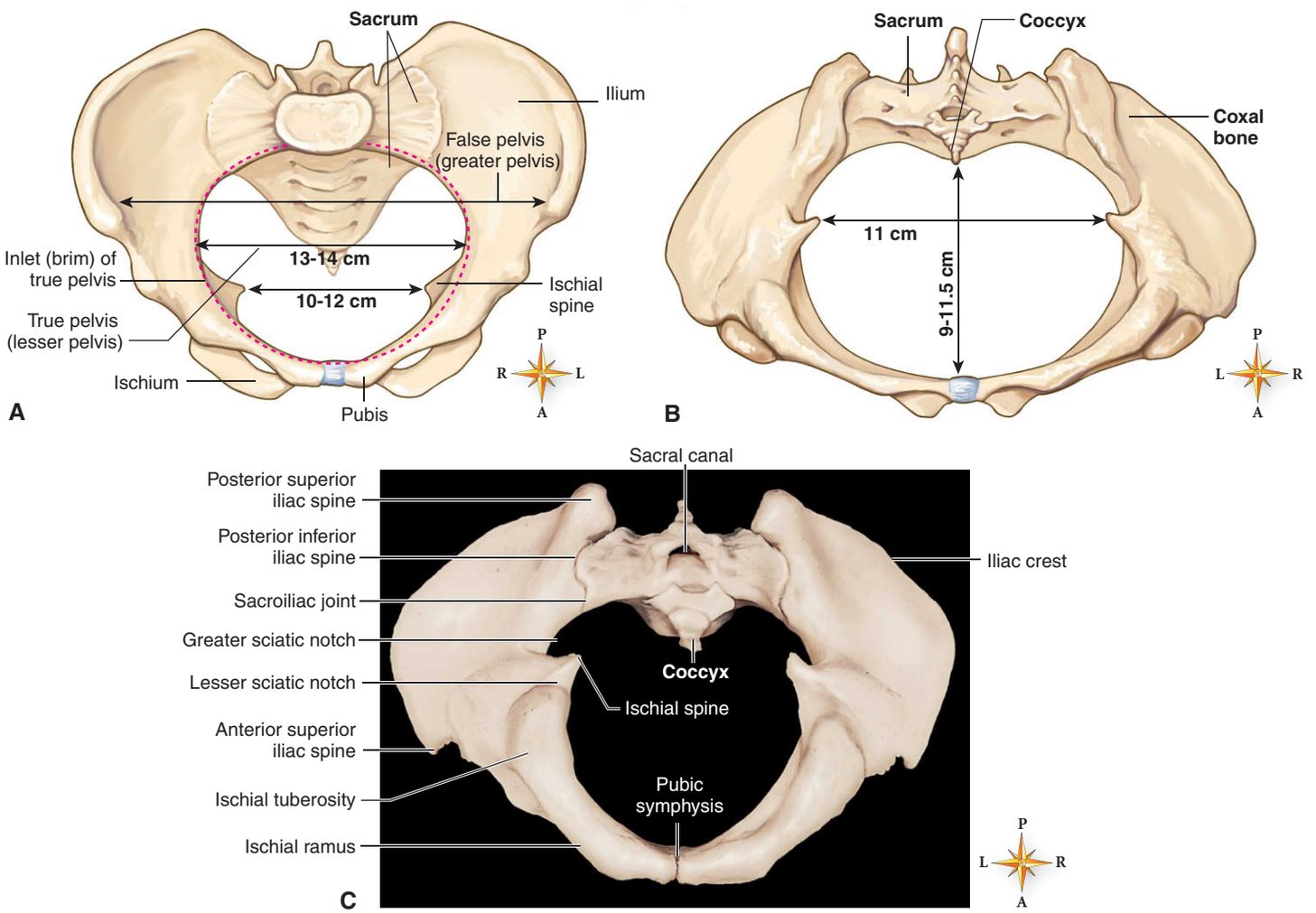


FIGURE 9-21

The female pelvis. A, Pelvis viewed from above. Note that the brim of the true pelvis (*dotted line*) marks the boundary between the superior false pelvis (*pelvis major*) and the inferior true pelvis (*pelvis minor*). **B** and **C,** Pelvis viewed from below. A comparison of the male pelvis and female pelvis is shown in Figure 9-26.

FIGURE 9-22

Left coxal (hip) bone. The left coxal bone is disarticulated from the bony pelvis and viewed from the side. Also see Figure 9-14, *H,* for a view of the right coxal bone outlining its three main regions.

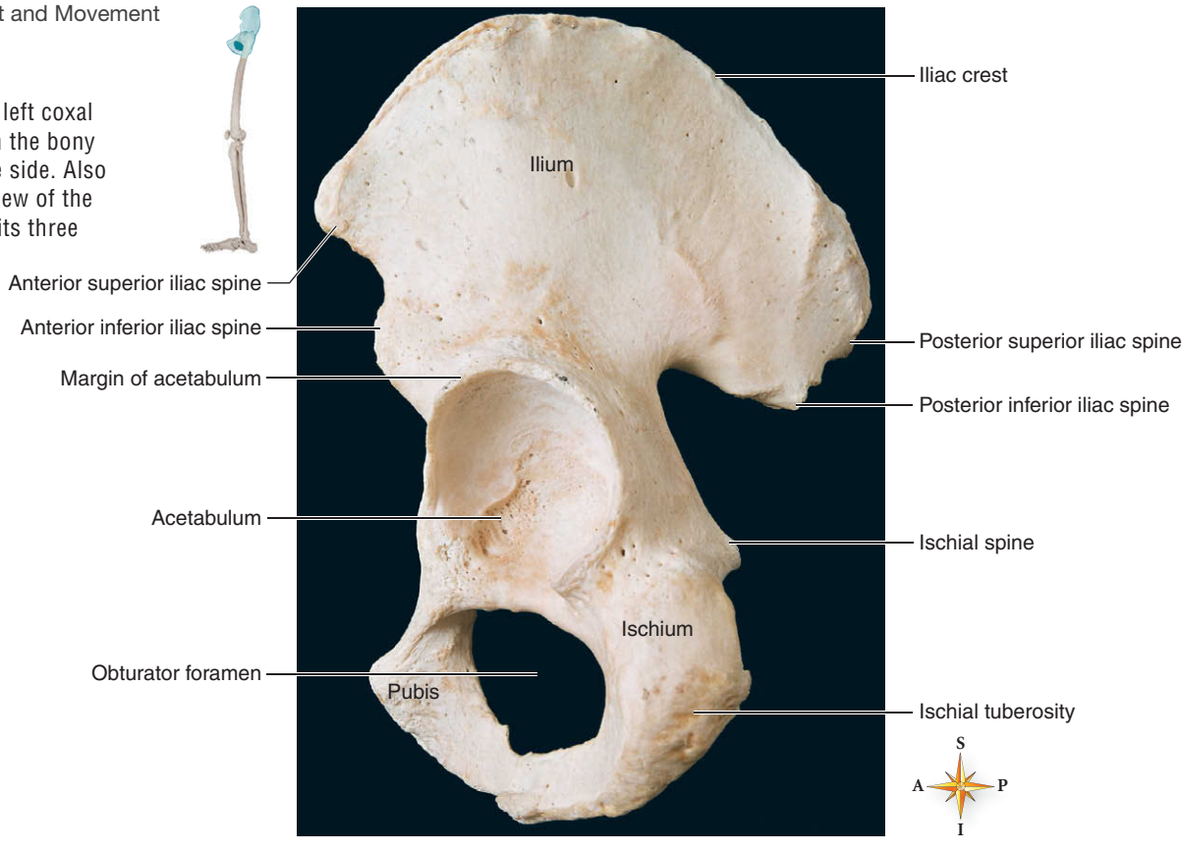


TABLE 9-8 Lower Extremity Bones and Their Markings

BONES AND MARKINGS	DESCRIPTION
Coxal	Large hip bone (pelvic bone); with the sacrum and coccyx, forms the basinlike pelvic cavity; lower extremities attached to the axial skeleton by the coxal bones
Ilium	Upper, flaring portion
Ischium	Lower, posterior portion
Pubis	Medial, anterior section
Acetabulum	Hip socket; formed by union of the ilium, ischium, and pubis
Iliac crests	Upper, curving boundary of the ilium
Iliac spines	
Anterior superior	Prominent projection at the anterior end of the iliac crest; can be felt externally as the “point” of the hip
Anterior inferior	Less prominent projection short distance below anterior superior spine
Posterior superior	At the posterior end of the iliac crest
Posterior inferior	Just below the posterior superior spine
Greater sciatic notch	Large notch on the posterior surface of the ilium just below the posterior inferior spine
Ischial tuberosity	Large, rough, quadrilateral process forming the inferior part of the ischium; in an erect sitting position the body rests on these tuberosities
Ischial spine	Pointed projection just above the tuberosity
Pubic symphysis	Cartilaginous, amphiarthrotic joint between the pubic bones
Superior pubic ramus	Part of the pubis lying between the symphysis and acetabulum; forms the upper part of the obturator foramen
Inferior pubic ramus	Part extending down from the symphysis; unites with the ischium
Pubic arch	Curve formed by the two inferior rami
Subpubic angle	Angle formed under the inferior pubic rami; generally larger in women than in men
Pubic crest	Upper margin of the superior ramus
Pubic tubercle	Rounded process at the end of the crest
Obturator foramen	Large hole in the anterior surface of the coxal bone; formed by the pubis and ischium; largest foramen in the body

TABLE 9-8 Lower Extremity Bones and Their Markings *(continued)*

BONES AND MARKINGS	DESCRIPTION
Pelvic inlet (or brim)	Boundary of the aperture leading into the true pelvis; formed by the pubic crests, iliopectineal lines, and sacral promontory; the size and shape of this inlet have obstetrical importance because if any of its diameters are too small, the infant's skull cannot enter the true pelvis for natural birth(or lesser pelvis)
True pelvis (or greater pelvis)	Space below the pelvic brim; true "basin" with bone and muscle walls and a muscle floor; pelvic organs located in this space
False pelvis (or lesser pelvis)	Broad, shallow space above the pelvic brim, or the pelvic inlet; name "false pelvis" is misleading because this space is actually part of the abdominal cavity, not the pelvic cavity
Pelvic outlet	Irregular circumference marking the lower limits of the true pelvis; bounded by the tip of the coccyx and two ischial tuberosities
Pelvic girdle (or bony pelvis)	Complete bony ring; composed of two hip bones (ossa coxae), the sacrum, and the coccyx; forms a firm base by which the trunk rests on the thighs and for attachment of the lower extremities to the axial skeleton
Femur	Thigh bone; largest, strongest bone of the body
Head	Rounded upper end of the bone; fits into the acetabulum
Neck	Constricted portion just below the head
Greater trochanter	Protuberance located inferiorly and laterally to the head
Lesser trochanter	Small protuberance located inferiorly and medially to the greater trochanter
Intertrochanteric line	Line extending between the greater and lesser trochanter
Linea aspera	Prominent ridge extending lengthwise along the concave posterior surface
Supracondylar ridges	Two ridges formed by division of the linea aspera at its lower end; the medial supracondylar ridge extends inward to the inner condyle, the lateral ridge to the outer condyle
Condyles	Large, rounded bulges at the distal end of the femur; one medial and one lateral
Epicondyles	Blunt projections from the sides of the condyles; one on the medial aspect and one on the lateral aspect
Adductor tubercle	Small projection just above the medial condyle; marks the termination of the medial supracondylar ridge
Trochlea	Smooth depression between the condyles on the anterior surface; articulates with the patella
Intercondylar fossa (notch)	Deep depression between the condyles on the posterior surface; the cruciate ligaments, which help bind the femur to the tibia, lodge in this notch
Patella	Kneecap; largest sesamoid bone of the body; embedded in the tendon of the quadriceps femoris muscle
Tibia	Shin bone
Condyles	Bulging prominences at the proximal end of the tibia; upper surfaces concave for articulation with the femur
Intercondylar eminence	Upward projection on the articular surface between the condyles
Crest	Sharp ridge on the anterior surface
Tibial tuberosity	Projection in the midline on the anterior surface
Medial malleolus	Rounded downward projection at the distal end of the tibia; forms the prominence on the medial surface of the ankle
Fibula	Long, slender bone of the lateral side of the leg
Lateral malleolus	Rounded prominence at the distal end of the fibula; forms the prominence on the lateral surface of the ankle

(continued on page 274)

conspicuous at each epiphysis: the head and greater and lesser trochanters proximally and the medial and lateral condyles and adductor tubercle distally (Figure 9-23). Both condyles and the greater trochanter may be felt externally. For a description of the various femur markings, see Table 9-8.

The largest sesamoid bone in the body, and one of the few that is almost universally present, is the **patella,** or kneecap, located in the tendon of the quadriceps femoris muscle as a projection to the underlying knee joint. Although some individuals have sesamoid bones in the tendons of other muscles, lists of bone names do not usually include them because they are not always present, are not found in any particular tendons, and are less important. (See the footnote in Table 9-1.) When the knee joint is extended, the patellar outline may be distinguished through the skin, but as the knee flexes, it sinks into the intercondylar notch of the femur and can no longer be easily distinguished.

The **tibia** is the larger and stronger and more medially and superficially located of the two leg bones. The **fibula** is smaller and more laterally and deeply placed. At its proximal end it articulates with the lateral condyle of the tibia. The proximal end of the tibia, in turn, articulates with the femur to form the knee joint, the largest and one of the most complex and frequently injured joints of the body. Distally, the tibia articulates with the fibula and also with the talus. The latter fits into a boxlike socket (ankle joint) formed by the medial and lateral malleoli, projections of the tibia and fibula, respectively. For other tibial markings, see

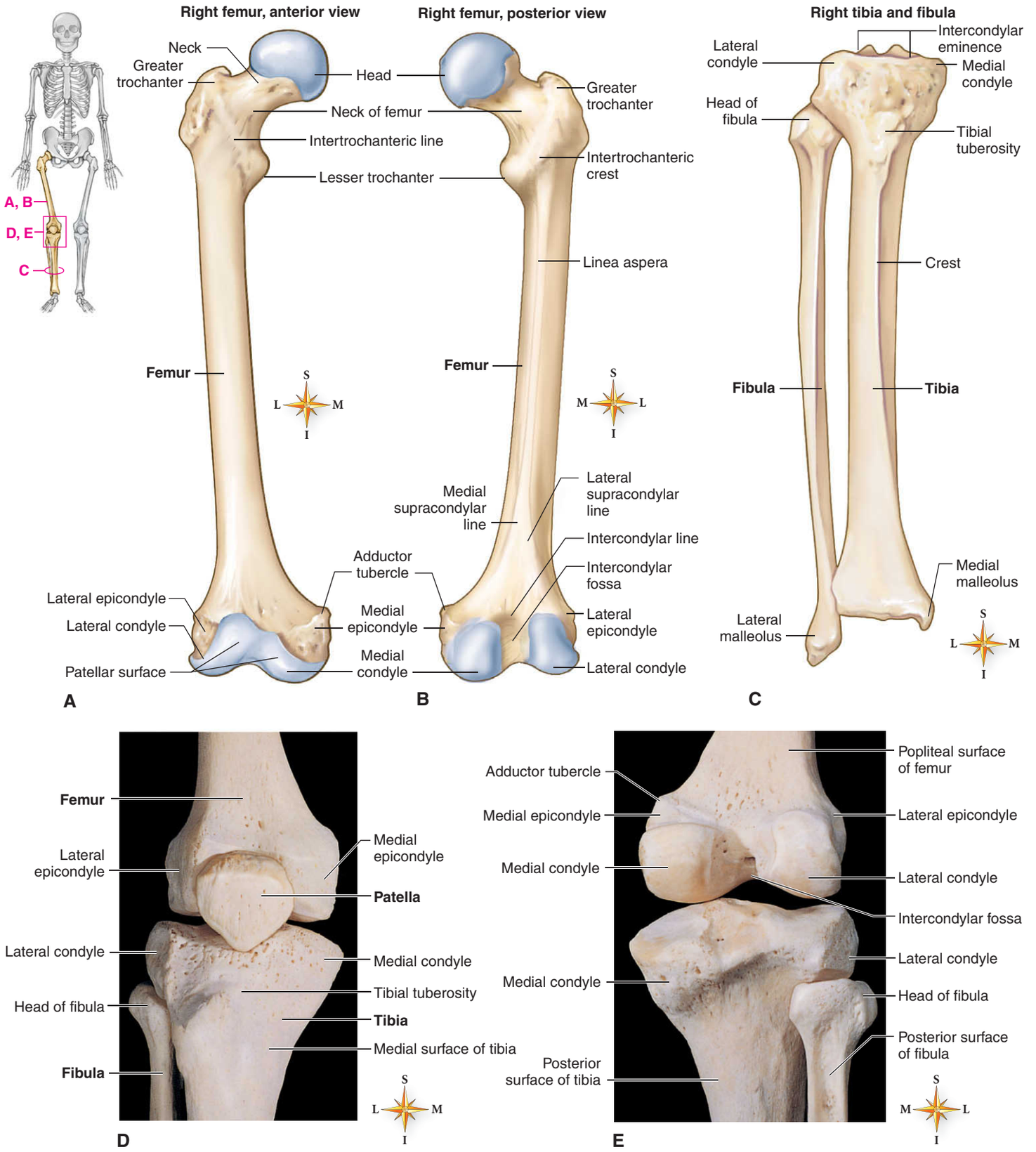


FIGURE 9-23

Bones of the thigh and leg. A, Right femur, anterior surface. **B,** Right femur, posterior view. **C,** Right tibia and fibula, anterior surface. **D,** Anterior aspect of the right knee skeleton. **E,** Right tibia and fibula, posterior aspect. (The skeleton inset shows the relative position of the bones of the thigh and leg within the entire skeleton.)

Box 9-2 | FYI

Palpable Bony Landmarks

Health professionals often identify externally palpable bony landmarks when dealing with the sick and injured. **Palpable** bony landmarks are bones that can be touched and identified through the skin. They serve as reference points in identifying other body structures.

Externally palpable bony landmarks are present throughout the body. Many skull bones, such as the zygomatic bone, can be palpated. The medial and lateral epicondyles of the humerus, the olecranon of the ulna, and the styloid process of the ulna and the radius at the wrist can be palpated on the upper extremity. The highest corner of the shoulder is the acromion process of the scapula.

When you put your hands on your hips, you can feel the superior edge of the ilium, called the iliac crest. The anterior end of the crest, called the anterior superior iliac spine, is a prominent landmark often used as a clinical reference. The sacral promontory is a prominent anteriorly projecting ridge or border on the superior aspect of the sacrum. Commonly, it serves as a palpable reference point when measuring the pelvis during obstetrical examinations. The medial malleolus of the tibia and the lateral malleolus of the fibula are prominent at the ankle. The calcaneus, or heel bone, is easily palpated on the posterior aspect of the foot. On the anterior aspect of the lower extremity, examples of palpable bony landmarks include the patella, or kneecap; the anterior border of the tibia, or shin bone; and the metatarsal bones and phalanges of the toes. Try to identify as many of the externally palpable bones of the skeleton as possible on your own body. Using these as points of reference will make it easier for you to visualize the placement of other bones that cannot be touched or palpated through the skin.

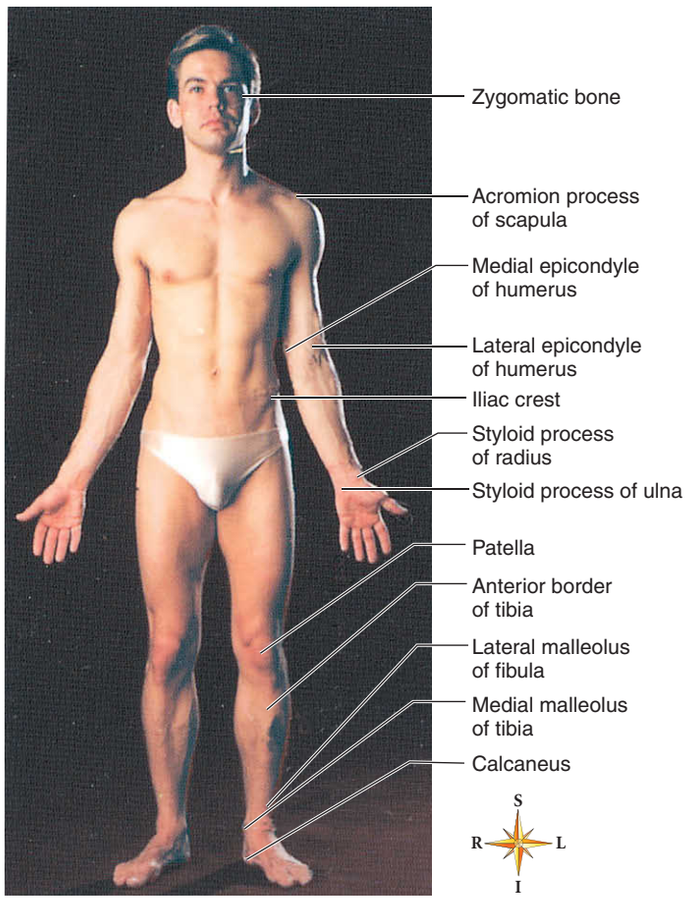


Table 9-8 and Figure 9-23. Box 9-2 explains how the malleoli and other bony prominences can be palpated through the skin.

The structure of the **foot** is similar to that of the hand, with certain differences that adapt it for supporting weight (Figure 9-24). One example is the much greater solidity and the more limited mobility of the great toe as compared to the thumb. Then, too, the foot bones are held together in such a way that they form springy lengthwise and crosswise arches (Figure 9-25). This arrangement is architecturally sound because arches furnish more supporting strength per given amount of structural material than does any other type of construction. Hence the two-way arch construction makes a highly stable base.

The **longitudinal arch** of the foot has an inner, or medial, portion and an outer, or lateral, portion. Both are formed by the placement of the tarsal and metatarsal bones. Specifically, some of the tarsal bones (calcaneus, talus, navicular, and cuneiforms) and the first three metatarsal bones (starting with the great toe) form the **medial longitudinal arch.** The calcaneus and cuboid tarsal bones plus the fourth and fifth metatarsal bones shape the **lateral longitudinal arch.** The **transverse arch** of the foot results from the relative placement of the distal row of tarsals and the five metatarsal bones. (See Table 9-8 for specific bones of different arches.)

Strong ligaments and leg muscle tendons normally hold the foot bones firmly in their arched positions. Not infrequently, however, these structures weaken and cause the arches to flatten—a condition aptly called **fallen arches,** or **flatfeet** (see Figure 9-25, *B*). Look at Figure 9-25, *D*, to see what shoes with high heels do to the position of the foot. They give a forward thrust to the body, which forces an undue amount of weight on the heads of the metatarsal bones. The resulting shift from the normal weight-bearing position of the feet may cause injury and chronic pain.

Normally, the tarsal and metatarsal bones have the major role in functioning of the foot as a supporting structure, with the phalanges being relatively unimportant. The reverse is true for the hand. Here, manipulation is the main function rather than support. Consequently, the phalanges of the fingers are all important, and the carpal and metacarpal bones are subsidiary.

In Chapter 8 the sesamoid bones were described as small rounded bones generally found embedded in the substance of tendons close to joints. The kneecap, or patella, is the largest of the sesamoid bones; other much smaller sesamoid bones are often found in tendons near the distal end (head) of the first metatarsal bone of the big toe (see Figure 9-24, *C*).

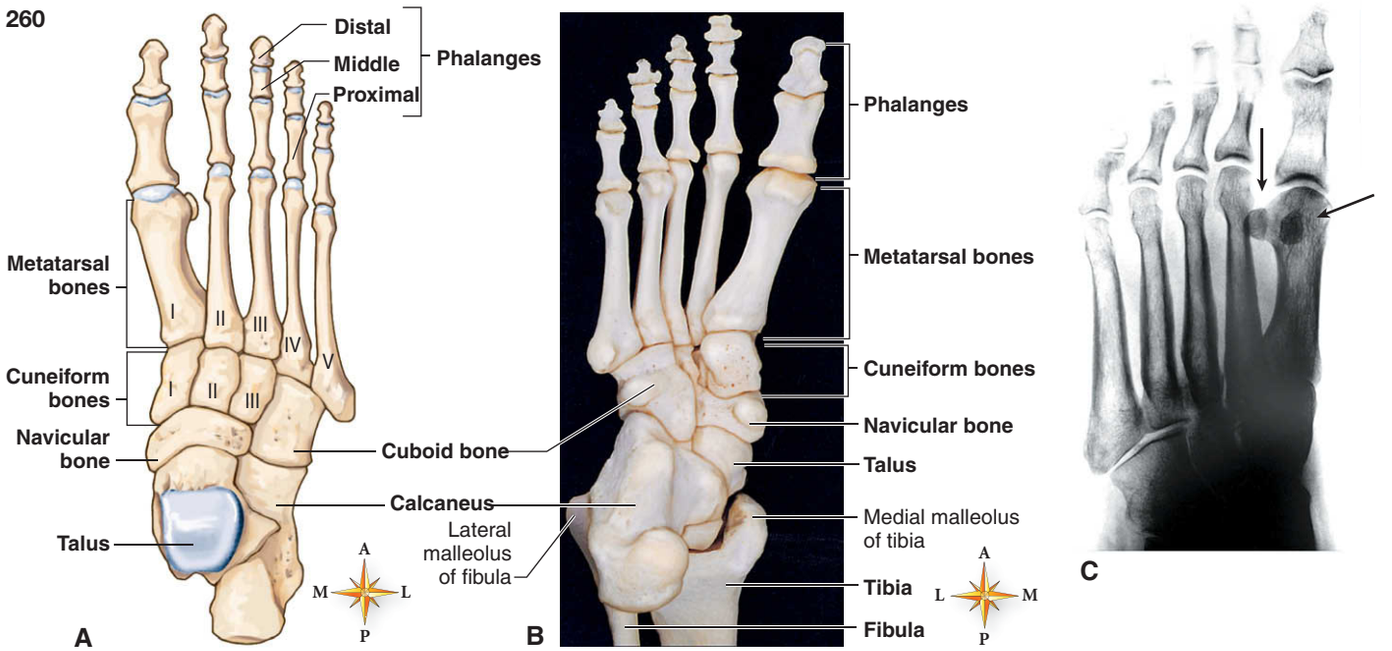


FIGURE 9-24 The foot. **A,** Bones of the right foot viewed from above. The tarsal bones consist of the cuneiforms, navicular, talus, cuboid, and calcaneus. **B,** Posterior aspect of the right ankle skeleton and inferior aspect of the right foot skeleton. **C,** X-ray film of the left foot showing prominent sesamoid bones (arrows) near the distal end (head) of the first metatarsal bone of the great toe.

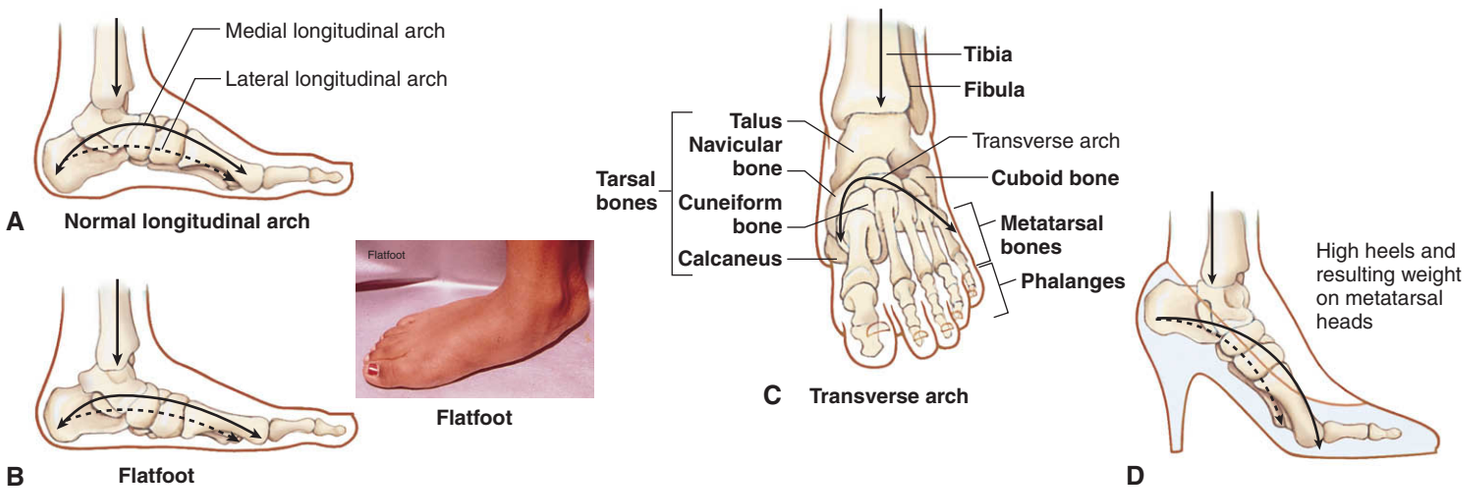


FIGURE 9-25 Arches of the foot. **A,** Longitudinal arch. The medial portion is formed by the calcaneus, talus, navicular, cuneiforms, and three metatarsal bones; the lateral portion is formed by the calcaneus, cuboid, and two lateral metatarsal bones. **B,** "Flatfoot" results when the tendons and ligaments attached to the tarsal bones are weakened. Downward pressure by the weight of the body gradually flattens out the normal arch of the bones. The photo shows the clinical appearance of a flatfoot. **C,** Transverse arch in the metatarsal region of the left foot. **D,** High heels throw the weight forward and cause the heads of the metatarsal bones to bear most of the body's weight. (*Arrows* show direction of force.)

TABLE 9-8 Lower Extremity Bones and Their Markings *(continued from p. 257)*

BONES AND MARKINGS	DESCRIPTION
Tarsal bones	Bones that form the heel and proximal or posterior half of the foot; include calcaneus, talus, navicular, cuboid, medial cuneiform (I), intermediate cuneiform (II), and lateral cuneiform (III)
Calcaneus	Heel bone
Talus	Uppermost of the tarsal bones; articulates with the tibia and fibula; boxed in the medial and lateral malleoli
Arches of foot	Curves of the bones of the foot and ankle that, along with muscles and other soft tissues, properly support the mass of the skeleton
Longitudinal arches	Tarsal and metatarsal bones so arranged as to form an arch from the front to the back of the foot
Medial	Formed by the calcaneus, talus, navicular, cuneiforms, and three medial metatarsal bones

BONES AND MARKINGS	DESCRIPTION
Lateral	Formed by the calcaneus, cuboid, and two lateral metatarsal bones
Transverse (or metatarsal) arch	Metatarsal and distal row of tarsal bones (cuneiforms and cuboid) articulated so as to form an arch across the foot; bones kept in two arched positions by means of powerful ligaments in the sole of the foot and by muscles and tendons
Metatarsal bones	Long bones of the feet; numbered (from medial side) I, II, III, IV, V
Phalanges	Miniature long bones of the toes; two in each great toe; three in the other toes; from metatarsal bone: proximal, middle (except first toe), distal; numbered (from medial side) I (except first toe), II, III, IV, V

SKELETAL DIFFERENCES BETWEEN MEN AND WOMEN

General and specific differences exist between male and female skeletons. The general difference is one of size and weight, the male skeleton being larger and heavier. The specific differences concern the shape of the pelvic bones and cavity. Whereas the male pelvis is deep and funnel shaped with a narrow subpubic angle (usually less than 90 degrees), the female pelvis, as Figure 9-26 shows, is shallow, broad, and flaring, with a wider subpubic angle (usually greater than 90 degrees). The childbearing

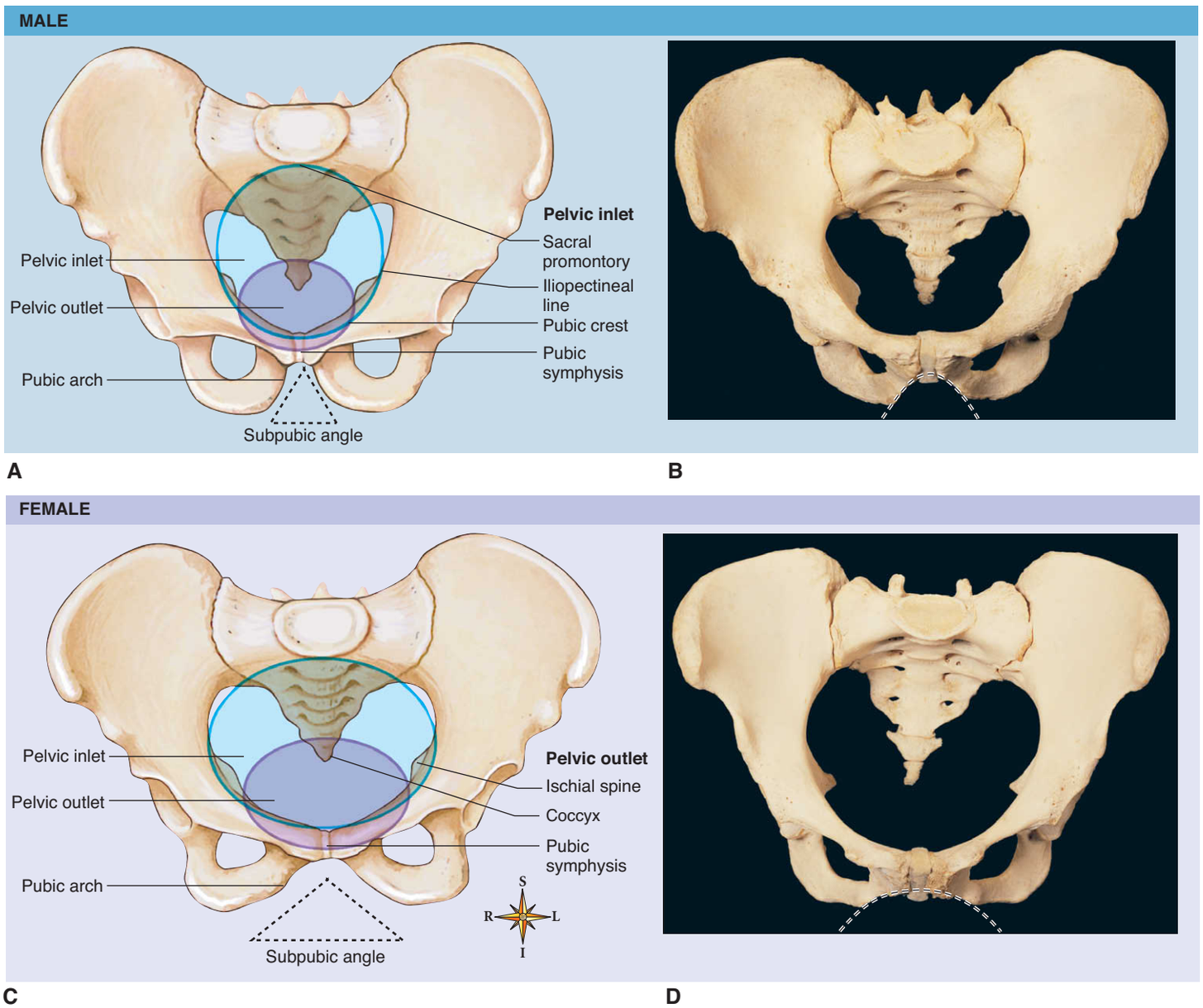


FIGURE 9-26

Comparison of the bony pelvis of the male and female skeletons. **A** and **C**, Diagrams showing components of the bony pelvis of the male and female. **B** and **D**, Photographs showing the bony pelvis of the male and female from in front and above.

TABLE 9-9 Comparison of Male and Female Skeletons

PORTION OF SKELETON	MALE	FEMALE
General form	Bones heavier and thicker Muscle attachment sites more massive Joint surfaces relatively large	Bones lighter and thinner Muscle attachment sites less distinct Joint surfaces relatively small
Skull	Forehead shorter vertically Mandible and maxillae relatively smaller Facial area rounder, with less pronounced features Processes less pronounced	Forehead more elongated vertically Mandible and maxillae relatively larger Facial area more pronounced Processes more prominent
Pelvis		
Pelvic cavity	Narrower in all dimensions Deeper Pelvic outlet relatively small	Wider in all dimensions Shorter and roomier Pelvic outlet relatively large
Sacrum	Long, narrow, with a smooth concavity (sacral curvature); sacral promontory more pronounced	Short, wide, flat concavity more pronounced in a posterior direction; sacral promontory less pronounced
Coccyx	Less movable	More movable and follows the posterior direction of the sacral curvature
Pubic arch	60- to 90-degree angle	90- to 120-degree angle
Pubic symphysis	Relatively deep	Relatively shallow
Ischial spine, ischial tuberosity, and anterior superior iliac spine	Turned more inward	Turned more outward and further apart
Greater sciatic notch	Narrow	Wide

function obviously explains the necessity for these and certain other modifications of the female pelvis. These and other differences between the skeletons of the male and female are summarized in Table 9-9.

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Check out the pictures of other skeletal differences between men and women in ***Skeletal Variations*** online at ***A&P Connect.***

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| QUICK CHECK |

10. Which three bones fuse during skeletal development to form the coxal (hip) bone?
11. List the bones of the lower extremity and indicate their positions in the skeleton.
12. What is the functional advantage of foot arches?
13. Name two differences between typical male and female skeletons.

Cycle of LIFE

Skeletal System

The changes that occur in the body's skeletal framework over the course of life result primarily from structural changes in bone, cartilage, and muscle tissues. For example, the resilience of incompletely ossified bone in young children allows their bones to withstand the mechanical stresses of childbirth and learning to walk with relatively little risk of fracturing. The density of bone and cartilage in a young to middle-aged adult permits the carrying of great loads. Loss of bone density in later adulthood can make a person so prone to fractures that simply walking or lifting with moderate force can cause bones to crack or break. Loss of skeletal tissue density may result in a compression of weight-bearing bones that causes a loss of height and perhaps an inability to maintain a standard posture. Degeneration of skeletal muscle tissue in late adulthood may also contribute to postural changes and loss of height. The effects of aging are discussed further in the Mechanisms of Disease section later in this chapter.

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Check out ***Skeletal Variations*** online at ***A&P Connect*** for graphic representations of changes in the skeleton throughout the life span.

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the BIG picture

Skeletal System

The skeletal system is a good example of increasing structural hierarchy or complexity in the body.

Recall from Chapter 1 that "levels of organization" characterize body structure so that all of our anatomical components logically fit together and function effectively (see Figure 1-3 on p. 7). In studying skeletal tissues in Chapter 8, we proceeded from the chemical level of organization (inorganic salts and organic matrix) to a discussion of the cells and tissues of bone and cartilage.

In this chapter, we have grouped skeletal tissues into discrete organs (bones) and then joined groups of individual bones together with varying numbers and kinds of other structures, such as blood vessels and nerves, to form a complex operational unit—the skeletal system. The "big picture" becomes more apparent when we integrate the skeletal system with other organ systems, which ultimately allows us to respond in a positive way to disruptions in homeostasis. The skeletal system, for example, plays a key role in purposeful movement, which in turn allows us to move away from potentially harmful stimuli. This organ system is much more than a collection of individual bones—it is a complex and interdependent functional unit essential for life.

MECHANISMS of DISEASE

SKELETAL CHANGES OVER THE LIFE SPAN

It is said that the body's aging processes begin at fertilization and continue until death. In the case of the skeletal system, a number of changes related to aging first become obvious early in uterine development. Other changes then occur at differing times and proceed at differing rates throughout life. Keep in mind that some of these changes are normal and produce positive outcomes whereas others are indicators of deterioration and disease.

Recall from Chapter 8 that flat bones enlarge during intramembranous ossification by appositional growth, which also permits the shafts of long bones to widen. It is endochondral ossification that replaces cartilaginous "models" of long bones present in the fetal skeleton with ossified matrix and then allows the new calcified bones to increase in length by interstitial growth until skeletal maturity occurs. The appearance and progression of these highly regulated skeletal aging processes is determined by genetic control factors, hormones, and other homeostatic control mechanisms.

Differing rates of bone deposition or reabsorption, including the nature and effectiveness of the remodeling process, often characterize aging-associated skeletal changes—both normal and pathological. For example, in the skull, fontanels close, sutures appear, teeth erupt, the paranasal sinuses enlarge and assume their adult placement, and the size of the cranium enlarges to accommodate a growing brain. All these changes occur in a predictable sequence over time and result from normal skeletal aging processes. In long bones, both the age of appearance of ossification centers and, later, the closure of epiphyseal growth plates are age-related skeletal changes important in clinical medicine (see Figure 8-9 on p. 207). Ossification centers (see Figure 8-8 and Figure 8-9 on p. 207) and epiphyseal growth plates appear, enlarge, mature, and close in an orderly fashion. Such orderly progression makes it possible to estimate a child's potential for growth and ultimate height from the number and location of ossification centers and the status of epiphyseal plate closures visible on radiographs. Once the epiphyseal plates in long bones ossify, they can no longer lengthen and growth in height ceases. Physicians often compare an individual's "**bone age**," which is determined by the number of ossification centers visible on a radiograph, with "**chronological age.**" This type of information can prove useful in the diagnosis or treatment of many genetic, metabolic, or inflammatory skeletal diseases characterized by abnormally rapid or delayed skeletal maturity.

In the absence of disease, new bone mass produced after puberty, and generally into the early thirties, is properly calcified but not brittle. It exhibits both the hardness and tensile strength required to resist fractures. During this period, osteoblastic activity results in the deposition of more bone than is resorbed in the remodeling process. Before puberty this process results in bones that continue to grow until they reach adult size and proportions. Instead of growth in bone size, the skeletal remodeling process in the immediate postpuberal years and, generally, into the second decade of life results in the replacement of younger and weaker bone with bone that is more dense and has higher-quality organic matrix. Thus the skeletal aging process in early adulthood produces a positive outcome—stronger bones. Unfortunately, the efficiency of the remodeling process during the next decade begins a progressive decline that can be slowed only by good nutrition and a healthy lifestyle, but never fully stopped. The negative outcomes of skeletal aging soon appear, and they continue over a lifetime.

Degenerative aging processes affect spongy bone before compact bone and generally begin between 30 and 40 years of age. In many cases, problems arise because of abnormalities in bone remodeling that result from both a decrease in osteoblasts and a gradual increase in osteoclast cell numbers and activity. In addition, the osteoblasts that are formed during late adulthood are less metabolically active and produce lower-quality bone matrix. Furthermore, in compact bone, older osteocytes tend to shrink and coalesce, resulting in the appearance of tiny, honeycomb-like open spaces. The result is bone thinning and loss of density. The

Box 9-3 | Balloon Kyphoplasty

Balloon kyphoplasty is an orthopedic procedure used to treat the vertebral compression fractures that occur in osteoporosis, as a result of certain tumors, or after prolonged use of steroid drugs. Fractured (collapsed) vertebrae (see Figure 8-22 on p. 214) result in shortened height and spinal deformity and may be the cause of chronic pain. The balloon kyphoplasty procedure involves the insertion of an inflatable balloonlike device called a **bone tamp** through a small incision in the skin and then through a channel drilled into the body of the fractured vertebra. Expansion of the balloon restores the vertebra to a normal height. The balloon is then deflated and removed, and the surgeon uses the needle to fill the cavity with a type of "super glue" bone cement that quickly hardens and thus stabilizes and seals the fracture. An earlier procedure, called **vertebroplasty,** also involves injecting bone cement, but without using a balloon. Both procedures are cost-effective, have short recovery periods, and in many cases may eliminate the need for difficult and expensive spinal surgery. However, as with all surgical procedures, both the physician and patient need to fully evaluate the risks and rewards beforehand. Specialized physician training and experience in performing the procedure are important, as is the availability of hospital spinal surgery service facilities and personnel if problems should occur.

skeleton as a whole loses strength, bones become brittle, and the risk for fracture increases.

It is the loss of trabeculae and resulting compression fractures in the spongy bone of vertebrae that cause the progressive decrease in height that is a typical consequence of aging. It's true—all of us "shrink with age." And the process begins earlier than you might think—about age 35. However, a regular weight-bearing exercise program coupled with good nutrition, especially adequate calcium and vitamin D intake, will help minimize the degenerative effects of skeletal aging.

The severe and repeated vertebral compression fractures common in osteoporosis cause not only a decrease in height but also spinal deformity and loss of mobility (Box 9-3). Recall that **osteoporosis** (see p. 216) is characterized by loss of bone mass, especially spongy bone, and demineralization of matrix. No discussion of skeletal aging is complete without emphasizing the importance of this very common and serious bone disease. You are encouraged to review the discussion of osteoporosis in Chapter 8. Unfortunately, advancing age is often accompanied by the appearance of other metabolic, genetic, or inflammatory disease conditions that affect skeletal tissues, bones, and joints.

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You can see some of the age-related changes in the skeleton for yourself at ***Skeletal Variations*** online at ***A&P Connect.***

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Bone Fractures

A *bone fracture* is defined as a partial or complete break in the continuity of a bone that most often occurs under mechanical stress. The most common cause of a fracture is traumatic injury. However, bone cancer, cysts, or metabolic bone disorders such as osteoporosis can also cause what are described as **pathological** or **spontaneous fractures.** In these types of fractures, the bone is so weak that it fractures under very little stress and in the absence of any significant trauma. Most fractures can be identified visually during physical examination or on a standard radiograph. One exception is the so-called **stress fracture,** which often occurs in the absence of any clinically visible damage to bone or surrounding tissue. In addition, most x-ray images appear normal with this type of fracture. The microscopic bone damage typical of a stress fracture frequently appears in one or more bones of the leg or foot after repetitive trauma. Long-distance (marathon) runners and ballet dancers are notoriously "at risk." Often called hidden or occult fractures because they frequently remain unseen on regular radiographs, they are clearly visible on bone scans.

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Check out ***Bone Scans*** online at ***A&P Connect.***

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A **displaced** or **open fracture,** also known as a *compound fracture* (Figure 9-27, *A*), is one in which broken bone projects through surrounding tissue and skin, thereby inviting the possibility of osteomyelitis (see p. 218) or other types of infection. A **nondisplaced** or **closed fracture,** also known as a simple fracture (Figure 9-27, *B*) does not produce a break in the skin and therefore does not pose an immediate danger of bone infection. A closed fracture that results in one end of the broken bone being driven into the marrow cavity or diaphysis of the other bone segment is called an **impacted fracture.** As Figure 9-27, *C*, shows, fractures also are classified as "complete" or "incomplete." A complete fracture involves a break across the entire section of bone, whereas an incomplete fracture involves only a partial break, with the bone fragments still being partially joined.

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The process of healing in a fractured bone is discussed in Chapter 8 (p. 213). Check out ***Bone Fractures*** online at ***A&P Connect*** for more on bone healing and types of bone fractures.

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Mastoiditis

Mastoiditis (mass-toyd-EYE-tis) is inflammation of the air spaces within the mastoid portion of the temporal bone. Infectious material may find its way into the mastoid air cells from middle ear infections and, unless treated promptly and successfully, can produce very serious medical problems. The mastoid air cells do not drain into the nose, as do the paranasal sinuses. As a result,

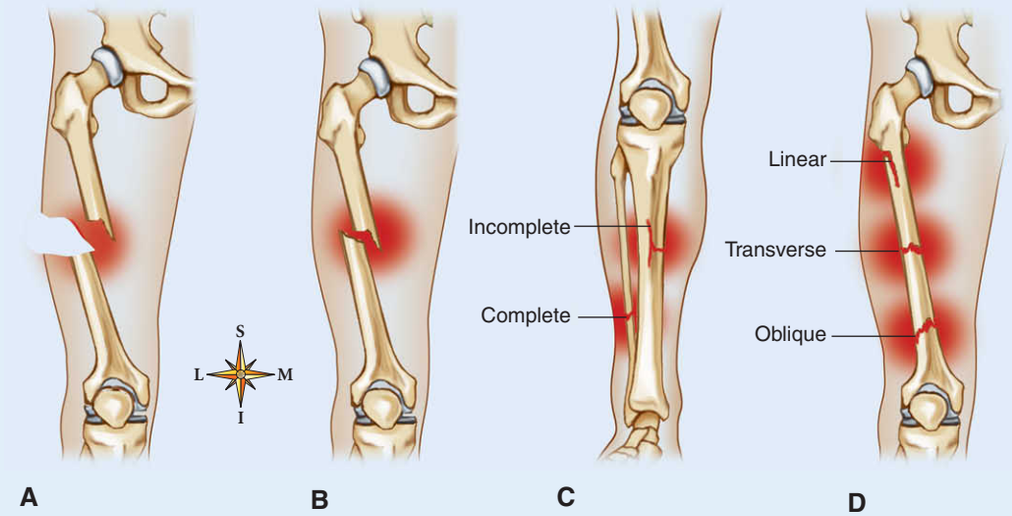


FIGURE 9-27

Bone fractures. A, Open. **B,** Closed. **C,** Incomplete and complete. **D,** Linear, transverse, and oblique.

infectious material that accumulates may erode the bony partition that separates the air cells from the cranial cavity. If such erosion develops, the inflammation may spread to the brain or its covering membranes. Infection and an accumulation of pus (abscess) may then develop in or on the surface of the brain. Should this occur, a localized infection within the middle ear and mastoid air cells in the substance of the temporal bone escalates into a life-threatening medical emergency involving the central nervous system. Externally, clinical signs of mastoiditis include redness and swelling of the external ear and the skin overlying the mastoid process. The area is very painful when touched. In severe cases, the external ear may be pushed forward and downward by the underlying swelling (Figure 9-28).

Prompt treatment of middle ear infection, or **otitis media,** with antibiotics has made life-threatening cases of mastoiditis rare. Exceptions occur in instances of antibiotic resistance or in cases of inadequate or untreated chronic middle ear infections. If intensive antibiotic therapy fails and the subsequent accumulation of infectious material that fills the middle ear and mastoid air cells threatens extension into the cranial cavity, surgical intervention may be required. A surgical incision of the eardrum is often performed to reduce pressure and release pus from the middle ear. Though rarely performed today, surgical removal of part of the diseased mastoid portion of the temporal bone, a procedure called **mastoidectomy,** may also be necessary to drain trapped infectious material from the air cells. Fortunately, modern antibiotics and prompt medical treatment have dramatically reduced the need for this procedure with its attendant scarring and hearing loss.



FIGURE 9-28

Mastoiditis. Note redness and swelling over the mastoid process of the temporal bone.

Abnormal Spinal Curvatures

The normal curvature of the spine is convex through the thoracic region and concave through the cervical and lumbar regions (see Figure 9-13). This gives the spine strength to support the weight of the rest of the body and makes it possible to also balance the weight of the body, which is necessary to stand and walk. A curved structure has more strength than does a straight one of the same size and material. Poor posture or disease may cause the lumbar curve to be abnormally accentuated—a condition known as "sway back," or **lordosis** (Figure 9-29, A). This condition is frequently

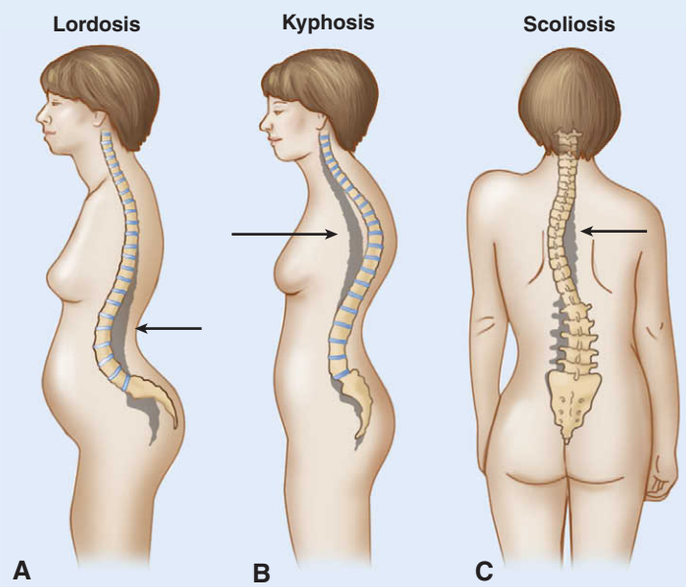


FIGURE 9-29

Abnormal spine curvatures. A, Lordosis. **B,** Kyphosis. **C,** Scoliosis. *Black arrows* highlight areas of abnormal curvature

seen during pregnancy as the woman adjusts to changes in her center of gravity. It may also be secondary to traumatic injury or a degenerative process of the vertebral bodies.

Kyphosis, or "hunchback," is an abnormally increased roundness in the thoracic curvature (Figure 9-29, *B*). It is frequently seen in elderly people with osteoporosis or chronic arthritis, those with neuromuscular diseases, or individuals with compression fractures of the thoracic vertebrae. In a condition called **Scheuermann disease,** kyphosis can develop in children at puberty.

Abnormal side-to-side curvature is called **scoliosis** (Figure 9-29, *C*). This too may be idiopathic or a result of damage to the supporting muscles along the spine. It is a relatively common condition that appears before adolescence.

All three abnormal curvatures can interfere with normal breathing, posture, and other vital functions. The degree of abnormal curvature and resulting deformity of the vertebral column determine the various treatments instituted. The traditional treatment of scoliosis is the use of a supportive brace, called the **Milwaukee brace,** that is worn on the upper part of the body 23 hours per day for up to several years. A newer approach to straightening abnormal curvature is **transcutaneous stimulation.** In this method, muscles on one side of the vertebral column are electrically stimulated to contract and pull the vertebrae into a more normal position. If these methods fail, correction may be achieved by surgical intervention in which pieces of bone from elsewhere in the skeleton, or metal rods, are grafted to the deformed vertebrae to hold them in proper alignment. If treated early enough, kyphosis resulting from poor posture can be corrected with special exercises and instructions for appropriate posture. Kyphosis resulting from pathological causes may also require special braces or surgical intervention.



Box 9-4 | SPORTS and FITNESS

Chondromalacia Patellae

Chondromalacia patellae is a degenerative process that results in softening (degeneration) of the articular surface of the patella. The symptoms associated with chondromalacia of the patella are a common cause of knee pain in many individuals—especially young athletes. The condition is usually caused by irritation of the patellar groove, with subsequent changes in the cartilage on the underside of the patella. The most common complaint is of pain arising from behind or beneath the kneecap, especially during activities that require flexion of the knee, such as climbing stairs, kneeling, jumping, or running.

LANGUAGE OF SCIENCE *(continued from p. 223)*

fontanel
(FON-tah-nel)
[*fontan-* **fountain,** *-el* **little**]

foot

frontal bone
(FRON-tal)
[*front-* **forehead,** *-al* **relating to**]

humerus
(HYOO-mer-us)
[*humerus* **arm**] *pl.,* humeri

ilium
(IL-ee-um)
[*ilium* **flank**] *pl.,* ilia

inferior nasal concha
(in-FEER-ee-or NAY-zal KONG-ke)
[*infer-* **lower,** *-or* **quality,** *nas-* **nose,** *-al* **relating to,** *concha* **sea shell**] *pl.,* conchae

ischium
(IS-kee-um)
[*ischium* **hip joint**] *pl.,* ischia

lacrimal bone
(LAK-ri-mal)
[*lacrima-* **tear,** *-al* **relating to**]

lateral longitudinal arch
(LAT-er-al lon-jih-TOO-di-nal)
[*later-* **side,** *-al* **relating to,** *longitud-* **length,** *-al* **relating to**]

longitudinal arch
(lon-ji-TOO-di-nal)
[*longitud-* **length,** *-al* **relating to**]

lumbar vertebra
(LUM-bar VER-teh-bra)
[*lumb-* **loin,** *-ar* **relating to,** *vertebra* **that which turns**] *pl.,* vertebrae

mandible
(MAN-di-bal)
[*mandere* **to chew**]

maxilla
(mak-SIH-lah)
[*maxilla* **upper jaw**] *pl.,* maxillae

medial longitudinal arch
(MEE-dee-al lon-ji-TOO-dih-nal)
[*medial* **middle,** *-al* **relating to,** *longitud* **length,** *-al* **relating to**]

metacarpal bone
(met-ah-KAR-pal)
[*meta-* **beyond,** *-carp-* **wrist,** *-al* **relating to**]

nasal bone
(NAY-zal)
[*nas-* **nose,** *-al* **relating to**]

occipital bone
(awk-SIP-it-al)
[*occipit-* **back of head,** *-al* **relating to**]

palatine bone
(PAL-ah-tine)
[*palat-* **palate (roof of mouth),** *-ine* **relating to**]

palpable
(PAL-pah-bul)
[*palp-* **touch gently,** *-able* **capable**]

parietal bone
(pah-RYE-i-tal)
[*parie-* **wall,** *-al* **relating to**]

patella
(pah-TEL-ah)
[*pat-* **dish,** *-ella* **small**] *pl.,* patellae

pelvic girdle
(PEL-vic GER-dul)
[*pelvi-* **basin,** *-ic* **relating to**]

pubis
(PYOO-biss)
[*pubis* **groin**] *pl.,* pubes

radius
(RAY-dee-us)
[*radius* **ray**] *pl.,* radii

scapula
(SKAP-yoo-lah)
[*scapula* **shoulder blade**] *pl.,* scapulae

shoulder girdle

sinus
(SYE-nus)
[*sinus* **hollow**]

sphenoid bone
(SFEE-noyd)
[*spheno-* **wedge,** *-oid* **like**]

sternum
(STER-num)
[*sternum* **breastbone**] *pl.,* sterna or sternums

suture
(SOO-chur)
[*sutur-* **seam**]

temporal bone
(TEM-poh-ral)
[*tempora-* **temple (of head),** *-al* **relating to**]

thoracic vertebra
(thoh-RASS-ik VER-teh-bra)
[*thorac-* **chest,** *-ic* **relating to,** *vertebra* **that which turns**] *pl.,* vertebrae

thorax
(THOH-raks)
[*thorax* **chest**] *pl.,* thoraces

tibia
(TIB-ee-ah)
[*tibia* **shin bone**] *pl.,* tibiae or tibias

transverse arch

ulna
(UL-nah)
[*ulna* **elbow**] *pl.,* ulnae or ulnas

vertebra
(VER-teh-bra)
[*vertebra* **that which turns**] *pl.,* vertebrae

vomer bone
(VOH-mer)
[*vomer* **plowshare**]

zygomatic bone
(zye-goh-MAT-ik)
[*zygo-* **union or yoke**, *-ic* **relating to**]

LANGUAGE OF MEDICINE

balloon kyphoplasty
(KYE-foh-plas-tee)
[*kypho-* **hump**, *-plasty* **surgical repair**]

bone age

bone tamp

chondromalacia patellae
(kon-droh-mah-LAY-shee-ah pah-TEL-ah)
[*chondro-* **cartilage**, *-malacia* **softening**, *pat-* **dish**, *-ella* **small**]

chronological age

complete fracture

displaced (open) fracture

fallen arches (flatfeet)

impacted fracture

incomplete fracture

kyphosis
(kye-FOH-sis)
[*kypho-* **hump**, *-osis* **condition**]

lordosis
(lor-DOH-sis)
[*lordos-* **bent backward**, *-osis* **condition**]

mastoidectomy
(mass-toyd-EK-toh-mee)
[*mast-* **breast**, *-oid-* **like**, *-ec-* **out**, *-tom-* **cut**, *-y* **action**]

mastoiditis
(mass-toyd-EYE-tis)
[*mast-* **breast**, *-oid-* **like**, *-itis* **inflammation**]

Milwaukee brace
(mil-WAWK-ee)
[*Milwaukee* **after the city in Wisconsin, U.S.A.**]

nondisplaced (closed) fracture

otitis media
(oh-TYE-tis MEE-dee-ah)
[*oti-* **ear**, *-itis* **inflammation**]

pathological (spontaneous) fracture

Scheuermann disease
(SHOY-er-man)
[*Holger W. Scheuermann,* **Danish surgeon**]

scoliosis
(skoh-lee-OH-sis)
[*scolio-* **twisted or crooked**, *-osis* **condition**]

stress fracture

transcutaneous stimulation
(trans-kyoo-TAYNE-ee-us)
[*trans-* **across**, *-cut-* **skin**, *-ous* **made of**]

vertebroplasty
(ver-tee-broh-PLAS-tee)
[*vertebra* **that which turns**, *-plasty* **surgical repair**]

UNIT 2

CASE study



No matter how much he turned the steering wheel, Robert's car just kept veering directly toward the guardrail as it slid across the black ice. The impact from the car slamming against an immovable object was horrendous. Even though he was wearing his seat belt, Robert was thrown violently forward and sideways as the car and railing collided. After the car came to a jolting stop, Robert's first thought was to unbuckle his seat belt so he could get out of the car, but a severe pain in his chest kept him from moving. Thankfully, the paramedics were on the scene in a matter of minutes. They gently moved Robert from his car to a backboard and strapped his head in place.

In the emergency department, a nurse gave Robert the news: his spine was fractured at "T6"; his fourth and fifth ribs were cracked; and he had a broken mandible and a shattered tibia.

1. Which bone in the spine was fractured?
   a. Thyroid vertebra
   b. Tibia
   c. Tarsal
   d. Thoracic vertebra
2. What is another name for the fourth and fifth ribs that were cracked in the accident?
   a. Floating ribs
   b. False ribs
   c. True ribs
   d. Costal ribs
3. What daily activity will be affected most by his broken mandible?
   a. Walking
   b. Eating
   c. Writing
   d. Sitting
4. What daily activity will be affected most by his shattered tibia?
   a. Walking
   b. Eating
   c. Writing
   d. Sitting

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

INTRODUCTION

A. Skeletal tissues form bones—the organs of the skeletal system
B. The relationship of bones to each other and to other body structures provides a basis for understanding the function of other organ systems
C. The adult skeleton is composed of 206 separate bones

DIVISIONS OF THE SKELETON (FIGURE 9-1; TABLE 9-1)

A. Axial skeleton—the 80 bones of the head, neck, and torso; composed of 74 bones that form the upright axis of the body and six tiny middle ear bones
B. Appendicular skeleton—the 126 bones that form the appendages to the axial skeleton; the upper and lower extremities

AXIAL SKELETON

A. Skull—made up of 28 bones in two major divisions: cranial bones and facial bones (Figures 9-2 to 9-7; Table 9-3)
   1. Cranial bones
      a. Frontal bone (Figure 9-8, *C*)
         (1) Forms the forehead and anterior part of the top of the cranium
         (2) Contains the frontal sinuses
         (3) Forms the upper portion of the orbits
         (4) Forms the coronal suture with the two parietal bones
      b. Parietal bones (Figure 9-8, *A*)
         (1) Form the bulging top of the cranium
         (2) Form several sutures: lambdoid suture with the occipital bone; squamous suture with the temporal bone and part of the sphenoid; and coronal suture with the frontal bone
      c. Temporal bones (Figure 9-8, *B*)
         (1) Form the lower sides of the cranium and part of the cranial floor
         (2) Contain the inner and middle ears
      d. Occipital bone (Figure 9-8, *D*)
         (1) Forms the lower, posterior part of the skull
         (2) Forms immovable joints with three other cranial bones and a movable joint with the first cervical vertebra
      e. Sphenoid bone (Figure 9-8, *E*)
         (1) A bat-shaped bone located in the central portion of the cranial floor
         (2) Anchors the frontal, parietal, occipital, and ethmoid bones and forms part of the lateral wall of the cranium and part of the floor of each orbit (Figure 9-7)
         (3) Contains the sphenoid sinuses
      f. Ethmoid bone (Figure 9-8, *F*)
         (1) A complex, irregular bone that lies anterior to the sphenoid and posterior to the nasal bones
         (2) Forms the anterior cranial floor, medial orbit walls, upper parts of the nasal septum, and sidewalls of the nasal cavity
         (3) The cribriform plate is located in the ethmoid
   2. Facial bones (Table 9-4)
      a. Maxilla (upper jaw) (Figure 9-8, *H*)
         (1) Two maxillae form the keystone of the face
         (2) Maxillae articulate with each other and with the nasal, zygomatic, inferior concha, and palatine bones
         (3) Forms parts of the orbital floors, roof of the mouth, and floor and sidewalls of the nose
         (4) Contains maxillary sinuses
      b. Mandible (lower jaw) (Figure 9-8, *M*)
         (1) Largest, strongest bone of the face
         (2) Forms the only movable joint of the skull with the temporal bone
      c. Zygomatic bone (Figure 9-8, *I*)
         (1) Shapes the cheek and forms the outer margin of the orbit
         (2) Forms the zygomatic arch with the zygomatic process of the temporal bones
      d. Nasal bone (Figures 9-8, *L* and 9-10)
         (1) Both nasal bones form the upper part of the bridge of the nose, whereas cartilage forms the lower part
         (2) Articulates with the ethmoid, nasal septum, frontal bone, maxillae, and the other nasal bone
      e. Lacrimal bone (Figure 9-8, *K*)
         (1) Paper-thin bone that lies just posterior and lateral to each nasal bone
         (2) Forms the nasal cavity and medial wall of the orbit
         (3) Contains a groove for the nasolacrimal (tear) duct
         (4) Articulates with the maxilla, frontal, and ethmoid bones
      f. Palatine bone (Figure 9-8, *J*)
         (1) Two bones form the posterior part of the hard palate
         (2) Vertical portion forms the lateral wall of the posterior part of each nasal cavity
         (3) Articulates with the maxillae and the sphenoid bone
      g. Inferior nasal conchae (turbinates)
         (1) Form the lower edge projecting into the nasal cavity and form the nasal meatus
         (2) Articulate with ethmoid, lacrimal, maxillary, and palatine bones
      h. Vomer bone (Figure 9-8, *G*)
         (1) Forms the posterior portion of the nasal septum
         (2) Articulates with the sphenoid, ethmoid, palatine, and maxillae
B. Eye orbits (Figure 9-7)
   1. Right and left eye orbits
      a. Contain eyes, associated eye muscles, lacrimal apparatus, blood vessels, and nerves
      b. Thin and fragile orbital walls separate orbital structures from the cranial and nasal cavities and paranasal sinuses
C. Fetal skull (Figure 9-11)

1. Characterized by unique anatomical features not seen in adult skull
2. Fontanels or "soft spots" (4) allow the skull to "mold" during the birth process and also allow for rapid growth of the brain (Table 9-5)
3. Permits differential growth or appearance of skull components over time
   a. Face—smaller proportion of total cranium at birth (⅛) than in adult (½)
   b. Head at birth is ¼ the total height; at maturity about ⅛ body height
   c. Sutures appear with skeletal maturity (Table 9-5)
   d. Paranasal sinuses—change in size and placement with skeletal maturity (Figure 9-9)
   e. Appearance of deciduous and, later, permanent teeth

D. Hyoid bone (Figure 9-12)
1. U-shaped bone located just above the larynx and below the mandible
2. Suspended from the styloid processes of the temporal bone
3. Only bone in the body that articulates with no other bones

E. Vertebral column (Figure 9-13)
1. Forms the flexible longitudinal axis of the skeleton
2. Consists of 24 vertebrae plus the sacrum and coccyx
3. Segments of the vertebral column:
   a. Cervical vertebrae, 7
   b. Thoracic vertebrae, 12
   c. Lumbar vertebrae, 5
   d. Sacrum—in adults, results from the fusion of five separate vertebrae
   e. Coccyx—in adults, results from the fusion of four or five separate vertebrae
4. Characteristics of the vertebrae (Figures 9-14; Table 9-6)
   a. All vertebrae, except the first, have a flat, rounded body anteriorly and centrally, a spinous process posteriorly, and two transverse processes laterally
   b. All but the sacrum and coccyx have a vertebral foramen
   c. Second cervical vertebrae has an upward projection, the dens, to allow rotation of the head
   d. Seventh cervical vertebra has a long, blunt spinous process
   e. Each thoracic vertebra has articular facets for the ribs
5. Vertebral column as a whole articulated with the head, ribs, and iliac bones
6. Individual vertebrae articulate with each other in joints between their bodies and between their articular processes

F. Sternum (Figure 9-15)
1. Dagger-shaped bone in the middle of the anterior chest wall made up of three parts:
   a. Manubrium—the upper handle part
   b. Body—middle blade part
   c. Xiphoid process—blunt cartilaginous lower tip, which ossifies during adult life
2. Manubrium articulates with the clavicle and first rib
3. Next nine ribs join the body of the sternum, either directly or indirectly, by means of the costal cartilages

G. Ribs (Figures 9-15 and 9-16)
1. Twelve pairs of ribs, with the vertebral column and sternum, form the thorax
2. Each rib articulates with the body and transverse process of its corresponding thoracic vertebra
3. Ribs 2 through 9 articulate with the body of the vertebra above
4. From its vertebral attachment, each rib curves outward, then forward and downward
5. Rib attachment to the sternum:
   a. Ribs 1 through 8 join a costal cartilage that attaches it to the sternum
   b. Costal cartilage of ribs 8 through 10 joins the cartilage of the rib above to be indirectly attached to the sternum
   c. Ribs 11 and 12 are floating ribs because they do not attach even indirectly to the sternum

APPENDICULAR SKELETON

A. Upper extremity (Table 9-7)
1. Consists of the bones of the shoulder girdle, upper and lower parts of the arm, wrist, and hand
2. Shoulder girdle (Figure 9-17)
   a. Made up of the scapula and clavicle
   b. Clavicle forms the only bony joint with the trunk, the sternoclavicular joint
   c. At its distal end, the clavicle articulates with the acromion process of the scapula
3. Humerus (Figures 9-18 and 9-19)
   a. The long bone of the upper part of the arm
   b. Articulates proximally with the glenoid fossa of the scapula and distally with the radius and ulna
4. Ulna
   a. The long bone found on the little finger side of the forearm
   b. Articulates proximally with the humerus and radius and distally with a fibrocartilaginous disk
5. Radius
   a. The long bone found on the thumb side of the forearm
   b. Articulates proximally with the capitulum of the humerus and the radial notch of the ulna; articulates distally with the scaphoid and lunate carpal bones and with the head of the ulna
6. Carpal bones (Figure 9-20)
   a. Eight small bones that form the wrist
   b. Carpal bones are bound closely and firmly by ligaments and form two rows of four carpals each
      (1) Proximal row is made up of the pisiform, triquetrum, lunate, and scaphoid
      (2) Distal row is made up of the hamate, capitate, trapezoid, and trapezium
   c. The joints between the radius and carpal bones allow wrist and hand movements
7. Metacarpal bones
   a. Form the framework of the hand
   b. The thumb metacarpal forms the most freely movable joint with the carpal bones
   c. Heads of the metacarpal bones (the knuckles) articulate with the phalanges

B. Lower extremity
1. Consists of the bones of the hip, thigh, leg, ankle, and foot (Table 9-8)

2. Pelvic girdle is made up of the sacrum and the two coxal bones bound tightly by strong ligaments (Figure 9-21)
   a. A stable circular base that supports the trunk and attaches the lower extremities to it
   b. Each coxal bone is made up of three bones that fuse together (Figure 9-22):
      (1) Ilium—largest and uppermost
      (2) Ischium—strongest and lowermost
      (3) Pubis—anterior most
3. Femur—longest and heaviest bone in the body (Figure 9-23)
4. Patella—largest sesamoid bone in the body
5. Tibia
   a. The larger, stronger, and more medially and superficially located of the two leg bones
   b. Articulates proximally with the femur to form the knee joint
   c. Articulates distally with the fibula and talus
6. Fibula
   a. The smaller, more laterally and deeply placed of the two leg bones
   b. Articulates with the tibia
7. Foot (Figures 9-24 and 9-25)
   a. Structure is similar to that of the hand with adaptations for supporting weight
   b. Foot bones are held together to form spring arches
      (1) Medial longitudinal arch is made up of the calcaneus, talus, navicular, cuneiforms, and medial three metatarsal bones
      (2) Lateral longitudinal arch is made up of the calcaneus, cuboid, and fourth and fifth metatarsal bones

SKELETAL DIFFERENCES BETWEEN MEN AND WOMEN

A. Male skeleton is larger and heavier than female skeleton
B. Pelvic differences (Figure 9-26; Table 9-9)
   1. Male pelvis—deep and funnel-shaped with a narrow pubic arch
   2. Female pelvis—shallow, broad, and flaring with a wider pubic arch

CYCLE OF LIFE: THE SKELETAL SYSTEM

A. Changes in the skeleton begin at fertilization and continue over a lifetime; changes can be positive or negative
B. Incompletely ossified skeleton in children provides the resiliency needed to withstand stress without breaking easily
C. Dense bone structure in young and middle adulthood permits bearing heavy loads
D. In later adulthood, reduced bone density makes fractures more likely and causes changes in posture and overall height
E. Details of aging effects are found in Mechanisms of Disease section

THE BIG PICTURE: SKELETAL SYSTEM

A. Skeletal system is a good example of increasing structural hierarchy in the body
   1. Skeletal tissues grouped into discrete organs—bones
   2. Skeletal system consists of bones, blood vessels, nerves, and other tissues grouped to form a complex operational unit
   3. Integration of skeletal system with other body organ systems permits homeostasis to occur
   4. Skeletal system more than a collection of individual bones—it represents a complex and interdependent functional unit of the body

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Describe the skeleton as a whole and identify its two major subdivisions.
2. Identify and differentiate the bones in the cranium and face.
3. Name and locate the fontanels and sutures of the skull.
4. Name the five pairs of bony sinuses in the skull.
5. Discuss the clinical (medical) importance of the cribriform plate of the ethmoid bone and the mastoid air cells in the temporal bone.
6. Identify and discuss the normal primary and secondary curves of the spine.
7. Describe and distinguish between the different kinds of bone fractures and discuss symptoms and treatments of broken bones.
8. Identify the bony components of the thorax.
9. Identify the bones of the shoulder and pelvic girdles.
10. Identify, compare, and organize the bones of the arm, forearm, wrist, and hand with those of the thigh, leg, ankle, and foot.
11. Discuss the arches of the foot and point out the functional importance of each.
12. Describe the role of the pubic symphysis during childbirth.
13. Describe vertebroplasty.

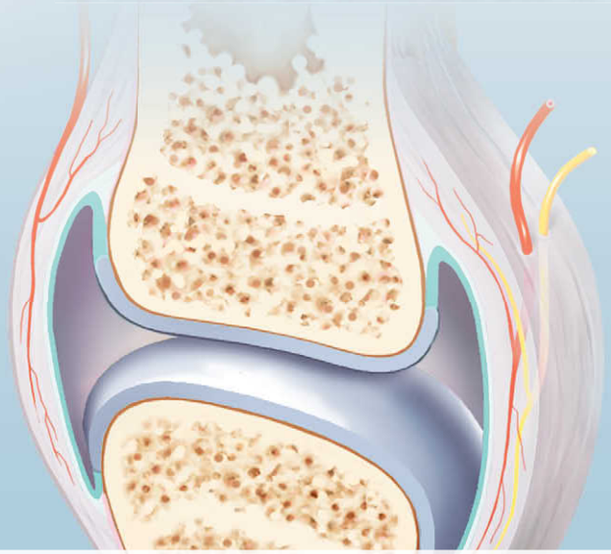
CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. How would you compare and contrast the differences between the skeletal structure of males and females? What are the physiological reasons for these differences?
2. What are some functional advantages of the fontanels of a baby's skull during the birth process?
3. Explain how the shoulder and pelvic girdles stabilize the appendages.
4. What are some of the functions of foramina in the skeleton?
5. What is the functional advantage of having air spaces in skull bones? What is a disadvantage to having these spaces lined with mucous membrane?
6. Why do many bones of the skeleton have prominent bumps? What is their purpose?

10 Articulations



CHAPTER OUTLINE

HINT *Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.*

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LANGUAGE OF SCIENCE

HINT *Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.*

abduction
(ab-DUK-shun)
[*ab-* **away,** *-duct-* **lead,** *-tion* **process**]

adduction
(ad-DUK-shun)
[*ad-* **toward,** *-duct-* **lead,** *-tion* **process**]

amphiarthrosis
(am-fee-ar-THROH-sis)
[*amphi-* **both sides,** *-arthr-* **joint,** *-osis* **condition**] *pl.,* amphiarthroses

angular movement

articular cartilage
(ar-TIK-yoo-lar KAR-ti-lij)
[*artic-* **joint,** *-ul-* **little,** *-ar* **relating to,** *cartilag* **cartilage**]

articulation
(ar-tik-yoo-LAY-shun)
[*artic-* **joint,** *-ul-* **little,** *-ation* **state**]

biaxial joint
(bye-AK-see-al)
[*bi-* **two,** *-axi-* **axle,** *-al* **relating to**]

bursa
(BER-sah)
[*bursa* **purse**] *pl.,* bursae

carpometacarpal joint
(kar-po-met-ah-KAR-pal)
[*carpo-* **wrist,** *-meta-* **beyond,** *-carp-* **wrist,** *-al* **relating to**]

circular movement

circumduction
(ser-kum-DUK-shun)
[*circum-* **around,** *-duct* **lead**]

depression
[*de-* **down,** *-press-* **press,** *-sion* **process**]

diarthrosis
(dye-ar-THROH-sis)
[*dia-* **between,** *-arthr-* **joint,** *-osis* **condition**] *pl.,* diarthroses

continued on p. 271

An articulation, or joint, is a point of contact between bones. Although most joints in the body allow considerable movement, some are completely immovable or permit only limited motion or motion in only one plane or direction. In the case of immovable joints, such as the sutures of the skull, adjacent bones are bound together into a strong and rigid protective plate. In other joints, movement is possible but highly restricted. For example, joints between the bodies of the spinal vertebrae perform two seemingly contradictory functions. They help firmly bind the components of the spine to each other and yet permit normal, but restricted movement to occur. Most joints in the body allow considerable movement to occur as a result of skeletal muscle contractions. It is the existence of such joints that permits us to execute complex, highly coordinated, and purposeful movements. Functional articulations between bones in the extremities, such as the shoulder, elbow, hip, and knee, contribute to controlled and graceful movement and provide a large measure of our enjoyment of life. This chapter begins by classifying joints and describing their identifying features. Coverage of joint classification and structure is followed by a discussion of body movements and a description of selected major joints. The chapter concludes by describing life cycle changes and some common joint diseases.

CLASSIFICATION OF JOINTS

Joints may be classified into three major categories by using a structural or a functional scheme. If a *structural classification* is used, joints are named according to the type of connective tissue that joins the bones together (fibrous or cartilaginous joints) or by the presence of a fluid-filled joint capsule (synovial joints). If a *functional classification* scheme is used, joints are divided into three classes according to the degree of movement they permit: **synarthroses** (immovable), **amphiarthroses** (slightly movable), and **diarthroses** (freely movable). Table 10-1 classifies joints according to structure, function, and range of movement. Refer often to this Table and to the illustrations that follow as you read about each of the major joint types in this chapter.

Fibrous Joints (Synarthroses)

The articulating surfaces of bones that form fibrous joints fit closely together. The different types and amount of connective tissue joining bones in this group may permit very limited movement in some fibrous joints, but most are fixed. There are three subtypes of fibrous joints: *syndesmoses*, *sutures*, and *gomphoses*.

SYNDESMOSES

Syndesmoses (SIN-dez-MO-seez) are joints in which fibrous bands (ligaments) connect two bones. The joint between the distal ends of the radius and ulna is joined by the *radioulnar interosseous ligament* (Figure 10-1). Although this joint is classified as a fibrous joint, some movement is possible because of ligament flexibility.

SUTURES

Sutures are found only in the skull. In most sutures, teethlike projections jut out from adjacent bones and interlock with each other with only a thin layer of fibrous tissue between them. Sutures become ossified in older adults and form extremely strong lines of fusion between opposing skull bones (see Figure 10-1).

GOMPHOSES

Gomphoses (gom-FOH-seez) are unique joints that occur between the root of a tooth and the alveolar process of the mandible or maxilla (see Figure 10-1). The fibrous tissue between the tooth's root and the alveolar process is a sheet made up of tiny ligaments and called the *periodontal membrane*.

Cartilaginous Joints (Amphiarthroses)

The bones that articulate to form cartilaginous joints are joined together by either hyaline cartilage or fibrocartilage. Joints characterized by the presence of hyaline cartilage between articulating bones are called *synchondroses*, and those joined by fibrocartilage are called *symphyses*. Cartilaginous joints permit only very limited movement between articulating bones in certain circumstances. During childbirth, for example, slight movement at the pubic symphysis facilitates the baby's passage through the pelvis.

SYNCHONDROSES

Note that joints identified as **synchondroses** (SIN-kon-DROH-seez) have hyaline cartilage between articulating bones. One example of a synchondrosis is the joint between the sphenoid bone and the

TABLE 10-1 Primary Joint Classifications

FUNCTIONAL NAME	STRUCTURAL NAME	DEGREE OF MOVEMENT PERMITTED	EXAMPLE
Synarthroses	Fibrous	Immovable	Sutures of the skull
Amphiarthroses	Cartilaginous	Slightly movable	Pubic symphysis
Diarthroses	Synovial	Freely movable	Shoulder joint

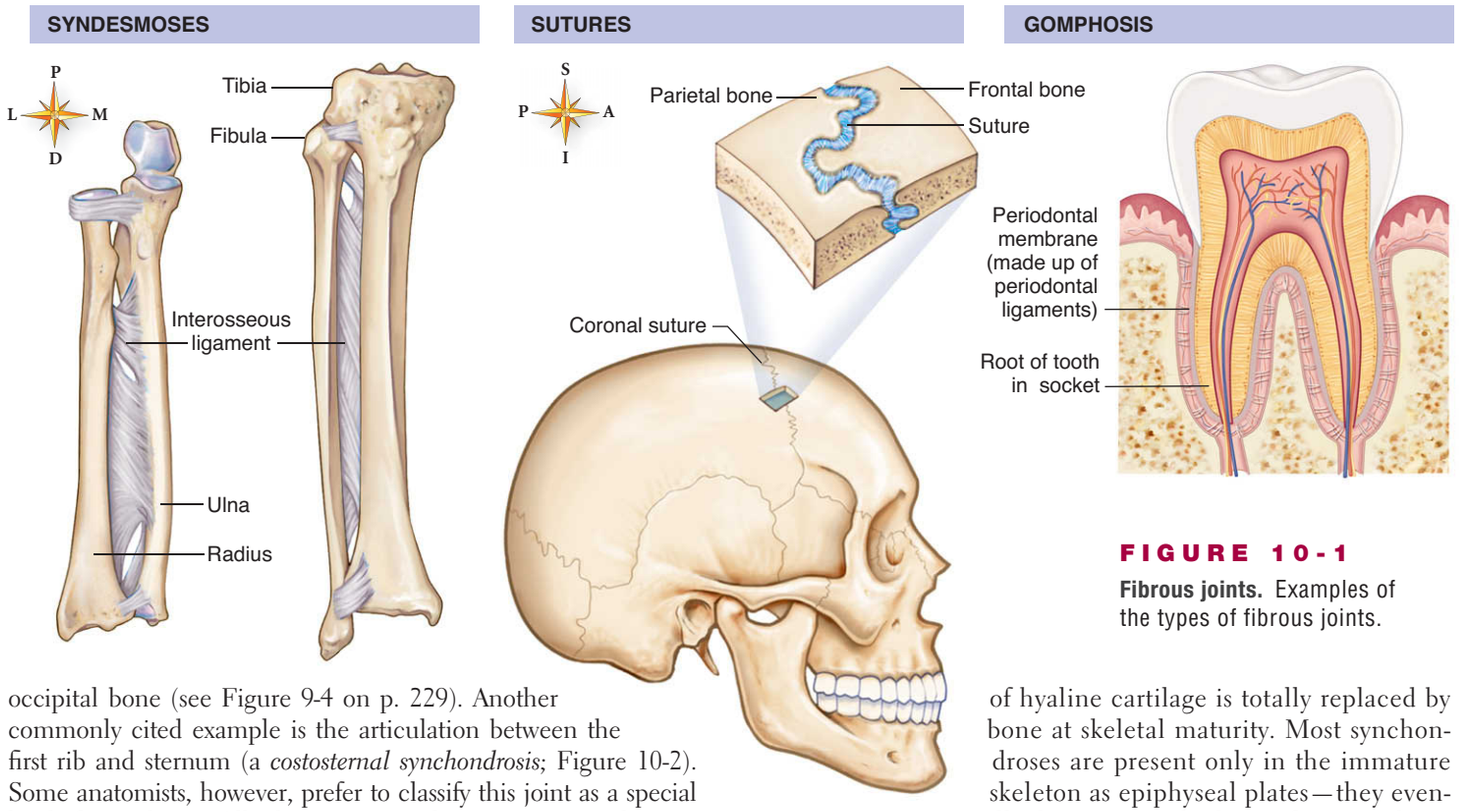


FIGURE 10-1
Fibrous joints. Examples of the types of fibrous joints.

occipital bone (see Figure 9-4 on p. 229). Another commonly cited example is the articulation between the first rib and sternum (a *costosternal synchondrosis*; Figure 10-2). Some anatomists, however, prefer to classify this joint as a special kind of synarthrosis. All other sternocostal joints are synovial joints, even though they often lack joint capsules.

The best example of a synchondrosis is the joint present during the growth years between the epiphyses of a long bone and its diaphysis (see Figure 10-2). The epiphyseal plate between the epiphysis and diaphyses of a long bone is a temporary synchondrosis that normally does not move. The plate of hyaline cartilage is totally replaced by bone at skeletal maturity. Most synchondroses are present only in the immature skeleton as epiphyseal plates—they eventually disappear as the bones fuse together.

SYMPHYSES

A **symphysis** (SIM-fi-sis) is a joint in which a pad or disk of fibrocartilage connects two bones. The tough fibrocartilage disks in these joints may permit slight movement when pressure is applied between the bones.

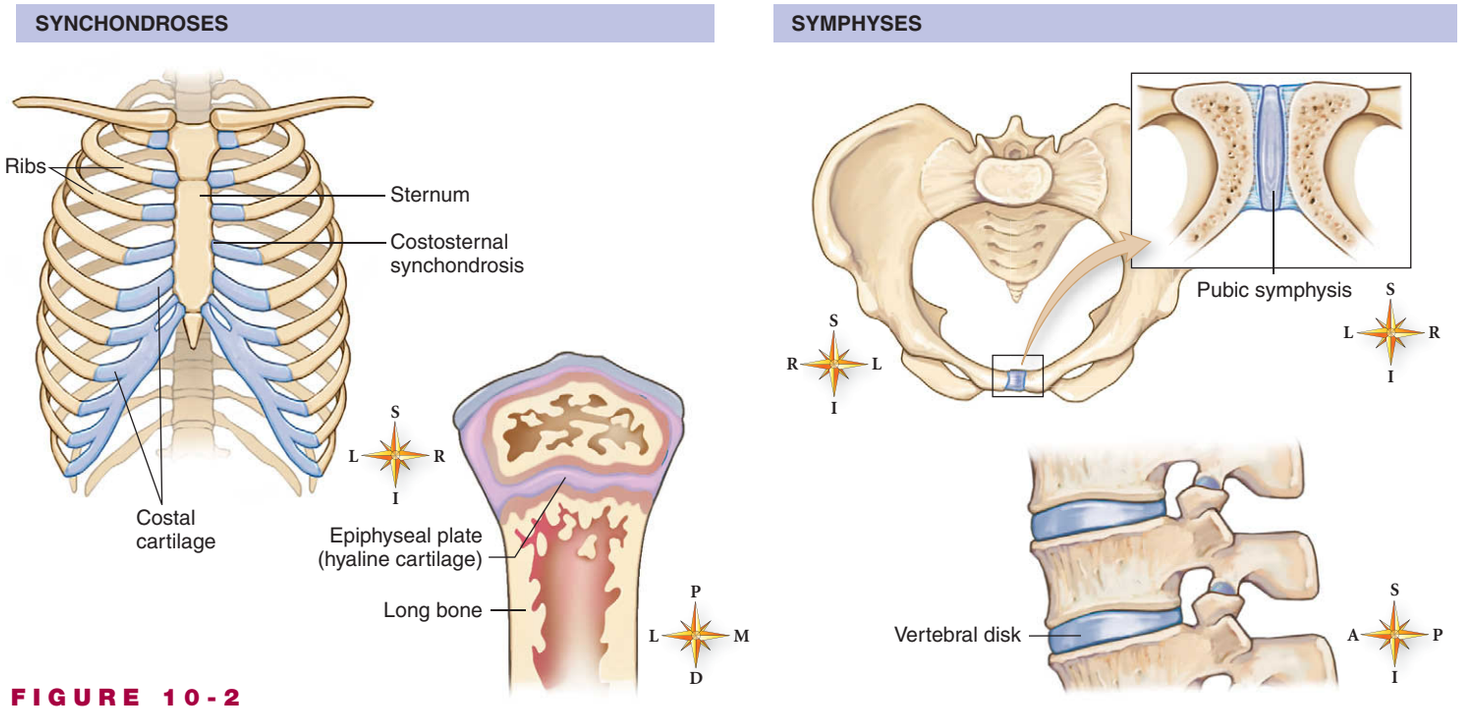


FIGURE 10-2
Cartilaginous joints. Examples of the types of cartilaginous joints.

Most symphyses are located in the midline of the body. Examples of symphyses include the pubic symphysis and the articulation between the *bodies* of adjacent vertebrae (see Figure 10-2). The intervertebral disk in these joints is composed of tough and resilient fibrocartilage that absorbs shock and permits limited movement. The bones of the vertebral column have numerous points of articulation between them. Collectively, these joints permit limited motion of the spine in a very restricted range. The articulation between the *bodies* of adjacent vertebrae is classified as a cartilaginous joint. The points of contact between the *articular facets* of adjacent vertebrae are, however, considered synovial joints and are described later in the chapter.

Table 10-2 summarizes the different kinds of fibrous and cartilaginous joints.

| QUICK CHECK |

1. Define the term *joint,* or *articulation.*
2. List the three major classes of joints according to both a structural and a functional scheme.
3. Name the three types of fibrous joints and give one example of each.
4. Identify the two types of cartilaginous joints and give one example of each.

Synovial Joints (Diarthroses)

Synovial joints are freely movable joints. They are not only the body's most mobile but also its most numerous and anatomically most complex joints. A majority of the joints between bones in the appendicular skeleton are synovial joints.

STRUCTURE OF SYNOVIAL JOINTS

The following seven structures characterize synovial, or freely movable, joints (Figure 10-3):

1. **Joint capsule.** Sleevelike extension of the periosteum of each of the articulating bones. The capsule forms a complete casing around the ends of the bones, thereby binding them to each other.
2. **Synovial membrane.** Moist, slippery membrane that lines the inner surface of the joint capsule. It attaches to the

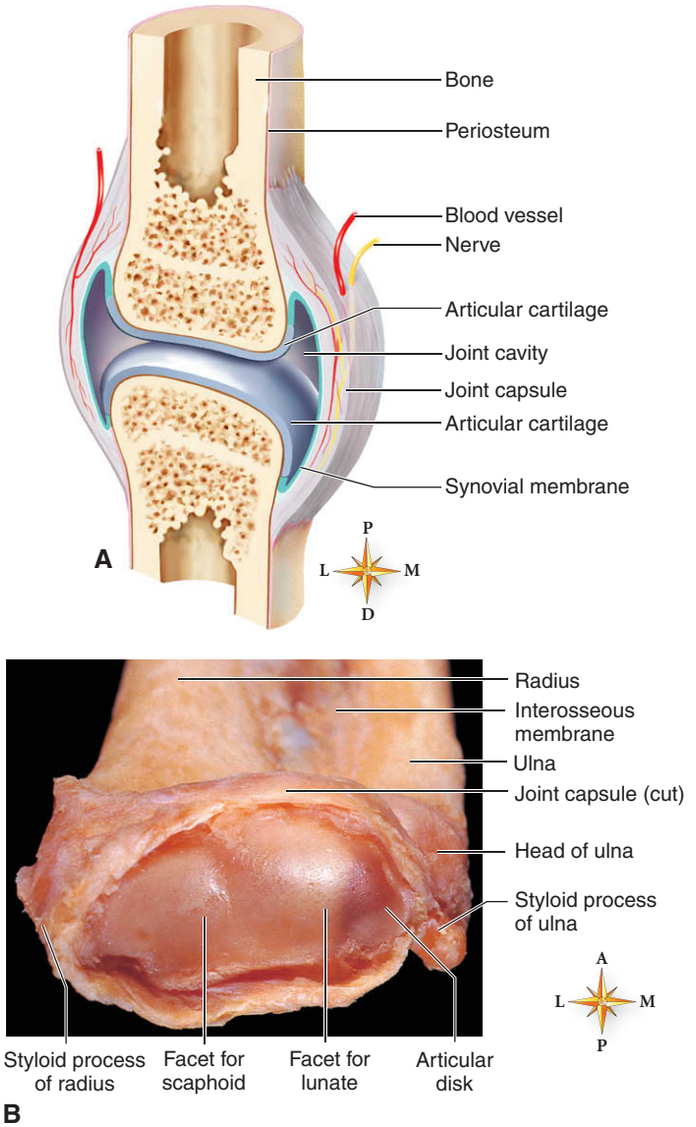


FIGURE 10-3

Structure of synovial joints. A, Artist's interpretation (composite drawing) of a typical synovial joint. **B,** Dissection photo showing the articular surface of a typical synovial joint—the distal radiocarpal joint (the joint capsule has been cut). See pp. 274–275 for a description of this joint.

TABLE 10-2 Classification of Fibrous and Cartilaginous Joints

TYPES	EXAMPLES	STRUCTURAL FEATURES	MOVEMENT
Fibrous Joints			
Syndesmoses	Joints between the distal ends of the radius and ulna	Fibrous bands (ligaments) connect articulating bones	Slight
Sutures	Joints between the skull bones	Teethlike projections of articulating bones interlock with a thin layer of fibrous tissue connecting them	None
Gomphoses	Joints between the roots of the teeth and the jaw bones	Fibrous tissue connects the roots of the teeth to the alveolar processes	None
Cartilaginous Joints			
Synchondroses	Costal cartilage attachments of the first rib to the sternum; epiphyseal plate between the diaphysis and epiphysis of a growing long bone	Hyaline cartilage connects articulating bones	Slight
Symphyses	Pubic symphysis; joints between *bodies* of vertebrae	Fibrocartilage between articulating bones	Slight

margins of the articular cartilage. It also secretes synovial fluid, which lubricates and nourishes the inner joint surfaces.

3. **Articular cartilage.** Thin layer of hyaline cartilage covering and cushioning the articular surfaces of bones.
4. **Joint cavity.** Small space between the articulating surfaces of the two bones of the joint. Absence of tissue between articulating bone surfaces permits extensive movement. Synovial joints are therefore diarthroses, or freely movable joints.
5. **Menisci (articular disks).** Pads of fibrocartilage located between the articulating ends of bones in some diarthroses. Usually these pads divide the joint cavity into two separate cavities. The knee joint contains two menisci (see Figure 10-10).
6. **Ligaments.** Strong cords of dense, white fibrous tissue at most synovial joints. They grow between the bones, and lash them even more firmly together than is possible with the joint capsule alone.
7. **Bursae.** Some synovial joints contain a closed pillowlike structure called a **bursa,** which consists of a synovial membrane filled with synovial fluid. Bursae tend to be associated with bony prominences (such as in the knee or the elbow), where they function to cushion the joint and facilitate movement of tendons.

TYPES OF SYNOVIAL JOINTS

Synovial joints are divided into three main groups: uniaxial, biaxial, and multiaxial. Each is subdivided further into two subtypes as follows:

1. **Uniaxial joints.** Synovial joints that permit movement around only one axis and in only one plane. Hinge and pivot joints are types of uniaxial joints (Figure 10-4, *A* and *B*).
   a. *Hinge joints.* Those in which the articulating ends of the bones form a hinge-shaped unit. Like a common door hinge, hinge joints permit only back-and-forth movements, namely, flexion and extension. If you have access to an articulated skeleton, examine the articulating end of the humerus (the trochlea) and the ulna (the semilunar notch). Observe their interaction as you flex and extend the forearm. Do you see why you can flex and extend your forearm but cannot move it in any other way at this joint? The shapes of the trochlea and the semilunar notch (see Figure 9-18, p. 252, and Figure 9-19, p. 253) permit only the uniaxial, horizontal-plane movements of flexion and extension at the elbow. Other hinge joints include the knee and interphalangeal joints.
   b. *Pivot joints.* Those in which a projection of one bone articulates with a ring or notch of another bone. Examples include a projection (dens) of the second cervical vertebra articulating with a ring-shaped portion of the first cervical vertebra and the head of the radius articulating with the radial notch of the ulna.
2. **Biaxial joints.** Diarthroses that permit movement around two perpendicular axes in two perpendicular planes. Saddle and condyloid joints are types of biaxial joints (Figure 10-4, *C* and *D*).
   a. *Saddle joints.* Those in which the articulating ends of the bones resemble reciprocally shaped miniature saddles. Only two saddle joints—one in each thumb—are present in the body. The thumb's metacarpal bone articulates in the wrist with a carpal bone (trapezium). The saddle-shaped articulating surfaces of these bones make it possible for the thumb to swing in an arc to touch the tips of the fingers—that is, to oppose the fingers. How important is this? To answer this for yourself, consider the following. Opposing the thumb to the fingers enables us

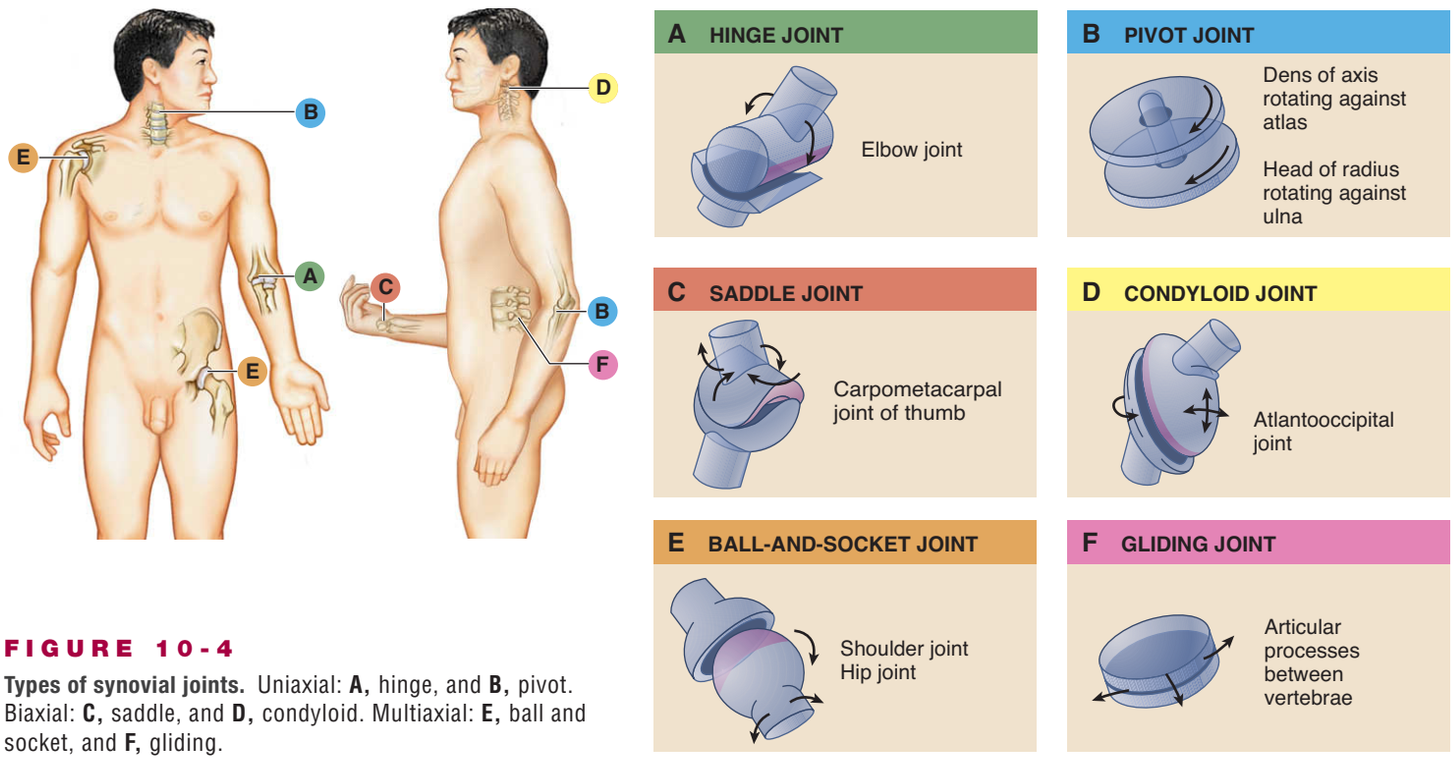


FIGURE 10-4

Types of synovial joints. Uniaxial: **A,** hinge, and **B,** pivot. Biaxial: **C,** saddle, and **D,** condyloid. Multiaxial: **E,** ball and socket, and **F,** gliding.

to grip small objects. Were it not for this movement, we would have much less manual dexterity. A surgeon could not grasp a scalpel or suture needle effectively, and none of us could easily hold a pen or pencil for writing.

b. *Condyloid (ellipsoidal) joints.* Those in which a condyle fits into an elliptical socket. Examples include condyles of the occipital bone fitting into elliptical depressions of the atlas and the distal end of the radius fitting into depressions of the carpal bones (scaphoid, lunate, and triquetrum).

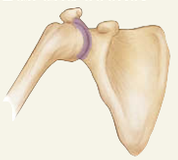
3. **Multiaxial joints.** Joints that permit movement around three or more axes and in three or more planes (Figure 10-4, *E* and *F*).

a. *Ball-and-socket joints (spheroid joints).* Our most movable joints. A ball-shaped head of one bone fits into a concave depression on another, thereby allowing the first bone to move in many directions. Examples include the shoulder and hip joints.

b. *Gliding joints.* Characterized by relatively flat articulating surfaces that allow limited gliding movements along various axes. Examples include the joints between the articular surfaces of successive vertebrae. (Articulations between the bodies of successive vertebrae are symphysis-type cartilaginous joints.) As a group, gliding joints are the least movable of the synovial joints.

Table 10-3 summarizes the classes of synovial joints.

TABLE 10-3 Classification of Synovial Joints

TYPES	EXAMPLES	STRUCTURE	MOVEMENT
Uniaxial			*Around one axis; in one place*
Hinge 	Elbow joint	Spool-shaped process fits into a concave socket	Flexion and extension only
Pivot 	Joint between the first and second cervical vertebrae	Arch-shaped process fits around a peglike process	Rotation
Biaxial			*Around two axes, perpendicular to each other; in two planes*
Saddle 	Thumb joint between the first metacarpal and carpal bone	Saddle-shaped bone fits into a socket that is concave-convex-concave	Flexion, extension in one plane; abduction, adduction in the other plane; opposing the thumb to the fingers
Condyloid (ellipsoidal) 	Joint between the radius and carpal bones	Oval condyle fits into an elliptical socket	Flexion, extension in one plane; abduction, adduction in the other plane
Multiaxial			*Around many axes*
Ball and socket 	Shoulder joint and hip	Ball-shaped process fits into a concave socket	Widest range of movement: flexion, extension, abduction, adduction, rotation, circumduction
Gliding 	Joints between the articular facets of adjacent vertebrae; joints between the carpal and tarsal bones	Relatively flat articulating surfaces	Gliding movements without any angular or circular movements

| QUICK CHECK |

5. List the seven structures that characterize synovial joints.
6. Name the three main categories of synovial joints grouped according to axial movement and list the two subtypes of joints found in each category.
7. Name one specific joint as an example of each of the six types of synovial joints.

REPRESENTATIVE SYNOVIAL JOINTS

Humeroscapular Joint

The joint between the head of the humerus and the glenoid cavity of the scapula is the one we usually refer to as the *shoulder joint* (Figure 10-5). It is our most mobile joint. One anatomical detail, the shallowness of the glenoid cavity, largely accounts for this mobility. The shallowness offers little interference to movement of the head of the humerus. Were it not for the *glenoidal labrum* (Figure 10-5, C), a narrow rim of fibrocartilage around the glenoid cavity, it would have scarcely any depth at all.

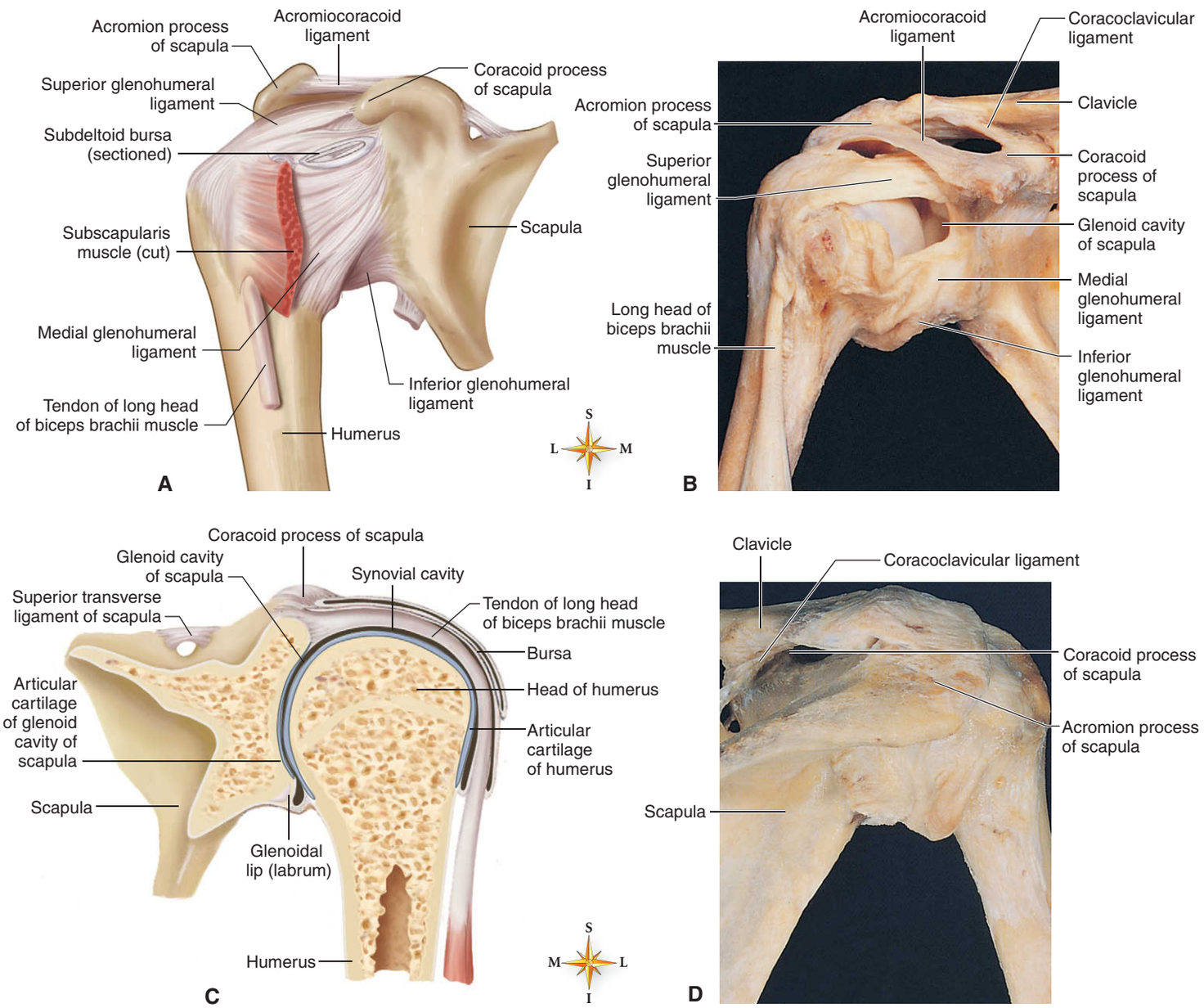


FIGURE 10-5

The shoulder joint. A, Artist's diagram, and **B,** dissection photo (anterior views). **C,** Artist's diagram, and **D,** dissection photo (viewed from behind through shoulder joint).

Some structures strengthen the shoulder joint and give it a degree of stability, notably several ligaments, muscles, tendons, and bursae. Note in Figure 10-5, *A*, for example, the superior, medial, and inferior glenohumeral ligaments. Each of these ligaments is a thickened portion of the joint capsule. Also in this figure, identify the subscapularis muscle, the tendon of the long head of the biceps brachii muscle, and a bursa.

Shoulder muscles and tendons form a cufflike arrangement around the joint. It is called the *rotator cuff*. Baseball pitchers frequently injure the rotator cuff in the shoulder of their pitching arms. The main bursa of the shoulder joint is the *subdeltoid bursa*. It lies wedged between the inferior surface of the deltoid muscle and the superior surface of the joint capsule. Other bursae of the shoulder joint are the subscapular, subacromial, and subcoracoid bursae. All in all, the shoulder joint is more mobile than stable. Dislocations of the head of the humerus from the glenoid cavity occur frequently.

| A&P CONNECT |

An x-ray photograph of the of the shoulder joint seen in ***Skeletal Radiography*** online at ***A&P Connect*** clearly shows the bony structures and their anatomical relationships in a living body. Other joints of the body are also illustrated there.

evolve

Elbow Joint

The elbow joint (Figure 10-6) is a classic hinge joint formed by two articulations occurring between the distal end of the humerus and the proximal ends of the radius and ulna. Laterally it is the capitulum of the humerus that articulates with the head of the radius in the *humeroradial joint*. Medially, the trochlea of the humerus articulates with the trochlear notch of the ulna in the *humeroulnar joint*. Both of these joint components are surrounded by a single joint capsule and by ligaments on either side, called *collateral ligaments*, that fuse with the capsule to stabilize the joint and help prevent disarticulation.

The articulation between the proximal ends of the radius and ulna just below the joint capsule is called the *proximal radioulnar joint*. The point of articulation is between the head of the radius and the radial notch of the ulna and is stabilized by the *annular ligament*. Although it is not a part of the elbow joint involved in hinge movements, it does permit rotation of the forearm as the radial head moves on the ulna. Dislocation of the radial head, called a "pulled elbow," is seen more often in young children than adults. The reason? The disk-shaped head of the radius does not attain its conical shape until late in childhood and therefore slips more easily from under the annular ligament. Figure 10-6, *B* shows the annular ligament attached to the proximal end of the ulna in an adult. It firmly holds the head of the radius against the articular surface of the radial notch on the ulna, thus allowing the radius to rotate freely.

A number of other anatomical or clinical "points of interest" are associated with the elbow joint. The medial and lateral epicondyles are palpable bony landmarks (see Box 9-2 on p. 227) on either side of the joint, and the **olecranon bursa,** which helps cushion the joint, is found just under the skin on its posterior surface overlying the olecranon of the ulna. **Olecranon bursitis** is inflammation of the bursa associated with prolonged pressure.

One of the most frequent sites for *venipuncture* (piercing a vein) to obtain blood is the median cubital vein located in the fossa just anterior to the joint.

Perhaps one of the most important structures near the joint is the ulnar nerve. It courses along the groove, sometimes called the "funny bone," between the olecranon and the medial epicondyle. Blows to this area produce unpleasant sensations in the hand and

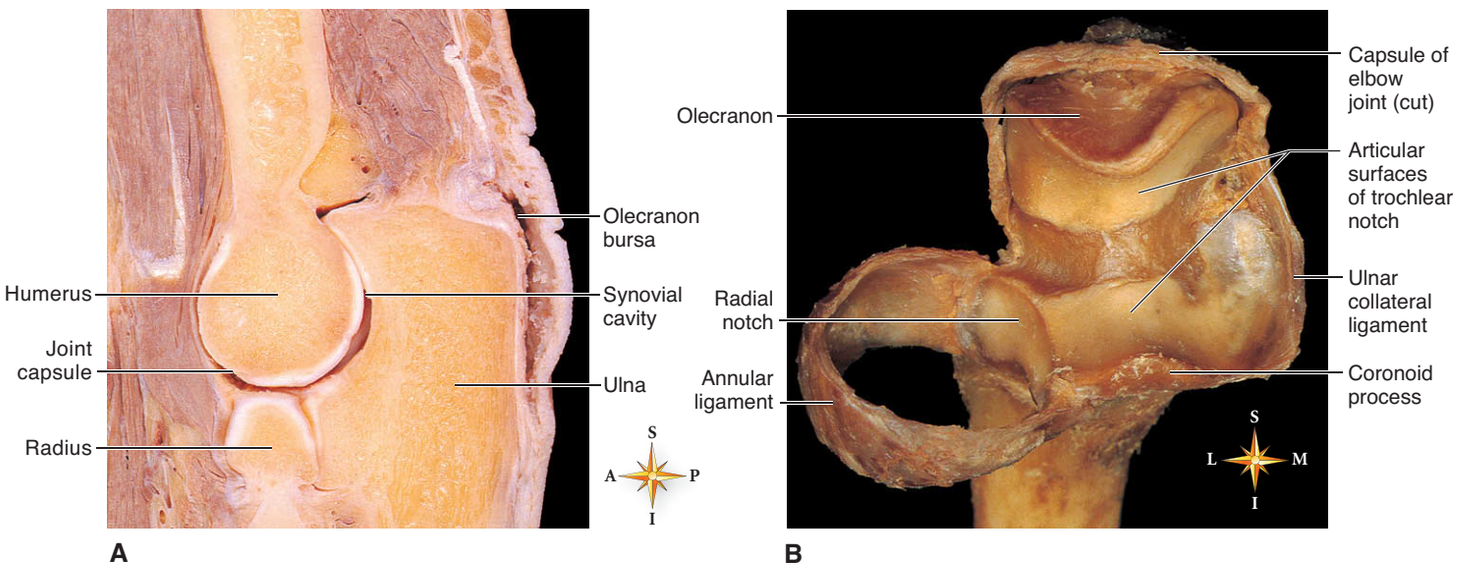


FIGURE 10-6

The elbow joint. A, Sagittal section through the elbow joint. **B,** Dissection photo showing the anterior view of the proximal end of the ulna with attached annular ligament.

fingers supplied by the nerve. More severe injuries may result in paralysis of hand muscles and produce "clawhand" or a reduction in wrist movements.

Forearm, Wrist, Hand, and Finger Joints

Proper function of the forearm, wrist, hand, and fingers, as well as the joints that permit movement in these areas, is often said to be the functional "reason" for the upper extremity. Our ability to grasp and manipulate small objects, to properly focus the movement and strength of our upper extremities, and the many movements required to coordinate or restore balance and equilibrium are only a few examples of activities that require normal functioning of our forearms, wrists, hands, and fingers.

In clinical medicine, treatment or repair of injuries to these important functional areas constitutes a highly specialized area of surgical practice. In addition to bones and joints, the relatively small area of the wrist and hand, especially, is packed with many other anatomical structures, such as muscles, ligaments, blood vessels, and nerves. Hand surgery, like many other forms of specialized surgery, requires both a mastery of complex techniques and an in-depth understanding of the anatomy involved.

There are seven categories of synovial joints between the bones of the forearm, wrist, hand, and fingers. They are named after the bones that touch or articulate with one another in the joints involved. Some of the movements produced are slight and subtle, whereas others are more apparent. All are important functionally and are illustrated later in the chapter.

RADIOULNAR JOINTS

The head of the radius and the radial notch of the ulna articulate just below the elbow joint to form the *proximal radioulnar joint* described earlier. Together with the *distal radioulnar joint*, which is the point of articulation between the ulnar notch of the radius and head of the ulna just above the wrist, the two **radioulnar joints** permit pronation and supination of the forearm.

RADIOCARPAL (WRIST) JOINTS

As the name in the heading implies, only the radius articulates directly with the wrist or carpal bones distally. The point of articulation between the head of the radius and the scaphoid and lunate carpal bones forms a typical synovial joint, in this case, a **radiocarpal joint,** and is shown in Figure 10-7. A full range of motions occur at the joint and are illustrated later in the chapter.

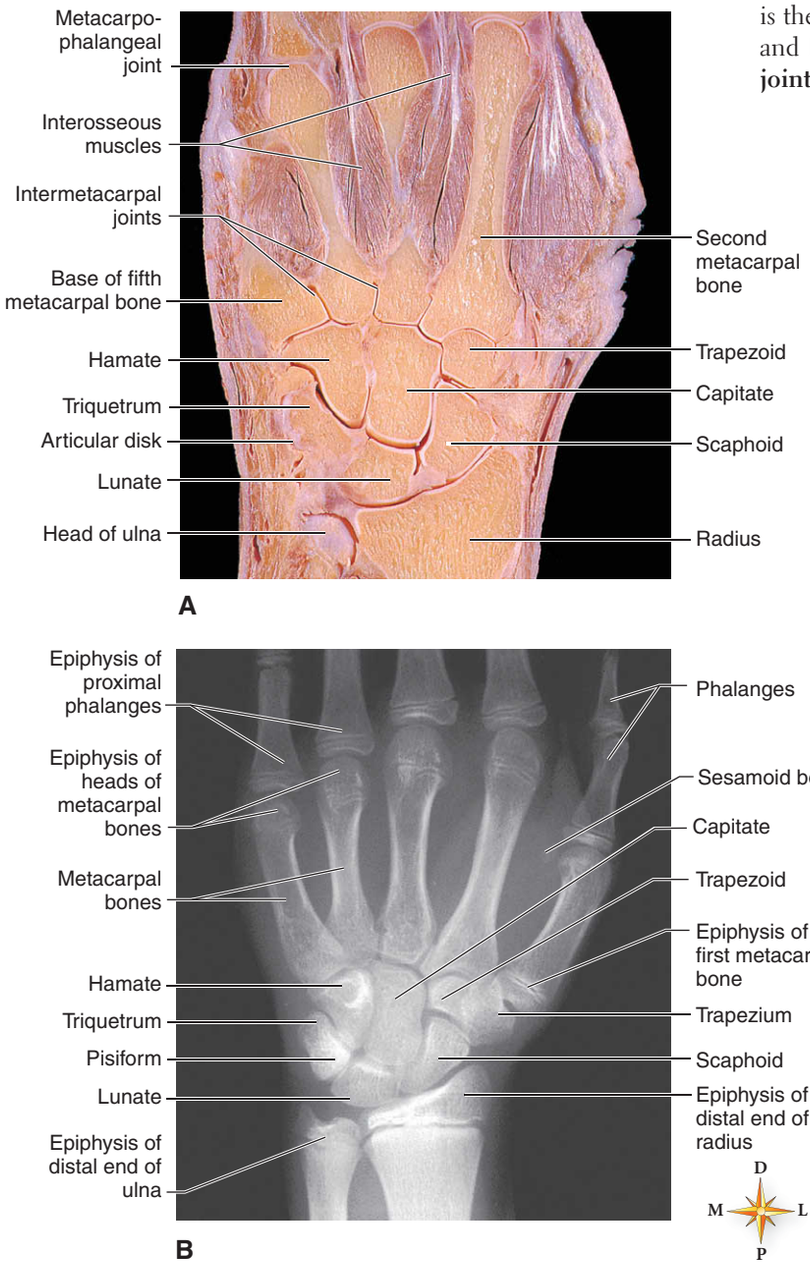


FIGURE 10-7

Joints of the wrist. A, Coronal section of the hand showing the joints of the wrist. Note that the thumb and little finger are not in the plane of section. **B,** Radiograph of an adolescent hand and wrist. Note that the epiphyseal plates are present. **C,** Major synovial spaces of the wrist: *1,* proximal; *2,* intermediate; *3,* distal.

Falls on an outstretched hand often result in fractures of the scaphoid bone. It is the scaphoid that transmits a majority of the applied force to the radial head. Unfortunately, loss of blood supply to a portion of the fractured scaphoid may result in necrosis of the broken fragment, which requires surgical removal or other specialized treatment. Note that a disk separates the distal part of the ulna from direct contact with the carpal bones.

INTERCARPAL JOINTS

The **intercarpal joints** occur at points of articulation between the eight carpal bones. Arranged in two rows (proximal and distal) of four bones each, the carpal bones and the joints between them are supported and stabilized by numerous ligaments. They are also stabilized by forearm muscle tendons acting on the wrist and digits that wrap around the wrist to form a sort of cuff.

The joint spaces usually communicate with each other, forming large joint spaces. You can see the three largest of these joint spaces in Figure 10-7, *C*. The relationships between the intercarpal joints are illustrated in Figure 10-7. Functionally, movements at the intercarpal joints are generally gliding with some abduction and flexion.

CARPOMETACARPAL JOINTS

There are a total of three **carpometacarpal joints,** one for the thumb and two for the fingers. The thumb carpometacarpal joint is unique in having both a loose-fitting joint capsule and a saddle-shaped articular surface between the first metacarpal bone and the trapezium. Movements possible at this joint include flexion, extension, adduction, abduction, and circumduction. In addition, because of the special anatomical features of this joint, a combination movement called *opposition* of the thumb (see p. 290) is possible. Opposition allows us to touch the tips of any of the fingers with the tip of the thumb. It is this unique movement that permits us to grasp and manipulate small objects—a functional movement of immense practical significance.

The remaining two carpometacarpal joints are much less mobile than the saddle-shaped one for the thumb and are limited to essentially gliding-type movements.

METACARPOPHALANGEAL JOINTS

In **metacarpophalangeal joints** the rounded heads of the metacarpal bones and the concave bases of the proximal phalanges articulate with each other (Figure 10-8). The capsule surrounding each joint is strengthened by collateral ligaments on both sides. The shape of the articular surfaces in these joints permits only limited adduction and abduction—and only when the fingers are extended. Much more extensive flexion and extension movements are possible.

INTERPHALANGEAL JOINTS

Interphalangeal joints are typical hinge-type synovial joints capable of flexion and extension. They exist between the heads of the phalanges and the bases of the more distal phalanges. In the fingers, two types of interphalangeal joints can be identified. The joints between the proximal and middle phalanges are called **proximal interphalangeal (PIP) joints,** whereas those between the middle and distal phalanges are called the **distal interphalangeal (DIP) joints.** Understanding the relationship of articulations between the phalanges will help in understanding the various finger movements discussed later in the chapter (see Figure 10-22).

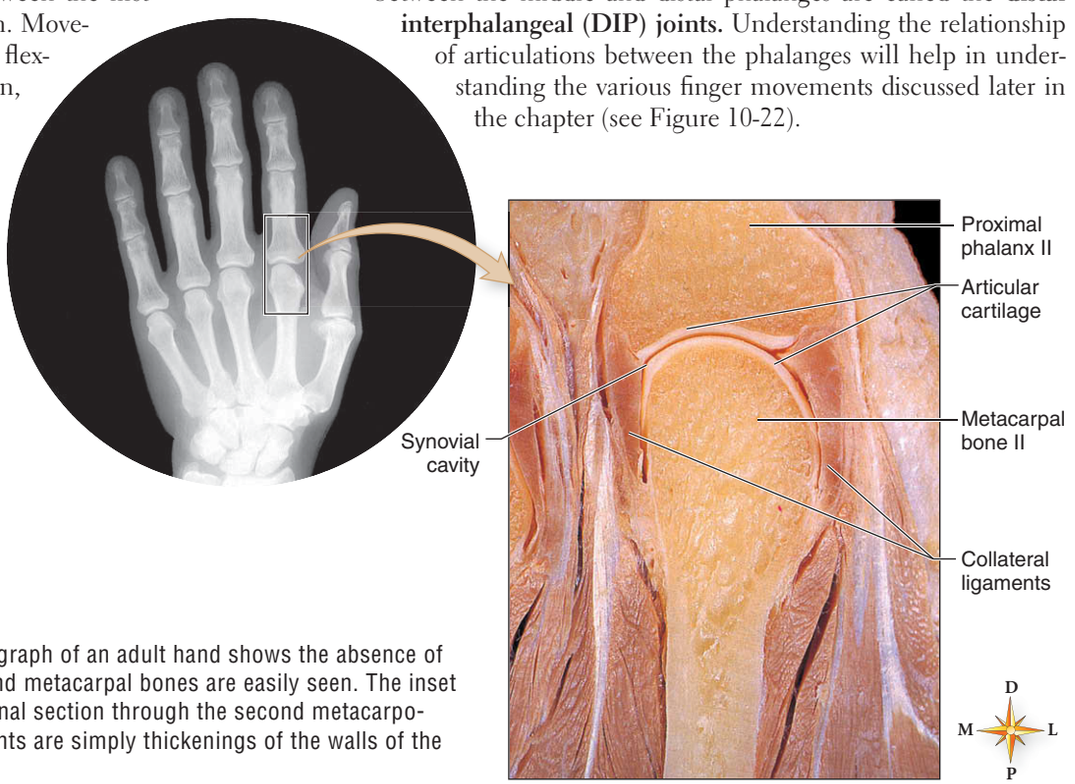


FIGURE 10-8

Joints of the hand and fingers. Radiograph of an adult hand shows the absence of epiphyseal plates. All the phalanges and metacarpal bones are easily seen. The inset shows a dissected specimen in a coronal section through the second metacarpophalangeal joint. The collateral ligaments are simply thickenings of the walls of the joint capsule.

Hip Joint

The first characteristic to remember about the hip joint is stability; the second is mobility (Figure 10-9). The stability of the hip joint derives largely from the shapes of the head of the femur and the acetabulum, the socket of the hip bone into which the femur head fits. Turn to Figure 9-22 and note the deep, cuplike shape of the acetabulum, and then observe the ball-like head of the femur in Figure 9-23, A. Compare these with the shallow, almost saucer-shaped glenoid cavity (see Figure 9-17, C) and the head of the humerus (see Figure 9-18). From these observations, do you see why the hip joint necessarily has a somewhat more limited range of movement than does the shoulder joint? Both joints, however, allow multiaxial movements. Both permit flexion, extension, abduction, adduction, rotation, and circumduction.

A joint capsule and several ligaments hold the femur and hip bones together and contribute to the hip joint's stability. The iliofemoral ligament connects the ilium with the femur, and the ischiofemoral and pubofemoral ligaments join the ischium and pubic bone to the femur. The iliofemoral ligament is one of the strongest ligaments in the body.

Knee Joint

The knee, or *tibiofemoral joint*, is the largest and one of the most complex and most frequently injured joints in the body

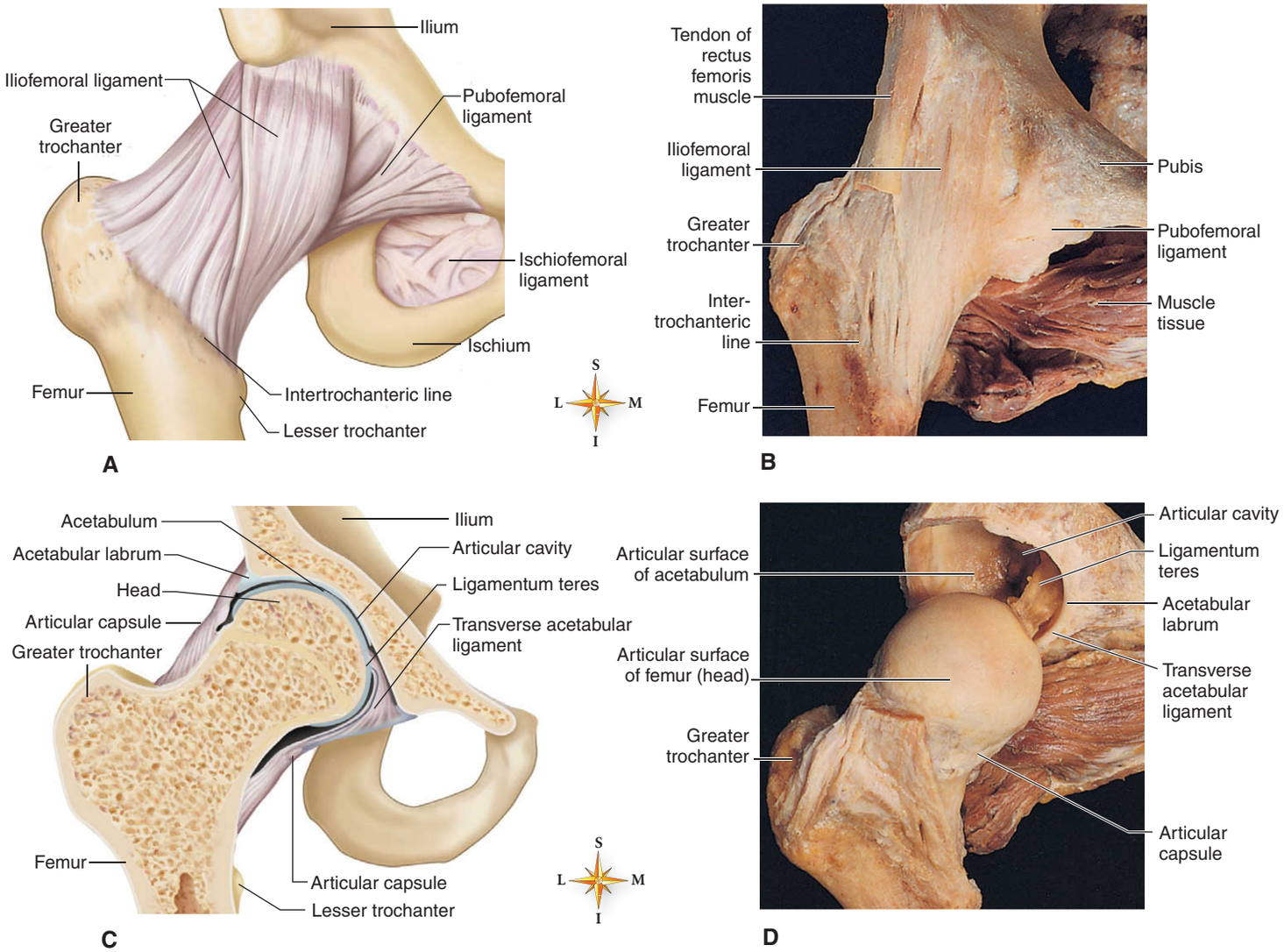


FIGURE 10-9

The hip joint. A, Artist's diagram, and **B,** dissection photo (anterior views). **C,** Artist's diagram, and **D,** dissection photo (frontal section).

(Figures 10-10 and 10-11, Box 10-1). The condyles of the femur articulate with the flat upper surface of the tibia. Although this arrangement is precariously unstable, counteracting forces are supplied by a joint capsule, cartilages, and numerous ligaments and muscle tendons. Note, for example, in Figure 10-10 the shape of the two cartilages labeled *medial meniscus* and *lateral meniscus.* They attach to the flat top of the tibia and, because of their concavity, form a kind of shallow socket for the condyles of the femur.

Of the many ligaments that hold the femur bound to the tibia, five can be seen in Figure 10-10. The *anterior cruciate ligament (ACL)* attaches to the anterior part of the tibia between its condyles, then crosses over and backward and attaches to the posterior part of the lateral condyle of the femur. The *posterior cruciate ligament (PCL)* attaches posteriorly to the tibia and lateral meniscus, then crosses over and attaches to the front part of the femur's medial condyle. The *posterior tibiofibular ligament* (ligament of Wrisberg) attaches posteriorly to the lateral meniscus and extends up and over to attach to the medial condyle behind the attachment of the posterior cruciate ligament (Figure 10-10, *C*). The *transverse ligament* connects the anterior margins of the two menisci. Strong ligaments, the *fibular* and *tibial collateral ligaments*, located at sides of the knee joint can be seen in Figure 10-10, *C*.

A baker's dozen of bursae serve as pads around the knee joint: four in front, four located laterally, and five medially. That is 13 in total. Of these, the largest is the *prepatellar bursa* (see Figure 10-11) inserted in front of the patellar ligament, between it and the skin. The painful ailment commonly called "housemaid's knee" or "surfer's knee" is **prepatellar bursitis.**

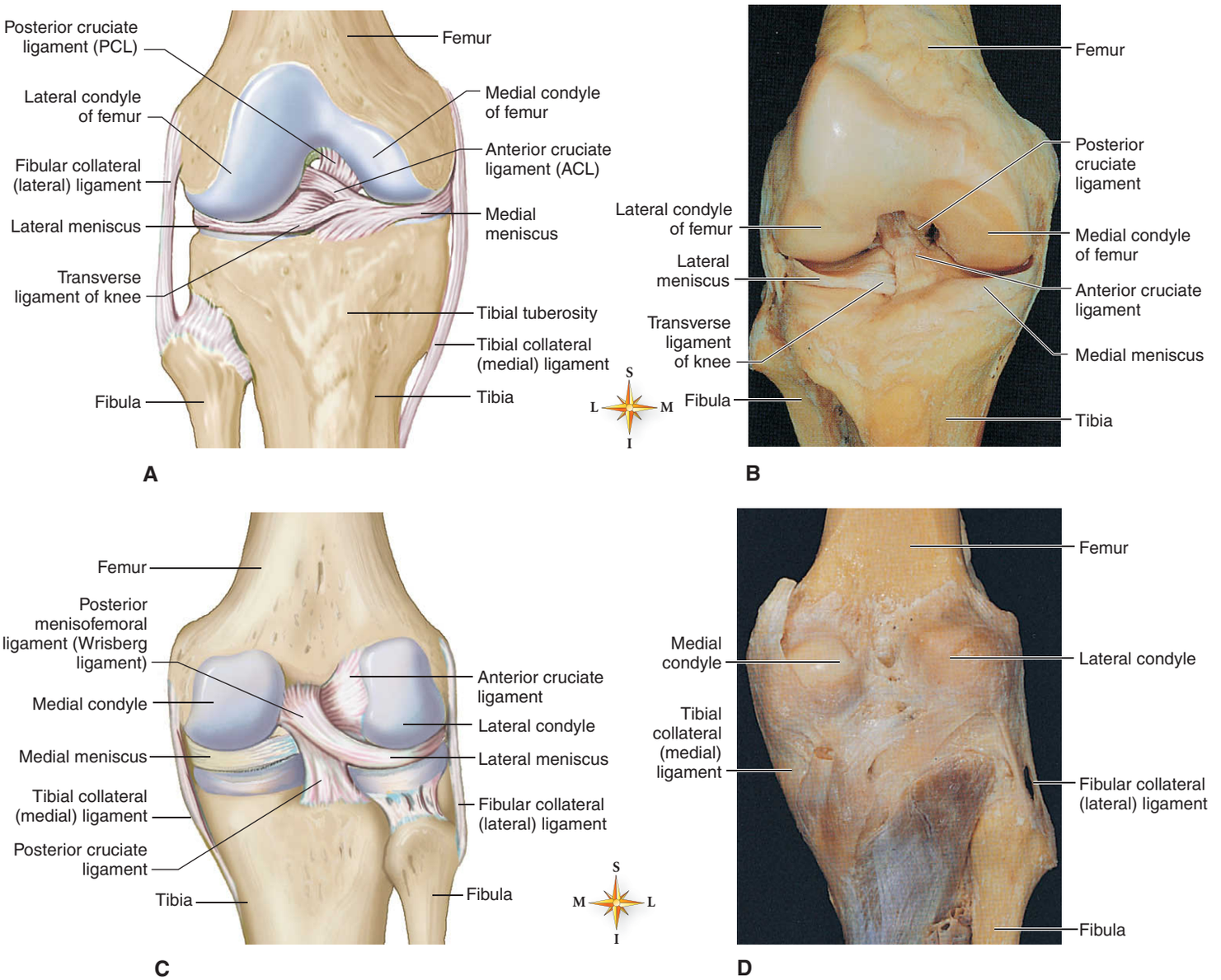


FIGURE 10-10

The right knee joint. A and **B,** Labeled dissection of the right knee viewed from in front. **C** and **D,** Viewed from behind.

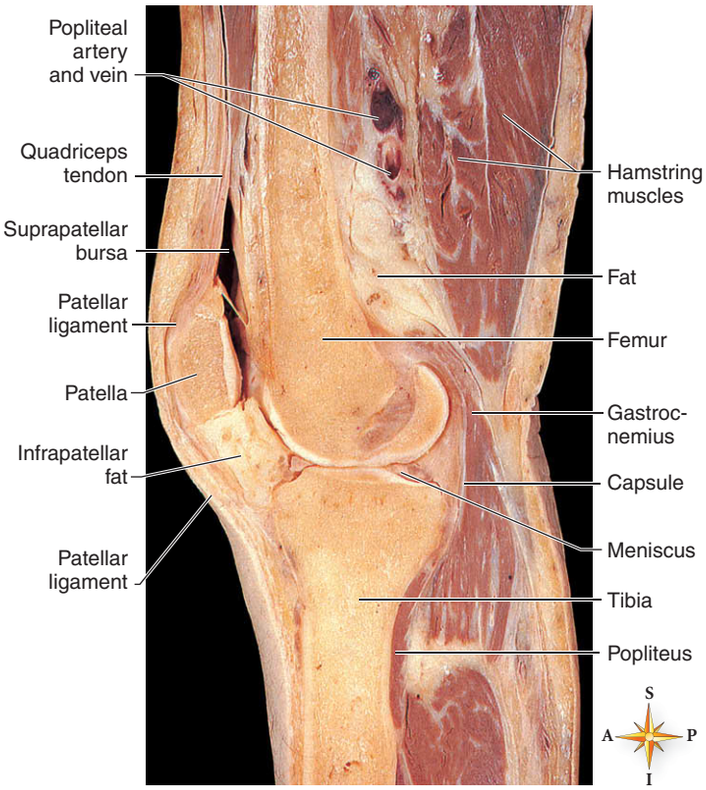


FIGURE 10-11

Knee joint (sagittal section). Cadaver dissection showing the articular surfaces and related structures.

When compared with the hip joint, the knee joint is relatively unprotected by surrounding muscles. Consequently, the knee, more often than the hip, is injured by blows or sudden stops and turns. Athletes, for example, are prone to tearing a knee cartilage, specifically, one of the menisci (see Figure 10-11).

The structure of the knee joint permits the hingelike movements of flexion and extension. Also, with the knee flexed, some internal and external rotation can occur. In most of our day-to-day activities—even such ordinary ones as walking, going up and down stairs, and getting into and out of chairs—our knees bear the brunt of the load; they are the main weight bearers. Knee injury or disease can therefore be crippling.

Ankle Joint

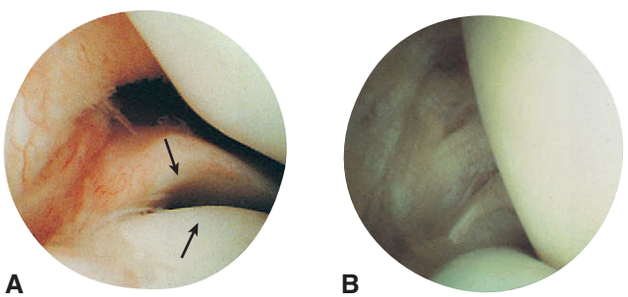
Anatomical comparisons of the wrist, hand, and fingers are often made with the ankle, foot, and toes. Although many anatomical similarities do exist, functional differences abound. Hand anatomy is a marvel of functional design intended to permit flexibility and, especially with the presence of a saddle joint between the first metacarpal bone and the trapezium, discrete and precisely controlled movement. The bony structure of the ankle and foot, as well as the joints that exist between them, enhance stability and weight bearing rather than flexibility and a wide range of different movements.

Box 10-1 | SPORTS and FITNESS

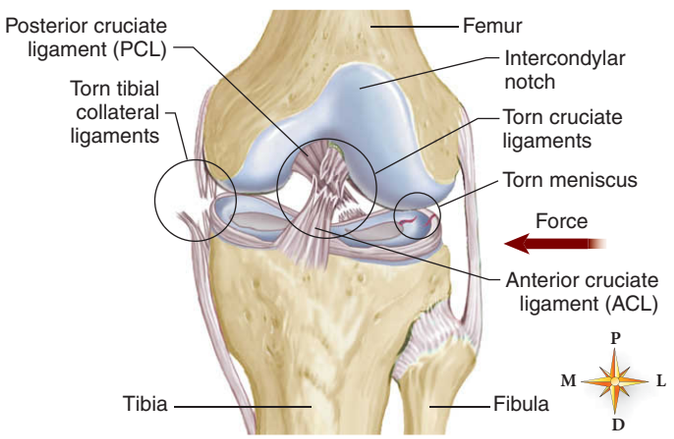
The Knee Joint

The knee is the largest and most vulnerable joint. Because the knee is often subjected to sudden, strong forces during athletic activity, knee injuries are among the most common type of athletic injury. Sometimes the articular cartilages on the tibia become torn when the knee twists while bearing weight. The ligaments holding the tibia and femur together and the medial and lateral menisci also can be injured in this way. Knee injuries also may occur when a weight-bearing knee collides with another person, especially from the side, as sometimes happens in sporting events.





Knee arthrogram **A,** Normal medial meniscus. Spot film showing the normal triangular shape of the meniscus (arrows). **B,** Linear tear of the medial meniscus.

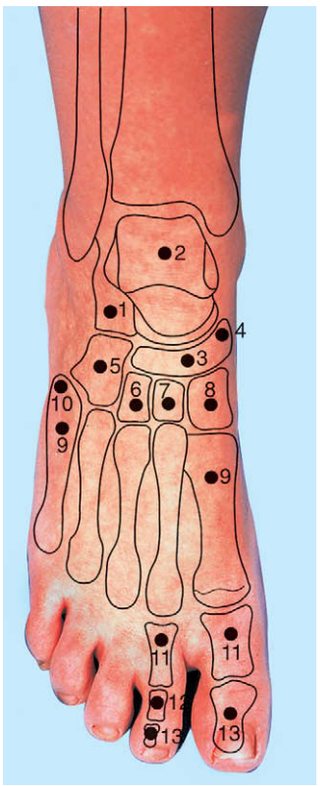


Compare the articulating bones, joint types, and movements in each area listed in Table 10-4. Note in Figure 10-12, *B*, that the lateral malleolus of the ankle joint is lower than the medial and contributes to a wedge or so-called *mortise-shaped* articulation with the talus below. The combination of a uniquely shaped articular surface and strong supporting ligaments results in an excellent platform for weight bearing during standing and walking. However, so-called rotational ankle injuries do occur—especially in certain types of dance or during athletic activity.

The most common type of **sprained ankle** is caused by an internal rotation injury to the anterior talofibular ligament, seen in Figure 10-12. Symptoms include pain and swelling over the lateral side of the ankle with severe "point tenderness" just anterior to the lateral malleolus. External ankle rotation injuries generally result in fractures rather than ligament tears. In first-degree ankle injuries the lateral malleolus is broken. Second-degree injuries result in fracture of both malleoli, and in third-degree injuries both malleoli and the articular surface of the tibia are fractured (OUCH!). The strong deltoid ligament, which helps maintain the medial longitudinal arch of the foot (see Chapter 9), is also frequently injured in severe twisting injuries affecting the ankle.

TABLE 10-4 Synovial (Diarthrotic) and Two Cartilaginous (Amphiarthrotic) Joints

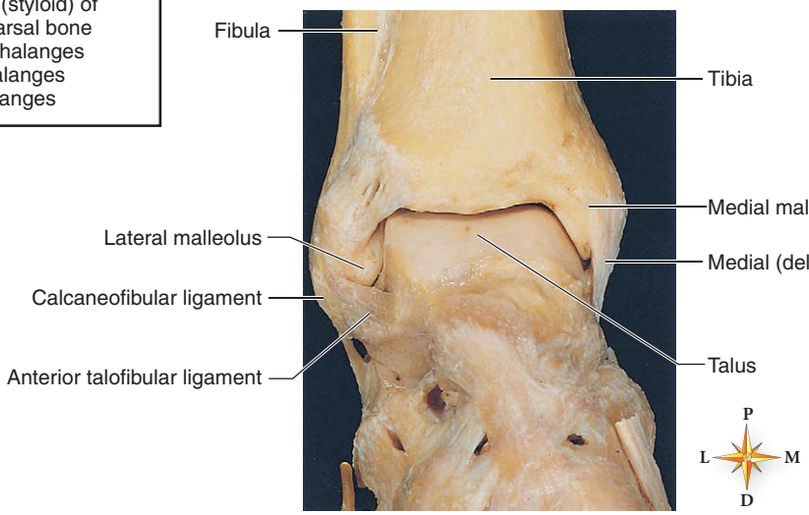
NAME	ARTICULATING BONES	TYPE	MOVEMENTS
Atlantoepistropheal	Anterior arch of the atlas rotates about the dens of the axis (epistropheus)	Synovial (pivot)	Pivoting or partial rotation of the head
Vertebral	Between bodies of vertebrae	Cartilaginous (symphyses)	Slight movement between any two vertebrae but considerable motility for the column as a whole
	Between articular processes	Synovial (gliding)	Gliding
Sternoclavicular	Medial end of the clavicle with the manubrium of the sternum	Synovial (gliding)	Gliding
Acromioclavicular	Distal end of the clavicle with the acromion of the scapula	Synovial (gliding)	Gliding; elevation, depression, protraction, and retraction
Thoracic	Heads of ribs with bodies of vertebrae	Synovial (gliding)	Gliding
	Tubercles of ribs with transverse processes of vertebrae	Synovial (gliding)	Gliding
Shoulder	Head of the humerus in the glenoid cavity of the scapula	Synovial (ball and socket)	Flexion, extension, abduction, adduction, rotation, and circumduction of the upper part of the arm
Elbow	Trochlea of the humerus with the semilunar notch of the ulna; head of the radius with the capitulum of the humerus	Synovial (hinge)	Flexion and extension
	Head of the radius in the radial notch of the ulna	Synovial (pivot)	Supination and pronation of the forearm and hand; rotation of the forearm on the upper extremity
Wrist	Scaphoid, lunate, and triquetral bones articulate with the radius and articular disk	Synovial (condyloid)	Flexion, extension, abduction, and adduction of the hand
Carpal	Between various carpal bones	Synovial (gliding)	Gliding
Hand	Proximal end of the first metacarpal bone with the trapezium	Synovial (saddle)	Flexion, extension, abduction, adduction, and circumduction of the thumb and opposition to the fingers
	Distal end of the metacarpal bones with the proximal end of the phalanges	Synovial (hinge)	Flexion, extension, limited abduction, and adduction of the fingers
	Between phalanges	Synovial (hinge)	Flexion and extension of finger sections
Sacroiliac	Between the sacrum and two ilia	Synovial (gliding)	None or slight
Pubic symphysis	Between two pubic bones	Cartilaginous (symphysis)	Slight, particularly during pregnancy and delivery
Hip	Head of the femur in the acetabulum of the coxal bone	Synovial (ball and socket)	Flexion, extension, abduction, adduction, rotation, and circumduction
Knee	Between the distal end of the femur and proximal end of the tibia	Synovial (hinge)	Flexion and extension; slight rotation of the tibia
Tibiofibular (proximal)	Head of the fibula with the lateral condyle of the tibia	Synovial (gliding)	Gliding
Ankle	Distal end of the tibia and fibula with the talus	Synovial (hinge)	Flexion (dorsiflexion) and extension (plantar flexion)
Foot	Between tarsal bones	Synovial (gliding)	Gliding; inversion and eversion
	Between metatarsal bones and phalanges	Synovial (hinge)	Flexion, extension, slight abduction, and adduction
	Between phalanges	Synovial (hinge)	Flexion and extension



Key for Figure A

1. Calcaneus
2. Talus
3. Navicular
4. Tubercle of navicular bone
5. Cuboid
6. Lateral cuneiform
7. Intermediate cuneiform
8. Medial cuneiform
9. Metatarsal bones
10. Tuberosity (styloid) of fifth metatarsal bone
11. Proximal phalanges
12. Middle phalanges
13. Distal phalanges

A



B

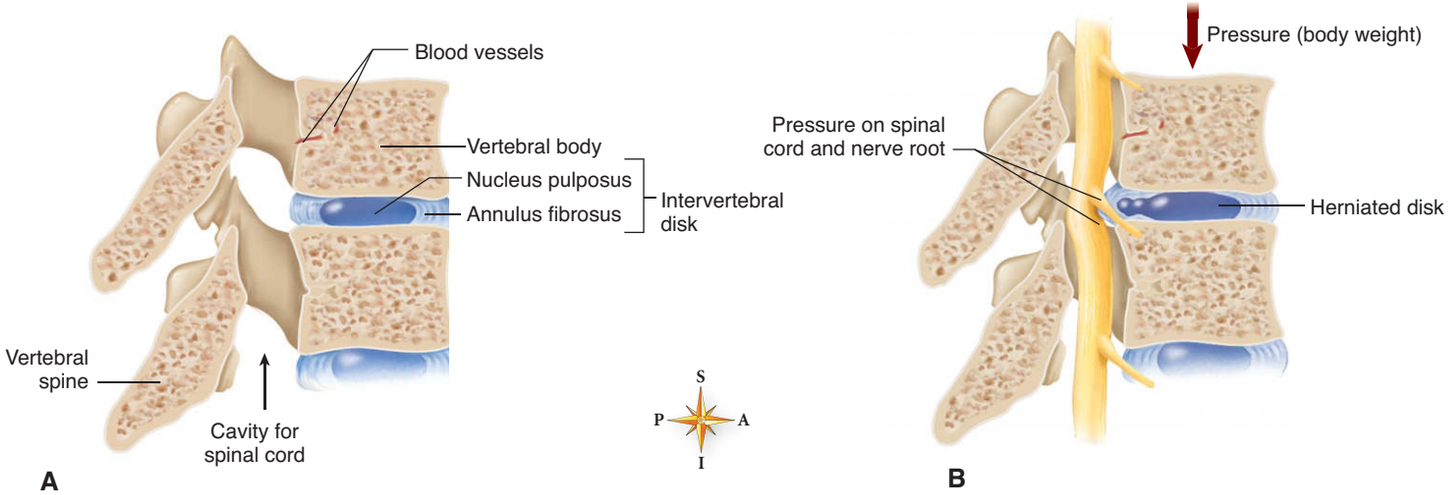
FIGURE 10-12

Ankle joint. A, Dorsum of the ankle and foot showing surface relationships to underlying bones. **B,** Dissection photo of the ankle joint.

Vertebral Joints

One vertebra connects to another by several joints—between their *bodies*, as well as between their articular, transverse, and spinous *processes*. Recall that the cartilaginous (amphiarthrotic) joints between the *bodies* of adjacent vertebrae permit only very slight movement and are classified as symphyses. However, the synovial (diarthrotic) joints between the articulating surfaces of the vertebral *processes* are more movable and are classified as **gliding joints.** These joints hold the vertebrae firmly together so that they are not easily dislocated, but these joints also form a flexible column. Consider how many ways you can move the trunk of your body. You can flex it forward or laterally, you can extend it, and you can circumduct or rotate it (see Figure 10-18).

The bodies of adjacent vertebrae are connected by intervertebral disks and strong ligaments. Fibrous tissue and fibrocartilage form a disk's outer rim (called the *annulus fibrosus*). Its central core (the *nucleus pulposus*), in contrast, consists of a pulpy, elastic substance (Figure 10-13, A). With age, the nucleus loses some of its resiliency. It may then be suddenly compressed by exertion or trauma and pushed through the annulus, with the herniating part protruding into the spinal canal and pressing on spinal



A B

FIGURE 10-13

Vertebrae. Sagittal section of vertebrae showing normal **(A)** and herniated **(B)** disks.

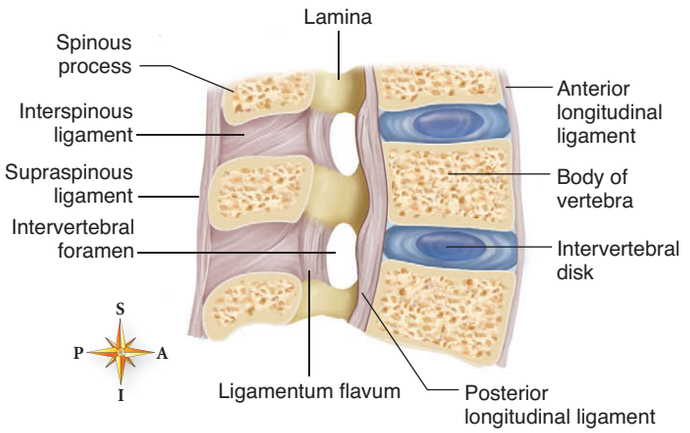


FIGURE 10-14

Vertebrae and their ligaments. Sagittal section of two lumbar vertebrae and their ligaments.

nerves or the spinal cord itself. Severe pain results. In medical terminology, this is called a **herniated disk** or *herniated nucleus pulposus* (HNP); in popular language, it is called a "slipped disk" (Figure 10-13, *B*).

In Figure 10-14 the following ligaments that bind the vertebrae together can be identified: The *anterior longitudinal ligament*, a strong band of fibrous tissue, connects the anterior surfaces of the vertebral bodies from the atlas down to the sacrum. Connecting the posterior surfaces of the bodies is the *posterior longitudinal ligament*. The *ligamenta flava* bind the laminae of adjacent vertebrae firmly together. Spinous processes are connected by *interspinous ligaments*. In addition, the tips of the spinous processes of the cervical vertebrae are connected by the *ligamentum nuchae*; its extension, the *supraspinous ligament*, connects the tips of the rest of the vertebrae down to the sacrum. And finally, *intertransverse ligaments* connect the transverse processes of adjacent vertebrae.

Table 10-4 summarizes the entire chapter with descriptions of most of the individual joints of the body.

| QUICK CHECK |

8. Which joint is the largest, most complex, and most frequently injured in the body?
9. List the two anatomical components of an intervertebral disk.

TYPES AND RANGE OF MOVEMENT AT SYNOVIAL JOINTS

The types of movement possible at synovial joints depend on the shapes of the articulating surfaces of the bones and on the positions of the joints' ligaments and nearby muscles and tendons. All synovial joints, however, permit one or more of the following types of movements:

1. Angular
2. Circular
3. Gliding
4. Special

Measuring Range of Motion

Measuring **range of motion (ROM)** is often one of the first assessment techniques used by a health care provider to determine the degree of damage in an injured joint. In the absence of disease or injury, major synovial joints should function within a normal ROM.

Joint ROM can be measured actively or passively. In active movements the individual moves the joint or body part through its ROM, and in passive movements the physician or other health care provider moves the part with the patient's muscles in a relaxed state. Normally, both active and passive ROM should be about equal.

If a joint has an obvious increase or limitation in its range of motion, an instrument called a **goniometer** is used to measure the angle (Figure 10-15). A goniometer consists of two rigid shafts that intersect at a hinge joint. A protractor is fixed to one shaft so that motion can be read directly from the scale in degrees. The starting position is defined as the point at which the movable segment is at 0 degrees (usually the anatomical position). Measuring joint ROM provides a physician, nurse, athletic trainer, or therapist with information required to assess normal joint function, accurately measure dysfunction, or gauge treatment and rehabilitative progress after injury or disease.

Illustrations in Figures 10-16 through 10-25 provide examples of types of movement at selected synovial joints. Refer to these illustrations frequently as you read about the various types of movement possible at synovial joints.

You will notice that the movements can often be classified as opposites: flexion is the opposite of extension, protraction is the opposite of retraction, and so on. Remembering this concept will be useful to you when the mechanism of antagonistic muscle groups is discussed in Chapter 11.

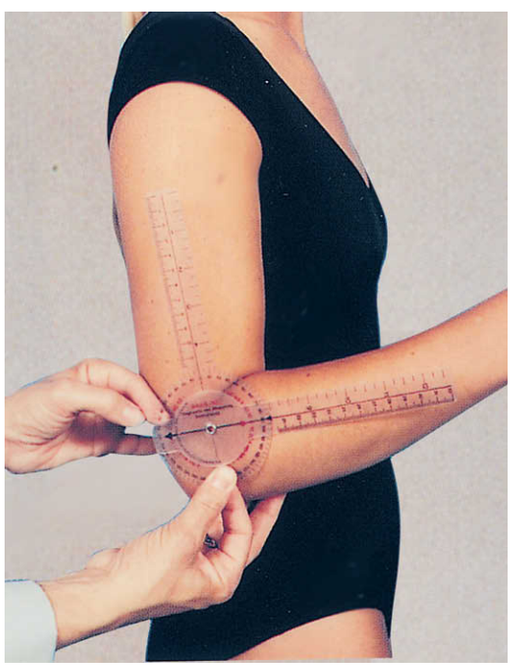


FIGURE 10-15

Use of a goniometer. Using a goniometer to measure range of motion (ROM) at the elbow.

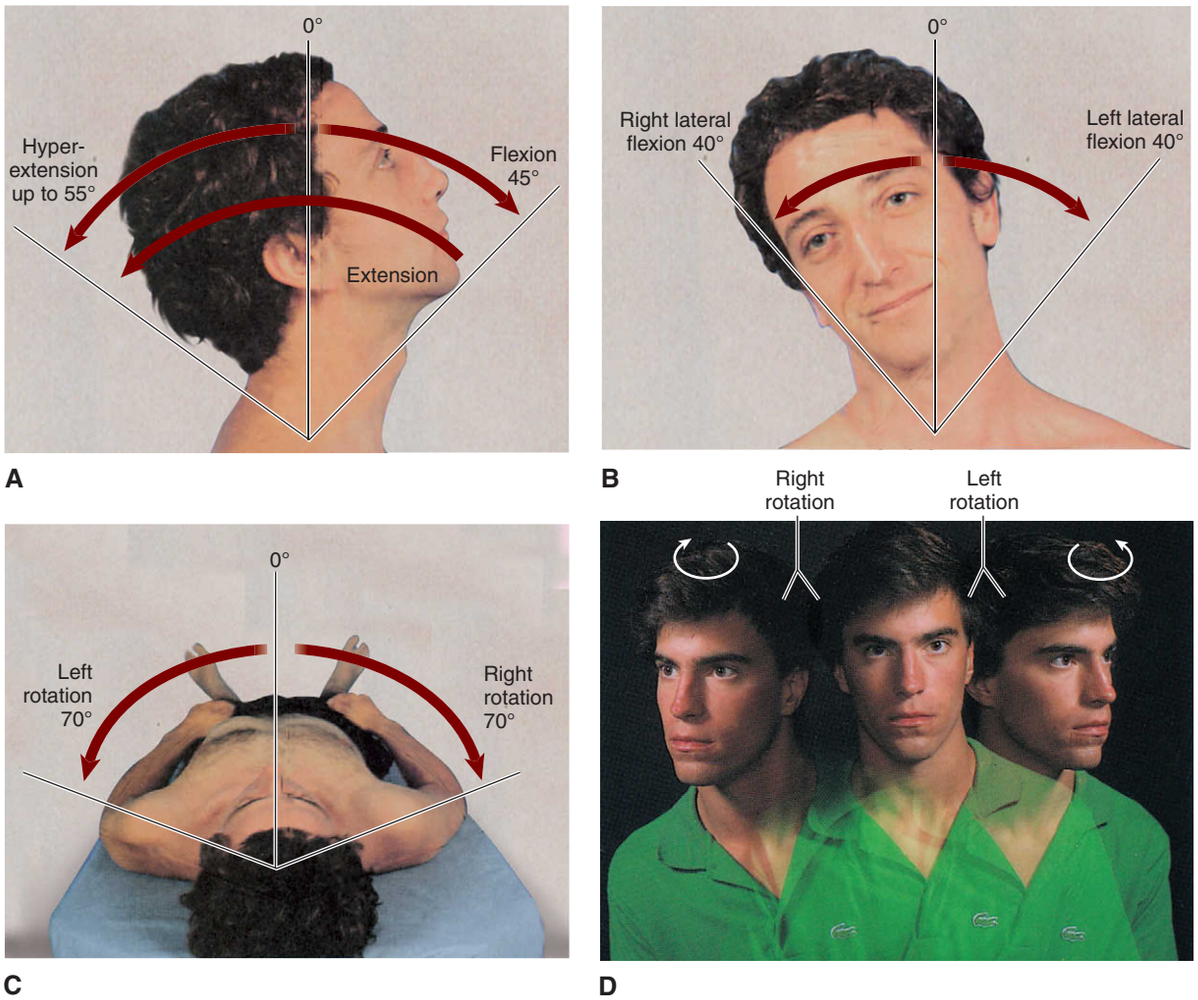


FIGURE 10-16

Movements and range of motion (ROM). A, Flexion and extension. Extension beyond the anatomical position is sometimes called *hyperextension.* **B,** Lateral bending. **C,** Rotation (supine position). **D,** Rotation (standing position).

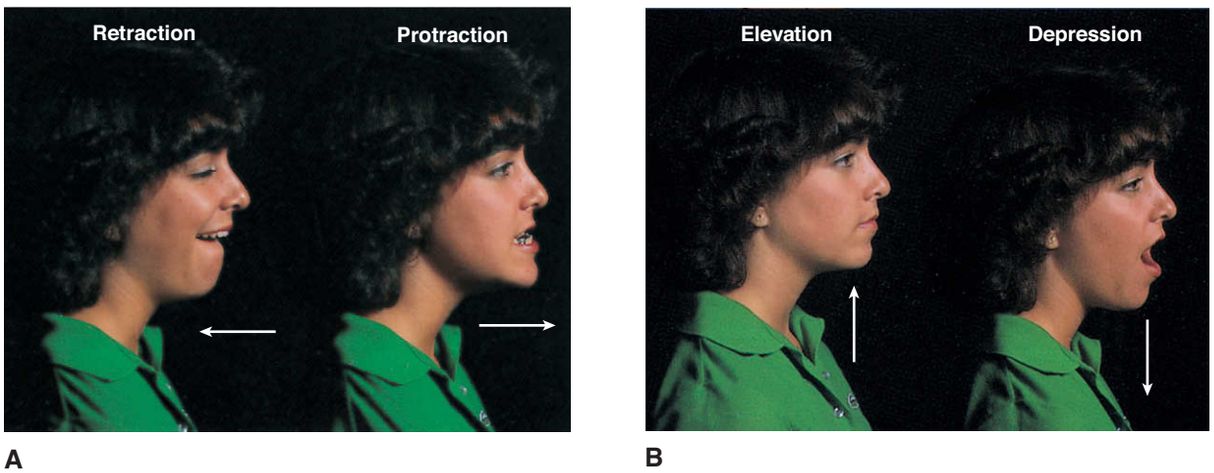
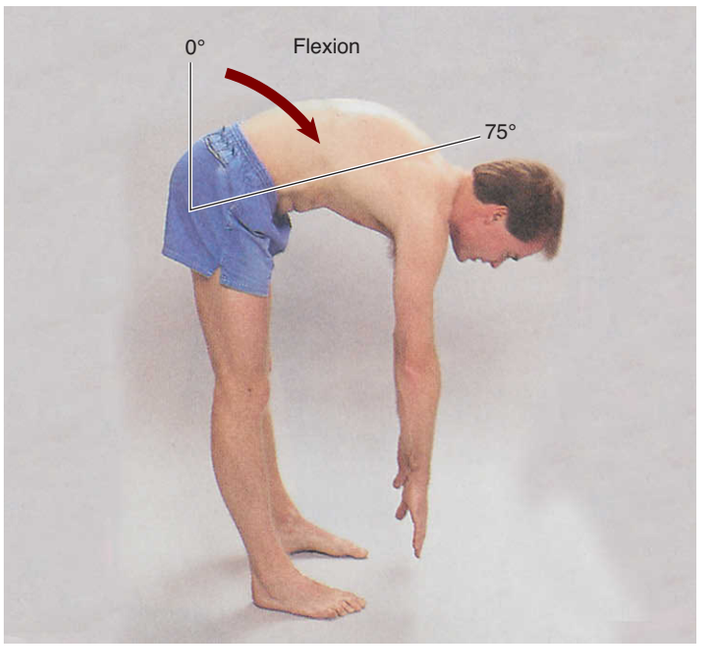
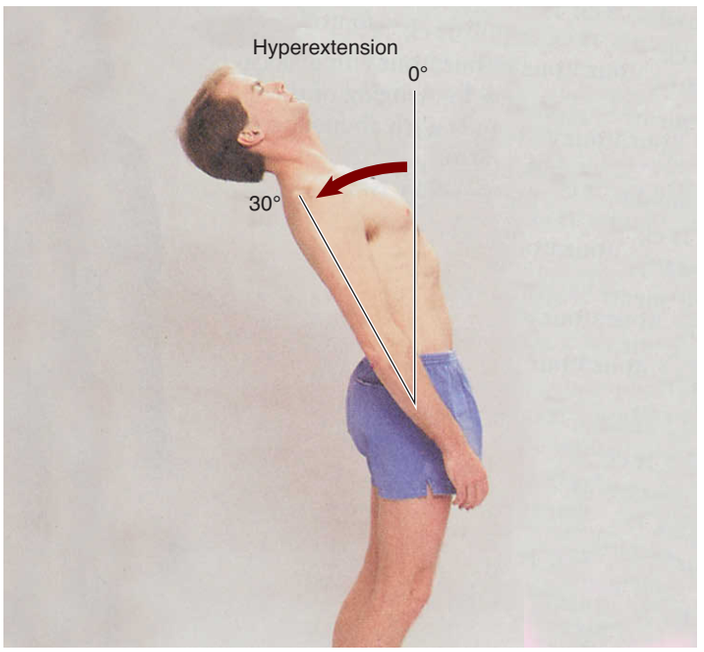


FIGURE 10-17

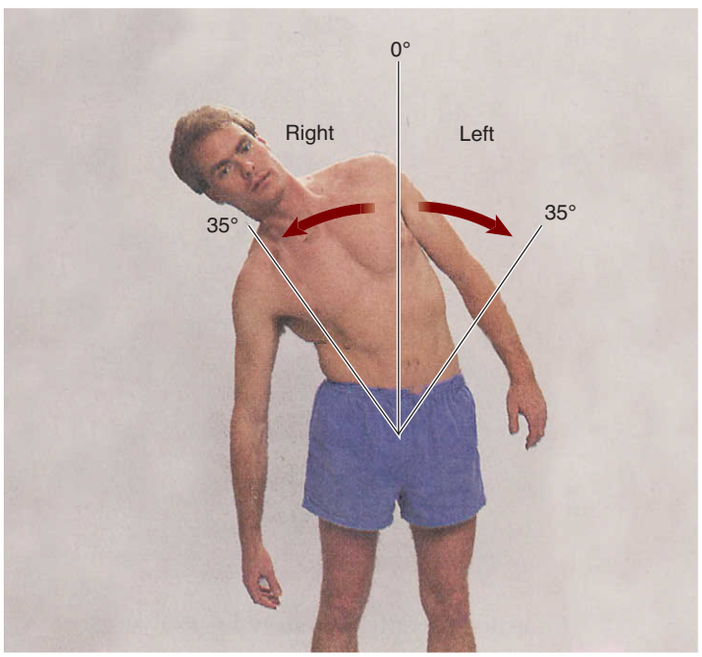
Movements of the jaw. A, Retraction and protraction. **B,** Elevation and depression.



A



B



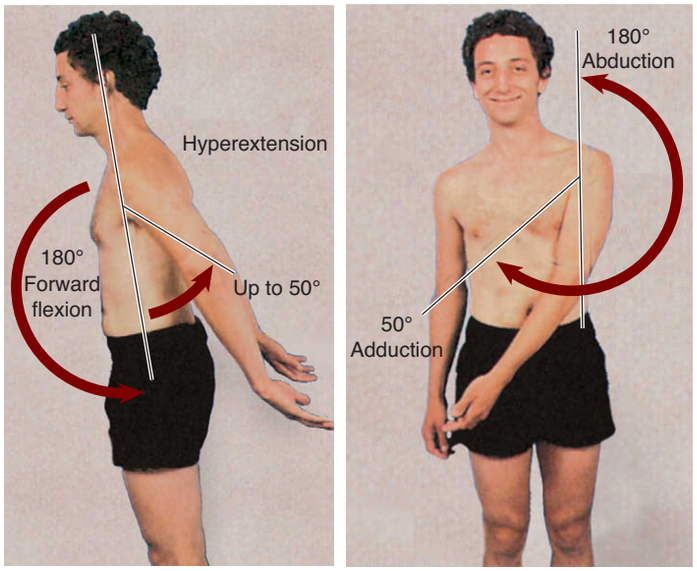
C



D

FIGURE 10-18

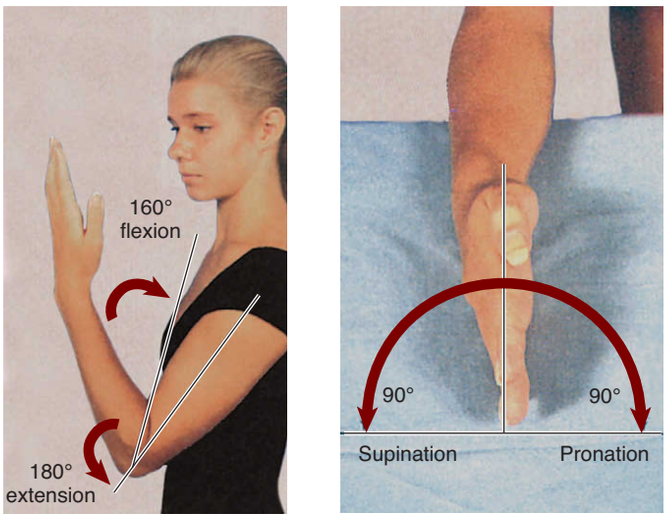
Movements and range of motion (ROM) of the thoracic and lumbar spine. A, Flexion. **B,** Hyperextension. **C,** Lateral bending. **D,** Rotation of the upper part of the trunk.



A B

FIGURE 10-19

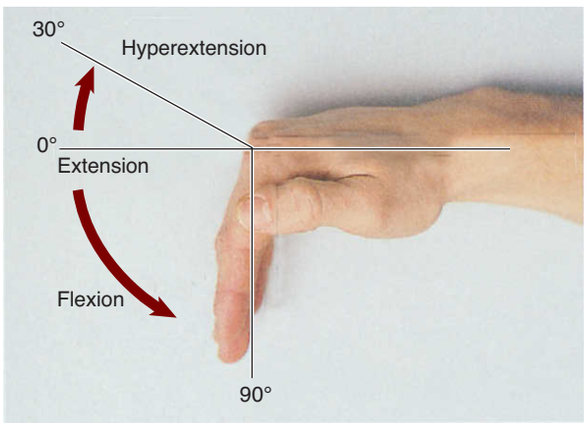
Movements and range of motion (ROM) of the shoulder. A, Forward flexion, extension (back to the anatomical position of 0 degrees), and backward hyperextension up to 50 degrees. **B,** Abduction and adduction.



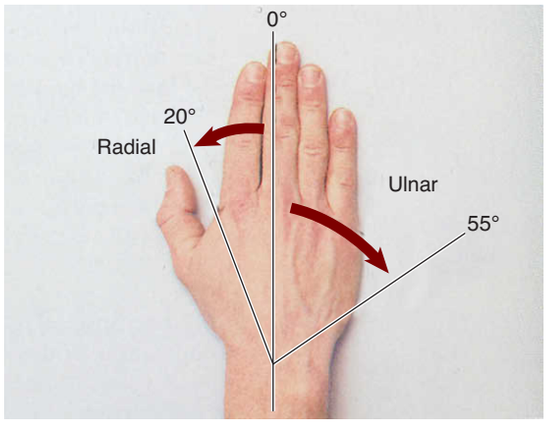
A B

FIGURE 10-20

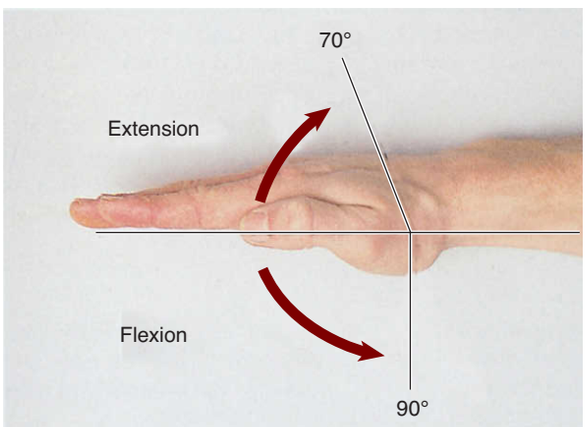
Movements and range of motion (ROM) of the elbow. A, Flexion and extension of the elbow. **B,** Supination and pronation.



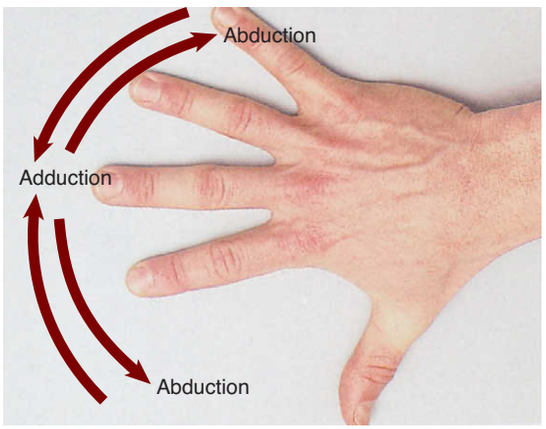
A



B



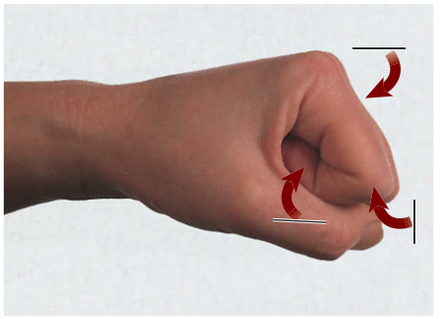
C



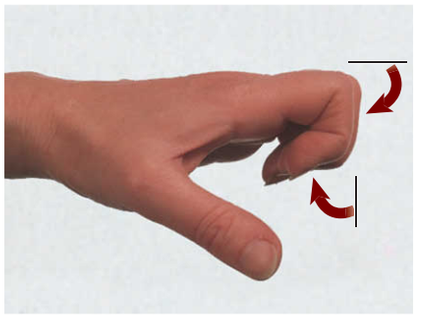
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FIGURE 10-21

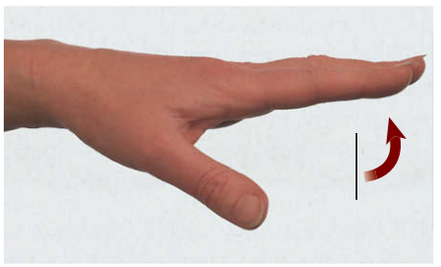
Movements and range of motion (ROM) of hand and wrist. A, Metacarpophalangeal flexion and hyperextension. **B,** Wrist radial and ulnar movement. **C,** Wrist flexion and hyperextension. **D,** Finger abduction and adduction.



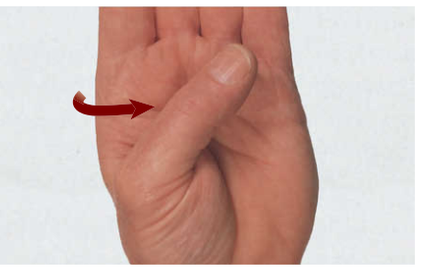
A



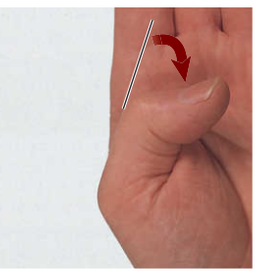
B



C



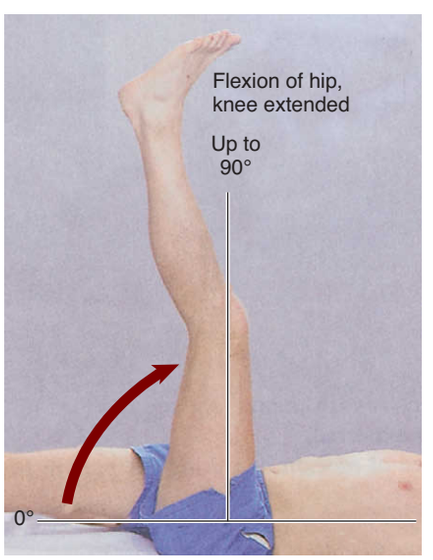
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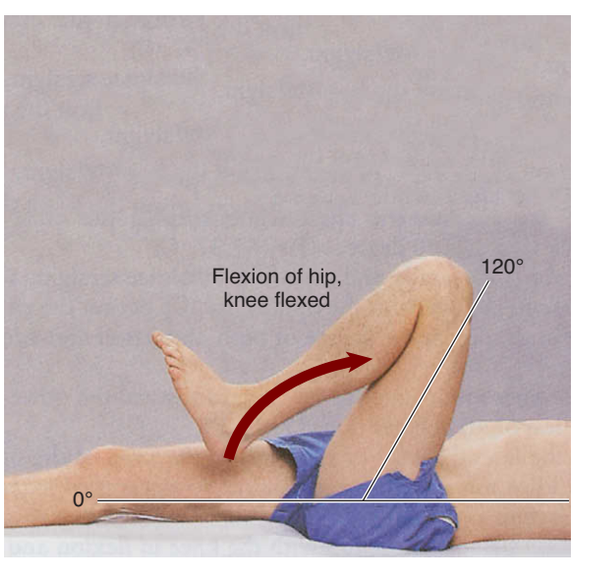
E

FIGURE 10-22

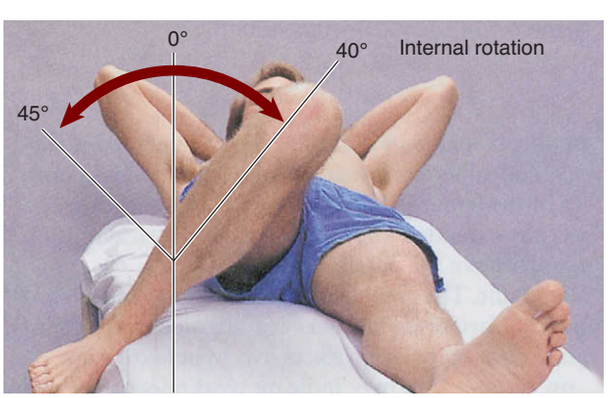
Movements of the fingers and thumb. A, Flexion of the metacarpophalangeal joints and flexion of the interphalangeal joints. **B,** Extension of the metacarpophalangeal joints and flexion of the interphalangeal joints. **C,** Extension of the metacarpophalangeal and interphalangeal joints. **D,** Opposition of the thumb. **E,** Flexion of the thumb.



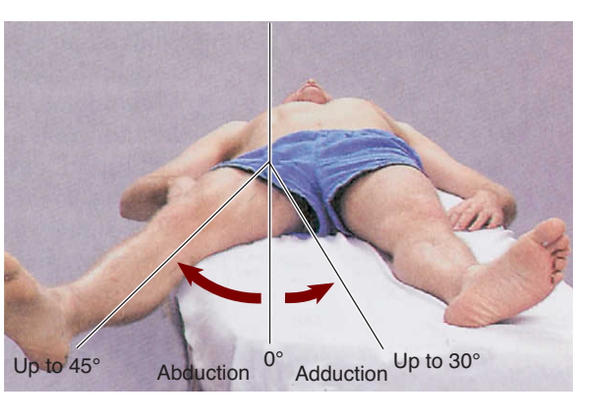
A



B



C



D

FIGURE 10-23

Movements and range of motion (ROM) of the hip. A, Hip flexion, knee extended. **B,** Hip flexion, knee flexed. **C,** Internal rotation. **D,** Abduction and adduction.

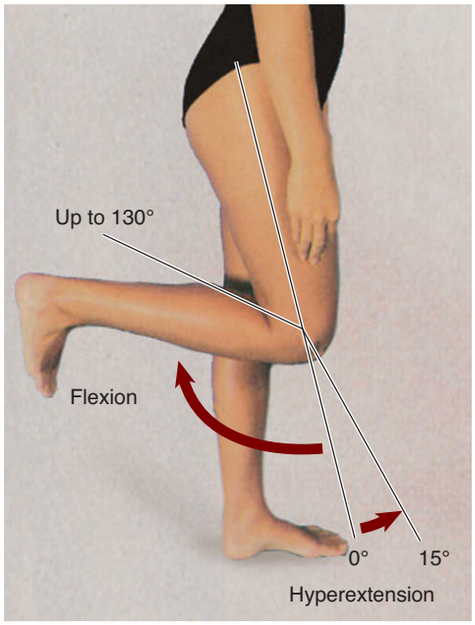


FIGURE 10-24

Movements and range of motion (ROM) of the knee. Flexion may reach 130 degrees. Extension occurs with movement from a 130-degree flexed position back to the 0-degree position. Hyperextension of 0 degrees to 15 degrees is possible in many individuals.

Angular Movements

Angular movements change the size of the angle between articulating bones. Flexion, extension, abduction, and adduction are some of the different types of angular movements.

FLEXION

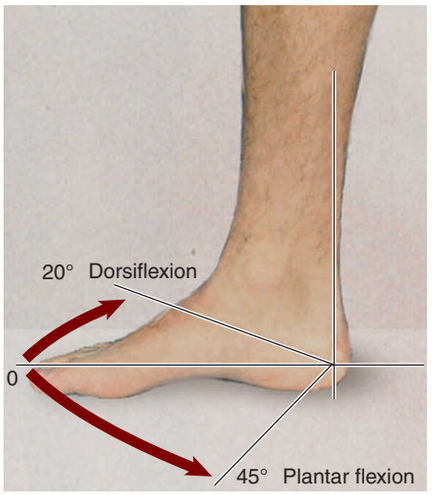
Flexion decreases the angle between bones. It bends or folds one part on another. For example, if you bend your head forward on your chest, you are flexing it. If you bend your arm at the elbow, you are flexing the lower part of your arm (see Figure 10-20, *A*). Flexion, in short, is bending, folding, or withdrawing a part. Flexion can also occur when an extended structure is returned to the anatomical position.

EXTENSION AND HYPEREXTENSION

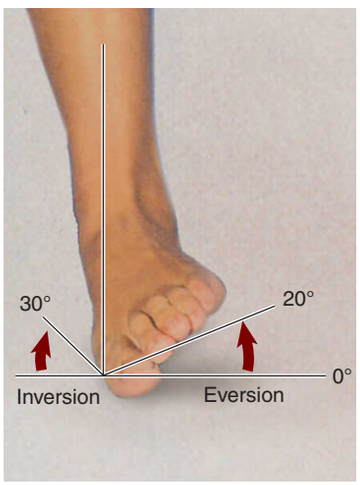
Extension increases the angle between bones. It returns a part from its flexed position to its anatomical position. Extensions are straightening or stretching movements. Extending a part beyond its anatomical position is sometimes called **hyperextension.** Hyperextension of the shoulder is illustrated in Figure 10-19, *A*, and of the knee in Figure 10-24. Clinically, hyperextension often refers to abnormal extension beyond a part's normal range of motion.

PLANTAR FLEXION AND DORSIFLEXION

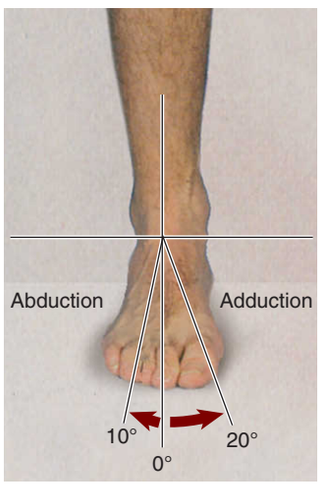
Plantar flexion occurs when the foot is stretched down and back (see Figure 10-25, *A*). This movement increases the angle between the top of the foot and the front of the leg. Recall that the definition of extension refers to an increase in the angle between articulating bones. Therefore, plantar flexion of the foot can also be described as extension. Look again at Figure 10-25, *A*, and note how the angle between the leg and the foot increases during plantar flexion.



A



B



C

FIGURE 10-25

Movements and range of motion (ROM) of the foot and ankle. **A,** Dorsiflexion and plantar flexion. **B,** Inversion and eversion. **C,** Abduction and adduction.

Dorsiflexion occurs when the foot is tilted upward, thus decreasing the angle between the top of the foot and the front of the leg (see Figure 10-25, *A*).

ABDUCTION AND ADDUCTION

Abduction moves a part away from the median plane of the body, as in moving the leg straight out to the side or fingers away from the midline of the hand. **Adduction** moves a part toward the median plane. Examples include bringing the arm back to the side or moving fingers toward the midline of the hand. Opposing movements in the shoulder can be seen in Figure 10-19, *B*.

Circular Movements

Circular movements result in the arclike rotation of a structure around an axis. The primary circular movements are rotation, circumduction, supination, and pronation (see Figure 10-16, *B*).

ROTATION AND CIRCUMDUCTION

Rotation consists of pivoting a bone on its own axis. For example, moving the head from side to side as in indicating "no" (see Figure 10-16, *D*). **Circumduction** moves a part so that its distal end moves in a circle. When a pitcher winds up to throw a ball, the pitcher circumducts the arm.

SUPINATION AND PRONATION

Supination and **pronation** of the hand are shown in Figure 10-20, *B*. Pronation twists the forearm, moving the palm so that the thumbs point medially. Supination twists the forearm in the opposite rotation, moving the palm so that the thumbs point laterally.

Gliding Movements

Gliding movements are the simplest of all movements. The articular surface of one bone moves over the articular surface of another without any angular or circular movement. Gliding movements occur between the carpal and tarsal bones and between the articular facets of adjoining spinal vertebrae.

Special Movements

Special movements are often unique or unusual movements that occur only in a very limited number of joints. These movements do not fit well into other movement categories and are generally described separately. Special movements include inversion, eversion, protraction, retraction, elevation, and depression.

INVERSION AND EVERSION

Inversion turns the sole of the foot inward, whereas **eversion** turns it outward (see Figure 10-25, *B*).

PROTRACTION AND RETRACTION

Protraction moves a part forward, whereas **retraction** moves it back. For instance, if you stick out your jaw, you protract it, and if you pull it back, you retract it (see Figure 10-17, *A*).

ELEVATION AND DEPRESSION

Elevation moves a part up, as in closing the mouth (see Figure 10-17, *B*). **Depression** lowers a part, moving it in the opposite direction from elevation.

| QUICK CHECK |

10. Name one example of each of the following types of movement at a synovial joint: angular, circular, gliding, and special.

Cycle of LIFE

Articulations

This chapter discusses the types of articulations that occur between bones and presents information on the common types of diseases that affect joints during the life cycle.

Changes in the way bones develop and in the sequence of ossification that occurs between birth and skeletal maturity also affect our joints. Fontanels, which exist between bones of the cranium, disappear with increasing age, and the epiphyseal plates, which serve as points of articulation between the epiphyses and diaphyses of growing long bones, ossify at skeletal maturity.

Range of motion at synovial joints is typically greater early in life. With advancing age, joints are often described as being "stiff," range of motion decreases, and changes in gait are common. The difficulty with locomotion that affects many elderly individuals may result from disease conditions that involve the functional unit comprising muscles, bones, and joints.

Some skeletal diseases have profound effects that are manifested as joint problems. Abnormal bone growth, or "lipping," which results in bone spurs, or sharp projections, on the articular surfaces of bones, dramatically influences joint function. Many of these disease conditions are associated with specific developmental periods, including early childhood, adolescence, and adulthood.

the BIG picture

Articulations

Anatomists sometimes refer to the hand as "the reason for the upper extremity" and the thumb as "the reason for the hand." Statements such as these, when they are used in a functional context, underscore the relationship that exists between structure and function. Furthermore, they serve as examples of how "big picture" thinking is helpful in examining the interaction between body structures and the rationale for how and why they function as they do. Proper functioning of the joints is crucial for meaningful, controlled, and purposeful movement to occur—movement that permits human beings to respond to and control their environment in ways that other animals are not capable of doing. The joints of the upper extremity are good examples.

The great mobility of the upper extremity is possible because of the following: (1) the arrangement of the bones in the shoulder girdle, arm, forearm, wrist, and hand; (2) the location and method of attachment of muscles to these bones; and (3) proper functioning of the joints involved. We give up a great deal of stability in the upper extremity (especially the shoulder joint) to achieve mobility. We need that mobility and extensive range of motion to position the entire upper extremity, and especially the hand, in ways that permit us to interact with objects in our physical environment effectively. It is the proper functioning of the thumb that allows us to grasp and manipulate objects with great dexterity and control. Although loss of mobility in the upper extremity as a whole presents a significant functional problem, loss of thumb function can present equally serious and disabling problems by dramatically decreasing the overall ability to manipulate and grasp objects. By enabling us to effectively interact with our external environment, the joints of the upper extremity contribute in a significant way to maintenance of homeostasis. It is in the "big picture" context that the hand and thumb are truly functional "reasons" for the upper extremity and the hand, respectively.

MECHANISMS of DISEASE

BURSITIS

Bursitis, or inflammation of a bursa, is a relatively common disorder. It is most often caused by prolonged pressure, excessive or repetitive exercise, or sudden trauma that involves one of these fluid-filled sacs. Although bursae are often associated with joints, where they may serve to cushion the joint or facilitate the movement of tendons over bony prominences, such as the olecranon of the elbow joint, the bursa itself is often completely separate from the joint space. Look again at Figure 10-6, *A*. It clearly shows the placement of the olecranon bursa just below the skin and independent of the joint space of the elbow. Therefore, inflammation of the olecranon bursa (Figure 10-26) may occur in the absence of any elbow joint inflammation or pathology. Bursitis near the knee joint is also common, especially in carpet layers, roofers, and others who work on their knees.

Joint Disorders

Joint disorders may be classified as **noninflammatory joint disease** or **inflammatory joint disease.** Serving as fulcrums, the joints permit smooth and precise movement to occur when a muscle contracts and pulls on bones. Because joints, bones, and muscles act together as a functional unit, joint disorders, regardless of type or classification, have profound effects on body mobility.

Noninflammatory Joint Disease

Noninflammatory types of joint disease can be distinguished from inflammatory joint conditions because they do not involve inflammation of the synovial membrane. Further, noninflammatory joint diseases do not produce systemic signs or symptoms, such as fever, or damage other body organs such as the heart and lungs.

Osteoarthritis, known also as *degenerative joint disease* (DJD), is the most common noninflammatory disorder of movable joints. It is characterized by "wear and tear" degeneration and fracturing of articular cartilage (Box 10-2) and by abnormal formation of new bone ("bone spurs") at joint surfaces. In DJD the articular cartilage no longer acts as a "shock absorber," the joint space narrows, the synovial membrane thickens, and the ligaments calcify.

Large weight-bearing joints, such as the hips and knees, are often involved first, followed by involvement of joints in the fingers. Swelling deformities of the *distal* interphalangeal joints called **Heberden nodes** and of the *proximal* interphalangeal joints called **Bouchard nodes** are common. Figure 10-27, *A*, shows the hands of a woman with osteoarthritis. The cause of osteoarthritis is unknown, but obesity, aging, and the "wear and tear" of mechanical stresses on joints over time are known to play a major role.

Unfortunately, no treatment is available to stop the degenerative joint disease process completely. Symptoms, which appear in many people in their fifties and sixties, include morning stiffness,

Box 10-2 | HEALTH matters

Joint Mice

The thin layer of cartilage that covers the articulating surfaces of bones in synovial joints may become cracked as a result of traumatic injury—especially to the knee. Such injuries are called **chondral fractures.** They result in fissuring of the articular cartilage, which can be likened to the cracking of an egg shell. If such an injury occurs, small fragments may become detached from the damaged layer of cartilage and enter the joint cavity. These fragments are called "loose bodies" or *joint mice* because they often cause clicking sounds or catching and locking sensations during joint movement. Symptoms often vary over time as cartilage fragments move about the joint cavity in the synovial fluid. Pain and loss of motion will occur if the fragments become lodged between opposing bone surfaces.



FIGURE 10-26

Olecranon bursitis. Pain, inflammation, and swelling of the bursa may limit motion, although the elbow joint itself may not be affected.



A



B



C

FIGURE 10-27

Types of arthritis. **A,** Osteoarthritis. Note Heberden nodes (*H*) on the distal interphalangeal joints and Bouchard nodes (*B*) on the proximal interphalangeal joints. **B,** Rheumatoid arthritis. Note the marked ulnar deviation of the fingers. **C,** Gouty arthritis. Note the tophi filled with sodium urate crystals.

deep "achy" pain on movement that worsens with use, and limited joint motion. In many cases, symptoms can be treated effectively with standard **nonsteroidal antiinflammatory drugs (NSAIDs),** such as aspirin or ibuprofen, or by nutritional supplements such as glucosamine or chondroitin sulfate (see Chapter 8, p. 204). Injection into the joint space, especially of the knee, of a gelatinous type of lubricating fluid containing *hyaluronic acid* has proved useful in some cases. If the disease is more advanced, various types of prescription medications or partial or total joint replacements may be necessary (Box 10-3). Although the severity of symptoms may plateau or stabilize for varying periods, the disease is generally progressive once established and will continue over a lifetime. Osteoarthritis is the leading cause of long-term disability in aging, but otherwise healthy, individuals.

Traumatic injuries are a frequent cause of joint injury. **Dislocation** (subluxation) of a joint as a result of trauma can be an emergency because of associated damage to important blood vessels and nerves. In a dislocation, the articular surfaces of bones forming the joint are no longer in proper contact. This displacement of bone alters the normal contour of the joint and can tear surrounding ligaments. Refer once again to Figure 10-6, *B*. Recall that the annular ligament is intended to hold the head of the radius firmly against the radial notch of the ulna at the proximal radioulnar joint. Functionally, it is this anatomic relationship that allows the radius to rotate freely without dislocation during pronation and supination of the forearm. In children younger than 5 years especially, dislocation of the radial head, called a "pulled elbow," is a common traumatic joint injury. Pain and soft tissue swelling are associated with dislocation injuries. Effective treatment involves early reduction or realignment.

One of the most common traumatic joint injuries associated with athletic activity involves damage to the cartilaginous menisci of the knee. Because the menisci act as shock absorbers and stabilize the knee, severe tears may produce edema, pain, instability, and limited motion. Arthroscopic surgical procedures are frequently used in both the diagnosis and treatment of this type of knee injury (Figure 10-28).

Arthroscopy is an imaging technique that allows a physician to examine the internal structure of a joint without the use of extensive surgery (see Figure 10-28, A). A narrow tube with lenses and a fiberoptic light source is inserted into the joint space through a small puncture. Isotonic saline (salt) solution is injected through a needle to expand the volume of the synovial space. This spreads the joint structures and makes viewing easier (see Figure 10-28, *B*).

Although arthroscopy is often used as a diagnostic procedure, it also can be used to perform joint surgery. While the surgeon views the internal structure of the joint through the arthroscope or on an attached video monitor, instruments can be inserted through puncture holes and used to repair or remove damaged tissue. Arthroscopic surgery is much less traumatic than previous methods in which the joint cavity was completely opened.

Box 10-3 | SPORTS and FITNESS

Joint Replacement

Arthroplasty is the total or partial replacement of a diseased joint with an artificial device called a **prosthesis.** Prosthetic joints or joint components must allow for considerable mobility and be durable, strong, and compatible with surrounding tissues. Development of new prosthetic materials and surgical techniques to replace diseased joints gained momentum with the first successful total hip replacement (THR) procedure. It was performed by noted English orthopedic surgeon Sir John Charnley in 1963. Currently, hip and knee replacements are performed in nearly equal numbers and are the most common orthopedic operations performed on older persons, performed more than 300,000 times each year in the United States. In addition, large numbers of elbow, shoulder, finger, and other joint replacement procedures are performed annually. Osteoarthritis and other types of degenerative bone disease frequently destroy or severely damage joints and cause unremitting pain. Total joint replacement is often the only effective treatment option available.



The THR procedure involves replacement of the femoral head by a metallic alloy prosthesis and the acetabular socket with a high-density polyethylene cup. In the past, both pieces were generally cemented into place with methyl methacrylate adhesive. Many of the newer prostheses, however, are "porous coated" to permit natural ingrowth of bone for stability and retention. The advantage of bone ingrowth is prevention of loosening that occurs if the cement bond weakens. With advanced surgical techniques and newer metal prostheses fabricated from alloys of titanium, cobalt/chrome, and surgical steel, 10-to 15-year THR and total knee replacement success rates have risen to approximately 85% in older patients. However, even more durable metal and plastic components are necessary to extend the 10- to 15-year lifespan of most hip and knee prostheses currently in use. At the present time, younger patients who stress artificial joints more than older adults are encouraged to delay replacement and rely instead on evolving therapies, which are intended to heal or regenerate diseased joint tissues. The x-ray illustration shows placement of a noncemented, porous-coated femoral prosthesis made of titanium alloy and a cemented acetabular socket made of high-density plastic.

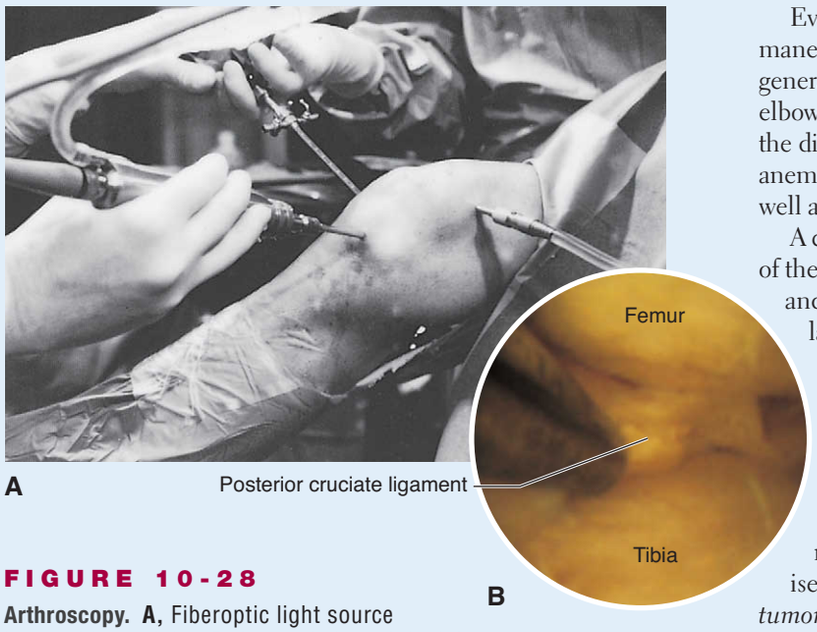


FIGURE 10-28

Arthroscopy. A, Fiberoptic light source inserted into a joint. **B,** Internal view of the joint.

A **sprain** is an acute musculoskeletal injury to the ligamentous structures surrounding a joint that disrupts the continuity of the synovial membrane. A common cause is a twisting or wrenching movement often associated with "whiplash"-type injuries. Blood vessels may be ruptured, and bruising and swelling may occur. Limitation of joint motion is common in all sprain injuries. External ankle rotation sprain injuries are discussed on p. 284.

Inflammatory Joint Disease

Arthritis is a general name for many different inflammatory joint diseases. Arthritis can be caused by a variety of factors, including infection, injury, genetic factors, and autoimmunity. Here is a brief list of the major types of arthritis:

Rheumatoid arthritis (RA) is a form of systemic autoimmune disease that involves chronic inflammation of many different tissues and organs of the body. Although organs such as the heart, lungs, skin, and muscles may become involved, the disease generally attacks joints first—and affects them most severely. A wide range of pathological joint changes are associated with RA. Initially, the synovial membrane becomes inflamed, thickened, and edematous. Soon, the diseased synovial membrane produces an aggregation of inflammatory cells, granulation tissue, and fibroblasts called **pannus** that adheres to the articular cartilage. It is the continued growth and spreading of pannus tissue that destroys articular cartilage and bridges the opposing bones.

Eventually, the bones fuse together, movement ceases, and permanent crippling occurs. Small joints in the hands and feet are generally affected first. As the disease progresses, the wrists, ankles, elbows, knees, and cervical spine may also be involved. Because the disease is systemic, most patients experience symptoms such as anemia, weight loss, fever, fatigue, and generalized muscle pain, as well as symptoms associated with specific types of joint pathology.

A characteristic deformity of the hands in RA is **ulnar deviation** of the fingers (Figure 10-27, *B*). A number of other common signs and symptoms are related to inflammation and loss of articular surface. They include reduction in joint mobility, pain, nodular swelling, and generalized aching and stiffness.

In the past, treatment for many patients was often limited to NSAIDs and other pain or antiinflammatory-type medication, corticosteroids, and so-called disease-modifying antirheumatic drugs such as methotrexate. Newer drugs influencing the altered immune system response in RA, called **TNF blockers,** are showing promise in many individuals suffering from this disease. *TNF,* or *tumor necrosis factor,* is a substance made in excess by the body's immune system in RA. It is involved in pannus formation, destruction of articular cartilage, and pain and swelling of joints. By blocking the effects of this substance, people with moderate RA often experience significant relief from symptoms and from continued damage to bone and joints.

Juvenile rheumatoid arthritis (JRA) is often more severe than the adult form but involves similar deterioration and deformity of joints. Onset is generally systemic and associated with rash, high fever, and swelling of the liver and spleen. Targeted joints, which include the wrists, elbows, knees, and ankles, are generally warm and swollen. The joint inflammatory process often destroys the growth of epiphyseal cartilage, and the growth of long bones is arrested. This form begins during childhood and is more common in girls. In addition to articular damage, JRA also affects the heart, lungs, muscles, and kidneys in many young patients.

Gouty arthritis is another type of inflammatory arthritis. It is a metabolic disorder in which excess blood levels of uric acid, a nitrogenous waste, are deposited as sodium urate crystals within the synovial fluid of joints and in other tissues. These deposits, called **tophi,** are often obvious in the soft tissues of patients with gouty arthritis (Figure 10-27, *C*). They trigger the chronic inflammation and tissue damage seen with the disease. Swelling, tenderness, or pain typically appears in the fingers, wrists, elbows, ankles, and knees. Allopurinol (Zyloprim) and febuxostat (Uloric) are drugs commonly used to treat the disease. They inhibit the synthesis of uric acid. Colchicine is an anti-inflammatory agent first used for treatment of articular pain in 1810. Today, it remains a preferred agent (Colcrys, others) in treatment of gouty arthritis.

LANGUAGE OF SCIENCE *(continued from p. 271)*

distal interphalangeal (DIP)
(DIS-tal inter-fah-LAN-gee-al)
[*dist-* **distance,** *-al* **relating to,** *inter-* **between,** *-phalang-* **finger bones (ref. from rows of soldiers),** *-al* **relating to**]

dorsiflexion
(dor-si-FLEK-shun)
[*dorsi-* **back,** *-flex-* **bend,** *-ion* **process**]

elevation
[*e(x)-* **up,** *-lev-* **raise,** *-at-* **perform,** *-tion* **process**]

eversion
(ee-VER-shun)
[*e(x)-* **outward,** *-ver-* **turn,** *-sion* **process**]

extension
[*ex- outward, -tens-* **stretch,** *-sion* **process**]

flexion
(FLEK-shun)
[*flex-* **bend,** *-ion* **process**]

gliding joint
gliding movement
gomphosis
(gom-FOH-sis)
[*gomphos-* **bolt,** *-osis* **condition**] *pl.,* gomphoses

goniometer
(gon-ee-OM-eh-ter)
[*gonio-* **angle,** *-meter* **measure**]

hyperextension
(hye-per-ek-STEN-shun)
[*hyper-* **excessive,** *-ex-* **out,** *-ten-* **stretch,** *-sion* **process**]

intercarpal joint
(in-ter-KAR-pal)
[*inter-* **between,** *-carp-* **wrist,** *-al* **relating to**]

interphalangeal joint
(in-ter-fah-LAN-jee-al)
[*inter-* **between,** *-phalang-* **finger bones (ref. from rows of soldiers),** *-al* **relating to**]

inversion
(in-VER-shun)
[*in- inward, -ver-* **turn,** *-sion* **process**]

joint capsule
joint cavity
ligament
(LIG-ah-ment)
[*liga-* **bind,** *-ment* **result of action**]

meniscus
(meh-NIS-kus)
[*meniscus* **crescent**] *pl.,* menisci

metacarpophalangeal joint
(met-ah-KAR-poh-fah-LAN-jee-al)
[*meta-* **beyond,** *-carpo-* **wrist,** *-phalang-* **finger bones (ref. from rows of soldiers),** *-al* **relating to**]

multiaxial joint
(mul-tee-AK-see-al)
[*multi-* **many,** *-axon* **axle**]

nonsteroidal antiinflammatory drug (NSAID)
(nahn-STAYR-oyd-al an-ti-in-FLAM-ah-toh-ree)
[*non-* **not,** *-stero-* **solid,** *-oid* **like,** *-al* **relating to,** *anti-* **against,** *-inflam-* **set afire,** *-ory* **relating to**]

olecranon bursa
(oh-LEK-rah-non BER-sah)
[*olecranon* **elbow,** *bursa* **purse**] *pl.,* bursae

plantar flexion
(PLAN-tar FLEK-shun)
[*planta-* **sole,** *-ar* **relating to,** *flex-* **bend,** *-ion* **process**]

pronation
(proh-NAY- shun)
[*pronat-* **bend forward,** *-tion* **process**]

protraction
(proh-TRAK- shun)
[*pro-* **forward,** *-tract-* **drag,** *-tion* **process**]

proximal interphalangeal (PIP)
(PROK-si-mal in-ter-fah-LAN-gee-al)
[*proxima-* **near,** *-al* **relating to,** *inter-* **between,** *-phalang-* **finger bones (ref. from rows of soldiers),** *-al* **relating to**]

radiocarpal joint
(RAY-dee-oh-KAR-pal)
[*radio-* **ray,** *-carp-* **wrist,** *-al* **relating to**]

radioulnar joint
(RAY-dee-oh-UL-nur)
[*radio-* **ray,** *-ulna-* **elbow or arm,** *-ar* **relating to**]

range of motion (ROM)
retraction
[*re-* **back,** *-tract-* **drag,** *-tion* **process**]

rotation
(roh-TAY-shun)
[*rot-* **turn,** *-ation* **process**]

special movement
supination
(soo-pi-NAY-shun)
[*supin-* **lying on the back,** *-ation* **process**]

suture
(SOO-chur)
[*suture-* **seam**]

symphysis
(SIM-fi-sis)
[*sym-* **together,** *-physis* **growth**] *pl.,* symphyses

synarthrosis
(sin-ar-THROH-sis)
[*syn-* **together,** *-arthr-* **joint,** *-osis* **condition**] *pl.,* synarthroses

synchondrosis
(SIN-kon-DROH-sis)
[*syn-* **together,** *-chondr-* **cartilage,** *-osis* **condition**] *pl.,* synchondroses

syndesmosis
(SIN-dez-MO-sis)
[*syn-* **together,** *-desmo-* **bond,** *-osis* **condition**] *pl.,* syndesmoses

synovial membrane
(si-NO-vee-all)
[*syn-* **together,** *-ovi-* **egg (white),** *-al* **relating to,** *membran-* **thin skin**]

uniaxial joint
(yoo-nee-AK-see-al)
[*uni-* **one,** *-axi-* **axle,** *-al* **relating to**]

LANGUAGE OF MEDICINE

arthritis
(ar-THRY-tis)
[*arthr-* **joint,** *-itis* **inflammation**]

Bouchard node
(boo-SHAR)
[*Charles J. Bouchard* **French physician,** *nod-* **knot**]

bursitis
(ber-SYE-tiss)
[*bursa-* **purse,** *-itis* **inflammation**]

chondral fracture
(KON-dral)
[*condr-* **cartilage,** *-al* **relating to,** *fracture* **a breaking**]

dislocation
[*dis-* **apart,** *-locat-* **to place,** *-tion* **process**]

gouty arthritis
(gow-TEE ar-THRY-tis)
[*gout-* **drop,** *-y* **of or like,** *arthr-* **joint,** *-itis* **inflammation**]

Heberden node
(HEB-er-den)
[*William Heberden* **English physician,** *nod-* **knot**]

herniated disk
(HER-nee-ayt-ed)
[*hernia-* **rupture,** *-ate* **act of**]

inflammatory joint disease
(in-FLAM-ah-toh-ree)
[*inflam-* **set afire,** *-ory* **relating to**]

juvenile rheumatoid arthritis (JRA)
(JOO-veh-neyel ROO-mah-toyd ar-THRY-tis)
[*juven-* **youth,** *-ile* **of or like,** *rheuma-* **flow,** *-oid* **like,** *arthr-* **joint,** *-itis* **inflammation**]

noninflammatory joint disease
(nahn-in-FLAM-ah-toh-ree)
[*non-* **not,** *- inflam-* **set afire,** *-ory* **relating to**]

olecranon bursitis
(oh-LEK-rah-nohn ber-SYE-tis)
[*olecranon* **elbow,** *burs-* **purse,** *-itis* **inflammation**]

osteoarthritis
(os-tee-oh-ar-THRY-tis)
[*osteo-* **bone,** *-arthr-* **joint,** *-itis* **inflammation**]

pannus
(PAN-us)
[*pannus* **tattered cloth**]

prepatellar bursitis
(pree-pah-TEL-er ber-SYE-tis)
[*pre-* **in front of,** *-pat-* **dish,** *-ella* **small,** *-ar* **relating to,** *bursa-* **purse,** *-itis* **inflammation**]

prosthesis
(pros-THEE-sis)
[*prosthesis* **addition**] *pl.,* prostheses

rheumatoid arthritis (RA)
(ROO-mah-toyd ar-THRY-tis)
[*rheuma-* **flow,** *-oid* **like,** *arthr-* **joint,** *-itis* **inflammation**]

sprain

sprained ankle

TNF (tumor necrosis factor) blocker

tophus
(TOH-fus)
[*tophus* **porous rock**] *pl.,* tophi

ulnar deviation
(UL-nur dee-vee-AY-shun)
[*ulna-* **elbow,** *-ar* **relating to, de-** **out of, -via- road or path,** *-ation* **process**]

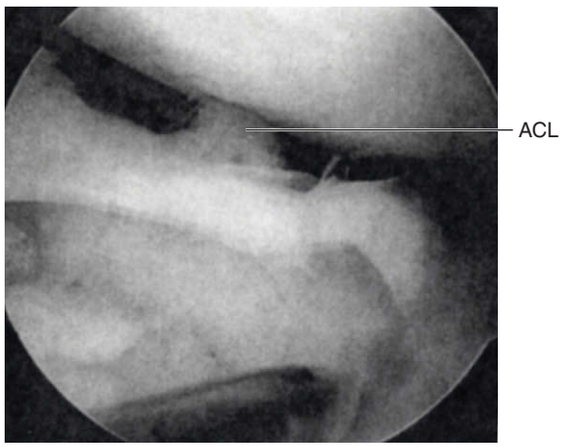
CASE study

While sprinting after the soccer ball, Julia was so intensely concentrating on making a goal that she didn't see the opposing team player coming at her from the side. The two players collided, and Julia felt a "pop" in her right knee followed by intense pain. In the emergency department, the resident told her that she had torn her ACL.

1. What knee structure is the resident referring to when she says "ACL"?
   a. Anterior cruciate ligament
   b. Anatomical connecting ligament
   c. Anterior collateral ligament
   d. Arthroscopic colloidal ligament
2. What two articulating bones form the knee joint?
   a. Femur and fibula
   b. Humerus and ulna
   c. Tibia and femur
   d. Fibula and tibia

Julia's main concern is whether she will be able to play soccer again. Unfortunately, some further tests verify that not only is the ACL torn, but Julia also has damaged the medial meniscus.

3. Which choice best describes a meniscus?
   a. A ligament
   b. A piece of cartilage
   c. A portion of bone
   d. A tendon



HINT

To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook, ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

INTRODUCTION

A. Articulation—point of contact between bones
B. Joints are mostly very movable, but some are immovable or allow only limited motion
C. Movable joints allow complex, highly coordinated, and purposeful movements to be executed

CLASSIFICATION OF JOINTS

A. Joints may be classified by using a structural or functional scheme (Table 10-1)
   1. Structural classification—joints are named according to:
      a. Type of connective tissue that joins bones together (fibrous or cartilaginous joints)
      b. Presence of a fluid-filled joint capsule (synovial joint)
   2. Functional classification—joints are named according to the degree of movement allowed
      a. Synarthroses—immovable joint
      b. Amphiarthroses—slightly movable
      c. Diarthroses—freely movable
B. Fibrous joints (synarthroses)—bones of joints fit together closely, thereby allowing little or no movement (Figure 10-1)
   1. Syndesmoses—joints in which ligaments connect two bones
   2. Sutures—found only in the skull; teethlike projections from adjacent bones interlock with each other
   3. Gomphoses—between the root of a tooth and the alveolar process of the mandible or maxilla
C. Cartilaginous joints (amphiarthroses)—bones of joints are joined together by hyaline cartilage or fibrocartilage; allow very little motion (Figure 10-2)
   1. Synchondroses—hyaline cartilage present between articulating bones
   2. Symphyses—joints in which a pad or disk of fibrocartilage connects two bones
D. Synovial joints (diarthroses)—freely movable joints (Figure 10-3)
   1. Structures of synovial joints
      a. Joint capsule—sleevelike casing around the ends of the bones that binds them together
      b. Synovial membrane—membrane that lines the joint capsule and also secretes synovial fluid
      c. Articular cartilage—hyaline cartilage covering the articular surfaces of bones
      d. Joint cavity—small space between the articulating surfaces of the two bones of the joint
      e. Menisci (articular disks)—pads of fibrocartilage located between articulating bones
      f. Ligaments—strong cords of dense white fibrous tissue that hold the bones of a synovial joint more firmly together
      g. Bursae—synovial membranes filled with synovial fluid; cushion joints and facilitate movement of tendons
   2. Types of synovial joints (Figure 10-4)
      a. Uniaxial joints—synovial joints that permit movement around only one axis and in only one plane
         (1) Hinge joints—articulating ends of bones form a hinge-shaped unity that allows only flexion and extension
         (2) Pivot joints—a projection of one bone articulates with a ring or notch of another bone
      b. Biaxial joints—synovial joints that permit movements around two perpendicular axes in two perpendicular planes
         (1) Saddle joints—synovial joints in which the articulating ends of the bones resemble reciprocally shaped miniature saddles; only example in the body is in the thumbs
         (2) Condyloid (ellipsoidal) joints—synovial joints in which a condyle fits into an elliptical socket
      c. Multiaxial joints—synovial joints that permit movements around three or more axes in three or more planes
         (1) Ball-and-socket (spheroid) joints—most movable joints; the ball-shaped head of one bone fits into a concave depression
         (2) Gliding joints—relatively flat articulating surfaces that allow limited gliding movements along various axes

REPRESENTATIVE SYNOVIAL JOINTS

A. Humeroscapular joint (Figure 10-5)
   1. Shoulder joint
   2. Most mobile joint because of the shallowness of the glenoid cavity
   3. Glenoid labrum—narrow rim of fibrocartilage around the glenoid cavity that lends depth to the glenoid cavity
   4. Structures that strengthen the shoulder joint are ligaments, muscles, tendons, and bursae
B. Elbow joint (Figure 10-6)
   1. Humeroradial joint—lateral articulation of the capitulum of the humerus with the head of the radius
   2. Humeroulnar joint—medial articulation of the trochlea of the humerus with the trochlear notch of the ulna
   3. Both components of the elbow joint surrounded by a single joint capsule and stabilized by collateral ligaments
   4. Classic hinge joint
   5. Medial and lateral epicondyles are externally palpable bony landmarks
   6. Olecranon bursa independent of elbow joint space
      a. Inflammation called *olecranon bursitis*
      b. Trauma to nerve results in unpleasant sensations in the fingers and part of the hand supplied by the nerve
      c. Severe injury may cause paralysis of hand muscles or reduction in wrist movements

C. Proximal radioulnar joint—between the head of the radius and the medial notch of the ulna
   1. Stabilized by the annular ligament
   2. Permits rotation of the forearm
   3. Dislocation of the radial head called a "pulled elbow"

D. Distal radioulnar joint—point of articulation between the ulnar notch of the radius and the head of the ulna
   1. Acts with the proximal radioulnar joint
   2. Permits pronation and supination of the forearm

E. Radiocarpal (wrist) joints (Figure 10-7)
   1. Only the radius articulates directly with the carpal bones distally (scaphoid and lunate)
   2. Joints are synovial
   3. Scaphoid bone is fractured frequently
   4. Portion of the fractured scaphoid may become avascular

F. Intercarpal joints (Figure 10-7)
   1. Present between eight carpal bones
   2. Stabilized by numerous ligaments
   3. Joint spaces usually communicate
   4. Movements generally gliding with some abduction and flexion

G. Carpometacarpal joints—total of three joints
   1. One joint for the thumb—wide range of movements
   2. Two joints for the fingers—movements largely gliding type
   3. Thumb carpometacarpal joint is unique and important functionally
      a. Loose-fitting joint capsule
      b. Saddle-shaped articular surface
      c. Movements—extension, adduction, abduction, circumduction, and opposition
      d. Opposition—ability to touch the tip of the thumb to the tip of other fingers—movement of great functional significance

H. Metacarpophalangeal joints (Figure 10-8)
   1. Rounded heads of metacarpal bones articulate with concave bases of the proximal phalanges
   2. Capsule surrounding joints strengthened by collateral ligaments
   3. Primary movements are flexion and extension

I. Interphalangeal joints
   1. Typical diarthrotic, hinge-type, synovial joints
   2. Exist between heads of phalanges and bases of more distal phalanges
   3. Two categories:
      a. PIP joints—proximal interphalangeal joints (between proximal and middle phalanges)
      b. DIP joints—distal interphalangeal joints (between middle and distal phalanges)

J. Hip joint (Figure 10-9)
   1. Stable joint because of the shape of the head of the femur and the acetabulum
   2. A joint capsule and ligaments contribute to the joint's stability

K. Knee joint (Figures 10-10 and 10-11)
   1. Largest and one of the most complex and most frequently injured joints
   2. Tibiofemoral joint is supported by a joint capsule, cartilage, and numerous ligaments and muscle tendons
   3. Permits flexion, extension, and with the knee flexed, some internal and external rotation

L. Ankle joint (Figure 10-12)
   1. Synovial-type hinge joint
   2. Articulation between the lower ends of the tibia and fibula and the upper part of the talus
   3. Joint is "mortise" or wedge shaped
      a. Lateral malleolus lower than medial malleolus
   4. Internal rotation injury results in common "sprained ankle"
      a. Involves anterior talofibular ligament
   5. Other ankle ligaments also may be involved in sprain injuries—example is deltoid ligament
   6. External ankle rotation injuries generally involve bone fractures rather than ligament tears
      a. First-degree ankle injury—lateral malleolus fractured
      b. Second-degree ankle injury—both malleoli fractured
      c. Third-degree ankle injury—fracture of both malleoli and articular surface of tibia

M. Vertebral joints (Figures 10-13 and 10-14)
   1. Vertebrae are connected to one another by several joints to form a strong flexible column
   2. Bodies of adjacent vertebrae are connected by intervertebral disks and ligaments
   3. Intervertebral disks are made up of two parts
      a. Annulus fibrosus—disk's outer rim, made of fibrous tissue and fibrocartilage
      b. Nucleus pulposus—disk's central core, made of a pulpy, elastic substance

TYPES AND RANGE OF MOVEMENT AT SYNOVIAL JOINTS

A. Measuring range of motion (Figure 10-15)
   1. Range of motion (ROM) assessment used to determine extent of joint injury
   2. ROM can be measured actively or passively; both are generally about equal
   3. ROM measured by instrument called a *goniometer*

B. Angular movements—change the size of the angle between articulating bones
   1. Flexion—decreases the angle between bones; bends or folds one part on another (Figures 10-16, *A*; 10-18; and 10-19)
   2. Extension and hyperextension (Figure 10-18)
      a. Extension—increases the angle between bones, returns a part from its flexed position to its anatomical position
      b. Hyperextension—stretching or extending part beyond its anatomical position (Figures 10-19, 10-21, and 10-23)
   3. Plantar flexion and dorsiflexion (Figure 10-25)
      a. Plantar flexion—increases the angle between the top of the foot and the front of the leg
      b. Dorsiflexion—decreases the angle between the top of the foot and the front of the leg

4. Abduction and adduction (Figures 10-19 and 10-23)
   a. Abduction—moves a part away from the median plane of the body
   b. Adduction—moves a part toward the median plane of the body

C. Circular movements
1. Rotation and circumduction
   a. Rotation—pivoting a bone on its own axis (Figure 10-16, *D*)
   b. Circumduction—moves a part so that its distal end moves in a circle
2. Supination and pronation (Figure 10-20, *B*)
   a. Supination—turns the hand palm side up
   b. Pronation—turns the hand palm side down

D. Gliding movements—simplest of all movements; articular surface of one bone moves over the articular surface of another without any angular or circular movement

E. Special movements
1. Inversion and eversion (Figure 10-25, *B*)
   a. Inversion—turning the sole of the foot inward
   b. Eversion—turning the sole of the foot outward
2. Protraction and retraction (Figure 10-17, *A*)
   a. Protraction—moves a part forward
   b. Retraction—moves a part backward
3. Elevation and depression (Figure 10-17, *B*)
   a. Elevation—moves a part up
   b. Depression—lowers a part

CYCLE OF LIFE: ARTICULATIONS

A. Bone development and the sequence of ossification between birth and skeletal maturity affect joints
1. Fontanels between cranial bones disappear
2. Epiphysial plates ossify at maturity

B. Older adults
1. ROM decreases
2. Changes in gait

C. Skeletal diseases manifested as joint problems
1. Abnormal bone growth (lipping)—influences joint motion
2. Disease conditions can be associated with specific developmental periods

THE BIG PICTURE: ARTICULATIONS

A. Hand—"reason for the upper extremity"; thumb—"reason for the hand"
1. Examples of "big picture" type of thinking when used in functional context

B. Mobility of the upper extremity is extensive because of the following:
1. Arrangement of bones in the shoulder girdle, arms, forearm, wrist, and hand
2. Location and method of attachment of muscles to bones
3. Proper functioning of joints

C. Mobility and extensive ROM needed to position upper extremity and hand to permit grasping and manipulation of objects, thus enabling effective interaction with objects in the external environment

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Classify joints and specify each group according to function and structure.
2. Define the terms *fibrous joints*, *cartilaginous joints*, and *synovial joints*.
3. Name and define three types of fibrous joints. Give an example of each.
4. Name and define two types of cartilaginous joints. Give an example of each.
5. List and describe the different types of synovial joints. Give an example of each.
6. Name and define four kinds of angular movements permitted by some synovial joints.
7. Define and give an example of the following: rotation, circumduction, pronation, supination.
8. Describe the function of a goniometer.
9. What joint makes possible much of the dexterity of the human hand? Describe it and the movements it permits.
10. Describe vertebral joints.
11. Describe and differentiate between the following joints: humeroscapular, hip, knee.
12. How do loose bodies, or cartilaginous "joint mice," differ from menisci?
13. Discuss the surgical procedure of total hip replacement (THR).
14. Name the two classifications of joint disorders and give examples of each.

CRITICAL THINKING QUESTIONS

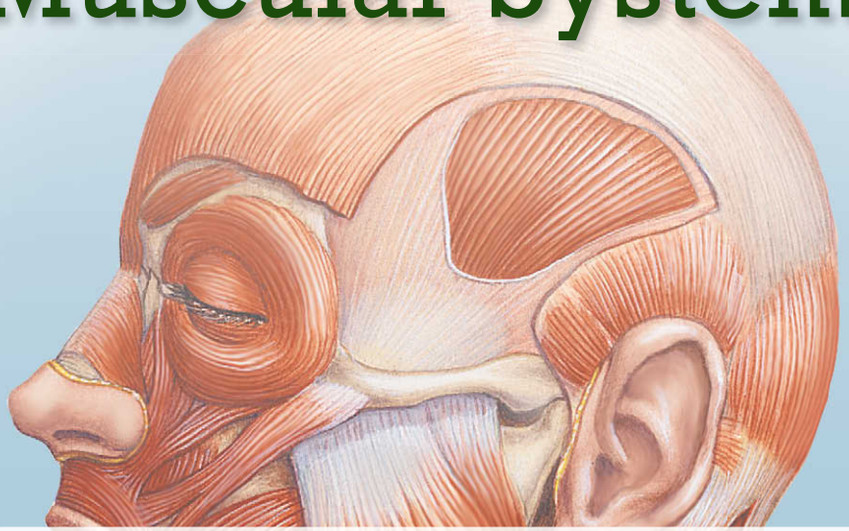


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. The elbow, the joint between the bodies of vertebrae, and the root of a tooth in the jaw are all joints given different functional names. What are these names and what characteristic distinguishes them from one another?
2. A synovial joint is the most freely moving type of joint in the body, but joints require stability and protection also. Evaluate the seven structural characteristics of a synovial joint as primarily necessary for stability, movement, and protection.
3. Compare the range of movement at different joints.
4. Describe the anatomical structure of the knee and explain why the knee joint is the most frequently injured joint in the body.

Anatomy of the Muscular System

11



UNIT 2

CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

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- Connective Tissue Components, 302
- Size, Shape, and Fiber Arrangement, 304
- Attachment of Muscles, 305
- Muscle Actions, 305
- Lever Systems, 306
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  - Third-Class Levers, 307

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- Muscles of Mastication, 313
- Muscles That Move the Head, 314

Trunk Muscles, 315
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Upper Limb Muscles, 322
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Posture, 341
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Cycle of Life: Muscular System, 342

The Big Picture: Skeletal Muscles and the Whole Body, 342

Case Study, 344

LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

agonist
(AG-ah-nist)
[*agon-* **struggle,** *-ist* **agent**]

anal triangle
[*an-* **ring** (**anus**), *-al* **relating to**]

antagonist
(an-TAG-oh-nist)
[*ant-* **against,** *-agon-* **struggle,** *-ist* **agent**]

aponeurosis
(ap-oh-nyoo-ROH-sis)
[*apo-* **from,** *-neur-* **sinew,** *-osis* **condition**] *pl.,* aponeuroses

belly

buccinator muscle
(BUK-si-NAY-tor)
[*buccinator* **trumpeter,** *mus-* **mouse,** *-cle* **little**]

bulbospongiosus muscle
(bul-boh-spun-jee-OH-ses)
[*bulbo-* **bulb,** *-spongiosus* **spongy,** *mus-* **mouse,** *-cle* **little**]

calcaneal tendon
(kal-KAH-nee-al)
[*calcane-* **heel,** *-al* **relating to,** *tend-* **pulled tight,** *-on* **unit**]

circular muscle
[*mus-* **mouse,** *-cle* **little**]

coccygeus muscle
(kohk-SIJ-ee-us)
[*coccygeus* **coccyx,** *mus-* **mouse,** *-cle* **little**]

convergent muscle
(kon-VER-jent)
[*con-* **together,** *-verg-* **incline,** *-ent* **state,** *mus-* **mouse,** *-cle* **little**]

corrugator supercilii muscle
(KOR-uh-gay-tor soo-per-SIL-ee-eye)
[*corrugator* **wrinkler,** *super-* **above,** *-cilli-* **eyelash,** *mus-* **mouse,** *-cle* **little**]

continued on p. 343

Survival depends on the ability to maintain a relatively constant internal environment. Such stability often requires movement of the body. Whereas many different systems of the body have some role in accomplishing movement, it is the skeletal and muscular systems acting together that actually produce most body movements. We have investigated the architectural plan of the skeleton and have seen how its firm supports and joint structures make movement possible. However, bones and joints cannot move themselves. They must be moved by something. Our subject for now, then, is the large mass of skeletal muscle that moves the framework of the body: the **muscular system.**

Movement is one of the most distinctive and easily observed "characteristics of life." When we walk, talk, run, breathe, or engage in a multitude of other physical activities that are under the "willed" control of the individual, we do so by contraction of skeletal muscle.

There are more than 600 skeletal muscles in the body. Collectively, they constitute 40% to 50% of our body weight. And, together with the scaffolding provided by the skeleton, muscles also determine the form and contours of our body.

Contraction of individual muscle cells is ultimately responsible for purposeful movement. In Chapter 12 the physiology of muscular contraction is discussed. In this preliminary chapter, however, we will learn how contractile units are grouped into unique functioning organs—or muscles.

The manner in which muscles are grouped, the relationship of muscles to joints, and how muscles attach to the skeleton determine purposeful body movement. A discussion of muscle shape and how muscles attach to and move bones is followed by information on specific muscles and muscle groups. The chapter ends with a review of the concept of posture.

SKELETAL MUSCLE STRUCTURE

Connective Tissue Components

The skeletal muscle cells, or *muscle fibers*, are covered by a delicate connective tissue membrane called the **endomysium** (Figure 11-1). Groups of skeletal muscle fibers, called *fascicles*, are then bound together into bundles by a tougher connective tissue envelope called the **perimysium.** The muscle as a whole is covered by a coarse sheath called the **epimysium.** Because all three of these structures are continuous with the fibrous structures that attach muscles to bones or other structures, muscles are firmly harnessed to the structures they pull on during contraction. The epimysium, perimysium, and endomysium of a muscle, for example, may be continuous with fibrous tissue that extends from the muscle as a **tendon,** a strong tough cord continuous at its other end with the fibrous periosteum covering a bone. Alternatively, the fibrous wrapping of a muscle may extend as a broad, flat sheet of connective tissue called an **aponeurosis,** which usually merges with the fibrous wrappings of another muscle. So tough and strong are tendons and aponeuroses that they are not often torn, even by injuries forceful enough to break bones or tear muscles. They are, however, occasionally pulled away from bones.

Fibrous connective tissue surrounding the muscle organ and located outside the epimysium and tendon is called **fascia.** *Fascia* is a general term for the fibrous connective tissue found under the skin and surrounding many deeper organs, including skeletal muscles and bones. Fascia just under the skin (the hypodermis) is sometimes called *superficial fascia*, and the fascia around muscles and bones is sometimes called *deep fascia*.

Sheets of fibrous connective tissue form double-walled tubes called **tendon sheaths** that enclose certain tendons, notably those of the wrist and ankle. Like bursae, the walls of tendon sheaths have a lining of synovial membrane. The moist, smooth surfaces that face each other within the double wall of a tendon sheath enables the tendon to move easily, almost without friction. Table 11-1 clarifies the arrangement of the fibrous coverings of a muscle organ.

TABLE 11-1 Fibrous Coverings of Muscle Organs

FIBROUS STRUCTURE*	PART COVERED
Fascia	External to muscles, bones, other organs
Superficial fascia	Under the skin
Deep fascia	Surrounds deeper organs, including epimysium of muscle
Tendon sheath	Tubelike tunnel around tendon of muscle; lined with synovial membrane
Epimysium†	Surrounds entire muscle organ
Perimysium†	Surrounds a fascicle (bundle) of muscle fibers
Endomysium†	Surrounds an individual muscle fiber

*Listed here from superficial to deep; all of these fibrous structures are continuous with one another (that is, their fibers blend together).
†Continue and fuse together to form a tendon or aponeurosis.

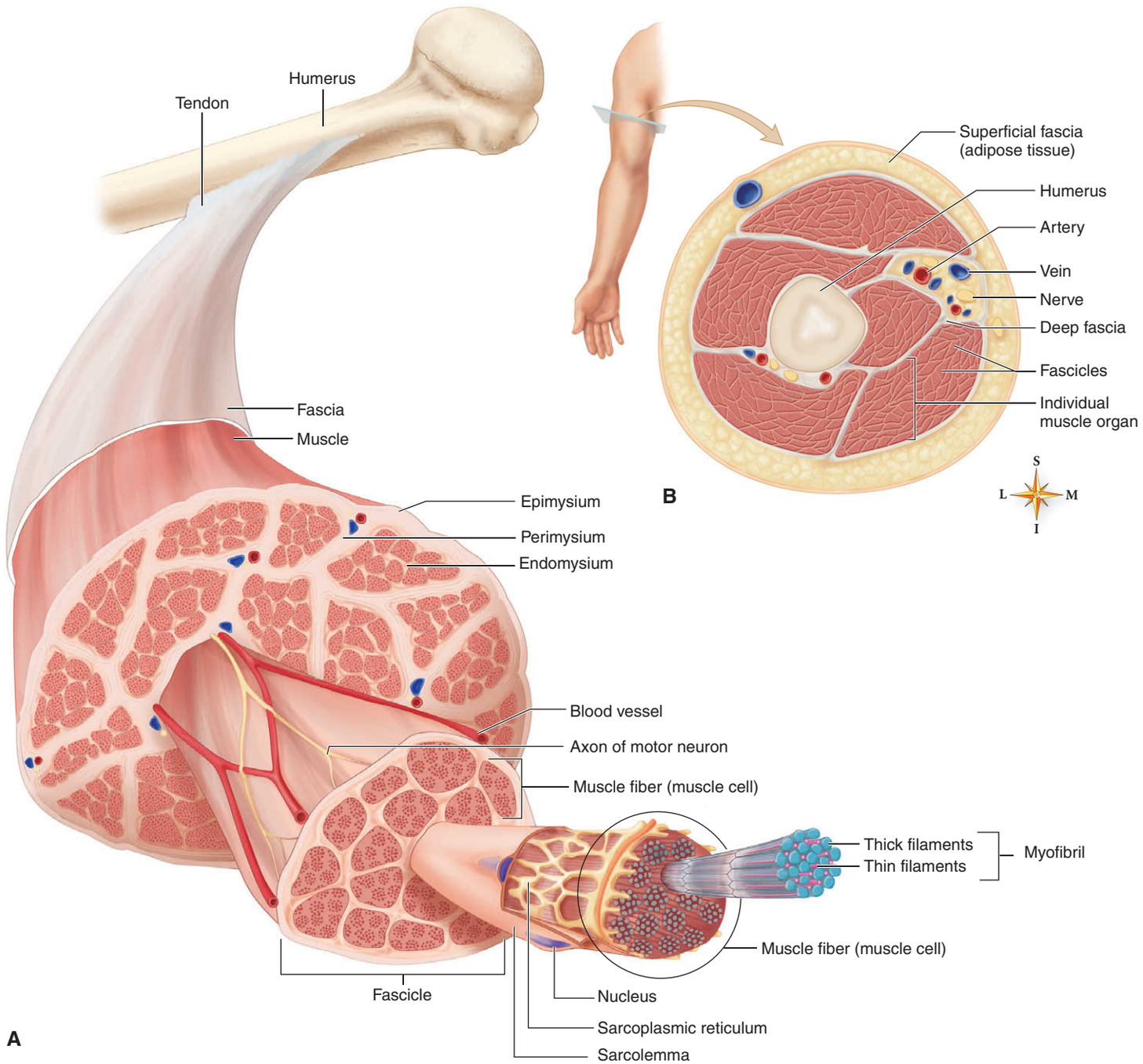


FIGURE 11-1

Structure of a muscle organ. A, Note that the connective tissue coverings, the epimysium, perimysium, and endomysium, are continuous with each other and with the tendon. Note also that muscle fibers are held together by the perimysium in groups called *fascicles.* **B,** Diagram showing the arm in cross section. Note the relationships of superficial and deep fascia to individual muscles and other structures in the plane of section.

Size, Shape, and Fiber Arrangement

The structures called *skeletal muscles* are organs. They consist mainly of skeletal muscle tissue plus important connective and nervous tissue components. Skeletal muscles vary considerably in size, shape, and arrangement of fibers. They range from extremely small strands, such as the stapedius muscle of the middle ear, to large masses, such as the muscles of the thigh. Some skeletal muscles are broad in shape and some are narrow. Some are long and tapering and some are short and blunt. Some are triangular, some quadrilateral, and some irregular. Some form flat sheets and others form bulky masses.

The strength and type of movement produced by the shortening of a muscle is related to the orientation of its fibers and overall shape, as well as its attachments to bone and involvement in joints. This is yet another example of the relationship between structure and function. Six muscle shapes are often used to describe and categorize skeletal muscles (Figure 11-2).

1. **Parallel muscles** can vary in length, but long straplike muscles with parallel fascicles are perhaps most typical. The sartorius muscle of the leg is a good example. The rectus abdominis muscles, which run the length of the anterior abdominal wall, have parallel muscle fascicles that are "interrupted" by transverse intersections.
2. **Convergent muscles** have fascicles that radiate out from a small to a wider point of attachment, much like the blades in a fan. The pectoralis major muscle is a good example.
3. **Pennate muscles** are said to be "featherlike" in appearance. Three categories of these muscles have uniquely different types of fascicle attachments that in some ways resemble the feathers in an old-fashioned plume pen. *Unipennate muscles*, such as the soleus, have fascicles that anchor to only one side of the connective tissue shaft. *Bipennate muscles*, such as the rectus femoris in the thigh, have a type of double-feathered attachment of fascicles. In *multipennate muscles*, such as the deltoid, the numerous interconnecting quill-like fascicles converge on a common point of attachment.
4. **Fusiform muscles** have fascicles that may be close to parallel in the center, or "belly," of the muscle but converge to a tendon at one or both ends. The brachioradialis is a good example.
5. **Spiral muscles,** such as the latissimus dorsi, have fibers that twist between their points of attachment.
6. **Circular muscles,** sometimes called *orbicular muscles* and *sphincters*, often circle body tubes or openings. The orbicularis oris around the mouth is an example. The external anal sphincter around the anus is another example.

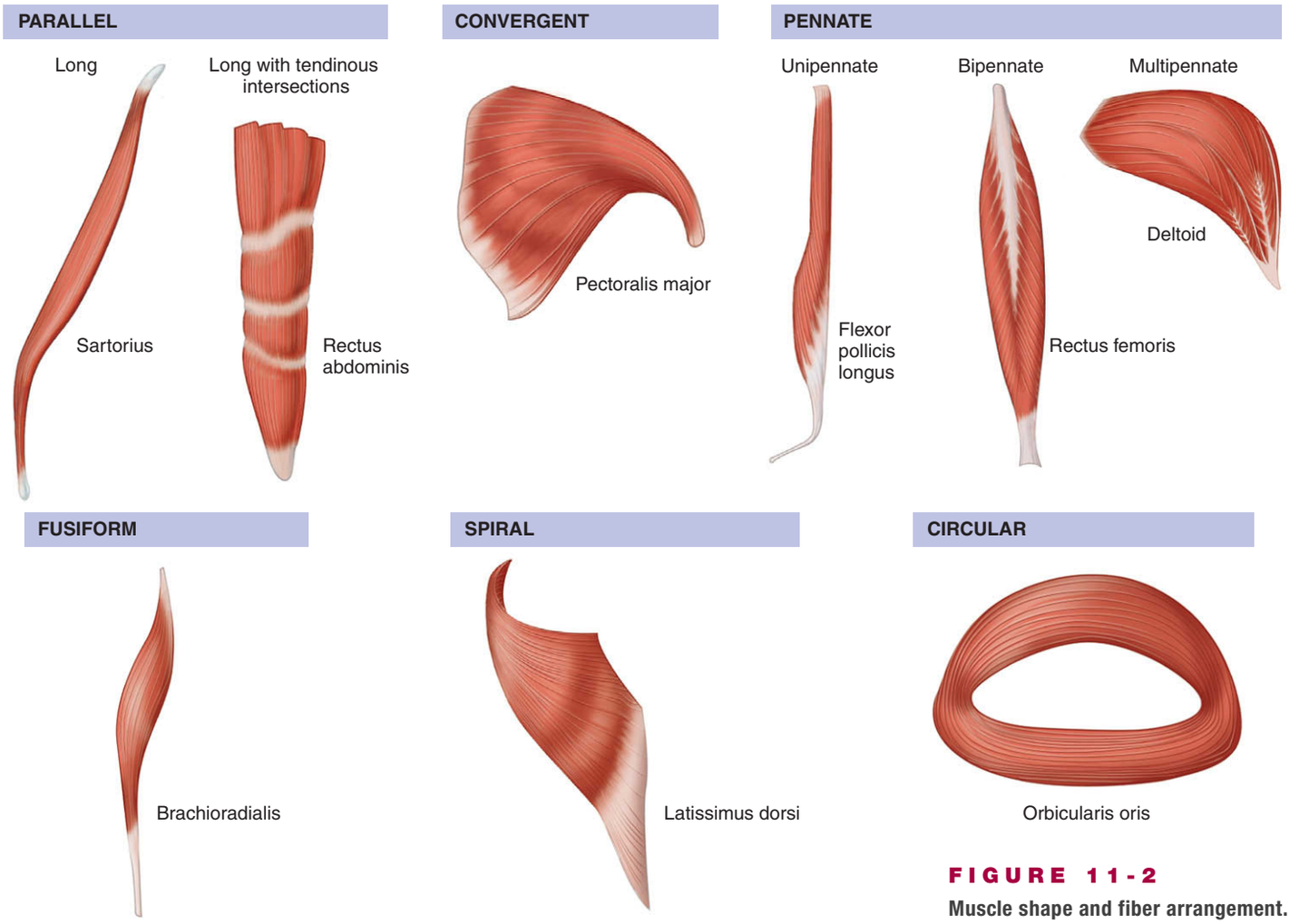


FIGURE 11-2
Muscle shape and fiber arrangement.

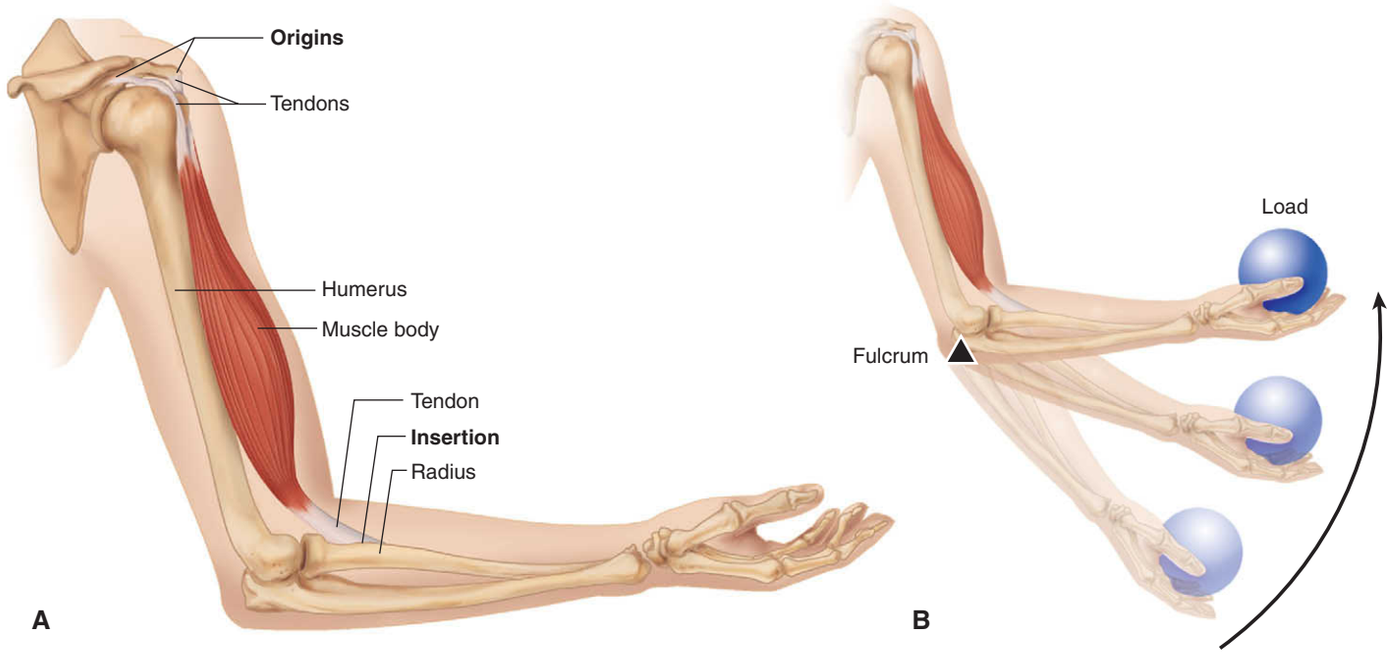


FIGURE 11-3

Attachments of a skeletal muscle. A, Origin and insertion of a skeletal muscle. A muscle originates at a relatively stable part of the skeleton (origin) and inserts at the skeletal part that is moved when the muscle contracts (insertion). **B,** Movement of the forearm during weightlifting. Muscle contraction moves bones, which serve as levers, and by acting on joints, which serve as fulcrums for those levers. See the text for discussion and review Figure 11-4, which illustrates types of levers.

| QUICK CHECK |

1. Identify (a) the connective tissue membrane that covers individual muscle fibers, (b) the membrane that surrounds groups of skeletal muscle fibers (fascicles), and (c) the membrane that covers the muscle as a whole.
2. Name the tough connective tissue cord that serves to attach a muscle to a bone.
3. Name three types of fiber arrangements seen in skeletal muscle.

Attachment of Muscles

Most of our muscles span at least one joint and attach to both articulating bones. When contraction occurs, one bone usually remains fixed and the other moves. The points of attachment are called the *origin* and *insertion*. The **origin** is the point of attachment that does not move when the muscle contracts. Therefore, the origin bone is the more stationary of the two bones at a joint when contraction occurs. The **insertion** is the point of attachment that moves when the muscle contracts (Figure 11-3). The insertion bone therefore moves toward the origin bone when the muscle shortens. In case you are wondering why both bones do not move because both are pulled on by the contracting muscle, the answer is one of them is normally stabilized by isometric contractions of other muscles or by certain features of its own that make it less mobile.

The terms *origin* and *insertion* provide us with useful points of reference. Many muscles have multiple points of origin or insertion. Understanding the functional relationship of these attachment points during muscle contraction helps in deducing muscle actions. The attachment points of the biceps brachii shown in Figure 11-3 help provide functional information. Distal insertion on the radius in the forearm causes flexion to occur at the elbow when contraction occurs. It should be realized, however, that origin and insertion are points that may change under certain circumstances. For example, not only can you grasp an object above your head and pull it down, but you can also pull yourself up to the object. Although origin and insertion are convenient terms, they do not always provide the necessary information needed to understand the full functional potential of muscle action.

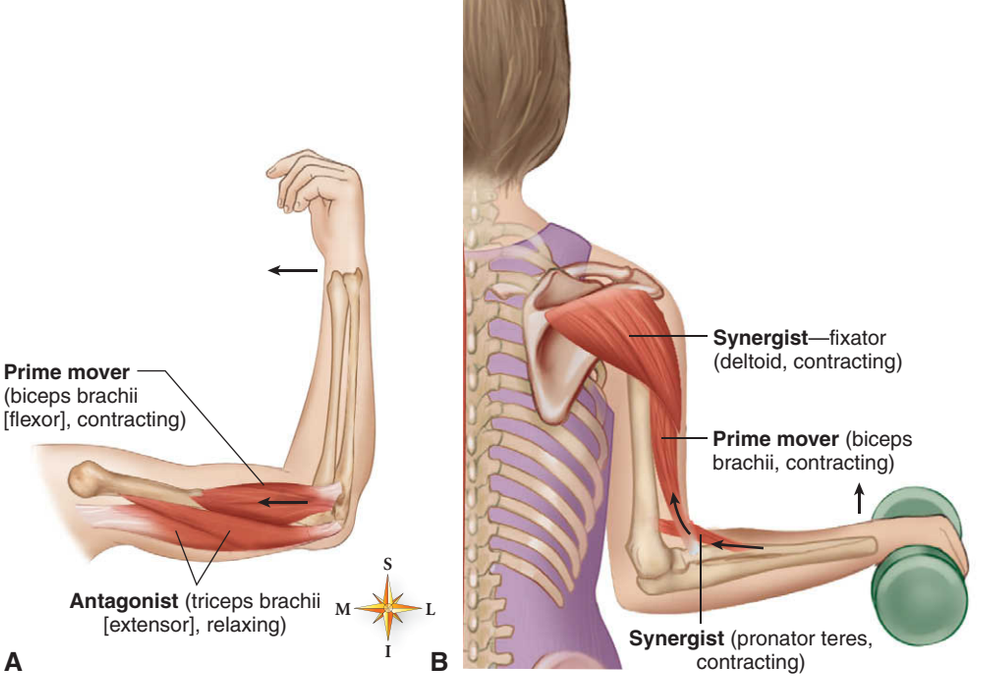
Muscle Actions

Skeletal muscles almost always act in groups rather than singly. As a result, most movements are produced by the coordinated action of several muscles. Some of the muscles in the group contract while others relax. The result is a movement pattern that allows for the functional classification of muscles or muscle groups. Several terms are used to describe muscle action during any particular movement pattern. The terms *prime mover (agonist)*, *antagonist*, *synergist*, and *fixator* are especially important and are discussed in the following paragraphs. Each term suggests an important concept that is essential to understanding such functional muscle patterns as flexion, extension, abduction, adduction, and other movements discussed in Chapter 10.

Any muscle that performs an action is a "mover." The term **prime mover** is used to describe a muscle that directly performs a specific movement. The movement produced by a muscle acting as a prime mover is described as the "action" or "function" of that

FIGURE 11-4

Muscle actions. A, The flexor muscle (biceps brachii) is the prime mover in flexing the elbow. The extensor muscle (triceps brachii) is the antagonist, which in this case must relax to permit easy flexion of the elbow. The pronator teres muscle acts as a synergist by also flexing the elbow. **B,** Here the biceps brachii is again the prime mover of flexion of the elbow. The pronator teres muscle acts as a synergist by also flexing the elbow. To prevent the biceps from also moving the shoulder while straining against a heavy weight, the posterior portion of the deltoid muscle tenses to stabilize the shoulder joint—thus acting as a fixator muscle in this action.



muscle. For example, the biceps brachii shown in Figures 11-3 and 11-4 is acting as a prime mover during flexion of the forearm. The term **agonist** can be applied to the prime mover, or any other "mover" muscle that directly contributes to the same action as the prime mover.

Antagonists are muscles that when contracting, directly oppose prime movers (or agonists). They are relaxed while the prime mover is contracting to produce movement (see Figure 11-4). Simultaneous contraction of a prime mover and its antagonist muscle results in rigidity and lack of motion. The term *antagonist* is perhaps unfortunate because muscles cooperate, rather than oppose, in normal movement patterns. Antagonists are important in providing precision and control during contraction of prime movers.

Synergists are muscles that contract at the same time as the prime mover. They facilitate or complement prime mover actions so that the prime mover produces a more effective movement.

Fixator muscles generally function as joint stabilizers (see Figure 11-4, *B*). They frequently serve to maintain posture or balance during contraction of prime movers acting on joints in the arms and legs. Because fixator muscles assist the prime mover in performing an action, they are a type of synergist.

Movement patterns are complex, and most muscles function not only as prime movers but also at times as antagonists, synergists, or fixators. A prime mover in a particular movement pattern, such as flexion, may be an antagonist during extension or a synergist or fixator in other types of movement.

| QUICK CHECK |

4. Identify the point of attachment of a muscle to a bone that (a) does not move when the muscle contracts and (b) one that does move when the muscle contracts.
5. What name is used to describe a muscle that directly performs a specific movement?
6. What type of muscles helps maintain posture or balance during contraction of muscles acting on joints in the arms and legs?
7. Name the type of muscles that generally function as joint stabilizers.

Lever Systems

When a muscle shortens, the central body portion, called the **belly,** contracts. The type and extent of movement are determined by the load or resistance that is moved, the attachment of the tendinous extremities of the muscle to bone (origin and insertion), and the particular type of joint involved. In almost every instance, muscles that move a part do not lie over that part. Instead, the muscle belly lies proximal to the part moved. Thus muscles that move the forearm lie proximal to it, that is, in the upper part of the arm.

Knowledge of lever systems is important in understanding muscle action. By definition, a **lever** is any rigid bar free to turn about a fixed point called its *fulcrum*. Bones serve as levers, and joints serve as fulcrums of these levers. A contracting muscle applies a pulling force on a bone lever at the point of the muscle's attachment to the bone (Box 11-1). This force causes the insertion bone to move about its joint fulcrum.

A **lever system** is a simple mechanical device that makes the work of moving a weight or other load easier in some way. Lever systems are composed of four component parts:

1. A rigid rod or bar (bone) called a *lever*
2. A fixed pivot, or fulcrum (F), around which the lever moves (joint)
3. A load (L), or resistance, that is moved
4. A force, or pull (P), which produces movement (muscle contraction).

Figure 11-5 shows the three different types of lever arrangements. All three types are found in the human body.

FIRST-CLASS LEVERS

As you can see in Figure 11-5, A, the fulcrum in a first-class lever lies between the effort, or pull (P), and the resistance, or load (W), as in a set of scales, a pair of scissors, or a child's seesaw. In the body the head being raised or tipped backward on the atlas is an example of a first-class lever in action. The facial portion of the skull is the load, the joint between the skull and atlas is the fulcrum, and the muscles of the back produce the pull. In the human body first-class levers are not abundant. They generally serve as levers of stability.

Box 11-1 | SPORTS and FITNESS

Assessing Muscle Strength

Physical therapists, certified athletic trainers, and other health care providers are often required to assess muscle strength. A basic principle of muscle action in a lever system is called the *optimum angle of pull.* An understanding of this principle is required for correct assessment of muscle strength.

Generally, the optimum angle of pull for any muscle is a right angle to the long axis of the bone to which it is attached. When the angle of pull departs from a right angle and becomes more parallel to the long axis, the strength of contraction decreases dramatically. Contraction of the brachialis muscle demonstrates this principle very well. The brachialis crosses the elbow from the humerus to the ulna. In the anatomical position the elbow is extended and the angle of pull of the brachialis is parallel to the long axis of the ulna (see Figure 11-21, *D*). Contraction of the brachialis at this angle is very inefficient. As the elbow is flexed and the angle of pull approaches a right angle, the contraction strength of the muscle is greatly increased. Therefore, to test brachialis muscle strength correctly, the forearm should be flexed at the elbow. Understanding the optimum angle of pull for any given muscle makes a rational approach to correct assessment of functional strength in that muscle possible.

SECOND-CLASS LEVERS

In second-class levers the load lies between the fulcrum and the joint at which the pull is exerted. The wheelbarrow is often used as an example. The presence of second-class levers in the human body is a controversial issue. Some authorities interpret the raising of the body on the toes as an example of this type of lever (see Figure 11-5, *B*). In this example the point of contact between the toes and the ground is the fulcrum, the load is located at the ankle, and pull is exerted by the gastrocnemius muscle through the Achilles tendon. Opening the mouth against resistance (depression of the mandible) is also considered to be an example of a second-class lever.

THIRD-CLASS LEVERS

In a third-class lever the pull is exerted between the fulcrum and the resistance or load to be moved. Flexing of the forearm at the elbow joint is a frequently used example of this type of lever (see Figure 11-5, C). Third-class levers permit rapid and extensive movement and are the most common type found in the body. They allow insertion of a muscle very close to the joint that it moves.

| A&P CONNECT |

Leverage is the change in effort needed when using a lever to do work. Want to know more about how muscles power the levers of the body? Check it out in ***Leverage*** online at ***A&P Connect.***

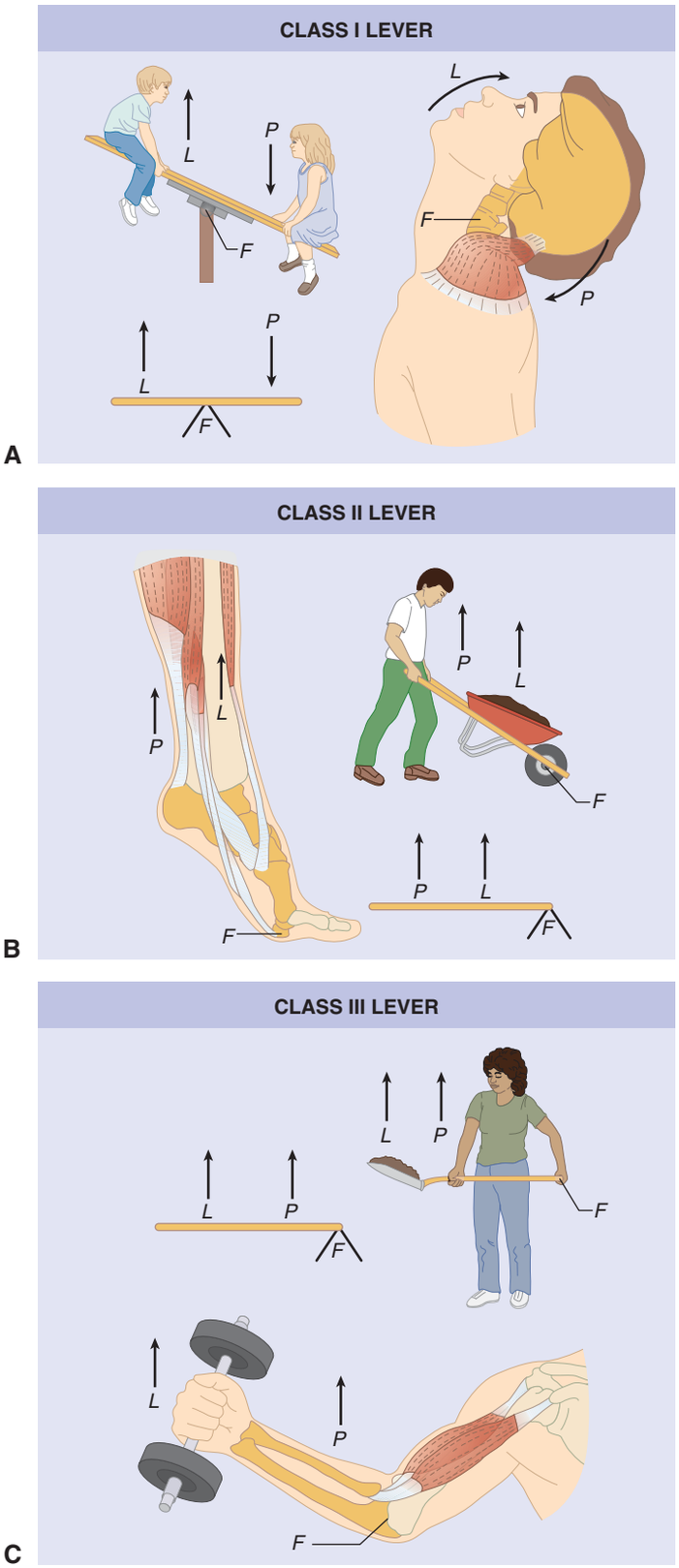


FIGURE 11-5

Lever classes. A, Class I: fulcrum (*F*) between the load (*L*) and force or pull (*P*). **B,** Class II: load (*L*) between the fulcrum (*F*) and force or pull (*P*). **C,** Class III: force or pull (*P*) between the fulcrum (*F*) and the load (*L*). The lever rod is *yellow* in each.

HOW MUSCLES ARE NAMED

The first thing you may notice as you start studying the muscles of the body is that many of the names seem difficult and foreign. The terms are less difficult if you keep in mind that most anatomical terms come from Latin.

Although we have strived to use only English names in this edition, some Latin terms still remain in common usage—especially in anatomy. This is certainly true in the health-related disciplines. For example, in some texts the deltoid muscle is called the *deltoideus* (Latin) and in others the *deltoid* (English). To minimize confusion, the terms used here will be the English versions from the *Terminologia Anatomica* (see Chapter 1). Even so, you will soon discover that the English versions are often the same or similar to the Latin versions!

Regardless of the muscle name used, when one understands the reasons for the term used, it will seem more logical and be easier to learn and understand. Many of the muscles of the body shown in Figure 11-6 or listed in Tables 11-2 through 11-6 are named according to one or more of the following features:

Location. Many muscles are named as a result of location. The *brachialis* (arm) muscle and *gluteus* (buttock) muscles

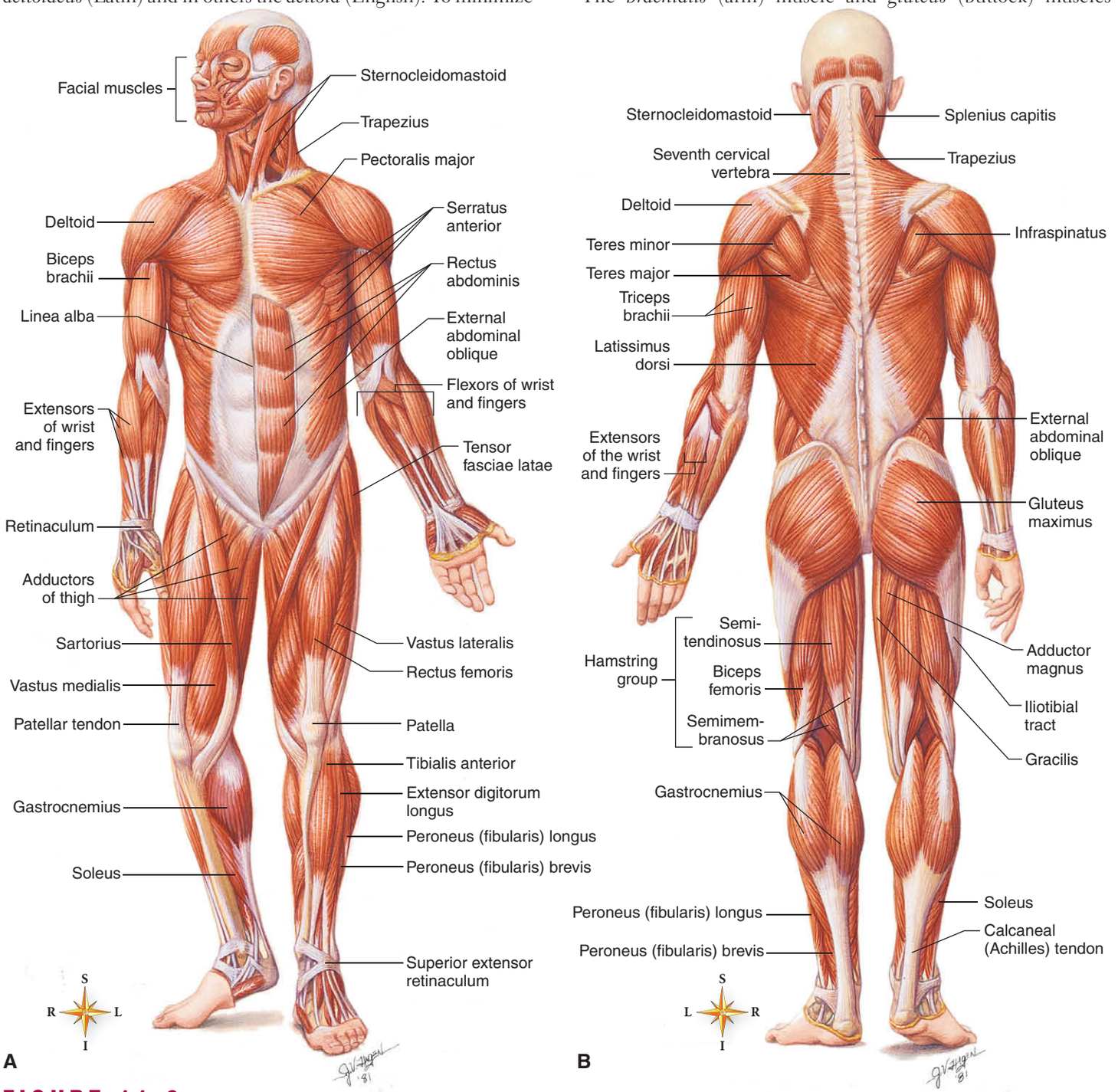


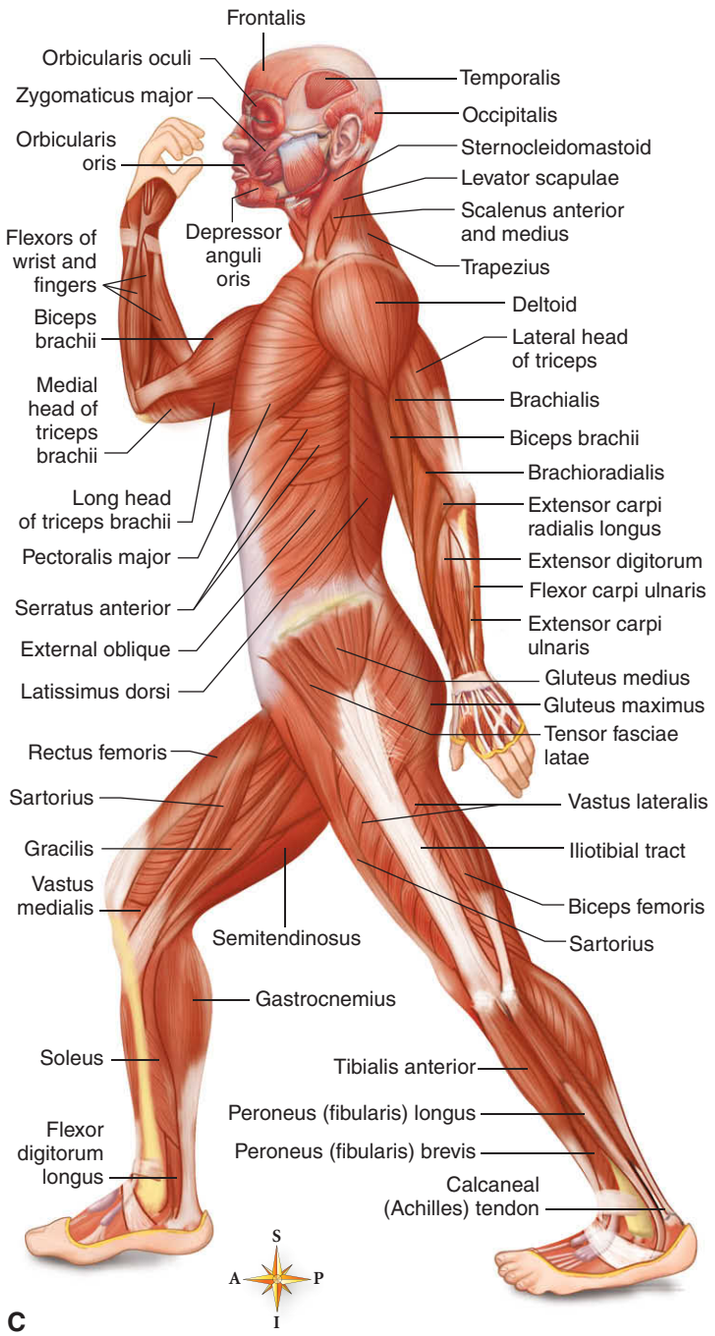
FIGURE 11-6

General overview of the body's musculature. A, Anterior view. **B,** Posterior view. **C,** Lateral view.

are examples. Table 11-2 gives a listing of some major muscles grouped by location.

Function. The function of a muscle often is a part of its name. The *adductor* muscles of the thigh adduct, or move, the leg toward the midline of the body. Table 11-3 lists selected muscles grouped according to function.

Shape. Shape is a descriptive feature used for naming many muscles. The *deltoid* (triangular) muscle covering the shoulder is deltoid, or triangular, in shape (see Table 11-4).



C

Direction of fibers. Muscles may be named according to the orientation of their fibers. The term *rectus* means straight. The fibers of the *rectus abdominis* muscle run straight up and down and are parallel to each other (see Table 11-5).

Number of heads or divisions. The number of divisions or heads (points of origin) may be used to name a muscle. The word part *-cep-* means *head. Biceps* (two), *triceps* (three), and *quadriceps* (four) refer to multiple heads, or points of origin. The *biceps brachii* is a muscle having two heads located in the arm (see Table 11-5).

Points of attachment. Origin and insertion points may be used to name a muscle. For example, the *sternocleidomastoid* has its origin on the sternum and clavicle and inserts on the mastoid process of the temporal bone.

TABLE 11-2 Selected Muscles Grouped According to Location

LOCATION	MUSCLES
Neck	Sternocleidomastoid
Back	Trapezius Latissimus dorsi
Chest	Pectoralis major Serratus anterior
Abdominal wall	External oblique
Shoulder	Deltoid
Arm	Biceps brachii Triceps brachii Brachialis
Forearm	Brachioradialis Pronator teres
Buttocks	Gluteus maximus Gluteus minimus Gluteus medius Tensor fascia latae
Thigh	
Anterior surface	Quadriceps femoris group Rectus femoris Vastus lateralis Vastus medialis Vastus intermedius
Medial surface	Gracilis Adductor group (brevis, longus, magnus)
Posterior surface	Hamstring group Biceps femoris Semitendinosus Semimembranosus
Leg	
Anterior surface	Tibialis anterior
Posterior surface	Gastrocnemius Soleus
Pelvic floor	Levator ani Coccygeus

TABLE 11-3 Selected Muscles Grouped According to Function

PART MOVED	EXAMPLE OF FLEXOR	EXAMPLE OF EXTENSOR	EXAMPLE OF ABDUCTOR	EXAMPLE OF ADDUCTOR
Head	Sternocleidomastoid	Semispinalis capitis		
Arm	Pectoralis major	Trapezius Latissimus dorsi	Deltoid	Pectoralis major with latissimus dorsi
Forearm	With forearm supinated: biceps brachii With forearm pronated: brachialis With semisupination or semipronation: brachioradialis	Triceps brachii		
Hand	Flexor carpi radialis and ulnaris Palmaris longus	Extensor carpi radialis, longus, and brevis Extensor carpi ulnaris	Flexor carpi radialis	Flexor carpi ulnaris
Thigh	Iliopsoas Rectus femoris (of quadriceps femoris group)	Gluteus maximus	Gluteus medius and minimus	Adductor group
Leg	Hamstrings	Quadriceps femoris group		
Foot	Tibialis anterior	Gastrocnemius Soleus	Evertors Fibularis longus Fibularis brevis	Invertor Tibialis anterior
Trunk	Iliopsoas Rectus abdominis	Erector spinae		

TABLE 11-4 Selected Muscles Grouped According to Shape

NAME	MEANING	EXAMPLE
Deltoid	Triangular	Deltoid
Gracilis	Slender	Gracilis
Trapezius	Trapezoid	Trapezius
Serratus	Notched	Serratus anterior
Teres	Round	Pronator teres
Rhomboid	Rhomboidal	Rhomboid major
Orbicularis	Round or circular	Orbicularis oris
Pectinate	Comblike	Pectineus
Piriformis	Wedge-shaped	Piriformis
Platys	Flat	Platysma
Quadratus	Square	Quadratus femoris
Lumbrical	Wormlike	Lumbricals

TABLE 11-5 Selected Muscles Grouped According to Number of Heads and Direction of Fiber

NAME	MEANING	EXAMPLE
Number of Heads		
Biceps	Two heads	Biceps brachii
Triceps	Three heads	Triceps brachii
Quadriceps	Four heads	Quadriceps
Digastric	Two bellies	Digastric
Direction of Fibers		
Oblique	Diagonal	External oblique rectus
Rectus	Straight	Rectus abdominis
Transverse	Transverse	Transversus abdominis
Circular	Around	Orbicularis oris
Spiral	Oblique	Supinator

TABLE 11-6 Selected Muscles Grouped According to Size

NAME	MEANING	EXAMPLE
Major	Large	Pectoralis major
Maximus	Largest	Gluteus maximus
Minor	Small	Pectoralis minor
Minimus	Smallest	Gluteus minimus
Longus	Long	Adductor longus
Brevis	Short	Extensor pollicis brevis
Latissimus	Very wide	Latissimus dorsi
Longissimus	Very long	Longissimus
Magnus	Very large	Adductor magnus
Vastus	Vast or huge	Vastus medialis

Size of muscle. The relative size of a muscle can be used to name a muscle, especially if it is compared to the size of nearby muscles (see Table 11-6). For example, the *gluteus maximus* is the largest muscle of the gluteal (Greek *glautos*, meaning "buttock") region. Nearby, there is a small gluteal muscle, the *gluteus minimus*, and a midsize gluteal muscle, the *gluteus medius*.

| QUICK CHECK |

8. Name the four major components of any lever system.
9. Identify the three types of lever systems found in the human body and give one example of each.
10. What type of lever system permits rapid and extensive movement and is the most common type found in the body?
11. List six criteria that may determine a muscle's name, and give an example of a specific muscle named according to each criterion.

Hints on How to Deduce Muscle Actions

To understand muscle actions, you first need to know certain anatomical facts, such as which bones muscles attach to and which joints they pull across. Then, if you relate these structural features to functional principles, you may find your study of muscles more interesting and less difficult than you may anticipate. Some specific suggestions for deducing muscle actions follow:

1. Start by making yourself familiar with the names, shapes, and general locations of the larger muscles by using Table 11-2 as a guide.
2. Try to deduce which bones the two ends of a muscle attach to from your knowledge of the shape and general location of the muscle. For example, look carefully at the deltoid muscle as illustrated in Figures 11-6 and 11-17. To which bones does it seem to attach? Check your answer with Table 11-14, p. 324.
3. Next, determine which bone moves when the muscle shortens. (The bone moved by a muscle's contraction is its insertion bone; the bone that remains relatively stationary is its origin bone.) In many cases you can tell which is the insertion bone by trying to move one bone and then another. In some cases either bone may function as the insertion bone. Although not all muscle attachments can be deduced as readily as those of the deltoid, they can all be learned more easily by using this deduction method than by relying on rote memory alone.
4. Deduce a muscle's actions by applying the principle that its insertion moves toward its origin. Check your conclusions with the text. Here, as in steps 2 and 3, the method of deduction is intended merely as a guide and is not adequate by itself for determining muscle actions.
5. To deduce which muscle produces a given action (instead of which action a given muscle produces, as in step 4), start by inferring the insertion bone (bone that moves during the action). The body and origin of the muscle will lie on one or more of the bones toward which the insertion moves—often a bone, or bones, proximal to the insertion bone. Couple these conclusions about origin and insertion with your knowledge of muscle names and locations to deduce the muscle that produces the action.

For example, if you wish to determine the prime mover for the action of raising the upper parts of the arms straight out to the sides, you infer that the muscle inserts on the humerus because this is the bone that moves. It moves toward the shoulder—that is, the clavicle and scapula—so the muscle probably has its origin on these bones. Because you know that the deltoid muscle fulfills these conditions, you conclude, and rightly so, that it is the muscle that raises the upper parts of the arms sideways.

IMPORTANT SKELETAL MUSCLES

The major skeletal muscles of the body are listed, grouped, and illustrated in the tables and figures that follow. Begin your study with an overview of important superficial muscles, shown in Figure 11-6. The remaining figures in this chapter illustrate individual muscles or important muscle groups.

Basic information about many muscles is given in Tables 11-7 to 11-19. Each table has a description of a group of muscles that move one part of the body. The actions listed for each muscle are those for which it is a prime mover. Remember, however, that a single muscle acting alone rarely accomplishes a given action. Instead, muscles act in groups as prime movers, synergists, antagonists, and fixators to bring about movements.

TABLE 11-7 Muscles of Facial Expression and Mastication

MUSCLE	ORIGIN	INSERTION	FUNCTION	NERVE SUPPLY
Muscles of Facial Expression				
Occipitofrontalis (part of epicranius)				
Frontal belly	Epicranial aponeurosis	Tissues of eyebrows and bridge of nose	Raises eyebrows, wrinkles forehead horizontally	Cranial nerve VII
Occipital belly	Occipital bone (highest nuchal line)	Epicranial aponeurosis	Draws scalp backward	Cranial nerve VII
Corrugator supercilii	Frontal bone (superciliary ridge	Skin of eyebrow	Wrinkles forehead vertically	Cranial nerve VII
Orbicularis oculi	Encircles eyelid		Closes eye	Cranial nerve VII
Zygomaticus major	Zygomatic bone	Angle of mouth	Laughing (elevates angle of mouth)	Cranial nerve VII
Orbicularis oris	Encircles mouth		Draws lips together	Cranial nerve VII
Buccinator	Maxillae	Skin of sides of mouth	Facilitates smiling; blowing, as in playing trumpet	Cranial nerve VII
Depressor anguli oris	Mandible	Angle of mouth	Draws ends of mouth downward, as when frowning	Cranial IV
Muscles of Mastication				
Masseter	Zygomatic arch	Mandible (external surface)	Elevates mandible, closing jaw	Cranial nerve V
Temporalis	Temporal bone	Mandible	Elevates mandible; closing jaw	Cranial nerve V
Pterygoids (lateral and medial)	Undersurface of skull	Mandible (medial surface)	Grates teeth	Cranial nerve V

Muscles of Facial Expression

The muscles of facial expression (Table 11-7 and Figures 11-7 and 11-8) are unique in that at least one of their points of attachment is to the deep layers of the skin over the face or neck. Contraction of these muscles produces a variety of facial expressions.

The **occipitofrontalis** (ok-sip-i-toh-fron-TAL-is) is in reality two muscles. One portion lies over the forehead (frontal bone); the other covers the occipital bone in back of the head. The two muscular parts, or bellies, are joined by a connective tissue aponeurosis (the *epicranial aponeurosis*) that covers the top of the skull. The two occipitofrontalis bellies, along with the epicranial aponeurosis, are together called the *epicranius muscle*. The frontal belly of the occipitofrontalis raises the

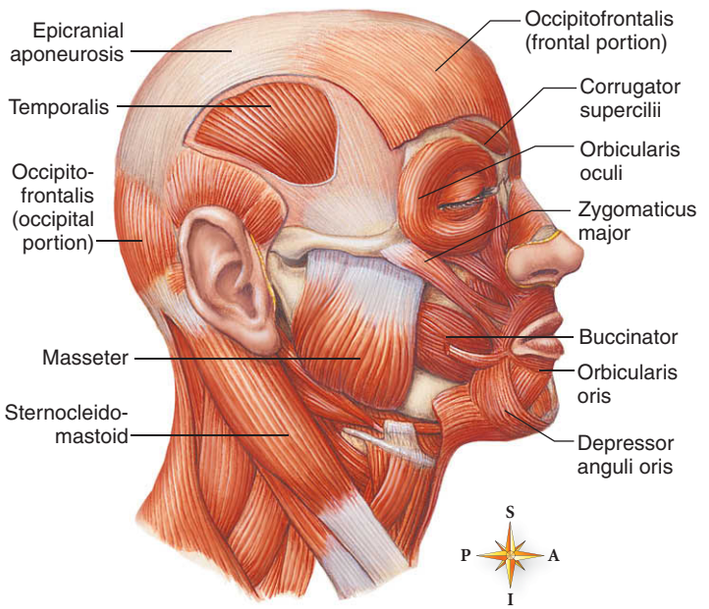


FIGURE 11-7

Muscles of facial expression and mastication. Lateral view.

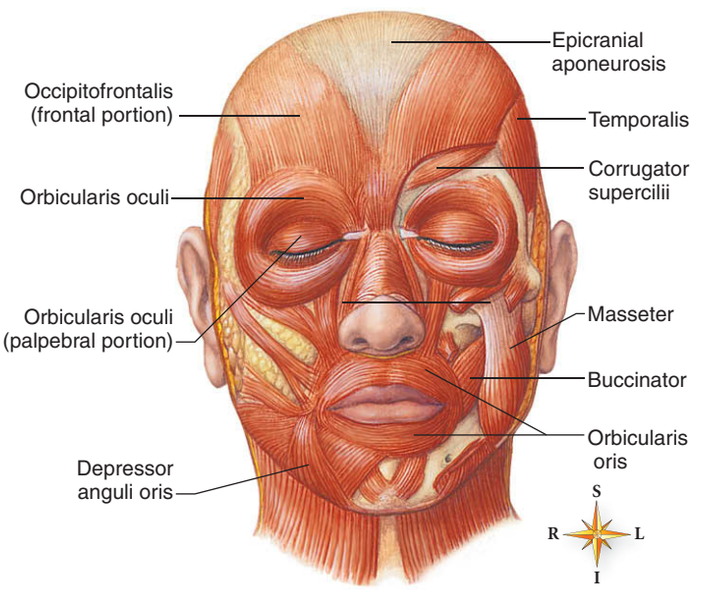


FIGURE 11-8

Muscles of facial expression and mastication. Anterior view.

eyebrows (surprise) and wrinkles the skin of the forehead horizontally. The posterior belly draws the scalp back toward the posterior neck.

The **corrugator supercilii** (COR-uh-gay-tor soo-per-SIL-ee-eye) draws the eyebrows together and produces vertical wrinkles above the nose (frowning). The **orbicularis oculi** (or-bik-yoo-LAIR-is OK-yoo-lye) encircles and closes the eye (blinking), whereas the **orbicularis oris** (OR-iss) and **buccinator** (BUK-si-NAY-tor) pucker the mouth (kissing) and press the lips and cheeks against the teeth. The **zygomaticus** (zye-goh-MAT-ik-us) **major** draws the corner of the mouth upward (laughing).

Muscles of Mastication

The muscles of **mastication** (mass-ti-KAY-shun) shown in Figure 11-9 are responsible for chewing movements. These powerful muscles (see Table 11-7) either elevate and retract the mandible (**masseter** [mah-SEE-ter] and **temporalis** [tem-poh-RAL-is]) or open and protrude it while causing sideways movement (**pterygoids** [TER-i-goidz]). The pull of gravity helps open the mandible during mastication, and the buccinator muscles play an important function by holding food between the teeth as the mandible moves up and down and from side to side.

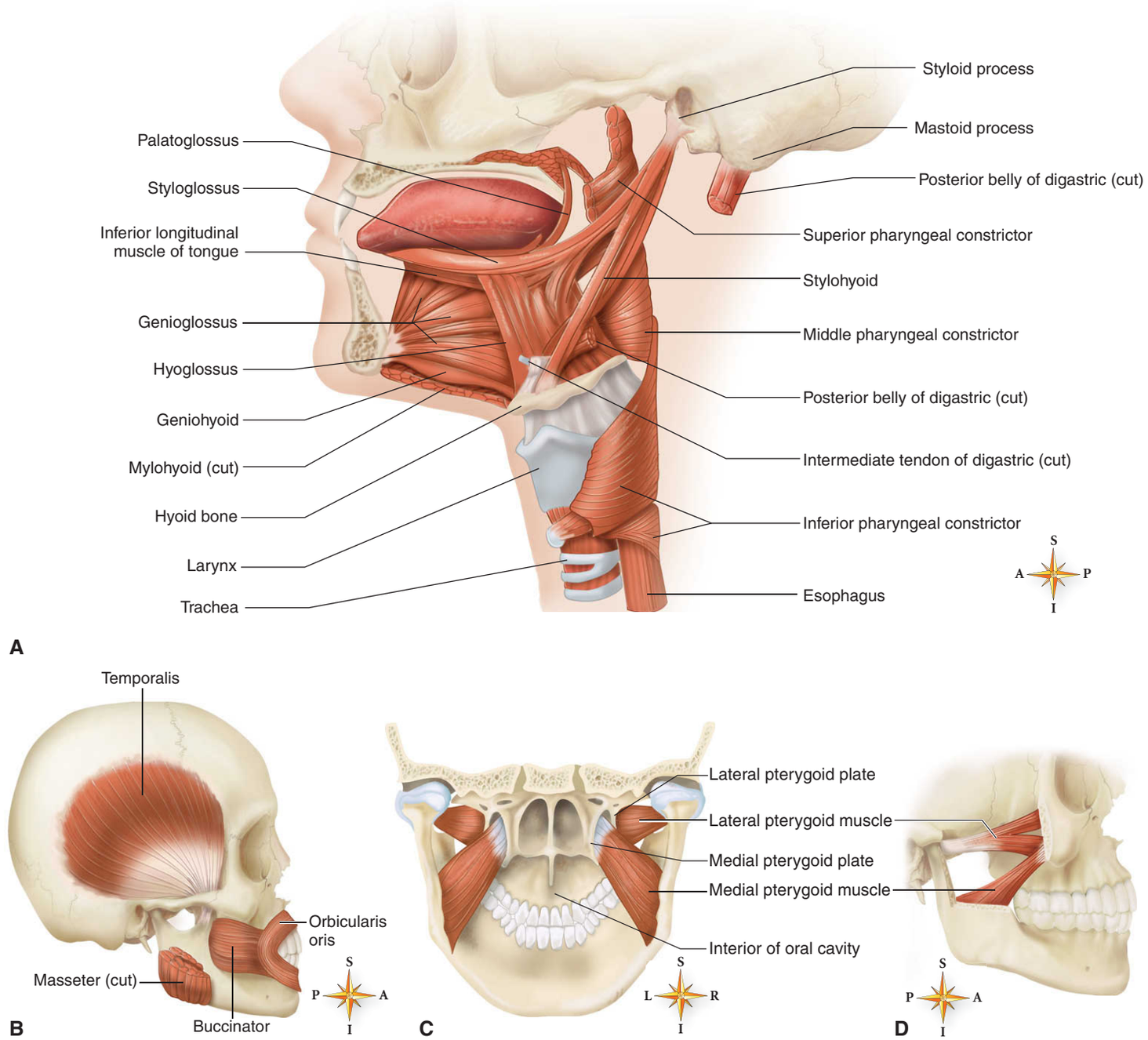


FIGURE 11-9

Muscles of mastication. A, Muscles of the tongue and pharynx. **B,** Right lateral dissection view showing the insertion of the temporalis muscle on the mandible—the masseter muscle is cut and part of the zygomatic arch has been removed. **C,** View of the pterygoids in a posterior dissection view. **D,** Lateral and medial pterygoid muscles viewed from the right side after removal of the zygomatic arch.

Muscles That Move the Head

Paired muscles on either side of the neck are responsible for head movements (Figure 11-10). Note the points of attachment and functions of important muscles in this group listed in Table 11-8. When both **sternocleidomastoid** (STERN-oh-KLYE-doh-MAS-toyd) muscles (see Figure 11-7) contract at the same time, the head is flexed on the thorax—hence the name "prayer muscle." If only one muscle contracts, the head and face are turned to the opposite side.

The broad *semispinalis capitis* (sem-ee-spi-NAL-is KAP-i-tis) is an extensor of the head and helps bend it laterally. Acting together, the **splenius capitis** (SPLE-nee-us KAP-i-tis) muscles serve as strong extensors that return the head to the upright position after flexion. When either muscle acts alone, contraction results in rotation and tilting toward that side. The bandlike **longissimus capitis** (lon-JIS-i-mus KAP-i-tis) muscles are covered and not visible in Figure 11-10. They run from the neck vertebrae to the mastoid process of the temporal bone on either side and cause extension of the head when acting together. One contracting muscle will bend and rotate the head toward the contracting side.

| QUICK CHECK |

12. What is meant by the terms *origin* and *insertion?*
13. Which muscle of facial expression has two parts, one lying over the forehead and the other covering the back of the skull?
14. What group of muscles facilitates chewing movements?
15. What is the action of the sternocleidomastoid muscle?

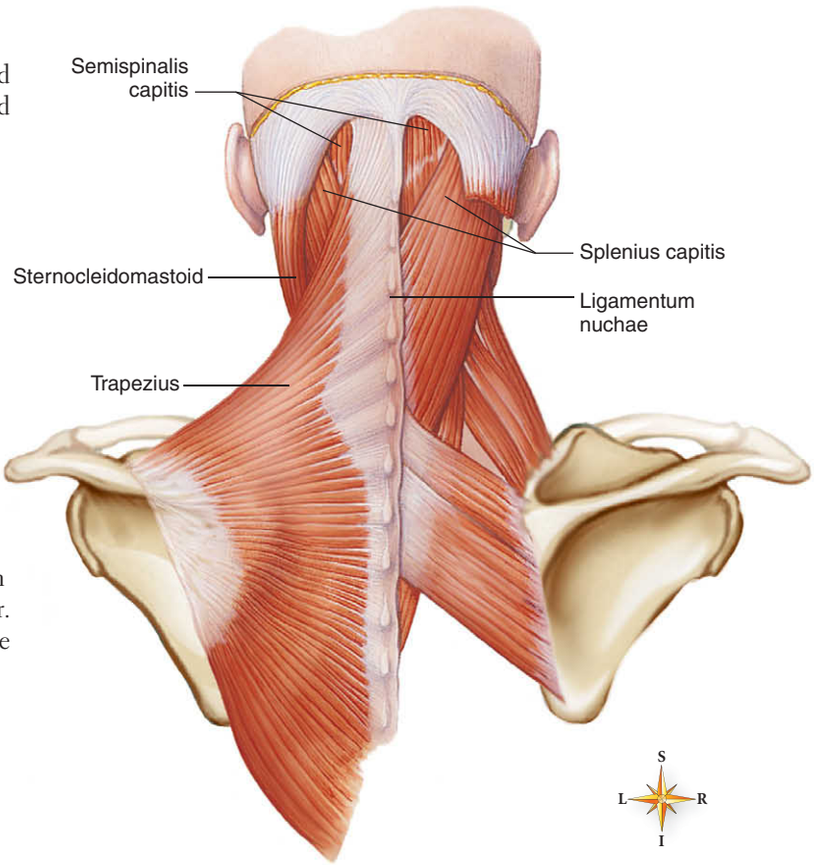


FIGURE 11-10

Muscles that move the head. Posterior view of muscles of the neck and the back.

TABLE 11-8 Muscles That Move the Head

MUSCLE	ORIGIN	INSERTION	FUNCTION	NERVE SUPPLY
Sternocleidomastoid	Sternum	Temporal bone (mastoid process)	Flexes head and neck (prayer muscle)	Accessory nerve
	Clavicle		One muscle alone, rotates head toward opposite side; spasm of this muscle alone or associated with trapezius called *torticollis,* or wryneck	
Semispinalis capitis	Vertebrae (transverse processes of upper six thoracic, articular processes of lower four cervical)	Occipital bone (between superior and inferior nuchal lines)	Extends head and neck; bends it laterally	First five cervical nerves
Splenius capitis	Ligamentum nuchae	Temporal bone (mastoid process)	Extends head/neck	Second, third, and fourth cervical nerves
	Vertebrae (spinous processes of upper three or four thoracic)	Occipital bone	Bends and rotates head toward same side as contracting muscle	
Longissimus capitis	Vertebrae (transverse processes of upper six thoracic, articular processes of lower four cervical)	Temporal bone (mastoid process)	Extends head and neck Bends and rotates head toward contracting side	Multiple innervation

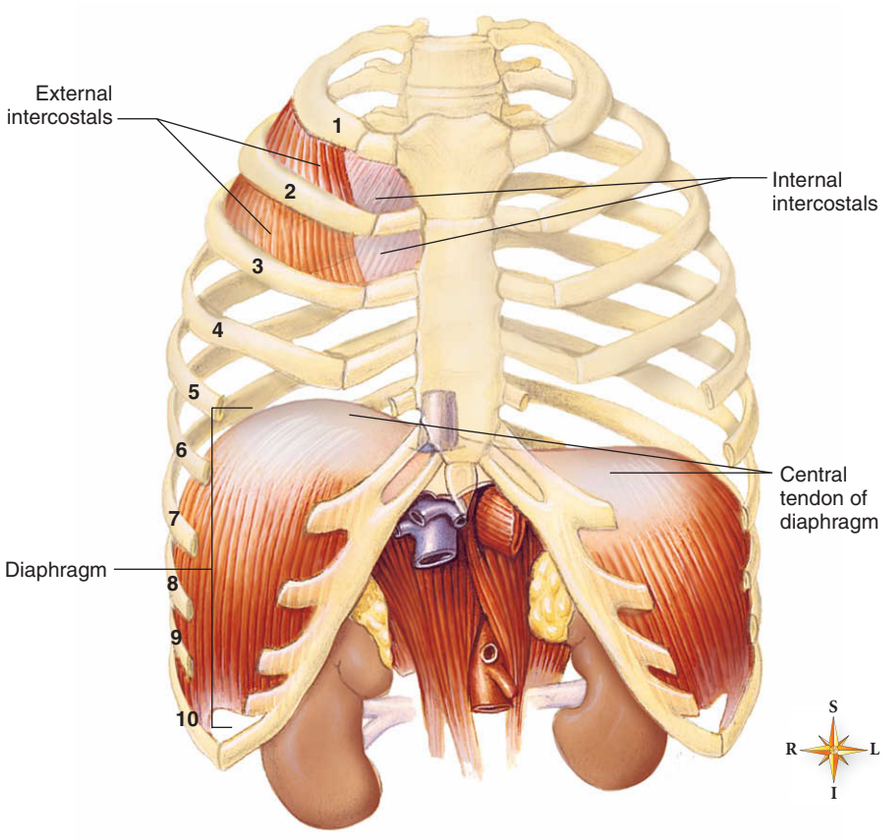


FIGURE 11-11

Muscles of the thorax. Anterior view. Note the relationship of the internal and external intercostal muscles and placement of the diaphragm.

TRUNK MUSCLES

Muscles of the Thorax

The muscles of the thorax are of critical importance in respiration (discussed in Chapter 27). Note in Figure 11-11 and Table 11-9 that the **internal** and **external intercostal** (IN-ter-KOS-tal) **muscles** attach to the ribs at different places and their fibers are oriented in different directions. As a result, contraction of the external intercostals elevates and contraction of the internal intercostals depresses the ribs—important in the breathing process. During inspiration the dome-shaped **diaphragm** (DYE-ah-fram) flattens, thus increasing the size and volume of the thoracic cavity. As a result, air enters the lungs.

TABLE 11-9 **Muscles of the Thorax**

MUSCLE	ORIGIN	INSERTION	FUNCTION	NERVE SUPPLY
External intercostals	Rib (lower border; forward fibers)	Rib (upper border of rib below origin)	Elevate ribs	Intercostal nerves
Internal intercostals	Rib (inner surface, lower border; backward fibers)	Rib (upper border of rib below origin)	Depress ribs	Intercostal nerves
Diaphragm	Lower circumference of thorax (of rib cage)	Central tendon of diaphragm	Enlarges thorax, thereby causing inspiration	Phrenic nerves

Muscles of the Abdominal Wall

The muscles of the anterior and lateral abdominal wall (Figures 11-12 and 11-13; Table 11-10) are arranged in three layers, with the fibers in each layer running in different directions much like the layers of wood in a sheet of plywood. The result is a very strong "girdle" of muscle that covers and supports the abdominal cavity and its internal organs.

The fibers in the three layers of muscle in the anterolateral wall are arranged to provide maximum strength. In the **external oblique** the muscle fascicles or fibers extend inferiorly and medially, whereas the fibers of the middle muscle layer, the **internal oblique,** run almost at right angles to those of the external oblique above it. The fibers of the **transversus abdominis,** the innermost muscle layer, are, as the name implies, directed transversely. In addition to these sheetlike muscles, the band- or strap-shaped

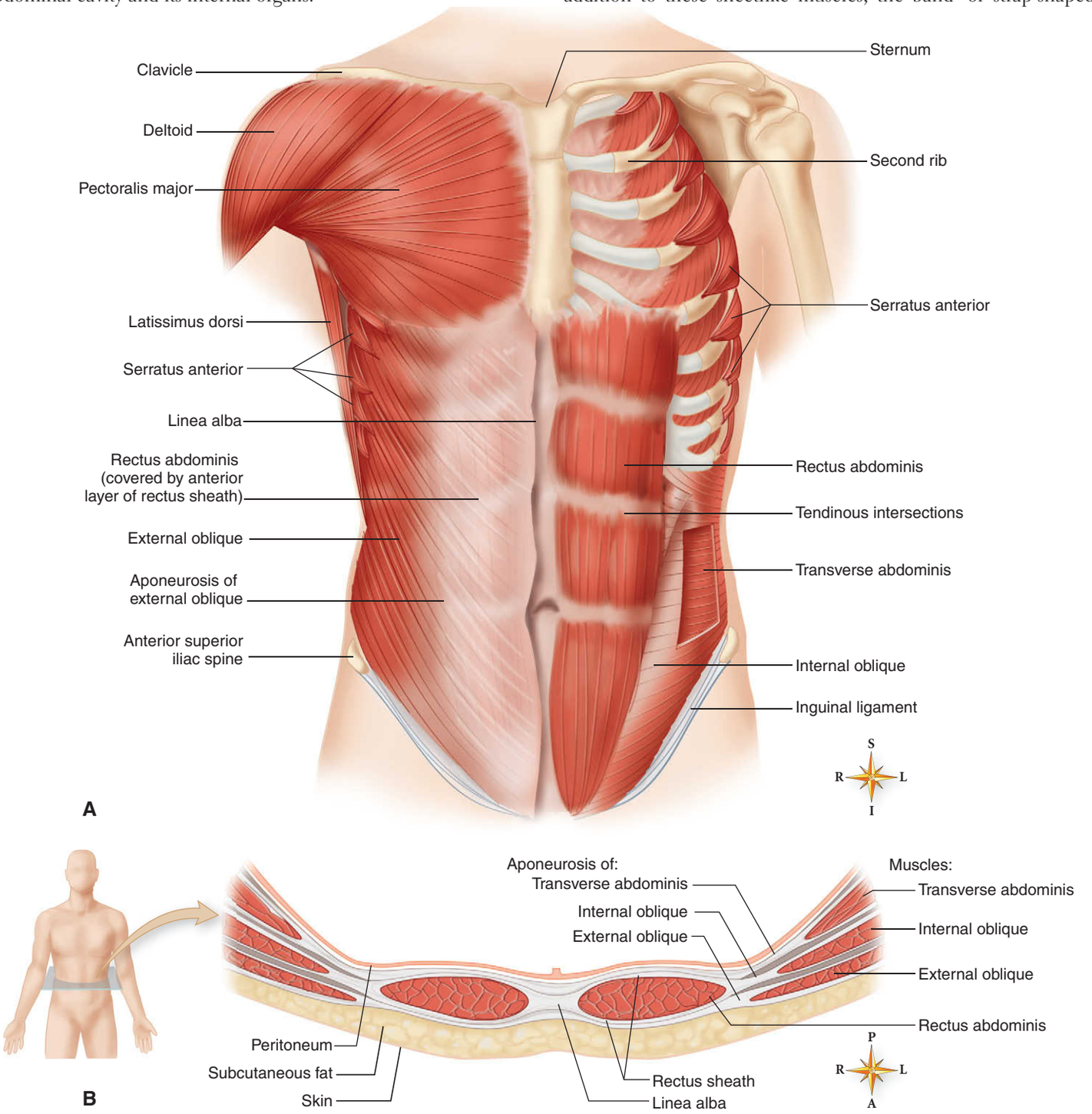


FIGURE 11-12

Muscles of the trunk and abdominal wall. A, Superficial muscles are visible on the right side of the body and deeper muscles on the left side of the body. **B,** Transverse section of the anterior wall above the umbilicus (see inset for location).

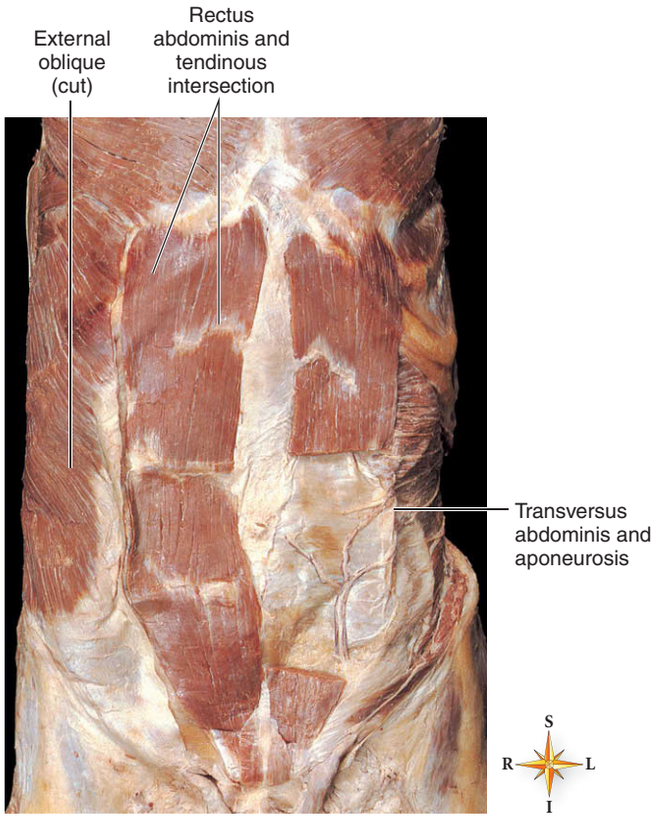


FIGURE 11-13

Dissection photo of the abdominal wall. The covering rectus sheaths, the left oblique muscles, and part of the left rectus have been removed.

rectus abdominis muscle runs down the midline of the abdomen from the thorax to the pubis. Note in Figure 11-12 that its parallel running fibers are "interrupted" by three tendinous intersections. When a surgeon "opens" or "closes" an incision through the anterolateral wall, attempts are made to maintain the inherent strength of the wall after surgery by sparing important nerves and blood vessels and by using suturing techniques during closure that will restore the direction of fibers in the cut layers of muscle.

In Figure 11-13, a number of superficial structures have been cut or partially removed. For example, part of the internal oblique has been removed to expose the underlying transversus abdominis, and the anterior (superficial) layer of the **rectus sheath** has been removed to better visualize the **rectus abdominis muscle** and its tendinous intersections. Note also in Figure 11-12, *B*, that the aponeuroses of the external oblique, internal oblique, and transversus abdominis muscles form the rectus sheaths that cover the rectus abdominis muscles and then fuse in the midline to form a tough band of connective tissue called the **linea alba** (white line), that extends from the xiphoid process to the pubis. Occasionally, a surgical procedure will permit an incision through the linea alba rather than through abdominal musculature. Since the linea alba is essentially avascular in some areas, blood loss in such procedures is generally less than what may occur in other approaches.

Working as a group, the abdominal muscles not only protect and hold the abdominal viscera in place, they are responsible for a number of vertebral column movements, including flexion, lateral bending, and some rotation. These important muscles are

TABLE 11-10 Muscles of the Abdominal Wall

MUSCLE	ORIGIN	INSERTION	FUNCTION	NERVE SUPPLY
External oblique	Ribs (lower eight)	Pelvis (iliac crest and pubis by way of the inguinal ligament)	Compresses abdomen	Lower seven intercostal nerves and iliohypogastric nerves
		Linea alba by way of an aponeurosis	Rotates trunk laterally	
Internal oblique	Pelvis (iliac crest and iliopsoas fascia)	Ribs (lower three)	Important postural function of all abdominal muscles is to pull the front of the pelvis upward, thereby flattening the lumbar curve of the spine; when these muscles lose their tone, common figure faults of protruding abdomen and lordosis develop	Last three intercostal nerves; iliohypogastric and ilioinguinal nerves
	Lumbodorsal fascia	Linea alba		
Transversus abdominis	Ribs (lower six) Pelvis (iliac crest, iliopsoas fascia)	Pubic bone Linea alba	Same as external oblique	Last three intercostal nerves; iliohypogastric and ilioinguinal nerves
	Lumbodorsal fascia	Ribs (costal cartilage of fifth, sixth, and seventh ribs)	Same as external oblique	Last five intercostal nerves; iliohypogastric and ilioinguinal nerves
Rectus abdominis	Pelvis (pubic bone and pubic symphysis)	Sternum (xiphoid process)	Same as external oblique; because abdominal muscles compress the abdominal cavity, they aid in straining, defecation, forced expiration, childbirth; abdominal muscles are antagonists of the diaphragm, relaxing as it contracts and vice versa Flexes trunk	Last six intercostal nerves
Quadratus lumborum	Iliolumbar ligament; iliac crest	Last rib; transverse process of vertebrae (L1-L4)	Flexes vertebral column laterally; depresses last rib	Lumbar

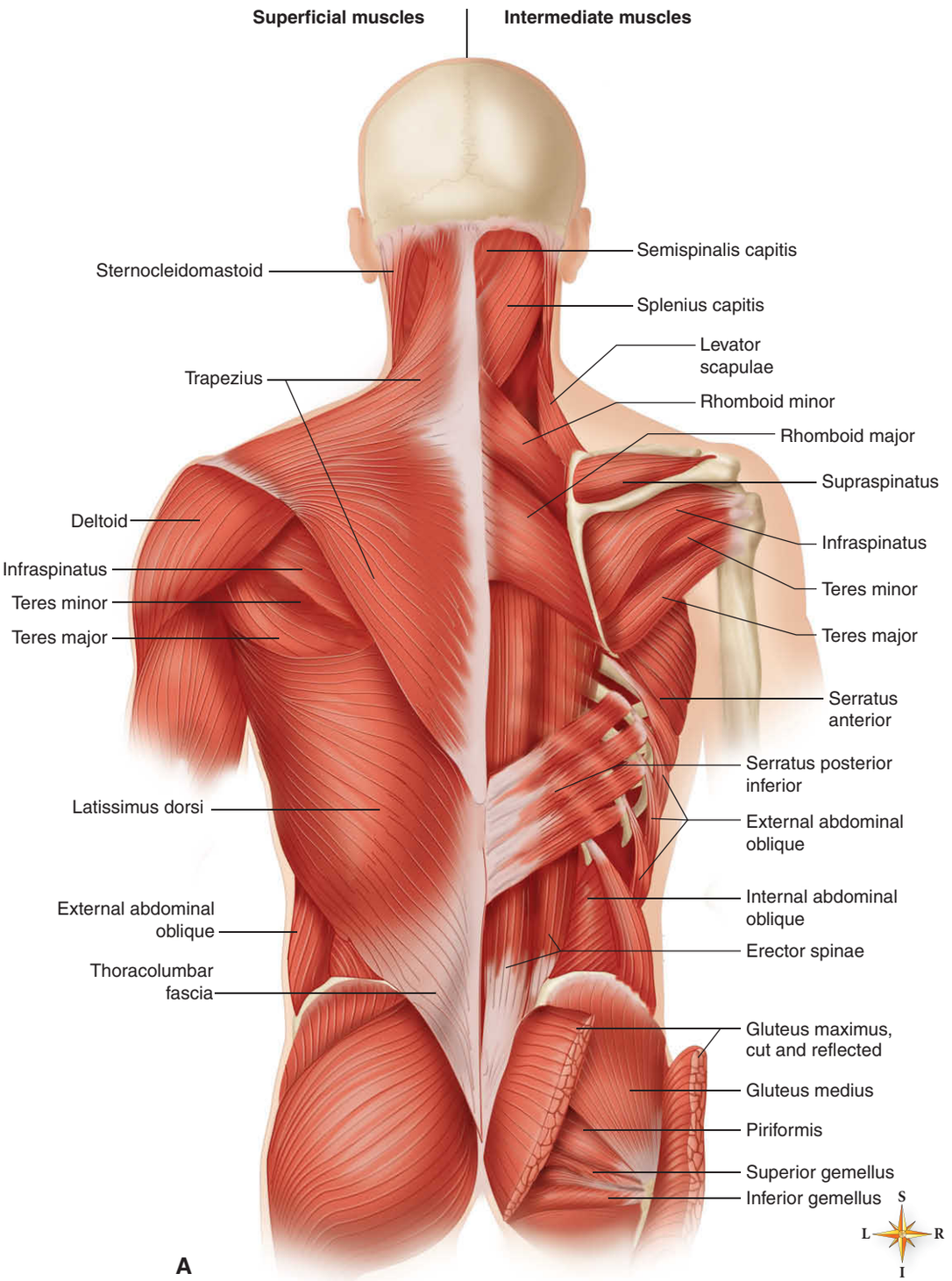
also involved in respiration and in helping "push" a baby through the birth canal during delivery. They also play a role in assisting in urination, defecation, and vomiting.

Muscles of the Back

Considering the large number of us who suffer from back pain, strain, and injury either occasionally or chronically, you can imagine the importance of the back muscles to health and fitness. Statistics show that 80% of the population in most areas of the world experience backache at some time in their lives. Although symptoms may vary from mild to disabling, "back problems" continue to plague large numbers of individuals and pose significant financial, social, and health care problems. The superficial back muscles play a major role in moving the head and limbs and are illustrated in Figure 11-14, *A*. The deep back muscles (Figure 11-14, *B*) not only allow us to move our vertebral column,

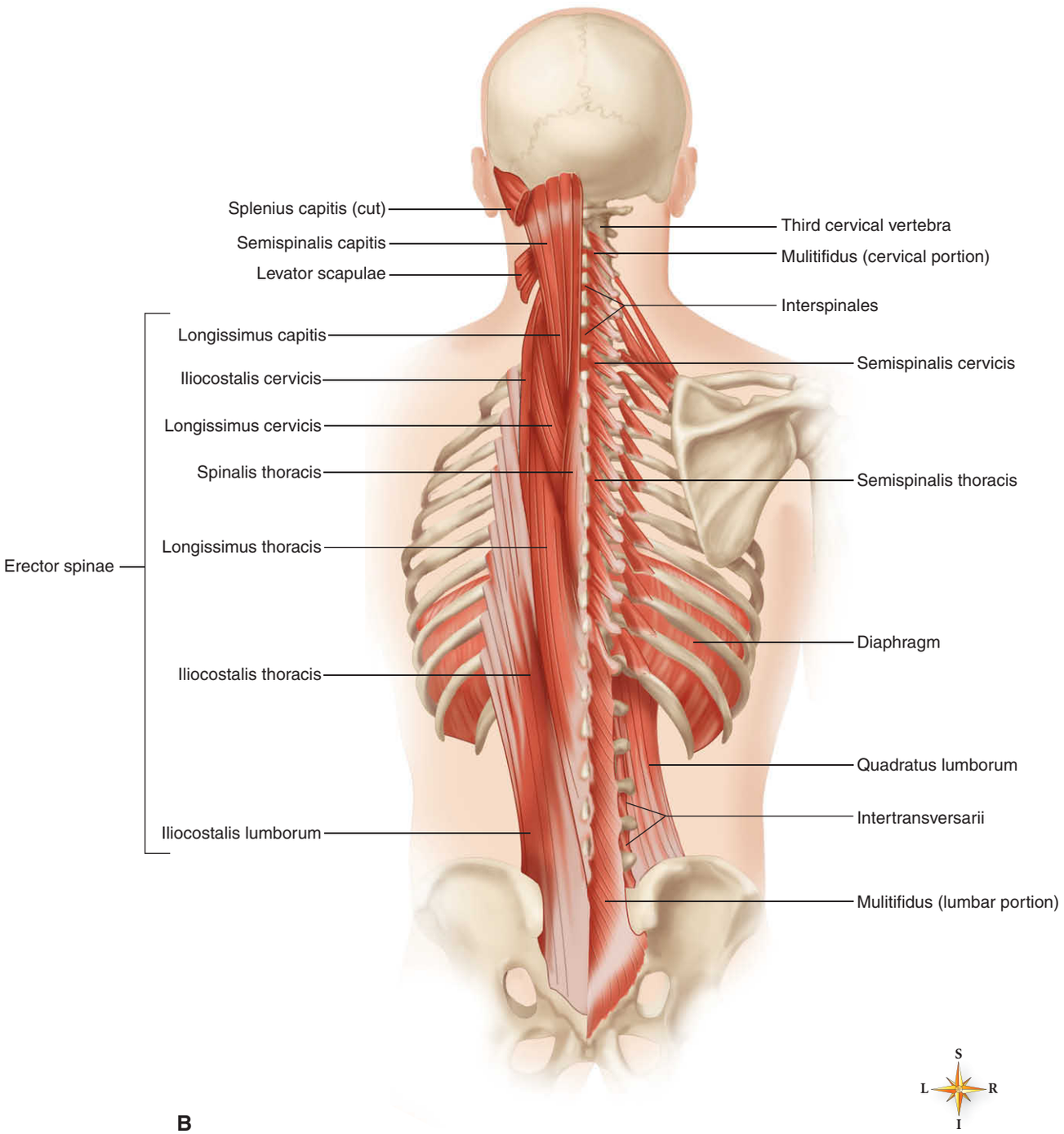
FIGURE 11-14

Muscles of the back. A, Superficial *(left)* and intermediate *(right)* muscle dissection of the back—posterior view. The illustration shows a two-stage dissection. Superficial muscles of the neck and back are shown on the left side and an intermediate-depth dissection is shown on the right. **B,** Deep muscle dissection of the back—posterior view. The superficial and intermediate muscles have been removed. The muscles in the gluteal region have been removed to expose the pelvic insertion of the multifidus.



thus helping us bend this way and that, but also stabilize our trunk so that we can maintain a stable posture. These muscles really get a work-out when we lift something heavy because they have to hold the body straight while the load is trying to bend the back.

The **erector spinae muscle** group consists of a number of long, thin muscles that travel all the way down our backs (see Figure 11-14). These muscles extend (straighten or pull back) the vertebral column and also flex the back laterally and rotate it a little. Even deeper than the erector spinae muscles are several additional back muscles. The **interspinales** and **multifidus groups,** for example, each connect one vertebra to the next; they also help extend the back and neck or flex them to the side. Table 11-11 and Figure 11-14 summarize some of the important deep back muscles.



B

TABLE 11-11 Muscles of the Back

MUSCLE	ORIGIN	INSERTION	FUNCTION	NERVE SUPPLY
Erector spinae group				
Iliocostalis group	Various regions of the pelvis and ribs	Ribs and vertebra (superior to the origin)	Extends, laterally flexes the vertebral column	Spinal, thoracic, or lumbar nerves
Longissimus group	Cervical and thoracic vertebrae, ribs	Mastoid process, upper cervical vertebrae, or upper lumbar vertebrae	Extends head, neck, or vertebral column	Cervical or thoracic and lumbar nerves
Spinalis group	Lower cervical or lower thoracic/upper lumbar vertebrae	Upper cervical or middle/upper thoracic vertebrae (superior to the origin)	Extends the neck or vertebral column	Cervical or thoracic nerves
Transversospinalis group				
Semispinalis group	Transverse processes of vertebrae (T2–T11)	Spinous processes of vertebrae (C2–T4)	Extends neck or vertebral column	Cervical or thoracic nerves
Multifidus group	Transverse processes of vertebrae; sacrum and ilium	Spinous processes of (next superior) vertebrae	Extends, rotates vertebral column	Spinal nerves
Rotatores group	Transverse processes of vertebrae	Spinous processes of (next superior) vertebrae	Extends, rotates vertebral column	Spinal nerves
Splenius	Spinous processes of vertebrae (C7–T1 or T3–T6)	Lateral occipital/mastoid or transverse processes of vertebrae (C1–C4)	Rotates, extends neck and flexes neck laterally	Cervical nerves
Interspinales group	Spinous processes of vertebrae	Spinous processes (of next superior vertebra)	Extends back and neck	Spinal nerves

Muscles of the Pelvic Floor

Structures in the pelvic cavity are supported by a reinforced muscular floor that guards the outlet below. The muscular pelvic floor filling the diamond-shaped outlet is called the **perineum** (pair-i-NEE-um). Passing through the floor are the anal canal and urethra in both sexes and the vagina in the female.

The two **levator ani** and **coccygeus muscles** form most of the pelvic floor. They stretch across the pelvic cavity like a hammock. This diamond-shaped outlet can be divided into two triangles by a line drawn from side to side between the ischial tuberosities. The **urogenital triangle** is anterior to this line (above) and extends to the pubic symphysis, and the **anal triangle** is posterior (behind it) and ends at the coccyx. Note in Figure 11-15 that structures in the urogenital triangle include the **ischiocavernosus** and **bulbospongiosus muscles** associated with the penis in the male and the vagina in the female. Constriction of muscles called the **urethral sphincter,** which encircle the urethra in both sexes, helps control urine flow. The anal triangle allows passage of the anal canal. The terminal portion of the canal is surrounded by the **external anal sphincter,** which regulates defecation. The origin, insertion, function, and innervation of important muscles of the pelvic floor are listed in Table 11-12. The coccygeus muscles lie behind the levator ani and are not visible in Figure 11-15.

| QUICK CHECK |

16. Name the skeletal muscles that produce respiratory movements.
17. Name two functions of the rectus abdominis muscle.
18. What is the perineum?

TABLE 11-12 Muscles of the Pelvic Floor

MUSCLE	ORIGIN	INSERTION	FUNCTION	NERVE SUPPLY
Levator ani	Pubis and spine of the ischium	Coccyx	Together with the coccygeus muscles form the floor of the pelvic cavity and support the pelvic organs	Pudendal nerve
Ischiocavernosus	Ischium	Penis or clitoris	Compress the base of the penis or clitoris	Perineal nerve
Bulbospongiosus				
Male	Bulb of the penis	Perineum and bulb of the penis	Constricts the urethra and erects the penis	Pudendal nerve
Female	Perineum	Base of the clitoris	Erects the clitoris	Pudendal nerve
Deep transverse perineal	Ischium	Central tendon (median raphe)	Supports the pelvic floor	Pudendal nerve
Urethral sphincter	Pubic ramus	Central tendon (median raphe)	Constricts the urethra	Pudendal nerve
External anal sphincter	Coccyx	Central tendon (median raphe)	Closes the anal canal	Pudendal and S4

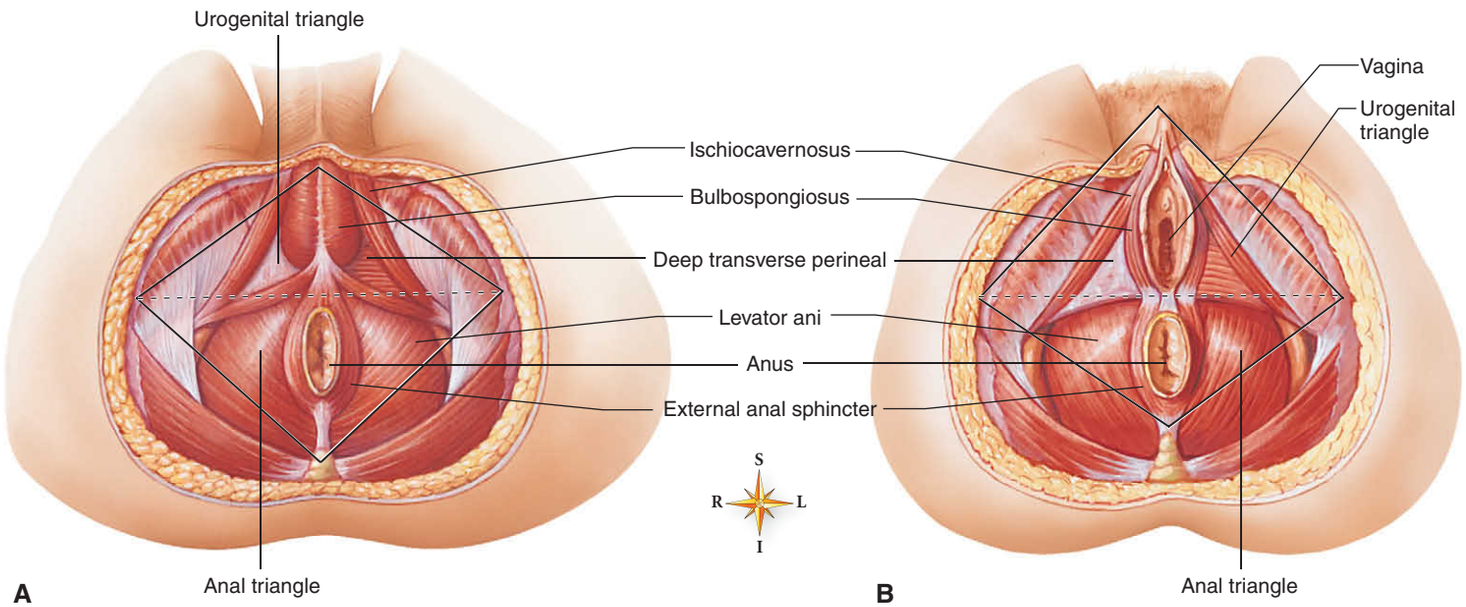


FIGURE 11-15

Muscles of the pelvic floor. A, Male, inferior view. **B,** Female, inferior view. Note the diamond-shaped outline of the perineum formed by the urogenital and anal triangles.

UPPER LIMB MUSCLES

The muscles of the upper limb include those acting on the shoulder or pectoral girdle and muscles located in the arm, forearm, and hand.

Muscles Acting on the Shoulder Girdle

Attachment of the upper extremity to the torso is by muscles that have an anterior location (chest) or posterior placement (back and neck). Six muscles (Table 11-13; Figure 11-16) that pass from the axial skeleton to the shoulder or pectoral girdle (scapula and clavicle) serve to not only "attach" the upper extremity to the body but also do so in such a way that extensive movement is possible. The clavicle can be elevated and depressed and moved forward and back. The scapula is capable of an even greater variety of movements.

The **pectoralis** (pek-toh-RAL-is) **minor** lies under the larger pectoralis major muscle on the anterior chest wall. It helps "fix" the scapula against the thorax and also raises the ribs during forced inspiration. Another anterior chest wall muscle—the **serratus** (ser-RAY-tus) **anterior**—helps hold the scapula against the thorax to prevent "winging" and is a strong abductor that is useful in pushing or punching movements.

The posterior muscles acting on the shoulder girdle include the **levator scapulae** (leh-VAY-tor SCAP-yoo-lee), which elevates the scapula; the **trapezius** (trah-PEE-zee-us), which is used to "shrug" the shoulders; and the **rhomboid** (ROM-boyd) **major** and **minor muscles,** which serve to adduct and elevate the scapula.

TABLE 11-13 Muscles Acting on the Shoulder Girdle

MUSCLE	ORIGIN	INSERTION	FUNCTION	NERVE SUPPLY
Trapezius	Occipital bone (protuberance)	Clavicle	Raises or lowers the shoulders and shrugs them	Spinal accessory; second, third, and fourth cervical nerves
	Vertebrae (cervical and thoracic)	Scapula (spine and acromion)	Extends the head and neck when the occiput acts as the insertion	
Pectoralis minor	Ribs (second to fifth)	Scapula (coracoid)	Pulls the shoulder girdle down and forward	Medial and lateral anterior thoracic nerve
Serratus anterior	Ribs (upper eight or nine)	Scapula (anterior surface, vertebral border)	Pulls the shoulder down and forward; abducts and rotates it upward	Long thoracic nerve
Levator scapulae	C1–C4 (transverse processes)	Scapula (superior angle)	Elevates and retracts the scapula and abducts the neck	Dorsal scapular nerve
Rhomboid				
Major	T1–T4	Scapula (medial border)	Retracts, rotates, and fixes the scapula	Dorsal scapular nerve
Minor	C6–C7	Scapula (medial border)	Retracts, rotates, elevates, and fixes the scapula	Dorsal scapular nerve

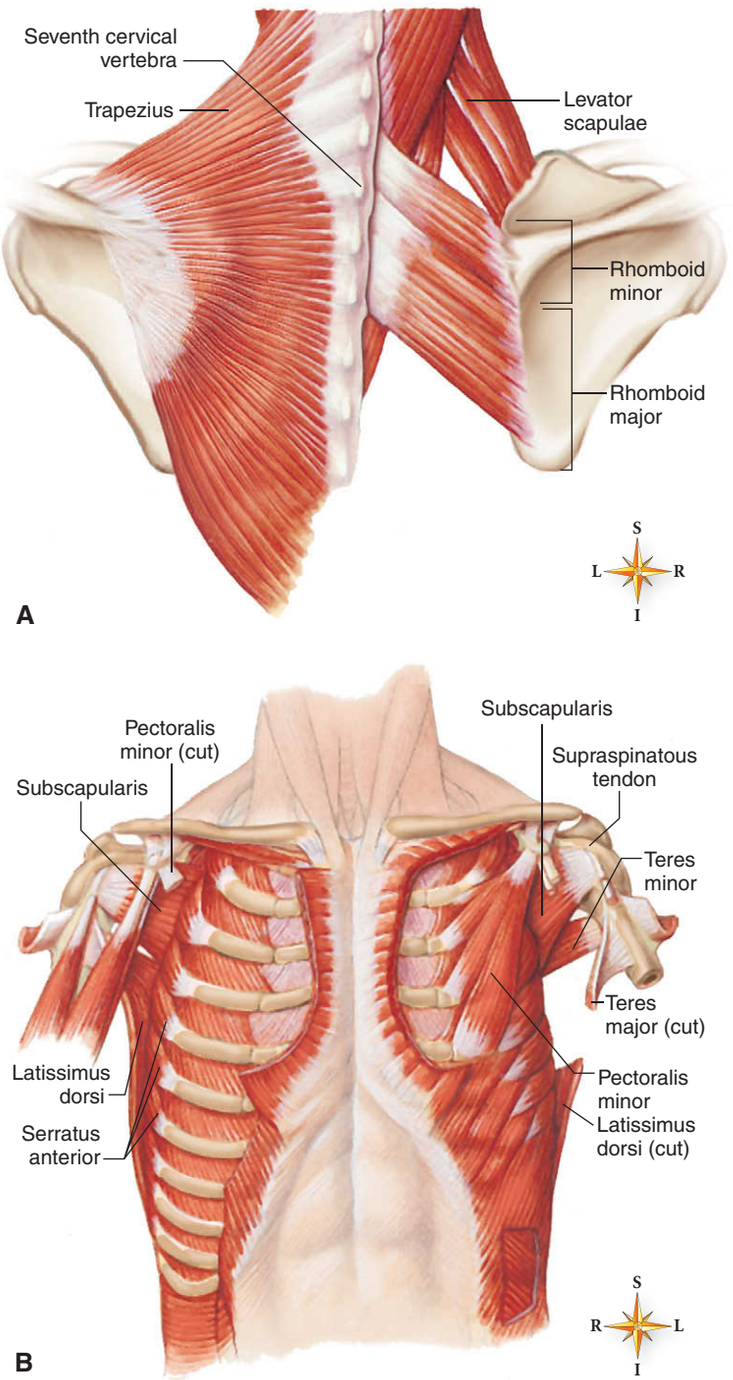


FIGURE 11-16

Muscles acting on the shoulder girdle. A, Posterior view. The trapezius has been removed on the right to reveal the deeper muscles. **B,** Anterior view. The pectoralis major has been removed on both sides. The pectoralis minor has also been removed on the right side.

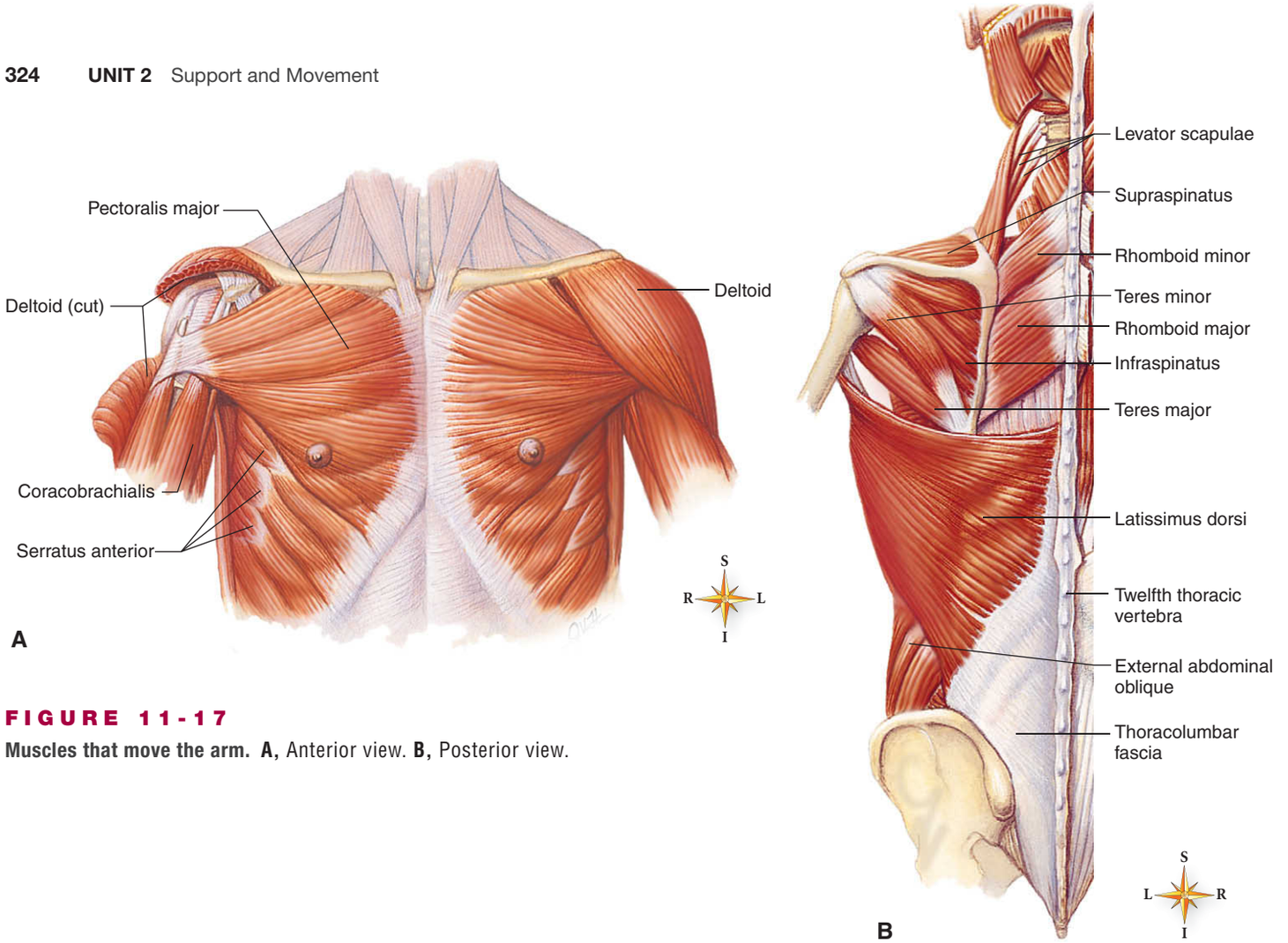


FIGURE 11-17

Muscles that move the arm. **A,** Anterior view. **B,** Posterior view.

TABLE 11-14 Muscles That Move the Arm

MUSCLE	ORIGIN	INSERTION	FUNCTION	NERVE SUPPLY
Axial*				
Pectoralis major	Clavicle (medial half) Sternum Costal cartilages of the true ribs	Humerus (greater tubercle)	Flexes the arm Adducts the arm anteriorly; draws it across the chest	Medial and lateral anterior thoracic nerves
Latissimus dorsi	Vertebrae (spines of the lower thoracic, lumbar, and sacral) Ilium (crest) Lumbodorsal fascia	Humerus (intertubercular groove)	Extends the arm Adducts the arm posteriorly	Thoracodorsal nerve
Scapular*				
Deltoid	Clavicle Scapula (spine and acromion)	Humerus (lateral side about halfway down—deltoid tubercle)	Abducts the arm Assists in flexion and extension of the arm	Axillary nerve
Coracobrachialis	Scapula (coracoid process)	Humerus (middle third, medial surface)	Adduction; assists in flexion and medial rotation of the arm	Musculocutaneous nerve
Supraspinatus†	Scapula (supraspinous fossa)	Humerus (greater tubercle)	Assists in abducting the arm	Suprascapular nerve
Teres minor†	Scapula (axillary border)	Humerus (greater tubercle)	Rotates the arm outward	Axillary nerve
Teres major	Scapula (lower part, axillary border)	Humerus (upper part, anterior surface)	Assists in extension, adduction, and medial rotation of the arm	Lower subscapular nerve
Infraspinatus†	Scapula (infraspinatus border)	Humerus (greater tubercle)	Rotates the arm outward	Suprascapular nerve
Subscapularis†	Scapula (subscapular fossa)	Humerus (lesser tubercle)	Medial rotation	Suprascapular nerve

**Axial* muscles originate on the axial skeleton. *Scapular* muscles originate on the scapula.
†Muscles of the rotator cuff (SITS muscles).

Muscles That Move the Arm

The shoulder is a synovial joint of the ball-and-socket type. As a result, extensive movement is possible in every plane of motion (Box 11-2). Muscles that move the upper part of the arm can be grouped according to function as flexors, extensors, abductors, adductors, and medial and lateral rotators (Table 11-14; Figure 11-17). The actions listed in Table 11-14 include primary actions and important secondary functions.

The **deltoid** (DEL-toyd) is a good example of a multifunction muscle. It has three groups of fibers and may act as three separate muscles. Contraction of the anterior fibers will flex the arm, whereas the lateral fibers abduct and the posterior fibers serve as extensors. Four other muscles serve as both a structural and functional cuff around the shoulder joint and are referred to as the **rotator cuff muscles** (Figure 11-18). They include the **supraspinatus, infraspinatus, teres minor,** and **subscapularis**—the so-called *SITS muscles*.

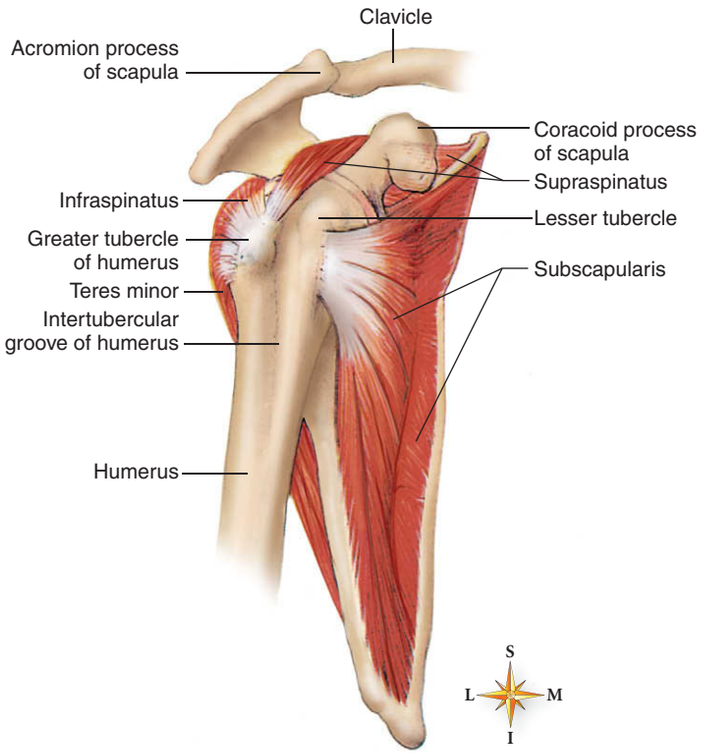


FIGURE 11-18

Rotator cuff muscles. Anterior view of the right shoulder showing the tendons of the teres minor, infraspinatus, supraspinatus, and subscapularis muscles surrounding the head of the humerus.



Box 11-2 | SPORTS and FITNESS

Shoulder Joint Stability

The disparity in size between the large and nearly hemispheric head of the humerus and the much smaller and shallow glenoid cavity of the scapula is of great clinical significance. Because the head of the humerus is more than two times larger than the shallow glenoid concavity that receives it, only about a quarter of the articular surface of the humeral head is in contact with the fossa in any given position of the joint. This anatomical fact helps explain the inherent instability of the shoulder—our most mobile joint. The soft tissues surrounding the shoulder, such as the joint capsule, ligaments, and adjacent muscles, provide the primary restraint against excessive motion and potential dislocation.

Unfortunately, only a thin articular capsule surrounds the shoulder joint. It is extremely loose and does not function to keep the articulating bones of the joint in contact. This fact is obviously correlated with both the great range of motion (ROM) possible at this articulation and its tendency to dislocate as a result of athletic injury or other trauma. The tendons of the supraspinatus, infraspinatus, teres minor, and subscapularis muscles (called the *SITS muscles*) all blend with and strengthen the articular capsule. The musculotendinous cuff resulting from this fusion is called the **rotator cuff** (see Figure 11-18). The rotator cuff provides the necessary strength to help prevent anterior, superior, and posterior displacement of the humeral head during most types of activity.



The rotator cuff stabilizes the shoulder during athletic activities.

Muscles That Move the Forearm

Selected superficial and deep muscles of the upper extremity are shown in Figures 11-19 and 11-20. Recall that most muscles acting on a joint lie proximal to that joint. Muscles acting directly on the forearm, therefore, are found proximal to the elbow and attach the bones of the forearm (ulna and radius) to the humerus or scapula above. Table 11-15 lists the muscles acting on the forearm and gives the origin, insertion, function, and innervation of each. Figure 11-21 shows the detail of attachment of several important muscles in this group.

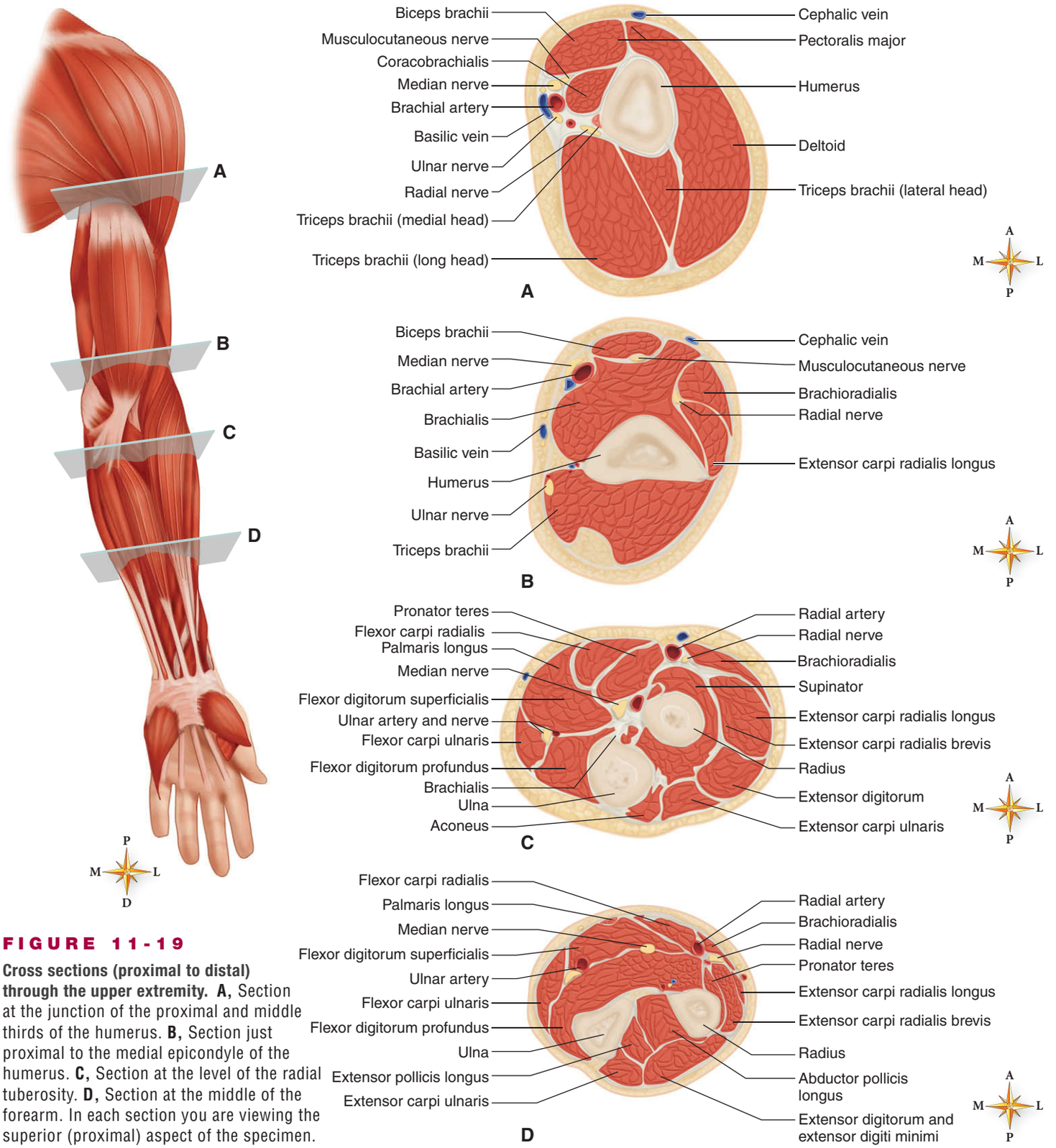


FIGURE 11-19

Cross sections (proximal to distal) through the upper extremity. A, Section at the junction of the proximal and middle thirds of the humerus. **B,** Section just proximal to the medial epicondyle of the humerus. **C,** Section at the level of the radial tuberosity. **D,** Section at the middle of the forearm. In each section you are viewing the superior (proximal) aspect of the specimen.

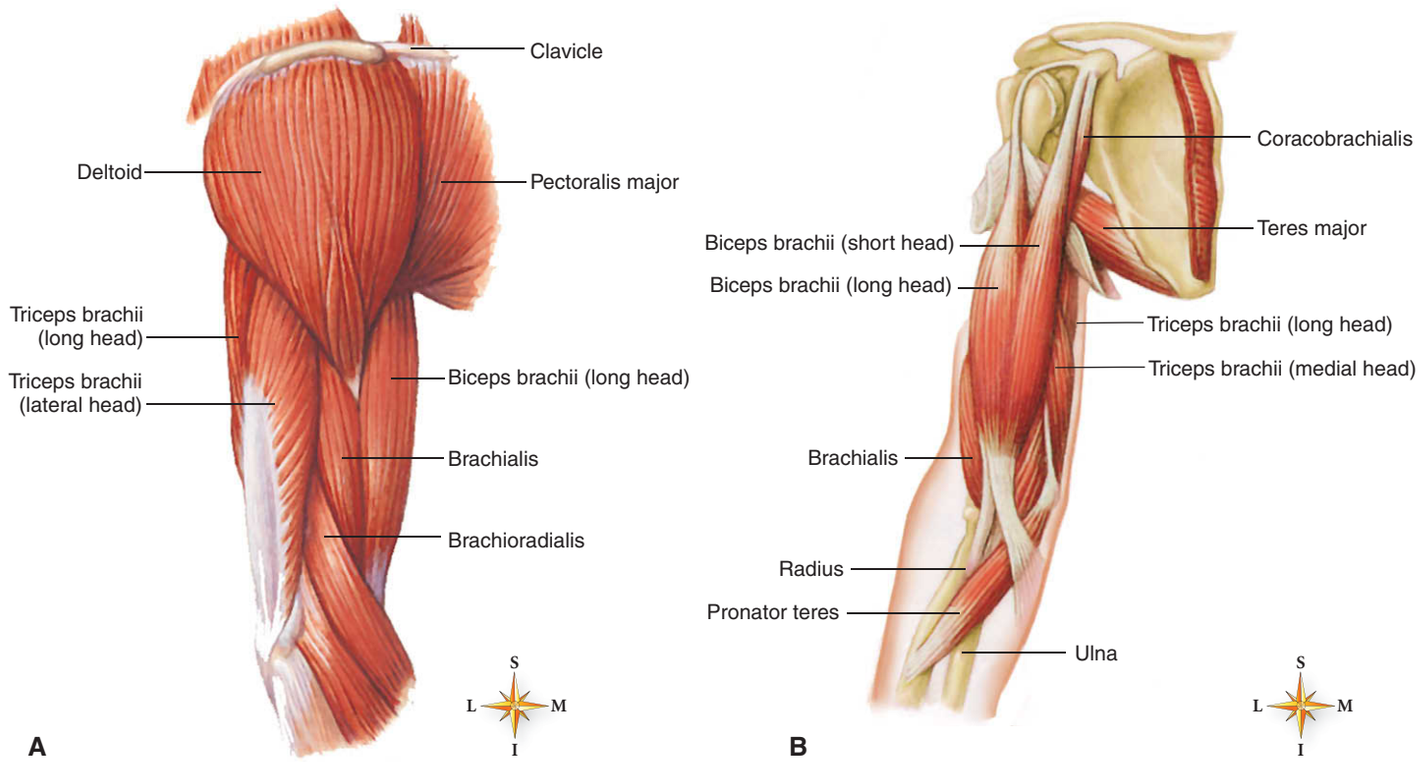


FIGURE 11-20

Muscles acting on the forearm. A, Lateral view of the right shoulder and arm. **B,** Anterior view of the right shoulder and arm (deep). The deltoid and pectoralis major muscles have been removed to reveal deeper structures.

TABLE 11-15 Muscles That Move the Forearm

MUSCLE	ORIGIN	INSERTION	FUNCTION	NERVE SUPPLY
Flexors				
Biceps brachii	Scapula (supraglenoid tuberosity) Scapula (coracoid)	Radius (tuberosity at the proximal end)	Flexes the supinated forearm Supinates the forearm and hand	Musculocutaneous nerve
Brachialis	Humerus (distal half, anterior surface)	Ulna (front of the coronoid process)	Flexes the pronated forearm	Musculocutaneous nerve
Brachioradialis	Humerus (above the lateral epicondyle)	Radius (styloid process)	Flexes the semipronated or semisupinated forearm; supinates the forearm and hand	Radial nerve
Extensor				
Triceps brachii	Scapula (infraglenoid tuberosity) Humerus (posterior surface—lateral head above the radial groove; medial head, below)	Ulna (olecranon)	Extends the lower arm	Radial nerve
Pronators				
Pronator teres	Humerus (medial epicondyle) Ulna (coronoid process)	Radius (middle third of the lateral surface)	Pronates and flexes the forearm	Median nerve
Pronator quadratus	Ulna (distal fourth, anterior surface)	Radius (distal fourth, anterior surface)	Pronates the forearm	Median nerve
Supinator				
Supinator	Humerus (lateral epicondyle) Ulna (proximal fifth)	Radius (proximal third)	Supinates the forearm	Radial nerve

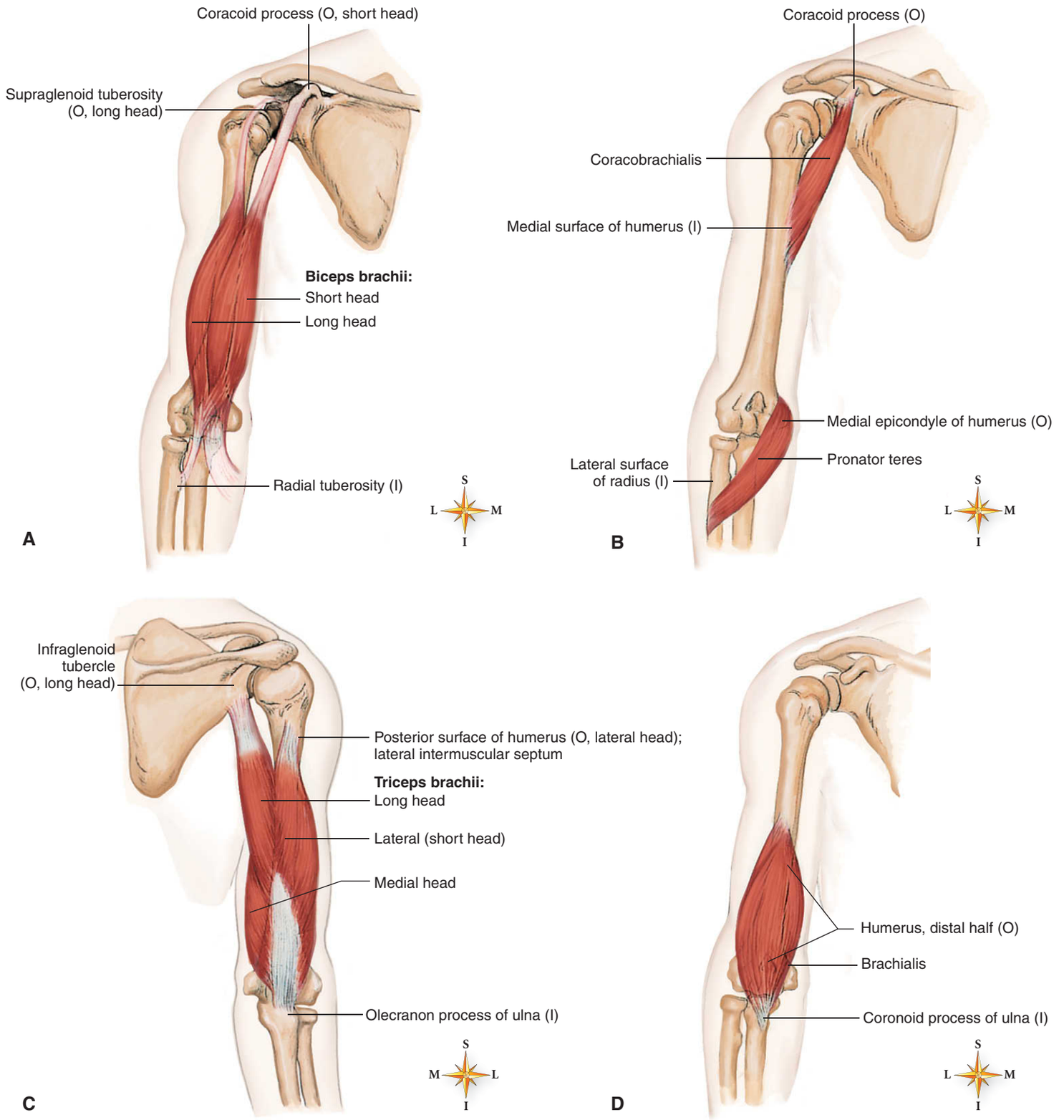


FIGURE 11-21

Muscles acting on the forearm. A, Biceps brachii. **B,** Coracobrachialis and pronator teres. **C,** Triceps brachii. **D,** Brachialis. *O,* Origin; *I,* insertion.

Muscles That Move the Wrist, Hand, and Fingers

Muscles that move the wrist, hand, and fingers can be **extrinsic muscles** or **intrinsic muscles.** The term *extrinsic* means *from the outside* and refers to muscles originating outside of the part of the skeleton moved. Extrinsic muscles originating in the forearm can pull on their insertions in the wrist, hand, and fingers to move them. The term *intrinsic*, meaning *from within*, refers to muscles that are actually within the part moved. Muscles that begin and end at different points within the hand can produce fine finger movements, for example.

Extrinsic muscles acting on the wrist, hand, and fingers are located on the anterior or the posterior surfaces of the forearm (Figure 11-22). In most instances, the muscles located on the anterior surface of the forearm are flexors and those on the posterior surface are extensors of the wrist, hand, and fingers (Table 11-16).

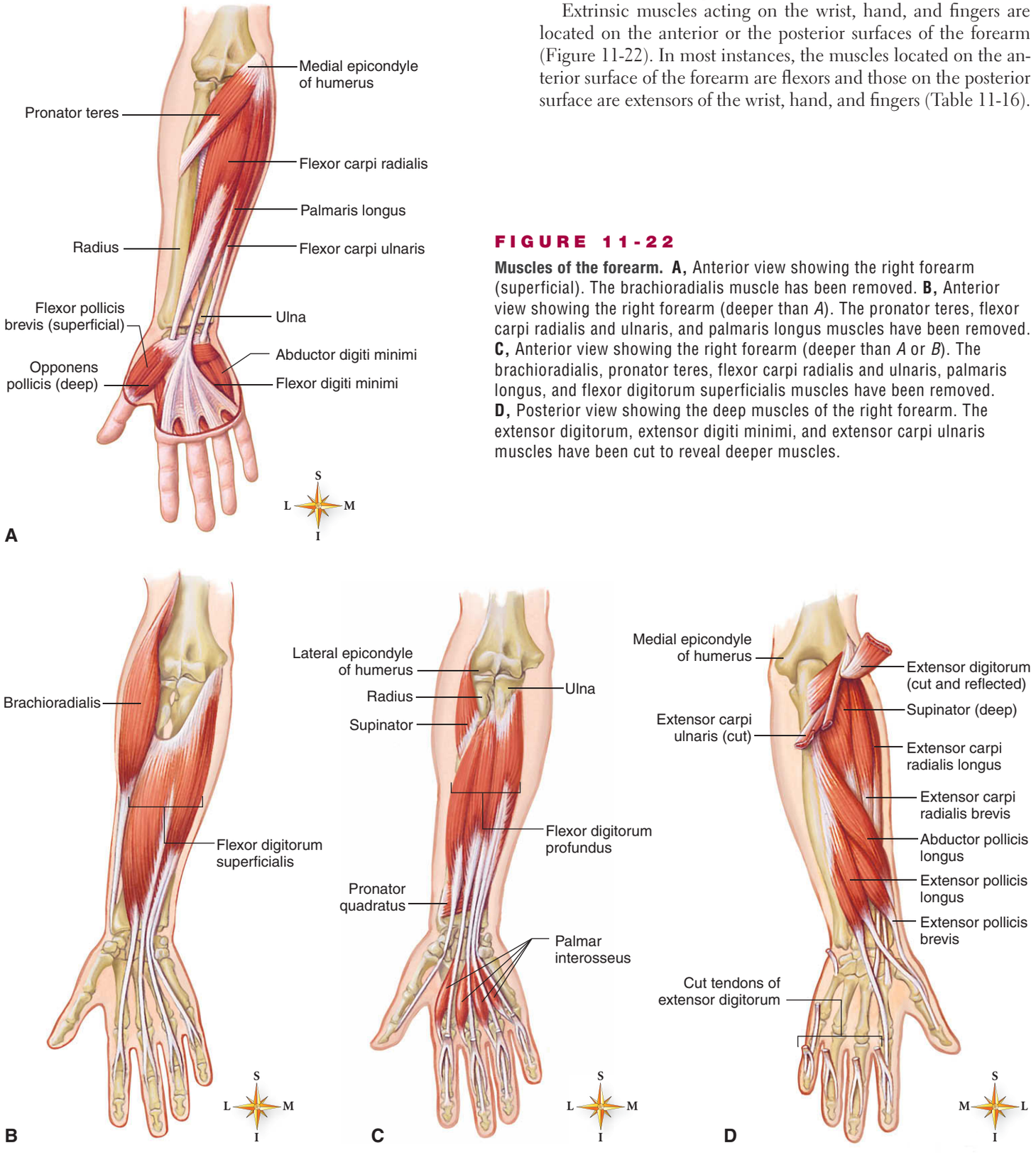


FIGURE 11-22

Muscles of the forearm. A, Anterior view showing the right forearm (superficial). The brachioradialis muscle has been removed. **B,** Anterior view showing the right forearm (deeper than *A*). The pronator teres, flexor carpi radialis and ulnaris, and palmaris longus muscles have been removed. **C,** Anterior view showing the right forearm (deeper than *A* or *B*). The brachioradialis, pronator teres, flexor carpi radialis and ulnaris, palmaris longus, and flexor digitorum superficialis muscles have been removed. **D,** Posterior view showing the deep muscles of the right forearm. The extensor digitorum, extensor digiti minimi, and extensor carpi ulnaris muscles have been cut to reveal deeper muscles.

TABLE 11-16 Muscles That Move the Wrist, Hand, and Fingers

MUSCLE	ORIGIN	INSERTION	FUNCTION	NERVE SUPPLY
Extrinsic				
Flexor carpi radialis	Humerus (medial epicondyle)	Second metacarpal (base of)	Flexes the hand Flexes the forearm	Median nerve
Palmaris longus	Humerus (medial epicondyle)	Fascia of the palm	Flexes the hand	Median nerve
Flexor carpi ulnaris	Humerus (medial epicondyle)	Pisiform bone	Flexes the hand	Ulnar nerve
	Ulna (proximal two thirds)	Third, fourth, and fifth metacarpals	Adducts the hand	
Extensor carpi radialis longus	Humerus (ridge above the lateral epicondyle)	Second metacarpal (base of)	Extends the hand Abducts the hand (moves toward the thumb side when the hand is supinated)	Radial nerve
Extensor carpi radialis brevis	Humerus (lateral epicondyle)	Second, third metacarpals (bases of)	Extends the hand	Radial nerve
Extensor carpi ulnaris	Humerus (lateral epicondyle) Ulna (proximal three fourths)	Fifth metacarpal (base of)	Extends the hand Adducts the hand (moves toward the little finger side when the hand is supinated)	Radial nerve
Flexor digitorum profundus	Ulna (anterior surface)	Distal phalanges (fingers 2 to 5)	Flexes the distal interphalangeal joints	Median and ulnar nerves
Flexor digitorum superficialis	Humerus (medial epicondyle) Radius Ulna (coronoid process)	Tendons of the fingers	Flexes the fingers	Median nerve
Extensor digitorum	Humerus (lateral epicondyle)	Phalanges (fingers 2 to 5)	Extends the fingers	Radial nerve
Intrinsic				
Opponens pollicis	Trapezium	Thumb metacarpal	Opposes the thumb to the fingers	Median nerve
Abductor pollicis brevis	Trapezium	Proximal phalanx of the thumb	Abducts the thumb	Median nerve
Adductor pollicis	Second and third metacarpals Trapezoid Capitate	Proximal phalanx of the thumb	Adducts the thumb	Ulnar nerve
Flexor pollicis brevis	Flexor retinaculum	Proximal phalanx of the thumb	Flexes the thumb	Median and ulnar nerves
Abductor digiti minimi	Pisiform	Proximal phalanx of the fifth finger (base of)	Abducts the fifth finger Flexes the fifth finger	Ulnar nerve
Flexor digiti minimi brevis	Hamate	Proximal and middle phalanx of the fifth finger	Flexes the fifth finger	Ulnar nerve
Opponens digiti minimi	Hamate Flexor retinaculum	Fifth metacarpal	Opposes the fifth finger slightly	Ulnar nerve
Interosseous (palmar and dorsal)	Metacarpals	Proximal phalanges	Adducts the second, fourth, and fifth fingers (palmar) Abducts the second, third, and fourth fingers (dorsal)	Ulnar nerve
Lumbricals	Tendons of the flexor digitorum profundus	Phalanges (2 to 5)	Flexes the proximal phalanges (2 to 5) Extends the middle and distal phalanges (2 to 5)	Median nerve (phalanges 2 and 3) Ulnar nerve (phalanges 4 and 5)

Box 11-3 | HEALTH matters

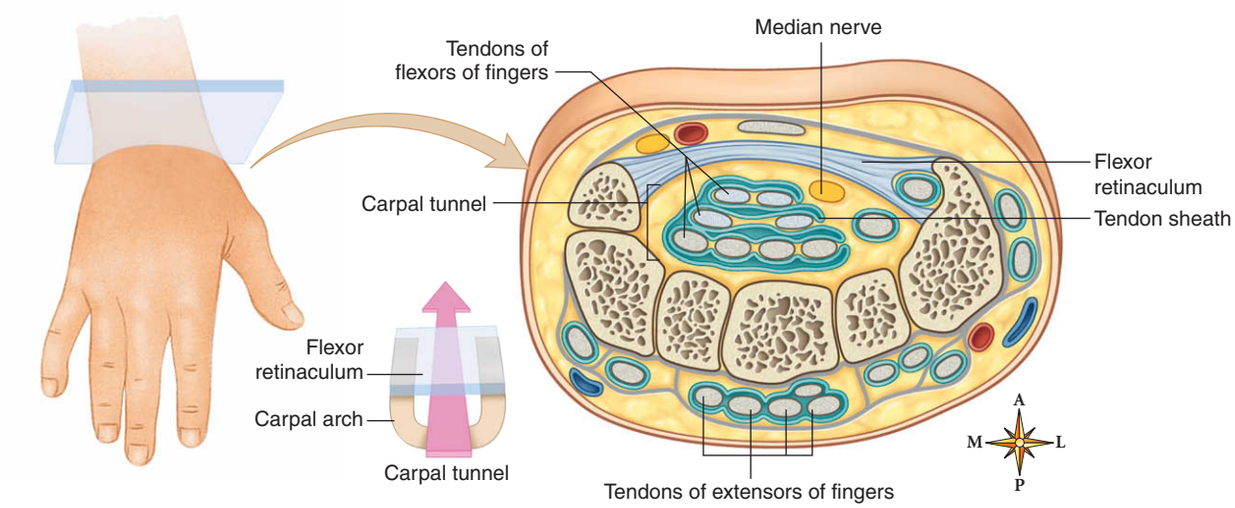
Carpal Tunnel Syndrome

Some epidemiologists specialize in the field of occupational health, the study of health matters related to work or the workplace. Many problems seen by occupational health experts are caused by repetitive motions of the wrists or other joints. Meat cutters and workers who use word processors, for example, are at risk for conditions caused by repetitive motion injuries.

One common problem often caused by such repetitive motion is **tenosynovitis** (ten-oh-sin-oh-VYE-tis)—inflammation of a tendon sheath. Tenosynovitis can be painful, and the swelling characteristic of this condition can limit movement in affected parts of the body. For example, swelling of the tendon sheath around tendons in an area of the wrist known as the *carpal tunnel* can limit movement of the wrist, hand, and fingers.

The figure shows the relative positions of the tendon sheath and median nerve within the carpal tunnel. The carpal tunnel is formed as a fibrous band called the *flexor retinaculum* wraps over the tendons of the flexor muscles that lie within an arch formed by the carpal bones. If swelling, or any other lesion within the carpal tunnel, presses on the *median nerve,* a condition called **carpal tunnel syndrome** may result. Because the median nerve connects to the palm and radial side (thumb side) of the hand, carpal tunnel syndrome is characterized by weakness, pain, and tingling in this part of the hand. The pain and tingling may also radiate to the forearm and shoulder. Prolonged or severe cases of carpal tunnel syndrome may be relieved by injection of antiinflammatory agents. A permanent cure is sometimes accomplished by surgically cutting the flexor retinaculum to relieve the pressure on the median nerve.

The procedure called *carpal tunnel release* is the most common hand operation in the United States. Such operations are performed more than 200,000 times every year. When the procedure was first introduced in 1933, it was performed as an "open" procedure. A less invasive endoscopic approach was introduced in 1989; that and many other innovative surgical techniques and advances are now being used.



The carpal tunnel. The median nerve and muscles that flex the fingers pass through a concavity in the wrist called the *carpal tunnel.*

Many of the flexors of the wrist and hand pass through a curve formed by the carpal bones called the *carpal tunnel*. The long tendons of these muscles slide through the carpal tunnel more easily because tendon sheaths lined with synovial membrane are present. Box 11-3 discusses the importance of the carpal tunnel in occupational health.

A number of intrinsic muscles are responsible for precise movements of the hand and fingers. Examples include the **lumbrical** (LUM-bri-kal) and **interosseous** (in-ter-OSS-ee-us) **muscles,** which originate from and fill the spaces between the metacarpal bones and then insert on the phalanges of the fingers. As a group, the intrinsic muscles abduct and adduct the fingers and aid in flexing them. Eight additional muscles serve the thumb and enable it to be placed in opposition to the fingers in tasks requiring grasping and manipulation. The **opponens pollicis** (oh-POH-nenz POL-i-cis) is a particularly important thumb muscle.

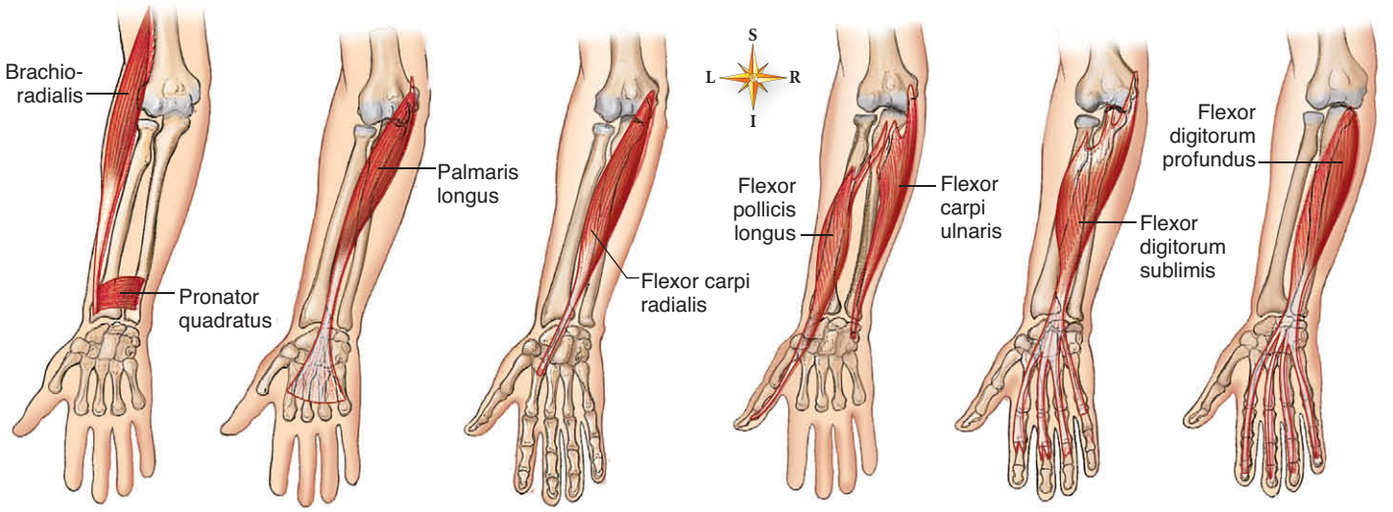


FIGURE 11-23

Some muscles of the anterior aspect of the right forearm.

It allows the thumb to be drawn across the palm to touch the tip of any finger—a critical movement for many manipulative-type activities. Figure 11-23 shows the placement and points of attachment for various individual extrinsic muscles acting on the wrist, hand, and fingers. Figure 11-24 provides a detailed illustration of many of the intrinsic muscles of the hand.

| QUICK CHECK |

19. What are the functions of the deltoid muscle?
20. What is the function of the biceps brachii muscle?
21. Distinguish the extrinsic from the intrinsic muscles of the hand and wrist.

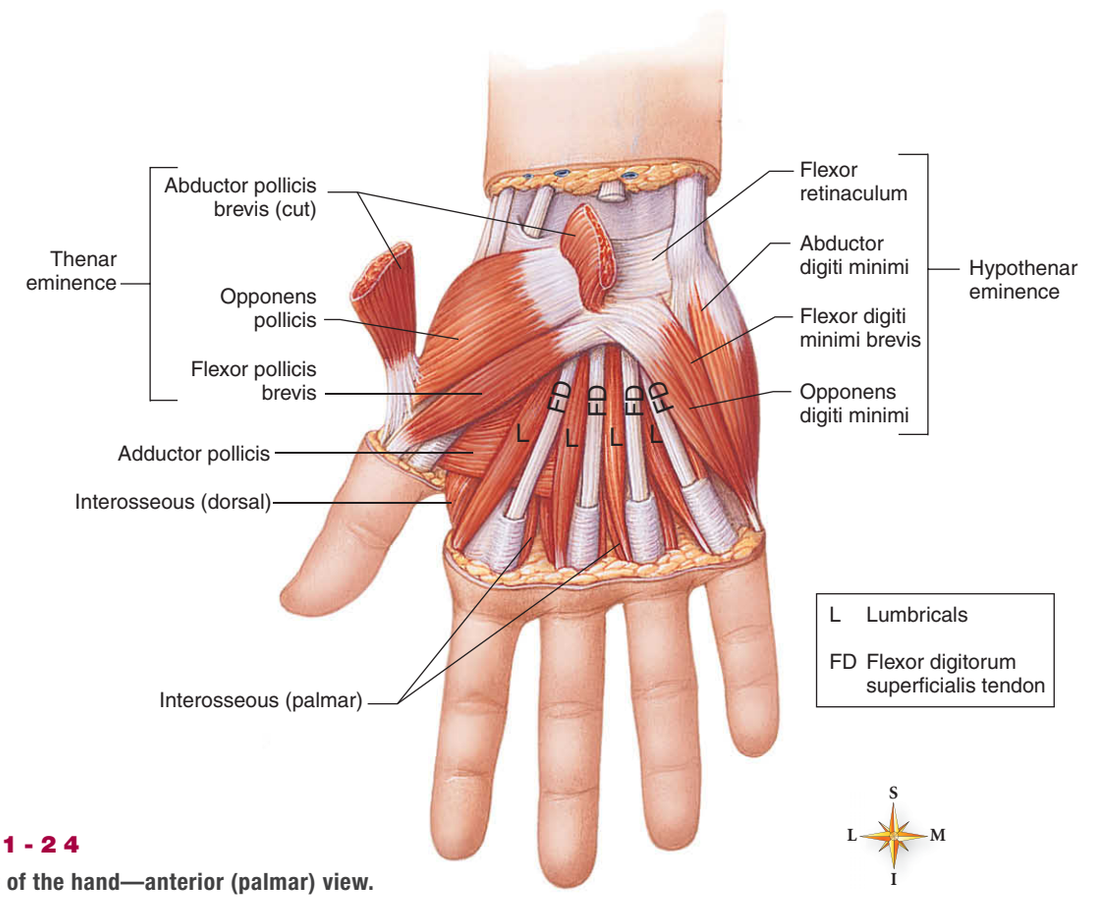


FIGURE 11-24

Intrinsic muscles of the hand—anterior (palmar) view.

TABLE 11-17 Muscles That Move the Thigh

MUSCLE	ORIGIN	INSERTION	FUNCTION	NERVE SUPPLY
Iliopsoas (iliacus, psoas major, and psoas minor)	Ilium (iliac fossa)	Femur (lesser trochanter)	Flexes the thigh	Femoral and second to fourth lumbar nerves
	Vertebrae (bodies of twelfth thoracic to fifth lumbar)		Flexes the trunk (when the femur acts as the origin)	
Rectus femoris	Ilium (anterior, inferior spine)	Tibia (by way of the patellar tendon)	Flexes the thigh Extends the leg	Femoral nerve
Gluteal group				
Maximus	Ilium (crest and posterior surface) Sacrum and coccyx (posterior surface) Sacrotuberous ligament	Femur (gluteal tuberosity) Iliotibial tract	Extends the thigh—rotates outward	Inferior gluteal nerve
Medius	Ilium (lateral surface)	Femur (greater trochanter)	Abducts the thigh—rotates outward; stabilizes the pelvis on the femur	Superior gluteal nerve
Minimus	Ilium (lateral surface)	Femur (greater trochanter)	Abducts the thigh; stabilizes the pelvis on the femur Rotates the thigh medially	Superior gluteal nerve
Tensor fasciae latae	Ilium (anterior part of the crest)	Tibia (by way of the iliotibial tract)	Abducts the thigh Tightens the iliotibial tract	Superior gluteal nerve
Adductor group				
Brevis	Pubic bone	Femur (linea aspera)	Adducts the thigh	Obturator nerve
Longus	Pubic bone	Femur (linea aspera)	Adducts the thigh	Obturator nerve
Magnus	Pubic bone	Femur (linea aspera)	Adducts the thigh	Obturator nerve
Gracilis	Pubic bone (just below the symphysis)	Tibia (medial surface behind the sartorius)	Adducts the thigh and flexes and adducts the leg	Obturator nerve

LOWER LIMB MUSCLES

The musculature, bony structure, and joints of the pelvic girdle and lower extremity function in locomotion and maintenance of stability. Powerful muscles at the back of the hip, at the front of the thigh, and at the back of the leg also serve to raise the full body weight from a sitting to a standing position. The muscles of the lower limb include those acting on the hip or pelvic girdle, as well as muscles located in the thigh, leg, and foot. Unlike the highly mobile shoulder girdle, the pelvic girdle is essentially fixed. Therefore, our study of muscles in the lower extremity begins with those arising from the pelvic girdle and passing to the femur; they produce their effects at the hip joint by moving the thigh.

Muscles That Move the Thigh and Leg

Table 11-17 identifies muscles that move the thigh and lists the origin, insertion, function, and nerve supply of each (Figure 11-25). Refer to Figure 11-6 and Figures 11-25 through 11-29, which show individual muscles, as you study the information provided in the table. Muscles acting on the thigh can be divided into three groups: (1) muscles crossing the front of the hip, (2) the three **gluteal** (GLOO-tee-al) **muscles,** and the **tensor fasciae latae** (TEN-sor FASH-ee LAT-tee), and (3) the thigh adductors. One of the gluteal muscles, the gluteus medius muscle, is often the site of intramuscular injections (Box 11-4).

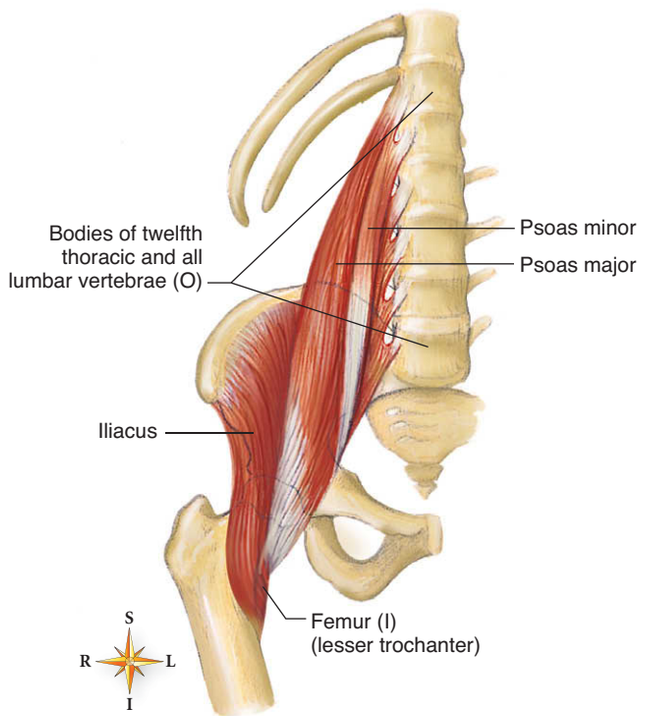


FIGURE 11-25

Iliopsoas muscle (iliacus, psoas major, and psoas minor muscles). *O,* Origin; *I,* insertion.

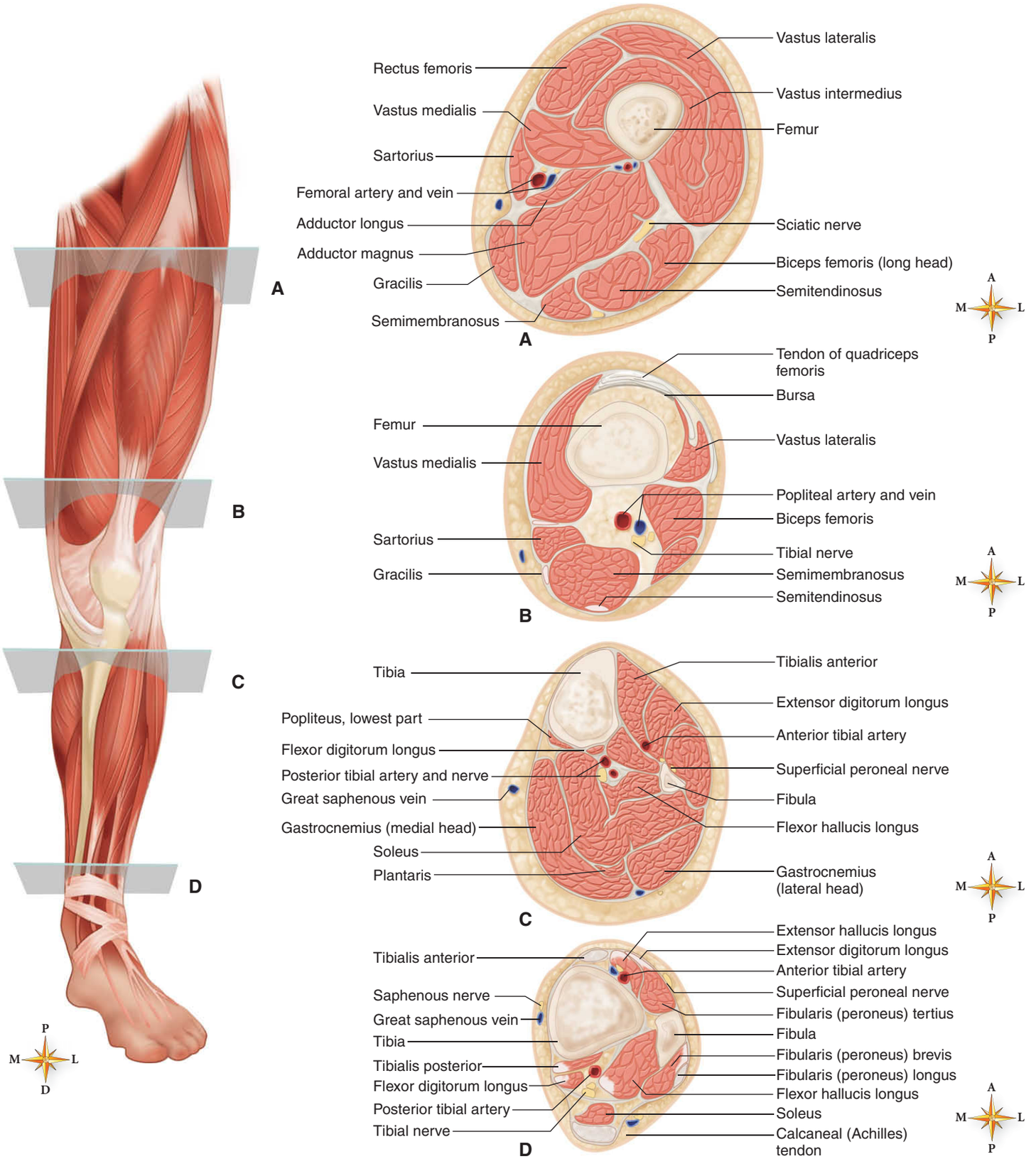


FIGURE 11-26

Cross sections (proximal to distal) through the lower extremity. A, Section through the middle of the femur. **B,** Section about 4 cm above the adductor tubercle of the femur. **C,** Section about 10 cm distal to the knee joint. **D,** Section about 6 cm above the medial malleolus. In each section you are viewing the superior (proximal) aspect of the specimen.

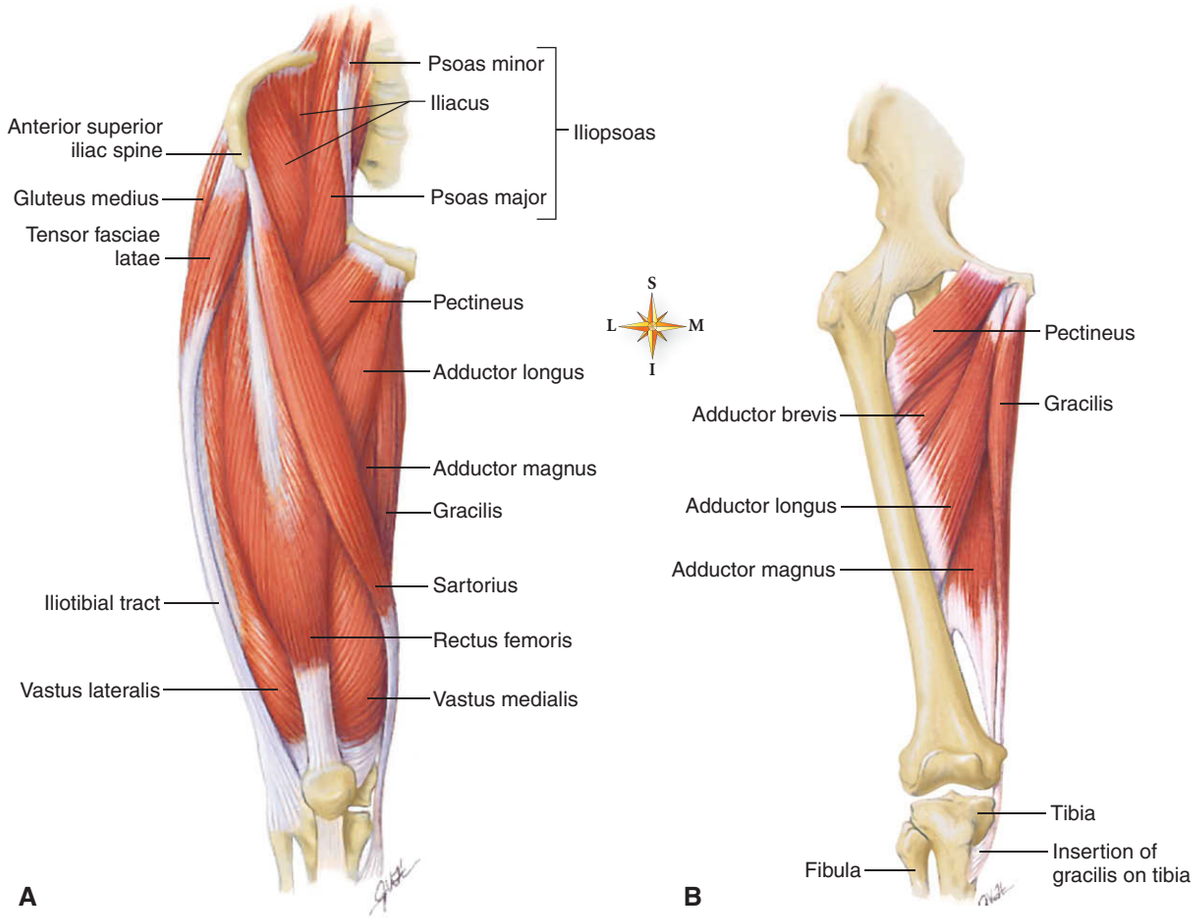


FIGURE 11-27

Muscles of the anterior aspect of the thigh. A, Anterior view of the right thigh. **B,** Adductor region of the right thigh. The tensor fasciae latae, sartorius, and quadriceps muscles have been removed.

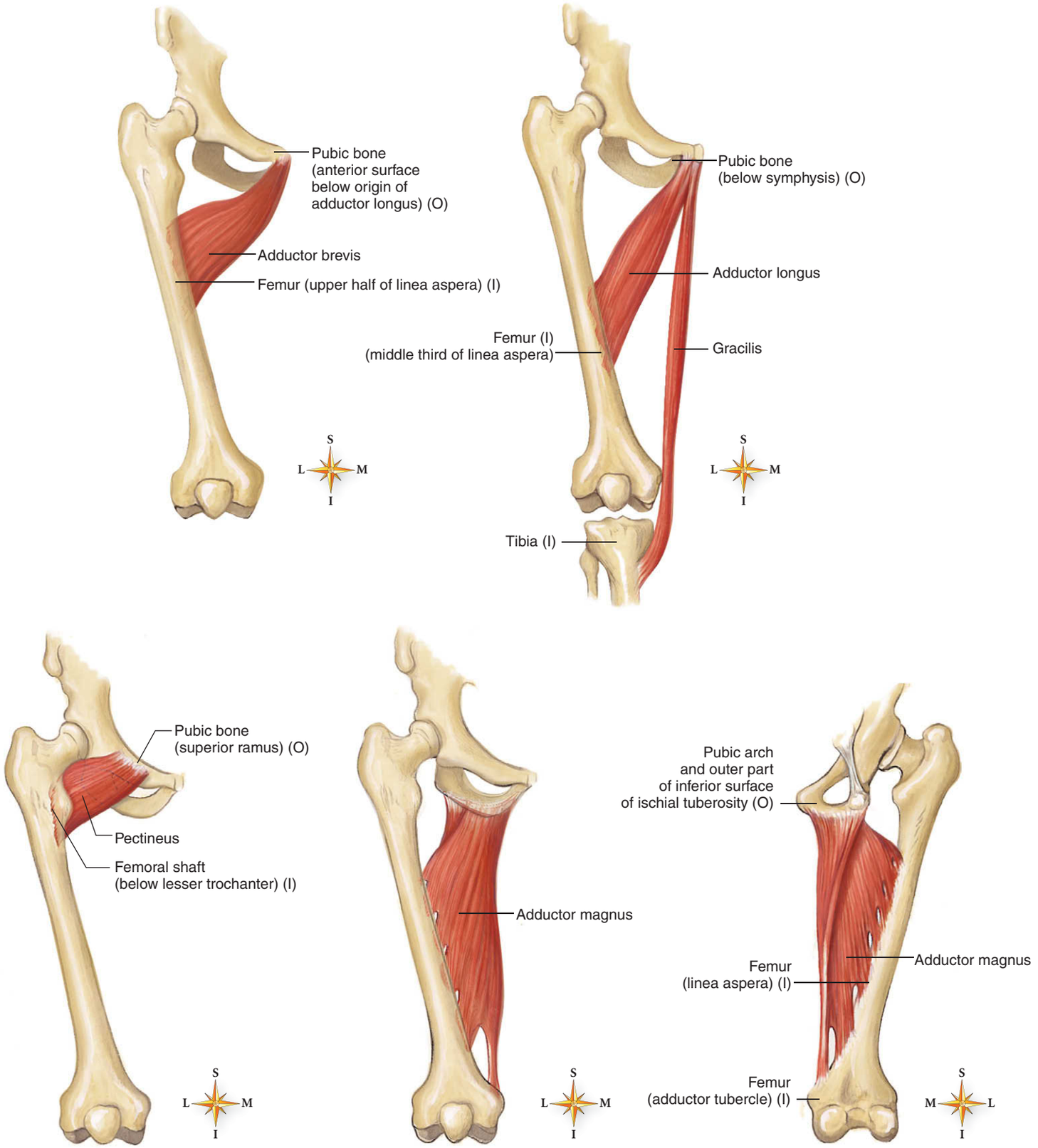


FIGURE 11-28

Muscles that adduct the thigh. *O,* Origin; *I,* insertion.

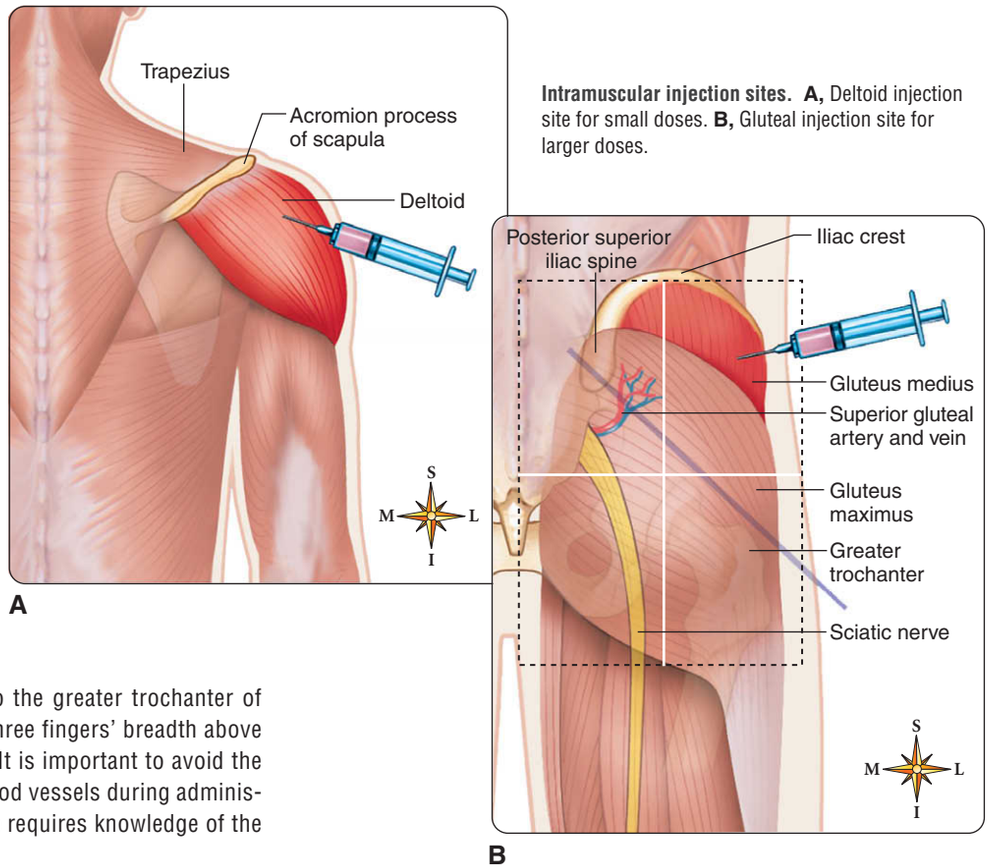
Box 11-4 | HEALTH matters

Intramuscular Injections

Many drugs are administered by **intramuscular injection.** If the amount to be injected is 2 ml or less, the deltoid muscle is often selected as the site of injection. Note that in part *A* of this figure, the needle is inserted into the muscle about two fingers' breadth below the acromion process of the scapula and lateral to the tip of the acromion.

If the amount of medication to be injected is 2 to 3 ml, the gluteal area shown in part *B* of the figure is often used. Injections are made into the gluteus medius muscle near the center of the upper outer quadrant.

Another technique of locating the proper injection site is to draw an imaginary diagonal line from a point of reference on the back of the bony pelvis (posterior superior iliac spine) to the greater trochanter of the femur. The injection is given about three fingers' breadth above and one third of the way down the line. It is important to avoid the sciatic nerve and the superior gluteal blood vessels during administration of the injection. Proper technique requires knowledge of the underlying anatomy.



Intramuscular injection sites. A, Deltoid injection site for small doses. **B,** Gluteal injection site for larger doses.

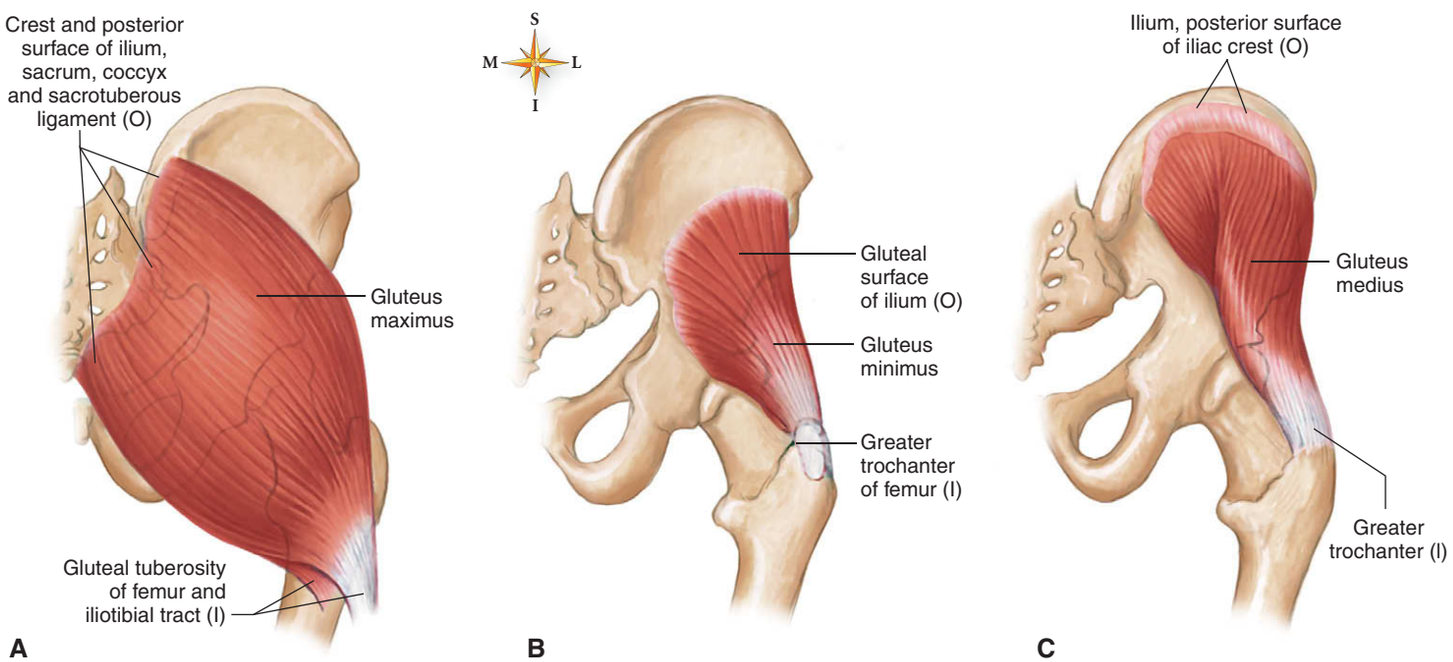


FIGURE 11-29

Gluteal muscles. A, Gluteus maximus. **B,** Gluteus minimus. **C,** Gluteus medius. *O,* Origin; *I,* insertion.

Table 11-18 identifies muscles that move the leg. Note that the quadriceps femoris group is made up of four large muscles that flex the thigh and extend the leg. The hamstring group is made up of three muscles that extend the thigh and flex the leg. Again, see Figure 11-6 and refer to Figures 11-30 and 11-31 as you study the table.

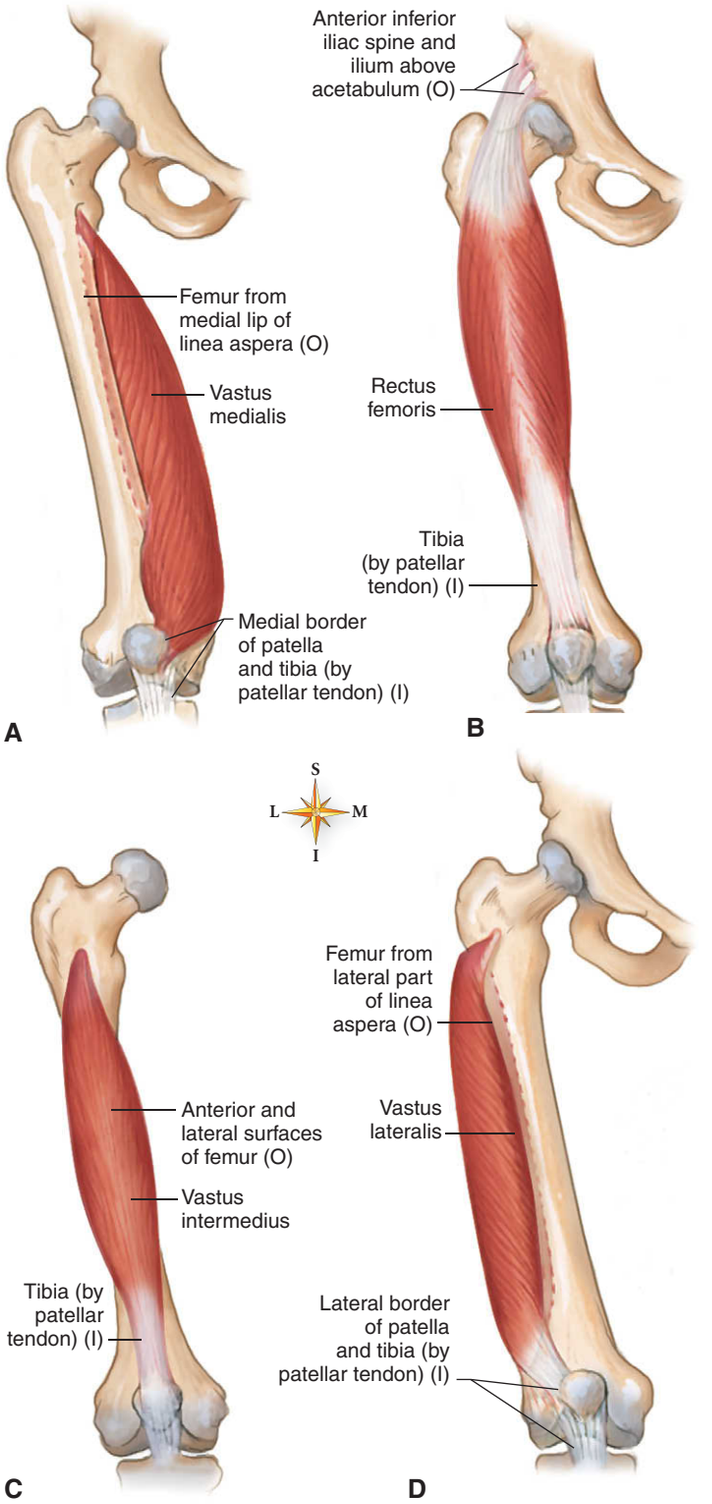


FIGURE 11-30

Quadriceps femoris group of thigh muscles. **A,** Vastus medialis. **B,** Rectus femoris. **C,** Vastus intermedius. **D,** Vastus lateralis. *O,* Origin; *I,* insertion.

TABLE 11-18 Muscles That Move the Lower Leg

MUSCLE	ORIGIN	INSERTION	FUNCTION	NERVE SUPPLY
Quadriceps femoris group				
Rectus femoris	Ilium (anterior inferior spine)	Tibia (by way of patellar tendon) Extends the leg	Flexes the thigh	Femoral nerve
Vastus lateralis	Femur (linea aspera)	Tibia (by way of the patellar tendon)	Extends the leg	Femoral nerve
Vastus medialis	Femur	Tibia (by way of the patellar tendon)	Extends the leg	Femoral nerve
Vastus intermedius	Femur (anterior surface)	Tibia (by way of the patellar tendon)	Extends the leg	Femoral nerve
Sartorius	Coxal (anterior superior iliac spines)	Tibia (medial surface of the upper end of the shaft)	Adducts and flexes the leg Permits crossing of the legs tailor fashion	Femoral nerve
Hamstring group				
Biceps femoris	Ischium (tuberosity)	Fibula (head of)	Extends the thigh; flexes the leg	Hamstring nerve (branch of the sciatic nerve)
	Femur (linea aspera)	Tibia (lateral condyle)	Flexes the leg	Hamstring nerve
Semitendinosus	Ischium (tuberosity)	Tibia (proximal end, medial surface)	Extends the thigh; flexes the leg	Hamstring nerve
Semimembranosus	Ischium (tuberosity)	Tibia (medial condyle)	Extends the thigh; flexes the leg	Hamstring nerve

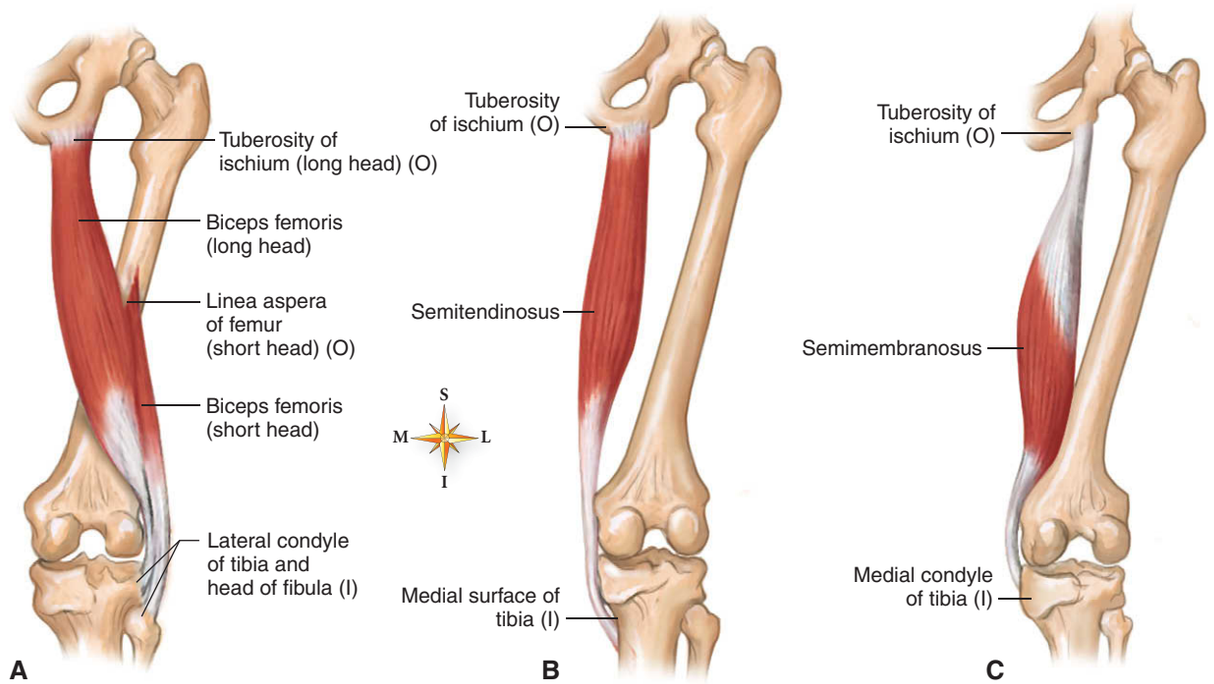


FIGURE 11-31

Hamstring group of thigh muscles. A, Biceps femoris. **B,** Semitendinosus. **C,** Semimembranosus. *O,* Origin; *I,* insertion.

Muscles That Move the Ankle and Foot

The muscles listed in Table 11-19 and shown in Figure 11-32 are responsible for movements of the ankle and foot. These muscles, called **extrinsic foot muscles,** are located in the leg but exert their actions by pulling on tendons that insert on bones in the ankle and foot. Extrinsic foot muscles are responsible for such movements as dorsiflexion, plantar flexion, inversion, and eversion of the foot. Muscles located within the foot itself are called **intrinsic foot muscles** (Figure 11-33). They are responsible for flexion, extension, abduction, and adduction of the toes.

The extrinsic muscles listed in Table 11-19 may be divided into four functional groups: (1) dorsal flexors, (2) plantar flexors, (3) invertors, and (4) evertors of the foot.

The superficial muscles located on the posterior surface of the leg form the bulging "calf." The common tendon of the **gastrocnemius** (GAS-trok-NEE-mee-us) and **soleus** is called the **calcaneal,** or *Achilles,* **tendon.** It inserts into the calcaneus, or heel bone. By acting together, these muscles serve as powerful flexors (plantar flexion) of the foot.

Dorsal flexors of the foot, located on the anterior surface of the leg, include the **tibialis** (tib-ee-AL-is) **anterior, fibularis tertius** (fib-yoo-LAIR-is TER-shee-us), and **extensor digitorum longus.** In addition to functioning as a dorsiflexor of the foot, the extensor digitorum longus also everts the foot and extends the toes. Note in Table 11-19 that the *fibularis* (fib-you-LAIR-is) muscles are also called *peroneus* (per-oh-NEE-us) muscles.

| QUICK CHECK |

22. Name the three gluteal muscles.
23. What is the function of the gastrocnemius muscle?

TABLE 11-19 Muscles That Move the Foot

MUSCLE	ORIGIN	INSERTION	FUNCTION	NERVE SUPPLY
Extrinsic				
Tibialis anterior	Tibia (lateral condyle of the upper body)	Tarsal (first cuneiform) Metatarsal (base of first)	Flexes the foot Inverts the foot	Common and deep peroneal nerves
Gastrocnemius	Femur (condyles)	Tarsal (calcaneus by way of the Achilles tendon)	Extends the foot Flexes leg	Tibial nerve (branch of the sciatic nerve)
Soleus	Tibia (underneath the gastrocnemius) Fibula	Tarsal (calcaneus by way of the Achilles tendon)	Extends the foot (plantar flexion)	Tibial nerve
Fibularis longus (peroneus longus)	Tibia (lateral condyle)	First cuneiform	Extends the foot (plantar flexion)	Common peroneal nerve
	Fibula (head and shaft)	Base of the first metatarsal	Everts the foot	
Fibularis brevis (peroneus brevis)	Fibula (lower two thirds of the lateral surface of the shaft)	Fifth metatarsal (tubercle, dorsal surface)	Everts the foot Flexes the foot	Superficial peroneal nerve
Fibularis tertius (peroneus tertius)	Fibula (distal third)	Fourth and fifth metatarsals (bases of)	Flexes the foot Everts the foot	Deep peroneal nerve
Extensor digitorum longus	Tibia (lateral condyle) Fibula (anterior surface)	Second and third phalanges (four lateral toes)	Dorsiflexion of the foot; extension of the toes	Deep peroneal nerve
Intrinsic				
Lumbricals	Tendons of the flexor digitorum longus	Phalanges (2 to 5)	Flex the proximal phalanges Extend the middle and distal phalanges	Lateral and medial plantar nerve
Flexor digiti minimi brevis	Fifth metatarsal	Proximal phalanx of the fifth toe	Flexes the fifth (small) toe	Lateral plantar nerve
Flexor hallucis brevis	Cuboid Medial and lateral cuneiform	Proximal phalanx of the first (great) toe	Flexes the first (great) toe	Medial and lateral plantar nerve
Flexor digitorum brevis	Calcaneus Plantar fascia	Middle phalanges of the toes (2 to 5)	Flexes toes 2 through 5	Medial plantar nerve
Abductor digiti minimi	Calcaneus	Proximal phalanx of the fifth (small) toe	Abducts the fifth (small) toe Flexes the fifth toe	Lateral plantar nerve
Abductor hallucis	Calcaneus	First (great) toe	Abducts the first (great) toe	Medial plantar nerve

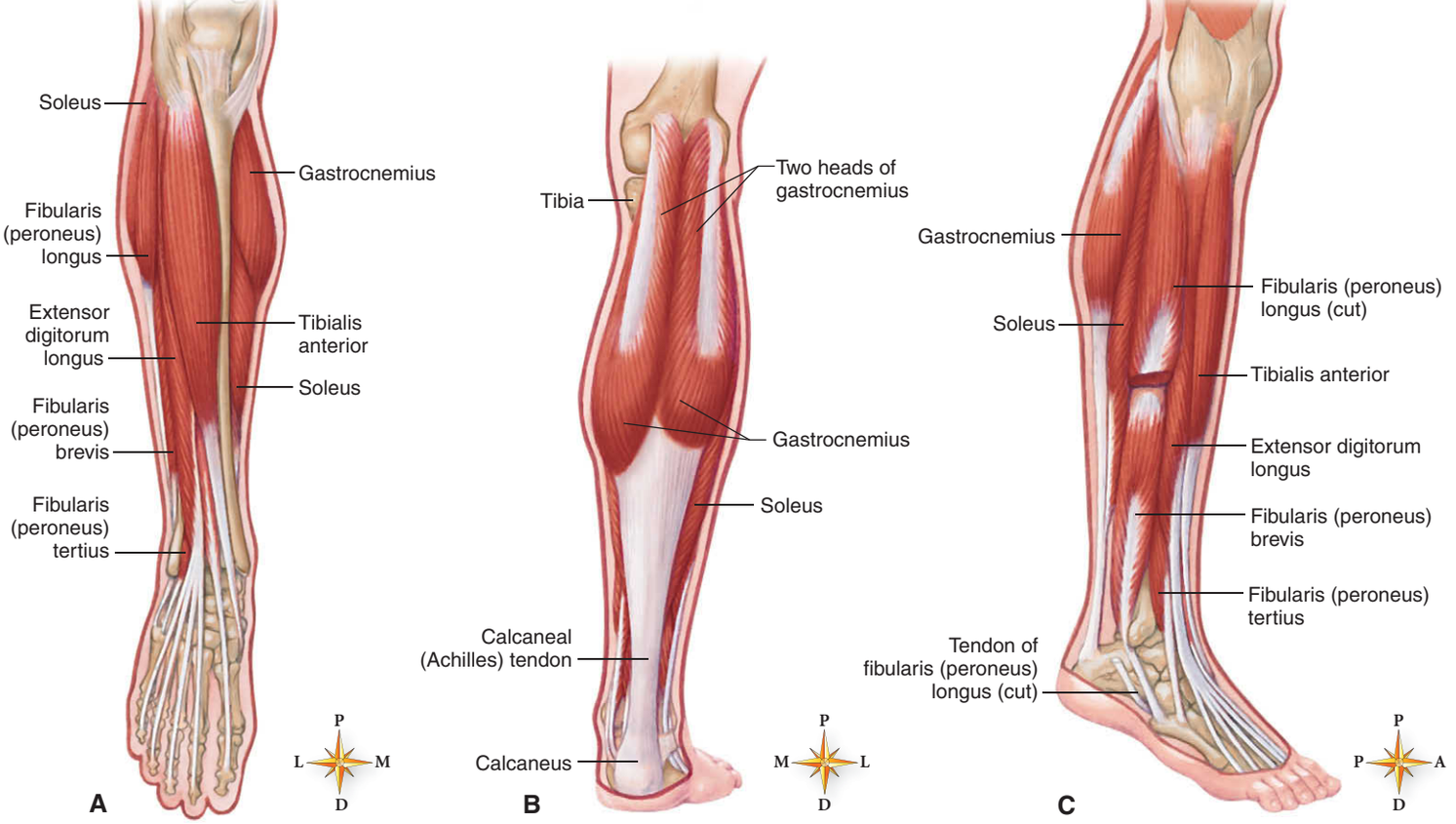


FIGURE 11-32

Superficial muscles of the leg. **A,** Anterior view. **B,** Posterior view. **C,** Lateral view.

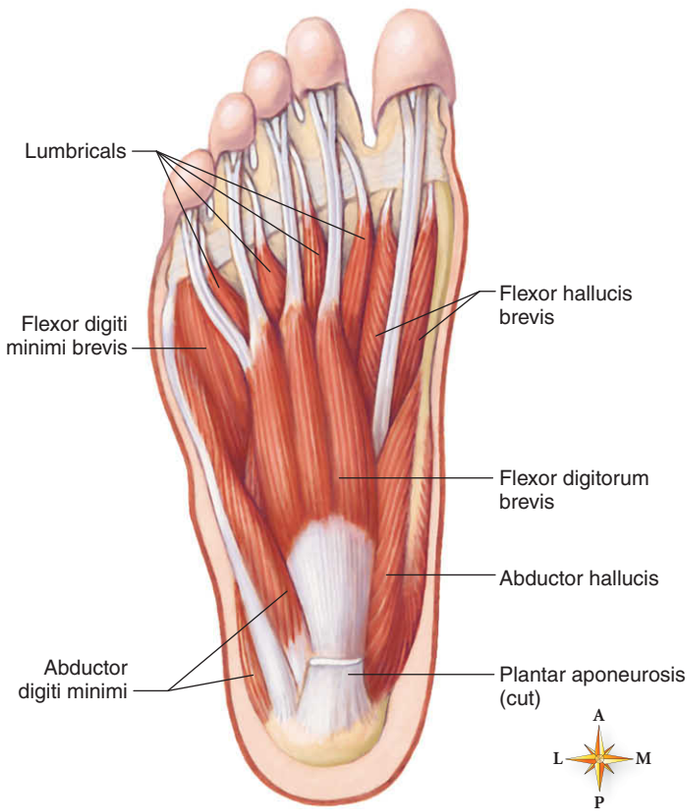


FIGURE 11-33

Intrinsic muscles of the foot. Inferior (plantar) view.

POSTURE

We have already discussed the major role of muscles in movement and heat production. We now turn our attention to a third way in which muscles serve the body as a whole—that of maintaining the posture of the body. Let us consider a few aspects of this important function.

The term **posture** means simply maintaining optimal body position. "Good posture" means many things. It means body alignment that most favors function; it means the position that requires the least muscular work to maintain, specifically, the position that places the least strain on muscles, ligaments, and bones; and often it means keeping the body's center of gravity over its base. Good posture in the standing position, for example, means the head and chest held high; the chin, abdomen, and buttocks pulled in; the knees bent slightly; and the feet placed firmly on the ground about 6 inches (15 cm) apart. Good posture in a sitting position varies with the position that one is trying to maintain. Good posture during exercise, such as riding a horse or dribbling a basketball, means moving or tensing different parts of the body frequently to avoid falling.

How Posture Is Maintained

Gravity pulls on the various parts of the body at all times. Because bones are too irregularly shaped to balance themselves on each other, the only way the body can be held in any particular position is for muscles to exert a continual pull on bones. The muscles must pull in the opposite direction from gravity or other forces that pull on body parts.

When the body is in a standing position, gravity tends to pull the head and trunk forward and downward. Extensor muscles must therefore pull backward and upward on the head and trunk. Likewise, as gravity pulls the lower jaw downward; muscles must pull upward on it—to keep the mouth closed.

Muscles exert their pull against gravity by virtue of a property called **tonicity.** Tonicity, or **muscle tone,** literally means *tension* and refers to the continuous, low level of sustained contraction maintained by all skeletal muscles. Because tonicity is absent during deep sleep, muscle pull does not then counteract the pull of gravity. Hence, we cannot sleep standing up. Interestingly, astronauts in the low-gravity conditions of space station missions *can* sleep in a standing position, as long as they are secured inside special sleeping bags on the wall of the space station.

Many structures other than muscles and bones play a part in the maintenance of posture. The nervous system triggers skeletal muscle contractions and is thus responsible for the existence of muscle tone. The nervous system regulates and coordinates the amount of pull exerted by the individual muscles. Breathing in the respiratory system, abdominal activity by the digestive system, and other systemic activities all can affect posture. This is one of many examples of the important principle that body functions are interdependent.

The importance of posture can perhaps be best evaluated by considering some of the effects of poor posture. Poor posture throws more work on muscles to counteract the pull of gravity and therefore leads to fatigue more quickly than does good posture. Poor posture puts more strain on ligaments. It puts abnormal strain on bones and may eventually produce deformities. It also interferes with various functions such as respiration, heart action, and digestion.

| A&P CONNECT |

As we discussed earlier in this chapter, it is important to remember that muscles, tendons, and fascia work in teams to maintain posture and produce movement. Explore one of the ways that they work together in ***Whole-Body Muscle Mechanics*** online at ***A&P Connect.***

evolve

Cycle of LIFE

Muscular System

Acting together, the muscular, skeletal, and nervous systems make it possible for us to move in a coordinated and controlled way. However, it is the contraction, or shortening, of muscles that ultimately provides the actual movement necessary for physical activity. Dramatic changes occur in the muscular system throughout the cycle of life. Muscle cells may increase or decrease in size and in their ability to shorten most effectively at different periods in life. In addition to age-related changes, many pathological conditions occurring at different ages may also affect the muscular system.

Because of the functional interdependence of the musculoskeletal and nervous systems, life cycle changes affecting the muscles are often manifested in other components of the functional unit. During infancy and childhood, the ability to coordinate and control the strength of muscle contraction permits a sequential series of developmental steps to occur. A developing youngster learns to hold the head up, roll over, sit up, stand alone, and then walk and run as developmental changes permit better control and coordination of muscular contraction.

Degenerative changes associated with advancing age often result in replacement of muscle cell volume with nonfunctional connective tissue. As a result, the strength of muscular contraction diminishes. Recent findings show that much, if not all, of this age-related decrease in muscle strength actually results from disuse atrophy (see Box 12-6 in Chapter 12) and may thus be avoidable. Pathological conditions associated with specific age ranges can also affect one or more components of the functional unit that permits us to move smoothly and effortlessly.

the BIG picture

Skeletal Muscles and the Whole Body

As you read through this chapter, what struck you most was probably the large number of individual muscles and their many actions. Although learning the names, locations, origins, insertions, and other details of the major muscles is a worthwhile endeavor, such an activity can cause you to lose sight of the "big picture." Step back from the details a moment to appreciate that the muscles work as coordinated teams of biological engines that move the various components of the flexible skeleton.

As a matter of fact, in this chapter you learned that the fibrous wrappings of each muscle are continuous with its tendons, which in turn are continuous with the fibrous structure of the bone to which they are attached. Thus we can see that the muscular and skeletal systems are in essence a single structure. This fact is very important in seeing a "big picture" comprising many individual muscles and bones. The entire skeletomuscular system, as it is often called, is actually a single, continuous structure that provides a coordinated, dynamic framework for the body.

Taking another step back, an even bigger picture comes into focus. Other systems of the body must play a role in the actions of the skeletomuscular system. For example, the nervous system senses changes in body position and degrees of movement—thereby permitting integration of feedback loops that ultimately regulate the muscular contractions that maintain posture and produce movements. The cardiovascular system maintains blood flow in the muscles, and the urinary and respiratory systems rid the body of wastes produced in the muscles. The respiratory and digestive systems bring in the oxygen and nutrients necessary for muscle function.

The picture is still not complete, however. We will see even more when Chapter 12 continues the story of muscle function by delving into the details of how each muscle works as an engine to drive the movement of the body.

LANGUAGE OF SCIENCE *(continued from p. 301)*

deltoid
(DEL-toyd)
[*delta-* **triangle**, *-oid* **like**]

diaphragm
(DYE-ah-fram)
[*dia-* **across**, *-phrag-* **enclose**]

endomysium
(en-doh-MEE-see-um)
[*endo-* **within**, *-mysium* **muscle**]

epimysium
(ep-i-MIS-ee-um)
[*epi-* **upon**, *-mysium* **muscle**]

erector spinae muscle
(eh-REK-tor SPINE-ee)
[*erector* **that which makes rigid or upright**, *spinae* **of the spine**, *mus-* **mouse**, *-cle* **little**]

extensor digitorum longus muscle
(ek-STEN-ser dij-i-TOH-rum LONG-gus)
[*extensor* **that which stretches**, *digit* **of the finger or toe**, *longus* **long**, *mus-* **mouse**, *-cle* **little**]

external anal sphincter muscle
(eks-TER-nal AY-nal SFINGK-ter)
[*extern-* **outside**, *-al* **relating to**, *an-* **ring** (**anus**), *-al* **relating to**, *sphinc-* **bind tight**, *-er* **agent**, *mus-* **mouse**, *-cle* **little**]

external intercostal muscle
(eks-TER-nal in-ter-KOS-tal)
[*extern-* **outside**, *-al* **relating to**, *inter-* **between**, *-costa-* **rib**, *-al* **relating to**, *mus-* **mouse**, *-cle* **little**]

external oblique muscle
(eks-TER-nal oh-BLEEK)
[*extern-* **outside**, *-al* **relating to**, *obliq-* **slanted**, *mus-* **mouse**, *-cle* **little**]

extrinsic foot muscle
(eks-TRIN-sik)
[*extrins-* **outside**, *-ic* **relating to**, *mus-* **mouse**, *-cle* **little**]

extrinsic muscle
(eks-TRIN-sik)
[*extrins-* **outside**, *-ic* **relating to**, *mus-* **mouse**, *-cle* **little**]

fascia
(FASH-ee-ah)
[*fascia* **band or bundle**]

fibularis tertius muscle
(per-oh-NEE-us TER-shee-us)
[*fibularis* **relating to a clasp** (**fibula**), *tertius* **third**, *mus-* **mouse**, *-cle* **little**]

fixator muscle
(fik-SAY-tor)
[*fixator* **fastener**, *mus-* **mouse**, *-cle* **little**]

fusiform muscle
(FYOO-si-form)
[*fusi-* **spindle**, *-form* **shape**, *mus-* **mouse**, *-cle* **little**]

gastrocnemius muscle
(GAS-trok-NEE-mee-us)
[*gastro-* **belly**, *-cnemius* **leg**, *mus-* **mouse**, *-cle* **little**]

gluteal muscle
(GLOO-tee-al)
[*glut-* **buttocks**, *-al* **relating to**, *mus-* **mouse**, *-cle* **little**]

infraspinatus muscle
(IN-frah-spy-nah-tus)
[*infra-* **below**, *-spina-* **spine**, *mus-* **mouse**, *-cle* **little**]

insertion
[*in-* **in**, *-ser-* **join**, *-tion* **process**]

internal intercostal muscle
(in-TER-nal in-ter-KOS-tal)
[*intern-* **inside**, *-al* **relating to**, *inter-* **between**, *-costal-* **rib**, *-al* **relating to**, *mus-* **mouse**, *-cle* **little**]

internal oblique muscle
(in-TER-nal oh-BLEEK)
[*intern-* **inside**, *-al* **relating to**, *obliq-* **slanted**, *mus-* **mouse**, *-cle* **little**]

interosseous muscle
(in-ter-OSS-ee-us)
[*inter-* **between**, *-os-* **bone**, *-ous* **relating to**, *mus-* **mouse**, *-cle* **little**]

interspinales group
(in-ter-spy-NAH-leez)
[*inter-* **between**, *-spina-* **spine**, *-al* **relating to**]

intrinsic foot muscle
(in-TRIN-sik)
[*intrins-* **inward**, *-ic* **relating to**, *mus-* **mouse**, *-cle* **little**]

intrinsic muscle
(in-TRIN-sik)
[*intrins-* **inward**, *-ic* **relating to**, *mus-* **mouse**, *-cle* **little**]

ischiocavernosus muscle
(iss-kee-oh-KAV-erno-sus)
[*ischio-* *hip joint*, *-cavern-* **hollow space**, *-osus* **relating to**, *mus-* **mouse**, *-cle* **little**]

levator ani muscle
(leh-VAY-tor)
[*levator* **lifter**, *ani* **of the anus**, *mus-* **mouse**, *-cle* **little**]

levator scapulae
(leh-VAY-tor SCAP-yoo-lee)
[*levator* **lifter**, *scapulae* **of the shoulder blade**]

lever
[*lev-* **lift**, *-er* **agent**]

lever system
[*lev-* **lift**, *-er* **agent**]

linea alba
(LIN-ee-ah AL-bah)
[*linea* **line**, *alba* **white**]

longissimus capitis muscle
(lon-JIS-i-mus KAP-i-tis)
[*longissimus* **longest or very long**, *capit-* **head**, *mus-* **mouse**, *-cle* **little**]

lumbrical muscle
(LUM-bri-kal)
[*lumbrical* **like a worm**, *mus-* **mouse**, *-cle* **little**]

masseter
(mah-SEE-ter)
[*masseter* **chewer**]

mastication
(mass-ti-KAY-shun)
[*mastica-* **chew**, *-ation* **process**]

multifidus muscle group
(mul-TIF-i-dus)
[*multi-* **many**, *-fidus* **split** (**into pieces**)]

muscle tone
[*mus-* **mouse**, *-cle* **little**, *ton-* **tension**]

muscular system
[*mus-* **mouse**, *-cul-* **little**, *-ar* **relating to**]

occipitofrontalis
(ok-sip-i-toh-fron-TAL-is)
[*occipit-* **back of head**, *front-* **forehead**, *-al* **relating to**]

opponens pollicis muscle
(oh-POH-nenz POL-i-cis)
[*oppenens* **opposing**, *pollicis* **pole**, *mus-* **mouse**, *-cle* **little**]

orbicularis oculi muscle
(or-bik-yoo-LAIR-is OK-yoo-lye)
[*orbi-* **circle**, *-cul-* **little**, *-ar* **relating to**, *ocul-* **eye**, *mus-* **mouse**, *-cle* **little**]

orbicularis oris muscle
(or-bik-yoo-LAR-is OR-iss)
[*orbi-* **circle**, *-cul-* **little**, *-ar* **relating to**, *oris* **mouth**, *mus-* **mouse**, *-cle* **little**]

origin
(OR-i-jin)

parallel muscle
[*para-* **beside**, *-llel* **one another**, *mus-* **mouse**, *-cle* **little**]

pectoralis minor
(pek-toh-RAL-is)
[*pector-* **breast**, *-al* **relating to**, *minor* **lesser**]

pennate muscle
(PEN-ayt)
[*penn-* **feather**, *-ate* **of or like**, *mus-* **mouse**, *-cle* **little**]

perimysium
(pair-i-MEE-see-um)
[*peri-* **around**, *-mysium* **muscle**]

perineum
(pair-i-NEE-um)
[*peri-* **around**, *-ine-* **excrete**, *-um* **thing**] *pl.,* perinea

posture
(POS-chur)
[*postur-* **position**]

prime mover
[*prime* **first order**]

pterygoid muscle
(TER-i-goid)
[*ptery-* **wing**, *-oid* **like**, *mus-* **mouse**, *-cle* **little**]

rectus abdominis muscle
(REK-tus ab-DOM-i-nus)
[*rectus* **straight**, *abdominis* **abdomen**, *mus-* **mouse**, *-cle* **little**]

rectus sheath
(REK-tus sheeth)
[*rectus* **straight**]

rhomboid major/minor muscles
(ROM-boyd)
[*rhombo-* **flatfish or equilateral parallelogram** (**rhombus**), *-oid* **like**, *major* **greater**, *minor* **lesser**, *-oid* **like**, *mus-* **mouse**, *-cle* **little**]

LANGUAGE OF SCIENCE *(continued from p. 343)*

rotator cuff muscle
(roh-TAY-tor)
[*rot-* **turn**, *-ator* **agent**, *mus-* **mouse**, *-cle* **little**]

serratus anterior muscle
(ser-RAY-tus)
[*serra-* **saw teeth**, *ante-* **front**, *-er-* **more**, *-or* **quality**, *mus-* **mouse**, *-cle* **little**]

soleus muscle
(SOH-lee-us)
[*soleus* **sole of foot**, *mus-* **mouse**, *-cle* **little**]

spiral muscle
[*mus-* **mouse**, *-cle* **little**]

splenius capitis
(SPLEH-nee-us KAP-i-tis)
[*splen-* **patch**, *capitis* **head**]

sternocleidomastoid muscle
(STERN-oh- KLYE-doh-MAS-toyd)
[*sterno-* **breastbone** (**sternum**), *-cleid-* **key** (**clavicle**), *-masto-* **breast** (**mastoid process**), *-oid* **like**, *mus-* **mouse**, *-cle* **little**]

subscapularis muscle
(sub-SKAP-yoo-lar-is)
[*sub-* **beneath**, *-scapula-* **shoulder blades**, *-ar* **relating to**, *mus-* **mouse**, *-cle* **little**]

supraspinatus muscle
(SOO-prah-spy-nah-tus)
[*supra-* **above**, *-spina-* **spine**, *mus-* **mouse**, *-cle* **little**]

synergist
(SIN-er-jist)
[*syn-* **together**, *-erg-* **to work**, *-ist* **agent**]

temporalis muscle
(tem-poh-RAL-is)
[*tempo-* **temple of head**, *-al* **relating to**, *mus-* **mouse**, *-cle* **little**]

tendon
[*tend-* **pulled tight**, *-on* **unit**]

tendon sheath
(sheeth)
[*tend-* **pulled tight**, *-on* **unit**]

tensor fasciae latae muscle
(TEN-sor FASH-ee LAT-tee)
[*tensor* **stretcher**, *fascia* **band or bundle**, *lat-* **side**, *mus-* **mouse**, *-cle* **little**]

teres minor
(TER-eez)
[*teres* **rounded**, *minor* **lesser**]

tibialis anterior muscle
(tib-ee-AL-is)
[*tibia* **shinbone**, *-al* **relating to**, *ante-* **front**, *-er-* **more**, *-or* **quality**, *mus-* **mouse**, *-cle* **little**]

tonicity
(toh-NIS-i-tee)
[*ton-* **stretch or tension**, *-ic* **relating to**, *-ty* **state**]

transversus abdominis muscle
(tranz-VERS-us ab-DAH-min-us)
[*trans-* **across**, *-vers-* **turn**, *abdo-min-* **belly**]

trapezius muscle
(trah-PEE-zee-us)
[*trapezion* **small table**, *mus-* **mouse**, *-cle* **little**]

urethral sphincter
(yoo-REE-thral SFINGK-ter)
[*ure-* **urine**, *-thr-* **agent or channel** (**urethra**), *-al* **relating to**, *mus-* **mouse**, *-cle* **little**, *sphinc-* **bind tight**, *-er* **agent**]

urogenital triangle
(YOO-roh-JEN-ih-tal)
[*uro-* **urine**, *-genit-* **reproduction**, *-al* **relating to**, *tri-* **three**, *-angle* **corner**]

zygomaticus major muscle
(zye-goh-MAT-ik-us)
[*-zygo-* **union or yoke**, *-ic* **relating to**, *major* **greater**, *mus-* **mouse**, *-cle* **little**]

LANGUAGE OF MEDICINE

carpal tunnel syndrome
(KAR-pul TUN-el SIN-drohm)
[*carp-* **wrist**, *-al* **relating to**, *syn-* **together**, *-drome* **running or** (**race**)**course**]

intramuscular injection
(in-trah-MUSS-kyoo-lar in-JEK-shun)
[*intra-* **within**, *mus-* **mouse**, *-cle* **little**, *-ar* **relating to**]

tenosynovitis
(ten-oh-sin-oh-VYE-tis)
[*teno-* **pulled tight** (**tendon**), *-syn-* **together**, *-ovi-***egg white** (**joint fluid**), *-itis* **inflammation**]

CASE study

At the sound of the starting pistol, Jeremy burst forward out of the blocks, sprinting down the track. About 20 meters into the race, he suddenly felt a sharp pain along the backside of his right thigh. Wincing, he slowed down and hobbled to a stop.



1. What muscle or muscle group has Jeremy likely injured?
   a. Quadriceps femoris group
   b. Hamstring group
   c. Gastrocnemius
   d. Triceps brachii
2. What muscle did Jeremy use when he closed his eyes in pain?
   a. Orbicularis oris
   b. Masseter
   c. Buccinator
   d. Orbicularis oculi

Jeremy made his way over to the grassy area beside the track and collapsed onto his side. In an effort to control the pain, he concentrated on taking deep, slow breaths in and out.

3. Which of the following muscles did Jeremy NOT use in breathing?
   a. Diaphragm
   b. External intercostals
   c. Latissimus dorsi
   d. Internal intercostals

After several minutes, Jeremy rolled onto his back and tried to sit up.

4. Which of the following muscles would contract to pull him to a sitting position?
   a. Rectus abdominis
   b. Pectoralis major
   c. Trapezius
   d. Pronator teres

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

INTRODUCTION (FIGURES 11-5 AND 11-6)

A. There are more than 600 skeletal muscles in the body
B. From 40% to 50% of our body weight is skeletal muscle
C. Muscles fill in the form and contour of the body

SKELETAL MUSCLE STRUCTURE (FIGURE 11-1)

A. Connective tissue components (Table 11-1)
   1. Endomysium—delicate connective tissue membrane that covers skeletal muscle fibers
   2. Perimysium—tough connective tissue binding together fascicles
   3. Epimysium—coarse sheath covering the muscle as a whole
   4. These three fibrous components continue and fuse to become a tendon or aponeurosis; a tendon sheath (lined with synovial membrane) covers some longer tendons
B. Size, shape, and fiber arrangement (Figure 11-2)
   1. Vary considerably in size, shape, and fiber arrangement
   2. Size—range from extremely small to large masses
   3. Shape—variety of shapes, such as broad, narrow, long, tapering, short, blunt, triangular, quadrilateral, irregular, flat sheets, or bulky masses
   4. Arrangement—variety of arrangements, such as parallel to a long axis, converging to a narrow attachment, oblique, pennate, bipennate, or curved; the direction of fibers is significant because of its relationship to function
C. Attachment of muscles (Figure 11-3)
   1. Origin—point of attachment that does not move when the muscle contracts
   2. Insertion—point of attachment that moves when the muscle contracts
D. Muscle actions (Figure 11-4)
   1. Most movements are produced by the coordinated action of several muscles; some muscles in the group contract while others relax
      a. Prime mover—a muscle that directly performs a specific movement
      b. Agonists—any "mover" muscle that directly performs a movement, including the prime mover
      c. Antagonist—muscles that when contracting, directly oppose prime movers; relax while the prime mover (agonist) is contracting to produce movement; provide precision and control during contraction of prime movers
      d. Synergists—muscles that contract at the same time as the prime movers; they facilitate prime mover actions to produce a more efficient movement
      e. Fixator muscles—joint stabilizers (type of synergist)
E. Lever systems
   1. In the human body, bones serve as levers and joints serve as fulcrums; contracting muscle applies a pulling force on a bone lever at the point of the muscle's attachment to the bone, which causes the insertion bone to move about its joint fulcrum
   2. Lever system—composed of four component parts (Figure 11-5)
      a. Rigid bar (bone)
      b. Fulcrum (F) around which the rod moves (joint)
      c. Load (L) that is moved
      d. Pull (P) that produces movement (muscle contraction)
   3. First-class levers
      a. Fulcrum lies between the pull and the load
      b. Not abundant in the human body; serve as levers of stability
   4. Second-class levers
      a. Load lies between the fulcrum and the joint at which the pull is exerted
      b. Presence of these levers in the human body is a controversial issue
   5. Third-class levers
      a. Pull is exerted between the fulcrum and load
      b. Permit rapid and extensive movement
      c. Most common type of lever found in the body

HOW MUSCLES ARE NAMED

A. Muscle names can be in Latin or English (this book uses English)
B. Muscles are named according to one or more of the following features:
   1. Location, function, shape (Tables 11-2; 11-3; 11-4)
   2. Direction of fibers—named according to fiber orientation (Table 11-5)
   3. Number of heads or divisions (Table 11-5)
   4. Points of attachment—origin and insertion points
   5. Relative size—small, medium, or large (Table 11-6)

IMPORTANT SKELETAL MUSCLES (FIGURE 11-6)

A. Muscles of facial expression—unique in that at least one point of attachment is to the deep layers of the skin over the face or neck (Figures 11-7 and 11-8; Table 11-7)
B. Muscles of mastication—responsible for chewing movements (Figure 11-9)
C. Muscles that move the head—paired muscles on either side of the neck are responsible for head movements (Figure 11-10; Table 11-8)

TRUNK MUSCLES

A. Muscles of the thorax—of critical importance in respiration (Figure 11-11; Table 11-9)
B. Muscles of the abdominal wall—arranged in three layers, with fibers in each layer running in different directions to increase strength (Figure 11-12; Table 11-10)
C. Muscles of the back—bend or stabilize the back (Figure 11-14; Table 11-11)

D. Muscles of the pelvic floor—support the structures in the pelvic cavity (Figure 11-15; Table 11-12)

UPPER LIMB MUSCLES

A. Muscles acting on the shoulder girdle—muscles that attach the upper extremity to the torso are located anteriorly (chest) or posteriorly (back and neck); these muscles also allow extensive movement (Figure 11-16; Table 11-13)
B. Muscles that move the arm—the shoulder is a synovial joint allowing extensive movement in every plane of motion (Figure 11-17; Table 11-14)
C. Muscles that move the forearm—found proximal to the elbow and attach to the ulna and radius (Figures 11-19, 11-20, and 11-21; Table 11-15)
D. Muscles that move the wrist, hand, and fingers—these muscles are located on the anterior or posterior surfaces of the forearm (Figures 11-22 through 11-24; Table 11-16)

LOWER LIMB MUSCLES

A. The pelvic girdle and lower extremity function in locomotion and maintenance of stability
B. Muscles that move the thigh and leg (Figures 11-6 and 11-25 through 11-29; Tables 11-17 and 11-18)
C. Muscles that move the ankle and foot (Figures 11-32 and 11-33; Table 11-19)
    1. Extrinsic foot muscles in the leg pull on tendons that insert on bones in the ankle and foot; responsible for dorsiflexion, plantar flexion, inversion, and eversion
    2. Intrinsic foot muscles are located within the foot; responsible for flexion, extension, abduction, and adduction of the toes

POSTURE

A. Maintaining body posture is a major role of muscles
B. "Good posture"—body alignment that most favors function; achieved by keeping the body's center of gravity over its base and requires the least muscular work to maintain
C. How posture is maintained
    1. Muscles exert a continual pull on bones in the opposite direction from gravity
    2. Structures other than muscle and bones have a role in maintaining posture
        a. Nervous system—responsible for the existence of muscle tone and also for regulation and coordination of the amount of pull exerted by individual muscles
        b. Respiratory, digestive, excretory, and endocrine systems all contribute to maintain posture

CYCLE OF LIFE: MUSCULAR SYSTEM

A. Muscle cells—increase or decrease in number, size, and ability to shorten at different periods
B. Pathological conditions at different periods of the life cycle may affect the muscular system
C. Life cycle changes—manifested in other components of functional unit:
    1. Infancy and childhood—coordination and control of muscle contraction permit sequential development steps
    D. Degenerative changes of advancing age result in replacement of muscle cells with nonfunctional connective tissue

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Define the terms *endomysium*, *perimysium*, and *epimysium*.
2. Identify/describe the most common type of lever in the body.
3. Give an example of a muscle named by location, function, shape, fiber direction, number of heads, and points of attachment.
4. Name the main muscles of the back, chest, abdomen, neck, shoulder, upper part of the arm, forearm, thigh, buttocks, leg, and pelvic floor.
5. Name the main muscles that flex, extend, abduct, and adduct the arm; that raise and lower the shoulder.
6. Name the main muscles that flex and extend the forearm; that flex and extend the wrist and hand.
7. Name the main muscles that flex, extend, abduct, and adduct the thigh; that flex and extend the leg and thigh; that flex and extend the foot.
8. Name the main muscles that flex, extend, abduct, and adduct the head.
9. Name the main muscles that move the abdominal wall; that move the chest wall.

CRITICAL THINKING QUESTIONS

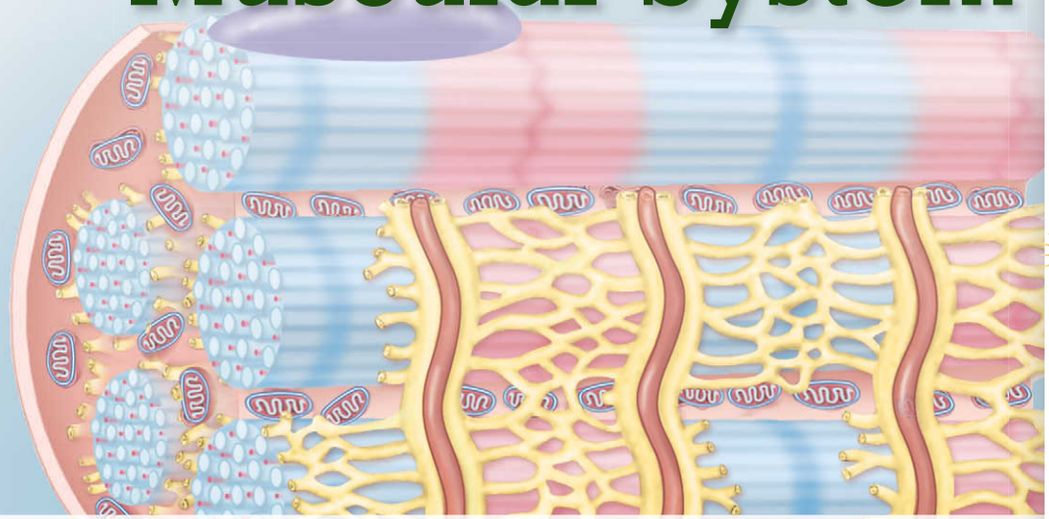


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Identify the muscles of facial expression. What muscles facilitate smiling and frowning?
2. How do the origin and insertion of a muscle relate to each other in regard to actual movement?
3. When the biceps brachii contracts, the elbow flexes. When the triceps brachii contracts, the elbow extends. Explain the role of both muscles in terms of agonist and antagonist in both of these movements.
4. Describe how the body maintains posture.
5. Describe the clinical significance regarding the difference in size between the large head of the humerus and the small and shallow glenoid cavity of the scapula.
6. If a person working as a word processor complained of weakness, pain, and tingling in the palm and thumb side of the hand, what type of problem might that person be experiencing? Explain specifically what would be happening to cause this discomfort.
7. Baseball players, particularly pitchers, often incur rotator cuff injuries. List the muscles that make up the rotator cuff and explain the importance of these muscles and their role in joint stability.

Physiology of the Muscular System

12



UNIT 2

CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

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Function of Skeletal Muscle Tissue, 348
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Function of Skeletal Muscle Organs, 360
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Graded Strength Principle, 364
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Function of Cardiac and Smooth Muscle Tissue, 368
- Cardiac Muscle, 368
- Smooth Muscle, 369

The Big Picture: Muscle Tissue and the Whole Body, 371

Mechanisms of Disease, 372

Case Study, 374

LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

A band

acetylcholine (ACh)
(ass-ee-til-KOH-leen)
[*acetyl-* **vinegar,** *-chol-* **bile,** *-ine* **made of**]

actin (AK-tin)
[*act-* **act or do,** *-in* **substance**]

concentric contraction
(kon-SEN-trik)
[*con-* **together,** *-centr-* **center,** *-ic* **relating to,** *con-* **together,** *-tract-* **drag or draw,** *-tion* **process**]

contractility
(kon-trak-TIL-i-tee)
[*con-* **together,** *-tract-* **drag or draw,** *-il-* **of or like,** *-ity* **quality of**]

creatine phosphate (CP)
(KREE-ah-tin FOS-fayt)
[*creat-* **flesh,** *-ine* **relating to,** *phosph-* **phosphorus,** *-ate* **oxygen**]

cross bridge

eccentric contraction
(ek-SENT-rik)
[*ec-* **out of,** *-centr-* **center,** *-ic* **relating to,** *con-* **together,** *-tract-* **drag or draw,** *-tion* **process**]

elastic filament
(eh-LAS-tik FIL-ah-ment)
[*elas-* **drive or beat out,** *-ic* **relating to,** *fila-* **thread,** *-ment* **thing**]

excitability
(ek-syte-eh-BIL-i-tee)
[*excit-* **arouse,** *-abil-* **capable,** *-ity* **state**]

extensibility
(ek-STEN-si-BIL-i-tee)
[*ex-* **outward,** *-tens-* **stretch,** *-abil-* **capable,** *-ity* **state**]

fast fiber

graded strength principle

continued on p. 373

In Chapter 11, we explored the anatomy of skeletal muscle organs and how they work together to accomplish specific body movements. In this chapter, we continue our study of the muscular system by examining the basic characteristics of skeletal muscle tissue. We uncover the mechanisms that permit skeletal muscle tissue to move the body's framework, as well as perform other functions vital to maintaining a constant internal environment. We also briefly examine smooth and cardiac muscle tissues and contrast them with skeletal muscle tissue.

GENERAL FUNCTIONS

If you have any doubts about the importance of muscle function to normal life, think about what it would be like without it. It is hard to imagine what life would be like if this matchless power were lost. However, as cardinal as it is, movement is not the only contribution muscles make to healthy survival. They also perform two other essential functions: production of a large proportion of body heat and maintenance of posture.

1. **Movement.** Skeletal muscle contractions produce movement of the body as a whole (locomotion) or movement of its parts.
2. **Heat production.** Muscle cells, like all cells, produce heat by the process known as catabolism (discussed in Chapters 4 and 30). The heat produced by just one cell is inconsequential, but because skeletal muscle cells are both highly active and numerous, together they produce a major share of total body heat. Skeletal muscle contractions therefore constitute one of the most important parts of the mechanism for maintaining homeostasis of temperature.
3. **Posture.** The continued partial contraction of many skeletal muscles makes possible standing, sitting, and maintaining a relatively stable position of the body while walking, running, or performing other movements.

FUNCTION OF SKELETAL MUSCLE TISSUE

Skeletal muscle cells have several characteristics that permit them to function as they do. One such characteristic is the ability to be stimulated, often called **excitability** or *irritability*. Because skeletal muscle cells are excitable, they can respond to regulatory mechanisms such as nerve signals.

Contractility of muscle cells, the ability to contract or shorten, allows muscle tissue to pull on bones and thus produce body movement. Sometimes muscle fibers do work by steadily resisting a load without actually becoming shorter. In such a case, the muscle cell is still said to be contracting. The term *contraction*, when applied to muscles, is meant in a broad sense of pulling the ends together—regardless of whether the cell actually gets shorter.

Extensibility, the ability to extend or stretch, allows muscles to return to their resting length after having contracted. Muscles may also extend while still exerting force, as when lowering a heavy object in your hand.

All of these characteristics of muscle cells are related to the microscopic structure of skeletal muscle cells. In the following passages, we first discuss the basic structure of a muscle cell. We then explain how a muscle cell's structural components allow it to perform its unique functions.

Overview of the Muscle Cell

Look at Figure 12-1. As you can see, a skeletal muscle is composed of bundles of skeletal muscle fibers that generally extend the entire length of the muscle. Muscle cells or *myocytes* are most frequently called "muscle fibers." One reason they are often called *fibers* instead of *cells* is their long, thin, threadlike shape. They are 1 to 40 mm long but have a diameter of only 10 to 100 μm. The gastrocnemius muscle of the calf, for example, has approximately a million threadlike muscle fibers.

During muscle tissue development, individual precursor cells fuse together to form a new, combined structure with many nuclei—the mature muscle fiber. That is why muscle fibers don't follow the general rule of one nucleus per cell: each fiber is made up of several cells that are combined into one. Some adult muscle fibers have one of these tiny precursor cells hugging their outer boundary. These *satellite cells* are stem cells that fuse with myocytes during strength training to make bigger muscle fibers. The satellite cells can also become active after a muscle injury to produce more muscle fibers. Scientists are now trying to understand this mechanism better in the hope of developing new therapies for replacing lost muscle tissues.

Skeletal muscle fibers have many of the same structural parts as other cells. Several of these parts, however, are referred to by different names in regard to muscle fibers. For example, **sarcolemma** is a name often used for the plasma membrane of a muscle fiber. **Sarcoplasm** is its cytoplasm.

Muscle fibers contain many more mitochondria than usually found in other types of cells (Figure 12-2), and as we have already learned, each fiber has several nuclei. Muscle cells contain networks of tubules and sacs known as the **sarcoplasmic reticulum (SR)**—the muscle fiber's version of smooth endoplasmic reticulum. The function of the SR is to temporarily store calcium ions (Ca^{++}). The membrane of the SR continually pumps Ca^{++} from the sarcoplasm and stores the ions within its sacs.

A structure unique to muscle cells is a system of transverse tubules, or **T tubules.** This name derives from the fact that these tubules extend transversely across the sarcoplasm, at a right angle to the long axis of the cell. As Figures 12-1, *B*, and 12-2 show, T tubules are formed by inward extensions of the sarcolemma. The chief function of T tubules is to allow electrical signals, or *impulses*, traveling along the sarcolemma to move deeper into the cell.

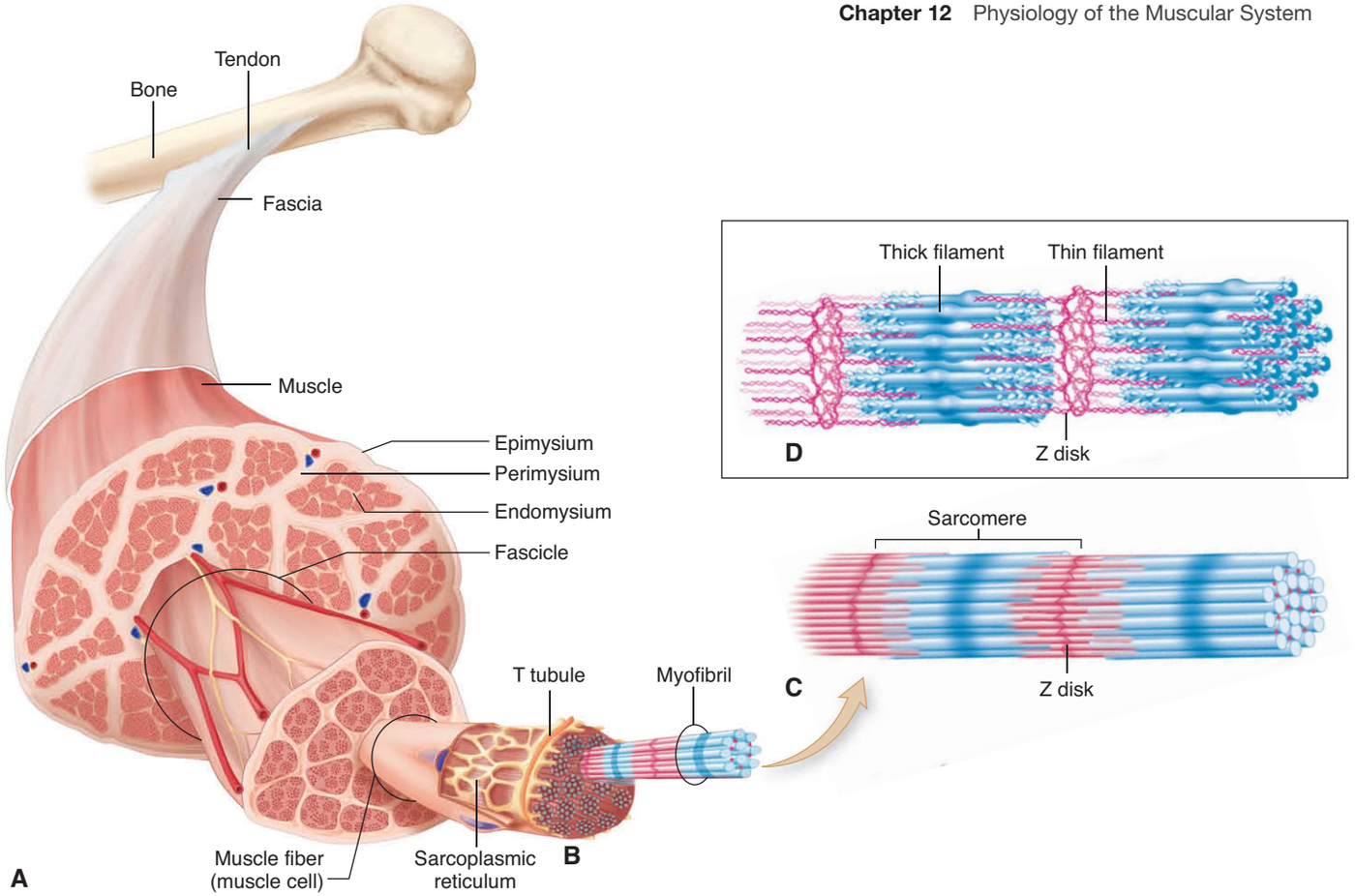


FIGURE 12-1

Structure of skeletal muscle. A, Skeletal muscle organ composed of bundles of contractile muscle fibers held together by connective tissue. **B,** Greater magnification of a single fiber showing smaller fibers—myofibrils—in the sarcoplasm. Note the sarcoplasmic reticulum and T tubules forming a three-part structure called a *triad.* **C,** Myofibril magnified further to show a sarcomere between successive Z disks (Z lines). Cross striae are visible. **D,** Molecular structure of a myofibril showing thick myofilaments and thin myofilaments.

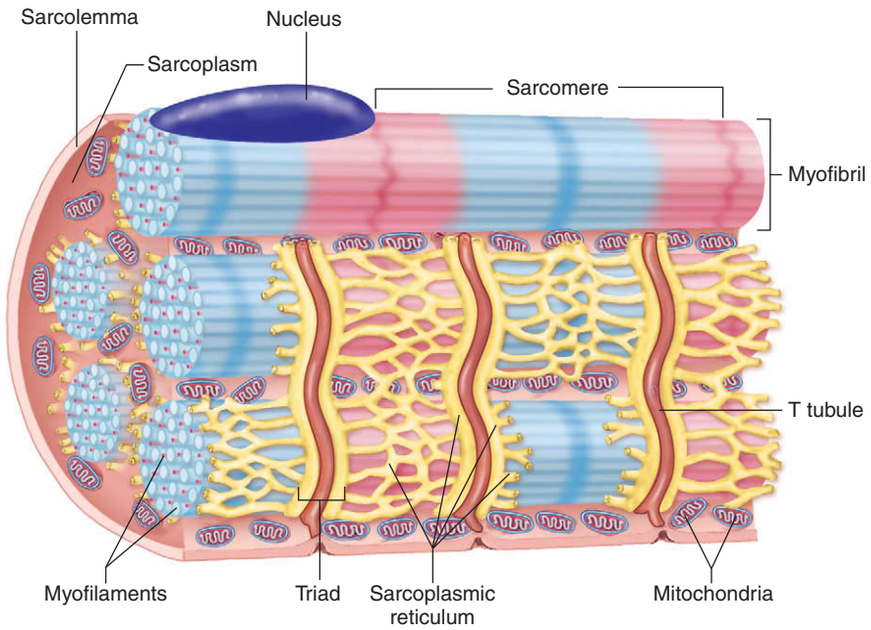


FIGURE 12-2

Unique features of the skeletal muscle cell. Notice especially the T tubules, which are extensions of the plasma membrane, or sarcolemma, and the sarcoplasmic reticulum (SR), a type of smooth endoplasmic reticulum that forms networks of tubular canals and sacs containing stored calcium ions. A triad is a triplet of adjacent tubules: a terminal (end) sac of the SR, a T tubule, and another terminal sac of the SR.

Notice in Figures 12-1, *B*, and 12-2 that a tubular sac of the SR butts up against each side of every T tubule in a muscle fiber. This triplet of tubules (a T tubule sandwiched between sacs of the SR) is called a **triad.** The triad is an important feature of the muscle cell because it allows an electrical impulse traveling along a T tubule to stimulate the membranes of adjacent sacs of the SR. Figure 12-3 shows how this works. At rest, calcium ion pumps in the SR membrane pump Ca^{++} into the terminal sacs of the SR. However, when an electrical impulse travels along the sarcolemma and down the T tubule, gated Ca^{++} channels in the SR open in response to the voltage fluctuation. This floods the sarcoplasm with calcium ions—an important step in initiating muscle contraction, as we shall see.

Additional structures not found in other cells are present in skeletal muscle fibers. For instance, the cytoskeleton of the muscle fiber is quite unique. **Myofibrils** are bundles of very fine cytoskeletal filaments that extend lengthwise along skeletal muscle fiber and almost fill the sarcoplasm. A typical muscle fiber may have somewhere in the neighborhood of a thousand or more myofibrils tightly packed inside it.

Myofibrils, in turn, are made up of still finer fibers called **myofilaments.** Notice in Figure 12-1, *D*, that there are two types of myofilaments in the myofibril: *thick filaments* and *thin filaments.* You can see at a glance that some of the filaments are much thicker than others. Although they appear in contrasting colors in the diagram, they are actually colorless.

A **sarcomere** is a segment of the myofibril between two successive **Z disks** (Z lines) (Box 12-1). Find the label *sarcomere* in Figure 12-1, *C*. You will note that each myofibril consists of a lineup of many sarcomeres. Each sarcomere functions as a contractile unit. The A bands of sarcomeres appear as relatively wide, dark stripes (cross striae) under the microscope, and they alternate with narrower, lighter-colored stripes formed by the I bands (see the figure in Box 12-1). Because of its cross striations (or *striae*), skeletal muscle is sometimes called *striated muscle.* Electron microscopy of skeletal muscle (Figure 12-4) reveals details that help us understand concepts of its structure and function.

| QUICK CHECK |

1. What are the three major functions of the skeletal muscles?
2. Name some features of the muscle cell that are not found in other types of cells.
3. What causes the striations observed in skeletal muscle fibers?
4. Why is the triad relationship between T tubules and the SR important?

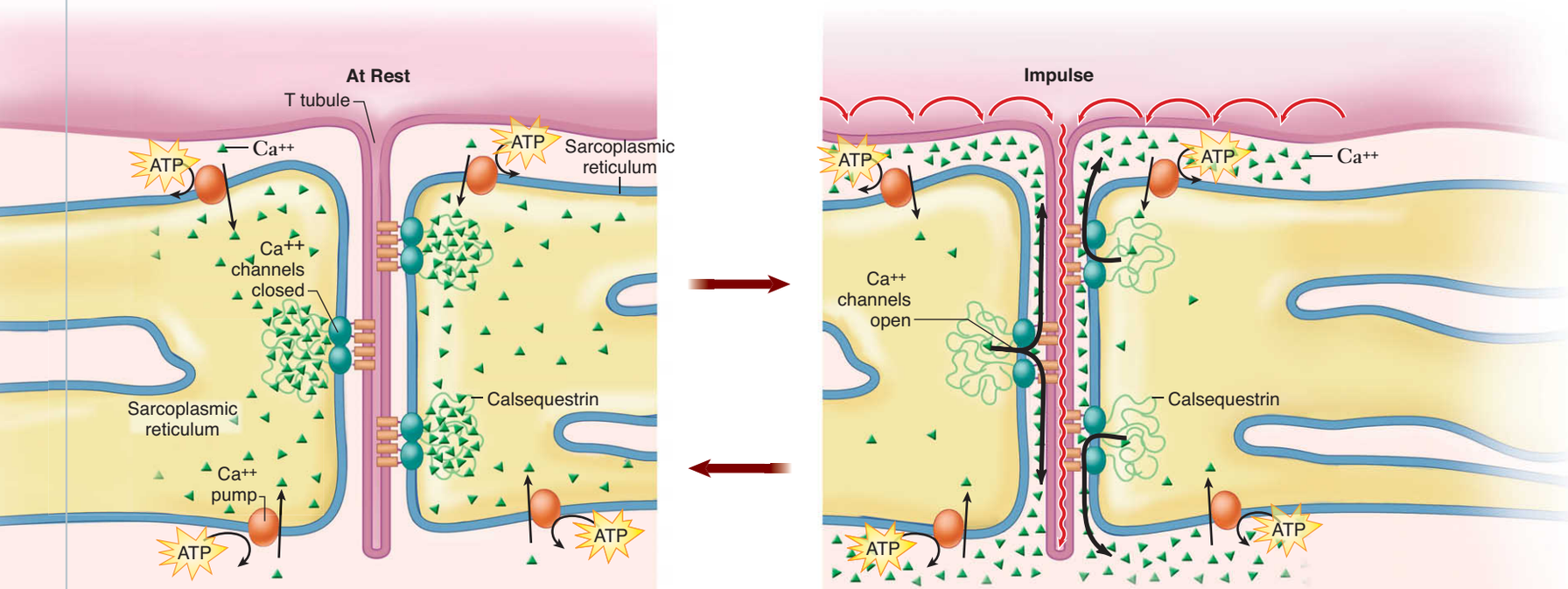


FIGURE 12-3

Storage and release of calcium ions at the triad. At rest *(left),* calcium ion pumps in the sarcoplasmic reticulum (SR) membrane actively pull Ca^{++} into the SR—thus creating a concentration gradient with very little Ca^{++} left in the sarcoplasm. Note that the Ca^{++} is sequestered by protein filaments *(calsequestrin)* in "bunches" just inside the closed Ca^{++} channels. When the fiber is stimulated *(right),* an electrical impulse travels from the sarcolemma and down the T tubule, where the voltage fluctuation triggers the opening of voltage-gated calcium channels. This allows passive diffusion of the Ca^{++} inside the SR out to the sarcoplasm, where it will trigger the contraction process. Almost immediately after stimulation, the calcium channels close and the Ca^{++} is once again pumped into the sacs of the SR *(left). ATP,* Adenosine triphosphate.

Box 12-1 | A More Detailed Look at the Sarcomere

The sarcomere is the basic contractile unit of the muscle cell. As you read the explanation of the sarcomere's structure and function, you might wonder what the Z disk, M line, and other components really are—and what they do for the muscle cell.

First of all, it is important that you appreciate the three-dimensional nature of the sarcomere. You can then realize that the Z disk (Z line), which often looks like a zigzag line in a flat diagram, is really a dense plate or disk to which the thin filaments directly anchor. Besides being an anchor for myofibrils, the Z disk is useful as a landmark separating one sarcomere from the next. The name Z disk comes from the German word *zwischen,* meaning "between."

Detailed analysis of the sarcomere also shows that the thick (myosin) filaments are held together and stabilized by *M-protein* molecules that form a middle line called the **M line.** Note that the regions of the sarcomere are identified by specific zones or bands:

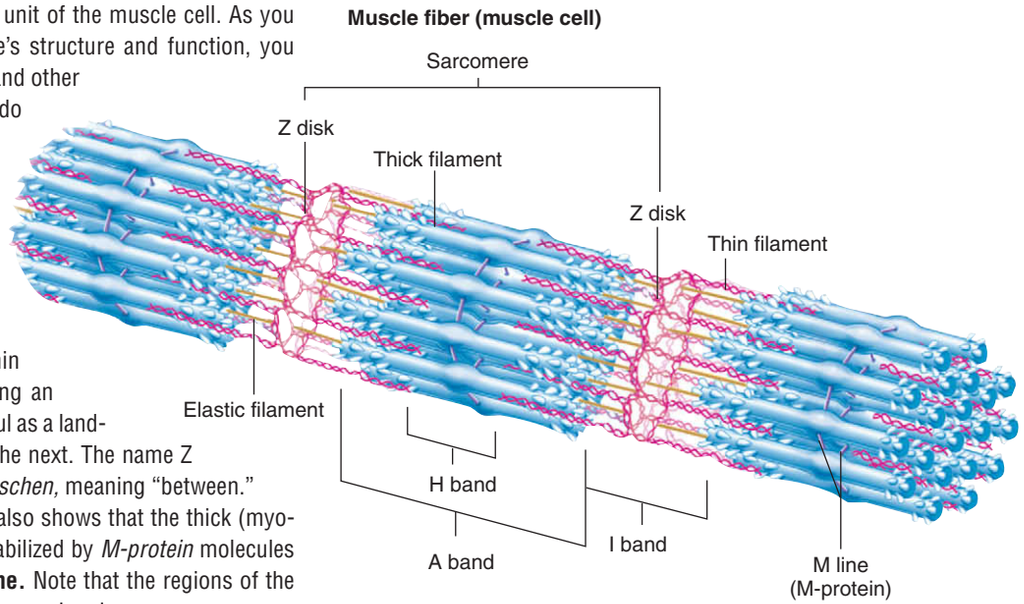
A band—the segment that runs the entire length of the thick filaments (also called *anisotropic band*)

I band—the segment that includes the Z disk and the ends of the thin filaments where they do not overlap the thick filaments (also called *isotropic band*)

H band—the middle region of the thick filaments where they do not overlap the thin filaments (H is German for *heller* "bright")

Note in Figure 12-2 that the T tubules in human muscle fibers align themselves along the borders between the A band and I band.

Later, as you review the process of contraction, note how the regions listed above change during each step of the process.



In addition to thin and thick filaments, each sarcomere has numerous **elastic filaments.** Elastic filaments, composed of a protein called *titin (connectin),* anchor the thick filaments to the Z disk, as the figure shows. The elastic filaments are believed to give myofibrils, and thus muscle fibers, their characteristic elasticity. *Dystrophin,* not shown here, is a protein that holds the actin filaments to the sarcolemma. Dystrophin and a complex of connected molecules anchors the muscle fiber to surrounding matrix so that the muscle does not break during a contraction. Dystrophin and its role in muscular dystrophy are discussed further on p. 373.

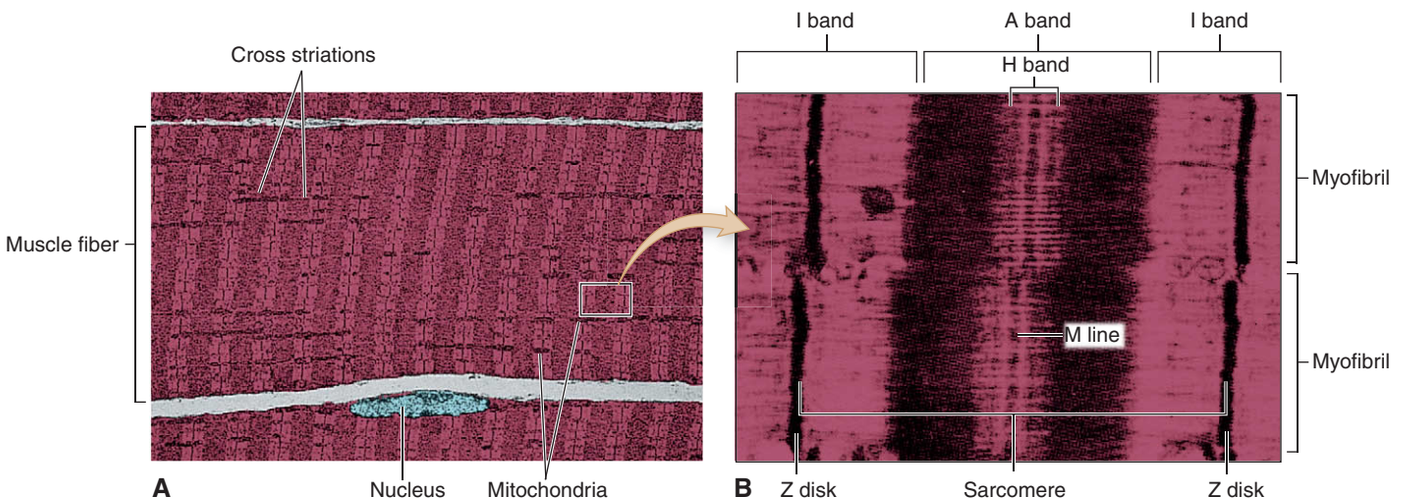


FIGURE 12-4

Skeletal muscle striations. Color-enhanced scanning electron micrographs (SEMs) showing longitudinal views of skeletal muscle fibers. **B** shows detail of **A** at greater magnification. Note that the myofilaments of each myofibril form a pattern that when viewed together, produces the striated (striped) pattern typical of skeletal muscle.

Myofilaments

Each muscle fiber contains a thousand or more parallel myofibrils that are only about 1 µm thick. Lying side by side in each myofibril are approximately 15,000 sarcomeres, each made up of hundreds of thick and thin filaments. The molecular structure of these myofilaments reveals the mechanism of how muscle fibers contract and do so powerfully. It is wise, therefore, to take a moment to first study the structure of myofilaments before discussing the detailed mechanism of muscle contraction.

First of all, four different kinds of protein molecules make up myofilaments: **myosin, actin, tropomyosin,** and **troponin.** The thin filaments are made of a combination of three proteins: actin, tropomyosin, and troponin. Figure 12-5, *A*, shows that globular actin molecules (*g-actin*) are strung together like beads to form two fibrous strands (*f-actin*) that twist around each other to form the bulk of each thin filament. Actin and myosin molecules have a chemical attraction for one another, but at rest, the active sites on the actin molecules are covered by long tropomyosin molecules. The tropomyosin molecules seem to be held in this blocking position by troponin molecules spaced at intervals along the thin filament (see Figure 12-5, *A*).

As Figure 12-5, *B*, shows, the thick filaments are made almost entirely of myosin molecules. Notice that the myosin molecules are shaped like two golf clubs twisted together. Their long shafts bundle together to form a thick filament and their doubled "heads" stick out from the bundle. The myosin heads are chemically attracted to the actin molecules of the nearby thin filaments, so they angle toward the thin filaments. When they bridge the gap between adjacent myofilaments, the myosin heads are usually called **cross bridges.** Recall from Figure 3-17 (p. 82) that myosin acts as a molecular motor. The myosin in thick filaments can actively pull on actin when adenosine triphosphate (ATP) is available.

Within a myofibril, the thick and thin filaments alternate, as shown in Figure 12-1, *D*. They are also very close to one another, as you can see in the cross section in Figure 12-5, *C*, and Figure 12-6. This arrangement is crucial for contraction. Another fact important for contraction is that the thin filaments attach to both Z disks (Z lines) of a sarcomere and that they extend in from the Z disks partway toward the center of the sarcomere. When the muscle fiber is relaxed, the thin filaments terminate at the outer edges of the H bands. In contrast, the thick myosin filaments do not attach directly to the Z disks, and they extend only to the length of the A bands of the sarcomeres.

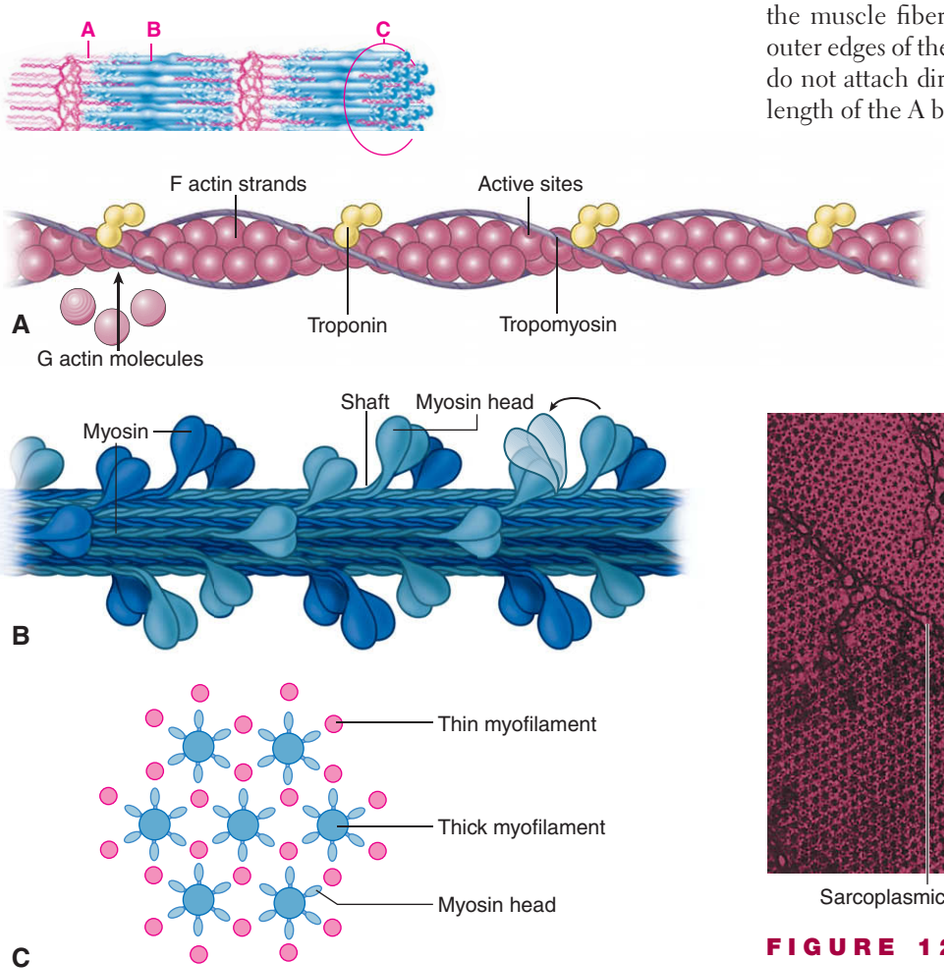


FIGURE 12-5

Structure of myofilaments. A, Thin myofilament. **B,** Thick myofilament. **C,** Cross section of several thick and thin myofilaments showing the relative positions of myofilaments and the myosin heads that will form cross bridges between them.

Mechanism of Contraction

To accomplish the powerful shortening, or contraction, of a muscle fiber, several processes must be coordinated in a stepwise fashion. These steps are summarized in the following sections and in Box 12-2.

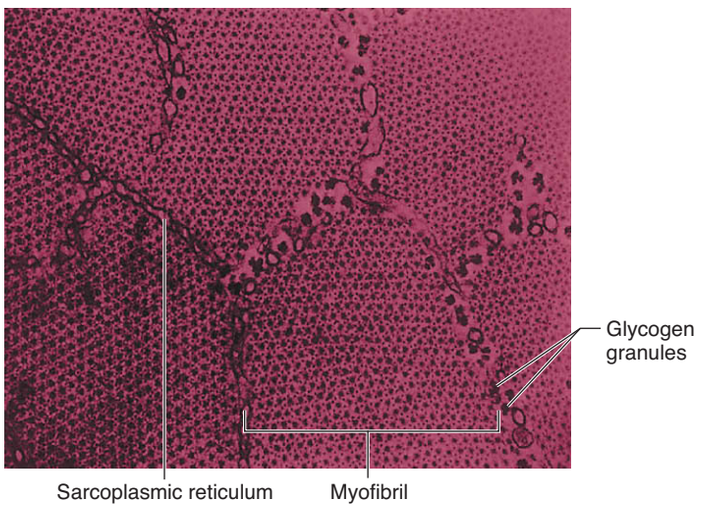


FIGURE 12-6

Cross section of myofibrils. Color-enhanced scanning electron micrographs (SEMs) showing a cross section from a skeletal muscle fiber. Note the dense arrangement of thick and thin filaments, seen here in cross section as mere dots. Note also the dark glycogen granules and sarcoplasmic reticulum tubules sandwiched between the myofibrils.

Box 12-2 | Major Events of Muscle Contraction and Relaxation

Excitation and Contraction

1. A nerve impulse reaches the end of a motor neuron and triggers release of the neurotransmitter acetylcholine (ACh).
2. ACh diffuses rapidly across the gap of the neuromuscular junction and binds to ACh receptors on the motor endplate of the muscle fiber.
3. Stimulation of ACh receptors initiates an impulse that travels along the sarcolemma, through the T tubules, to the sacs of the sarcoplasmic reticulum (SR).
4. Ca^{++} is released from the SR into the sarcoplasm, where it binds to troponin molecules in the thin myofilaments.
5. Tropomyosin molecules in the thin myofilaments shift and thereby expose actin's active sites.
6. Energized myosin cross bridges of the thick myofilaments bind to actin and use their energy to pull the thin myofilaments toward the center of each sarcomere. This cycle repeats itself many times per second, as long as adenosine triphosphate is available.
7. As the filaments slide past the thick myofilaments, the entire muscle fiber shortens.

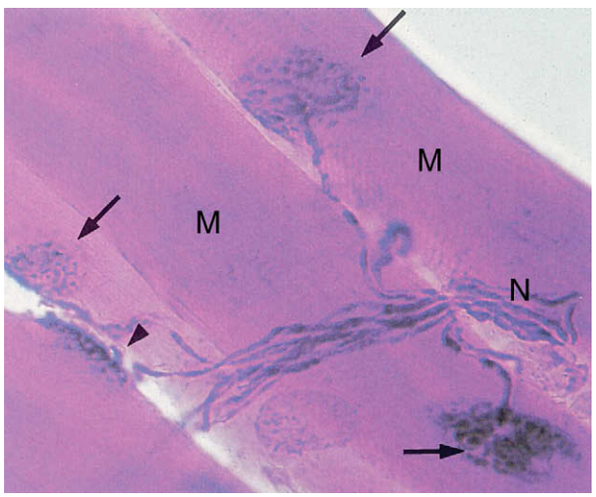
Relaxation

1. After the impulse is over, the SR begins actively pumping Ca^{++} back into its sacs.
2. As Ca^{++} is stripped from troponin molecules in the thin myofilaments, tropomyosin returns to its position and blocks actin's active sites.
3. Myosin cross bridges are prevented from binding to actin and thus can no longer sustain the contraction.
4. Because the thick and thin myofilaments are no longer connected, the muscle fiber may return to its longer, resting length.

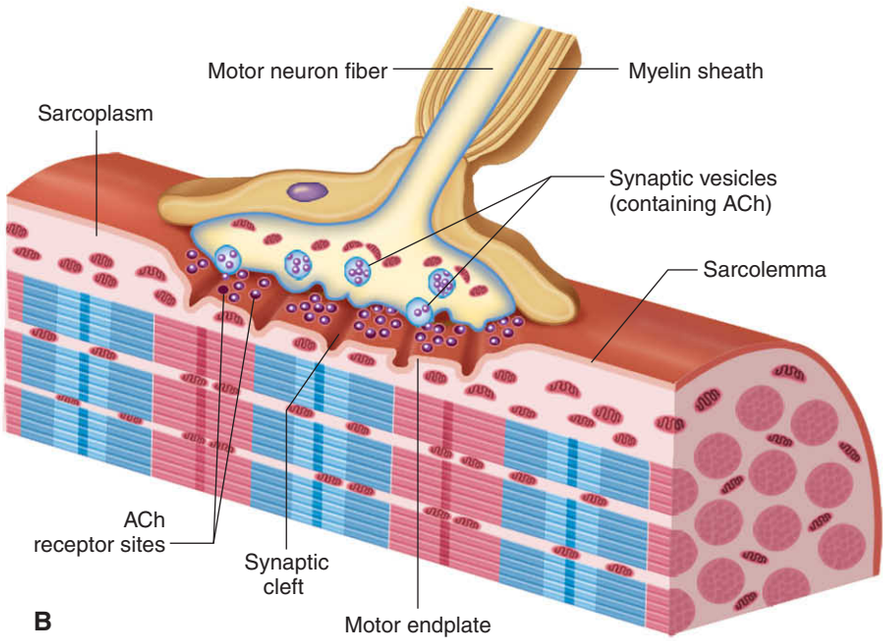
EXCITATION OF THE SARCOLEMMA

Under normal circumstances, a skeletal muscle fiber remains "at rest" until it is stimulated by a signal from a special type of nerve cell called a **motor neuron.** As Figure 12-7 shows, motor neurons connect to the sarcolemma of a muscle fiber at a folded **motor endplate** to form a junction called a *neuromuscular junction.*

A **neuromuscular junction (NMJ)** is a type of connection called a *synapse* and is characterized by a narrow gap, or synaptic cleft, across which *neurotransmitter* molecules transmit signals. When nerve impulses reach the end of a motor neuron fiber, small vesicles release a neurotransmitter, **acetylcholine (ACh),** into the synaptic cleft. Diffusing swiftly across this microscopic gap, acetylcholine molecules contact the sarcolemma of the adjacent muscle fiber. There they stimulate acetylcholine receptors and thereby initiate an electrical impulse in the sarcolemma. The process of synaptic transmission and induction of an impulse—a process often called *excitation*—is discussed in detail in Chapter 13.



A



B

FIGURE 12-7

Neuromuscular junction (NMJ). A, Micrograph showing four neuromuscular junctions (NMJs). Three are surface views *(arrows)* and one is a side view *(arrowhead). N,* Nerve fibers; *M,* muscle fibers. **B,** This sketch shows a side view of the NMJ. Note how the distal end of a motor neuron fiber forms a synapse, or "chemical junction," with an adjacent muscle fiber. Neurotransmitter molecules (specifically, acetylcholine, or ACh) are released from the neuron's synaptic vesicles and diffuse across the synaptic cleft. There they stimulate receptors in the motor endplate region of the sarcolemma.

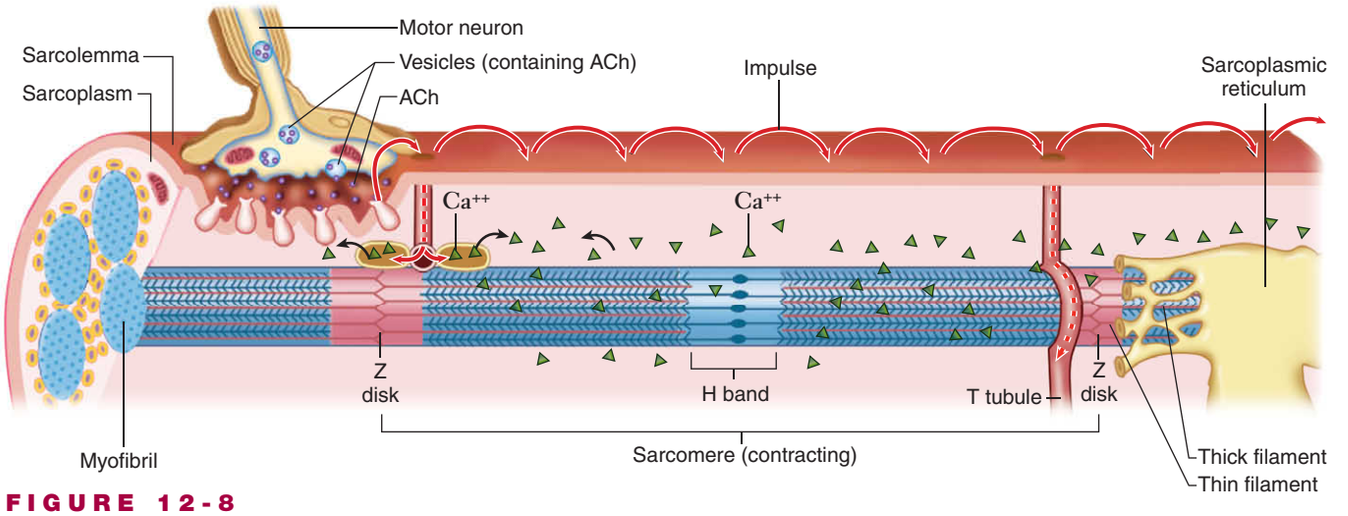


FIGURE 12-8

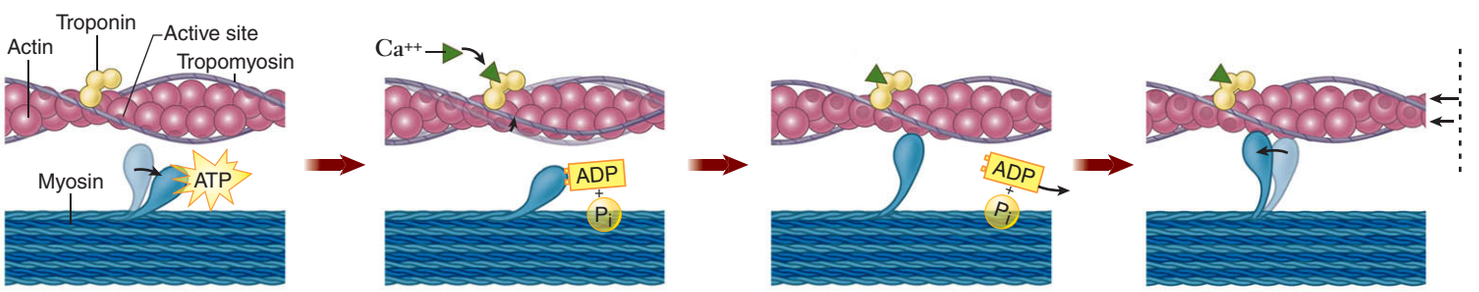
Effects of excitation on a muscle fiber. Excitation of the sarcolemma by a nerve impulse initiates an impulse in the sarcolemma. The impulse travels across the sarcolemma and through the T tubules, where it triggers adjacent sacs of the sarcoplasmic reticulum to release a flood of calcium ions (Ca^{++}) into the sarcoplasm. Ca^{++} is then free to bind to troponin molecules in the thin filaments. This binding, in turn, initiates the chemical reactions that produce a contraction.

CONTRACTION

The impulse, a temporary electrical voltage imbalance, is conducted over the muscle fiber's sarcolemma and inward along the T tubules (Figure 12-8). The impulse in the T tubules triggers the release of a flood of calcium ions from the adjacent sacs of the SR (see Figures 12-3 and 12-8).

In the sarcoplasm, the calcium ions combine with troponin molecules in the thin filaments of the myofibrils (Figure 12-9). Recall that troponin normally holds tropomyosin strands in a position that blocks the chemically active sites of actin. When calcium binds to troponin, however, the tropomyosin shifts to expose active binding sites on the actin molecules (Figure 12-10). Once the active sites are exposed, energized myosin heads of the thick filaments bind to actin molecules in the nearby thin filaments. The myosin head temporarily forms a *cross bridge* between the thick and thin filaments (Figure 12-11). After forming cross bridges, the myosin heads bend with great force, literally pulling the thin filaments past them. Each head then releases itself, binds to the next active site, and pulls again. Figure 12-12 shows how sliding of the thin filaments toward the center of each sarcomere quickly shortens the entire myofibril—and thus the entire muscle fiber.

This model of muscle contraction has been called the **sliding-filament model.** Perhaps a better name might be



1. Each myosin head in the thick filament moves into a resting position after an ATP molecule binds and transfers its energy.
2. Calcium ions released from the sarcoplasmic reticulum bind to troponin in the thin filament, thereby allowing tropomyosin to shift from its position blocking the active sites of actin molecules.
3. Each myosin head then binds to an active site on a thin filament and displaces the remnants of ATP hydrolysis—adenosine diphosphate (ADP) and inorganic phosphate (P_i).
4. The release of stored energy from step 1 provides the force needed for each head to move back to its original position and pull actin along with it. Each head will remain bound to actin until another ATP molecule binds to it and pulls it back into its resting position (step 1).

FIGURE 12-9

The molecular basis of muscle contraction.

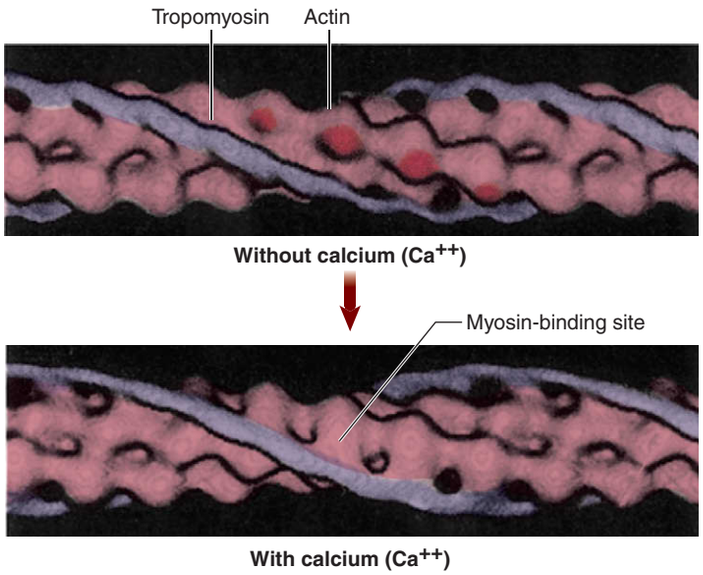


FIGURE 12-10

Role of calcium in muscle contraction. Color-enhanced scanning electron micrograph (SEM) of a thin filament. When calcium is absent, the active myosin binding sites on actin are covered by tropomyosin. However, after calcium becomes available and binds to troponin, the tropomyosin is pulled out of its blocking position and reveals the active binding sites on actin.

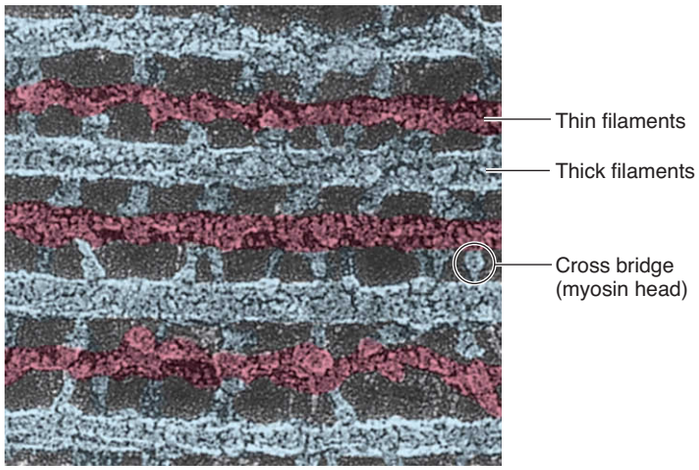


FIGURE 12-11

Cross bridges. Color-enhanced scanning electron micrograph (SEM) showing the myosin heads functioning as cross bridges that connect the thick filaments to the thin filaments, pulling on the thin filaments and causing them to slide.

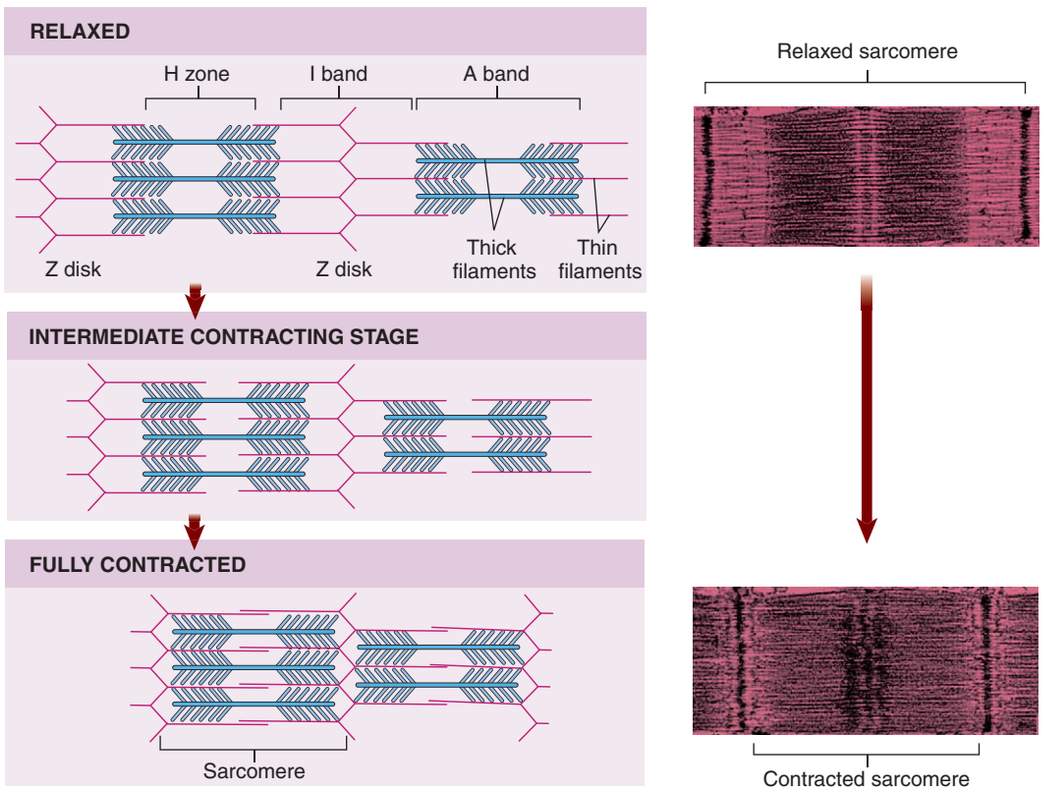


FIGURE 12-12

Sliding-filament model. A, During contraction, myosin cross bridges pull the thin filaments toward the center of each sarcomere, thus shortening the myofibril and the entire muscle fiber. **B,** Color-enhanced transmission electron micrographs (TEMs) showing the shortening of a sarcomere caused by the sliding of filaments during muscle contraction.

ratcheting-filament model because the myosin heads actively ratchet the thin filaments toward the center of the sarcomere with great force.

Muscle fibers usually contract to about 80% of their starting length—rarely to 60% or 70%. Some muscle fibers contract hardly at all because they are pulling on an unmoving load. Even so, such muscle fibers are still said to be "contracting" in a broad sense. Their sarcomeres are still working hard to pull the ends toward one another, as though they are at a steady "draw" in a game of tug-of-war (Figure 12-13). Because the actin-myosin bond is not permanent, the sarcomere cannot "lock up" once it has shortened to hold its position passively. Thus it takes energy to actively maintain a shortened position—by continually repeating the actin-myosin reaction as long as necessary.

RELAXATION

Almost immediately after the SR releases its flood of calcium ions into the sarcoplasm, it begins actively pumping them back into its sacs once again. Within a few milliseconds, much of the calcium is recovered. Because the active transport carriers of the SR have greater affinity for calcium than the troponin molecules do, the calcium ions are stripped off the troponin molecules and returned to the sacs of the SR. As you might suspect, this shuts down the entire process of contraction. Troponin without its bound calcium allows the tropomyosin to once again block actin's active sites. Myosin heads reaching for the next active site on actin are blocked, and thus the thin filaments are no longer being held—or pulled—by the thick filaments.

If no new nerve impulse immediately follows, the muscle fiber relaxes. The relaxed muscle fiber may remain at its contracted length, but forces outside the muscle fiber are likely to pull it back to its longer resting length.

As we have seen, the contraction process in a skeletal muscle fiber automatically shuts itself off within a small fraction of a second after the initial stimulation. However, a muscle fiber may sustain a contraction for some time if there are many stimuli in rapid succession, thus permitting calcium ions to remain available in the sarcoplasm for a longer period.

| QUICK CHECK |

5. Describe the structure of thin and thick myofilaments, and name the kinds of proteins that compose them.
6. What is a neuromuscular junction (NMJ)? How does it work?
7. What is the role of calcium ions (Ca^{++}) in muscle contraction?

Energy Sources for Muscle Contraction

ATP

The energy required for muscular contraction is obtained by hydrolysis of a nucleotide called *adenosine triphosphate*, or *ATP*. Recall from Chapter 2 (Figure 2-33, p. 59) that this molecule has an adenine and ribose group (together called *adenosine*) attached to three phosphate groups. Two of the three phosphate groups in ATP are attached to the molecule by *high-energy bonds*. Breaking of these high-energy bonds provides the energy necessary to pull the thin myofilaments during muscle contraction.

As Figure 12-9, *Step 1*, shows, before contraction occurs, each myosin cross-bridge head moves into a resting position when an ATP molecule binds to it. The ATP molecule breaks its outermost high-energy bond, thereby releasing inorganic phosphate (P_i) and transferring the energy to the myosin head. In a way, this is like pulling back the elastic band of a slingshot—the apparatus is "at rest" but ready to spring. When myosin binds to actin, the stored energy is released, and the myosin head does indeed spring back to its original position. Thus the energy transferred from ATP is used to do the work of pulling the thin filaments during contraction. Another ATP molecule then binds to the myosin head, which then releases actin and moves into its resting position again—all set for the next "pull." This cycle repeats as long as ATP is available and actin's active sites are unblocked.

Muscle fibers must continually resynthesize ATP because they can store only small amounts of it. There is only enough ATP in a muscle fiber for about 2 to 4 seconds of maximum contraction. However, energy for the resynthesis of ATP can be quickly supplied by the breakdown of another high-energy compound, **creatine phosphate (CP)**, as you can see in Figure 12-14. CP is a sort of backup energy molecule that provides enough energy for about 20 additional seconds of maximal contraction. Both ATP and CP

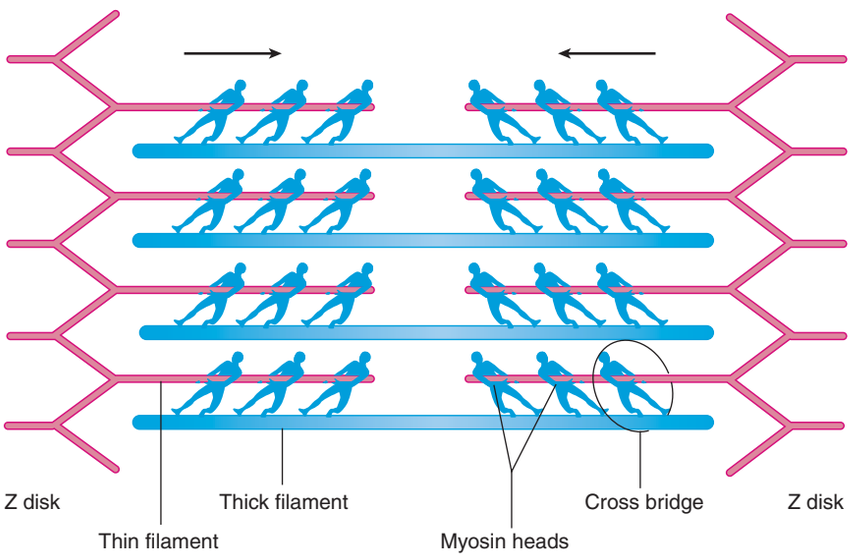


FIGURE 12-13

Simplified contracting sarcomere. This diagram illustrates the concept of muscle contraction as a sort of tug-of-war game in which the myosin heads (shown here as little people) hold onto thin filament "ropes"—thus forming cross bridges. As the myosin heads pull on the thin filaments, the Z disks (Z lines) get closer together—thus shortening the sarcomere. Likewise, the short length of a sarcomere may be held in position by the continued effort of the myosin heads.

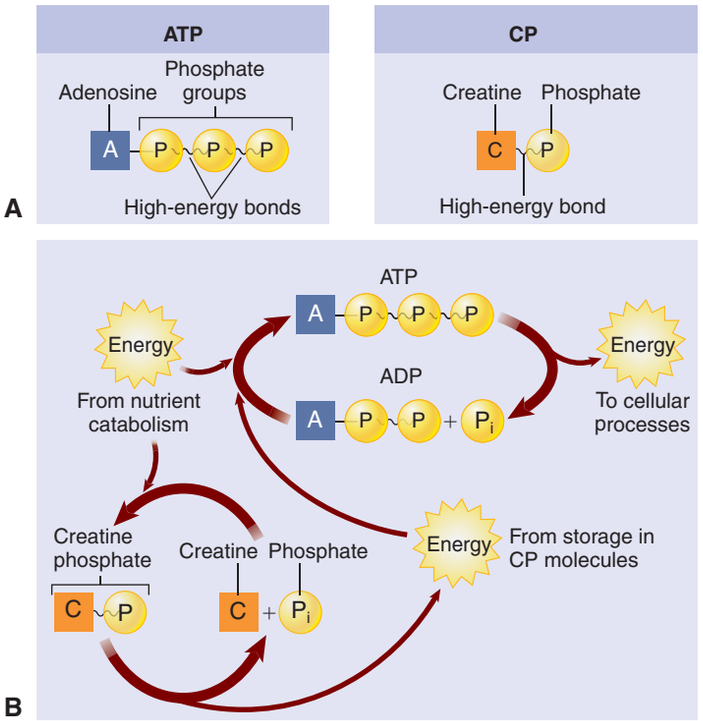


FIGURE 12-14

Energy sources for muscle contraction. A, The basic structure of two high-energy molecules in the sarcoplasm: adenosine triphosphate (ATP) and creatine phosphate (CP). **B,** This diagram shows how energy released during the catabolism of nutrients can be transferred to the high-energy bonds of ATP directly or, instead, stored temporarily in the high-energy bond of CP. During contraction, ATP is hydrolyzed and the energy of the broken bond is transferred to a myosin head.

are continually resynthesized—or "recharged"—by cellular respiration. Ultimately, energy for both ATP and CP synthesis comes from the catabolism of food.

If a cell runs out of ATP completely and cannot resynthesize more, contraction stops—possibly resulting in stiffness caused by the inability of myosin heads to disengage from actin (see Figure 12-9). When this happens after death, it is called *rigor mortis* (Box 12-3).

GLUCOSE AND OXYGEN

Continued, efficient nutrient catabolism by muscle fibers requires two essential ingredients: glucose and oxygen.

Glucose is a nutrient molecule that contains many chemical bonds. The potential energy stored in these chemical bonds is released during catabolic reactions in the sarcoplasm and mitochondria and transferred to ATP or CP molecules. Ultimately, all the glucose needed by muscle fibers comes from the blood. Skeletal muscle fibers are surrounded by a network of blood capillaries, the tiny "exchange" vessels that allow molecules to enter or leave the blood (Figure 12-15). Some muscle fibers ensure an uninterrupted supply of glucose by storing it in the form of *glycogen*. Recall from Chapter 2 that glycogen is a polysaccharide made up of thousands of glucose subunits.

Box 12-3 | FYI

Rigor Mortis

The term **rigor mortis** is a Latin phrase that means "stiffness of death." In a medical context the term *rigor mortis* refers to the stiffness of skeletal muscles sometimes observed shortly after death. What causes rigor mortis? At the time of death, stimulation of muscle cells ceases. However, the muscle fibers of postural muscles may have been in midcontraction at the time of death—when the myosin-actin cross bridges are still intact. In addition, the sarcoplasmic reticulum (SR) releases much of the Ca^{++} it had been storing, thereby causing even more cross bridges to form. Adenosine triphosphate (ATP) is required to release the cross bridges and "energize" the myosin heads for their next attachment. Because the last of a cell's ATP supply is used up at the time it dies, many cross bridges may be left "stuck" in the contracted position. Thus muscles in a dead body may be stiff because individual muscle fibers ran out of the ATP required to "turn off" a muscle contraction.

Oxygen, which is needed for a catabolic process known as *aerobic respiration*, also ultimately comes from the blood. Most of the oxygen carried in the blood is temporarily bound to *hemoglobin* molecules—a reddish pigment inside red blood cells.

Oxygen can also be stored by cells to ensure an uninterrupted supply. During rest, excess oxygen molecules in the sarcoplasm are attracted to a large protein molecule called **myoglobin.** Like hemoglobin, myoglobin is a reddish pigment with iron (Fe) groups that attract oxygen molecules and hold them temporarily. When the oxygen concentration inside a muscle fiber decreases rapidly—as it does during exercise—it can be quickly resupplied from myoglobin. Muscle fibers that contain large amounts of

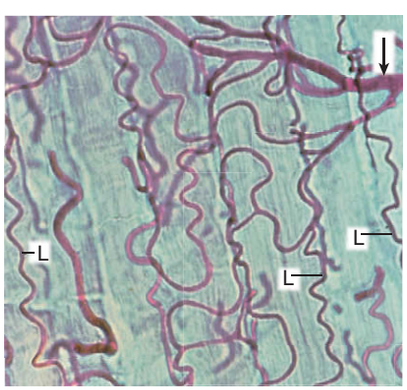


FIGURE 12-15

Blood supply of muscle fibers. Tiny "exchange" vessels called *capillaries* branch out longitudinally *(L)* from small arteries *(arrow)* to form a network that supplies muscle fibers with glucose and oxygen and removes carbon dioxide and lactic acid. In this micrograph, the muscle fibers appear translucent and the blood vessels appear reddish.

myoglobin take on a deep red appearance and are often called *red fibers.* Muscle fibers with little myoglobin in them are light pink and are often called *white fibers.* Most muscle tissues contain a mixture of red and white fibers (Box 12-4).

CATABOLIC PATHWAYS

The *aerobic* (oxygen-requiring) *pathway* is a catabolic process that produces the maximum amount of energy available from each glucose molecule. When the oxygen concentration is low, however,

Box 12-4 | SPORTS and FITNESS

Types of Muscle Fibers

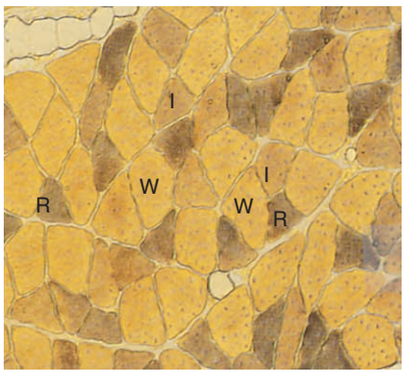
Skeletal muscle fibers can be classified into three types according to their structural and functional characteristics: (1) *slow* (red) *fibers,* (2) *fast* (white) *fibers,* and (3) *intermediate fibers.* Each type is best suited to a particular type or style of muscular contraction—a fact that is useful in considering how different muscles are used during different athletic activities. Although each muscle organ contains a mix of all three fiber types (part *A* of the figure), different organs have these fibers in different proportions, depending on the types of contraction that they most often perform (part *B* of the figure).

Slow fibers are also called *red fibers* because they contain a high concentration of myoglobin, the reddish pigment used by muscle cells to store oxygen. They are called *slow fibers* because their thick myofilaments are made of a type of myosin (type I) that reacts at a slow rate. Because they contract so slowly, slow fibers are usually able to produce ATP quickly enough to keep pace with the energy needs of the myosin and thus avoid fatigue. This effect is enhanced by the larger number of mitochondria, more than found in other fiber types, and the rich oxygen store provided by the myoglobin. The slow, nonfatiguing characteristics of slow fibers make them especially well suited to the sustained contractions exhibited by postural muscles. Postural muscles containing a high proportion of slow fibers can hold the skeleton upright for long periods without fatigue.

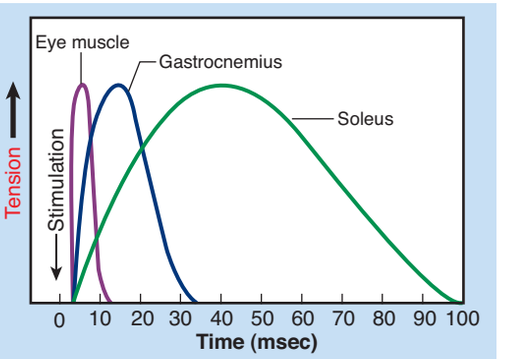
Fast fibers are also called *white fibers* because they contain very little myoglobin. Fast fibers can contract much more rapidly than slow fibers because they have a faster type of myosin (type IIx) and because their system of T tubules and sarcoplasmic reticulum (SR) is more efficient at quickly delivering Ca^{++} to the sarcoplasm. The price of a rapid contraction mechanism is rapid depletion of ATP. Despite the fact that fast fibers typically contain a high concentration of glycogen, they have few mitochondria and thus must rely primarily on anaerobic processes to regenerate ATP. Because the anaerobic pathway produces relatively small amounts of ATP, fast fibers cannot produce enough ATP to sustain a contraction for very long. Because they can generate great force very quickly but not for a long duration, fast fibers are best suited for muscles that move the fingers and eyes in darting motions.

Intermediate fibers have characteristics somewhere in between fast and slow fibers because they have moderately fast myosin (type IIa). They are more fatigue resistant than fast fibers and can generate more force more quickly than slow fibers. This type of muscle fiber predominates in muscles that both provide postural support and are occasionally required to generate rapid, powerful contractions. One example is the *gastrocnemius* of the calf, which helps support the leg but is also used in walking, running, and jumping (part *B* of the figure).

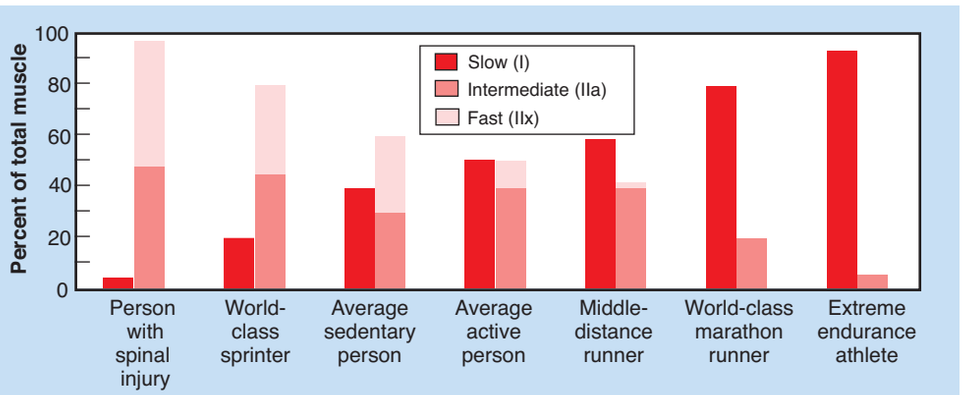
The bar graph in part *C* of the figure shows that the relative proportions of muscle fiber types, body wide, varies with the type of work a person does with his or her muscles. This graph underscores the fact that athletic training, for example, can produce changes in the mix of different fiber types in muscle tissue.



A

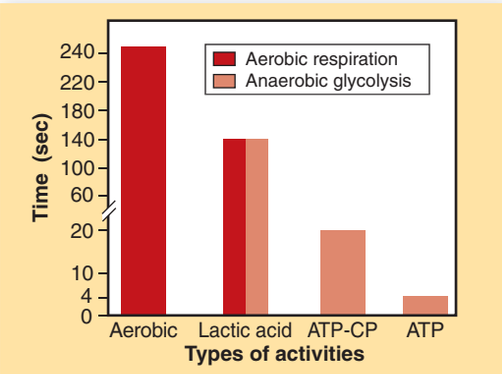


B

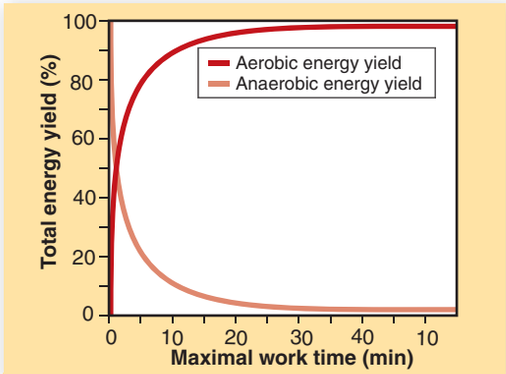


C

A, Types of muscle fibers. Using a special staining technique, this micrograph of a cross section of skeletal muscle tissue shows a mix of fiber types: *R,* red (slow) fibers; *W,* white (fast) fibers; and *I,* intermediate fibers.
B, Three styles of twitch contraction. Different muscle organs have different proportions of slow, fast, and intermediate fibers and thus produce different styles of twitch contractions in a myogram. **C,** Proportions of fiber types in muscle tissue. A person with a spinal cord injury eventually loses nearly all of the postural slow fibers while retaining mostly intermediate and fast fibers. In an extreme endurance athlete, on the other hand, the slow fibers develop so much that they greatly dominate the faster fiber types.



A



Duration of maximal exercise									
	Seconds			Minutes					
	10	30	60	2	4	10	30	60	120
Anaerobic (%)	90	80	70	50	35	15	5	2	1
Aerobic (%)	10	20	30	50	65	85	95	98	99

B

FIGURE 12-16

Aerobic and anaerobic pathways during muscular activity. A, The aerobic pathway (dark bars) can supply energy for muscle contraction for a longer time than can the anaerobic pathway (light bars). **B,** The lines show that 100% of the energy used at the beginning of maximal exercise comes from anaerobic processes. However, the muscles soon switch to aerobic sources of energy so after 1 hour of maximal exercise, nearly 100% of the energy comes from aerobic respiration in the muscle fibers. More information on aerobic and anaerobic energy metabolism is found in Chapter 30.

muscle fibers can shift toward increased use of another catabolic process: the *anaerobic pathway*. As its name implies, the anaerobic pathway does not require the immediate use of oxygen. Besides its ability to produce ATP without oxygen, the anaerobic pathway has the added advantage of being very rapid. Muscle fibers having difficulty getting oxygen—or fibers that generate a great deal of force very quickly—may rely on the anaerobic pathway to resynthesize their ATP molecules.

Anaerobic processes may allow the body to avoid the use of oxygen in the short term, but not in the long term (Figure 12-16). Anaerobic processes called *fermentation* result in the formation of an incompletely catabolized molecule called **lactic acid.** Lactic acid may accumulate in muscle tissue during exercise and cause a burning sensation. As oxygen becomes available, it may be converted back to glucose and used for energy. Any lactic acid not converted in the muscle fiber may eventually diffuse into the blood and be delivered to the liver, where an oxygen-consuming process later converts it back into glucose. This is one of the reasons that after heavy exercise, when the lack of oxygen in some tissues has caused the production of lactic acid, a person may still continue to breathe heavily. The body is repaying the so-called *oxygen debt* by using the extra oxygen gained by heavy breathing to process the lactic acid that was produced during exercise. This "oxygen debt" is often called the *excess postexercise oxygen consumption (EPOC)*.

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There is more to the oxygen debt than first meets the eye! Discover more about this important process of physical exercise in ***The Oxygen Debt*** online at ***A&P Connect.***

evolve

HEAT PRODUCTION

Because the catabolic processes of cells are never 100% efficient, some of the energy released is lost as heat. Because skeletal muscle tissues produce such a massive amount of heat—even when they are doing hardly any work—they have a great effect on body temperature. Recall from Chapter 7 that various heat loss mechanisms of the skin can be used to cool the body when it becomes overheated (see Figure 7-15, p. 183). Skeletal muscle tissues can likewise be used when the body's temperature falls below the set point value determined by the "thermostat" in the hypothalamus of the brain. As Figure 12-17 shows, a low external temperature can reduce body temperature below the set point. Temperature

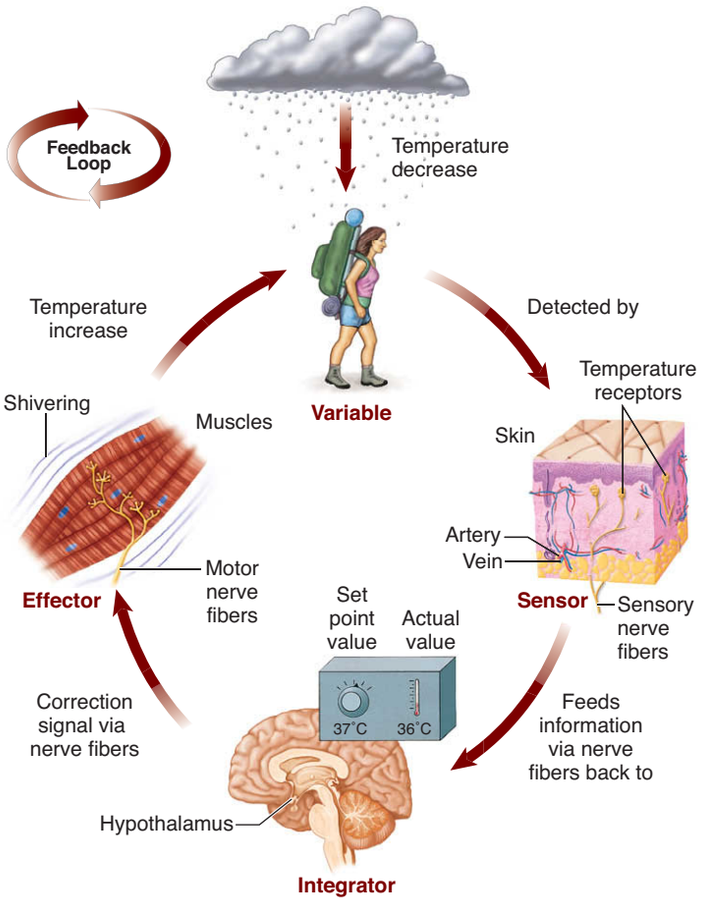


FIGURE 12-17

The role of skeletal muscle tissues in maintaining a constant body temperature. This diagram shows that a drop in body temperature caused by cold weather can be corrected by a negative feedback mechanism that triggers shivering (muscle contraction), which in turn produces enough heat to warm the body.

sensors in the skin and other parts of the body feed this information back to the hypothalamus, which compares the actual value with the set point value (usually about 37° C). The hypothalamus responds to a decrease in body temperature by signaling skeletal muscles to contract. The shivering contractions that result produce enough waste heat to warm the body back to the set point temperature—and homeostatic balance is maintained.

The subject of energy metabolism is discussed more thoroughly in Chapter 30.

| QUICK CHECK |

8. Where does the energy stored in ATP come from?
9. Contrast the aerobic pathway and anaerobic pathway in muscle fibers.
10. What is the role of myoglobin in muscle fibers?

FUNCTION OF SKELETAL MUSCLE ORGANS

Although each skeletal muscle fiber is distinct from all other fibers, it operates as part of the large group of fibers that form a skeletal muscle organ. Skeletal muscle organs, often simply called *muscles*, are composed of bundle upon bundle of muscle fibers held together by fibrous connective tissues (see Figure 12-1, A). The details of muscle organ anatomy are discussed in Chapter 11. For now, we turn attention to the matter of how skeletal muscle organs function as a single unit.

Motor Unit

Recall that each muscle fiber receives its stimulus from a motor neuron. This neuron, often called a *somatic motor neuron*, is one of several nerve cells that enter a muscle organ together in a bundle called a *motor nerve*. One of these motor neurons, plus the muscle fibers to which it attaches, constitutes a functional unit called a **motor unit** (Figure 12-18).

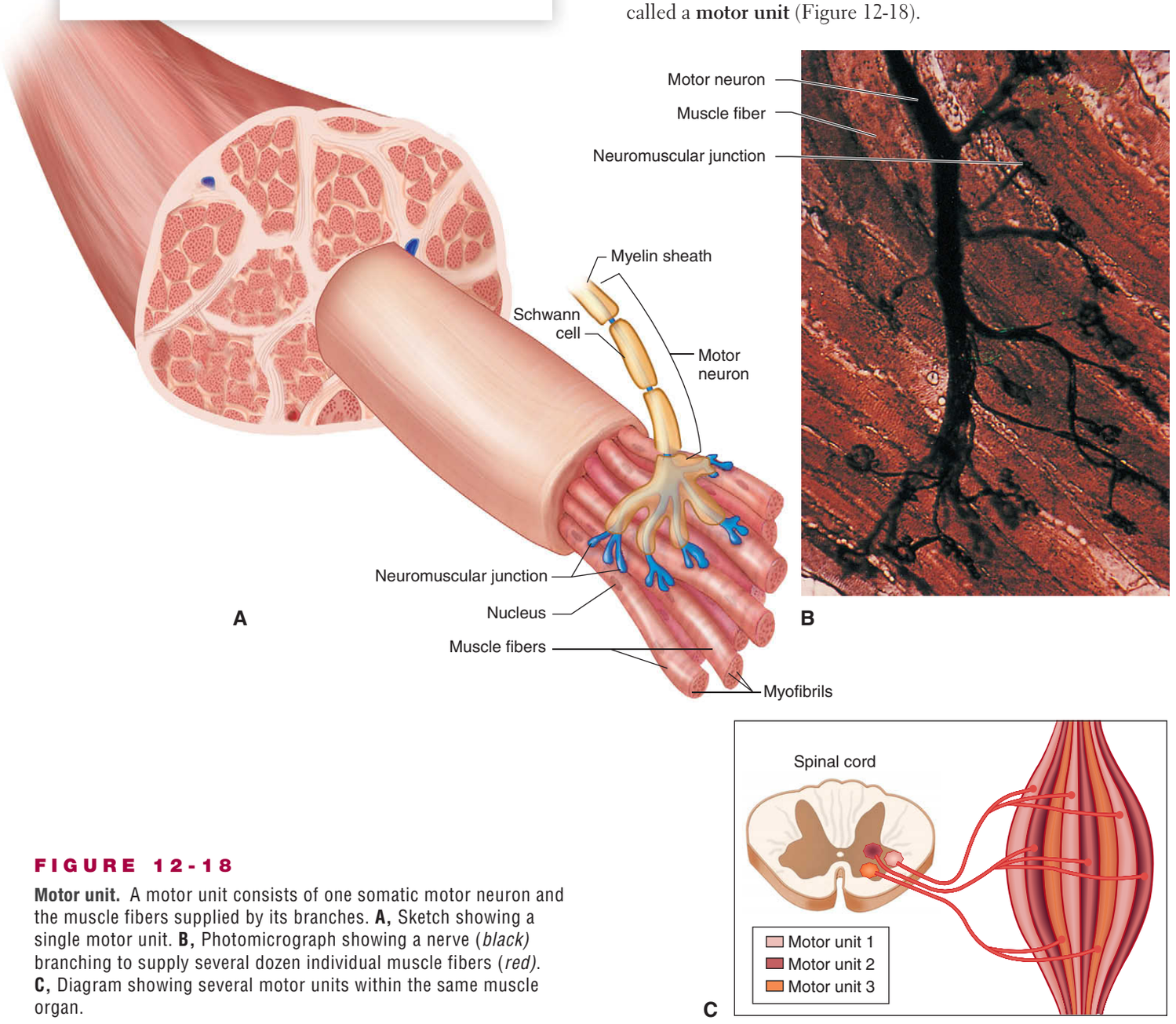


FIGURE 12-18

Motor unit. A motor unit consists of one somatic motor neuron and the muscle fibers supplied by its branches. **A,** Sketch showing a single motor unit. **B,** Photomicrograph showing a nerve (*black*) branching to supply several dozen individual muscle fibers (*red*). **C,** Diagram showing several motor units within the same muscle organ.

The single fiber of a somatic motor neuron divides into a variable number of branches upon entering the skeletal muscle. The neuron branches of some motor units terminate in only a few dozen muscle fibers, whereas others terminate in a few thousand fibers. Consequently, impulse conduction by one motor unit may stimulate only a small part of a muscle organ, whereas conduction by another motor unit may activate a much larger portion of a muscle organ. This fact bears a relationship to the function of the muscle as a whole. As a rule, the fewer the number of fibers supplied by a skeletal muscle's individual motor units, the more precise the movements that muscle can produce. For example, in certain small muscles of the hand, each motor unit includes only a few muscle fibers, and these muscles produce precise finger movements. In contrast, motor units in large abdominal muscles that do not produce precise movements may have thousands of muscle fibers.

Myography

Many experimental methods have been used to study the contractions of skeletal muscle organs. They vary from relatively simple procedures, such as observing or palpating muscles in action, to the more complicated method of *electromyography* (recording electrical impulses from muscles as they contract). One method of studying muscle contraction particularly useful for the purposes of our discussion is called simply *myography*, a term that means "muscle graphing." This is a procedure in which the force or tension from the contraction of an isolated muscle is recorded as a line that rises and falls as the muscle contracts and relaxes (Figure 12-19). To get the muscle to contract, an electrical stimulus of sufficient intensity (the **threshold stimulus**) is applied to the muscle. A single, brief threshold stimulus produces a quick jerk of the muscle, called a **twitch contraction.**

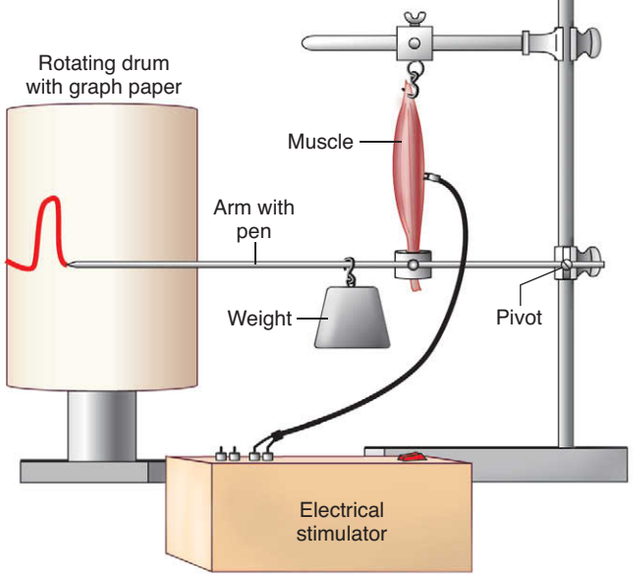


FIGURE 12-19

Myography. This classic type of myograph, called a *kymograph,* records muscle contractions as graphs showing changes in length. An isolated muscle moves the pen upward during contraction, and the weight pulls the muscle and pen downward as the muscle relaxes. A change in tension produces this change in length. Electrical voltage simulates a nerve impulse to stimulate the fibers in the muscle. Modern myography often uses computer-based systems that record similar muscle tension graphs.

The Twitch Contraction

The quick, jerky twitch contraction seen in a myogram serves as the fundamental model for how muscles operate. The myogram of a twitch contraction shown in Figure 12-20 shows that the muscle does not begin to contract at the instant of stimulation but rather a fraction of a second later. The muscle then increases its tension (or shortens) until a peak is reached, after which it gradually returns to its resting state. These three phases of the twitch contraction are called, respectively, the *latent period*, the *contraction phase*, and the *relaxation phase*. The entire twitch usually lasts less than one tenth of a second.

During the latent period, the impulse initiated by the stimulation travels through the sarcolemma and T tubules to the SR, where it triggers the release of calcium ions into the sarcoplasm. It is not until the calcium binds to troponin and sliding of the myofilaments begins that contraction is observed. After a few milliseconds, the forceful sliding of the myofilaments ceases and relaxation begins. By the end of the relaxation phase, all of the myosin-actin reactions in all the fibers have ceased.

Twitch contractions of muscle organs rarely happen in the body. Even if we tried to make our muscles twitch voluntarily, they won't. Instead, our nervous system subconsciously "smoothes out" the movements to prevent injury and to make our movements more useful to us. Sustaining a smooth contraction is something that we will discuss a little later. But, to begin our discussion, a look at the twitch contraction gives us important insight about the mechanisms of more typical types of muscle organ contractions.

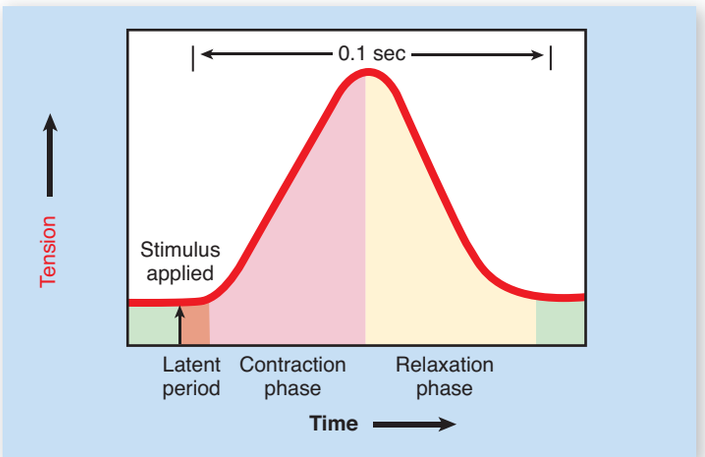


FIGURE 12-20

The twitch contraction. Three distinct phases are apparent: **(1)** the latent period, **(2)** the contraction phase, and **(3)** the relaxation phase.

Treppe: The Staircase Phenomenon

One interesting effect that can be seen in myographic studies of the twitch contraction is called **treppe,** or the *staircase phenomenon.* Treppe is a gradual, steplike increase in the strength of contraction that can be observed in a series of twitch contractions that occur about 1 second apart (Figure 12-21, *B*).

In other words, a muscle contracts more forcefully after it has contracted a few times than when it first contracts—a principle used by athletes when they warm up. Several factors contribute to this phenomenon. For example, in warm muscle fibers, calcium ions diffuse through the sarcoplasm more efficiently and more actin-myosin reactions occur. In addition, calcium ions accumulate in the sarcoplasm of muscles that have not had time to relax and pump much of the calcium back into their SR. Thus, up to a point, a warm fiber contracts more strongly than does a cool fiber. Thus, after the first few stimuli, muscle responds to successive stimuli with maximal contractions. Eventually though, it will respond with less and less strong contractions. The relaxation phase becomes shorter and finally disappears entirely. In other words, the muscle stays partially contracted—an abnormal state of prolonged contraction called *contracture.*

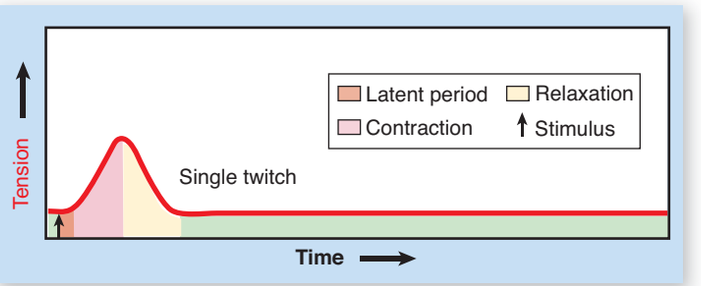
Repeated stimulation of muscle in time lessens its excitability and contractility and may result in **muscle fatigue,** a condition in which the muscle does not respond to the strongest stimuli. Complete muscle fatigue can be readily induced in an isolated muscle but very seldom occurs in the body (Box 12-5).

Tetanus

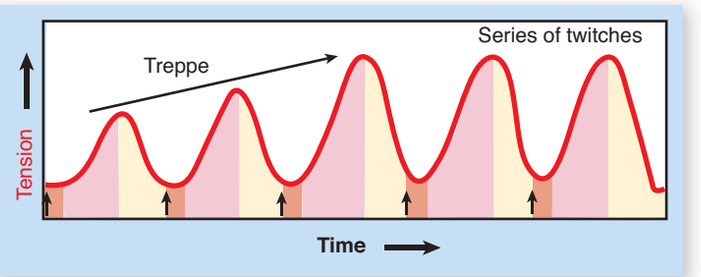
The concept of the simple twitch can help us understand the smooth, sustained types of contraction that are commonly observed in the body. Such smooth, sustained contractions are called *tetanic contractions* or, simply, **tetanus.** Figure 12-21, *C,* shows that if a series of stimuli come in a rapid enough succession, the muscle does not have time to relax completely before the next contraction phase begins. Muscle physiologists describe this effect as *multiple wave summation*—so named because it seems as though multiple twitch waves have been added together to sustain muscle tension for a longer time. The type of tetanus produced when very short periods of relaxation occur between peaks of tension is called *incomplete tetanus.* It is "incomplete" because the tension is not sustained at a completely constant level. Figure 12-21, *D,* shows that when the frequency of stimuli increases, the distance between peaks of tension decrease to a point at which they seem to fuse into a single, sustained peak. This produces a very smooth type of tetanic contraction called *complete tetanus.*

Figure 12-22 shows the role of calcium in maintaining tetanus. Recall that it is a surge in intracellular calcium (from the SR) that triggers contraction (see Box 12-2, p. 349). When there is a single stimulus, there is a single surge in intracellular calcium and thus a single, rapid contraction. When there is a series of stimuli, close together in time, the intracellular calcium surges overlap and maintain a high level of calcium availability for a longer time. The force of contraction can be maintained as long as the calcium remains at a high enough level in the muscle fibers.

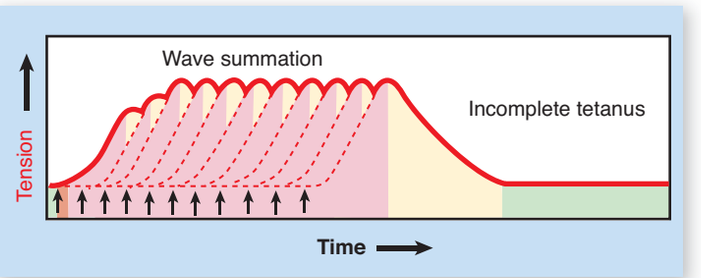
In a normal body, tetanus results from two factors working at the same time. One factor is the rapid-fire stimulation of nerve fibers



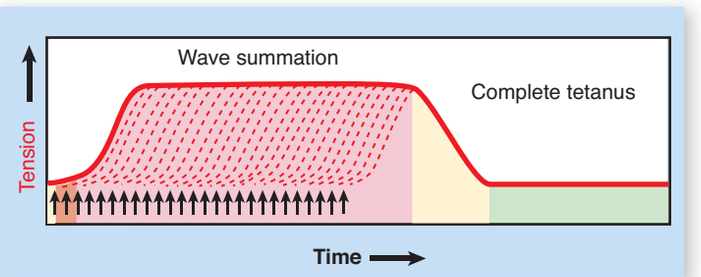
A



B



C



D

FIGURE 12-21

Myograms of various types of muscle contractions. A, A single twitch contraction. **B,** The treppe phenomenon, or "staircase effect," is a steplike increase in the force of contraction over the first few in a series of twitches. **C,** Incomplete tetanus occurs when a rapid succession of stimuli produces "twitches" that seem to add together (wave summation) to produce a rather sustained contraction. **D,** Complete tetanus is a smoother sustained contraction produced by the summation of "twitches" that occur so close together that the muscle cannot relax at all.

Box 12-5 | SPORTS and FITNESS

Muscle Fatigue

Broadly defined, **muscle fatigue** is simply a state of exhaustion (a loss of strength or endurance) produced by strenuous muscular activity.

Physiological muscle fatigue is caused by any combination of local failure in the steps of muscle contraction (see Box 12-2 on p. 349).

For example, failure of the sodium-potassium pumps to maintain the ion concentration gradients needed to produce action potentials may cause fatigue. Individual muscle fibers become less contractile until the proper Na^+ and K^+ gradients can be restored.

Depending on the muscle fiber type and the kind of activity, the cause may be a relative lack of ATP, which renders the myosin heads incapable of producing the force required for further muscle contractions. The low levels of adenosine triphosphate (ATP) that produce fatigue may result from depletion of oxygen or glucose in muscle fibers or from an inability to regenerate ATP quickly enough. Thus depletion of glycogen in the muscle often produces fatigue.

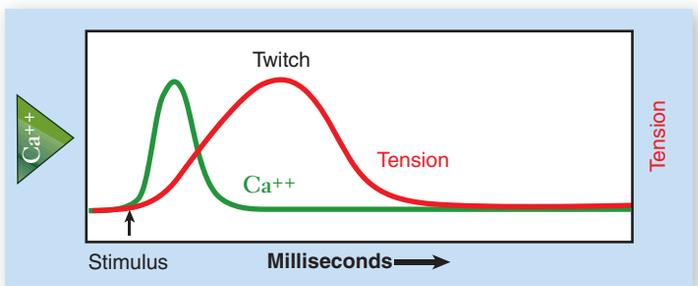
Accumulation of phosphate molecules (from the breakdown of ATP) may further interfere with contraction by binding to calcium ions that would otherwise be participating in the contraction process. Decreased pH from the buildup of lactic acid may also contribute to physiological fatigue by interfering with normal chemical reactions in the muscle fiber.

Muscle tissue can limit physiological fatigue by increasing blood flow, thus bringing in additional oxygen and glucose—and taking away more CO_2 and lactic acid. Muscle tissue also produces hormones that trigger the release of more glucose and other nutrients into the bloodstream. But eventually a muscle may not be able to sustain its work.

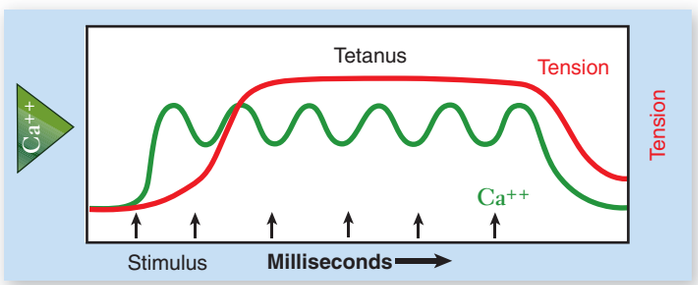
Under ordinary circumstances, however, complete physiological fatigue seldom occurs. It is usually *psychological fatigue* that produces the exhausted feeling that stops us from continuing a muscular activity. Such fatigue is regulated by feedback loops that increase our feelings of fatigue as muscles work hard and thus protect the muscles from reaching a point where they could become seriously impaired.

In physiological muscle fatigue we *cannot* contract our muscles, but in psychological muscle fatigue, we simply *will not* contract our muscles because we feel tired.

that permits wave summation to occur in each fiber. Another factor is the coordinated contractions of different motor units within the muscle organ. These motor units fire in an asynchronous, overlapping time sequence to produce a "relay team" effect that results in a sustained contraction. Tetanus is the kind of contraction exhibited by normal skeletal muscle organs most of the time.



A



B

FIGURE 12-22

Role of calcium in twitch and tetanus. A, A single, sudden increase in calcium (Ca^{++}) availability triggers the twitch contraction. **B,** Repeated stimuli maintain a high level of calcium, permitting sustained (tetanic) contraction.

| QUICK CHECK |

11. What are the three phases of a twitch contraction? What molecular events occur during each of these phases?
12. What is the difference between a twitch contraction and a tetanic contraction?
13. How does the treppe effect relate to the warm-up exercises of athletes?
14. What is tetanus? Is it normal?

Muscle Tone

A **tonic contraction** (*tonus*, "tone") is a continual, partial contraction in a muscle organ. At any one moment a small number of the total fibers in a muscle contract and produce tautness of the muscle rather than a recognizable contraction and movement. Different groups of fibers scattered throughout the muscle contract in relays. Tonic contraction, or **muscle tone,** is the low level of continuous contraction characteristic of the muscles of normal individuals when they are awake. It is particularly important for maintaining posture. A striking illustration of this fact is the following: when a person loses consciousness, muscles lose their tone, and the person collapses in a heap, unable to maintain a sitting or standing posture. Muscles with less tone than normal are described as *flaccid*, and those with more than normal tone are called *spastic*.

Muscle tone is maintained by negative feedback mechanisms centered in the nervous system, specifically in the spinal cord. Stretch sensors in the muscles and tendons detect the degree of stretch in a muscle organ and feed this information back to an integrator mechanism in the spinal cord. When the actual stretch (detected by the stretch receptors) deviates from the set point stretch, signals sent via the somatic motor neurons adjust the strength of tonic contraction. This type of subconscious mechanism is often called a *spinal reflex* (discussed further in Chapters 13 to 15).

GRADED STRENGTH PRINCIPLE

Skeletal muscles contract with varying degrees of strength at different times—a fact called the **graded strength principle.** Because muscle organs can generate different grades of strength, we can match the force of a movement to the demands of a specific task (Box 12-6).

Various factors contribute to the phenomenon of graded strength. We have already discussed some of these factors. For example, we stated that the metabolic condition of individual fibers influences their capacity to generate force. Thus, if many fibers of a muscle organ are unable to maintain a high level of ATP and become fatigued, the entire muscle organ suffers some loss in its ability to generate maximum force of contraction. On the other hand, the improved metabolic conditions that produce the treppe effect allow a muscle organ to increase its contraction strength.

Another factor that influences the grade of strength exhibited by a muscle organ is the number of fibers contracting simultaneously. Obviously, the more muscle fibers contracting at the same time, the stronger the contraction of the entire muscle organ. How large this number is depends on how many motor units are activated or **recruited.** Recruitment of motor units, in turn, depends on the

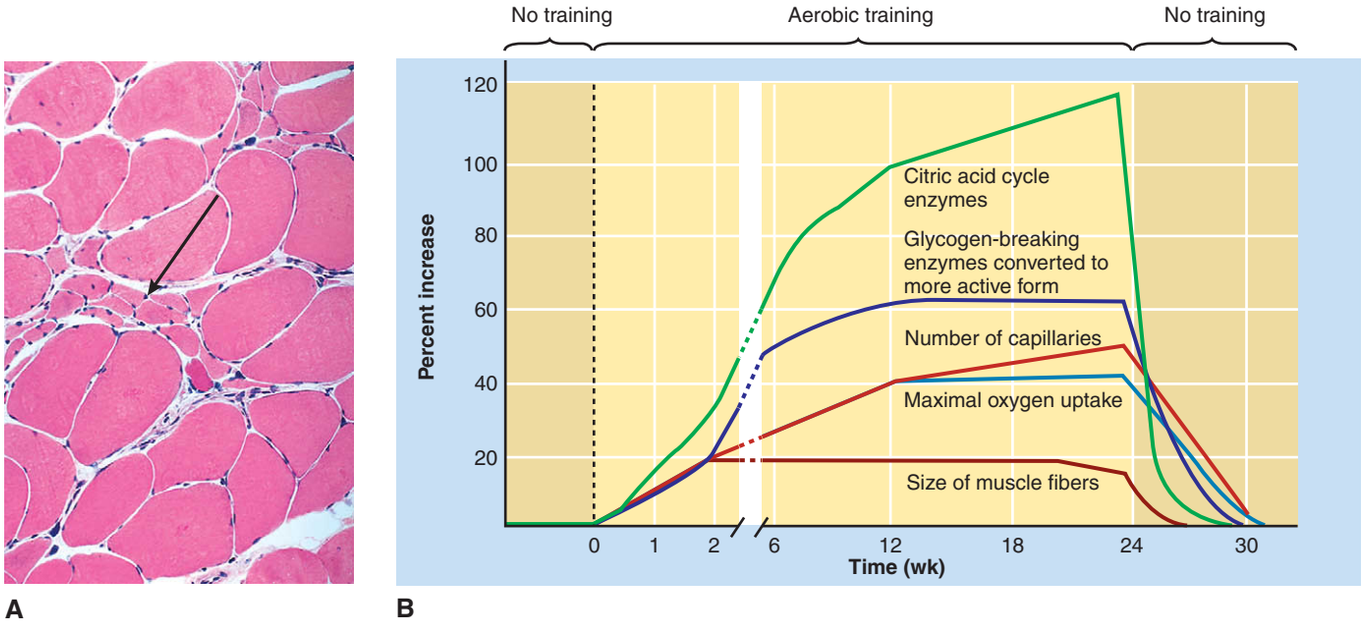
Box 12-6 | Effects of Exercise on Skeletal Muscles

Most of us believe that exercise is good for us, even if we have no idea what or how many specific benefits can come from it. Some of the good consequences of regular, properly practiced exercise are greatly improved muscle tone, better posture, more efficient heart and lung function, less fatigue, and looking and feeling better.

Skeletal muscles undergo changes that correspond to the amount of work that they normally do. During prolonged inactivity, muscles usually shrink in mass, a condition called **disuse atrophy** (part *A* of the figure). Disuse atrophy may result from general lack of use, but it is most often seen when a body part is immobilized by a cast or when the motor nerves are damaged. Exercise, on the other hand, may cause an increase in muscle size called **hypertrophy.**

Muscle hypertrophy can be enhanced by **strength training,** which involves contracting muscles against heavy resistance. Isometric exercises and weightlifting are common strength-training activities. This type of training results in increased numbers of satellite cells merging with muscle fibers to form additional myofilaments in each muscle fiber. Although the number of muscle fibers stays the same, the increased number of myofilaments greatly increases the mass of the muscle. When strength training stops, the extra myofilaments are dismantled and the muscle atrophies. However, the extra nuclei may remain for years and thus enable a quick restoration of muscle mass and strength if strength training resumes.

Endurance training, often called **aerobic training** (part *B* of the figure), does not usually result in as much muscle hypertrophy as strength training does. Instead, this type of exercise program increases a muscle's ability to sustain moderate exercise over a long period. Aerobic activities such as running, bicycling, or other primarily isotonic movements increase the number of blood vessels in a muscle (see Figure 12-15). The increased blood flow allows more efficient delivery of oxygen and glucose to muscle fibers during exercise. Aerobic training also causes an increase in the number of mitochondria in muscle fibers. This allows production of more ATP as a rapid energy source.



A, Disuse atrophy. The arrow points to a group of muscle fibers that have atrophied from disuse (in this case from nerve damage). Notice how much smaller they are than the surrounding, normal fibers. **B, Effects of aerobic training.** The graph shows that aerobic training increases the metabolic condition of muscles mainly by increasing levels of enzymes and the availability of oxygen. Only moderate increases in muscle fiber size occur.

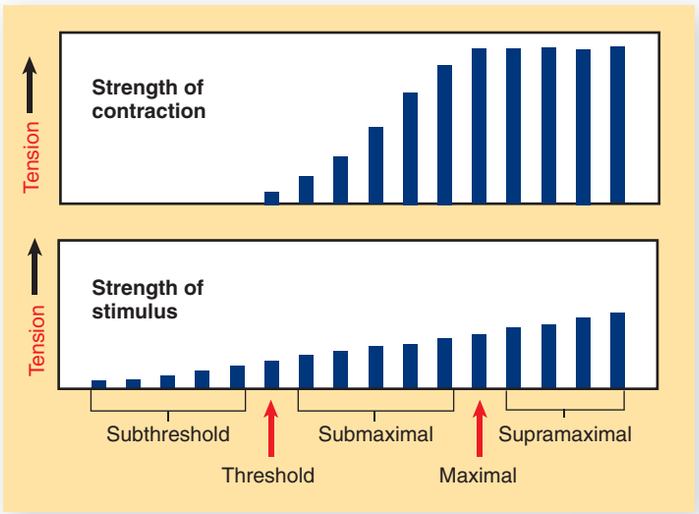


FIGURE 12-23

The strength of muscle contraction compared with the strength of the stimulus. After the threshold stimulus is reached, a continued increase in stimulus strength produces a proportional increase in muscle strength until the maximal level of contraction strength is reached.

intensity and frequency of stimulation. In general, the more intense and the more frequent a stimulus, the more motor units that are recruited and the stronger the contraction. Figure 12-23 shows that increasing the strength of the stimulus beyond the threshold level of the most sensitive motor units causes an increase in the strength of contraction. As the threshold level of each additional motor unit is reached, the strength of contraction increases. This process continues as the strength of stimulation increases until the maximal level of contraction is reached. At this point, the limits of the muscle organ to recruit new motor units have been reached. Even if stimulation increases above the maximal level, the muscle cannot contract any more strongly. As long as the supply of ATP holds out, the muscle organ can sustain a tetanic contraction at the maximal level, with motor units contracting and relaxing in overlapping "relays" (see Figure 12-21, *D*).

The maximal strength that a muscle can develop is directly related to the initial length of its fibers—this is the *length-tension relationship* (Figure 12-24). A muscle that begins a contraction from a short initial length cannot develop much tension because its sarcomeres are already compressed. Conversely, a muscle that begins a contraction from an overstretched initial length cannot develop much tension because the thick myofilaments are too far away from the thin myofilaments to effectively pull them and thus compress the sarcomeres. The strongest maximal contraction is possible only when the muscle organ has been stretched to an optimal initial length. To illustrate this point, extend your elbow fully and try to contract the *biceps brachii* muscle on the ventral side of the upper part of your arm. Now flex the elbow just a little and contract the biceps again. Try it a third time with the elbow completely flexed. The greatest tension—seen as the largest "bulge" of the biceps—occurs when the elbow is partly flexed and the biceps only moderately stretched.

Another factor that influences the strength of a skeletal muscle contraction is the amount of load imposed on the muscle. Within certain limits, the heavier the load, the stronger the contraction. Lift your hand with palm up in front of you and then put this book in your palm. You can feel your arm muscles contract more strongly as the book is placed in your hand. This occurs because of a *stretch reflex*, a response in which the body tries to maintain

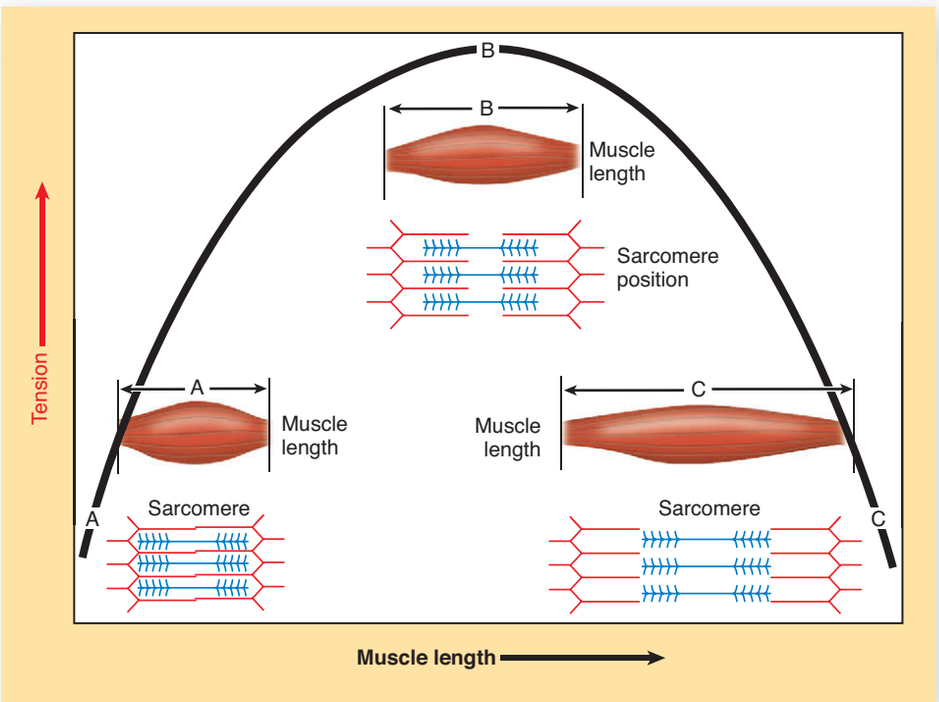


FIGURE 12-24

The length-tension relationship. As this graph of muscle tension shows, the maximum strength that a muscle can develop is directly related to the initial length of its fibers. At a short initial length, the sarcomeres are already compressed, and thus the muscle cannot develop much tension (position *A*). Conversely, the thick and thin myofilaments are too far apart in an overstretched muscle to generate much tension (position *C*). Maximum tension can be generated only when the muscle has been stretched to a moderate, optimal length (position *B*).

constancy of muscle length (Figure 12-25). An increased load threatens to stretch the muscle beyond the set point length that you are trying to maintain. Your body exhibits a negative feedback response when it detects the increased stretch caused by an increased load, feeds the information back to an integrator in the nervous system, and increases its stimulation of the muscle to counteract the stretch. This reflex maintains a relatively constant muscle length as load is increased up to a maximum sustainable level. When the load becomes too heavy and thus threatens to cause injury to the muscle or skeleton, the body abandons this reflex and forces you to relax and drop the load.

The major factors involved in the graded strength principle are summarized in Figure 12-26.

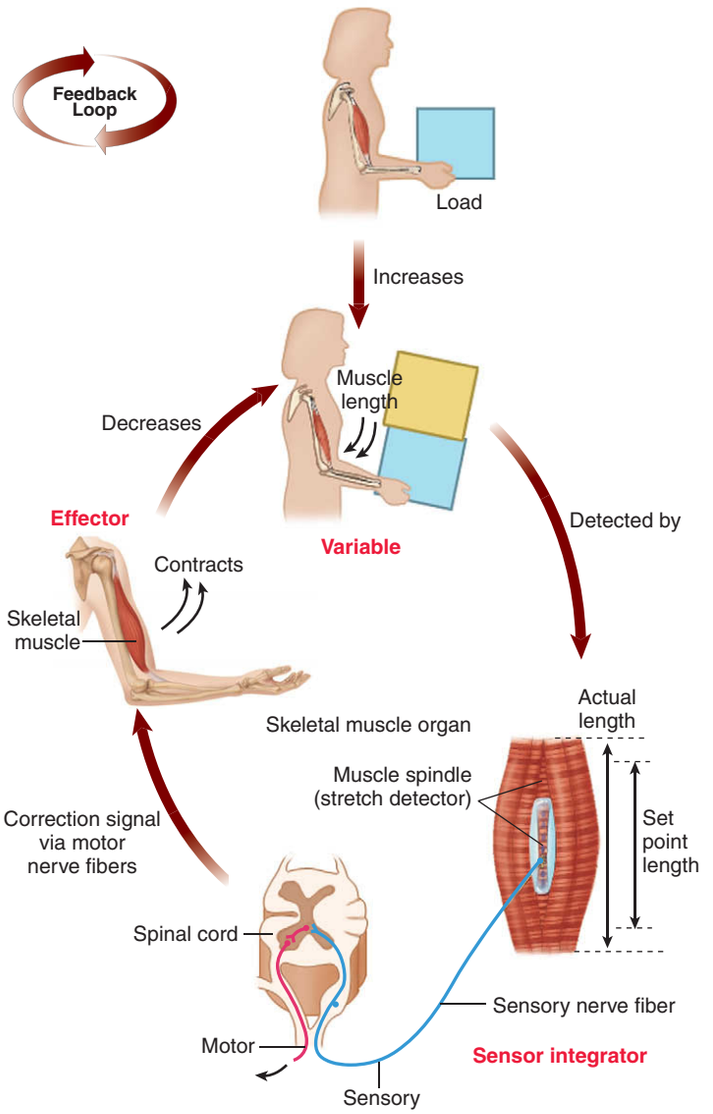


FIGURE 12-25

The stretch reflex. The strength of a muscle organ can be matched to the load imposed on it by a negative feedback response centered in the spinal cord. Increased stretch (caused by increased load) is detected by a sensory nerve fiber attached to a muscle cell (called a *muscle spindle*). The information is integrated in the spinal cord and a correction signal is relayed through motor neurons back to the same muscle, which increases tension to return to the set point muscle length.

Isotonic and Isometric Contractions

The term *isotonic* literally means "same tension" (*iso-*, "equal," *-tonic*, "relating to tension"). An **isotonic contraction** is a contraction in which the tone or tension within a muscle remains the same as the length of the muscle changes (Figure 12-27, A). Because the muscle is moving against its resistance (load) in an isotonic contraction, the energy of contraction is used to pull on the thin myofilaments and thus change the length of a fiber's sarcomeres. Put another way, in isotonic contractions the myosin cross bridges "win" the tug-of-war against a light load and are thus able to pull the thin myofilaments. Because the muscle is moving in an isotonic contraction, it is also called *dynamic tension*.

There are two basic varieties of isotonic contractions (see Figure 12-27, A). **Concentric contractions** are those in which the movement results in shortening of the muscle, as when you pick up this book. **Eccentric contractions** are those in which the movement results in lengthening of the muscle being contracted. For example, when you slowly lower the book you have just picked up, you are contracting the same muscle you just used to lift it—but this time you are lengthening the muscle, not shortening it.

An **isometric contraction,** in contrast to an isotonic contraction, is a contraction in which muscle length remains the same while muscle tension increases (Figure 12-27, *B*). The term *isometric* literally means "same length." You can observe isometric contraction by lifting up on a stationary handrail and feeling the tension increase in your arm muscles. Isometric contractions can

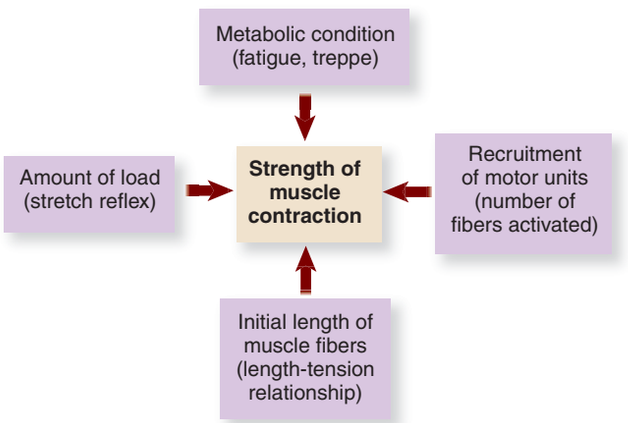


FIGURE 12-26

Factors that influence the strength of muscle contraction.

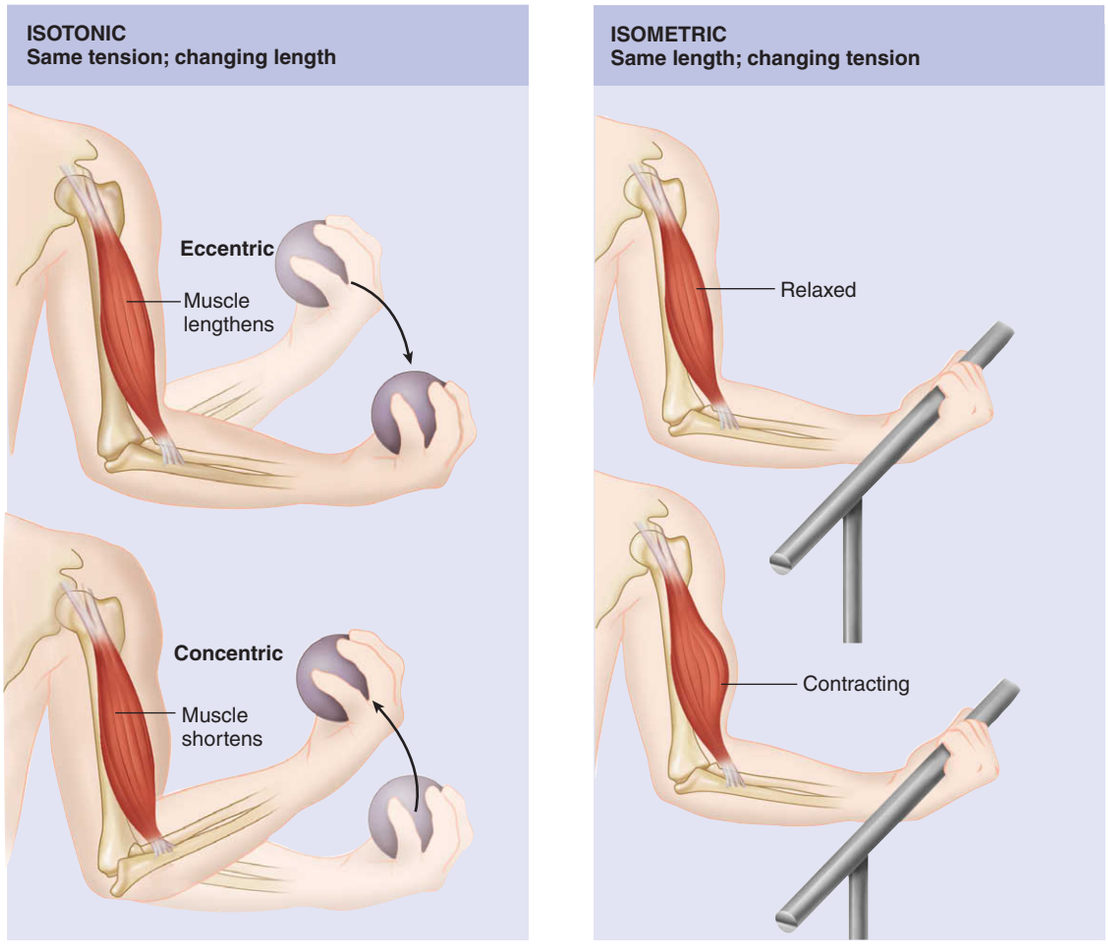


FIGURE 12-27

Isotonic and isometric contraction. A, In isotonic contraction the muscle shortens and produces movement. Concentric contractions occur when the muscle shortens during the movement. Eccentric contractions occur when the contracting muscle lengthens. **B,** In isometric contraction the muscle pulls forcefully against a load but does not shorten because it cannot overcome the resistance.

do work by "tightening" to resist a force, but they do not produce movements. In isometric contractions, the tension produced by the "power stroke" of the myosin cross bridges cannot overcome the load placed on the muscle. Using the tug-of-war analogy, we can say that in isometric contractions the myosin cross bridges reach a "draw"—they hold their own against the load placed on the muscle but do not make any progress in sliding the thin myofilaments. Because muscles remain stable during isometric contraction, it is also called *static tension*.

| QUICK CHECK |

15. What is meant by the term *muscle tone?*
16. Name four factors that influence the strength of a skeletal muscle contraction.
17. What is meant by the phrase "recruitment of motor units?"
18. What is the difference between isotonic and isometric contractions? Concentric and eccentric?

FUNCTION OF CARDIAC AND SMOOTH MUSCLE TISSUE

Cardiac and smooth muscle tissues operate by mechanisms similar to those in skeletal muscle tissues. Detailed study of cardiac and smooth muscle function will be set aside until we discuss specific smooth and cardiac muscle organs in later chapters. However, it may be helpful to preview some of the basic principles of cardiac and smooth muscle physiology so that we can compare them with those that operate in skeletal muscle tissue. Table 12-1 summarizes the characteristics of the three major types of muscle.

Cardiac Muscle

Cardiac muscle, also known as *striated involuntary muscle*, is found in only one organ of the body: the heart. Forming the bulk of the wall of each heart chamber, cardiac muscle contracts rhythmically and continuously to provide the pumping action necessary to maintain a relative constancy of blood flow through the internal environment. As you shall see, its physiological mechanisms are well adapted to this function.

The functional anatomy of cardiac muscle tissue resembles that of skeletal muscle to a degree, but it exhibits certain unique features related to its role of continuously pumping blood. As Figure 12-28 shows, each cardiac muscle fiber contains parallel myofibrils. Each myofibril includes sarcomeres that give the whole fiber a striated appearance. However, cardiac muscle fiber does not taper like skeletal muscle fiber but, instead, forms strong, electrically coupled junctions (intercalated disks) with other fibers. This feature, along with the branching exhibited by individual cells, allows cardiac fibers to form a continuous, electrically coupled mass called a **syncytium** (meaning "unit of combined cells"). Cardiac muscles thus form a continuous, contractile band around the heart chambers that conducts a single impulse across a virtually continuous sarcolemma—features necessary for an efficient, coordinated pumping action.

Unlike skeletal muscle, in which a nervous impulse excites the sarcolemma to produce its own impulse, cardiac muscle is self-exciting. Cardiac muscle cells thus exhibit a continuing rhythm of excitation and contraction on their own, although the rate of self-induced impulses can be altered by nervous or hormonal input. Figure 12-29 shows that impulses triggering

TABLE 12-1 Characteristics of Muscle Tissues

	SKELETAL	CARDIAC	SMOOTH
Principal location	Skeletal muscle organs	Wall of heart	Walls of many hollow organs
Principal functions	Movement of bones, heat production, posture	Pumping of blood	Movement in walls of hollow organs (peristalsis, mixing of fluids)
Type of control	Voluntary	Involuntary	Involuntary
Structural features			
Striations	Present	Present	Absent
Nucleus	Many near the sarcolemma	Single (sometimes double); near the center of the cell	Single; near the center of the cell
T tubules	Narrow; form triads with the SR	Large diameter; form diads with the SR, regulate Ca^{++} entry into the sarcoplasm	Absent
Sarcoplasmic reticulum	Extensive; stores and releases Ca^{++}	Less extensive than in skeletal muscle	Very poorly developed
Cell junctions	No gap junctions	Intercalated disks	*Single-unit*:* many gap junctions *Multiunit:* few gap junctions
Contraction style	Rapid twitch contractions of motor units usually summate to produce sustained tetanic contractions; must be stimulated by a neuron	Syncytium of fibers compress the heart chambers in slow, separate contractions (does not exhibit tetanus or fatigue); exhibits autorhythmicity	*Single-unit:* electrically coupled sheets of fibers contract autorhythmically and produce peristalsis or mixing movements *Multiunit:* individual fibers contract when stimulated by a neuron

*Also referred to as *visceral smooth muscle tissue.*
SR, Sarcoplasmic reticulum.

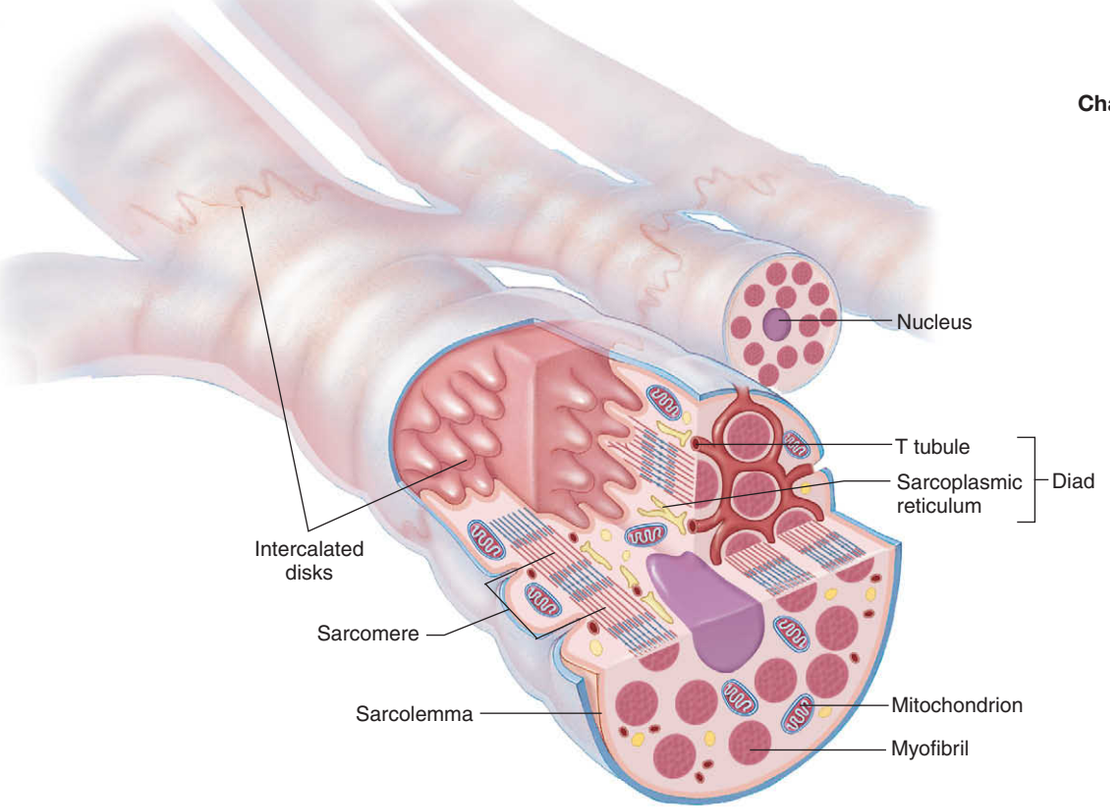


FIGURE 12-28

Cardiac muscle fiber. Unlike other types of muscle fibers, cardiac muscle fiber is typically branched and forms junctions, called *intercalated disks,* with adjacent cardiac muscle fibers. Like skeletal muscle fibers, cardiac muscle fibers contain sarcoplasmic reticula and T tubules—although these structures are not as highly organized as in skeletal muscle fibers.

cardiac muscle contractions are much more prolonged than those triggering skeletal muscle contractions. Because the sarcolemma of cardiac muscle sustains each impulse longer than in skeletal muscle, Ca^{++} remains in the sarcoplasm longer. This means that even though many adjacent cardiac muscle cells contract simultaneously, they exhibit a prolonged contraction rather than a rapid twitch. It also means that impulses cannot come rapidly enough to produce tetanus. Because it cannot sustain long tetanic contractions, cardiac muscle does not normally run low on ATP and thus does not experience fatigue. Obviously, this characteristic of cardiac muscle is vital to keeping the heart continuously pumping.

Although cardiac muscle fiber has T tubules and SR, they are arranged a little differently than in skeletal muscle fibers. The T tubules are larger, and they form diads (double structures) rather than triads (triple structures), with a rather sparse SR. Much of the calcium that enters the sarcoplasm during contraction enters from outside the cells through the T tubules rather than from storage in the SR.

The structure and function of the heart are discussed further in Chapters 21 and 22.

Smooth Muscle

As we mentioned in Chapter 6, smooth muscle is composed of small, tapered cells with single nuclei. Smooth muscle cells do not have T tubules and have only loosely organized sarcoplasmic reticula. The calcium required for contraction comes from

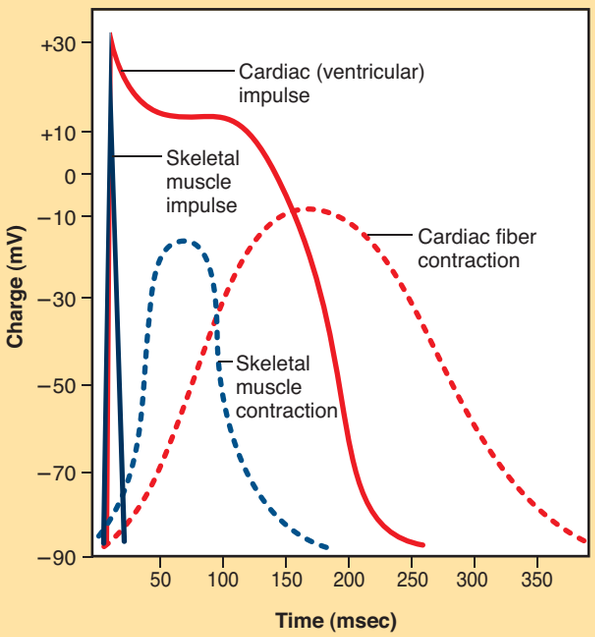


FIGURE 12-29

Cardiac and skeletal muscle contractions compared. A brief nerve impulse triggers a brief twitch contraction in skeletal muscle *(blue)*, but a prolonged impulse in the heart tissue produces a rather slow, drawn out contraction in cardiac muscle *(red)*.

outside the cell and binds to a protein called *calmodulin*, rather than to troponin, to trigger a contraction event.

The lack of striations in smooth muscle fibers results from the fact that the thick and thin myofilaments are arranged quite differently than in skeletal or cardiac muscle fibers. As Figure 12-30 shows, thin arrangements of myofilaments crisscross the cell and attach at their ends to the cell's plasma membrane. When cross bridges pull the thin filaments together, the muscle "balls up" and thus contracts the cell. Because the myofilaments are not organized into sarcomeres, they have more freedom of movement and as a result can contract a smooth muscle fiber to shorter lengths than in skeletal and cardiac muscle.

There are two types of smooth muscle tissue: *single-unit* and *multiunit* (Figure 12-31) smooth muscle.

In *visceral*, or **single-unit, smooth muscle,** gap junctions join individual smooth muscle fibers into large, continuous sheets—much like the syncytium of fibers observed in cardiac muscle. This type of smooth muscle is the most common, and it forms a muscular layer in the walls of many hollow structures such as the digestive, urinary, and reproductive tracts. Like cardiac muscle, this type of smooth muscle commonly exhibits a rhythmic self-excitation, or *autorhythmicity* (meaning "self-rhythm"), that spreads across the entire tissue. When these rhythmic, spreading waves of contraction become strong enough, they can push the contents of a hollow organ progressively along its lumen. This phenomenon, called *peristalsis*, moves food along the digestive tract, assists the flow of urine to the bladder, and pushes a baby out of the womb during labor. Such contractions can also be coordinated to produce mixing movements in the stomach and other organs.

Multiunit smooth muscle tissue does not act as a single unit (as in visceral muscle) but instead is composed of many independent single-cell units. Each independent fiber does not usually generate its own impulse but rather responds only to nervous input. Although this type of smooth muscle can form thin sheets, as in the walls of large blood vessels, it is more often found in bundles (for example, the *arrector pili* muscles of the skin or muscles that control the lens of the eye) or as single fibers (such as those surrounding small blood vessels).

The structure and function of smooth muscle organs are discussed in later chapters.

| QUICK CHECK |

19. How do slow, separate, autorhythmic contractions of cardiac muscle make it well suited to its role in pumping blood?
20. What produces the striations in cardiac muscle?
21. How are myofilaments arranged in a smooth muscle fiber?
22. What is the difference between single-unit and multiunit smooth muscle?

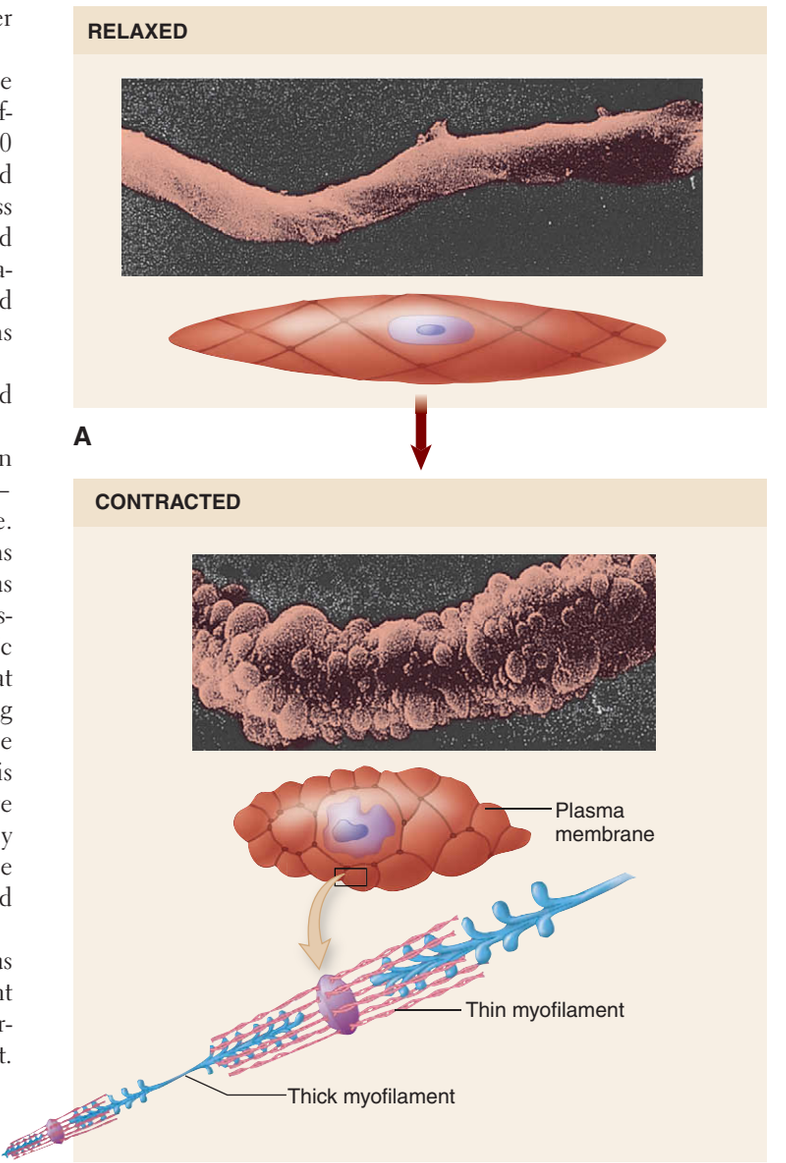


FIGURE 12-30

Smooth muscle fiber. A, Thin bundles of myofilaments span the diameter of a relaxed fiber. The scanning electron micrograph *(above)* shows that the surface of the cell is rather flat when the fiber is relaxed. **B,** During contraction, sliding of the myofilaments causes the fiber to shorten by "balling up." The micrograph *(above)* shows that the fiber becomes shorter and thicker and exhibits "dimples" where the myofilament bundles are pulling on the plasma membrane.

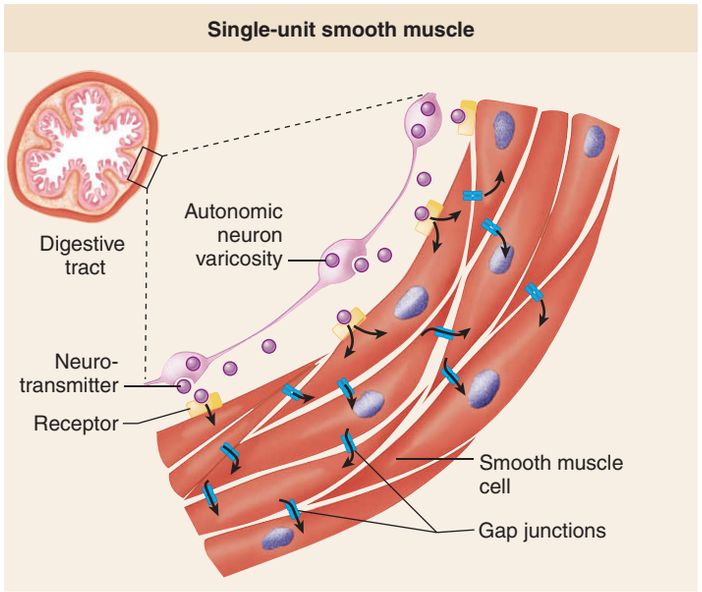


FIGURE 12-31

Types of smooth muscle. A, Single-unit (visceral) smooth muscle. Neurotransmitters released from varicosities (bulges) in the nerve fiber trigger impulses in the smooth muscle membranes—an event that is transmitted to adjacent muscle fibers through gap junctions. Thus a large mass of muscle fibers acts as a single unit. **B,** Multiunit smooth muscle. Each muscle fiber is triggered independently by nerve stimulation.

the BIG picture

Muscle Tissue and the Whole Body

The function of all three major types of muscle (skeletal, smooth, and cardiac) is integral to the function of the entire body. What does the function of muscle tissue contribute to homeostasis of the whole body? First, all three types of muscle tissue provide the movement necessary for survival. Skeletal muscle moves the skeleton so that we can seek shelter, gather food, and defend ourselves. All three muscle types produce movements that power vital homeostatic mechanisms such as breathing, blood flow, digestion, and urine flow.

The relative constancy of the body's internal temperature could not be maintained in a cool external environment if not for the "waste" heat generated by muscle tissue—especially the large mass of skeletal muscle found throughout the body. Maintenance of a relatively stable body position—posture—is also a primary function of the skeletal muscular system. Posture, specific body movements, and other contributions of the skeletal muscular system to homeostasis of the whole body were discussed in Chapter 11. The homeostatic roles of smooth muscle organs and the cardiac muscle organ (the heart) are examined in later chapters.

Like all tissues of the body, muscle tissue gives and takes. A number of systems support the function of muscle tissues. Without these systems, muscle would cease to operate. For example, the nervous system directly controls the contraction of skeletal muscle and multiunit smooth muscle. It also influences the rate of rhythmic contractions in cardiac muscle and visceral smooth muscle. The endocrine system produces hormones that assist the nervous system in regulation of muscle contraction throughout the body. The blood delivers nutrients and carries away waste products. Nutrients for the muscle are ultimately procured by the respiratory system (oxygen) and digestive system (glucose and other foods). The respiratory system also helps get rid of the waste of muscle metabolism, as does the urinary system. The liver processes lactic acid produced by muscles and converts it back to glucose. The immune system helps defend muscle tissue against infection and cancer—as it does for all body tissues. The fibers that make up muscle tissues, then, are truly members of the large, interactive "society of cells" that forms the human body.

MECHANISMS of DISEASE

MAJOR MUSCULAR DISORDERS

As you might expect, muscle disorders, or **myopathies,** generally disrupt the normal movement of the body. In mild cases, these disorders vary from inconvenient to slightly troublesome. Severe muscle disorders, however, can impair the muscles used in breathing—a life-threatening situation.

Muscle Injury

Injuries to skeletal muscles caused by overexertion or trauma usually result in a muscle **strain.** Figure 12-32 shows an unusually severe muscle strain that resulted in a massive tear in the entire muscle organ. Muscle strains are characterized by muscle pain, or **myalgia** (my-AL-jee-ah), and involve overstretching or tearing of muscle fibers. If an injury occurs in the area of a joint and a ligament is damaged, the injury may be called a **sprain.** Any muscle inflammation, including that caused by a muscle strain, is termed **myositis** (my-oh-SYE-tis). If tendon inflammation occurs with myositis, as with a "charley horse," the condition is termed **fibromyositis** (fye-broh-my-oh-SYE-tis). Although inflammation may subside in a few hours or days, it usually takes weeks for damaged muscle fibers to repair. Some damaged muscle cells may be replaced by fibrous tissue, thereby forming scars. Occasionally, hard calcium is deposited in the scar tissue.

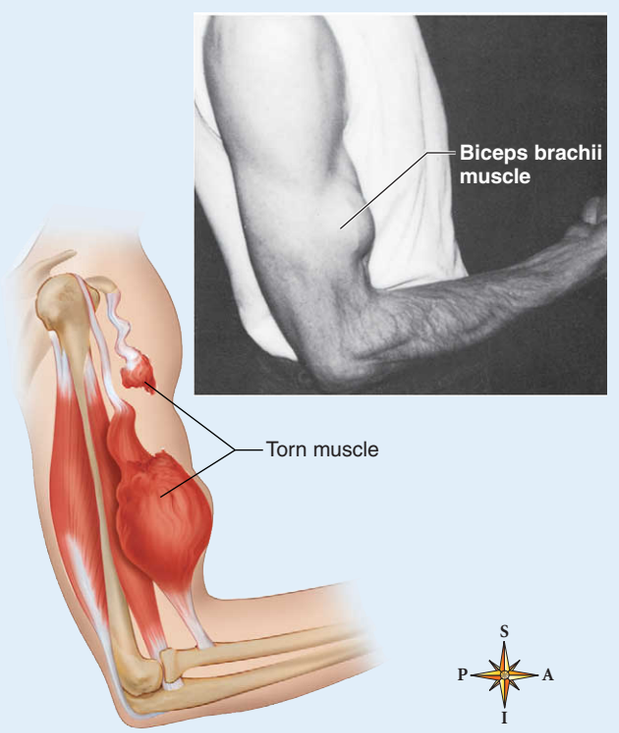


FIGURE 12-32

Muscle strain. Severe strain of the biceps brachii muscle. In a severe muscle strain, a muscle may break in two pieces and result in a visible gap in muscle tissue under the skin. Notice how the broken ends of the muscle reflexively contract (spasm) to form a knot of tissue.

Box 12-7 | HEALTH matters

Abnormal Muscle Contractions

Cramps are painful muscle spasms (involuntary twitches). Cramps often occur when a muscle organ is fatigued or mildly inflamed, but they can be a symptom of any irritation or ion and water imbalance.

Convulsions are abnormal, uncoordinated tetanic contractions of varying groups of muscles. Convulsions may result from a disturbance in the brain, or seizure, in which the output along motor nerves increases and becomes disorganized.

Fibrillation is an abnormal type of contraction in which individual fibers contract asynchronously rather than at the same time. This produces a flutter of the muscle but no effective movement. Fibrillation can also occur in cardiac muscle, where it reduces the heart's ability to pump blood.

Cramps often result from mild myositis or fibromyositis, but they can be a symptom of any irritation or an ion and water imbalance. Box 12-7 outlines a few types of abnormal muscle contractions.

Minor trauma to the body, especially a limb, may cause a muscle bruise, or **contusion.** Muscle contusions involve local internal bleeding and inflammation. Severe trauma to a skeletal muscle may cause a *crush injury.* Crush injuries greatly damage the affected muscle tissue, and the release of muscle fiber contents into the bloodstream can be life threatening. For example, the reddish muscle pigment myoglobin can accumulate in the blood and cause kidney failure.

Stress-induced muscle tension can result in myalgia and stiffness in the neck and back and is thought to be one cause of "stress headaches." Headache and back pain clinics use various strategies to treat stress-induced muscle tension. These treatments include massage, biofeedback, and relaxation training.

Muscle Infections

Several bacteria, viruses, and parasites may infect muscle tissue—often producing local or widespread myositis. For example, in trichinosis, widespread myositis is common. The muscle pain plus stiffness that sometimes accompanies influenza is another example.

One bacterial infection you have probably heard of is called *tetanus*—a confusing name because that word also refers to normal, sustained muscle contractions (see Figure 12-21). However, tetanus *the infection* is an abnormal condition caused by infection of the central nervous system with the bacterium *Clostridium tetani.* This bacterium releases a toxin called *tetanospasmin* that triggers overactivity of the nervous system, often involving painful spasms of the muscles throughout the body. Because the spasms frequently begin in the head and cause the jaw muscles to tense involuntarily, the infection is often called "lockjaw."

Once a tragically common disease, **poliomyelitis** is a viral infection of the nerves that control skeletal muscle movement. Although the disease can be asymptomatic, it often causes paralysis

that may progress to death. Although virtually eliminated in the United States as a result of a comprehensive vaccination program, it still affects millions in other parts of the world.

Muscular Dystrophy

Muscular dystrophy (DISS-troh-fee) is not a single disorder but a group of genetic diseases characterized by atrophy (wasting) of skeletal muscle tissues. Some, but not all, forms of muscular dystrophy can be fatal.

The common form of muscular dystrophy is **Duchenne** (doo-SHEN) **muscular dystrophy (DMD).** This form of the disease is also called *pseudohypertrophy* (meaning "false muscle growth") because the atrophy of muscle is masked by excessive replacement of muscle by fat and fibrous tissue. DMD is characterized by mild leg muscle weakness that progresses rapidly to include the shoulder muscles. The first signs of DMD are apparent at about 3 years of age, and the stricken child is usually severely affected within 5 to 10 years. Death from respiratory or cardiac muscle weakness often occurs by the time the individual is 21 years old.

DMD is caused by a mutation in the X chromosome, although other factors may be involved. DMD occurs primarily in boys. Because girls have two X chromosomes and boys only one, genetic diseases involving X chromosome abnormalities are more likely to occur in boys. This is true because girls with one damaged X chromosome may not exhibit an "X-linked" disease if their other X chromosome is normal (see Chapter 37). The gene involved in DMD normally codes for the protein **dystrophin** (DIS-trof-in), which forms strands in each skeletal muscle fiber and helps hold the cytoskeleton to the sarcolemma (see Figure 3-21 on p. 85). Dystrophin thus helps keep the muscle fiber from breaking during contractions. Normal dystrophin is missing in those with DMD because a deletion or mutation of part of the dystrophin gene causes the resulting protein to be nonfunctional (it has the wrong shape to do the job). Therefore, in DMD muscle fibers break apart more easily—causing the symptoms of progressive muscle weakness.

Myasthenia Gravis

Myasthenia gravis (my-es-THEE-nee-ah GRAH-vis) is a chronic disease characterized by muscle weakness, especially in the face and throat. Most forms of this disease begin with mild weakness and chronic muscle fatigue in the face, then progress to wider muscle involvement. An acute episode of widespread and severe muscle weakness is called a *myasthenic crisis*. A person in myasthenic crisis is in danger of dying of respiratory failure because of weakness in the respiratory muscles.

Myasthenia gravis is an autoimmune disease in which the immune system attacks the acetylcholine receptors in the sarcolemma of muscle cells and results in a defect in the conduction of nerve impulses at the neuromuscular junction. Nerve impulses from motor neurons are then unable to fully stimulate the affected muscle (see figures 12-7 and 12-8).

Hernias

Weakness of abdominal muscles can lead to a *hernia*, or protrusion, of an abdominal organ (commonly the small intestine or stomach) through an opening in the abdominal wall. There are several types of hernias.

| A&P CONNECT |

If you have not experienced a hernia before now, there is a good chance that one day you may. Hernias are quite common. See some examples of the common hernia types in ***Hernias*** online at ***A&P Connect.***

Evolve

LANGUAGE OF SCIENCE *(continued from p. 347)*

H band

hypertrophy
(hye-PER-troh-fee)
[*hyper-* **excessive**, *-troph-* **nourishment**, *-y* **state**]

I band

intermediate fiber
(in-ter-MEE-dee-it)
[*inter-* **between**, *-medi-* **middle**, *-ate* **of or like**]

isometric contraction
(eye-soh-MET-rik)
[*iso-* **equal**, *-metr-* **measure**, *-ic* **relating to**, *con-* **together**, *-tract-* **drag or draw**, *-tion* **process**]

isotonic contraction
(eye-soh-TON-ik)
[*iso-* **equal**, *ton-* **stretch or tension**, *-ic* **relating to**, *con-* **together**, *-tract-* **drag or draw**, *-tion* **process**]

lactic acid
(LAK-tik)
[*lact-* **milk**, *-ic* **relating to**, *acid* **sour**]

M line
(EM lyne)
[*M mittel* **middle**]

motor endplate
[*mot-* **movement**, *-or* **agent**]

motor neuron
(NOO-ron)
[*mot-* **movement**, *-or* **agent**, *neuron* **nerve**]

motor unit
[*mot-* **movement**, *-or* **agent**]

multiunit smooth muscle
[*multi-* **many**, *mus-* **mouse**, *-cle* **little**]

muscle fatigue
(fah-TEEG)
[*mus-* **mouse**, *-cle* **little**, *fatig-* **tire**]

muscle tone
[*mus-* **mouse**, *-cle* **little**, *ton-* **stretch or tension**]

myofibril
(my-oh-FYE-bril)
[*myo-* **muscle**, *-fibr-* **fiber**, *-il* **little**]

myofilament
(my-oh-FIL-ah-ment)
[*myo-* **muscle**, *-fila-* **thread**, *-ment* **thing**]

myoglobin
(my-oh-GLOH-bin)
[*myo-* **muscle**, *-glob-* **ball**, *-in* **substance**]

myosin (MY-oh-sin)
[*myos-* **muscle**, *-in* **substance**]

neuromuscular junction (NMJ)
(noo-roh-MUSS-kyoo-lar)
[*neuro-* **nerve**, - *mus-* **mouse**, *-cul-* **little**, *-ar* **relating to**]

posture
(POS-chur)
[*postur-* **position**]

recruit
[*re-* **again**, *-cruit* **grow**]

sarcolemma
(sar-koh-LEM-ah)
[*sarco-* **flesh**, *-lemma* **sheath**]
pl., sarcolemmae

sarcomere
(SAR-koh-meer)
[*sarco-* **flesh**, *-mere* **part**]

sarcoplasm
(SAR-koh-plaz-em)
[*sarco-* **flesh**, *-plasm* **substance**]

sarcoplasmic reticulum (SR)
(sar-koh-PLAZ-mik reh-TIK-yoo-lum)
[*sarco-* **flesh**, *-plasm-* **substance**, *-ic* **relating to**, *ret-* **net**, *-ic-* **relating to**, *-ul-* **little**, *-um* **thing**] *pl.,* reticula

LANGUAGE OF SCIENCE *(continued from p. 373)*

single-unit smooth muscle
[*mus-* **mouse**, *-cle* **little**]

sliding-filament model
(SLY-ding FILL-ah-ment MOD-uhl)

slow fiber

syncytium
(sin-SISH-ee-em)
[*syn-* **together**, *-cyt-* **cell**, *-um* **a thing**] *pl.,* syncytia

T tubule
(TEE TOOB-yool)
[*T* **transverse**]

tetanus
(TET-ah-nus)
[*tetanus* **tension**]

threshold stimulus
(THRESH-hold STIM-yoo-lus)
[*stimul-* **to excite**, *-us* **thing**]
pl., stimuli

tonic contraction
(TAHN-ik)
[*ton-* **to stretch**, *-ic* **relating to**, *con-* **together**, *-tract-* **drag or draw**, *-tion* **process**]

treppe
(TREP-ee)
[*treppe* **staircase**]

triad
(TRY-ad)
[*triad* **group of three**]

tropomyosin
(troh-poh-MY-oh-sin)
[*tropo-* **to turn**, *-myo-* **muscle**, *-in* **substance**]

troponin
(troh-POH-nin)
[*tropo-* **turn**, *-in* **substance**]

twitch contraction
[*con-* **together**, *-tract-* **drag or draw**, *-tion* **process**]

Z disk (also called Z line)
(ZEE lyne)
[*Z zwischen* **between**]

LANGUAGE OF MEDICINE

aerobic training
(air-OH-bik)
[*aero-* **air**, *-ic* **relating to**]

contusion
(kon-TOO-zhun)
[*contus-* **bruise**, *-sion* **result**]

convulsion
(kon-VUL-shun)
[*convuls-* **pull violently**, *-sion* **result**]

cramp

disuse atrophy
(DIS-yoos AT-roh-fee)
[*dis-* **absence of**, *a-* **without**, *-troph* **nourishment**]

Duchenne muscular dystrophy (DMD)
(doo-SHEN MUSS-kyoo-lar DISS-troh-fee)
[*Guillaume B.A. Duchenne de Boulogne* **French neurologist**, *mus-* **mouse**, *-cul-* **little**, *-ar* **relating to**, *dys-* **bad**, *-troph-* **nourishment**, *-y* **state**]

dystrophin
(DIS-trof-in)
[*dys-* **bad**, *-troph-* **nourishment**, *-in* **substance**]

endurance training

fibrillation
(fi-bri-LAY-shun)
[*fibril-* **small fiber**, *-ation* **process**]

fibromyositis
(fye-broh-my-oh-SYE-tis)
[*fibro-* **fiber**, *-myos-* **muscle**, *-itis* **inflammation**]

muscular dystrophy
(MUSS-kyoo-lar DISS-troh-fee)
[*mus-* **mouse**, *-cul-* **little**, *-ar* **relating to**, *dys-* **bad**, *-troph-* **nourishment**, *-y* **state**]

myalgia
(my-AL-jee-ah)
[*my-* **muscle**, *-algia* **pain**]

myasthenia gravis
(my-es-THEE-nee-ah GRAH-vis)
[*my-* **muscle**, *-asthenia* **weakness**, *gravis* **severe**]

myopathy
(my-OP-ah-thee)
[*myo-* **muscle**, *-path-* **disease**, *-y* **state**]

myositis
(my-oh-SYE-tis)
[*myos-* **muscle**, *-itis* **inflammation**]

poliomyelitis
(pol-ee-oh-my-eh-LYE-tis)
[*polio-* **gray**, *-mye-* **marrow**, *-itis* **inflammation**]

rigor mortis
(RIG-or MOR-tis)
[*rigor* **stiffness**, *mortis* **of death**]

sprain

strain

strength training

CASE study

"It can't be snowing again!" Isabel was so tired of shoveling snow, and it was only the beginning of February—at least 6 more weeks of winter to go. As she pushed the snow shovel across the driveway and tossed the snow onto an ever-growing mountain, she could feel her muscles begin to ache.

1. By what process would Isabel's muscles first get their energy for contraction?
a. Anaerobic pathway
b. Aerobic pathway
c. Recruitment
d. Breakdown of creatine phosphate

2. What substance in her muscles may be causing the aching or burning sensation?
a. Lactase
b. Glucose
c. Lactic acid
d. Glycogen

3. What protein molecules are interacting to allow Isabel's muscles to contract?
a. Myosin and troponin
b. Actin and myosin
c. Actin and tropomyosin
d. Troponin and tropomyosin

After several minutes of shoveling, Isabel stopped to take off her coat. She was surprised to find she was sweating even though it was below freezing.

4. What was causing Isabel's increased body temperature?
a. Contraction of cardiac muscle cells
b. Her increased respirations
c. Contraction of skeletal muscle cells
d. Conversion of ATP to glucose

5. To pick up a heavier shovelful of snow, Isabel will recruit more _____.
a. Motor units
b. Myoglobin
c. Individual muscle fibers
d. Myosin

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect****, and other resources.*

CAREER choices

Massage Therapist

Massage therapy improves circulation and helps correct imbalances in the soft tissue areas of the body, as in muscles and fascia. As a massage therapist, I am self-employed. My clientele consists of hospital-referred patients for lymph drainage therapy (see Chapter 23) and people who seek traditional massage for various reasons. The majority of my work consists of home visits; however, I also do some work at health facilities and with organized groups.

Some of the current trends in the massage profession are La Stone Therapy, treatment of cancer patients (with a doctor's approval), and stress and pain relief.

My job is extremely rewarding. I rarely encounter a client in a bad mood before a massage, and never after completion! It is very rewarding to see that a client or patient's problem has improved after massage therapy, or simply to see a look of contentment on that person's face. There is a personal, respectful bond between the therapist and the client. In addition, this profession can be financially rewarding.



Monteo Myers, CMT

Knowledge of anatomy and physiology is definitely needed to effectively treat muscular/skeletal problems because isolation of the involved muscle is necessary. I still review anatomy and physiology of the muscular, skeletal, and lymphatic areas all the time. My advice is to study anatomy and physiology in a quiet room, do not study an entire chapter in one sitting, spread the chapter out, and take notes!

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

INTRODUCTION

A. Muscular system is responsible for moving the framework of the body
B. In addition to movement, muscle tissue performs various other functions

GENERAL FUNCTIONS

A. Movement of the body as a whole or movement of its parts
B. Heat production
C. Posture

FUNCTION OF SKELETAL MUSCLE TISSUE

A. Characteristics of skeletal muscle cells
   1. Excitability (irritability)—ability to be stimulated
   2. Contractility—ability to contract, or shorten, and produce body movement
   3. Extensibility—ability to extend, or stretch, thereby allowing muscles to return to their resting length

B. Overview of the muscle cell (Figures 12-1 and 12-2)
   1. Muscle cells are called *fibers* because of their threadlike shape
   2. Sarcolemma—plasma membrane of muscle fibers
   3. Sarcoplasmic reticulum (SR)
      a. T tubules—network of tubules and sacs found within muscle fibers
      b. Membrane of the SR continually pumps calcium ions from the sarcoplasm and stores the ions within its sacs for later release (Figure 12-3)
   4. Muscle fibers contain many mitochondria and several nuclei
   5. Myofibrils—numerous fine fibers packed close together in sarcoplasm
   6. Sarcomere
      a. Segment of myofibril between two successive Z disks
      b. Each myofibril consists of many sarcomeres
      c. Contractile unit of muscle fibers
   7. T tubules
      a. Transverse tubules extend across the sarcoplasm at right angles to the long axis of the muscle fiber
      b. Formed by inward extensions of the sarcolemma
      c. Membrane has ion pumps that continually transport Ca^{++} ions inward from the sarcoplasm
      d. Allow electrical impulses traveling along the sarcolemma to move deeper into the cell

8. Striated muscle (Figure 12-4)
   a. Dark stripes called *A bands;* light H band runs across the midsection of each dark A band
   b. Light stripes called *I bands;* dark Z disk extends across the center of each light I band
9. Triad
   a. Triplet of tubules; a T tubule sandwiched between two sacs of sarcoplasmic reticulum
   b. Allows an electrical impulse traveling along a T tubule to stimulate the membranes of adjacent sacs of the sarcoplasmic reticulum

C. Myofilaments (Figures 12-5 and 12-6)
1. Each myofibril contains thousands of thick and thin myofilaments
2. Four different kinds of protein molecules make up myofilaments
   a. Myosin
      (1) Makes up almost all the thick filament
      (2) Myosin "heads" are chemically attracted to actin molecules
      (3) Myosin "heads" are known as *cross bridges* when attached to actin
   b. Actin—globular protein that forms two fibrous strands twisted around each other to form the bulk of the thin filament
   c. Tropomyosin—protein that blocks the active sites on actin molecules
   d. Troponin—protein that holds tropomyosin molecules in place
3. Thin filaments attach to both Z disks (Z lines) of a sarcomere and extend part way toward the center
4. Thick myosin filaments do not attach to the Z disks

D. Mechanism of contraction
1. Excitation and contraction (Figures 12-7 through 12-13; Table 12-1)
   a. A skeletal muscle fiber remains at rest until stimulated by a motor neuron
   b. Neuromuscular junction—motor neurons connect to the sarcolemma at the motor endplate (Figure 12-7)
   c. Neuromuscular junction is a synapse where neurotransmitter molecules transmit signals
   d. Acetylcholine—the neurotransmitter released into the synaptic cleft that diffuses across the gap, stimulates the receptors, and initiates an impulse in the sarcolemma
   e. Nerve impulse travels over the sarcolemma and inward along the T tubules, which triggers the release of calcium ions
   f. Calcium binds to troponin, which causes tropomyosin to shift and expose active sites on actin
   g. Sliding filament model (Figures 12-12 and 12-13)
      (1) When active sites on actin are exposed, myosin heads bind to them
      (2) Myosin heads bend and pull the thin filaments past them
      (3) Each head releases, binds to the next active site, and pulls again
      (4) The entire myofibril shortens
2. Relaxation
   a. Immediately after the Ca^{++} ions are released, the sarcoplasmic reticulum begins actively pumping them back into the sacs (Figure 12-3)
   b. Ca^{++} ions are removed from the troponin molecules, thereby shutting down the contraction
3. Energy sources for muscle contraction (Figure 12-14)
   a. Hydrolysis of ATP yields the energy required for muscular contraction
   b. ATP binds to the myosin head and then transfers its energy to the myosin head to perform the work of pulling the thin filament during contraction
   c. Muscle fibers continually resynthesize ATP from the breakdown of creatine phosphate (CP)
   d. Catabolism by muscle fibers requires glucose and oxygen
   e. Glucose and oxygen supplied to muscle fibers by blood capillaries (Figure 12-15)
   f. At rest, excess O_2 in the sarcoplasm is bound to myoglobin (Box 12-4)
      (1) Red fibers—muscle fibers with high levels of myoglobin
      (2) White fibers—muscle fibers with little myoglobin
   g. Catabolic pathways
      (1) Aerobic pathway
         (a) Occurs when adequate O_2 is available from blood (Figure 12-15)
         (b) Slower than anaerobic pathway, thus supplies energy for the long term rather than the short term
      (2) Anaerobic pathway (Figure 12-16)
         (a) Very rapid, providing energy during first minutes of maximal exercise (Figure 12-16)
         (b) May occur when low levels of O_2 are available
         (c) Results in the formation of lactic acid, which requires oxygen to convert back to glucose, the producing of an "oxygen debt" or excess postexercise oxygen consumption (EPOC)
   h. Skeletal muscle contraction produces waste heat that can be used to help maintain the set point body temperature (Figure 12-17)

FUNCTION OF SKELETAL MUSCLE ORGANS

A. Muscles are composed of bundles of muscle fibers held together by fibrous connective tissue

B. Motor unit (Figure 12-18)
1. Motor unit—motor neuron plus the muscle fibers to which it attaches
2. Some motor units consist of only a few muscle fibers, whereas others consist of numerous fibers
3. Generally, the smaller the number of fibers in a motor unit, the more precise the movements available; the larger the number of fibers in a motor unit, the more powerful the contraction available

C. Myography—method of graphing the changing tension of a muscle as it contracts (Figure 12-19)

D. Twitch contraction (Figure 12-20)
   1. A quick jerk of a muscle that is produced as a result of a single, brief threshold stimulus (generally occurs only in experimental situations)
   2. The twitch contraction has three phases
      a. Latent phase—nerve impulse travels to the sarcoplasmic reticulum to trigger release of Ca^{++}
      b. Contraction phase—Ca^{++} binds to troponin and sliding of filaments occurs
      c. Relaxation phase—sliding of filaments ceases

E. Treppe—the staircase phenomenon (Figure 12-21, *B*)
   1. Gradual, steplike increase in the strength of contraction that is seen in a series of twitch contractions that occur 1 second apart
   2. Eventually, the muscle responds with less forceful contractions, and the relaxation phase becomes shorter
   3. If the relaxation phase disappears completely, a contracture occurs

F. Tetanus—smooth, sustained contractions
   1. Multiple wave summation—multiple twitch waves are added together to sustain muscle tension for a longer time
   2. Incomplete tetanus—very short periods of relaxation occur between peaks of tension (Figure 12-21, *C*)
   3. Complete tetanus—the stimulation is such that twitch waves fuse into a single, sustained peak (Figure 12-21, *D*)
   4. The availability of calcium determines whether a muscle will contract; if the calcium is continuously available, then contraction will be sustained (Figure 12-22)

G. Muscle tone
   1. Tonic contraction—continual, partial contraction of a muscle
   2. At any one time, a small number of muscle fibers within a muscle contract and produce a tightness or muscle tone
   3. Muscles with less tone than normal are flaccid
   4. Muscles with more tone than normal are spastic
   5. Muscle tone is maintained by negative feedback mechanisms

GRADED STRENGTH PRINCIPLE

A. Graded strength principle—skeletal muscles contract with varying degrees of strength at different times

B. Factors that contribute to the phenomenon of graded strength (Figure 12-26)
   1. Metabolic condition of individual fibers
   2. Number of muscle fibers contracting simultaneously; the greater the number of fibers contracting, the stronger the contraction
   3. Number of motor units recruited
   4. Intensity and frequency of stimulation (Figure 12-23)
   5. Length-tension relationship (Figure 12-24)
      a. Maximal strength that a muscle can develop bears a direct relationship to the initial length of its fibers
      b. A shortened muscle's sarcomeres are compressed; therefore, the muscle cannot develop much tension
      c. An overstretched muscle cannot develop much tension because the thick myofilaments are too far from the thin myofilaments
      d. Strongest maximal contraction is possible only when the skeletal muscle has been stretched to its optimal length
   6. Stretch reflex (Figure 12-25)
      a. The load imposed on a muscle influences the strength of a skeletal contraction
      b. Stretch reflex—the body tries to maintain constancy of muscle length in response to increased load
      c. Maintains a relatively constant length as load is increased up to a maximum sustainable level

C. Isotonic and isometric contractions (Figure 12-27)
   1. Isotonic contraction
      a. Contraction in which the tone or tension within a muscle remains the same as the length of the muscle changes
         (1) Concentric—muscle shortens as it contracts
         (2) Eccentric—muscle lengthens while contracting
      b. Isotonic—literally means "same tension"
      c. All of the energy of contraction is used to pull on thin myofilaments and thereby change the length of a fiber's sarcomeres
   2. Isometric contraction
      a. Contraction in which muscle length remains the same while muscle tension increases
      b. Isometric—literally means "same length"
   3. Most body movements occur as a result of both types of contractions

FUNCTION OF CARDIAC AND SMOOTH MUSCLE TISSUE (TABLE 12-1)

A. Cardiac muscle (Figure 12-28)
   1. Found only in the heart; forms the bulk of the wall of each chamber
   2. Also known as *striated involuntary muscle*
   3. Contracts rhythmically and continuously to provide the pumping action needed to maintain constant blood flow
   4. Cardiac muscle resembles skeletal muscle but has unique features related to its role in continuously pumping blood
      a. Each cardiac muscle contains parallel myofibrils (Figure 12-28)
      b. Cardiac muscle fibers form strong, electrically coupled junctions (intercalated disks) with other fibers; individual cells also exhibit branching
      c. Syncytium—continuous, electrically coupled mass
      d. Cardiac muscle fibers form a continuous, contractile band around the heart chambers that conducts a single impulse across a virtually continuous sarcolemma
      e. T tubules are larger and form diads with a rather sparse sarcoplasmic reticulum
      f. Cardiac muscle sustains each impulse longer than in skeletal muscle; therefore, impulses cannot come rapidly enough to produce tetanus (Figure 12-29)
      g. Cardiac muscle does not run low on ATP and does not experience fatigue
      h. Cardiac muscle is self-stimulating

B. Smooth muscle
   1. Smooth muscle is composed of small, tapered cells with single nuclei (Figure 12-30)
   2. No T tubules are present, and only a loosely organized sarcoplasmic reticulum is present
   3. Ca^{++} comes from outside the cell and binds to calmodulin instead of troponin to trigger a contraction
   4. No striations because thick and thin myofilaments are arranged differently than in skeletal or cardiac muscle fibers; myofilaments are not organized into sarcomeres
   5. Two types of smooth muscle tissue (Figure 12-31)
      a. Single-unit (visceral) smooth muscle
         (1) Gap junctions join smooth muscle fibers into large, continuous sheets
         (2) Most common type; forms a muscular layer in the walls of hollow structures such as the digestive, urinary, and reproductive tracts
         (3) Exhibits autorhythmicity and produces peristalsis
      b. Multiunit smooth muscle
         (1) Does not act as a single unit but is composed of many independent cell units
         (2) Each fiber responds only to nervous input

THE BIG PICTURE: MUSCLE TISSUE AND THE WHOLE BODY

A. Function of all three major types of muscle is integral to function of the entire body
B. All three types of muscle tissue provide the movement necessary for survival
C. Relative constancy of the body's internal temperature is maintained by "waste" heat generated by muscle tissue
D. Maintains the body in a relatively stable position

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Define the terms *sarcolemma*, *sarcoplasm*, and *sarcoplasmic reticulum*.
2. Describe the function of the sarcoplasmic reticulum.
3. How are acetylcholine, Ca^{++}, and adenosine triphosphate (ATP) involved in the excitation and contraction of skeletal muscle?
4. Describe the general structure of ATP and tell how it relates to its function.
5. How does ATP provide energy for muscle contraction?
6. Describe the anatomical arrangement of a motor unit.
7. List and describe the different types of skeletal muscle contractions.
8. Define the term *recruited* as it applies to muscles.
9. Describe rigor mortis.
10. What are the effects of exercise on skeletal muscles?

CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Explain how skeletal muscles provide movement, heat, and posture. Are all of these functions unique to muscles? Explain your answer.
2. The characteristic of excitability is shared by what other system? Relate contractility and extensibility to the concept of agonist and antagonist discussed in Chapter 11.
3. What structures are unique to skeletal muscle fibers? Which of the structures are involved primarily in contractility and which are involved in excitability?
4. Explain how the structure of myofilaments is related to their function.
5. Explain how the sliding filament theory allows for the shortening of a muscle fiber.
6. Compare and contrast the role of Ca^{++} in excitation, contraction, and relaxation of skeletal muscle.
7. People who exercise seriously are sometimes told to work a muscle until they "feel the burn." In terms of how the muscle is able to release energy, explain what is going on in the muscle early in the exercise and when the muscle is "burning."
8. Using fiber types, design a muscle for a marathon runner and a different muscle for a 100-yard–dash sprinter. Explain your choice.
9. Explain the meaning of a "unit of combined cells" as it relates to cardiac muscle. How does this structural arrangement affect its function?
10. Which of the two smooth muscle types would be most affected by damage to the nerves that stimulate them?

Unit Three

Communication, Control, and Integration

The anatomical structures and functional mechanisms that permit communication, control, and integration of bodily functions are discussed in the chapters of Unit Three. To maintain homeostasis, the body must have the ability to monitor and then respond appropriately to changes that may occur in either the internal or external environment. The nervous and endocrine systems provide this capability. Information originating in sensory nerve endings found in complex special sense organs such as the eye and in simple receptors located in skin or other body tissues provides the body with the necessary input. Nervous signals traveling rapidly from the brain and spinal cord over nerves to muscles and glands initiate immediate coordinating and regulating responses. Slower-acting chemical messengers, hormones produced by endocrine glands, serve to effect more long-term changes in physiological activities to maintain homeostasis.

SEEING THE BIG PICTURE



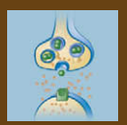
13 Nervous System Cells, 380



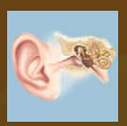
14 Central Nervous System, 420



15 Peripheral Nervous System, 463



16 Autonomic Nervous System, 488



17 Sense Organs, 505

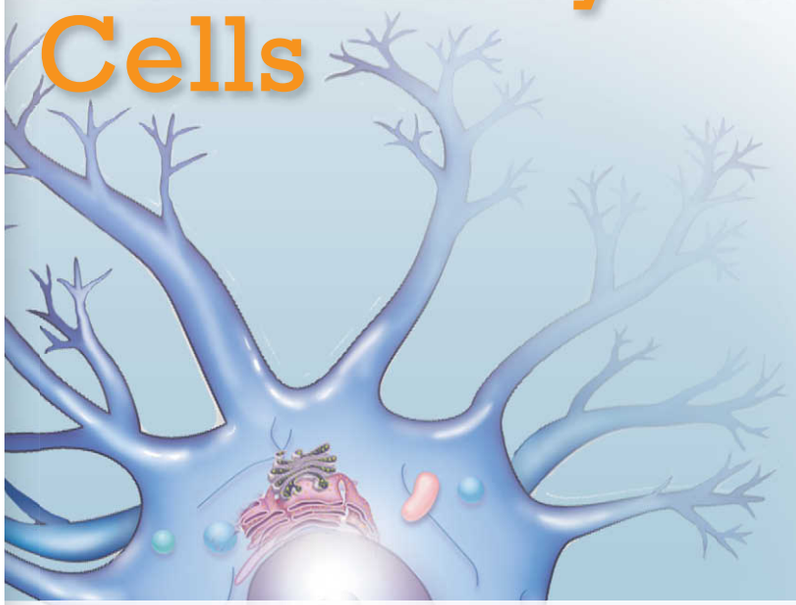


18 Endocrine Regulation, 545



19 Endocrine Glands, 563

13 Nervous System Cells



LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

absolute refractory period
(AB-so-loot ree-FRAK-toh-ree)
[*absolut-* **unrestricted,** *refract-* **break apart,** *-ory* **relating to,** *period* **circuit**]

acetylcholine (ACh)
(ass-ee-til-KOH-leen)
[*acetyl-* **vinegar,** *-chole-* **bile,** *-ine* **made of**]

action potential
(AK-shun poh-TEN-shal)
[*potent-* **power,** *-ial* **relating to**]

afferent division
(AF-fer-ent)
[*a-* **toward,** *-fer-* **carry,** *-ent* **relating to**]

afferent (sensory) neuron
(AF-fer-ent NOO-ron)
[*ad-* **toward,** *-fer-* **carry,** *-ent* **relating to**]

amine
(AM-een)
[*amine* **ammonia compound**]

astrocyte
(ASS-troh-sytes)
[*astro-* **star shaped,** *-cyte* **cell**]

autonomic nervous system (ANS)
(aw-toh-NOM-ik)
[*auto-* **self,** *-nom-* **rule,** *-ic* **relating to,** *nerv-* **nerves,** *-ous* **relating to**]

axon
(AK-son)
[*axon* **axle**]

axon hillock
(AK-son HILL-ok)
[*axon* **axle,** *hill-* **hill** *-ock* **little**]

axonal transport
(AK-soh-nal trans-PORT)
[*axon* **axle,** *-al* **relating to,** *trans-* **across,** *-port* **carry**]

bipolar neuron
(bye-POH-lar NOO-ron)
[*bi-* **two,** *-pol-* **pole,** *-ar* **relating to,** *neuron* **nerve**]

continued on p. 412

CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

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The nervous system and the endocrine system together perform a vital function for the body—communication. Communication provides the means to control and integrate the many different functions performed by organs, tissues, and cells. Integrating means unifying. Unifying body functions allows them to work together like a machine to maintain homeostasis and thus survival.

The nervous system—*made up of the brain, spinal cord, and nerves—is probably the most intriguing body system (Figure 13-1). Facts, theories, and questions about this system are as fascinating as they are abundant. We shall begin our study of the nervous system in this chapter by considering the cells of the nervous system and how they work together to accomplish their function. Then in Chapter 14 we discuss the brain and spinal cord. Chapter 15 presents the major peripheral nerves of the body and Chapter 16 discusses the role of the autonomic nervous system in the subconscious control of body functions. Chapter 17 continues the discussion by describing the structure and function of the sense organs.*

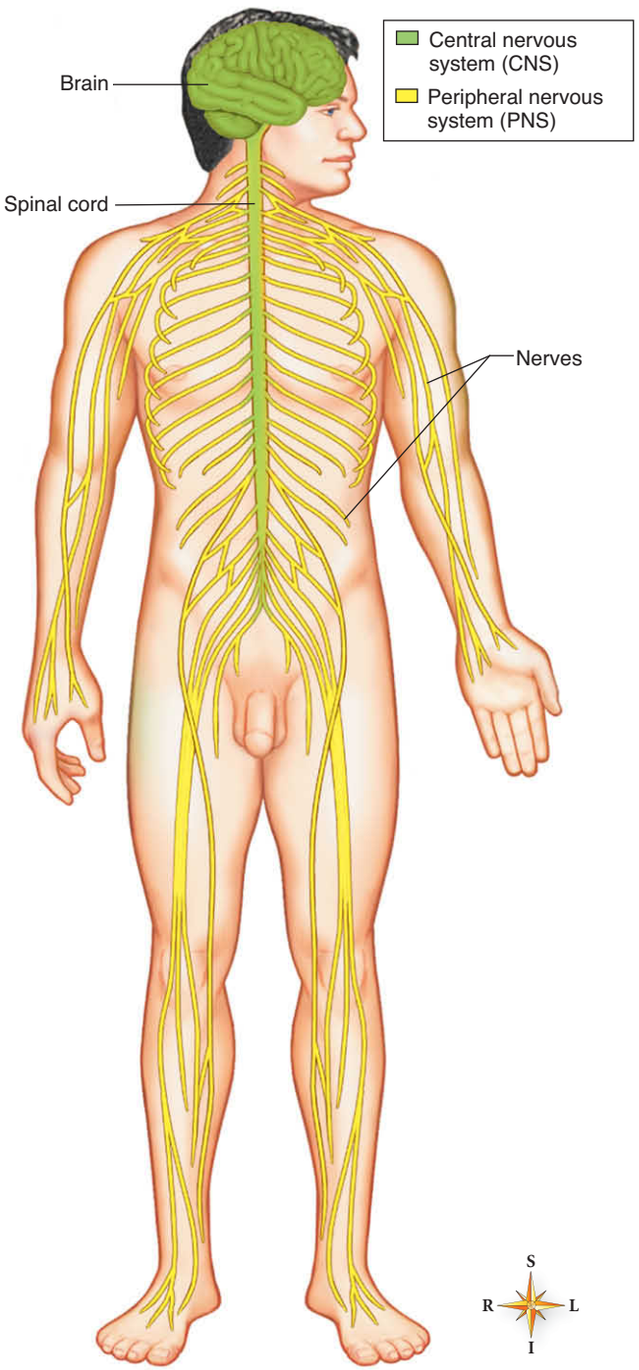


FIGURE 13-1

The nervous system. Major anatomical features of the human nervous system include the brain, the spinal cord, and each of the individual nerves. The brain and spinal cord make up the central nervous system (CNS), and all the nerves and their branches make up the peripheral nervous system (PNS). Nerves originating from the brain are classified as *cranial nerves,* and nerves originating from the spinal cord are called *spinal nerves.*

ORGANIZATION OF THE NERVOUS SYSTEM

The nervous system is organized to detect changes (stimuli) in the internal and external environment, evaluate that information, and possibly respond by initiating changes in muscles or glands. To make this complex network of information lines and processing circuits easier to understand, biologists have subdivided the nervous system into the smaller "systems" and "divisions" described in the following paragraphs and illustrated in Figure 13-2. Note as you read through the next several sections that the nervous system can be divided in various ways: according to structure, direction of information flow, or control of effectors.

Central and Peripheral Nervous Systems

The classical manner of subdividing the nervous system is based on the gross dissections of early anatomists. It simply categorizes all nervous system tissues according to their relative positions in the body: central or peripheral.

The **central nervous system** (CNS) is, as its name implies, the structural and functional center of the entire nervous system. Consisting of the brain and spinal cord, the CNS integrates incoming pieces of sensory information, evaluates the information, and initiates an outgoing response. Today, neurobiologists include only those cells that begin and end within the anatomical boundaries of the brain and spinal cord as part of the CNS. Cells that begin in the brain or cord but extend out through a nerve are thus not included in the central nervous system.

The **peripheral nervous system** (PNS) consists of the nerve tissues that lie in the periphery, or "outer regions," of the nervous system. Nerves that originate from the brain or exit through the skull are called *cranial nerves*, and nerves that originate from the spinal cord and do not exit the skull are called *spinal nerves*.

The terms *central* and *peripheral* are often used as directional terms in the nervous system. For example, nerve cell extensions called *nerve fibers* may be called *central fibers* if they extend from the cell body toward the CNS. Likewise, they may be called

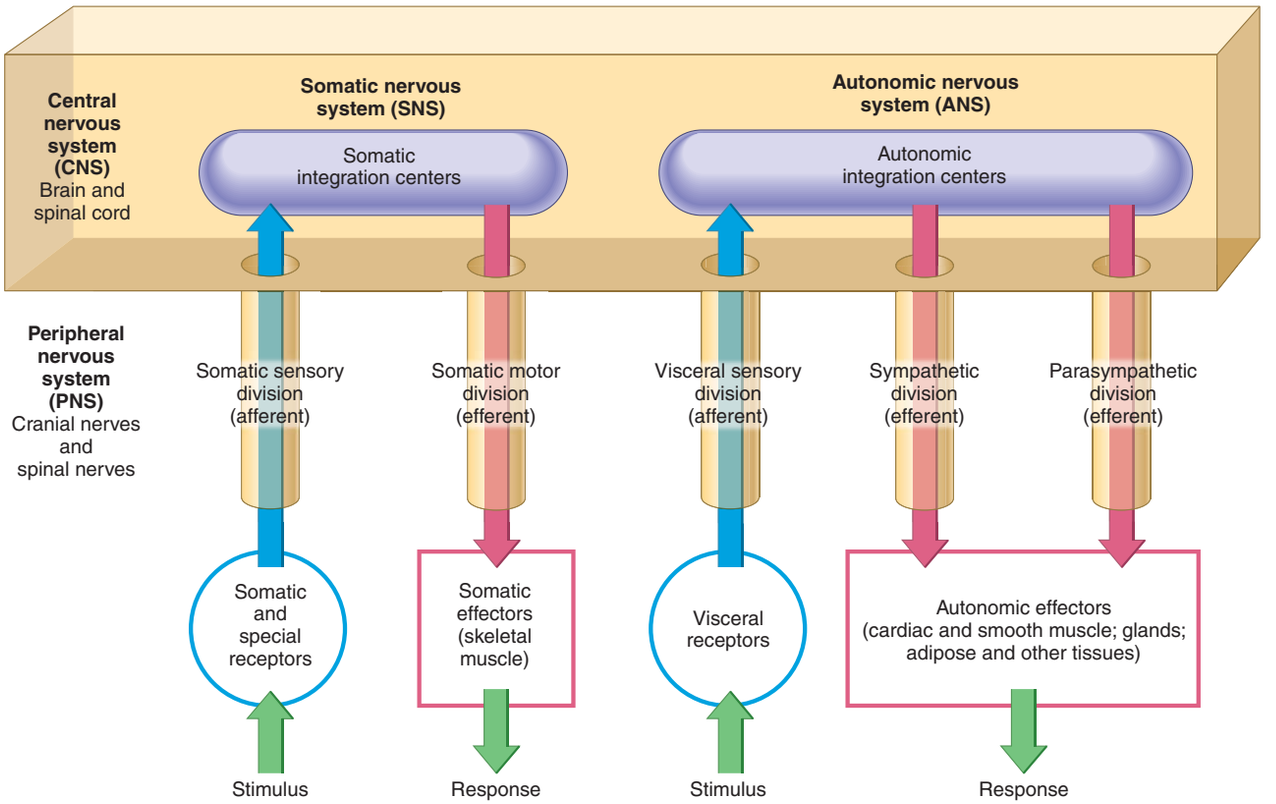


FIGURE 13-2

Organizational plan of the nervous system. Diagram summarizes the scheme used by most neurobiologists in studying the nervous system. Both the somatic nervous system (SNS) and the autonomic nervous system (ANS) include components in the central nervous system (CNS) and peripheral nervous system (PNS). Somatic sensory pathways conduct information toward integrators in the CNS, and somatic motor pathways conduct information toward somatic effectors. In the ANS, visceral sensory pathways conduct information toward CNS integrators, whereas the sympathetic and parasympathetic pathways conduct information toward autonomic effectors.

peripheral fibers if they extend from the cell body away from the CNS.

Figure 13-1 represents the anatomical components of the CNS and PNS and their relative positions in the body. Figure 13-2 represents the relationship of the CNS and PNS in diagram form.

Afferent and Efferent Divisions

The tissues of both the central and the peripheral nervous systems include nerve cells that form incoming information pathways and outgoing pathways. For this reason, it is often convenient to categorize the nervous pathways into divisions according to the direction in which they carry information. The **afferent division** of the nervous system consists of all of the incoming *sensory* or *afferent* pathways. The **efferent division** of the nervous system consists of all the outgoing *motor* or *efferent* pathways. The literal meanings of the terms *afferent* (carry toward) and *efferent* (carry away) may help you distinguish between these two divisions of the nervous system more easily.

Look at Figure 13-2 and try to distinguish the afferent and efferent pathways represented there. Here, and throughout the rest of this book, afferent pathways are typically represented in blue and efferent pathways in red.

Somatic and Autonomic Nervous Systems

Yet another way to organize the components of the nervous system for ease of study is to categorize them according to the type of effectors they regulate. Some pathways of the **somatic nervous system (SNS)** carry information to the *somatic effectors*, which are the skeletal muscles. These motor pathways make up the somatic motor division. As Figure 13-2 shows, the somatic nervous system also includes the afferent pathways, making up the **somatic sensory division,** that provide feedback from the somatic effectors. The SNS also includes the integrating centers that receive the sensory information and generate the efferent response signal.

Efferent pathways of the **autonomic nervous system (ANS)** carry information to the *autonomic*, or *visceral*, effectors, which are mainly the smooth muscles, cardiac muscle, glands, adipose tissue, and other "involuntary" tissue. As its name implies, the autonomic nervous system seems autonomous of voluntary control—it usually appears to govern itself without our conscious knowledge. We now know that the autonomic nervous system is influenced by the conscious mind, but the historical name for this part of the nervous system has remained.

The efferent pathways of the ANS can be divided into the *sympathetic division* and the *parasympathetic division*. The sympathetic division, made up of pathways that exit the middle portions of the spinal cord, is involved in preparing the body to deal with immediate threats to the internal environment. It produces the "fight-or-flight" response. The parasympathetic pathways exit at the brain or lower portions of the spinal cord and coordinate the body's normal resting activities. The parasympathetic division is thus sometimes called the "rest-and-repair" division.

The afferent pathways of the ANS belong to the **visceral sensory division,** which carries feedback information to the autonomic integrating centers in the central nervous system.

Figure 13-2 summarizes the various ways in which the nervous system is subdivided and combines these approaches into a single "big picture."

| QUICK CHECK |

1. List the major subdivisions of the human nervous system.
2. What two organs make up the central nervous system?
3. Contrast the somatic nervous system with the autonomic nervous system.

CELLS OF THE NERVOUS SYSTEM

Two main types of cells compose the nervous system, namely, *neurons* and *glia*. **Neurons** are excitable cells that conduct the impulses that make possible all nervous system functions. In other words, they form the "wiring" of the nervous system's information circuits. **Glia,** or *glial cells,* on the other hand, do not usually conduct information themselves but support the function of neurons in various ways. Some of the major types of glia and neurons are described in the following sections.

Glia

Our understanding of glia, or **neuroglia** as they are sometimes called, has been slow in coming. In the late nineteenth century the Italian cell biologist Camillo Golgi (after whom the Golgi apparatus is named) accidentally dropped a piece of brain tissue in a bath of silver nitrate. When he finally found it, Golgi could see a vast network of various kinds of darkly stained cells surrounding the neurons—proof that glia existed. However, they were almost immediately set aside as mere packing material. In fact, *glia* literally means "glue." For more than a century almost all research efforts focused on neurons. Fortunately, the tide has turned, and studies of glia and their functions are one of the hottest areas in *neurobiology*, the study of the nervous system. We are now finding that they have a major role in how the nervous system works.

The number of glia in the human nervous system is beyond imagination. One estimate places the figure at a staggering 900 billion, or nine times the estimated number of stars in our galaxy! Unlike some neurons, glial cells retain their capacity for cell division throughout adulthood. Although this characteristic gives them the ability to replace themselves, it also makes them susceptible to abnormalities of cell division—such as cancer. Most benign and malignant tumors found in the nervous system originate in glial cells.

As stated earlier, glia serve various roles in supporting the function of neurons. To get a sense of this variety of functions, we shall briefly examine five major types of glia (Figure 13-3):

1. Astrocytes
2. Microglia
3. Ependymal cells
4. Oligodendrocytes
5. Schwann cells

The first four glial types in this list are located in the CNS. Only the Schwann cells are located in the PNS.

The star-shaped glia, **astrocytes** (Figure 13-3, A), derive their name from the Greek *astron*, "star." Found only in the central nervous system, they are the largest and most numerous type of glia. Their long, delicate "points" extend through brain tissue, attaching to both neurons and the tiny blood capillaries of the brain. Astrocytes have recently been called "stars of the nervous system" because of the many important functions they perform. Astrocytes actually "feed" the neurons by picking up glucose from the blood, converting it to lactic acid, and passing it along to the neurons to which they are connected. (See Chapter 30 for a fuller discussion of the role of lactic acid in cellular respiration.)

Because webs of astrocytes form tight sheaths around the brain's blood capillaries, they help form the *blood-brain barrier* (BBB). The

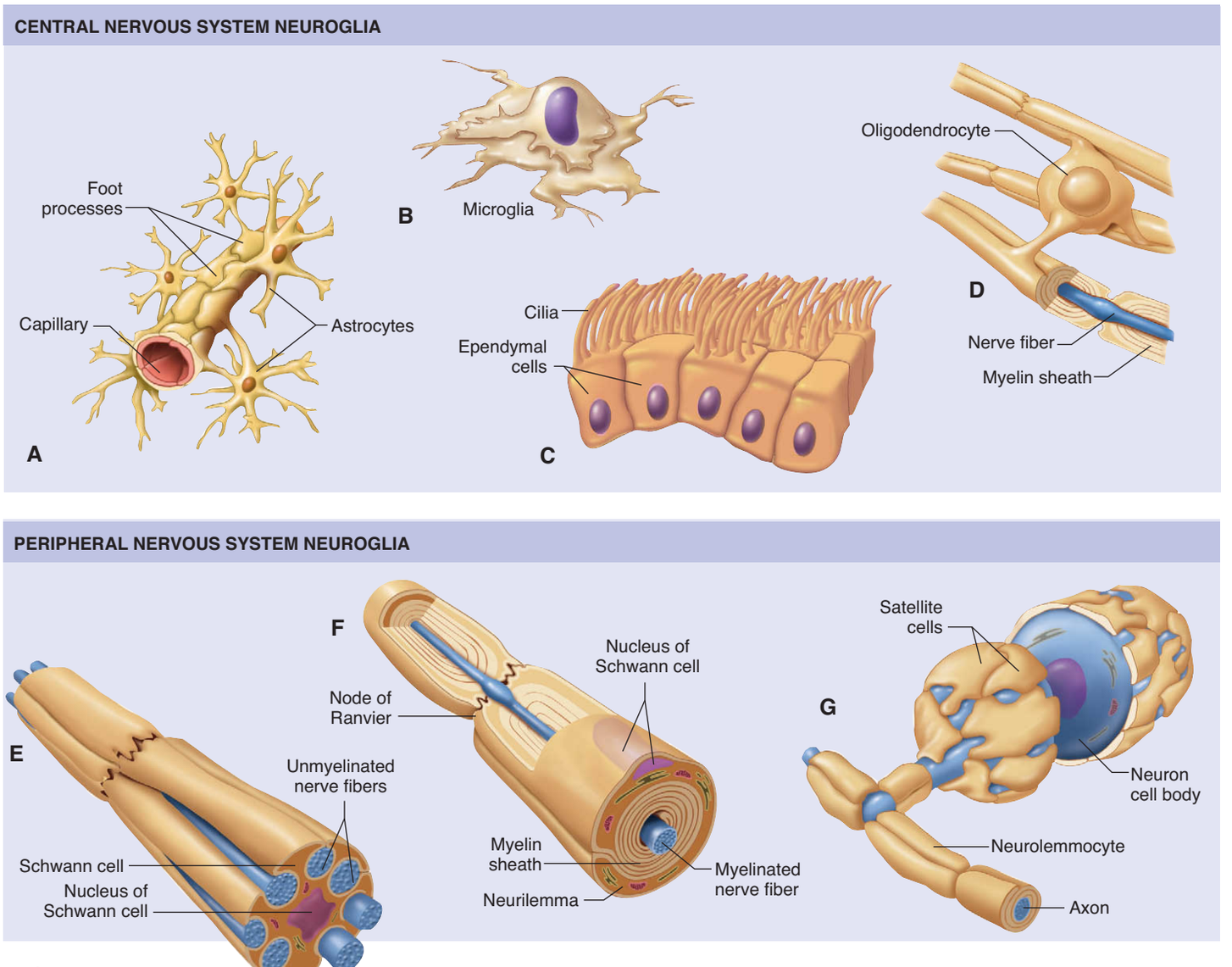


FIGURE 13-3

Types of neuroglia. Neuroglia of the central nervous system (CNS): **A,** Astrocytes attached to the outside of a capillary blood vessel in the brain. **B,** A phagocytic microglial cell. **C,** Ciliated ependymal cells forming a sheet that usually lines fluid cavities in the brain. **D,** An oligodendrocyte with processes that wrap around nerve fibers in the CNS to form myelin sheaths. Neuroglia of the peripheral nervous system (PNS): **E,** A Schwann cell supporting a bundle of nerve fibers in the PNS. **F,** Another type of Schwann cell wrapping around a peripheral nerve fiber to form a thick myelin sheath. **G,** Satellite cells, another type of Schwann cell, surround and support cell bodies of neurons in the PNS.

BBB is a double barrier made up of astrocyte "feet" and the endothelial cells that make up the walls of the capillaries. Small molecules (e.g., oxygen, carbon dioxide, water, alcohol) diffuse rapidly through the barrier to reach brain neurons and other glia. Larger molecules penetrate it slowly or not at all (Box 13-1). More recent findings suggest that astrocytes may not only influence the growth of neurons and how the neurons connect to form circuits but also transmit information along "astrocyte pathways" themselves.

Microglia (Figure 13-3, *B*) are small, usually stationary cells found in the central nervous system. In inflamed or degenerating brain tissue, however, microglia enlarge, move about, and carry on phagocytosis. In other words, they engulf and destroy microorganisms and cellular debris. Although classified as glia, microglia are functionally and developmentally unrelated to other nervous system cells.

Ependymal cells (Figure 13-3, *C*) are glia that resemble epithelial cells, forming thin sheets that line fluid-filled cavities in the brain and spinal cord. Some ependymal cells take part in producing the fluid that fills these spaces. Other ependymal cells have cilia that help keep the fluid circulating within the cavities.

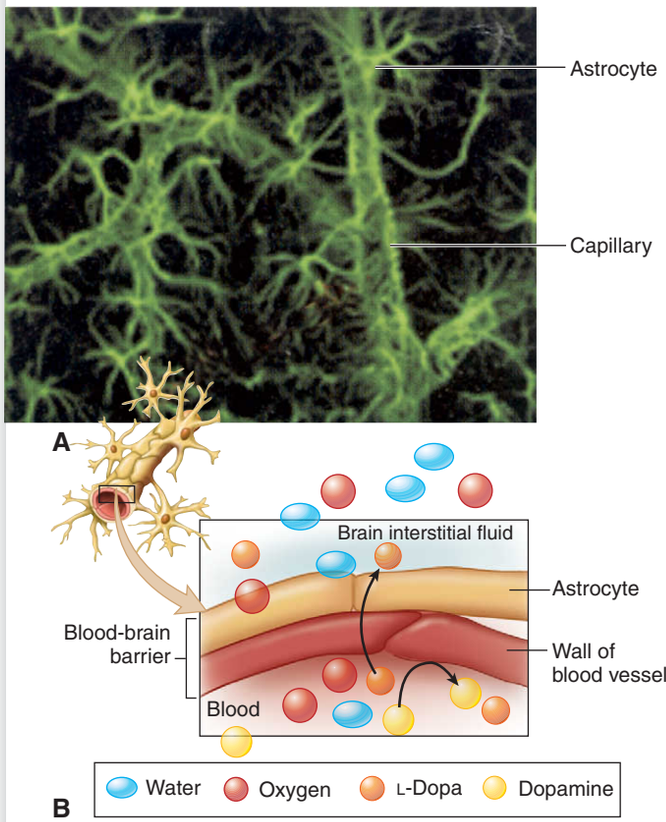
Oligodendrocytes (Figure 13-3, *D*) are smaller than astrocytes and have fewer processes. The name *oligodendrocytes* literally means "cell with few branches" (*oligo-* few, *-dendro-* branch, *-cyte* cell). Some oligodendrocytes lie clustered around nerve cell

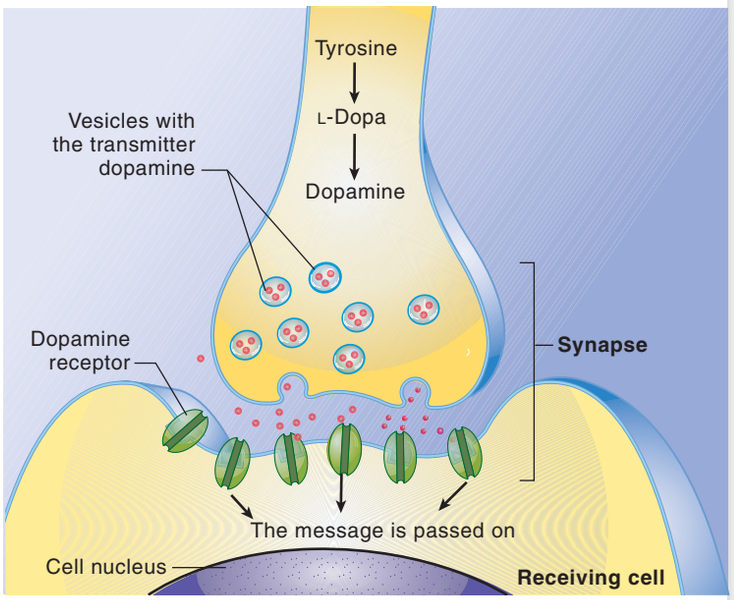
Box 13-1 | HEALTH matters

The Blood-Brain Barrier

The **blood-brain barrier (BBB)** helps maintain the very stable environment required for normal functioning of the brain. The BBB is formed as astrocytes wrap their "feet" around capillaries in the brain (part *A* of figure). The tight junctions between epithelial cells in the capillary wall, along with the covering formed by footlike extensions of the astrocytes, form a barrier that regulates the passage of most ions between the blood and the brain tissue (part *B* of figure). If they crossed to and from the brain freely, ions such as sodium (Na^+) and potassium (K^+) could disrupt the transmission of nerve impulses. Water, oxygen, carbon dioxide, and glucose can cross the barrier easily. Small, lipid-soluble molecules such as alcohol can also diffuse easily across the barrier.

The blood-brain barrier must be considered by researchers trying to develop new drug treatments for brain disorders. Many drugs and other chemicals simply will not pass through the barrier, although they might have therapeutic effects if they could get to the cells of the brain. For example, the abnormal control of muscle movements characteristic of **Parkinson disease (PD)** can often be alleviated by the substance dopamine, which is deficient in the brains of PD patients. Because dopamine cannot cross the blood-brain barrier, dopamine injections or tablets are ineffective. Researchers found that the chemical used by brain cells to make dopamine, **levodopa (L-dopa),** can cross the barrier. Part *C* of the figure shows how L-dopa is used in brain cells to form dopamine. Levodopa administered to patients with Parkinson disease crosses the barrier and converts to dopamine, and the effects of the condition are thereby reduced.





Blood-brain barrier. A, Micrograph of fluorescent-stained astrocytes shows how they attach to capillaries, forming a coating around these tiny blood vessels. **B,** Diagram showing a cross section of the blood-brain barrier, made up of the foot processes of astrocytes and the wall of the blood capillary. **C,** Diagram showing how dopamine is formed from L-dopa before being released as a neurotransmitter. See Figure 13-31 for a more detailed look at the formation of dopamine.

UNIT 3

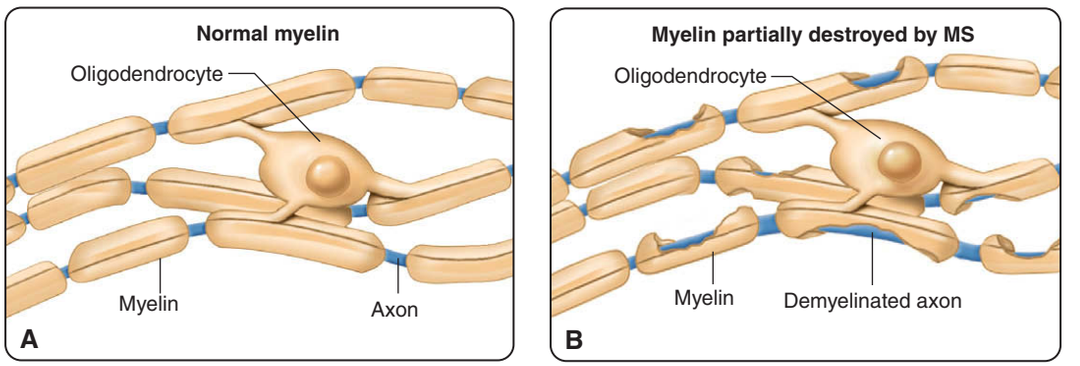
Box 13-2 | HEALTH matters

Multiple Sclerosis (MS)

Several diseases are associated with disorders of the oligodendrocytes. Because these glial cells are involved in myelin formation, the diseases are called **myelin disorders.** The most common primary disease of the central nervous system is a myelin disorder called **multiple sclerosis (MS).** It is characterized by myelin loss and destruction accompanied by varying degrees of oligodendrocyte injury and death. The result is demyelination throughout the white matter of the central nervous system. Hard plaquelike lesions replace the destroyed myelin, and affected areas are invaded by inflammatory cells. As the myelin surrounding nerve fibers is lost, nerve conduction is impaired and weakness, loss of coordination, visual impairment, and speech disturbances occur. Although the disease occurs in both sexes and among all age-groups, it is most common in women between 20 and 40 years of age.

The cause of MS is thought to be related to autoimmunity and to viral infections in some individuals. Susceptibility to MS is inherited in some individuals. MS is characteristically relapsing and chronic in nature, but some cases of acute and unremitting disease have been reported. In most instances, the disease is prolonged, with remissions and relapses occurring over a period of many years. There is no known cure.

Effects of multiple sclerosis (MS). **A,** A normal myelin sheath allows rapid conduction. **B,** In MS, the myelin sheath is damaged, disrupting nerve conduction.



bodies; and some are arranged in rows between nerve fibers in the brain and cord. They help hold nerve fibers together and also serve another and probably more important function—they produce the fatty **myelin sheath** around nerve fibers in the central nervous system (Box 13-2).

Notice in Figure 13-3, *D*, how their processes wrap around surrounding nerve fibers to form this sheath.

Schwann cells (Figure 13-3, *E* to G) are found only in the peripheral nervous system. Here they serve as the functional equivalent of the oligodendrocytes, supporting nerve fibers and sometimes forming a myelin sheath around them. As Figure 13-3, *F*, shows, many Schwann cells can wrap themselves around a single nerve fiber. The myelin sheath is formed by layers of Schwann cell membrane containing the white, fatty substance **myelin.** Microscopic gaps in the sheath, between adjacent Schwann cells, are called **nodes of Ranvier** or simply *myelin sheath gaps.* The myelin sheath and its tiny gaps are important in the proper conduction of impulses along nerve fibers in the peripheral nervous system. As you can see in Figure 13-4, the developing Schwann cell wraps around the nerve fiber in a way that forms an inner core of many layers of plasma membrane, made up mostly of the myelin (a type of phospholipid). Notice that the Schwann cell's

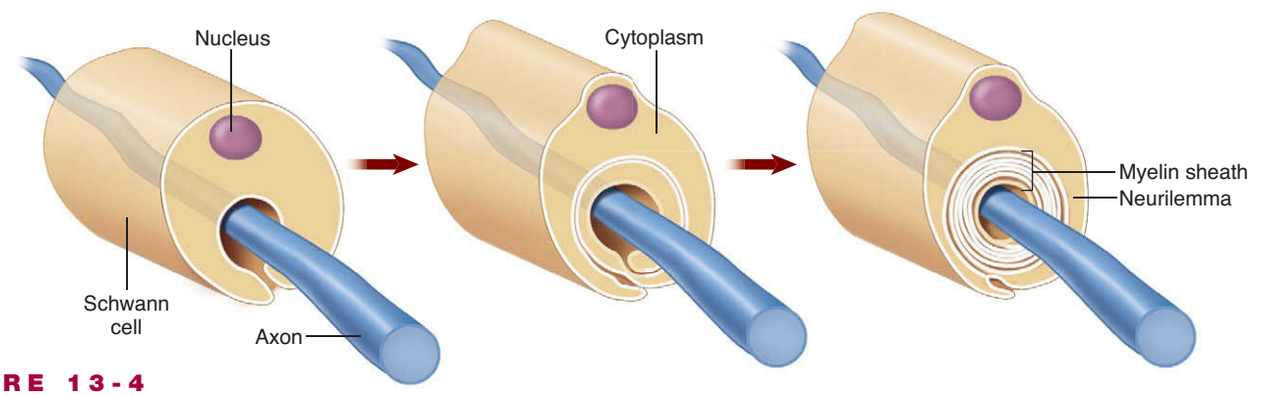


FIGURE 13-4

Development of the myelin sheath. A Schwann cell (neurolemmocyte) migrates to a neuron and wraps around an axon. The Schwann cell's cytoplasm is pushed to the outer layer, leaving a dense multilayered covering of plasma membrane around the axon. Because the plasma membrane of the Schwann cell is mostly the phospholipid myelin, the dense wrapping around the axon is called a *myelin sheath.* The outer layer of cytoplasm is called the *neurilemma.* The extensions of oligodendrocytes also wrap around axons to form a myelin sheath.

nucleus and cytoplasm are squeezed to the perimeter to form the **neurilemma.** The neurilemma is essential to normal nerve growth and the regeneration of injured nerve fibers. Schwann cells are also called *neurolemmocytes.* The myelin sheath along with the neurilemma is sometimes called the *neuronal sheath.*

Figure 13-3, *E,* shows that some Schwann cells do not wrap around nerve fibers to form a thick myelin sheath but simply hold fibers together in a bundle. Nerve fibers with many Schwann cells forming a thick myelin sheath are called **myelinated fibers,** or *white fibers.* When several nerve fibers are held by a single Schwann cell that does not wrap around them to form a thick myelin sheath, the fibers are called *unmyelinated fibers,* or *gray fibers.*

Figure 13-3, *G,* shows a type of Schwann cell often called a **satellite cell.** Like satellites positioned around a planet, these special Schwann cells surround the cell body of a neuron. Satellite cells support neuronal cell bodies in regions called *ganglia* in the peripheral nervous system.

| QUICK CHECK |

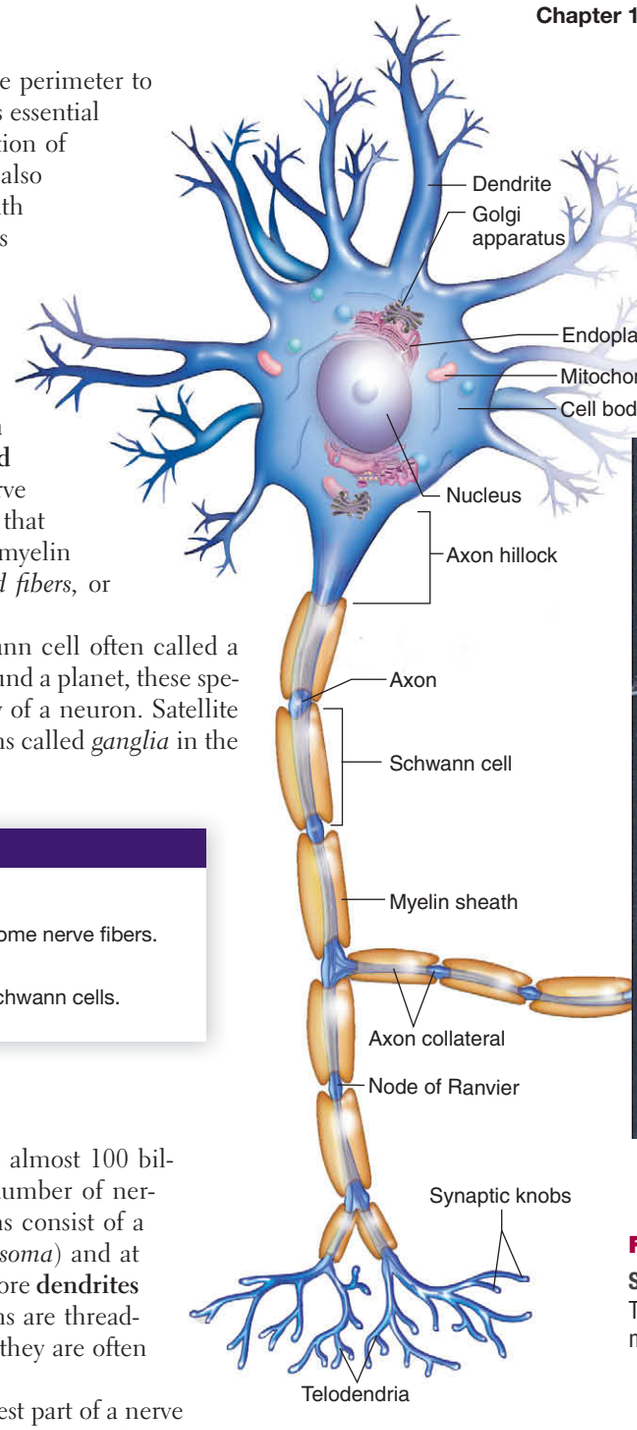
4. What are the five main types of glia?
5. Describe the myelin sheath found on some nerve fibers.
6. What is a neurilemma?
7. Describe the three different forms of Schwann cells.

Neurons

The human brain is estimated to contain almost 100 billion neurons, or about half of the total number of nervous system cells in the brain. All neurons consist of a **cell body** (also called the **perikaryon,** or *soma*) and at least two processes: one **axon** and one or more **dendrites** (Figure 13-5). Because dendrites and axons are thread-like extensions from a neuron's cell body, they are often called **nerve fibers.**

In many respects the cell body, the largest part of a nerve cell, resembles other cells. It contains a nucleus, cytoplasm, and various organelles found in other cells, for example, mitochondria and a Golgi apparatus. The location of the nucleus in the cell body not only makes it easy to find in a microscopic specimen but also provides the name *perikaryon* (literally, "surrounding the nucleus"). A neuron's cytoplasm extends through its cell body and its processes. A plasma membrane encloses the entire neuron.

In the cell body, rough endoplasmic reticulum (ER) and its attached ribosomes provide protein molecules for the neuron. Some of these proteins are then processed and packaged into vesicles by the Golgi apparatus. Some protein molecules in these vesicles are needed for the transmission of nerve signals from one neuron to another. Such proteins are called **neurotransmitters.** Other proteins are used in the maintenance and repair of the neuron.



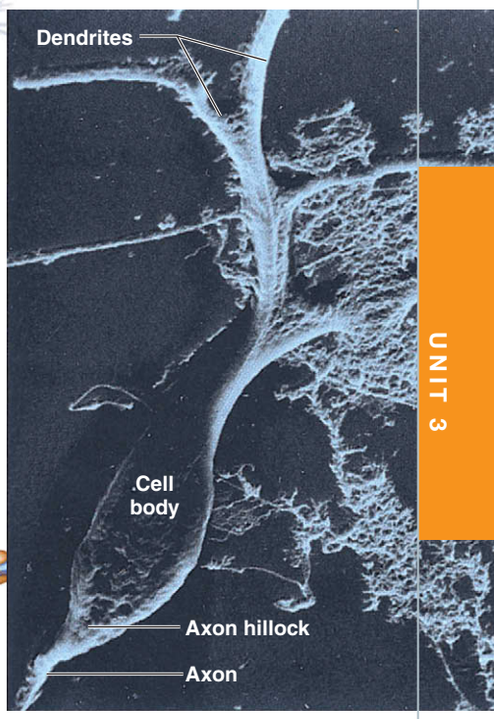


FIGURE 13-5

Structure of a typical neuron. The inset is a scanning electron micrograph of a neuron.

The cell body also contains many mitochondria, which replicate themselves in the cell body. Some of the resulting mitochondria are transported to the end of the axon to provide energy (adenosine triphosphate [ATP]) for nerve signaling there.

Dendrites usually branch extensively from the cell body—like tiny trees. In fact, their name derives from the Greek word for *tree.* The distal ends of dendrites of sensory neurons may be called *receptors* because they receive the stimuli that initiate nerve signals. Some dendrites in the brain have small knoblike *dendritic spines,* which serve as connection points for other neurons. Dendrites receive stimuli and conduct electrical signals toward the cell body and/or axon of the neuron.

The axon of a neuron is a single process that usually extends from a tapered portion of the cell body called the **axon hillock.** Axons conduct impulses away from the cell body. Although a neuron has only one axon, that axon often has one or more side branches, called *axon collaterals.* Moreover, the distal tips of axons form branches called **telodendria** that each terminate in a **synaptic knob** (see Figure 13-5). Each synaptic knob contains mitochondria and numerous vesicles.

Some axons have *varicosities*, or swellings, which act as points of contact with other cells such as smooth muscle fibers (see Figure 12-31 on p. 371). Axons vary in both length and diameter. Some are a meter long. Some, however, measure only a few millimeters. Axon diameters also vary considerably, from about 20 µm down to about 1 µm—a point of interest because axon diameter relates to velocity of impulse conduction. In general, the larger the diameter, the more rapid the conduction.

Whether an axon is myelinated or not also affects the speed of impulse conduction. Figure 13-6 shows a cross section of a typical myelinated axon. Notice in the figure how a series of Schwann cells have grown over the axon in a spiral fashion to form the myelin sheath and neurilemma (see also Figure 13-4). Only axons may have a myelin sheath—dendrites do not. The role of the myelin sheath and nodes of Ranvier in impulse conduction is discussed later.

Extending through the cytoplasm of each neuron are fine strands sometimes called **neurofibrils** (see Figure 13-6). Neurofibrils are bundles of intermediate filaments called *neurofilaments.* Microtubules and microfilaments are additional components of the neuron's cytoskeleton. Along with providing structural support, a neuron's cytoskeleton forms a sort of "railway" for the rapid transport of small organelles to and from the far ends of a neuron. Figure 13-7 shows how small "motor molecules" attach to mitochondria and vesicles containing neurotransmitters and carry them to the end of the axon. The "used" vesicles and transmitters are then returned to the cell body by the same process, but in reverse, for recycling. This type of movement is called **axonal transport.**

Figure 13-8 summarizes the different functional regions of the neurons, based on their role in receiving and conducting nerve signals. The dendrites and cell body act primarily as an *input zone*, receiving nerve stimulation and initiating nerve

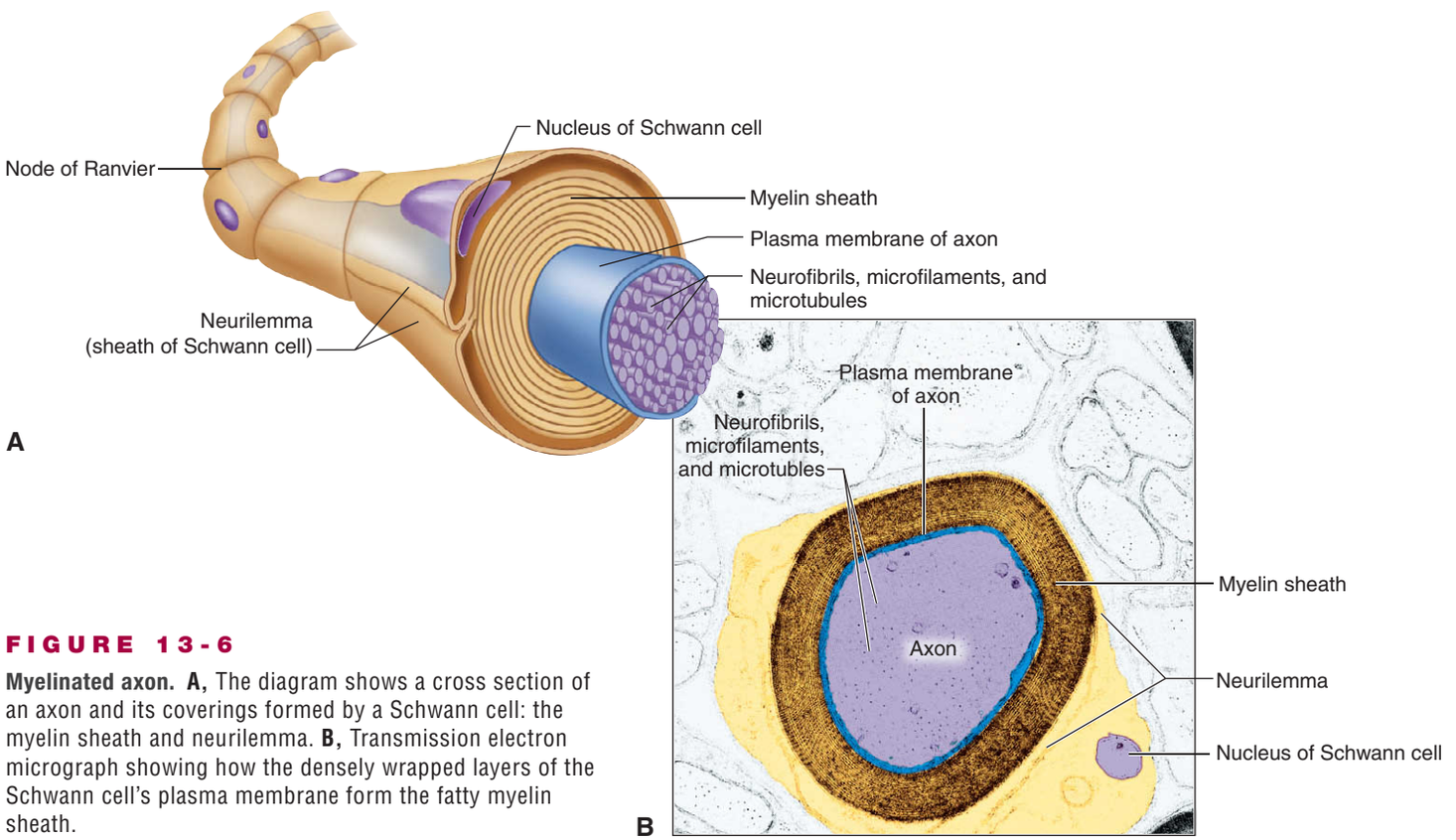


FIGURE 13-6

Myelinated axon. A, The diagram shows a cross section of an axon and its coverings formed by a Schwann cell: the myelin sheath and neurilemma. **B,** Transmission electron micrograph showing how the densely wrapped layers of the Schwann cell's plasma membrane form the fatty myelin sheath.

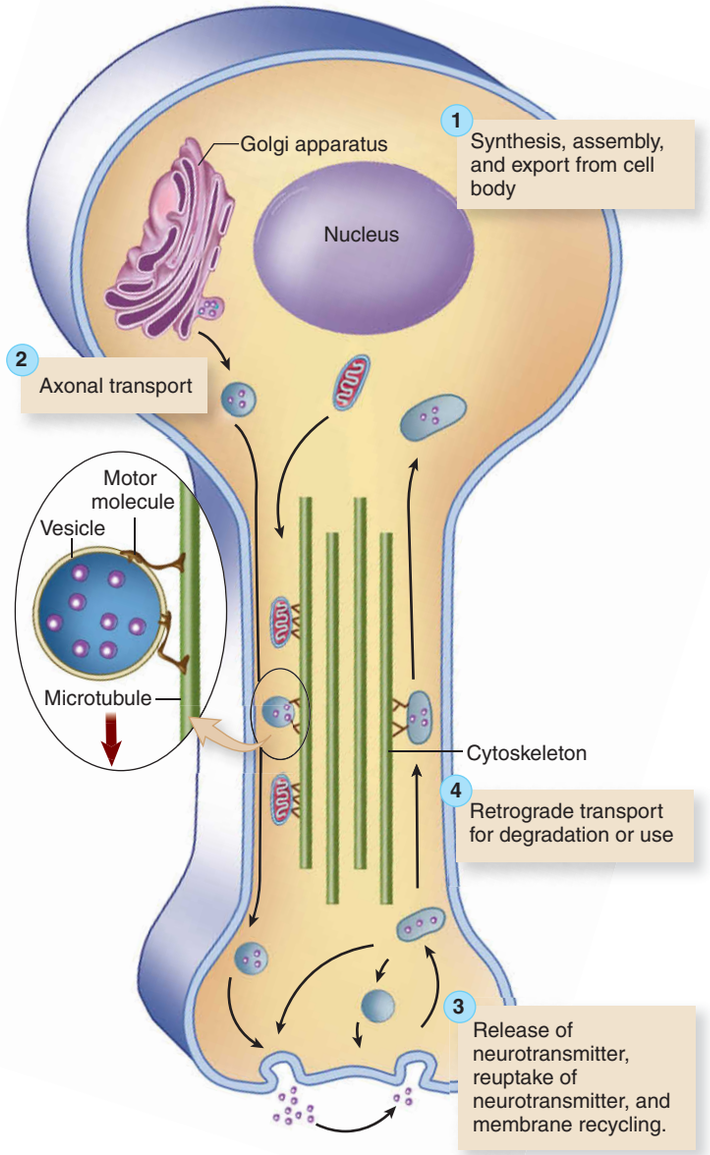


FIGURE 13-7

Axonal transport. Various cellular materials such as mitochondria and vesicles containing neurotransmitter can be shuttled quickly and efficiently from their point of origin in the soma (perikaryon) all the way to the end of the axon by using the neuron's cytoskeleton as a kind of railway system. The inset shows how motor molecules "walk" the material along a microtubule in the axon. The system also permits reverse transport, such as bringing the membranes of spent neurotransmitter vesicles back up to the soma.

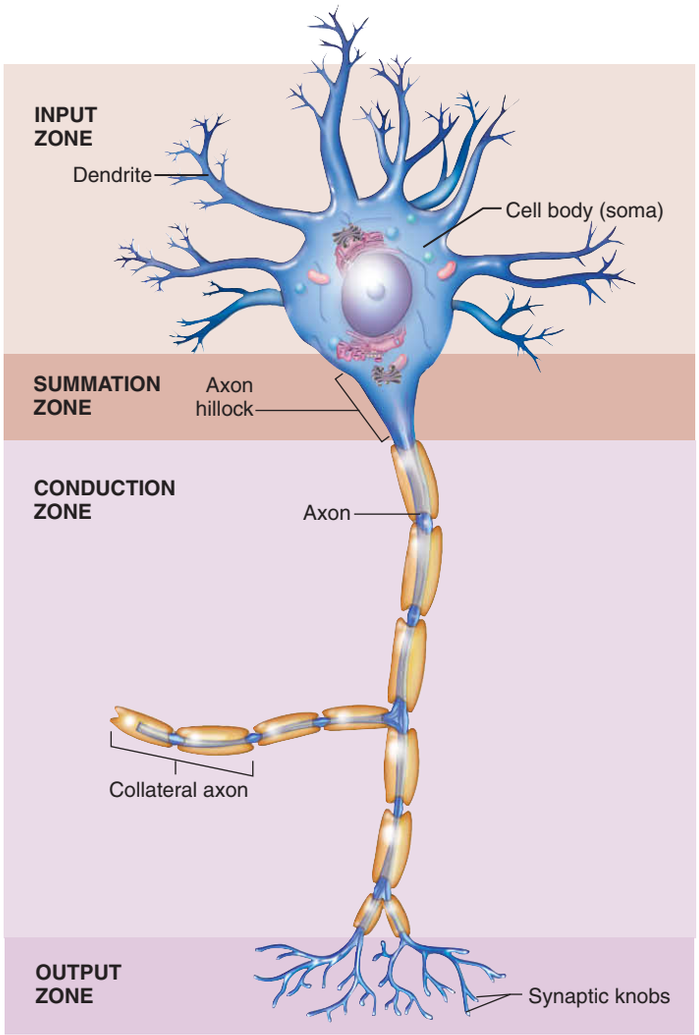


FIGURE 13-8

Functional regions of the neuron's plasma membrane. The *input zone* (dendrites and soma) receives input from other neurons or from sensory stimuli (stimulus-gated ion channels present). The *summation zone* (axon hillock) serves as the site where the nerve impulses combine and possibly trigger an impulse that will be conducted along the axon—or *conduction zone.* Both the summation (trigger) zone and conduction zone have many voltage-gated Na^+ channels and K^+ channels imbedded in the plasma membrane. The *output zone* (distal end of axon) is where the nerve impulse triggers the release of neurotransmitters. The output zone includes many voltage-gated Ca^{++} channels in the membrane.

impulses in response. The axon hillock acts as a *summation zone* by adding together all the nerve impulses arriving from the cell body and dendrites—and deciding whether to send the impulse any farther along the neuron. The axon is the *conduction zone* because its primary job is to conduct the nerve impulse from the axon hillock all the way to the end of the neuron. The telodendria of the axon, along with their synaptic knobs, together act as an *output zone* where vesicles of neurotransmitter are released for possible reception by a nearby neuron or effector cell (muscle or gland cell).

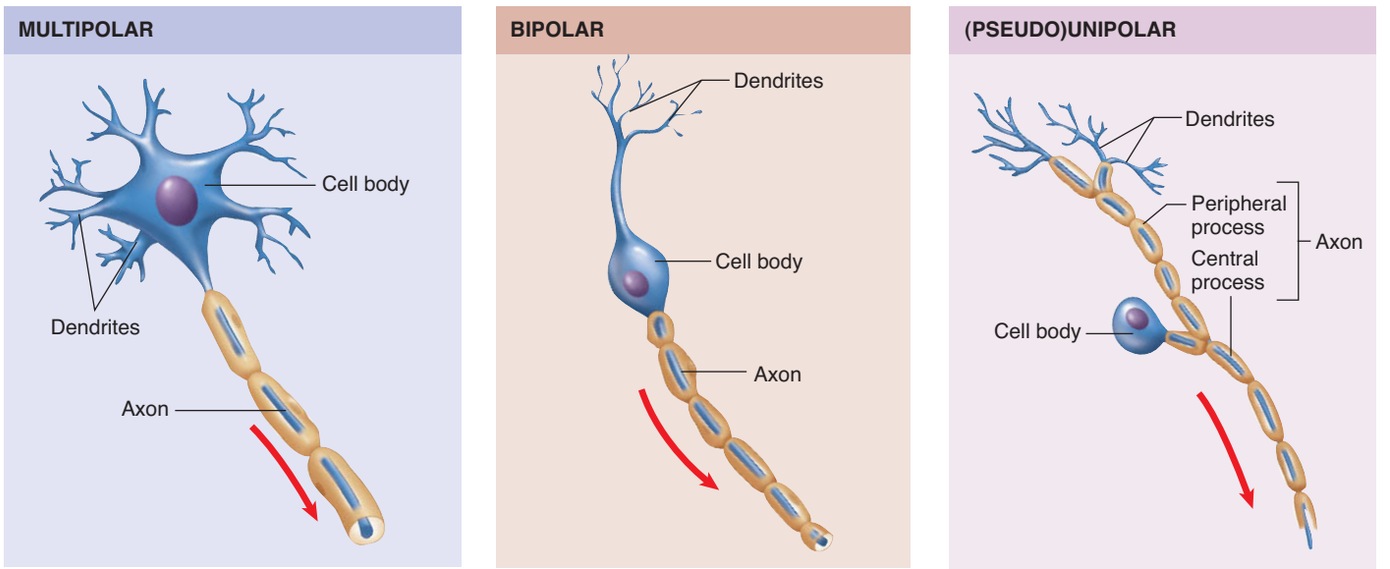


FIGURE 13-9

Structural classification of neurons. A, Multipolar neuron: neuron with multiple extensions from the cell body. **B,** Bipolar neuron: neuron with exactly two extensions from the cell body. **C,** (Pseudo) unipolar neuron: neuron with only one extension from the cell body. The central process is an axon; the peripheral process is a modified axon with branched dendrites at its extremity. (The *red arrows* show the direction of impulse travel.)

Classification of Neurons

STRUCTURAL CLASSIFICATION

The three types of neurons classified according to the number of their extensions from the cell body (Figure 13-9) are as follows:

1. Multipolar
2. Bipolar
3. Unipolar

Multipolar neurons have only one axon but several dendrites. Most of the neurons in the brain and spinal cord are multipolar. **Bipolar neurons** have only one axon and also only one highly branched dendrite. Bipolar neurons are the least numerous kind of neuron. They are found in the retina of the eye, in the inner ear, and in the olfactory pathway. **Unipolar (pseudounipolar) neurons** have a single process extending from the cell body. This single process branches to form a central process (toward the CNS) and a peripheral process (away from the CNS). These two processes together form an axon, conducting impulses away from the dendrites found at the distal end of the peripheral process. Unipolar neurons are always sensory neurons, conducting information toward the central nervous system.

FUNCTIONAL CLASSIFICATION

The three types of neurons classified according to the direction in which they conduct impulses are as follows:

1. Afferent neurons
2. Efferent neurons
3. Interneurons

Figure 13-10 shows one neuron of each of these types. **Afferent (sensory) neurons** transmit nerve impulses to the spinal cord or brain. **Efferent (motor) neurons** transmit nerve impulses away from the brain or spinal cord to or toward muscles or glands. **Interneurons** conduct impulses from afferent neurons to or toward motor neurons. Interneurons lie entirely within the central nervous system (brain and spinal cord).

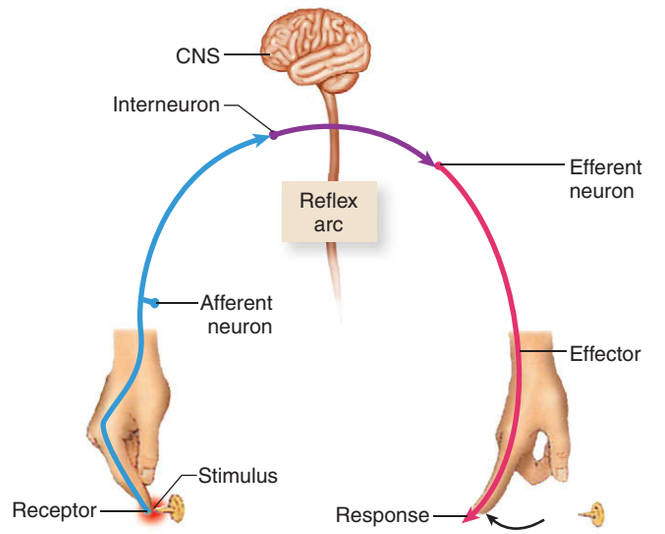


FIGURE 13-10

Functional classification of neurons in a reflex arc. Neurons can be classified according to the direction in which they conduct impulses. Notice that the most basic route of signal conduction follows a pattern called the *reflex arc.*

Reflex Arc

Notice in Figure 13-10 that neurons are often arranged in a pattern called a **reflex arc.** Basically, a reflex arc is a signal conduction route to and from the central nervous system (the brain and spinal cord). The most common form of reflex arc is the three-neuron arc (Figure 13-11, *A*). It consists of an afferent neuron, an interneuron, and an efferent neuron. Afferent, or sensory, neurons conduct signals to the central nervous system from *sensory receptors* in the peripheral nervous system. Efferent neurons, or *motor neurons*, conduct signals from the central nervous system to effectors. An effector is muscle tissue or glandular tissue. Interneurons conduct signals from afferent neurons toward or to motor neurons. In its simplest form, a reflex arc consists of an afferent neuron and an efferent neuron; this is called a *two-neuron arc.* In essence, a reflex arc is a signal conduction route from receptors to the central nervous system and out to effectors. By now you should recognize that the reflex arc is an example of the information pathway described in Chapter 1 as a regulatory *feedback loop.* To confirm this point, compare the reflex arc (see Figure 13-10) with the feedback loop illustrated in Figure 1-13, *B*, p. 22.

Now look again at Figure 13-11, *A.* Note the two labels for synapse. A **synapse** is the place where nerve information is transmitted from one neuron to another. Synapses are located between the synaptic knobs on one neuron and the dendrites or cell body of another neuron. For example, in Figure 13-11, *A*, the first synapse lies between the sensory neuron's synaptic knobs and the interneuron's dendrites. The second synapse lies between the interneuron's synaptic knobs and the motor neuron's dendrites. This reflex arc is called an *ipsilateral reflex arc* because the receptors and effectors are located on the same side of the body. Figure 13-11, *B*, shows a *contralateral reflex arc*, one whose receptors and effectors are located on opposite sides of the body.

Besides simple two-neuron and three-neuron arcs, *intersegmental arcs* (Figure 13-11, *C*)—even more complex multineuron, multisynaptic arcs—also exist. An important principle is this: all electrical signals that start in receptors do not invariably travel over a complete reflex arc and terminate in effectors. Many signals fail to be conducted across synapses. Moreover, all signals that terminate in effectors do not invariably start in receptors. Many of them, for example, are thought to originate in the brain.

| QUICK CHECK |

8. What is the difference between an axon and a dendrite?
9. What are the three structural categories of neurons?
10. What are the three main functional categories of neurons?
11. What are the essential components of a reflex arc?

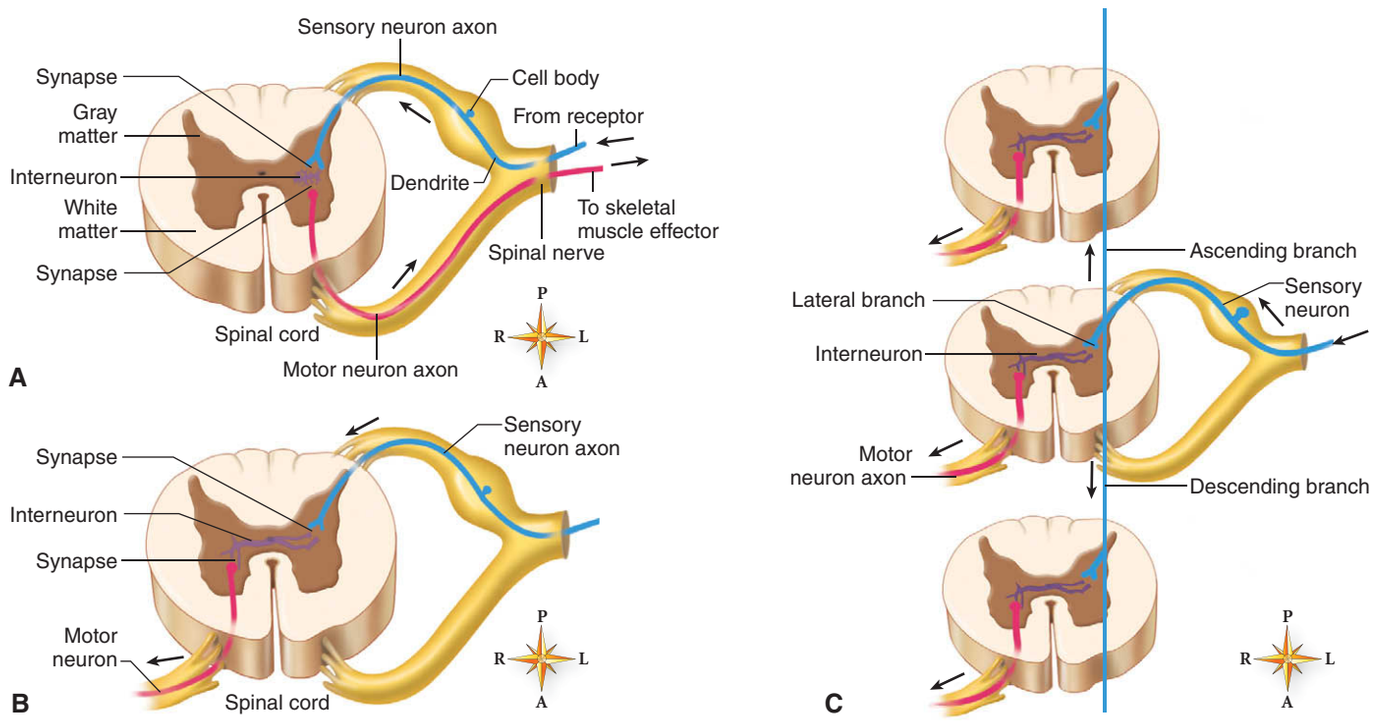


FIGURE 13-11

Examples of reflex arcs. A, Three-neuron ipsilateral reflex arc. Sensory information enters the central nervous system (CNS) and motor information leaves the CNS on the same side. **B,** Three-neuron contralateral reflex arc. Sensory information enters on the side of the CNS that is opposite from the side where motor information exits the CNS. **C,** Intersegmental contralateral reflex arc. Divergent branches of a sensory neuron bring information to several segments of the CNS at the same time. Motor information leaves each segment on the opposite side of the CNS.

NERVES AND TRACTS

Nerves are bundles of peripheral nerve fibers held together by several layers of connective tissues (Figure 13-12). Surrounding each nerve fiber is a delicate layer of fibrous connective tissue called the **endoneurium.** Bundles of fibers (each with its own endoneurium), called *fascicles*, are held together by a connective tissue layer called the **perineurium.** Numerous fascicles, along with the blood vessels that supply them, are held together to form a complete nerve by a fibrous coat called the **epineurium.** As you can see in Figure 13-2, the epineurium has a superficial part that surrounds the whole nerve and a deep part that extends between the fascicles. The deep epineurium is made up of wavy collagen bundles along with adipose tissue and blood vessels.

Within the central nervous system, however, bundles of nerve fibers are called **tracts** rather than nerves. Unlike nerves, tracts do not have connective tissue coverings. Individual nerve fibers that originate in the peripheral nervous system and pass through a nerve may continue into the spinal cord or brain as part of a tract. Likewise, an individual nerve fiber that originates in the brain or spinal cord and passes through a tract may continue into the peripheral nervous system within a nerve.

The creamy white color of myelin distinguishes bundles of myelinated fibers from surrounding unmyelinated tissues, which appear darker in comparison. Bundles of myelinated fibers make up the so-called **white matter,** or *white substance*, of the nervous system. In the peripheral nervous system, white matter consists of myelinated nerves; in the central nervous system, white matter consists of myelinated tracts.

Cell bodies and unmyelinated fibers make up the darker **gray matter,** or *gray substance*, of the nervous system. Small, distinct regions of gray matter within the central nervous system are usually called *nuclei*. In peripheral nerves, similar regions of gray matter are more often called *ganglia*.

Most nerves in the human nervous system are *mixed nerves*. That is, they contain both sensory (afferent) and motor (efferent) fibers. Nerves that contain predominantly afferent fibers are often called *sensory nerves*. Likewise, nerves that contain mostly efferent fibers are called *motor nerves*.

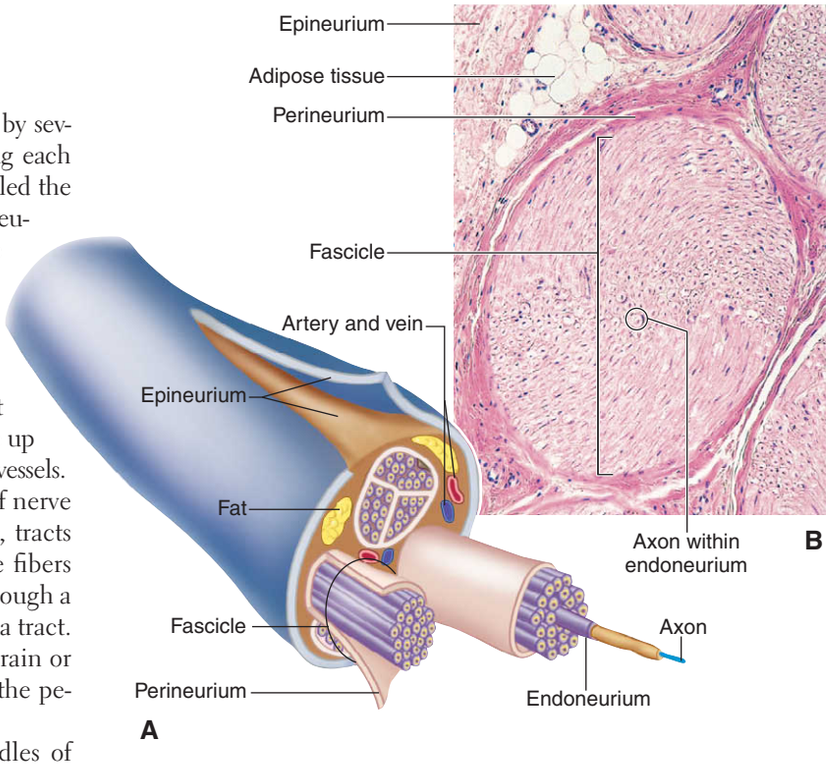


FIGURE 13-12

The nerve. A, Each nerve contains axons bundled into fascicles. A fibrous endoneurium surrounds each axon and its Schwann cells within a fascicle. A perineurium surrounds each fascicle. A connective tissue epineurium wraps the entire nerve. The superficial epineurium is shown in blue and the deep epineurium (collagen fibers, adipose tissue, and blood vessels) is shown in brown. **B,** A light micrograph of a cross section of a nerve.

REPAIR OF NERVE FIBERS

For a long time, neuroscientists believed that mature neurons could not be replaced—and therefore nervous tissue had severe limitations to self-healing of damage. Evidence now clearly shows that neurons are in fact replaced. In fact, fresh new neurons are often added to the existing network. As we learn more about this process, neuroscientists hope to understand the details of these mechanisms and develop therapies to prevent and treat nerve damage or degeneration.

Another option in the body for healing injured or diseased nervous tissue is repairing the neurons that are already present. Unfortunately, neurons have a somewhat limited capacity to repair themselves. Nerve fibers can sometimes be repaired if the damage is not extensive, when the cell body and neurilemma remain intact, and when scarring has not occurred. Figure 13-13 shows the stages of the healing process in the axon of a peripheral motor neuron.

Immediately after the injury occurs, the distal portion of the axon degenerates, as does its myelin sheath. Macrophages then move into the area and remove the debris. The remaining neurilemma and endoneurium form a pathway or tunnel from the point of injury to the effector. New Schwann cells grow within this tunnel, maintaining a path for regrowth of the axon.

Meanwhile, the cell body of the damaged neuron has reorganized its ribosomes (sometimes called Nissl bodies, or *Nissl substance*) to provide the proteins necessary to extend the remaining healthy portion of the axon. Several growing axon "sprouts" appear. When one of these growing fibers reaches the tunnel, it increases its growth rate—growing as much as 3 to 5 mm per day. If all goes well, the neuron's connection with the effector is quickly reestablished.

Notice in Figure 13-13 that the skeletal muscle cell supplied by the damaged neuron atrophies during the absence of nervous input. Only after the nervous connection is reestablished and stimulation resumed does the muscle cell grow back to its original size. If the damaged axon fails to repair itself, a nearby, undamaged axon from an adjacent neuron may form a sprout that reaches the effector cell and thus reestablishes a connection with the nervous system.

If the damaged nerve is connected to another nerve, the receiving nerve may also wither and die. In fact, because the preceding neuron may now have no functioning neuron to send a signal to, it may wither as well. In short, damage to a single axon can shut down an entire nerve pathway if not repaired—and repaired quickly.

In the central nervous system, similar repair of damaged nerve fibers is very unlikely. First of all, neurons in the central nervous system lack the neurilemma needed to form the guiding tunnel from the point of injury to the distal connection. Second, astrocytes quickly fill

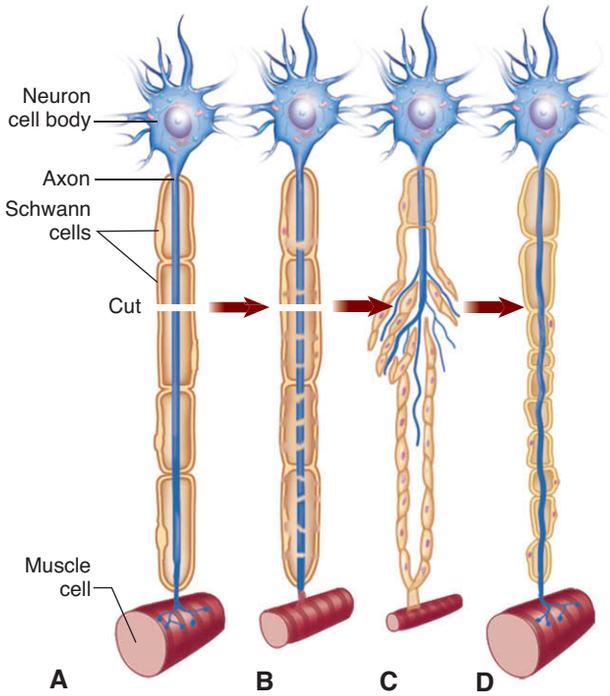


FIGURE 13-13

Repair of a peripheral nerve fiber. A, An injury results in a cut nerve. **B,** Immediately after the injury occurs, the distal portion of the axon degenerates, as does its myelin sheath. **C,** The remaining neurilemma tunnels from the point of injury to the effector. New Schwann cells grow within this tunnel, maintaining a path for regrowth of the axon. Meanwhile, several growing axon "sprouts" appear. When one of these growing fibers reaches the tunnel, it increases its growth rate—growing as much as 3 to 5 mm per day. (The other sprouts eventually disappear.) **D,** The neuron's connection with the effector is reestablished.

damaged areas and thus block regrowth of the axon with scar tissue. Despite great strides made by researchers looking for ways to stimulate the repair of neurons in the central nervous system, most injuries to the brain and spinal cord cause permanent damage (Box 13-3).

| QUICK CHECK |

12. What are the three layers of connective tissues that hold the fibers of a nerve together?
13. What is the difference between a nerve and a tract?
14. How does white matter differ from gray matter?
15. Under what circumstances can a nerve fiber be repaired?

Box 13-3 | Neuroglobin

Neuroglobin (Ngb) is a protein molecule very similar to the oxygen-binding proteins *hemoglobin (Hb)* in red blood cells (see Chapters 20 and 27) and *myoglobin* in muscle fibers (see Chapter 12). As the myoglobin in muscle fibers, neuroglobin temporarily stores a "backup" supply of oxygen for times when oxygen availability is low. In brain tissues, such a circumstance may occur during a stroke, or *cerebrovascular accident (CVA),* when the blood supply to the brain is disrupted. It could also occur during respiratory accidents, such as suffocation. Until normal blood flow is restored, neuroglobin can supply oxygen to the cell for a short time.

NERVE IMPULSES

Neurons are remarkable among cells because they initiate and conduct signals called *nerve impulses.* Expressed differently, neurons exhibit both *excitability* and *conductivity.* What exactly is a nerve impulse? How is a neuron able to conduct this signal along its entire length—sometimes a full meter? These questions, and more, are answered in the paragraphs that follow.

Membrane Potentials

One way to describe a nerve impulse is as a wave of electrical fluctuation that travels along the plasma membrane. To understand this phenomenon more fully, however, requires some familiarity with the electrical nature of the plasma membrane.

All living cells, including neurons, maintain a difference in the concentration of ions across their membranes. There is a slight excess of positive ions on the outside of the membrane and a slight excess of negative ions on the inside of the membrane. This, of course, results in a difference in electrical charge across their plasma membranes called the **membrane potential.** This difference in electrical charge is called a *potential* because it is a type of stored energy called *potential energy.* Whenever opposite electrical charges (in this case, opposite ions) are thus separated by a membrane, they have the potential to move toward one another if they are allowed to cross the membrane. When a membrane potential is maintained by a cell, opposite ions are held on opposite sides of the membrane like water behind a dam—ready to rush through with force when the proper membrane channels open.

A membrane that exhibits a membrane potential is said to be *polarized.* That is, its membrane has a negative pole (the side on which there is an excess of negative ions) and a positive pole (the side on which there is an excess of positive ions). The magnitude of potential difference between the two sides of a polarized membrane is measured in volts (V) or millivolts (mV). The voltage across a membrane can be measured by a device called a *voltmeter,* which is shown in Figure 13-14. The sign of a membrane's voltage indicates the charge on the inside surface of a polarized membrane. For example, the value –70 mV indicates that the potential difference has a magnitude of 70 mV and that the inside of the membrane is negative with respect to the outside surface (see Figure 13-14). A value of +30 mV indicates a

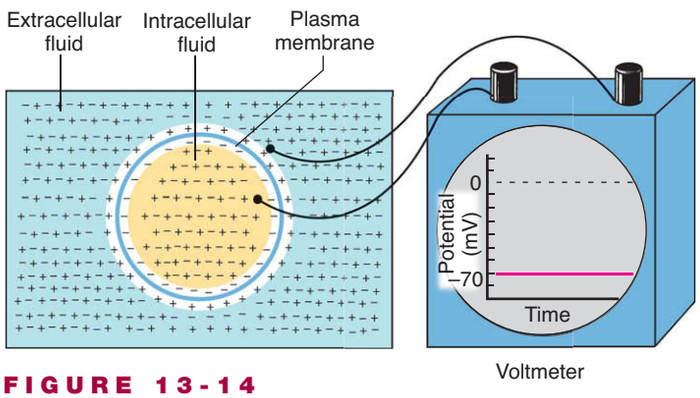


FIGURE 13-14

Membrane potential. The diagram on the left represents a cell maintaining a very slight difference in the concentration of oppositely charged ions across its plasma membrane. The voltmeter records the magnitude of electrical difference over time, which, in this case, does not fluctuate from –70 mV (voltage recorded over time as a red line).

potential difference of 30 mV and that the inside of the membrane is positive (and thus the outside of the membrane is negative).

To understand the electrical activity of the neuron—which is an essential concept of neurobiology—we will need to understand the different membrane potentials that occur in different circumstances in the plasma membrane of a neuron.

Resting Membrane Potentials

When a neuron is not conducting electrical signals, it is said to be "resting." At rest, a neuron's membrane potential is typically maintained at about –70 mV (see Figure 13-14). The membrane potential maintained by a nonconducting neuron's plasma membrane is called the **resting membrane potential (RMP).** Although the RMP can vary somewhat, we will use –70 mV as our typical value for the sake of discussion.

The mechanisms that produce and maintain the RMP do so by promoting a slight ionic imbalance across the neuron's plasma membrane. Specifically, these mechanisms produce a slight excess of positive ions on its outer surface. This imbalance of ion concentrations is produced primarily by ion transport mechanisms in the neuron's plasma membrane.

Recall from Chapters 3 and 4 that the permeability characteristics of each cell's plasma membrane are determined in part by the presence of specific membrane transport channels. Many of these channels are *gated channels*, allowing specific molecules to diffuse across the membrane only when the "gate" of each channel is open (see Figure 4-6 on p. 95).

In the neuron's plasma membrane, channels for the transport of the major anions (negative particles) are either nonexistent or closed. For example, there are no channels to allow the exit of the large anionic protein molecules that dominate the intracellular fluid. Chloride ions (Cl^-), the dominant extracellular anions, are likewise "trapped" on one side of the membrane because chloride ions are repelled by the protein anions inside the cell. This means that the only ions that can move efficiently across a neuron's membrane are the positive ions sodium and potassium.

In a resting neuron, some of the potassium channels are open, but most of the sodium channels are closed (Figure 13-15). This means that potassium ions pumped into the neuron can diffuse back out of the cell in an attempt to equalize its concentration gradient, but very little of the sodium pumped out of the cell can diffuse back into the neuron (Figure 13-16). Thus the membrane's selective permeability characteristics create and maintain a slight excess of positive ions on the outer surface of the membrane.

Another mechanism also operates to maintain the RMP. The sodium-potassium pump is an active transport mechanism in the plasma membrane that transports sodium ions (Na^+) and potassium ions (K^+) in opposite directions and at different rates (see Figure 13-16). It moves three sodium ions out of a neuron for every two potassium ions it moves into it. If, for instance, the pump transports 100 potassium ions into a neuron from the extracellular fluid, it concurrently transports 150 sodium ions out of the cell. The sodium-potassium pump thus maintains an imbalance in the distribution of positive ions, maintaining a difference in electrical charge across the membrane. As this pump operates, the inside surface of the membrane becomes slightly less positive—that is, slightly negative—with respect to its outer surface.

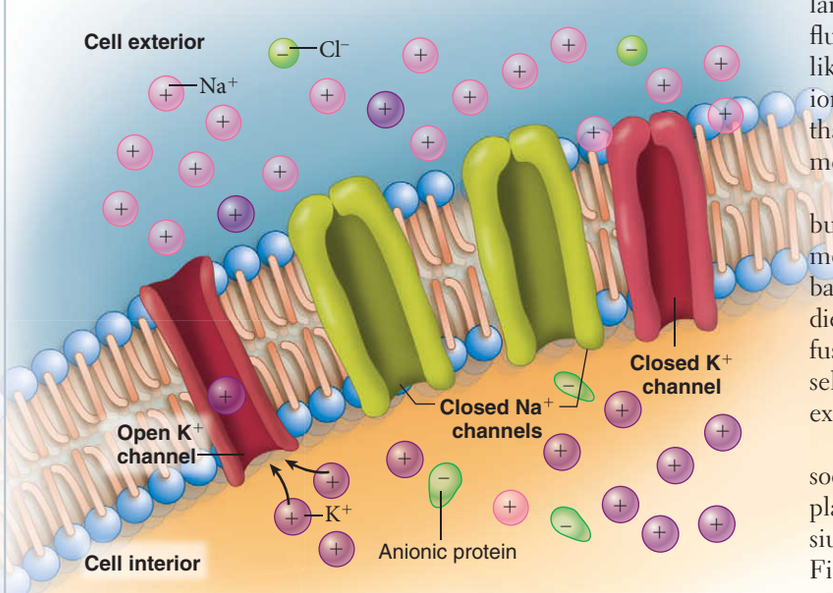


FIGURE 13-15

Role of ion channels in maintaining the resting membrane potential (RMP). Some K^+ channels are open in a "resting" membrane, allowing K^+ to diffuse down its concentration gradient (out of the cell) and thus add to the excess of positive ions on the outer surface of the plasma membrane. Diffusion of Na^+ in the opposite direction would counteract this effect but is prevented from doing so by closed Na^+ channels. Compare this figure with Figure 13-16.

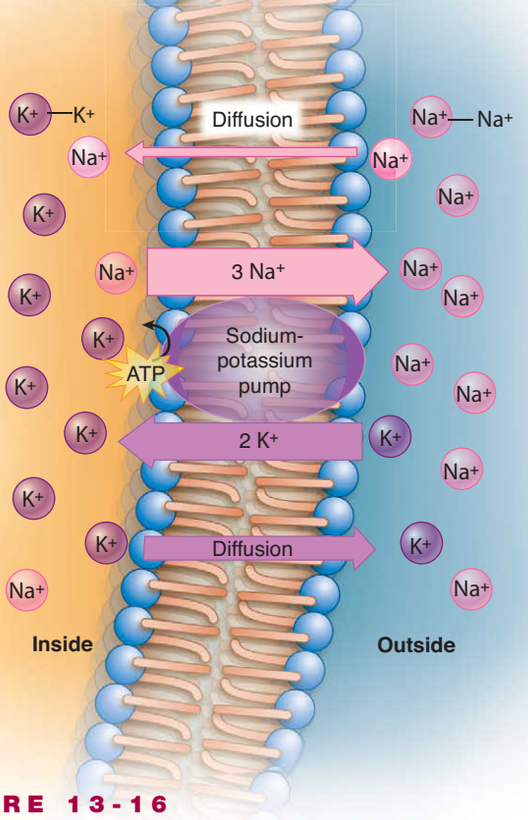


FIGURE 13-16

Sodium-potassium pump. This mechanism in the plasma membrane actively pumps sodium ions (Na^+) out of the neuron and potassium ions (K^+) into the neuron—at an unequal (3:2) rate. Because very little sodium reenters the cell via diffusion, this maintains an imbalance in the distribution of ions and thus maintains the resting potential. (See Figure 13-15 for the role of ion channels in the diffusion of ions.)

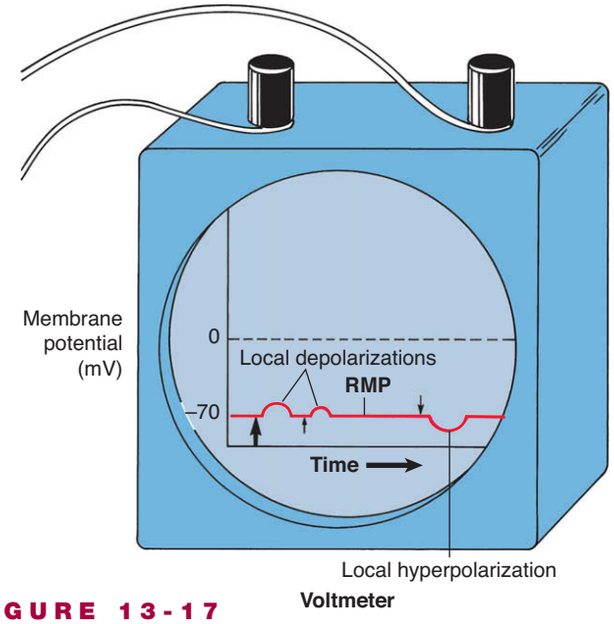


FIGURE 13-17

Local potentials. Recording voltmeter shows that excitatory stimuli (↑) cause depolarizations (movements toward 0 mV) in proportion to the strength of the stimuli. Inhibitory stimuli (↓) cause hyperpolarizations, local deviations away from 0 mV that cause the membrane potential to dip below the level of the resting membrane potential (RMP). Voltage is recorded as a red line on the screen of the voltmeter. Upward deviations of the red line are depolarizations; downward deviations of the red line are hyperpolarizations.

The RMP can be maintained by a cell as long as its sodium-potassium pumps continue to operate and its permeability characteristics remain stable. If either of these mechanisms is altered, the RMP is altered as well.

Local Potentials

In neurons, membrane potentials can fluctuate above or below the resting membrane potential in response to certain stimuli (Figure 13-17). A slight shift away from the RMP in a specific region of the plasma membrane is often called a **local potential.**

Excitation of a neuron occurs when a stimulus triggers the opening of stimulus-gated Na^+ channels. **Stimulus-gated channels** are ion channels that open in response to a sensory stimulus or a chemical stimulus from another neuron. Many stimulus-gated channels are located in the membrane of the neuron's input zone—the dendrites and soma (see Figure 13-8). The opening of stimulus-gated Na^+ channels in response to a stimulus permits more Na^+ to enter the cell. As the excess of positive ions outside the plasma membrane decreases, the magnitude of the membrane potential is reduced. Such movement of the membrane potential toward zero is called **depolarization.** In *inhibition*, a stimulus triggers the opening of stimulus-gated K^+ channels. As more K^+ diffuses out of the cell, the excess of positive ions outside the plasma membranes increases—increasing the magnitude of the membrane potential. Movement of the membrane potential away from zero (thus below the usual RMP) is called **hyperpolarization.**

Local potentials are called *graded potentials* because the magnitude of deviation from the RMP is proportional to the magnitude of the stimulus. In short, local potentials can be large or small—they are not all-or-none events. Local potentials exhibit *decremental* conduction, which means that their magnitude decreases as they travel along a membrane. Local potentials are called "local" nerve signals because they are more or less isolated to a particular region of the plasma membrane. That is, local potentials do not spread all the way to the end of a neuron's axon.

| QUICK CHECK |

16. What mechanisms are involved in producing the resting membrane potential?
17. In a resting neuron, what positive ion is most abundant outside the plasma membrane? What positive ion is most abundant inside the plasma membrane?
18. How does depolarization of a membrane differ from hyperpolarization?

ACTION POTENTIAL

An **action potential** is, as the term suggests, the membrane potential of an active neuron, that is, one that is conducting an impulse. A synonym commonly used for action potential is *nerve impulse.* The action potential is an electrical fluctuation that travels along the surface of a neuron's plasma membrane.

As with local potentials, understanding how action potentials are generated requires familiarity with gated ion channels. Table 13-1 summarizes the types and functions of gated channels for sodium and potassium that are important for understanding changes in membrane potential.

TABLE 13-1 Sodium and Potassium Channel Types and Functions

CHANNEL	EFFECT ON ION TRANSPORT*	EFFECT ON MEMBRANE POTENTIAL	TYPES	TRIGGER	RESPONSE
Sodium (Na^+) channels	Na^+ ions diffuse into cell	Increase (more positive)	Stimulus-gated	Sensory stimulus	Rapid response
				Chemical stimulus (neurotransmitter)	Rapid response
			Voltage-gated	Increase in membrane potential (to threshold potential [–59 mV] or beyond)	Rapid response
Potassium (K^+) channels	K^+ ions diffuse out of cell	Decrease (more negative)	Stimulus-gated	Sensory stimulus	Rapid response
				Chemical stimulus (neurotransmitter)	Rapid response
			Voltage-gated	Increase in membrane potential (to threshold potential [–59 mV] or beyond)	Slow response

*Net diffusion of ions down their respective concentration gradients.

TABLE 13-2 Steps of the Mechanism That Produces an Action Potential

STEP	DESCRIPTION
1	A stimulus triggers stimulus-gated Na^+ channels to open and allow inward Na^+ diffusion. This causes the membrane to depolarize.
2	As the threshold potential is reached, voltage-gated Na^+ channels open.
3	As more Na^+ enters the cell through voltage-gated Na^+ channels, the membrane depolarizes even further.
4	The magnitude of the action potential peaks (at +30 mV) when voltage-gated Na^+ channels close.
5	Repolarization begins when voltage-gated K^+ channels open, allowing outward diffusion of K^+.
6	After a brief period of hyperpolarization, the resting potential is restored by the sodium-potassium pump and the return of ion channels to their resting state.

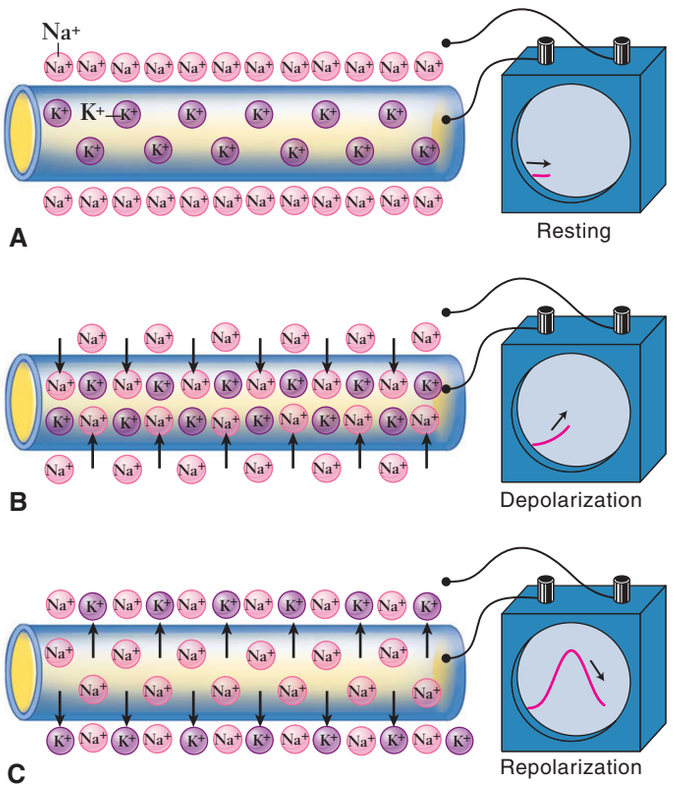


FIGURE 13-18

Depolarization and repolarization. A, Resting membrane potential (RMP) results from an excess of positive ions on the outer surface of the plasma membrane. More Na^+ ions are on the outside of the membrane than K^+ ions are on the inside of the membrane. **B,** Depolarization of a membrane occurs when Na^+ channels open, allowing Na^+ to move to an area of lower concentration (and more negative charge) *inside* the cell—reversing the polarity to an inside-positive state. **C,** Repolarization of a membrane occurs when K^+ channels then open, allowing K^+ to move to an area of lower concentration (and more negative charge) *outside* the cell—reversing the polarity back to an inside-negative state. Each voltmeter records the changing membrane potential as a red line.

A step-by-step description of the mechanism that produces the action potential is given in the following paragraphs and in Table 13-2. Refer to Figures 13-18 and 13-19 as you read each step.

1. When an adequate stimulus is applied to a neuron, the stimulus-gated Na^+ channels at the point of stimulation open. Na^+ diffuses rapidly into the cell because of the concentration gradient and electrical gradient, producing a local depolarization (see Figure 13-18, *B*).
2. If the magnitude of the local depolarization surpasses a limit called the **threshold potential** (for example, −59 mV), voltage-gated Na^+ channels are stimulated to open. **Voltage-gated channels** are ion channels that open in response to voltage fluctuations, usually at least −50 mV to −60 mV. There are many voltage-gated Na^+ channels and K^+ channels in the membrane of the neuron's summation zone (axon hillock) and conduction zone (axon) (see Figure 13-8). The threshold potential is the minimum magnitude a voltage fluctuation in the summation or conduction zone must have to trigger the opening of a voltage-gated ion channel.
3. As more Na^+ rushes into the cell, the membrane moves rapidly toward 0 mV and then continues in a positive direction to a peak of +30 mV (see Figure 13-19). The positive value at the peak of the action potential indicates that there is an excess of positive ions *inside* the membrane. If the local depolarization fails to cross the threshold of −59 mV, the voltage-gated Na^+ channels do not open, and the membrane simply recovers back to the resting potential of −70 mV without producing an action potential.
4. Voltage-gated Na^+ channels stay open for only about 1 millisecond (ms) before they automatically close. This means that once they are stimulated, the Na^+ channels always allow sodium to rush in for the same amount of time, which in turn

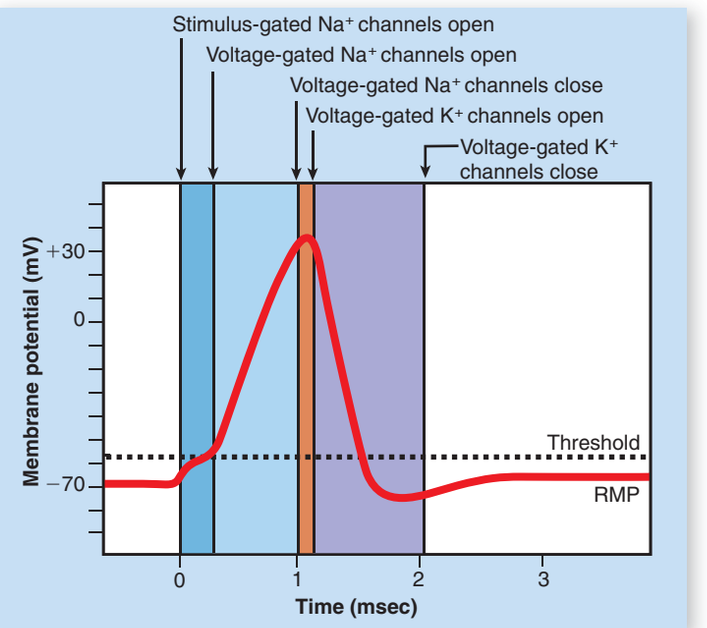


FIGURE 13-19

The action potential. Changes in membrane potential in a local area of a neuron's membrane result from changes in membrane permeability.

TABLE 13-3 Types of Membrane Potentials

MEMBRANE POTENTIAL	POLARIZATION	TYPICAL VOLTAGE*	SUMMATION	CONDUCTION	DESCRIPTION
Resting membrane potential (RMP)	Polarized	–70 mV	Not applicable	Not applicable	Membrane voltage when the neuron is not excited and not conducting an impulse
Local potential	Depolarized (excitatory; EPSP)	Graded; varies higher than –70 mV	Yes	Decremental	Temporary fluctuation in a local region of the membrane in response to a sensory or nerve stimulus; may be an upward or downward fluctuation in voltage; loses amplitude as it spreads along membrane
	Hyperpolarized (inhibitory; IPSP)	Graded; varies lower than –70 mV	Yes	Decremental	
Threshold potential	Depolarized	–59 mV	Yes	Triggers action potential	Minimum local depolarization needed to trigger voltage-gated channels that produce the action potential
Action potential	Depolarized	+30 mV	No	Nondecremental	Temporary maximum depolarization of membrane voltage that travels to end of axon without losing amplitude

*Example used in this chapter; actual values in body vary depending on many diverse factors.
EPSP, Excitatory postsynaptic potential; *IPSP,* inhibitory postsynaptic potential.

produces the same magnitude of action potential. In other words, the action potential is an *all-or-none* response. If the threshold potential is surpassed, the full peak of the action potential is always reached; if the threshold potential is not surpassed, no action potential will occur at all.

5. Once the peak of the action potential is reached, the membrane potential begins to move back toward the resting potential (–70 mV) in a process called **repolarization.** Surpassing the threshold potential triggers the opening of not only voltage-gated Na^+ channels but also voltage-gated K^+ channels. The voltage-gated K^+ channels are slow to respond, however, and thus do not begin opening until the inward diffusion of Na^+ ions has caused the membrane potential to reach +30 mV. Once the K^+ channels open, K^+ rapidly diffuses out of the cell because of the concentration gradient and because it is repulsed by the now-positive interior of the cell. The outward rush of K^+ restores the original excess of positive ions on the outside surface of the membrane—thus repolarizing the membrane (see Figure 13-18).
6. Because the K^+ channels often remain open as the membrane reaches its resting potential, too much K^+ may rush out of the cell. This causes a brief period of hyperpolarization before the resting potential is restored by the action of the sodium-potassium pump and the return of ion channels to their resting state.

Table 13-3 summarizes essential characteristics of the action potential along with other important types of membrane potentials discussed so far in this chapter.

Refractory Period

The refractory period is a brief period during which a local area of an axon's membrane resists restimulation (Figure 13-20, *A*). For

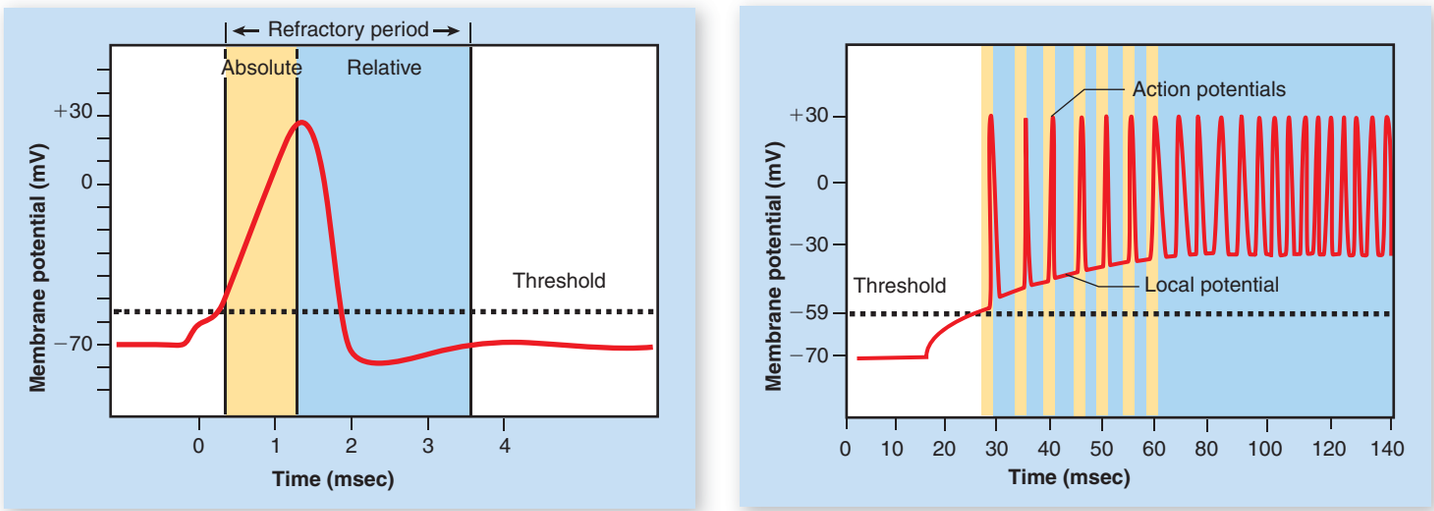


FIGURE 13-20

Refractory period. A, During the absolute refractory period, the membrane will not respond to any stimulus. During the relative refractory period, however, a very strong stimulus may elicit a response in the membrane. **B,** As the local potential increases, a new action potential may begin during the relative refractory period. The higher the local potential, the sooner a new action potential can be generated. As the graph shows, high local potentials produce a higher frequency of action potentials than lower local potentials.

about 0.5 ms after the membrane surpasses the threshold potential, it will not respond to any stimulus, no matter how strong. This is called the **absolute refractory period.** The **relative refractory period** is the few milliseconds after the absolute refractory period—the time during which the membrane is repolarizing and restoring the resting membrane potential. During the relative refractory period the membrane will respond only to very strong stimuli.

Because only very strong stimuli can produce an action potential during the relative refractory period, a series of closely spaced action potentials can occur only when the magnitude of the stimulus is great. The greater the magnitude of the stimulus, the earlier a new action potential can be produced, and thus the greater the frequency of action potentials (Figure 13-20, *B*). This means that although the magnitude of the stimulus does not affect the magnitude of the action potential, which is an all-or-none response, it does cause a proportional increase in the frequency of impulses. Thus the nervous system uses the frequency of nerve impulses to code for the strength of a stimulus—not changes in the magnitude of the action potential.

Conduction of the Action Potential

At the peak of the action potential, the inside of the axon's plasma membrane is positive relative to the outside. That is, its polarity is now the reverse of that of the resting membrane potential. Such reversal in polarity causes electrical current to flow between the site of the action potential and the adjacent regions of membrane. This local current flow triggers voltage-gated Na^+ channels in the next segment of membrane to open. As Na^+ rushes inward, this next segment exhibits an action potential. The action potential thus has moved from one point to the next continuously along the axon's membrane (Figure 13-21). This cycle repeats itself because each action potential always causes enough local current flow to surpass the threshold potential for the next region of membrane. Because each action potential is an all-or-none phenomenon, the fluctuation in membrane potential moves along the membrane without any decrement, or decrease, in magnitude.

The action potential never moves backward, restimulating the region from which it just came. It is prevented from doing so because the previous segment of membrane remains in a refractory period too long to allow such restimulation. This is the mechanism responsible for the one-way movement of action potentials along axons.

In myelinated fibers, the insulating properties of the thick myelin sheath resist ion movement and the resulting local flow of current. Electrical changes in the membrane can only occur at gaps in the myelin sheath, that is, at the nodes of Ranvier. Figure 13-22 shows that when an action potential occurs at one node, most of the current flows *under* the insulating myelin sheath to the next node. This stimulates regeneration of an action potential at that node by opening voltage-gated channels, which in turn stimulates the next node. Thus the action potential seems to "leap" from

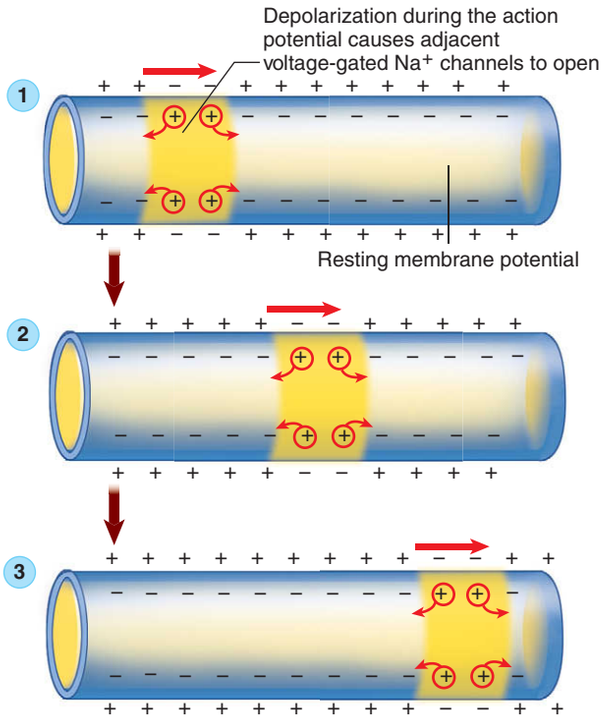


FIGURE 13-21

Continuous conduction of the action potential. The reverse polarity characteristic of the peak of the action potential causes local current flow to adjacent regions of the membrane *(small arrows).* This stimulates voltage-gated Na^+ channels to open and thus create a new action potential. This cycle continues, producing wavelike conduction of the action potential from point to point along a nerve fiber. Adjacent regions of membrane behind the action potential do not depolarize again because they are still in their refractory period.

node to node along the myelinated fiber. This type of impulse regeneration is called **saltatory conduction** (from the Latin verb *saltare*, "to leap").

How fast does a nerve fiber conduct impulses? It depends on its diameter and on the presence or absence of a myelin sheath. The speed of conduction of a nerve fiber is proportional to its diameter: the larger the diameter, the faster it conducts impulses. Myelinated fibers conduct impulses more rapidly than unmyelinated fibers. This is because saltatory conduction is more rapid than point-to-point, continuous conduction. The fastest fibers, such as those that innervate the skeletal muscles, can conduct impulses up to about 130 meters per second (close to 300 miles per hour). The slowest fibers, such as those from sensory receptors in the skin, may conduct impulses at only about 0.5 meter per second (little more than 1 mile per hour).

Box 13-4 outlines how disrupting conduction of nerve impulses can be used to block pain signals.

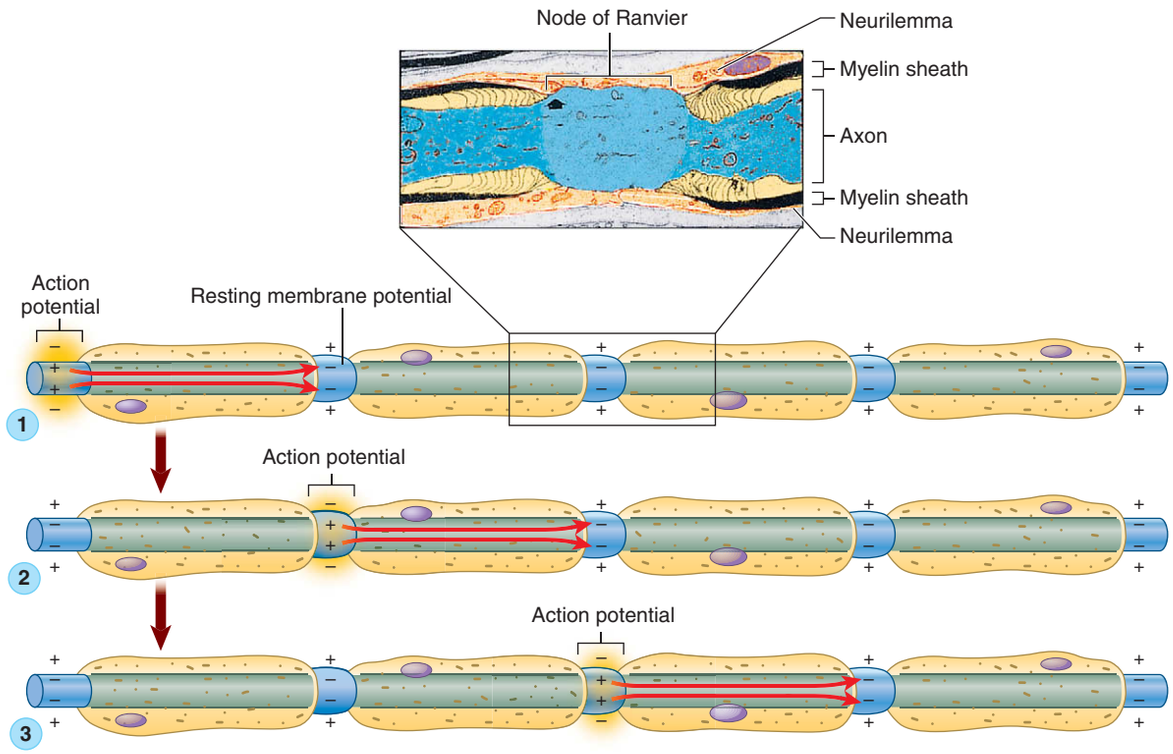


FIGURE 13–22

Saltatory conduction. This series of diagrams shows that the insulating nature of the myelin sheath prevents ion movement everywhere but at the nodes of Ranvier. The action potential at one node triggers current flow *(arrows)* across the myelin sheath to the next node—producing an action potential there. The action potential thus seems to "leap" rapidly from node to node. The inset is a transmission electron micrograph showing a node of Ranvier in a myelinated fiber.

Box 13-4 | HEALTH matters

Reducing Damage to Nerve Fibers

Crushing and bruising cause most injuries to the spinal cord—often damaging nerve fibers irreparably. This usually results in **paralysis** or loss of function in the muscles normally supplied by the damaged fibers. Unfortunately, the inflammation of the injury site usually damages even more fibers and thus increases the extent of the paralysis. However, early treatment of the injury with the antiinflammatory drug *methylprednisolone* can reduce the inflammatory response in the damaged tissue and thus limit the severity of a spinal cord injury. Although early studies failed to confirm the effectiveness of standard doses of this steroid drug, later studies showed that very large doses administered within 8 hours of the injury reduced the extent of nerve cell damage dramatically. Since about 95% of the 10,000 Americans suffering spinal cord injuries each year are admitted for treatment well before the 8-hour limit, this drug may prove to be the first effective therapy for spinal cord injuries.

| QUICK CHECK |

19. List the events that lead to the initiation of an action potential.
20. What is meant by the term *threshold potential?*
21. How does impulse conduction in an unmyelinated fiber differ from impulse conduction in a myelinated fiber?

SYNAPTIC TRANSMISSION

Structure of the Synapse

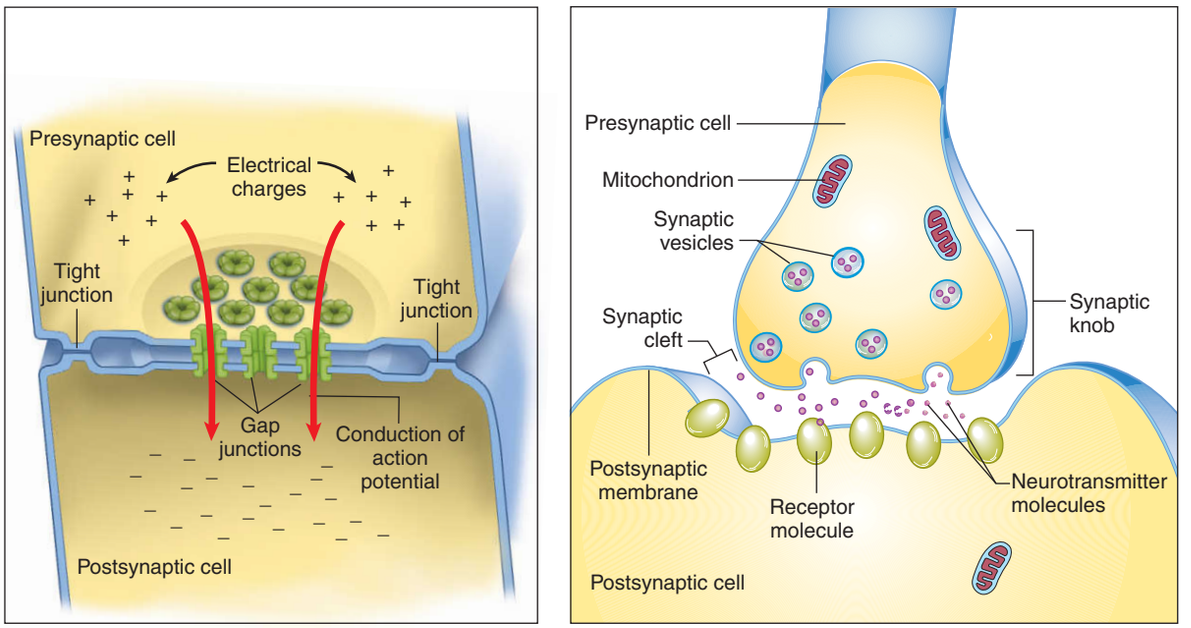
A synapse is the place where signals are transmitted from one neuron, called the *presynaptic neuron*, to another neuron, called the *postsynaptic neuron*. The postsynaptic cell could also be an effector, such as a muscle. There are many such connections in our nervous system—over 100 trillion synapses in our brain alone!

Types of Synapses

There are two types of synapses: electrical synapses and chemical synapses.

FIGURE 13-23

Electrical and chemical synapses. A, Electrical synapses involve gap junctions that allow action potentials to move from cell to cell directly by allowing electrical current to flow between cells. **B,** Chemical synapses involve transmitter chemicals (neurotransmitters) that signal postsynaptic cells, possibly inducing an action potential.



Electrical synapses occur where two cells are joined end-to-end by gap junctions (Figure 13-23, A). Because the plasma membranes and cytoplasm are functionally continuous in this type of junction, an action potential can simply continue along the postsynaptic plasma membrane as if it belonged to the same cell. Electrical synapses occur between cardiac muscle cells and between some types of smooth muscle cells. Electrical synapses are found throughout the nervous system early in development. These early electrical synapses are thought to be eventually replaced by the more complex chemical synapses. However, evidence suggests that electrical synapses may be more abundant, and more critical to certain functions, in adults than previously thought.

Chemical synapses are called that because they use a chemical transmitter called a *neurotransmitter* to send a signal from the **presynaptic** cell to the **postsynaptic** cell (Figure 13-23, *B*). Because of its importance and complexity, it is the chemical synapse that we will consider carefully in the following paragraphs.

CHEMICAL SYNAPSE

Three structures make up a chemical synapse:

1. A synaptic knob
2. A synaptic cleft
3. The plasma membrane of a postsynaptic neuron

A *synaptic knob* is a tiny bulge at the end of a terminal branch of a presynaptic neuron's axon (see Figure 13-23). Each synaptic knob, or synaptic terminal, contains numerous small sacs or vesicles. Each vesicle contains about 10,000 neurotransmitter molecules. Some of these are released from the presynaptic neuron into a **synaptic cleft**—the space between a synaptic knob and the plasma membrane of a postsynaptic neuron.

The synaptic cleft is an incredibly narrow space—only 20 to 30 nanometers (nm), or about one millionth of an inch in width.

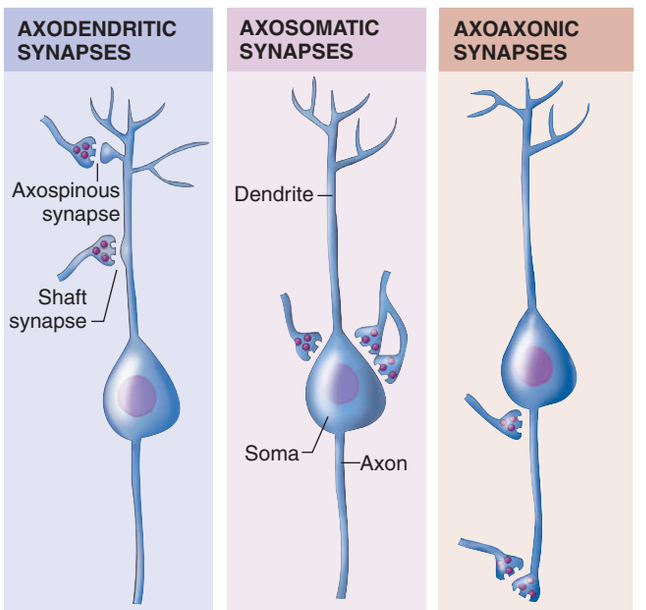


FIGURE 13-24

Arrangements of synapses. The axon of a presynaptic neuron may form a synapse at the dendrite, soma, or axon of another neuron.

Identify the synaptic cleft in Figure 13-23. The synaptic cleft is not an empty space—it contains fluid, enzymes, adhesion molecules, and other substances.

Figure 13-24 shows that an axon may form a synapse at any of several points along a postsynaptic neuron:

- At the dendrite (axodendritic synapses)
- At the soma (axosomatic synapses)
- At the axon (axoaxonic synapses)

Synapses at the dendrite or soma are the most common arrangements in many areas of the nervous system. Synapses of an axon with the axon of another neuron are less common but offer a way for one neuron to inhibit or facilitate synaptic transmission by another neuron.

The plasma membrane of a postsynaptic neuron has protein molecules embedded in it, each facing toward the synaptic knob (see Figure 13-23). These membrane molecules serve as receptors to which neurotransmitter molecules bind and trigger responses in the postsynaptic cell.

Mechanisms of Synaptic Transmission

An action potential that has traveled the length of a neuron stops at its axon terminals. Action potentials cannot cross synaptic clefts, minuscule barriers though they are. Instead, neurotransmitters are released from the synaptic knob, cross the synaptic cleft, and bring about a response by the postsynaptic neuron. *Excitatory* neurotransmitters cause depolarization of the postsynaptic membrane, whereas *inhibitory* neurotransmitters cause hyperpolarization of the postsynaptic membrane (see Figure 13-17).

The mechanism of synaptic transmission, summarized in Figures 13-23 and 13-25, consists of the following sequence of events:

1. When an action potential reaches a synaptic knob, voltage-gated calcium channels in its membrane open and allow calcium ions (Ca^{++}) to diffuse into the knob rapidly. Many voltage-gated Ca^{++} channels are present in the membrane of the neuron's output zone (see Figure 13-8).
2. The increase in intracellular Ca^{++} concentration triggers the movement of neurotransmitter vesicles to the plasma

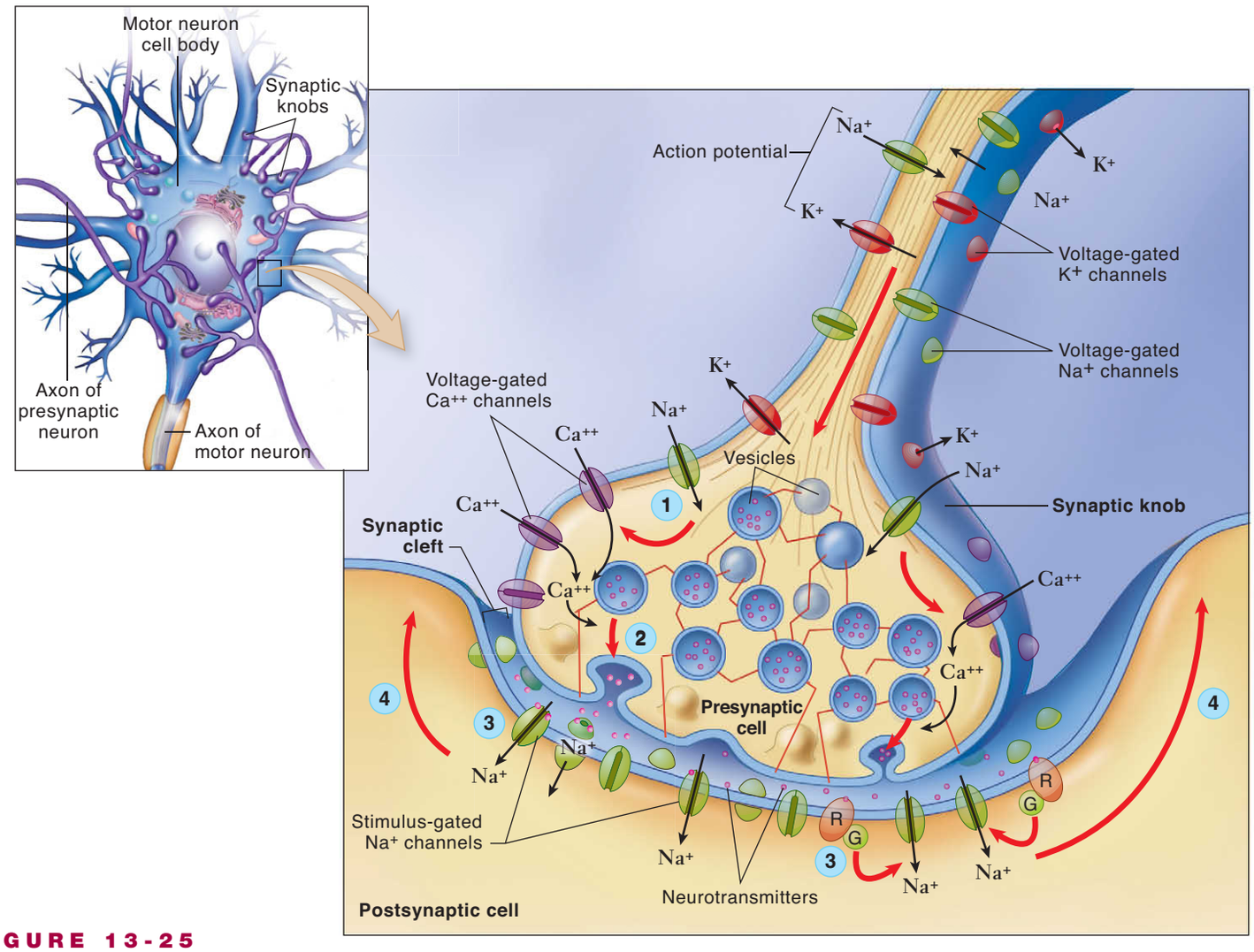


FIGURE 13-25

The chemical synapse. Diagram shows detail of synaptic knob, or axon terminal, of presynaptic neuron, the plasma membrane of a postsynaptic neuron, and a synaptic cleft. On the arrival of an action potential at a synaptic knob, voltage-gated Ca^{++} channels open and allow extracellular Ca^{++} to diffuse into the presynaptic cell *(step 1)*. In step 2, the Ca^{++} triggers the rapid exocytosis of neurotransmitter molecules from vesicles in the knob. In step 3, neurotransmitter diffuses into the synaptic cleft and binds to receptor molecules in the plasma membrane of the postsynaptic neuron. The postsynaptic receptors directly or indirectly trigger the opening of stimulus-gated ion channels, initiating a local potential in the postsynaptic neuron. In step 4, the local potential may move toward the axon, where an action potential may begin.

membrane of the synaptic knob. Once there, they fuse with the membrane and release their neurotransmitter via exocytosis. Thousands of neurotransmitter molecules spurt out of the open vesicles into the synaptic cleft.

3. The released neurotransmitter molecules almost instantaneously diffuse across the narrow synaptic cleft and contact the postsynaptic neuron's plasma membrane. Here, neurotransmitters briefly bind to receptor molecules that are also gated channels or that are coupled to gated channels. Binding of neurotransmitters triggers the channels to open.
4. The opening of ion channels in the postsynaptic membrane may produce a local potential called a **postsynaptic potential.** Excitatory neurotransmitters cause both Na^+ channels and K^+ channels to open. Because Na^+ rushes inward faster than K^+ rushes outward, there is a temporary depolarization called an **excitatory postsynaptic potential (EPSP).** Inhibitory neurotransmitters cause K^+ channels and/or Cl^- channels to open. If K^+ channels open, K^+ rushes outward; if Cl^- channels open, Cl^- rushes inward. Either event makes the inside of the membrane even more negative than at the resting potential. This temporary hyperpolarization is called an **inhibitory postsynaptic potential (IPSP).**
5. Once a neurotransmitter binds to its postsynaptic receptors, its action is quickly terminated (Figure 13-26). Several mechanisms bring this about. Some neurotransmitter molecules are transported back into the synaptic knobs, where they can be repacked into vesicles and used again. Some neurotransmitter molecules are metabolized into inactive compounds by synaptic enzymes. Other neurotransmitter molecules simply diffuse out of the synaptic cleft and are transported into nearby glial cells. The glial cells may release them again for reuptake by the presynaptic neuron, sometimes after breaking them down into another form.

Some mechanisms of synaptic transmission are illustrated in Figures 13-25 and 13-26. The diagram in Figure 13-27 summarizes all the main events of synaptic transmission.

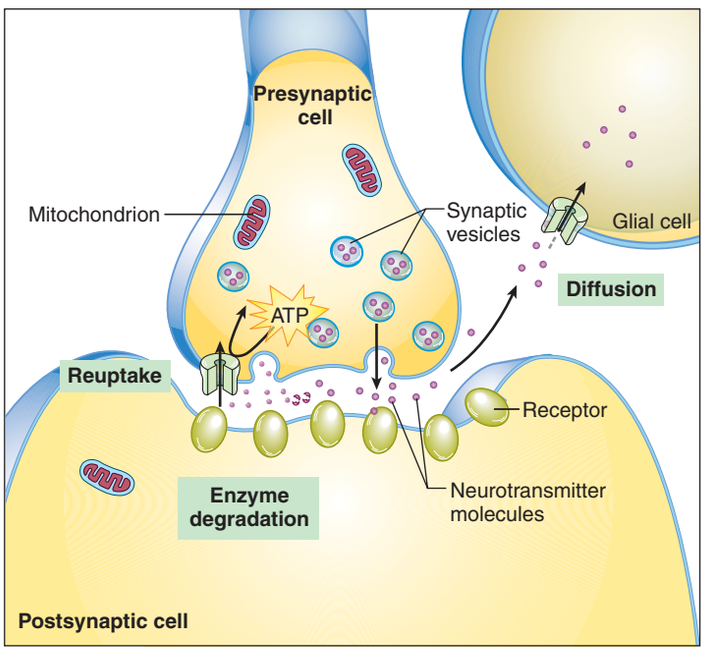


FIGURE 13-26

Fate of neurotransmitters. After synaptic transmission, the signal must be stopped by removing neurotransmitters from the synaptic cleft. Many neurotransmitters are immediately transported back into the presynaptic neuron in a process called *reuptake.* Some neurotransmitters are broken down by enzymes in the synaptic cleft, and the resulting molecules are transported back into the presynaptic neuron for recycling. Some neurotransmitter molecules may diffuse out of the synapse and be transported into a nearby glial cell (which may return an altered form of the molecule to the presynaptic neuron).

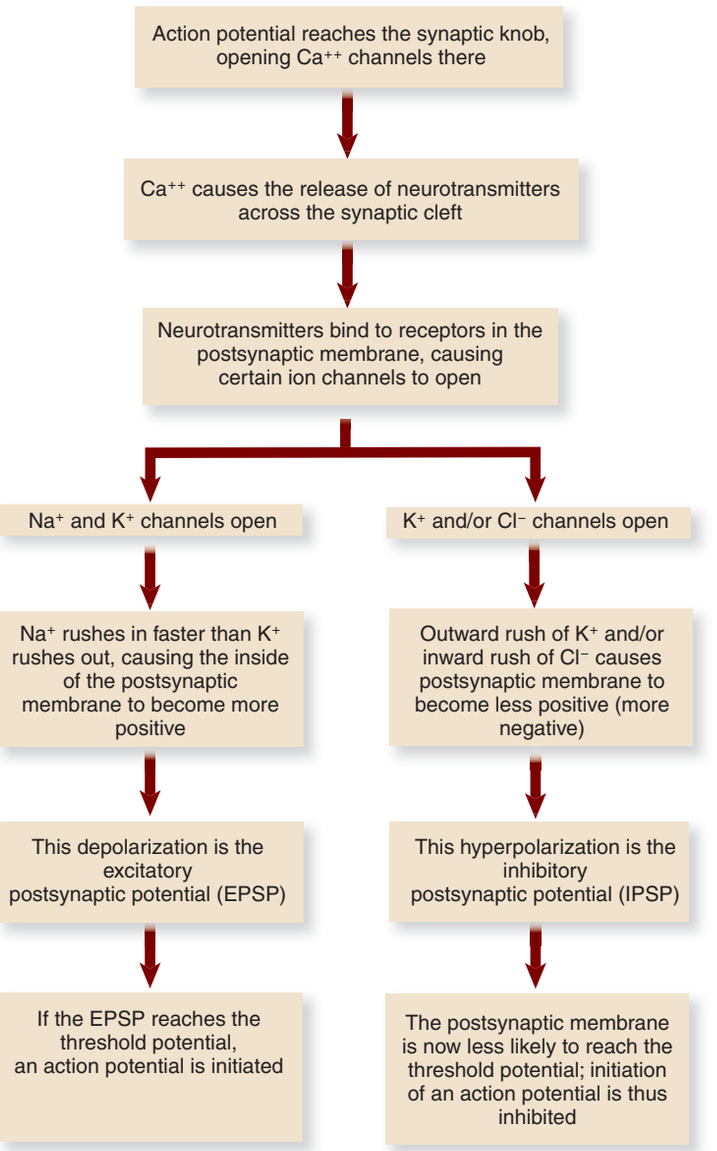
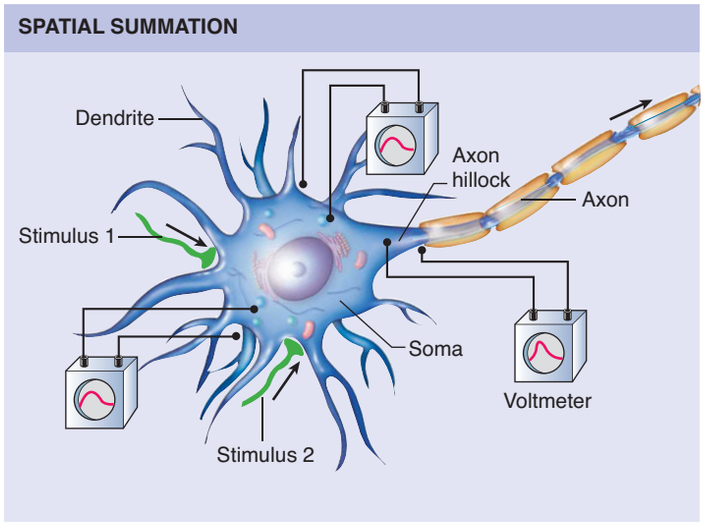
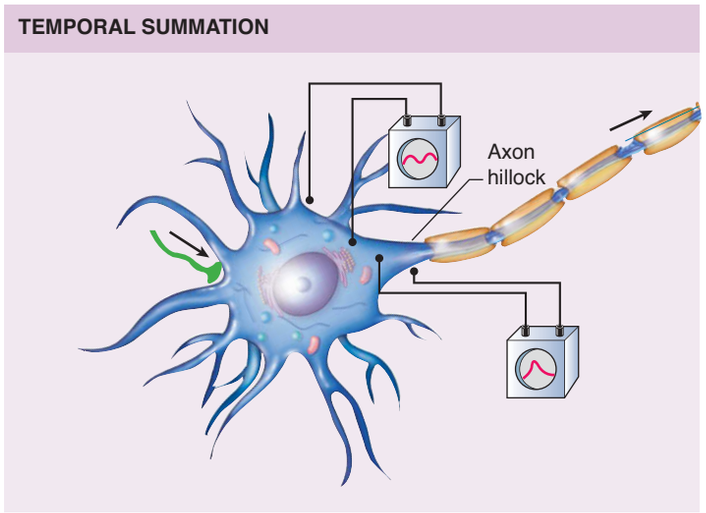


FIGURE 13-27

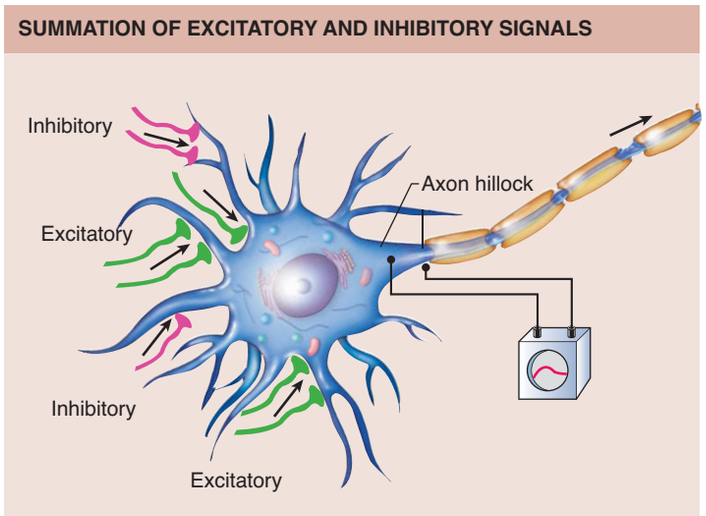
Summary of synaptic transmission.



A



B



C

Summation

At least several, usually thousands, and in some cases more than 100,000, knobs synapse with a single postsynaptic neuron. The amount of excitatory neurotransmitter released by one knob is not enough to trigger an action potential. It may, however, *facilitate* initiation of an action potential by producing a local depolarization of the synaptic membrane—an EPSP. When several knobs are activated simultaneously, neurotransmitters stimulate different locations on the postsynaptic membrane. These local potentials may spread far enough to reach the axon hillock, where they may add together, or *summate*. If the sum of the local potentials reaches the threshold potential, voltage-gated channels in the axon membrane open, producing an action potential (Figure 13-28, *A*). This phenomenon is called **spatial summation.**

Likewise, when synaptic knobs stimulate a postsynaptic neuron in rapid succession, their effects can add up over a brief period of time to produce an action potential (Figure 13-28, *B*). This type of summation is called **temporal summation.**

Usually both excitatory and inhibitory transmitters are released at the same postsynaptic neuron. The excitatory neurotransmitters produce local EPSPs, and the inhibitory neurotransmitters produce local IPSPs. Summation of these opposing local potentials occurs at the axon hillock, where many voltage-gated ion channels are located. If the EPSPs predominate over the IPSPs enough to depolarize the membrane to the threshold potential, the voltage-gated channels will respond and produce an action potential (Figure 13-28, *C*). The action potential is then conducted without decrement along the axon's membrane.

On the other hand, if the IPSPs predominate over the EPSPs, the membrane will not reach the threshold potential. The voltage-gated channels at the axon hillock will not respond, and no action potential will be conducted along the axon.

One reason summation is important for our understanding of the nervous system is that it helps explain how information can be processed as it moves through a network of neurons. For example, not all of the sensory information your sensory neurons are receiving right now is actually getting to the conscious part of your brain.

FIGURE 13-28

Summation. A, Spatial summation is the effect produced by simultaneous stimulation by a number of synaptic knobs on the same postsynaptic neuron. Voltmeters placed near the site of stimulation show small depolarizations, and a voltmeter at the axon hillock shows the large depolarization resulting from the combined effect of both smaller depolarizations. **B,** Temporal summation is the effect produced by a rapid succession of stimuli on a single postsynaptic neuron. The figure shows two stimuli in a short burst that produce two small depolarizations that combine at the axon hillock to produce a large depolarization. **C,** Summation of many excitatory and inhibitory effects produces the potential at the axon hillock. Here, depolarizations triggered by five excitatory presynaptic neurons *(green),* are partially offset by hyperpolarizations triggered by three inhibitory presynaptic neurons *(red)* to produce only a small depolarization at the axon hillock. This will occur only if there is sufficient depolarization to surpass the threshold potential.

Of course, it would be overwhelming if all that information did get into your consciousness. Much of it would have been stopped at synapses where threshold was not reached, as described in the preceding paragraphs. Thus summation is a mechanism for *making decisions* about what information should continue onward in the neural network.

Synapses and Memory

Current theories of memory state that synapses play a key role in how memories are stored in the nervous system. The most widely held idea is that information is stored in the form of an increased flow of information at synapses in particular pathways (depending on the memory stored). In other words, memories form when the flow of information is facilitated at synapses.

Short-term memories, lasting only a few seconds or minutes, may result from presynaptic facilitation or inhibition at particular synapses. Go back to Figure 13-24 on p. 401 to see how an axoaxonic synapse would permit one neuron to influence the presynaptic events of another neuron.

Intermediate long-term memory lasts from minutes to weeks. To get these memories to remain that long, facilitation of presynaptic activity has to last longer. One way that the nervous system does this involves the neurotransmitter *serotonin*. Serotonin is released at an axoaxonal synapse and triggers the axon terminal of a presynaptic neuron to block its potassium channels for up to several weeks. Thus whenever there is an action potential arriving at that presynaptic neuron, it lasts longer (because potassium fails to rapidly repolarize the membrane as shown in Figure 13-19 on p. 396). A prolonged action potential means that the presynaptic calcium channels stay open longer and trigger the release of more neurotransmitter than usual—thus facilitating synaptic transmission.

Long-term memories, the kind of memories needed for learning anatomy and physiology, last for months or years. Such long-term facilitation of synaptic transmission requires longer-lasting structural changes in the synapses. These changes may involve just one element or be a combination of the following: an increase in the number of vesicles stored, an increase in membrane locations from which the vesicles can release their neurotransmitters, an increase in the number of presynaptic axon terminals, and/or changes in the dendrites that permit postsynaptic facilitation.

Because nearby astrocytes can enhance or alter synaptic transmission by releasing transmitters of their own, they may also play a role in storing memories. Prion proteins (PrP), which can change shape and then cause other proteins in a neuron to change shape, have also been suggested as a memory mechanism.

| QUICK CHECK |

22. What are the three structural components of a synapse?
23. List the steps of synaptic transmission.
24. What is an EPSP? What is an IPSP?
25. How does temporal summation differ from spatial summation?
26. How are memories formed?

NEUROTRANSMITTERS

Neurotransmitters are the means by which neurons talk to one another. At billions, or more likely, trillions, of synapses throughout the body, presynaptic neurons release neurotransmitters that act to facilitate, stimulate, or inhibit postsynaptic neurons and effector cells. More than 50 compounds are known to be neurotransmitters. At least 50 other compounds are suspected of being neurotransmitters. For the most part, they are not distributed diffusely or at random throughout the nervous system. Instead, specific neurotransmitters are localized in discrete groups of neurons and thus released in specific nerve pathways (Box 13-5).

Classification of Neurotransmitters

Neurotransmitters are commonly classified by their function or by their chemical structure, depending on the context in which they are discussed. You are already familiar with two major functional classifications: *excitatory neurotransmitters* and *inhibitory neurotransmitters*. Some neurotransmitters can have inhibitory effects at some synapses and excitatory effects at other synapses. For example, the neurotransmitter *acetylcholine*, discussed in Chapter 12, excites skeletal muscle cells but inhibits cardiac muscle cells. This illustrates an important point about the action of neurotransmitters: their function is determined by the postsynaptic receptors, not by the neurotransmitters themselves.

Another way to classify neurotransmitters by function is to identify the mechanism by which they cause a change in the postsynaptic neuron or effector cell. Some neurotransmitters trigger the opening or closing of ion channels directly, by binding to one or both receptor sites on the channel itself (see figure in Box 13-6). This "direct mechanism" is illustrated in Figure 13-29.

Box 13-5 | HEALTH matters

Anesthetics

Anesthetics are substances that are administered to reduce or eliminate the sensation of pain—thus producing a state called **anesthesia.** Many anesthetics produce their effects by inhibiting the opening of sodium channels and thus blocking the initiation and conduction of nerve impulses. Anesthetics such as bupivacaine (Marcaine) are often used in dentistry to minimize pain involved in tooth extractions and other dental procedures. Procaine has likewise been used to block the transmission of electrical signals in sensory pathways of the spinal cord. Benzocaine and phenol, local anesthetics found in several over-the-counter products that relieve pain associated with teething in infants, sore throat pain, and other ailments, also produce their effect by blocking initiation and conduction of nerve impulses.

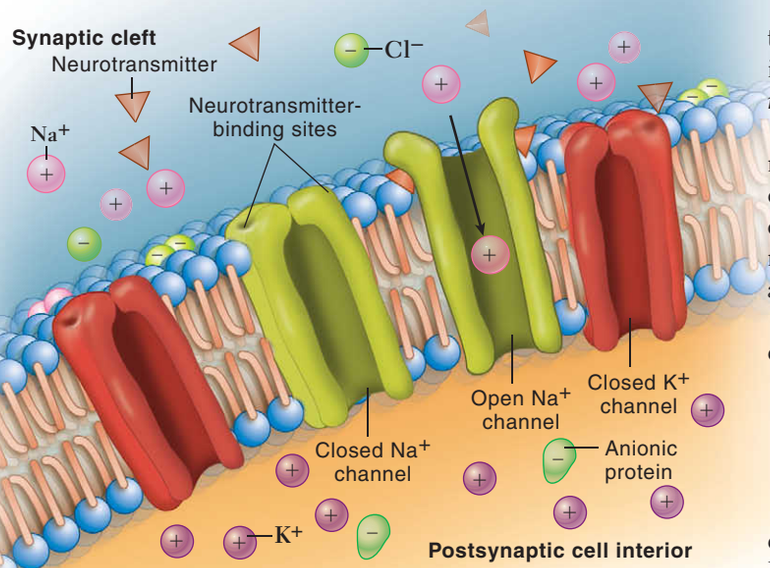


FIGURE 13-29

Direct stimulation of postsynaptic receptor. Some neurotransmitters, such as acetylcholine, initiate nerve signals by binding directly to one or both neurotransmitter-binding sites on the stimulus-gated ion channel. Such binding causes the channel to change its shape to an open position. When the neurotransmitter is removed, the channel again closes.

their chemical structure. Neurotransmitters can thus be grouped into two main groupings: *small-molecule transmitters* and *large-molecule transmitters.*

Small-molecule neurotransmitters are, as their name implies, molecules of a smaller size than those in the large-molecule category. Small-molecule neurotransmitters are amino acids or are derived from individual amino acids. Large-molecule neurotransmitters, on the other hand, are made up of more than one amino acid—usually chains of 2 to 40 amino acids.

Small-molecule transmitters are subdivided into four main chemical classes:

Class I Acetylcholine
Class II Amines
Class III Amino acids
Class IV Other small molecules

Large-molecule neurotransmitters are all neuropeptides—chains of several amino acids strung together by peptide bonds. Examples of neurotransmitters in each of these groupings are

Other neurotransmitters produce their effects by binding to receptors linked to G proteins that, in turn, activate chemical messengers within the postsynaptic cell. An example of this *second messenger* mechanism occurs when the neurotransmitter *norepinephrine* binds to **G-protein–coupled receptors (GPCRs).** Triggering the GPCR causes G proteins to activate the membrane-bound enzyme adenyl cyclase. The adenyl cyclase removes phosphate groups from adenosine triphosphate (ATP) to form cyclic adenosine monophosphate (cAMP). Cyclic AMP is the "second messenger," triggering the activation of the protein kinase A enzyme that eventually causes Na^+ channels in the postsynaptic membrane to open (Figure 13-30).

The second messenger mechanism is usually slower and longer lasting than the direct mechanism. And because the second messenger mechanism involves intracellular messengers, it can regulate other cellular processes, such as cytoskeleton movement, gene expression, and shuttling of proteins along the axonal transport system.

Learning about these mechanisms of neurotransmitter signaling has revolutionized our understanding of neurobiology—and thus our ability to prevent and treat illnesses. Many drugs and herbal supplements used in prevention and therapy today either enhance or inhibit particular steps of the mechanisms just described.

Because the functions of specific neurotransmitters vary by location, it is often most useful to classify them according to

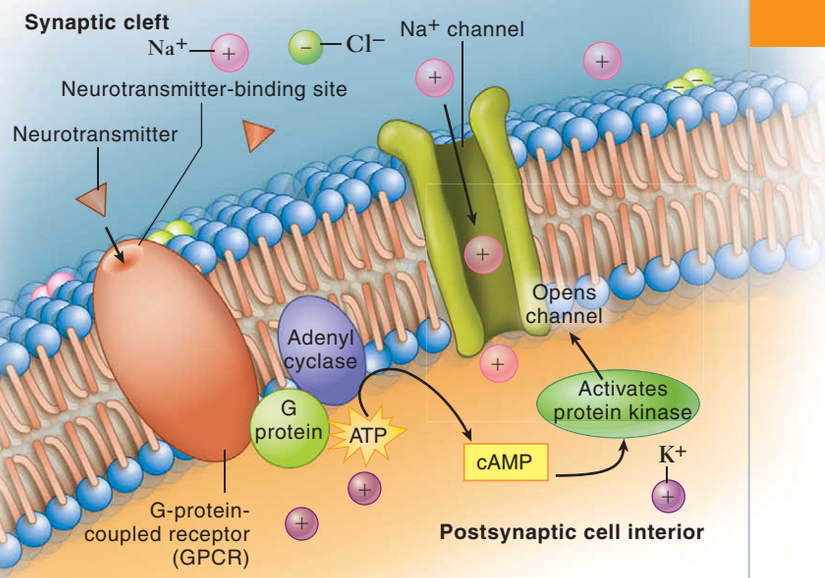


FIGURE 13-30

Second messenger stimulation of postsynaptic receptor. Norepinephrine and many other neurotransmitters initiate nerve signals indirectly by binding to a G-protein–coupled receptor (GPCR) that changes shape to activate the enzyme *adenylate cyclase,* which in turn catalyzes the conversion of ATP to cyclic AMP (cAMP). cAMP is a "second messenger" that induces a change in the shape of a stimulus-gated channel. (Compare with Figure 13-29.)

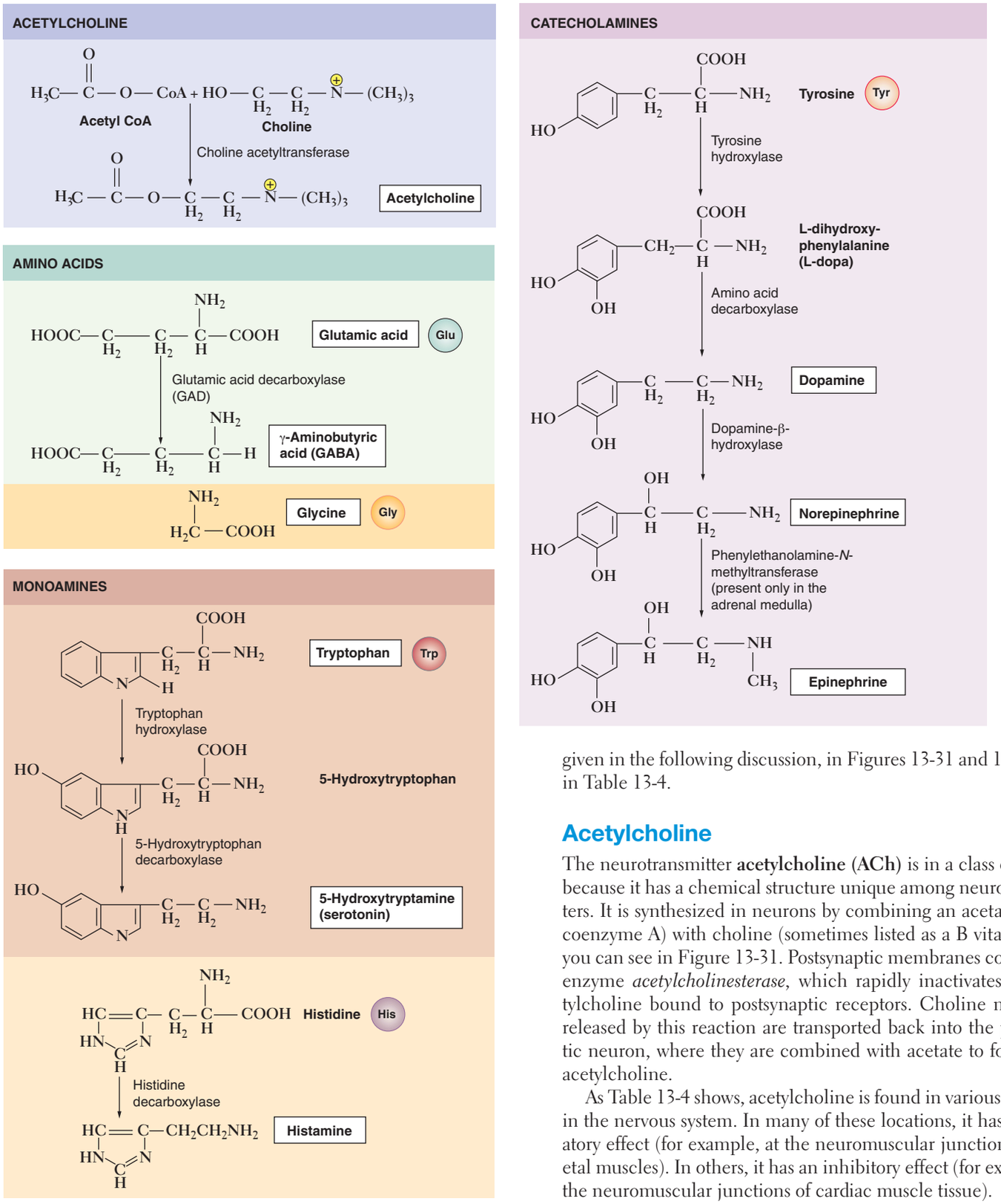


FIGURE 13-31

Examples of small-molecule neurotransmitters. Many of the small-molecule transmitters are amino acid molecules or are derived from the amino acids tryptophan, histidine, or tyrosine.

given in the following discussion, in Figures 13-31 and 13-32, and in Table 13-4.

Acetylcholine

The neurotransmitter **acetylcholine (ACh)** is in a class of its own because it has a chemical structure unique among neurotransmitters. It is synthesized in neurons by combining an acetate (acetyl coenzyme A) with choline (sometimes listed as a B vitamin)—as you can see in Figure 13-31. Postsynaptic membranes contain the enzyme *acetylcholinesterase*, which rapidly inactivates the acetylcholine bound to postsynaptic receptors. Choline molecules released by this reaction are transported back into the presynaptic neuron, where they are combined with acetate to form more acetylcholine.

As Table 13-4 shows, acetylcholine is found in various locations in the nervous system. In many of these locations, it has an excitatory effect (for example, at the neuromuscular junctions of skeletal muscles). In others, it has an inhibitory effect (for example, at the neuromuscular junctions of cardiac muscle tissue).

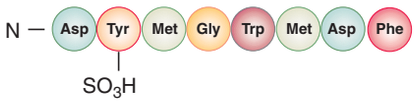
Amines

Amine neurotransmitters are synthesized from amino acid molecules, such as tyrosine, tryptophan, or histidine. Amines include

Vasoactive intestinal peptide (VIP)



Cholecystokinin-like peptide (CCK8)



Met-enkephalin



Substance P



Leu-enkephalin



β-Endorphin



FIGURE 13-32

Examples of neuropeptides. Large-molecule transmitters are made up of more than one amino acid.

TABLE 13-4 Examples of Neurotransmitters

NEUROTRANSMITTER	LOCATION*	FUNCTION*
Small-Molecule Transmitters		
Class I		
Acetylcholine (ACh)	Junctions with motor effectors (muscles, glands); many parts of brain	Excitatory or inhibitory; involved in memory
Class II: Amines		
Monoamines		
Serotonin (5-HT†)	Several regions of the CNS	Mostly inhibitory; involved in moods and emotions, sleep
Histamine	Brain	Mostly excitatory; involved in emotions and regulation of body temperature and water balance
Catecholamines		
Dopamine (DA)	Brain; autonomic system	Mostly inhibitory; involved in emotions/moods and in regulating motor control
Epinephrine	Several areas of the CNS and in the sympathetic division of the ANS	Excitatory or inhibitory; acts as a hormone when secreted by sympathetic neurosecretory cells of the adrenal gland
Norepinephrine (NE)	Several areas of the CNS and in the sympathetic division of the ANS	Excitatory or inhibitory; regulates sympathetic effectors; in brain, involved in emotional responses
Class III: Amino Acids		
Glutamate (glutamic acid, Glu)	CNS	Excitatory; most common excitatory neurotransmitter in CNS
Gamma-aminobutyric acid (GABA)	Brain	Inhibitory; most common inhibitory neurotransmitter in brain
Glycine (Gly)	Spinal cord	Inhibitory; most common inhibitory neurotransmitter in brain
Class IV: Other Small Molecules		
Nitric oxide (NO)	Several regions of the nervous system	May be a signal from postsynaptic to presynaptic neuron

*These are examples only; most of these neurotransmitters are also found in other locations, and many have additional functions.
†5-hydroxytryptamine (synonym for serotonin).
CNS, Central nervous system; *ANS,* autonomic nervous system.

(continued)

TABLE 13-4 Examples of Neurotransmitters *(continued)*

NEUROTRANSMITTER	LOCATION*	FUNCTION*
Large-Molecule Transmitters		
Neuropeptides		
Vasoactive intestinal peptide (VIP)	Brain; some ANS and sensory fibers; retina; gastrointestinal tract	Function in nervous system uncertain
Cholecystokinin (CCK)	Brain; retina	Function in nervous system uncertain
Substance P	Brain, spinal cord, sensory pain pathways; gastrointestinal tract	Mostly excitatory; transmits pain information
Enkephalins	Several regions of CNS; retina; intestinal tract	Mostly inhibitory; act like opiates to block pain
Endorphins	Several regions of CNS; retina; intestinal tract	Mostly inhibitory; act like opiates to block pain
Neuropeptide Y (NPY)	Brain, some ANS fibers	Variety of functions including enhancing blood vessel constriction by ANS, regulation of energy balance, learning, and memory

*These are examples only; most of these neurotransmitters are also found in other locations, and many have additional functions.
†5-hydroxytryptamine (synonym for serotonin).
CNS, Central nervous system; *ANS,* autonomic nervous system.

the neurotransmitters of the **monoamine** subclass: *serotonin* and *histamine*. Also included are neurotransmitters of the **catecholamine** subclass: *dopamine*, *epinephrine*, and *norepinephrine*.

Figure 13-31 shows how these subclasses of neurotransmitters are derived from different amino acids. It is not important to focus on the detailed chemical structures shown in the diagram. However, seeing that these neurotransmitters are chemically related to amino acids—and to each other—will help you better understand concepts in nutrition, pharmacology, and other health science applications.

The amine neurotransmitters are found in various regions of the brain, where they affect learning, emotions, motor control, and other activities (Box 13-6). In a previous section, we discussed the role of serotonin in forming memories. Dopamine, another amine, has an inhibitory effect on certain somatic motor pathways. When dopamine is deficient, the tremors and general overstimulation of muscles characteristic of *parkinsonism* occur. This effect will be discussed further in Chapter 14. Epinephrine and norepinephrine are also involved in motor control, specifically in the sympathetic pathways of the autonomic nervous system. Some autonomic neurons in the adrenal gland do not terminate at a postsynaptic effector cell but instead release their neurotransmitters directly into the bloodstream. When this occurs, epinephrine and norepinephrine are called *hormones* instead of neurotransmitters.

Amino Acids

Many biologists now believe that amino acids are among the most common neurotransmitters in the central nervous system. For example, it is thought that the amino acid *glutamate (glutamic acid)* is responsible for up to 75% of the excitatory signals in the brain. *Gamma-aminobutyric acid (GABA)*, which is derived from glutamate, is the most common inhibitory neurotransmitter in the brain. In the spinal cord, the most widely distributed inhibitory neurotransmitter is the simple amino acid *glycine*. These three neurotransmitters are shown in Figure 13-31.

Amino acids are found in all cells of the body, where they are used to synthesize various structural and functional proteins. In the nervous system, however, they are also stored in synaptic vesicles and used as neurotransmitters. Certain membrane receptors in the postsynaptic membrane are sensitive to high quantities of certain amino acids and thus trigger specific responses in the postsynaptic cell. It is believed that an imbalance of certain amino acids in the body could produce similar effects, and thus alter the function of the nervous system.

Other Small-Molecule Transmitters

The term "other" is not a very descriptive term for a category of compounds, but the discovery of a new group of small neurotransmitter molecules is so recent that a standard name for Class IV neurotransmitters has not been adopted. The prime example of this group is **nitric oxide (NO).** Nitric oxide is a small gas molecule that the cell makes from the amino acid arginine. NO was the first gas to be identified as a transmitter, but carbon monoxide (CO) may be another. Nitric acid is released from postsynaptic neurons and *diffuses backward* toward the presynaptic neuron, where it has its biochemical effects. This gives postsynaptic neurons a mechanism by which they can "talk back" to the presynaptic neuron, establishing the opportunity for feedback.

Neuropeptides

The **neuropeptide** neurotransmitters are short strands of amino acids called *polypeptides* or, more simply, *peptides*. Neuropeptide neurotransmitters are often called *neuroactive peptides*. Because they are made up of chains of amino acids, peptides are very large molecules compared to the neurotransmitters previously discussed, most of which are derived from a single amino acid (see Figure 13-32).

Box 13-6 | Neural Networks

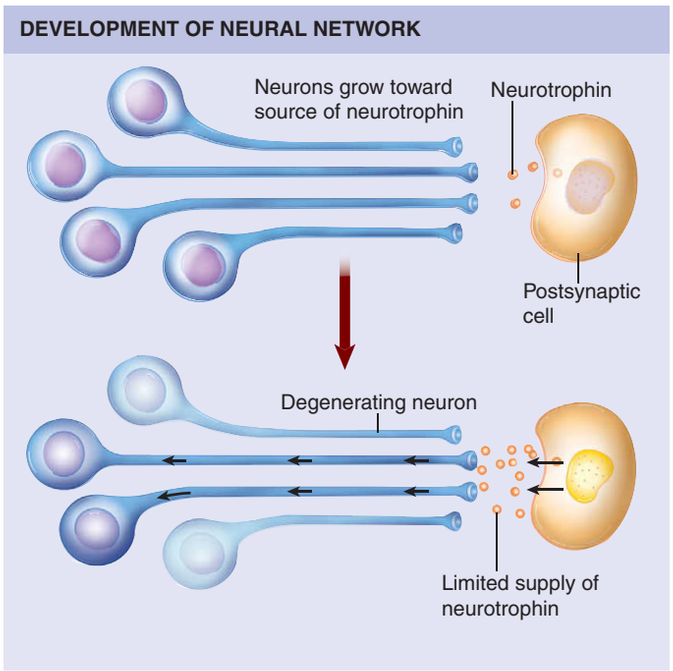
Nervous pathways, or **neural networks,** conduct information along complex series of neurons joined together by synapses.

Research shows that such networks develop during a person's early life and are influenced by the various sensory learning experiences that we have as our nerve tissue develops. One process that facilitates the formation of connections involves *neurotrophic factors* or *neurotrophins*—nerve growth factors that are released by various cells of the body. As part *A* of the figure shows, the axons of several developing neurons grow toward the cell that releases neurotrophins. However, only those axons that can be supported by the amount of available neurotrophin will remain—the rest of the neurons will degenerate. Many other factors, such as repeated stimulation of a pathway, influence this process. Once neural networks become mature in adulthood, they are less likely to accept the addition of new neurons—even though neural stem cells do exist in the adult nervous system.

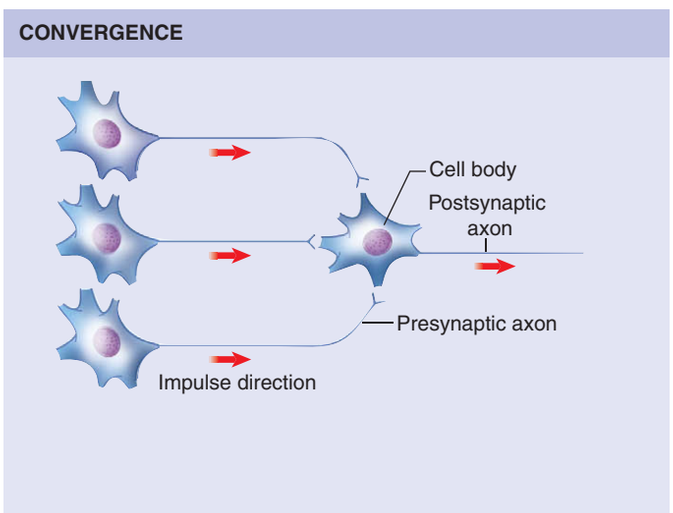
Something that makes the pathways of neural networks complex is that they often *converge* and *diverge.*

Convergence occurs when more than one presynaptic axon synapses with a single postsynaptic neuron (part *B* of the figure). Convergence allows information from several different pathways to be funneled into a single pathway. For example, the pathways that innervate the skeletal muscles may originate in several different areas of the central nervous system. Because pathways from each of these motor control areas converge on a single motor neuron, each area has an opportunity to control the same muscle.

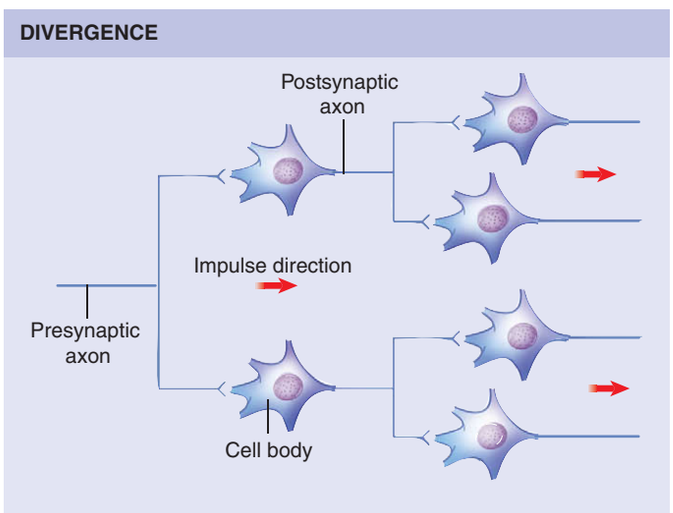
Divergence occurs when a single presynaptic axon synapses with many different postsynaptic neurons (part *C* of the figure). Divergence allows information from one pathway to be "split" or "copied" and sent to different destinations in the nervous system. For example, a single bit of visual information may be sent to many different areas of the brain for processing.



A



B



C

Peptides were first discovered to have regulatory effects in the digestive tract, where they act as hormones and regulate digestive function. In the 1970s some of these "gut" polypeptides, such as *vasoactive intestinal peptide (VIP)*, *cholecystokinin (CCK)*, and *substance P*, were also found to be acting as neurotransmitters in the brain. In addition, researchers found that receptors of many of the gut-brain peptides also bind morphine and other opium derivatives. For example, two subclasses of peptides—*enkephalins* and *endorphins*—that bind to the opiate receptors serve as the body's own supply of opiates. Enkephalins and endorphins have important pain-relieving effects in the body.

Although neuropeptides may be secreted by a synaptic knob by themselves, some may be secreted along with a second, or even third, neurotransmitter. In such cases, the neuropeptide is thought to act as a **neuromodulator.** A neuromodulator is a "cotransmitter" that regulates or modulates the effects of the neurotransmitter(s) released along with it.

An important class of neuropeptides in the nervous system is the **neurotrophins,** or *neurotrophic factors*. When first discovered, researchers found that they stimulate neuron development, hence the name neurotrophin (literally, "nerve growth factor"). Box 13-6, part *A* of the figure, shows how neurotrophins help regulate neuron growth. More recently, we have discovered that neurotrophins also participate in synaptic transmission and neuromodulation. In fact, one type of neurotrophin released by neurons is required to form any memory lasting more than a day.

ROLE OF NERVOUS SYSTEM CELLS

From the very birth of neuroscience, biologists have argued about which metaphor is best to describe the role of cells in the nervous system. One camp has argued on behalf of the *neuron doctrine*, which states that the neuron is the basic structural and functional unit of the nervous system and that neurons are independent units connected by chemical synapses. The competing *reticular theory* stated that the nervous system is best understood as a large integrated network—one endless piece. Once the presence of chemical synapses separating independent neurons was confirmed, it seemed as if the neuron doctrine was proved true and the reticular theory proved wrong.

However, today neuroscience has advanced to a point at which the neuron doctrine has been expanded to include concepts of the reticular theory. For example, we now know that along with chemical synapses, there are many electrical synapses that functionally unite neurons into large information-processing networks. We also know that signals can be sent both forwards and backwards in the chemical synapses of the neural network. We know that the concentration of neurotransmitters at synapses in certain neural pathways can affect health (Box 13-7). And today, we are learning more about how neuroglia communicate with each other and regulate the information-carrying functions of neurons. In fact, a very active area of neuroscience research relates to studying the integrated behavior of large neural networks. Our understanding of the role of nervous system cells is growing rapidly.

| A&P CONNECT |

The concept that signals can be sent "backwards" at a synapse is called *retrograde signaling.* See how this works at ***Retrograde Signaling*** online at ***A&P Connect.***

evolve

| QUICK CHECK |

27. How do excitatory neurotransmitters differ from inhibitory neurotransmitters?
28. What are the four chemical classes of neurotransmitters?
29. What are neuromodulators?

Box 13-7 | HEALTH matters

Antidepressants

Severe psychic depression occurs when a deficit of norepinephrine, dopamine, serotonin, and other amines exists in certain brain synapses. This fact led to the development of **antidepressant** drugs.

Certain of these antidepressants inhibit *catechol-O-methyl transferase* (COMT), the enzyme that inactivates norepinephrine. When COMT is inhibited by an antidepressant drug, the amount of active norepinephrine in brain synapses increases—relieving the symptoms of depression. Antidepressants such as phenelzine (Nardil) block the action of *monoamine oxidase* (MAO), the enzyme that inactivates dopamine and serotonin. Such drugs are in a class called *MAOIs (monoamine oxidase inhibitors).*

Widely used antidepressants such as imipramine (Tofranil) and amitriptyline (Elavil) increase amine levels at brain synapses by blocking their uptake into the axon terminals. The popular drugs fluoxetine (Prozac), citalopram (Celexa), and related drugs called *SSRIs (serotonin-specific reuptake inhibitors)* produce antidepressant effects by inhibiting the uptake of serotonin. *Norepinephrine reuptake inhibitors (NRIs)* such as atomoxetine (Strattera) selectively reduce the reuptake of noradrenaline. *SNRIs (serotonin and norepinephrine reuptake inhibitors)* such as venlafaxine (Effexor) and duloxetine (Cymbalta) are also used to treat depression.

Cocaine, which is often used in medical practice as a local anesthetic, produces a temporary feeling of well being in cocaine abusers by similarly blocking the uptake of dopamine. Unfortunately, cocaine and similar drugs can also adversely affect blood flow and heart function when taken in large amounts—leading to death in some individuals.

Cycle of LIFE

Nervous System Cells

The development of nerve tissue begins from the *ectoderm* during the first weeks after conception and exhibits many complicated stages before becoming mature by early adulthood. The most rapid and obvious development of nervous tissue occurs in the womb and for several years shortly after birth.

One of the most remarkable aspects of neural development involves the way in which nervous cells become organized to form a coordinated network spread throughout the body. Although we know very little about these processes, we do know that neurons require the coordinated actions of several agents to promote proper "wiring" of the nervous system. For example, we know that *nerve growth factors* released by effector cells stimulate the growth of neuron processes and help direct them to the proper destination.

During the first years of neural development, synapses are made, broken, and reformed until the basic organization of the nervous system is intact. Neurobiologists believe that the sensory stimulation that serves as the essence of early learning in infants and children has a critical role in directing the formation of synapses in the nervous system. The formation of new synapses, selective strengthening of existing synapses, and selective removal of synapses are thought to be primary physiological mechanisms of learning and memory.

In older adulthood, our brain processing may slow a bit. But that often allows us to make better use of stored memories and learned problem-solving skills to exhibit enhanced wisdom. In advanced old age, degeneration of neurons, glia, and the blood vessels that supply them may destroy certain portions of nervous tissue. This, coupled with age-related syndromes such as *Alzheimer disease (AD)*, may produce a loss of memory, coordination, and other neural functions sometimes referred to as *senility*.

the BIG picture

Nervous System Cells and the Whole Body

Neurons, the conducting cells of the nervous system, act as the "wiring" that connects the structures needed to maintain the internal constancy that is so vital to our survival. They also form processing "circuits" that make decisions regarding appropriate responses to stimuli that threaten our internal constancy. Sensory neurons act as sensors or receptors that detect changes in our external and internal environment that may be potentially threatening. Sensory neurons then relay this information to integrator mechanisms in the central nervous system. There, the information is processed—often by one or more interneurons—and an outgoing response signal is relayed to effectors by way of motor neurons. At the effector, a chemical messenger or neurotransmitter triggers a response that tends to restore homeostatic balance. Neurotransmitters released into the bloodstream, where they are called *hormones,* can enhance and prolong such homeostatic responses.

Of course, neurons do much more than simply respond to stimuli in a preprogrammed manner. Circuits of interneurons are capable of remembering, learning new responses, generating rational and creative thought, and implementing other complex processes. The exact mechanisms of many of these complex integrative functions are yet to be discovered, but you will learn some of what we already know in Chapter 14, in our discussion of the central nervous system.

UNIT 3

MECHANISMS of DISEASE

DISORDERS OF NERVOUS SYSTEM CELLS

Most disorders of nervous system cells involve glia rather than neurons. **Multiple sclerosis (MS),** one of the **myelin disorders** discussed in Box 13-2 (p. 386), is a good example of this principle. A few other important disorders involving glia are described in the following paragraphs.

The general name for tumors arising in nervous system structures is **neuroma** (noo-ROH-mah). Tumors do not usually develop directly from neurons but from glia, membrane tissues, and blood vessels. A common type of brain tumor—**glioma** (glee-OH-mah)—occurs in glia. Gliomas are usually benign but may still be life threatening. Because they often develop in deep areas of the brain, they are difficult to treat. Untreated gliomas may grow to a size that disrupts normal brain function—perhaps leading to death. Most malignant tumors of glia and other tissues in the nervous system do not originate there but are secondary tumors resulting from metastasis of cancer cells from the breast, lung, or other organs.

Tumors in the Central Nervous System

Astrocytoma is a type of glioma that originates from astrocytes. It is a slow-growing, infiltrating tumor of the brain that usually appears during the fourth decade of life. Seizures, headaches, or neurological deficits indicative of the area of the brain involved are usual presenting symptoms. **Glioblastoma multiforme,** a highly malignant form of astrocytic tumor, spreads throughout the white matter of the brain. Because of its invasive nature, surgical removal is difficult and the average survival is less than 1 year. **Ependymoma** is a glial tumor arising from ependymal cells, which line the fluid-filled cavities *(ventricles)* of the brain and spinal cord. This is the most common glioma in

children but can occur in adults. Because of its location, fluid pathways are obstructed, causing increased pressure in the brain, which in turn causes neurological damage. Surgical correction is possible, and the average postoperative survival is roughly 5 years. Glioma of oligodendrocytes is called **oligodendroglioma.** This tumor commonly occurs in the anterior portion of the brain and has a peak incidence at 40 years of age. The prognosis is better, with an average survival of 10 years after the onset of symptoms.

Tumors in the Peripheral Nervous System

Glial tumors can also develop in or on the cranial nerves. **Acoustic neuroma** is a lesion of the sheath of Schwann cells surrounding the eighth cranial nerve, responsible for hearing and balance. This tumor may be only the size of a pea or walnut, but the afflicted person typically experiences difficulty deciphering speech through the affected ear, dizziness, tinnitus (ringing in the ear), and a slow, progressive hearing loss. With the use of microsurgical techniques, the tumor can be removed, but some nerve damage caused by the surgical procedure is common.

Glial tumors can also appear in other regions of the peripheral nervous system. **Neurofibromatosis** (nooroh-fye-broh-mah-TOH-sis) is a group of genetic diseases often characterized by numerous fibrous neuromas and skin spots throughout the body (Figure 13-33). Although usually inherited, many cases occur from spontaneous mutations of the genetic code in an individual—who can then pass along the disease to offspring. The tumors are benign, appearing first as small nodules in the Schwann cells of nerve fibers in the skin. In some cases, involvement spreads in the form of large, disfiguring fibrous tumors that develop in many areas of the body, including muscles, bones, and internal organs.



FIGURE 13-33

Neurofibromatosis. Multiple tumors of supportive cells in nerves of the skin that are characteristic of this group of genetic conditions.

UNIT 3

LANGUAGE OF SCIENCE (continued from p. 380)

catecholamine
(kat-eh-KOHL-ah-meen)
[*catech-* **melt**, *-ol-* **alchohol**, *-amine* **ammonia compound**]

cell body
[*cell* **storeroom**]

central nervous system (CNS)
[*centr-* **center**, *-al* **relating to**, *nerv-* **nerves**, *-ous* **relating to**]

convergence
(kon-VER-jens)
[*con-* **together**, *-verg-* **incline**, *-ence* **state**]

dendrite
(DEN-dryte)
[*dendr-* **tree**, *-ite* **part** (**branch**) **of**]

depolarization
(dee-poh-lar-i-ZAY-shun)
[*de-* **opposite**, *-pol-* **pole**, *-ar-* **relating to**, *-ization* **process**]

divergence
(dye-VER-jens)
[*di-* **to separate**, *-verg-* **incline**, *-ence* **state**]

efferent division
(EF-fer-ent)
[*e-* **away**, *-fer-* **carry**, *-ent* **relating to**]

efferent (motor) neuron
(EF-fer-ent NOO-ron)
[*e-* **away**, *-fer-* **carry**, *-ent* **relating to**]

endoneurium
(en-doh-NOO-ree-um)
[*endo-* **inward**, *-neuri-* **nerve**, *-um* **thing**] *pl.,* endoneuria

ependymal cell
(eh-PEN-di-mal)
[*ep-* **over**, *-en-* **on**, *-dyma-* **put**, *-al* **relating to**, *cell* **storeroom**]

epineurium
(ep-i-NOO-ree-um)
[*epi-* **upon**, *-neuri-* **nerve**, *-um* **thing**] *pl.,* epineuria

excitatory postsynaptic potential (EPSP)
(ek-SYE-tah-toh-ree post-si-NAP-tik poh-TEN-shal)
[*excita-* **arouse**, *-ory* **relating to**, *post-* **after**, *-syn-* **together**, *-apt-* **join**, *-ic* **relating to**, *potent-* **power**, *-ial* **relating to**]

G-protein–coupled receptor (GPCR)
(jee-PROH-teen-kup-eld ree-SEP-ter)
[*G* **for guanine nucleotide binding**, *-prote-* **first rank**, *-in* **substance**, *recept-* **receive**, *-or* **agent**]

glia
(GLEE-ah)
[*glia* **glue**] *sing.*, **glial cell**

gray matter

hyperpolarization
(hye-per-pol-lar-i-ZAY-shun)
[*hyper-* **excessive**, *-pol-* **pole**, *-ar-* **relating to**, *-ization* **process**]

inhibitory postsynaptic potential (IPSP)
(in-HIB-i-tor-ee post-si-NAP-tik poh-TEN-shal)
[*inhib-* **restrain**, *-ory* **relating to**, *post-* **after**, *-syn-* **together**, *-apt-* **join**, *-ic* **relating to**, *potent-* **power**, *-ial* **relating to**]

interneuron
(in-ter-NOO-ron)
[*inter-* **between**, *-neuron* **nerve**]

local potential
[*potent-* **power**, *-ial* **relating to**]

membrane potential
[*membran-* **thin skin**, *potent-* **power**, *-ial* **relating to**]

microglia
(my-KROG-lee-ah)
[*micro-* **small** *-glia* **glue**] *sing.*, **microglial cell**

monoamine
(mon-oh-ah-MEEN)
[*mono-* **single**, *-amine* **ammonia compound** (**amino acid**)]

multipolar neuron
(mul-ti-POL-ar NOO-rons)
[*multi-* **many**, *-pol-* **pole**, *-ar* **relating to**, *neuron* **nerve**]

myelin
(MY-eh-lin)
[*myel-* **marrow**, *-in* **substance**]

myelin sheath
(MY-eh-lin sheeth)
[*myel-* **marrow**, *-in* **substance**]

myelinated fiber
(MY-eh-li-nay-ted)
[*myel-* **marrow**, *-in-* **substance**, *-ate* **act of**]

nerve

nerve fiber

nervous system
[*nerv-* **nerves**, *-ous* **relating to**]

neurilemma
(noo-ri-LEM-mah)
[*neuri-* **neuron**, *-lemma* **sheath**]
pl., neurilemmae

neurofibril
(noo-roh-FYE-bril)
[*neuro-* **nerves**, *-fibr-* **fiber**, *-il* **small**]

neuroglia
(noo-ROG-lee-ah)
[*neuro-* **nerve**, *-glia* **glue**] *sing.*, **neuroglial cell**

neuroglobin (Ngb)
(NOO-roh-gloh-bin)
[*neuro-* **nerves**, *-glob-* **ball**, *-in* **substance**]

neuromodulator
(noo-roh-MOD-yoo-lay-tor)
[*neuron-* **nerves**, *-modul-* **regulate**, *-ate* **act of**]

neuron
(NOO-ron)
[*neuron* **nerve**]

neuropeptide
(noo-roh-PEP-tyde)
[*neuro-* **nerves**, *-pept-* **digest**, *-ide* **chemical**]

neurotransmitter
(noo-roh-trans-MIT-ter)
[*neuro-* **nerves**, *-trans-* **across**, *-mitt-* **send**, *-er* **agent**]

neurotrophin
(noo-roh-TROF-in)
[*neuro-* **nerve**, *-troph-* **nutrition**, *-in* **substance**]

nitric oxide (NO)
(NYE-trik AWK-side)
[*nitr-* **nitrogen**, *-ic* **relating to**, *ox-* **oxygen**, *-ide* **chemical**]

node of Ranvier
(rahn-vee-AY)
[*nod-* **knot**, *Louis A. Ranvier* **French pathologist**]

oligodendrocyte
(ohl-i-go-DEN-droh-syte)
[*oligo-* **few**, *-dendr-* **part** (**branch**) **of**, *-cyte* **cell**]

perikaryon
(pair-i-KAR-ee-on)
[*peri-* **around**, *-karyon* **nut or kernel**]

perineurium
(pair-i-NOO-ree-um)
[*peri-* **around**, *-neuri-* **nerve**, *-um* **thing**] *pl.,* perineuria

peripheral nervous system (PNS)
(peh-RIF-er-al)
[*peri-* **around**, *-phera-* **boundary**, *-al* **relating to**, *nerv-* **nerves**, *-ous* **relating to**]

postsynaptic
(post-si-NAP-tik)
[*post-* **after**, *-syn-* **together**, *-apt-* **join**, *-ic* **relating to**]

postsynaptic potential
(post-sih-NAP-tik poh-TEN-shal)
[*post-* **after**, *-syn-* **together**, *-apt-* **join**, *-ic* **relating to**, *potent-* **power**, *-ial* **relating to**]

presynaptic
(pree-sih-NAP-tik)
[*pre-* **before**, *-syn-* **together**, *-apt-* **join**, *-ic* **relating to**]

reflex arc
[*re-* **back or again**, *-flex* **bend**, *arc* **curve**]

relative refractory period
(ree-FRAK-tor-ee)
[*refract-* **break apart**, *-ory* **relating to**, *period* **circuit**]

repolarization
(ree-poh-lah-ri-ZAY-shun)
[*re-* **back or again**, *-pol-* **pole**, *-ar* **relating to**, *-zation* **process**]

resting membrane potential (RMP)
[*membran-* **thin skin**, *potent-* **power**, *-ial* **relating to**]

retrograde signaling
(RET-roh-grayd SIG-nah-ling)
[*retro-* **backward**, *-grad-* **step**, *sign-* **mark**, *-al* **relating to**]

saltatory conduction
(SAL-tah-tor-ee)
[*salta-* **leap**, *-ory* **relating to**]

satellite cell
(SAT-i-lyte)
[*satell-* **attendant**, *-ite* **relating to**, *cell* **storeroom**]

Schwann cell
(shwon *or* shvon)
[*Theodor Schwann* **German anatomist**]

somatic nervous system (SNS)
(so-MAH-tik)
[*soma-* **body**, *-ic* **relating to**, *nerv-* **nerves**, *-ous* **relating to**]

somatic sensory division
(so-MAH-tik)
[*soma-* **body**, *-ic* **relating to**, *sens-* **feel**, *-ory* **relating to**]

spatial summation
(SPAY-shal sum-MAY-shun)
[*spati-* **space**, *-al* **relating to**, *summa-* **total**, *-tion* **process**]

stimulus-gated channel
(STIM-yoo-lus GAY-ted)
[*stimulus* **incitement**]

synapse
(SIN-aps)
[*syn-* **together**, *-aps-* **join**]

synaptic cleft
(si-NAP-tik kleft)
[*syn-* **together**, *-apt-* **join**, *-ic* **relating to**]

synaptic knob
(si-NAP-tik nob)
[*syn-* **together**, *-apt-* **join**, *-ic* **relating to**]

telodendrion
(tel-oh-DEN-dree-on)
[*telo-* **end**, *-dendr-* **part** (**branch**) **of**]
pl., telodendria

temporal summation
(TEM-poh-ral sum-MAY-shun)
[*tempor-* **time**, *-al* **relating to**]

threshold potential
(THRESH-hold poh-TEN-shal)
[*potent-* **power**, *-ial* **relating to**]

tract
(trakt)
[*trac-* **course**]

unipolar (pseudounipolar) neuron
(yoo-nee-POH-lar [SOO-doh-yoo-nee-POH-lar] NOO-ron)
[*uni-* **single**, *-pol-* **pole**, *-ar* **relating to**, *pseudo-* **false**, *neuron* **nerve**]

visceral sensory division
(VISS-er-al)
[*viscer-* **internal organs**, *-al* **relating to**, *sens-* **feel**, *-ory* **relating to**]

voltage-gated channel
(VOL-tij GAY-ted)
[*volt-* **unit of electrical force** (**after** *Alessandro Volta* **Italian physicist**), *-age* **amount**]

white matter

LANGUAGE OF MEDICINE

acoustic neuroma
(ah-KOOS-tik noo-ROH-mah)
[*acoust-* **hear**, *-ic* **relating to**, *neuro-* **nerve**, *-oma* **tumor**]

anesthesia
(an-es-THEE-zhah)
[*an-* **absence**, *-esthesia* **feeling**]

antidepressant
(an-tee-deh-PRESS-ant)
[*anti-* **against**, *-de-* **down**, *-press-* **press**, *-ant* **agent**]

astrocytoma
(ass-troh-sye-TOH-mah)
[*astro-* **star**, *-cyt-* **cell**, *-oma* **tumor**]

blood-brain barrier (BBB)

ependymoma
(eh-pen-di-MOH-mah)
[*ep-* **over**, *-en-* **on**, *-dyma-* **put**, *-oma* **tumor**]

glioblastoma multiforme
(glye-oh-blas-TOH-ma mul-ti-FOR-mee)
[*glio-* **glue**, *-blasto-* **bud**, *-oma* **tumor**, *multi-* **many**, *-form-* **shape**]

glioma
(glee-OH-mah)
[*glio-* **neuroglia**, *-oma* **tumor**]

levodopa (L-dopa)
(LEEV-oh-doh-pah)
[*levo-* **left** (**form of molecule**), *-dopa* **acronym denoting 3.4-** ***d*****ihydr****o****xy-*** ***p*****henyl*****a*****lanine**]

multiple sclerosis (MS)
(MUL-ti-pul skleh-ROH-sis)
[*multi-* **many**, *-pl-* **fold**, *sclera-* **hard**, *-osis* **condition**]

myelin disorder
(MY-eh-lin)
[*myel-* **marrow**, *-in* **substance**]

neural network
(NOOR-al)
[*neur-* **nerves**, *-al* **relating to**]

neurofibromatosis
(noo-roh-fye-broh-mah-TOH-sis)
[*neuro-* **nerves**, *-fibr-* **fiber**, *-oma-* **tumor**, *-osis* **condition**]

neuroma
(noo-ROH-mah)
[*neur-* **nerves**, *-oma* **tumor**]

oligodendroglioma
(ohl-i-go-DEN-droh-glye-OH-mah)
[*oligo-* **few**, *-dendro-* **part** (**branch**) **of**, *-glio-* **glue**, *-oma* **tumor**]

paralysis
(pah-RAL-i-sis)
[*para-* **beside**, *-lysis* **loosening**]

Parkinson disease (PD)
(PARK-in-son)
[*James Parkinson* **English physician**]

UNIT 3

CASE study

Kelly had been having difficulty focusing her eyes for a couple of weeks. She assumed her recent lack of sleep was the cause. But when she started dropping her keys and feeling unsteady when walking down the stairs, she became worried enough to go to the doctor. After the results of several tests were known, the doctor told her she had myasthenia gravis. This is a disease in which the body's own white blood cells start attacking acetylcholine receptors.

1. What's the connection between acetylcholine and Kelly's symptoms?
   a. Acetylcholine is a hormone released during stress
   b. Acetylcholine is found primarily in sensory neuron connections
   c. Acetylcholine is found primarily in motor neuron connections
   d. Acetylcholine affects communication primarily with smooth muscles

2. If the binding of acetylcholine opened sodium channels on the postsynaptic membrane, this would cause a temporary _____, called an _____.
   a. depolarization; excitatory postsynaptic potential
   b. hyperpolarization; excitatory postsynaptic potential
   c. depolarization; inhibitory postsynaptic potential
   d. hyperpolarization; inhibitory postsynaptic potential

Some muscle relaxants used during surgery bind to acetylcholine receptors, effectively blocking the action of acetylcholine—just as in myasthenia gravis. The drugs (anticholinesterases) used after surgery to reverse the relaxants are the same as those used to treat myasthenia gravis.

3. What do you think the action of these drugs would be?
   a. Blocking the release of acetylcholine
   b. Blocking the action of acetylcholinesterase
   c. Increasing the production of choline
   d. Increasing the action of acetylcholinesterase

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

INTRODUCTION

A. Function of nervous system, along with the endocrine system, is to communicate
B. Nervous system made up of the brain, spinal cord, and nerves (Figure 13-1)

ORGANIZATION OF THE NERVOUS SYSTEM

A. Organized to detect changes in internal and external environments, evaluate the information, and initiate an appropriate response
B. Subdivided into smaller "systems" by location (Figure 13-2)
   1. Central nervous system (CNS)
      a. Structural and functional center of the entire nervous system
      b. Consists of the brain and spinal cord
      c. Integrates sensory information, evaluates it, and initiates an outgoing response
   2. Peripheral nervous system (PNS)
      a. Nerves that lie in the "outer regions" of the nervous system
      b. Cranial nerves—originate from the brain
      c. Spinal nerves—originate from the spinal cord
C. Afferent and efferent divisions
   1. Afferent division—consists of all incoming sensory pathways
   2. Efferent division—consists of all outgoing motor pathways
D. "Systems" categorized according to types of organs they innervate (Figure 13-2)
   1. Somatic nervous system (SNS)
      a. Somatic motor division carries information to the somatic effectors (skeletal muscles)
      b. Somatic sensory division carries feedback information to somatic integration centers in the CNS
   2. Autonomic nervous system (ANS)
      a. Efferent division of ANS carries information to the autonomic or visceral effectors (smooth and cardiac muscles, glands, and adipose and other tissues)
         (1) Sympathetic division—prepares the body to deal with immediate threats to the internal environment; produces "fight-or-flight" response
         (2) Parasympathetic division—coordinates the body's normal resting activities; sometimes called the "rest-and-repair" division

b. Visceral sensory division carries feedback information to autonomic integrating centers in the CNS

CELLS OF THE NERVOUS SYSTEM

A. Glia (neuroglia)
1. Glial cells support the neurons
2. Five major types of glia (Figure 13-3)
   a. Astrocytes (in CNS)
      (1) Star-shaped, largest, and most numerous type of glia
      (2) Cell extensions connect to both neurons and capillaries
      (3) Astrocytes transfer nutrients from the blood to the neurons
      (4) Form tight sheaths around brain capillaries, which, with tight junctions between capillary endothelial cells, constitute the blood-brain barrier (BBB)
   b. Microglia (in CNS)
      (1) Small, usually stationary cells
      (2) In inflamed brain tissue, they enlarge, move about, and carry on phagocytosis
   c. Ependymal cells (in CNS)
      (1) Resemble epithelial cells and form thin sheets that line fluid-filled cavities in the CNS
      (2) Some produce fluid; others aid in circulation of fluid
   d. Oligodendrocytes (in CNS)
      (1) Smaller than astrocytes with fewer processes
      (2) Hold nerve fibers together and produce the myelin sheath
   e. Schwann cells (in PNS)
      (1) Found only in peripheral neurons
      (2) Support nerve fibers and form myelin sheaths (Figure 13-4)
      (3) Myelin sheath gaps are often called *nodes of Ranvier*
      (4) Neurilemma is formed by cytoplasm of Schwann cell (neurolemmocyte) wrapped around the myelin sheath; essential for nerve regrowth
      (5) Neuronal sheath is the myelin sheath plus the neurilemma (that is, the whole Schwann wrapping around the axon)
      (6) Satellite cells are Schwann cells that cover and support cell bodies in the PNS

B. Neurons
1. Excitable cells that initiate and conduct impulses that make possible all nervous system functions
2. Components of neurons (Figure 13-5)
   a. Cell body (perikaryon)
      (1) Ribosomes, rough endoplasmic reticulum (ER), Golgi apparatus
         (a) Provide protein molecules (neurotransmitters) needed for transmission of nerve signals from one neuron to another
         (b) Neurotransmitters are packaged into vesicles
         (c) Provide proteins for maintaining and regenerating nerve fibers
      (2) Mitochondria provide energy (ATP) for neuron; some are transported to end of axon
   b. Dendrites
      (1) Each neuron has one or more dendrites, which branch from the cell body
      (2) Conduct nerve signals to the cell body of the neuron
      (3) Distal ends of dendrites of sensory neurons are receptors
      (4) Dendritic spines—small knoblike protrusions on dendrites of some brain neurons; serve as connection points for axons of other neurons
   c. Axon
      (1) A single process extending from the axon hillock, sometimes covered by a fatty layer called a *myelin sheath* (Figure 13-6)
      (2) Conducts nerve impulses away from the cell body of the neuron
      (3) Distal tips of axons are telodendria, each of which terminates in a synaptic knob
      (4) Axon varicosities—swellings that make contact (synapse) with other cells
   d. Cytoskeleton
      (1) Microtubules and microfilaments, as well as neurofibrils (bundles of neurofilaments)
      (2) Allow the rapid transport of small organelles (Figure 13-7)
         (a) Vesicles (some containing neurotransmitters), mitochondria
         (b) Motor molecules shuttle organelles to and from the far ends of a neuron
   e. Functional regions of the neuron (Figure 13-8)
      (1) Input zone—dendrites and cell body
      (2) Summation zone—axon hillock
      (3) Conduction zone—axon
      (4) Output zone—telodendria and synaptic knobs of axon

C. Classification of neurons
1. Structural classification—classified according to number of processes extending from cell body (Figure 13-9)
   a. Multipolar—one axon and several dendrites
   b. Bipolar—only one axon and one dendrite; least numerous kind of neuron
   c. Unipolar (pseudounipolar)—one process comes off neuron cell body but divides almost immediately into two fibers: central fiber and peripheral fiber
2. Functional classification (Figure 13-10)
   a. Afferent (sensory) neurons—conduct impulses to spinal cord or brain
   b. Efferent (motor) neurons—conduct impulses away from spinal cord or brain toward muscles or glandular tissue
   c. Interneurons

D. Reflex arc
1. A signal conduction route to and from the CNS, with the electrical signal beginning in receptors and ending in effectors

2. Three-neuron arc—most common; consists of afferent neurons, interneurons, and efferent neurons (Figure 13-11)
   a. Afferent neurons—conduct impulses to the CNS from the receptors
   b. Efferent neurons—conduct impulses from the CNS to effectors (muscle or glandular tissue)
3. Two-neuron arc—simplest form; consists of afferent and efferent neurons
4. Synapse
   a. Where nerve signals are transmitted from one neuron to another
   b. Two types: electrical and chemical; chemical synapses are typical in the adult
   c. Chemical synapses are located at the junction of the synaptic knob of one neuron and the dendrites or cell body of another neuron

NERVES AND TRACTS

A. Nerves—bundles of peripheral nerve fibers held together by several layers of connective tissue (Figure 13-12)
   1. Endoneurium—delicate layer of fibrous connective tissue surrounding each nerve fiber
   2. Perineurium—connective tissue holding together fascicles (bundles of fibers)
   3. Epineurium—fibrous coat surrounding numerous fascicles and blood vessels to form a complete nerve
B. Tracts—bundles of nerve fibers within the CNS
   1. Unlike nerves, tracts do not have connective tissue coverings
   2. Individual fibers may extend through both a nerve and a tract as it passes into or out of the CNS
C. White matter
   1. PNS—myelinated nerves
   2. CNS—myelinated tracts
D. Gray matter
   1. Made up of cell bodies and unmyelinated fibers
   2. CNS—referred to as *nuclei*
   3. PNS—referred to as *ganglia*
E. Mixed nerves
   1. Contain sensory and motor neurons
   2. Sensory nerves—nerves with predominantly sensory neurons
   3. Motor nerves—nerves with predominantly motor neurons

REPAIR OF NERVE FIBERS

A. Mature neurons are incapable of cell division; therefore damage to nervous tissue can be permanent
B. Neurons have limited capacity to repair themselves
C. If the damage is not extensive, the cell body and neurilemma are intact, and scarring has not occurred, nerve fibers can be repaired
D. Stages of repair of an axon in a peripheral motor neuron (Figure 13-13)
   1. Following injury, distal portion of axon and myelin sheath degenerates
   2. Macrophages remove the debris
   3. Remaining neurilemma and endoneurium form a tunnel from the point of injury to the effector
   4. New Schwann cells grow in the tunnel to maintain a path for regrowth of the axon
   5. Cell body reorganizes its Nissl bodies to provide the needed proteins to extend the remaining healthy portion of the axon
   6. Axon "sprouts" appear
   7. When "sprout" reaches tunnel, its growth rate increases
   8. The skeletal muscle cell atrophies until the nervous connection is reestablished
E. In CNS, similar repair of damaged nerve fibers is unlikely

NERVE IMPULSES

A. Membrane potentials
   1. All living cells maintain a difference in the concentration of ions across their membranes
   2. Membrane potential—slight excess of positively charged ions on the outside of the membrane and slight deficiency of positively charged ions on the inside of the membrane (Figure 13-14)
   3. Difference in electrical charge is called *potential* because it is a type of stored energy
   4. Polarized membrane—a membrane that exhibits a membrane potential
   5. Magnitude of potential difference between the two sides of a polarized membrane is measured in volts (V) or millivolts (mV); the sign of a membrane's voltage indicates the charge on the inside surface of a polarized membrane
B. Resting membrane potential (RMP)
   1. Membrane potential maintained by a nonconducting neuron's plasma membrane; typically –70 mV
   2. The slight excess of positive ions on a membrane's outer surface is produced by ion transport mechanisms and the membrane's permeability characteristics
   3. The membrane's selective permeability characteristics help maintain a slight excess of positive ions on the outer surface of the membrane (Figure 13-15)
   4. Sodium-potassium pump (Figure 13-16)
      a. Active transport mechanism in plasma membrane that transports Na^+ and K^+ in opposite directions and at different rates
      b. Maintains an imbalance in the distribution of positive ions, resulting in the inside surface becoming slightly negative with respect to its outer surface
C. Local potentials
   1. Local potentials—slight shift away from the resting membrane in a specific region of the plasma membrane (Figure 13-17)
   2. Excitation—when a stimulus triggers the opening of additional Na^+ channels, allowing the membrane potential to move toward zero (depolarization)
   3. Inhibition—when a stimulus triggers the opening of additional K^+ channels, increasing the membrane potential (hyperpolarization)

4. Local potentials are called *graded potentials* because the magnitude of deviation from the resting membrane potential is proportional to the magnitude of the stimulus

ACTION POTENTIAL

A. Action potential—the membrane potential of a neuron that is conducting an impulse; also known as a *nerve impulse*
B. Mechanism that produces the action potential (Figures 13-18 and 13-19)
   1. When an adequate stimulus triggers stimulus-gated Na^+ channels to open, allowing Na^+ to diffuse rapidly into the cell, a local depolarization is produced
   2. As threshold potential is reached, voltage-gated Na^+ channels open and more Na^+ enters the cell, causing further depolarization
   3. As more Na^+ rushes into cell, the membrane moves rapidly toward and continues in a positive direction to the peak of the action potential
   4. Voltage-gated Na^+ channels stay open for only about 1 ms before they automatically close; action potential is an all-or-none response
   5. After action potential peaks, membrane begins to move back toward the resting membrane potential when K^+ channels open, allowing outward diffusion of K^+; process is known as *repolarization*
   6. Brief period of hyperpolarization occurs, and then the resting membrane potential is restored by the sodium-potassium pumps
C. Refractory period (Figure 13-20)
   1. Absolute refractory period—brief period (lasting approximately 0.5 ms) during which a local area of a neuron's membrane resists restimulation and will not respond to a stimulus, no matter how strong
   2. Relative refractory period—time during which the membrane is repolarized and restoring the resting membrane potential; the few milliseconds after the absolute refractory period; will respond only to a very strong stimulus
D. Conduction of the action potential
   1. At the peak of the action potential, the plasma membrane's polarity is now the reverse of the RMP
   2. The reversal in polarity causes electrical current to flow between the site of the action potential and the adjacent regions of membrane and triggers voltage-gated Na^+ channels in the next segment to open; this next segment exhibits an action potential (Figure 13-21)
   3. This cycle continues to repeat, producing continuous conduction
   4. The action potential never moves backward because of the refractory period
   5. In myelinated fibers, action potentials in the membrane only occur at the nodes of Ranvier; this type of impulse conduction is called *saltatory conduction* (Figure 13-22)
   6. Speed of nerve conduction depends on diameter and on the presence or absence of a myelin sheath

SYNAPTIC TRANSMISSION

A. Two types of synapses (junctions) (Figure 13-23)
   1. Electrical synapses occur where cells joined by gap junctions allow an action potential to simply continue along postsynaptic membrane
   2. Chemical synapses occur where presynaptic cells release chemical transmitters (neurotransmitters) across a tiny gap to the postsynaptic cell, possibly inducing an action potential there
B. Structure of the chemical synapse (Figure 13-25)
   1. Synaptic knob—tiny bulge at the end of a terminal branch of a presynaptic neuron's axon that contains vesicles housing neurotransmitters
   2. Synaptic cleft—space between a synaptic knob and the plasma membrane of a postsynaptic neuron
   3. Arrangements of synapses
      a. Axodendritic—axon signals postsynaptic dendrite; common
      b. Axosomatic—axon signals postsynaptic soma; common
      c. Axoaxonic—axon signals postsynaptic axon; may regulate action potential of postsynaptic axon
   4. Plasma membrane of a postsynaptic neuron—has protein molecules that serve as receptors for the neurotransmitters
C. Mechanism of synaptic transmission (Figure 13-25)—sequence of events is as follows:
   1. Action potential reaches a synaptic knob, causing calcium ions to diffuse into the knob rapidly
   2. Increased calcium concentration triggers the release of neurotransmitter by way of exocytosis
   3. Neurotransmitter molecules diffuse across the synaptic cleft and bind to receptor molecules, causing ion channels to open
   4. Opening of ion channels produces a postsynaptic potential, either an excitatory postsynaptic potential (EPSP) or an inhibitory postsynaptic potential (IPSP)
   5. The neurotransmitter's action is quickly terminated by neurotransmitter molecules being transported back into the synaptic knob (reuptake) and/or metabolized into inactive compounds by enzymes and/or diffused and taken up by nearby glia (Figure 13-26)
D. Summation (Figure 13-28)
   1. Spatial summation—adding together the effects of several knobs being activated simultaneously and stimulating different locations on the postsynaptic membrane, producing an action potential
   2. Temporal summation—when synaptic knobs stimulate a postsynaptic neuron in rapid succession, their effects can summate over a brief period of time to produce an action potential
E. Synapses and memory
   1. Memories are stored by facilitating (or inhibiting) synaptic transmission
   2. Short-term memories (seconds or minutes) may result from axoaxonic facilitation or inhibition of the presynaptic axon terminal

3. Intermediate long-term memory (minutes to weeks) happens when serotonin blocks potassium channels in the presynaptic terminal—thus prolonging the action potential and increasing the amount of neurotransmitter released
4. Long-term memories (months or years) require structural changes at the synapse—for example, more vesicles, more vesicle release sites, more presynaptic terminals, more sensitive postsynaptic membranes

NEUROTRANSMITTERS

A. Neurotransmitters—means by which neurons communicate with one another; there are more than 50 compounds known to be neurotransmitters, and dozens of others are suspected
B. Classification of neurotransmitters—commonly classified by the following:
   1. Function—the function of a neurotransmitter is determined by the postsynaptic receptor; two major functional classifications are excitatory neurotransmitters and inhibitory neurotransmitters; can also be classified according to whether the receptor directly opens a channel or instead uses a second messenger mechanism involving G-protein–coupled receptors (GPCRs) and intracellular signals (Figures 13-29 and 13-30)
   2. Chemical structure—the mechanism by which neurotransmitters cause a change; there are four main classes; since the functions of specific neurotransmitters vary by location, they are usually classified according to chemical structure
C. Small-molecule neurotransmitters (Figure 13-31)
   1. Acetylcholine
      a. Unique chemical structure; acetate (acetyl coenzyme A) with choline
      b. Acetylcholine is deactivated by acetylcholinesterase, with the choline molecules being released and transported back to presynaptic neuron to combine with acetate
      c. Present at various locations, sometimes in an excitatory role; other times, inhibitory
   2. Amines
      a. Synthesized from amino acid molecules
      b. Two categories: monoamines and catecholamines
      c. Found in various regions of the brain, affecting learning, emotions, motor control, and so on
   3. Amino acids
      a. Believed to be among the most common neurotransmitters of the CNS
      b. In the PNS, amino acids are stored in synaptic vesicles and used as neurotransmitters
   4. Other small-molecule transmitters
      a. Nitric oxide (NO) derived from an amino acid
      b. NO from a postsynaptic cell signals the presynaptic neuron, providing feedback in a neural pathway
D. Neuropeptides—large-molecule neurotransmitters
   1. Neuropeptides are short strands of amino acids called polypeptides or peptides (Figure 13-32)
   2. Peptides first discovered to have regulatory effects in the digestive tract; also act as neurotransmitters in the brain
   3. May be secreted by themselves or in conjunction with a second or third neurotransmitter; in this case, neuropeptides act as a neuromodulator, a "co-transmitter" that regulates the effects of the neurotransmitter released along with it
   4. Neurotrophins (neurotrophic [nerve growth] factors) stimulate neuron development but also can act as neurotransmitters or neuromodulators

ROLE OF NERVOUS SYSTEM CELLS

A. Neuron doctrine—proposes neuron is basic structural and functional unit of the nervous system and neurons are independent units connected by chemical synapses
B. Reticular theory—proposes nervous system is best understood as a large integrated network
C. Today, the dominant neuron doctrine has expanded to include concepts of the reticular theory—neurons are distinct units but also participate in a network; some neurons are functionally connected by electrical synapses, and chemical signals can move in two directions at the same synapse
D. Because neuroglia also participate in the neural network, the whole concept of nervous system cell function is rapidly expanding

CYCLE OF LIFE: NERVOUS SYSTEM CELLS

A. Nerve tissue development
   1. Begins in ectoderm
   2. Occurs most rapidly in womb and in first 2 years
B. Nervous cells organize into body network
C. Synapses
   1. Form and re-form until nervous system is intact
   2. Formation of new synapses and strengthening or elimination of old synapses stimulate learning and memory
D. Aging causes degeneration of the nervous system, which may lead to senility

THE BIG PICTURE: NERVOUS SYSTEM CELLS AND THE WHOLE BODY

A. Neurons act as the "wiring" that connects structures needed to maintain homeostasis
B. Sensory neurons—act as receptors to detect changes in the internal and external environment; relay information to integrator mechanisms in the CNS
C. Information is processed, and a response is relayed to the appropriate effectors through the motor neurons
D. At the effector, neurotransmitter triggers a response to restore homeostasis
E. Neurotransmitters released into the bloodstream are called *hormones*
F. Neurons are responsible for more than just responding to stimuli; circuits are capable of remembering or learning new responses, generation of thought, and so on

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Briefly explain the general function the nervous system performs for the body.
2. Identify the other body system that performs the same general function.
3. Describe the function of sodium and potassium in the generation of an action potential.
4. Why is an action potential an all-or-none response?
5. How does the myelin sheath affect the speed of an action potential? What about the diameter of the nerve fiber?
6. Describe the structure of a synapse.
7. Describe the series of events that mediate conduction across synapses.
8. List and describe the four main chemical classes of transmitters.
9. Describe the actions of acetylcholine.
10. List and describe disorders of the nervous system cells.

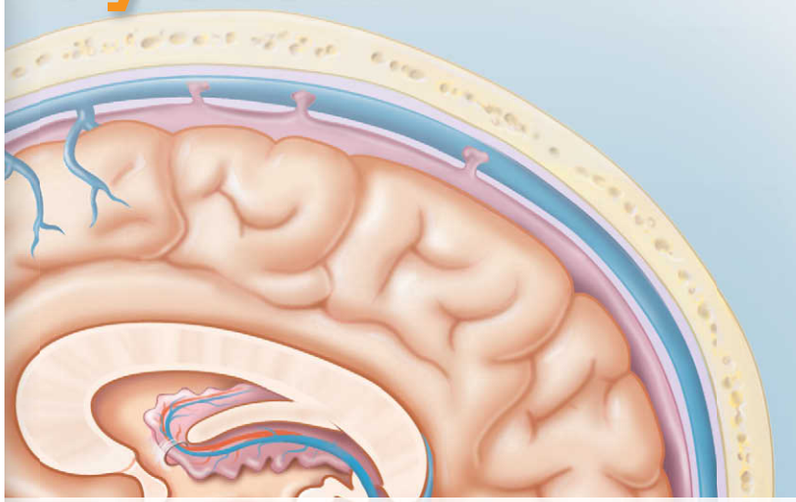
CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Compare and contrast the characteristics of the central nervous system and the peripheral nervous system. Also, explain how the somatic and autonomic nervous systems could be included in the afferent and efferent divisions.
2. There are relatively few neurons in the brain. How would you describe the other cells in the brain? What do they do?
3. All neurons have axons and dendrites. Explain where these parts of the neuron are located in multipolar, bipolar, and unipolar neurons.
4. Compare and contrast white and gray matter. What would result if there were a loss of myelination?
5. Explain how high doses of methylprednisolone act to reduce the severity of spinal cord injuries.
6. Nerve fibers in the peripheral nervous system are much more successful than nerve fibers in the central nervous system in repairing themselves. How would you explain this difference?
7. Define *potential*. The following is a list of times and charges taken during a nerve impulse. Identify them as being either an action potential or not and as occurring either during the absolute or relative refractory period. (Assume the stimulus starts at 0 msec.)
   0 mV at 1 msec
   −50 mV at 0.5 msec
   +25 mV at 1.5 msec
   +25 mV at 3 msec
8. Describe the mechanisms that allow subthreshold stimuli to generate an action potential.
9. Many antibiotics that should kill the causative agents of meningitis are ineffective if given orally. Can you explain the anatomical mechanism that could cause this ineffectiveness?
10. Explain one of the ways an anesthetic may relieve the sensation of pain.
11. Referred pain is a condition in which the pain is not felt where the injury is actually occurring but rather is felt over a wider area or in some other part of the body. What structural aspect of the nervous system might explain referred pain?

14 Central Nervous System



LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

amygdaloid nucleus
(ah-MIG-dah-loyd NOO-klee-us)
[*amygdal-* **almond,** *-oid* **like**] *pl.,* nuclei

anterior corticospinal tract
(an-TEER-ee-or KOR-ti-koh-spy-nal)
[*ante-* **front,** *-er-* **more,** *-or* **quality,** *cortic-* **bark,** *-spin-* **backbone,** *-al* **relating to,** *tract-* **trail**]

anterior spinothalamic tract
(an-TEER-ee-or SPY-no-tha-lam-ik)
[*ante-* **front,** *-er-* **more,** *-or* **quality,** *spino-* **backbone,** *-thalam-* **inner chamber,** *-ic* **relating to**]

arbor vitae
(AR-bor VI-tay)
[*arbor* **tree,** *vitae* **of life**] *pl.,* arbores vitae

ascending tract
(ah-SEND-ing)
[*ascend-* **climb,** *tract-* **trail**]

basal nuclei
(BAY-sal NOO-klee-eye)
[*bas-* **foundation,** *-al* **relating to,** *nucle-* **nut or kernel**] *sing.,* nucleus

biological clock
(bye-oh-LOJ-i-kal)
[*bio-* **life,** *-o-* **combining form,** *-log-* **words (study of),** *-ical* **relating to**]

brainstem

cauda equina
(KAW-da eh-KWY-nah)
[*caud-* **tail,** *equina* **of a horse**]
pl., caudae equinae

caudate nucleus
(KAW-dayt NOO-klee-us)
[*caud-* **tail,** *-ate* **of or like,** *nucleus* **nut or kernel**] *pl.,* nuclei

continued on p. 454

CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

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Recall from Chapter 13 that the nervous system is said to be composed of two major divisions: the central nervous system (CNS) and the peripheral nervous system (PNS). The reason for designating two distinct divisions is to make the study of the nervous system easier. In this chapter, we discuss the part of the nervous system that lies at the center of the regulatory process: the central nervous system. Comprising both the brain and the spinal cord, the central nervous system is the principal integrator of sensory input and motor output. Thus the central nervous system is capable of evaluating incoming information and formulating responses to changes that threaten our homeostatic balance.

This chapter begins with a description of the protective coverings of the brain and spinal cord. After that, we briefly discuss the watery cerebrospinal fluid (CSF) *and the spaces in which it is found. We then outline the overall structure and function of the major organs of the central nervous system, beginning at the bottom with the spinal cord; this is the simplest and least complex part of the CNS. Then our focus moves upward to the more complex brain, beginning first with the narrow brainstem (Figure 14-1) and the roughly spherical cerebellum attached to its dorsal surface. Again shifting our attention upward, we describe the structure and function of the diencephalon and then move on to a discussion of the cerebrum. As we move up the central nervous system, the complexity of both structure and function increases. The spinal cord mediates simple reflexes, whereas the brainstem and diencephalon are involved in the regulation of the more complex maintenance functions, such as regulation of heart rate and breathing. The cerebral hemispheres, which together form the largest part of the brain, perform complex integrative functions such as conscious thought, learning, memory, language, and problem solving. We end the chapter with a discussion of the somatic sensory pathways and the somatic motor pathways. This prepares us for Chapter 15, which covers the peripheral nervous system, Chapter 16, which covers autonomic regulation of vital functions, and Chapter 17, which covers the sense organs.*

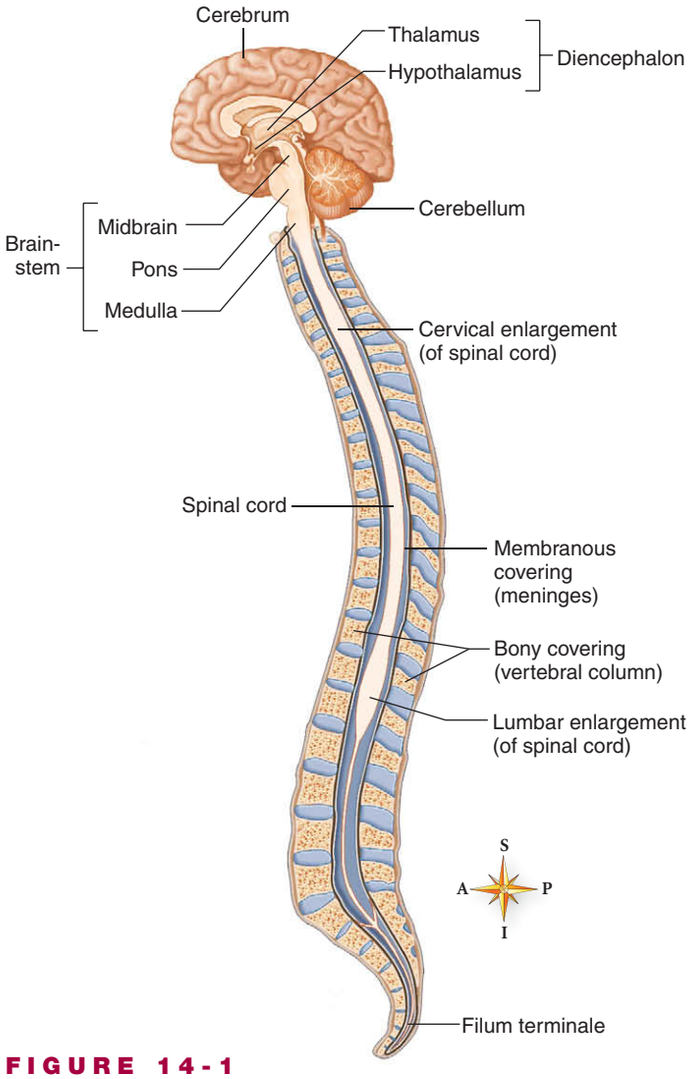


FIGURE 14-1

The central nervous system. Details of both the brain and the spinal cord are easily seen in this figure.

COVERINGS OF THE BRAIN AND SPINAL CORD

Because the brain and spinal cord are both delicate and vital, nature has provided them with two protective coverings. The outer covering consists of bone: cranial bones encase the brain; vertebrae encase the spinal cord. The inner covering consists of membranes known as **meninges.** Three distinct layers compose the meninges:

1. Dura mater
2. Arachnoid mater
3. Pia mater

Observe their respective locations in Figures 14-2 and 14-3. The dura mater, made of strong white fibrous tissue, serves as the outer layer of the meninges and also as the inner periosteum of the cranial bones. The arachnoid mater, a delicate, spiderweb-like layer, lies between the dura mater and the pia mater, or innermost layer of the meninges. The transparent pia mater adheres to the outer surface of the brain and spinal cord and contains blood vessels.

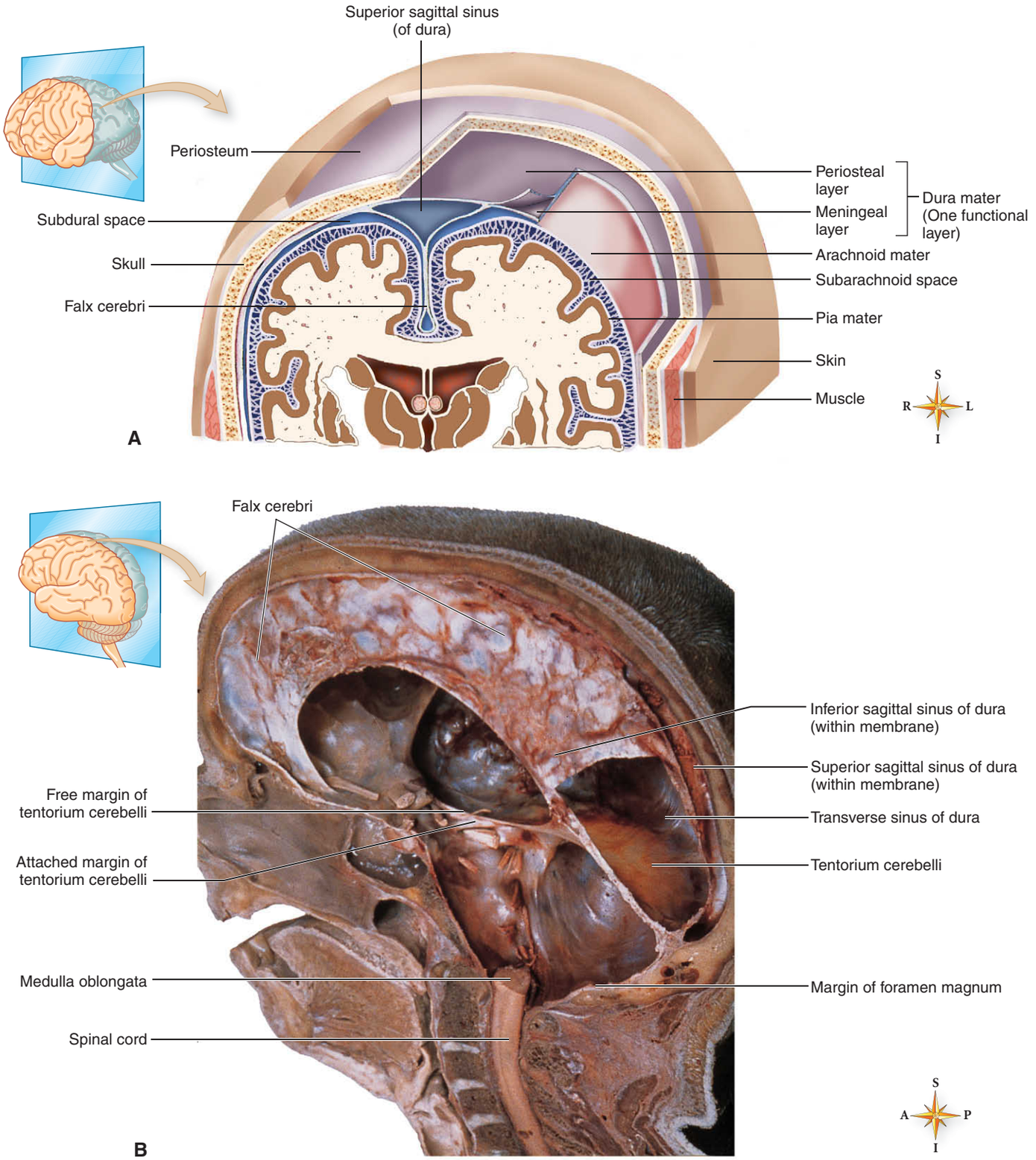


FIGURE 14-2

Coverings of the brain. A, Frontal section of the superior portion of the head, as viewed from the front. Both the bony and the membranous coverings of the brain can be seen. **B,** Sagittal section of the skull, viewed from the left. The dura mater has been retained in this specimen to show how it lines the inner roof of the cranium and the falx cerebri extending inward.

The dura mater has three important inward extensions:

1. **Falx cerebri.** The falx cerebri projects downward into the longitudinal fissure to form a kind of partition between the two cerebral hemispheres. The Latin word *falx* means "sickle" and refers to the curving sickle shape of this partition as it extends from the roof of the cranial cavity (see Figure 14-2, *B*).
2. **Falx cerebelli.** The falx cerebelli is a sickle-shaped extension that separates the two halves, or hemispheres, of the cerebellum.

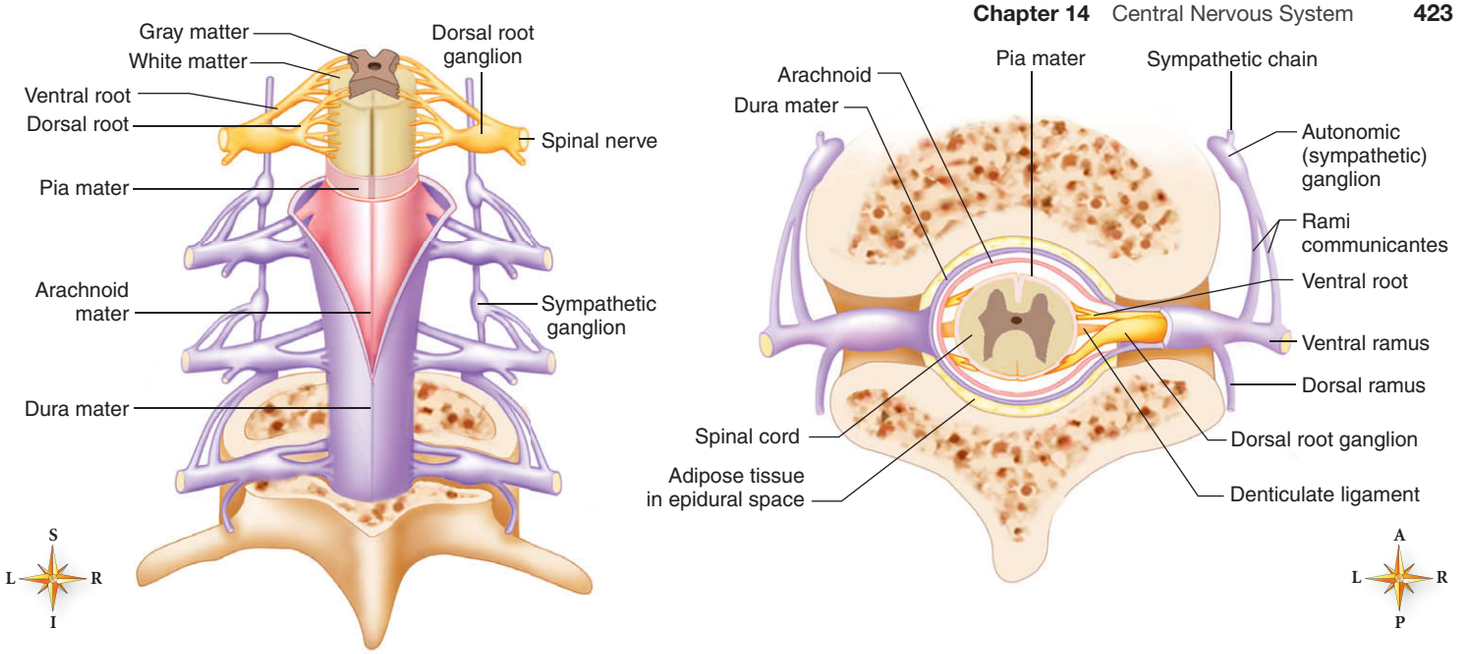


FIGURE 14-3

Coverings of the spinal cord. The dura mater is shown in purple. Note how it extends to cover the spinal nerve roots and nerves. The arachnoid is highlighted in pink and the pia mater in orange.

3. **Tentorium cerebelli.** The tentorium cerebelli separates the cerebellum from the cerebrum. It is called a *tentorium* (meaning "tent") because it forms a tentlike covering over the cerebellum.

Figure 14-2 shows a large space within the dura, where the falx cerebri begins to descend between the left and right cerebral hemispheres. This space, called the *superior sagittal sinus*, is one of several dural sinuses. Dural sinuses function as venous reservoirs, collecting blood from brain tissues for the return trip to the heart.

A number of spaces lie between and around the meninges (see Figure 14-2). Three of these spaces are the following:

1. **Epidural space.** The epidural ("on the dura") space is immediately outside the dura mater but inside the bony coverings of the spinal cord. It contains a supporting cushion of fat and other connective tissues. Around the brain, because the dura mater is continuous with the periosteum on the inside face of the cranial bones, no epidural space is normally present.
2. **Subdural space.** The subdural ("under the dura") space is between the dura mater and arachnoid mater. The subdural space contains a small amount of lubricating serous fluid.
3. **Subarachnoid space.** As its name suggests, the *subarachnoid space* is under the arachnoid and outside the pia mater. This space contains a significant amount of cerebrospinal fluid.

The meninges of the cord (see Figure 14-3) continue on down inside the spinal cavity for some distance below the end of the spinal cord. The pia mater forms a slender filament known as the **filum terminale** (see Figure 14-1). At the level of the third segment of the sacrum, the filum terminale blends with the dura mater to form a fibrous cord that disappears in the periosteum of the coccyx.

Infections of the meninges are discussed in Box 14-1.

Box 14-1 | HEALTH matters

Meningitis

Infection or inflammation of the meninges is termed *meningitis.* It most often involves the arachnoid and pia mater, or the *leptomeninges* ("thin meninges"). Meningitis is most commonly caused by bacteria such as *Neisseria meningitidis* (meningococcus), *Streptococcus pneumoniae,* or *Haemophilus influenzae.* However, viral infections, mycoses (fungal infections), and tumors also may cause inflammation of the meninges. Individuals with meningitis usually complain of fever and severe headaches, as well as neck stiffness and pain. Signs also include avoidance of bright lights and loud sounds, lethargy, and confusion. Persons experiencing these symptoms, some of which mimic the flu, should seek medical help immediately. In infants and very young children, so-called projective vomiting is common. College campuses are often the sites for localized outbreaks of meningitis, and several bacterial forms are highly contagious.

Depending on the primary cause, meningitis may be mild and self-limiting or may progress to a severe, even fatal, condition. If only the spinal meninges are involved, the condition is called *spinal meningitis.* A lumbar puncture ("spinal tap") can be diagnostic, especially for bacterial meningitis such as the type caused by *H. influenzae.* Spinal meningitis must be treated immediately to avoid an increase in intracranial pressure and damage to the nervous system. If not treated quickly, meningitis can lead to deafness, deficits in cognitive ability, and permanent brain disorders such as epilepsy. Meningitis caused by *H. influenzae* type B, pneumococci bacteria, or the mumps virus can be prevented by immunization.

CEREBROSPINAL FLUID

In addition to its bony and membranous coverings, nature has further protected the brain and spinal cord against injury by providing a cushion of fluid both around the organs and within them. This fluid is the **cerebrospinal fluid (CSF).** The CSF does more than simply provide a supportive, protective cushion, however. It is also a reservoir of circulating fluid that, along with blood, the brain monitors for changes in the internal environment. For example, changes in the carbon dioxide (CO_2) content of CSF trigger homeostatic responses in the respiratory control centers of the brainstem that help regulate the overall CO_2 content and pH of the body.

Fluid Spaces

Cerebrospinal fluid is found in the subarachnoid space around the brain and spinal cord and within the cavities and canals of the brain and spinal cord.

The four large, fluid-filled spaces within the brain are called **ventricles.** Two of them, the lateral (or first and second) ventricles, are located one in each hemisphere of the cerebrum. As you can see in Figure 14-4, the third ventricle is little more than a thin, vertical pocket of fluid below and medial to the lateral ventricles. The fourth ventricle is a tiny, diamond-shaped space where the cerebellum attaches to the back of the brainstem. Actually, the fourth ventricle is simply a slight expansion of the central canal extending up from the spinal cord.

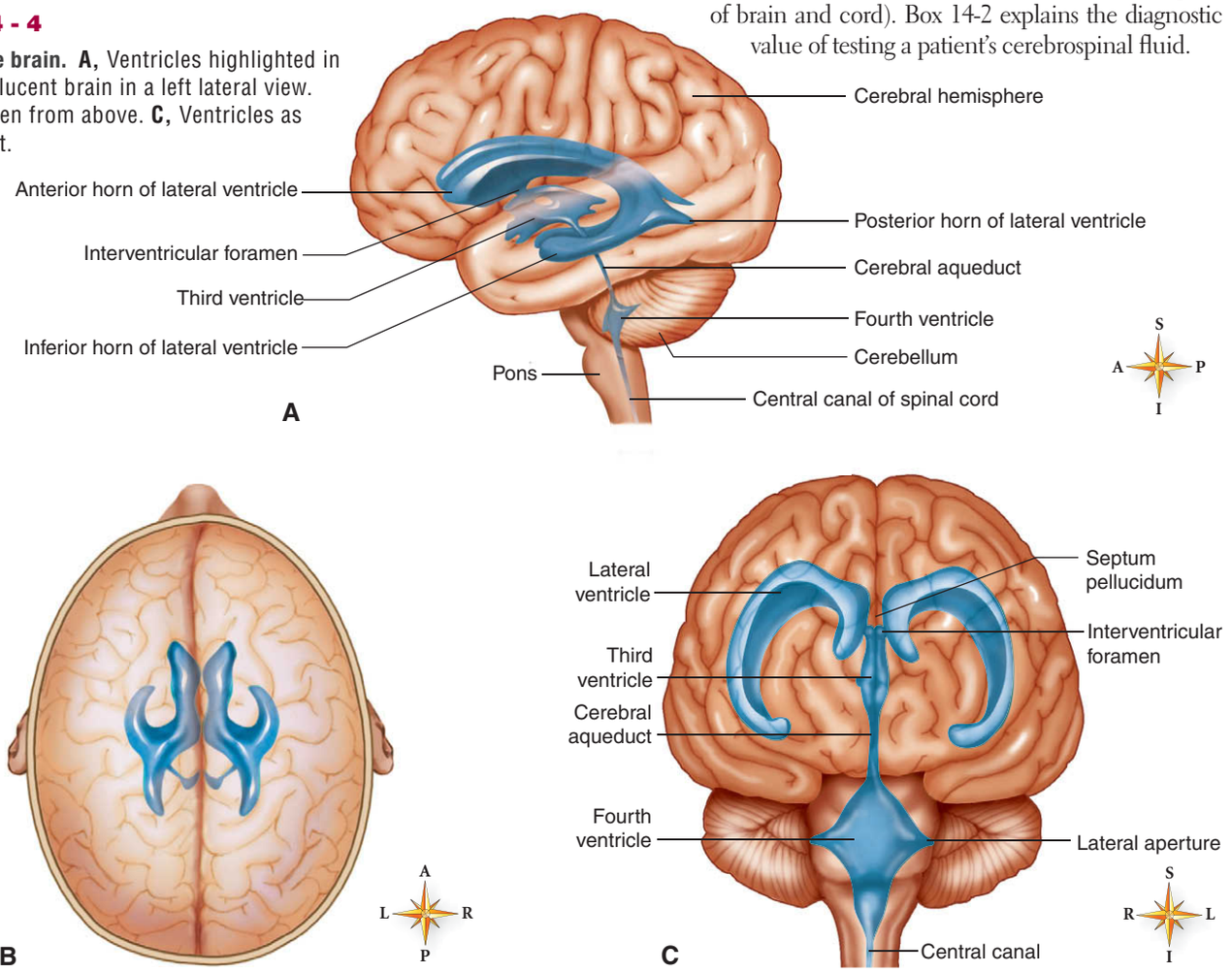
Formation and Circulation of Cerebrospinal Fluid

Formation of CSF occurs mainly by separation of fluid from blood in the **choroid plexuses.** Choroid plexuses are networks of capillaries that project from the pia mater into the lateral ventricles and into the roofs of the third and fourth ventricles. Each choroid plexus is covered with a sheet of a special type of ependymal (glial) cell that releases the CSF into the fluid spaces. From each lateral ventricle the fluid seeps through an opening, the *interventricular foramen (of Monro)*, into the third ventricle, then through a narrow channel, the *cerebral aqueduct (of Sylvius)*, into the fourth ventricle (Figure 14-5). Some of the fluid moves from the fourth ventricle directly into the central canal of the cord. Some of it moves out of the fourth ventricle through openings in its roof, two *lateral foramina (of Luschka)* and one *median foramen (of Magendie)*. These openings allow CSF to move into the *cisterna magna*, a space behind the medulla that is continuous with the subarachnoid space around the brain and cord. The fluid circulates in the subarachnoid space and then is absorbed into venous blood through the *arachnoid villi* (fingerlike projections of the arachnoid mater into the brain's venous sinuses). Briefly, here is the circulation route of cerebrospinal fluid: it is formed as fluid is separated from blood in the choroid plexuses, then it flows into the ventricles of the brain, circulates through the ventricles and into the central canal and subarachnoid spaces, and is then absorbed back into blood.

The amount of CSF in the average adult is about 140 ml (about 23 ml in the ventricles and 117 ml in the subarachnoid space of brain and cord). Box 14-2 explains the diagnostic value of testing a patient's cerebrospinal fluid.

FIGURE 14-4

Fluid spaces of the brain. A, Ventricles highlighted in blue within a translucent brain in a left lateral view. **B,** Ventricles as seen from above. **C,** Ventricles as seen from the front.



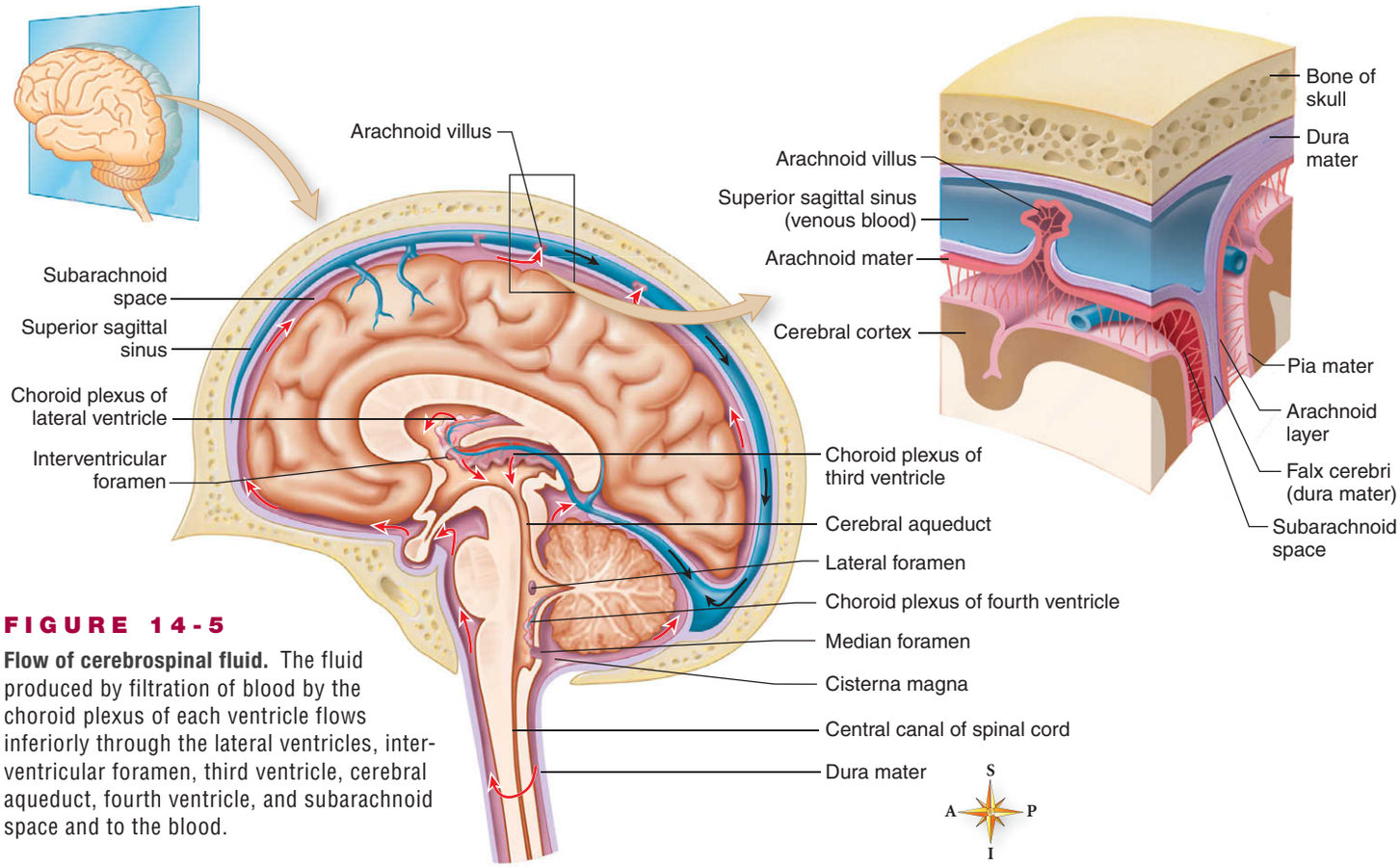


FIGURE 14-5

Flow of cerebrospinal fluid. The fluid produced by filtration of blood by the choroid plexus of each ventricle flows inferiorly through the lateral ventricles, interventricular foramen, third ventricle, cerebral aqueduct, fourth ventricle, and subarachnoid space and to the blood.

Box 14-2 | DIAGNOSTIC study

Lumbar Puncture

The meninges extends beyond the cord, which provides a convenient location for performing lumbar punctures without danger of injuring the spinal cord. A **lumbar puncture** is a withdrawal of some of the cerebrospinal fluid (CSF) from the subarachnoid space in the lumbar region of the vertebral column. The physician inserts a needle just above or below the fourth lumbar vertebra, knowing that the spinal cord ends 2 or more centimeters (about an inch) above that level (Figure 1). The fourth lumbar vertebra can be easily located because it lies on a line with the iliac crest. Placing a patient on his or her side with the knees and chest drawn together to arch the back separates the vertebrae sufficiently to create a space in which the needle can be inserted. As the needle enters the CSF, the thin nerve roots roll off the tip of the needle—thus allowing collection of CSF without damaging nerve tissue.

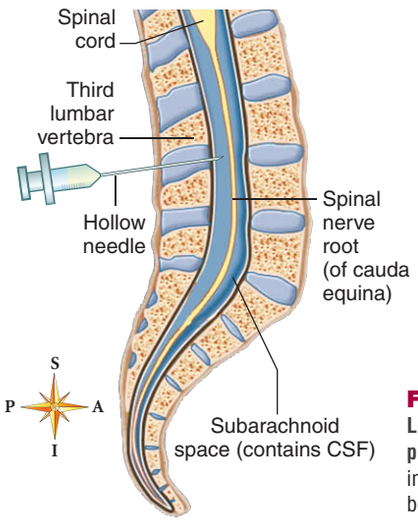


FIGURE 1

Location of lumbar puncture. The needle is inserted a few centimeters below the spinal cord.

Cerebrospinal fluid removed through a lumbar puncture can be tested for the presence of blood cells, bacteria, or other abnormal characteristics that may indicate an injury or infection, such as meningitis (Figure 2). A sensor called a *manometer* is sometimes attached to the needle to determine the pressure of the CSF within the subarachnoid space. The lumbar puncture can also be used to introduce diagnostic agents, such as radiopaque dyes for **x-ray photography,** into the subarachnoid space.



FIGURE 2

Cerebrospinal fluid (CSF) examination. These samples were taken by a lumbar puncture or "spinal tap." The top sample shows the normal, clear appearance of CSF. The bottom sample was taken from a patient with hemorrhage in the subarachnoid space. Blood is seen settling to the bottom of the sample. The yellowish tinge of the fluid is from the breakdown of blood cells before the fluid was removed from the body.

| A&P CONNECT |

When the circulation of cerebrospinal fluid (CSF) is blocked, there can be dramatic effects on the structure of the brain. An example is **hydrocephalus,** a condition in which the CSF produces abnormal fluid pressure in the brain. A brief description of hydrocephalus and how it can be treated, along with some dramatic clinical images, can be found in ***Hydrocephalus*** online at ***A&P Connect.***

evolve

| QUICK CHECK |

1. Name the three membranous coverings of the central nervous system in order, beginning with the outermost layer.
2. Trace the path of cerebrospinal fluid from its formation by a choroid plexus to its reabsorption into the blood.

SPINAL CORD

Structure of the Spinal Cord

The spinal cord lies within the spinal cavity, extending from the foramen magnum to the lower border of the first lumbar vertebra (Figure 14-6), a distance of about 45 cm (18 inches) in the average body. The spinal cord does not completely fill the spinal cavity—which also contains the meninges, CSF, a cushion of adipose tissue, and blood vessels.

The spinal cord is an oval-shaped cylinder that tapers slightly as it descends and has two bulges, one in the cervical region and the other in the lumbar region (see Figure 14-6). Two deep grooves, the *anterior median fissure* and the *posterior median sulcus*, just miss dividing the cord into separate symmetrical halves. The anterior fissure is the deeper and the wider of the two grooves—a useful factor to remember when you examine spinal cord diagrams. It enables you to tell at a glance which part of the cord is anterior and which is posterior.

Two bundles of nerve fibers called *nerve roots* project from each side of the spinal cord (see Figure 14-6). Fibers comprising the **dorsal (posterior) nerve root** carry sensory information into the spinal cord. Cell bodies of these unipolar, sensory neurons make up a small region of gray matter in the dorsal nerve root called the *dorsal (posterior) root ganglion*. Fibers of the **ventral (anterior) nerve root** carry motor information out of the spinal cord. Cell bodies of these multipolar, motor neurons are in the gray matter that composes the inner core of the spinal cord. Numerous interneurons are also located in the gray matter core of the spinal cord. On each side of the spinal cord, the dorsal and ventral nerve roots join together to form a single mixed nerve called, simply, a **spinal nerve.** Spinal nerves, components of the peripheral nervous system, are considered in more detail in the next chapter.

The spinal cord ends at vertebra L1 in a tapered cone called the **conus medullaris.** As you can see in Figure 14-7, many nerve roots extending from the conus medullaris form a sort of "horse tail" of spinal nerve roots called the **cauda equina.** Within the cauda equina the long cordlike *filum terminale* is formed from the spinal meninges.

Although the gray matter core of the spinal cord looks like a flat letter H in transverse sections of the cord, it actually has three dimensions, because the gray matter extends the length of the cord. The H-shaped rod of gray matter is made up of anterior, lateral, and posterior **gray columns.** When viewed in a cross section, as in Figure 14-6, the columns forming the H appear to spread out like animal horns—and thus are also called *anterior, posterior,* and *lateral gray horns.* The left and right gray columns are joined in the middle by a band called the **gray commissure.** It is through the gray commissure that the central canal carries CSF through the spinal cord. The gray columns consist predominantly of cell bodies of interneurons and motor neurons.

White matter surrounding the gray matter is subdivided in each half of the cord into three white columns or **funiculi:** the anterior,

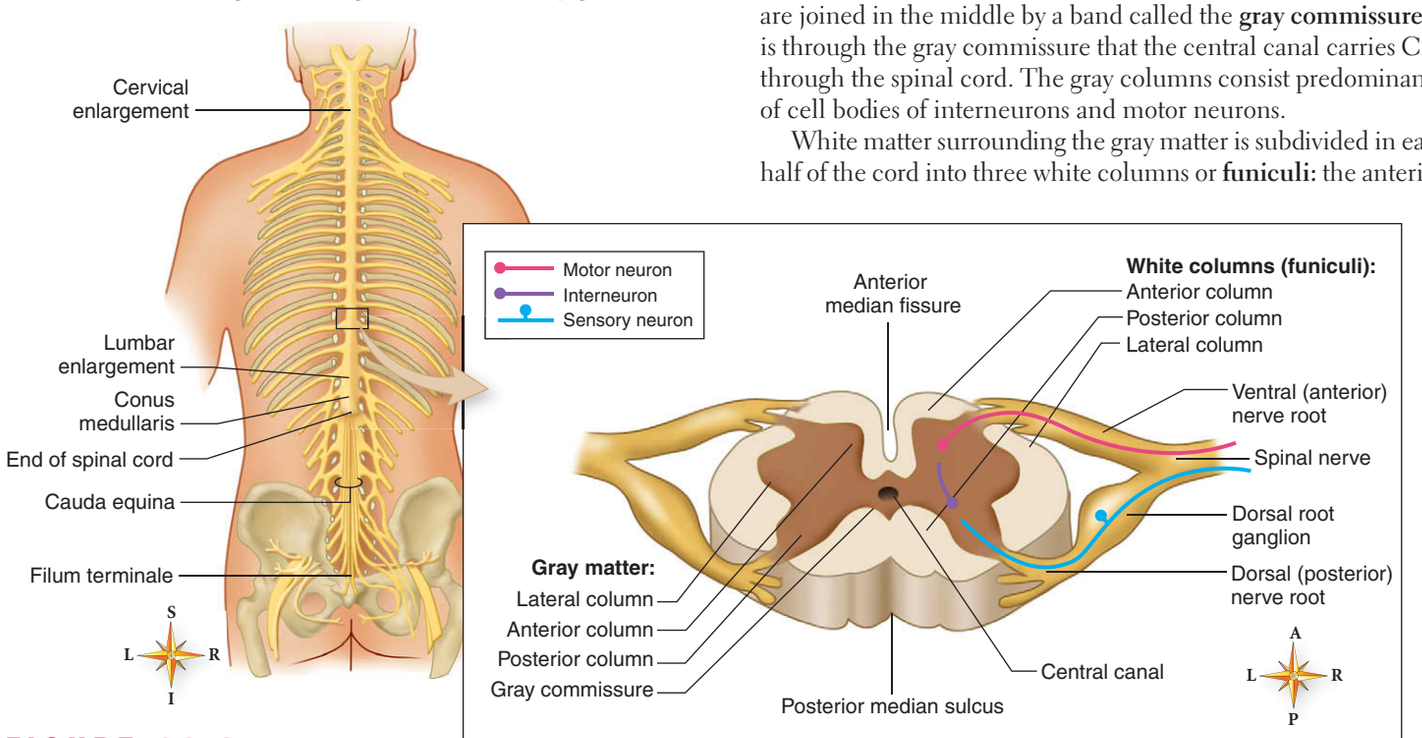


FIGURE 14-6

Spinal cord. The inset illustrates a transverse section of the spinal cord shown in the broader view.

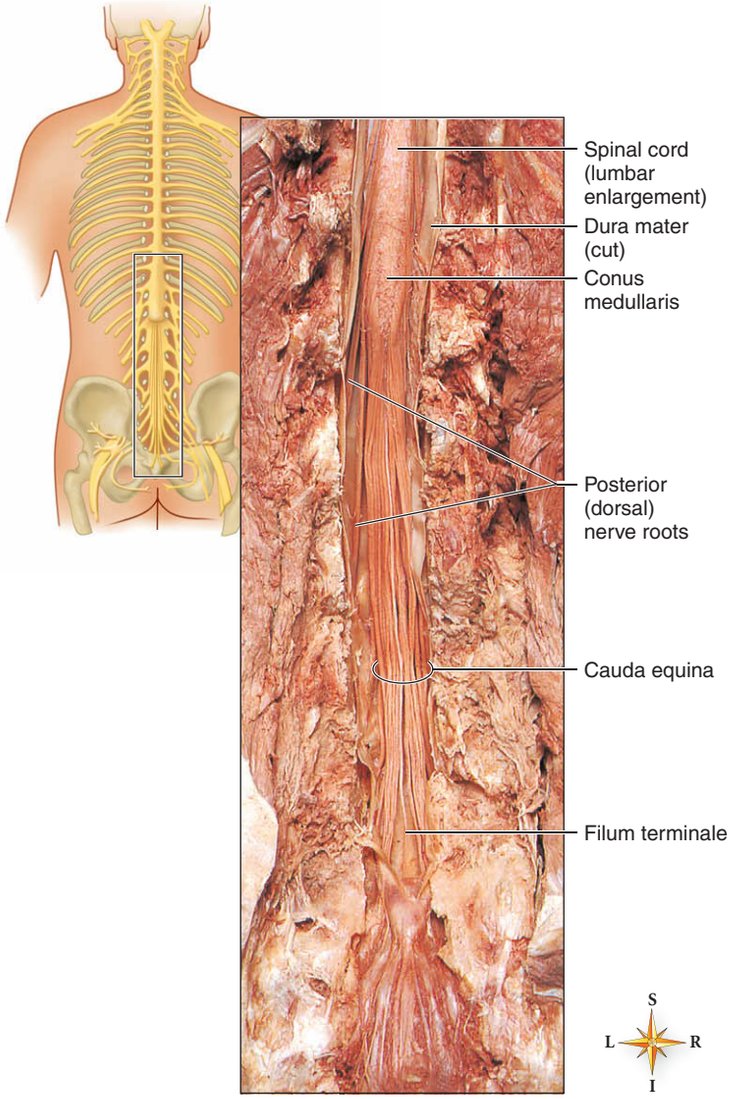


FIGURE 14-7

Cauda equina. Photograph shows the inferior portion of the dura mater dissected posteriorly, revealing the cauda equine and nearby structures.

posterior, and lateral white columns. Each white column, or funiculus, consists of a large bundle of nerve fibers (axons) divided into smaller bundles called **spinal tracts,** shown in Figure 14-8. The names of most spinal cord tracts indicate the white column in which the tract is located, the structure in which the axons that make up the tract originate, and the structure in which they terminate. For example, the lateral corticospinal tract is located in the lateral white column of the cord. The axons that compose it originate from neuron cell bodies in the spinal cortex (of the cerebrum) and terminate in the spinal cord. The anterior spinothalamic tract lies in the anterior white column. The axons that compose it originate from neuron cell bodies in the spinal cord and terminate in a portion of the brain called the *thalamus.*

You may wish to refer to the atlas that accompanies this book, where you will find detailed photographs of a human spinal cord. How many structures can you identify in the atlas by sight?

Functions of the Spinal Cord

The spinal cord performs two general functions. Briefly, it provides conduction routes to and from the brain and serves as the integrator, or reflex center, for all spinal reflexes.

Spinal cord tracts provide conduction paths to and from the brain. **Ascending tracts** conduct sensory impulses up the cord to the brain. **Descending tracts** conduct motor impulses down the cord from the brain. Bundles of axons compose all tracts.

Tracts are both structural and functional organizations of the nerve fibers of the spinal cord. They are *structural* organizations in that all the axons of any one tract originate from neuron cell bodies located in the same area of the central nervous system, and all the axons terminate in a single structure elsewhere in the central nervous system. For example, all the fibers of the spinothalamic tract are axons originating from neuron cell bodies located in the spinal cord and terminating in the thalamus. Tracts are *functional* organizations in that all the axons that compose one tract serve one general function. For instance, fibers of the spinothalamic tracts serve a sensory function. They transmit impulses that produce the sensations of crude touch, pain, and temperature.

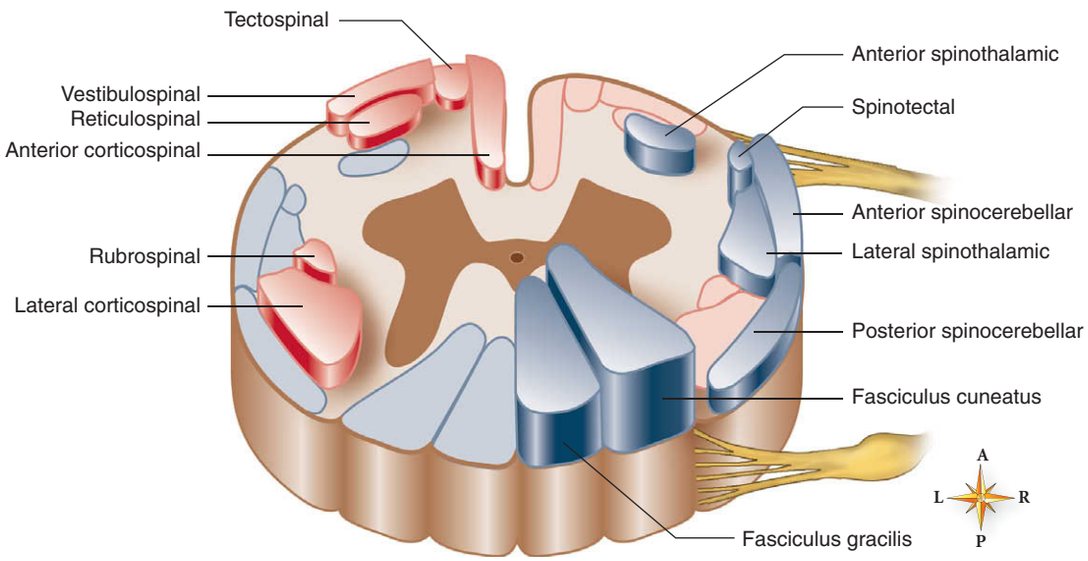


FIGURE 14-8

Major tracts of the spinal cord. The major ascending (sensory) tracts are highlighted in blue. The major descending (motor) tracts are highlighted in red.

TABLE 14-1 Major Ascending Tracts of Spinal Cord

NAME	FUNCTION	LOCATION	ORIGIN*	TERMINATION†
Lateral spinothalamic	Pain, temperature, and crude touch on opposite side	Lateral white columns	Posterior gray column on opposite side	Thalamus
Anterior spinothalamic	Crude touch and pressure	Anterior white columns	Posterior gray column on opposite side	Thalamus
Fasciculi gracilis and cuneatus	Discriminating touch and pressure sensations, including vibration, stereognosis, and two-point discrimination; also conscious kinesthesia	Posterior white columns	Spinal ganglia on same side	Medulla
Anterior and posterior spinocerebellar	Unconscious kinesthesia	Lateral white columns	Anterior or posterior gray column	Cerebellum
Spinotectal	Touch related to visual reflexes	Lateral white columns	Posterior gray columns	Superior colliculus (midbrain)

*Location of cell bodies of neurons from which axons of tract arise.
†Structure in which axons of tract terminate.

Because so many different tracts make up the white columns of the cord, we mention only a few of the more important ones. Locate each tract in Figure 14-8. Consult Tables 14-1 and 14-2 for a brief summary of these tracts.

Five important ascending, or sensory, tracts and their functions, stated very briefly, are as follows:

1. **Lateral spinothalamic tracts:** crude touch, pain, and temperature
2. **Anterior spinothalamic tracts:** crude touch and pressure
3. **Fasciculi gracilis** and **cuneatus tracts:** discriminating touch and conscious sensation of position and movement of body parts (kinesthesia)
4. **Spinocerebellar tracts:** subconscious kinesthesia
5. **Spinotectal tracts:** touch that triggers visual reflexes

Further discussion of the sensory neural pathways may be found on pp. 506–507.

Six important descending, or motor, tracts and their functions described in brief are as follows:

1. **Lateral corticospinal tracts:** voluntary movement; contraction of individual or small groups of muscles, particularly those moving hands, fingers, feet, and toes on opposite side of body
2. **Anterior corticospinal tracts:** same as preceding except mainly muscles of same side of body
3. **Reticulospinal tracts:** help maintain posture during skeletal muscle movements
4. **Rubrospinal tracts:** transmit impulses that coordinate body movements and maintenance of posture
5. **Tectospinal tracts:** head and neck movement related to visual reflexes
6. **Vestibulospinal tracts:** coordination of posture and balance

Further discussion of motor neural pathways may be found on pp. 490–491.

TABLE 14-2 Major Descending Tracts of Spinal Cord

NAME	FUNCTION	LOCATION	ORIGIN*	TERMINATION†
Lateral corticospinal (or crossed pyramidal)	Voluntary movement, contraction of individual or small groups of muscles, particularly those moving hands, fingers, feet, and toes of opposite side	Lateral white columns	Motor areas or cerebral cortex of opposite side from tract location in cord	Lateral or anterior gray columns
Anterior corticospinal (direct pyramidal)	Same as lateral corticospinal except mainly muscles of same side	Anterior white columns	Motor cortex but on same side as location in cord	Lateral or anterior gray columns
Reticulospinal	Maintain posture during movement	Anterior white columns	Reticular formation (midbrain, pons, medulla)	Anterior gray columns
Rubrospinal	Coordination of body movement and posture	Lateral white columns	Red nucleus (of midbrain)	Anterior gray columns
Tectospinal	Head and neck movement during visual reflexes	Anterior white columns	Superior colliculus (midbrain)	Medulla and anterior gray columns
Vestibulospinal	Coordination of posture/balance	Anterior white columns	Vestibular nucleus (pons, medulla)	Anterior gray columns

*Location of cell bodies of neurons from which axons of tract arise.
†Structure in which axons of tract terminate.

The spinal cord also serves as the reflex center for all spinal reflexes. The term *reflex center* means the center of a reflex arc or the place in the arc where incoming sensory impulses become outgoing motor impulses. They are structures that switch impulses from afferent to efferent neurons. In two-neuron arcs, reflex centers are merely synapses between neurons. In all other arcs, reflex centers consist of interneurons interposed between afferent and efferent neurons. Spinal reflex centers are located in the gray matter of the cord.

| A&P CONNECT |

Reflex centers can act as **pain control areas.** Pain control areas can inhibit the pain information heading toward the conscious processing centers of the brain. Identifying pain control areas and how they work has lead to the development of **transcutaneous electrical nerve stimulation (TENS)** units and other therapies to reduce pain. To learn more about this check out ***Pain Control Areas*** online at ***A&P Connect.***

evolve

| QUICK CHECK |

3. What are spinal nerve roots? How does the dorsal root differ from the ventral root?
4. Name the regions of the white and gray matter seen in a horizontal section of the spinal cord.
5. Contrast ascending tracts and descending tracts of the spinal cord. Can you give an example of each?

BRAIN

The brain is one of the largest organs in adults (Box 14-3). It consists, in round numbers, of almost 100 billion neurons and roughly the same number of glia. In most adults, it weighs about 1.4 kg (3 pounds).

Most of the production of new neurons in the brain occurs during prenatal development and during the first few months of postnatal life. Malnutrition during the crucial prenatal months of neuron multiplication can result in fewer brain cells. After birth, the neurons grow mainly in size rather than in number. The brain attains full size by about the eighteenth year but grows rapidly only during the first 9 years or so. However, some regions of the brain retain *neural stem cells (NSCs)* that can continue to add small numbers of new neurons to the brain throughout adulthood. Throughout life many new synapses form while others are broken, making the brain a very dynamic and adaptive structure.

Six major divisions of the brain, named from below, upward, are as follows: *medulla oblongata*, *pons*, *midbrain*, *cerebellum*, *diencephalon*, and *cerebrum*. Very often the medulla oblongata, pons, and midbrain are referred to collectively as the *brainstem*. Look at these three structures in Figure 14-9. Do you agree that they seem to form a stem for the rest of the brain?

Structure of the Brainstem

Three divisions of the brain make up the **brainstem.** The **medulla oblongata** forms the lowest part of the brainstem, the **midbrain** forms the uppermost part, and the **pons** lies between them, that is, above the medulla and below the midbrain. Ten of the twelve pairs of cranial nerves arise from the brainstem.

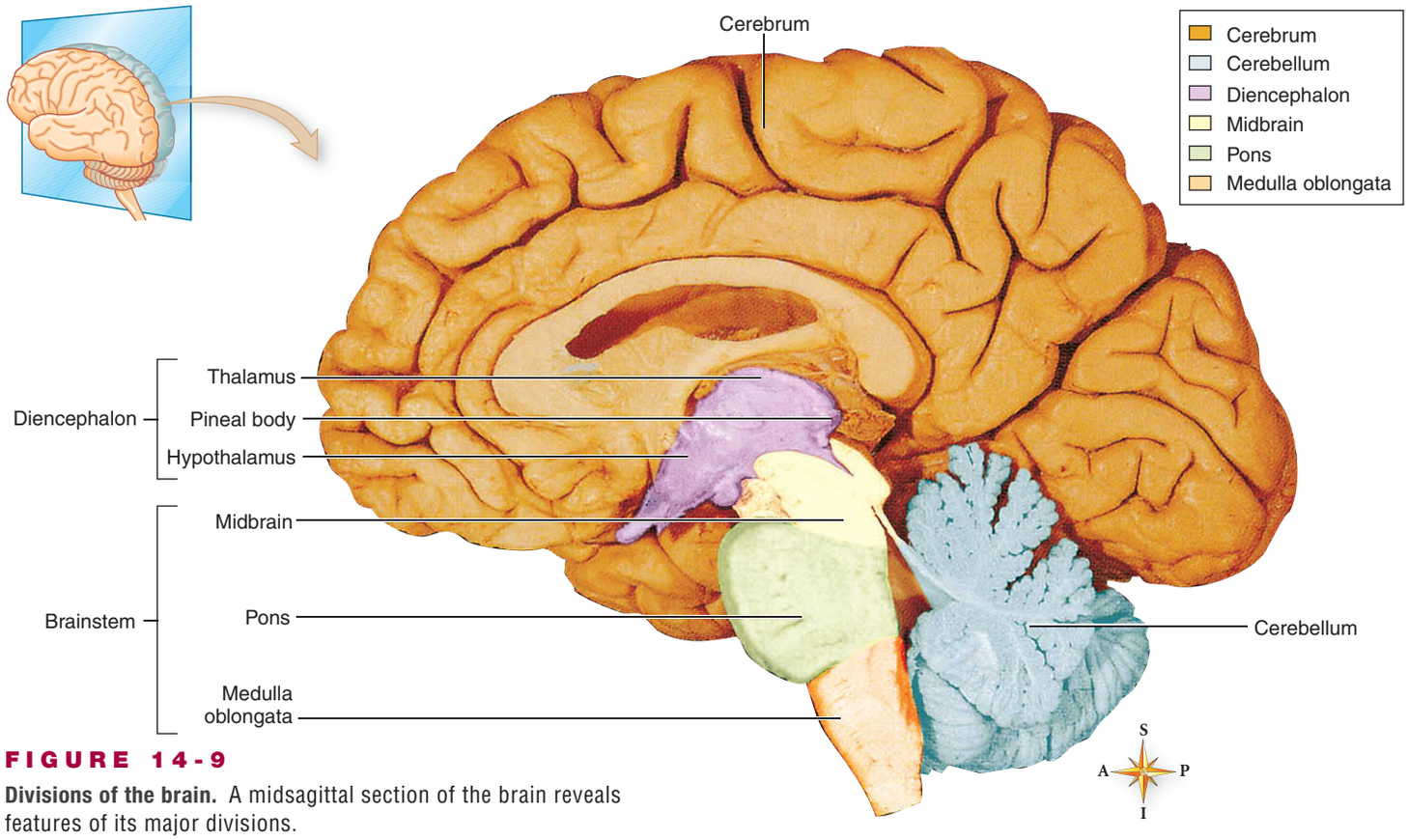


FIGURE 14-9

Divisions of the brain. A midsagittal section of the brain reveals features of its major divisions.

Box 14-3 | FYI

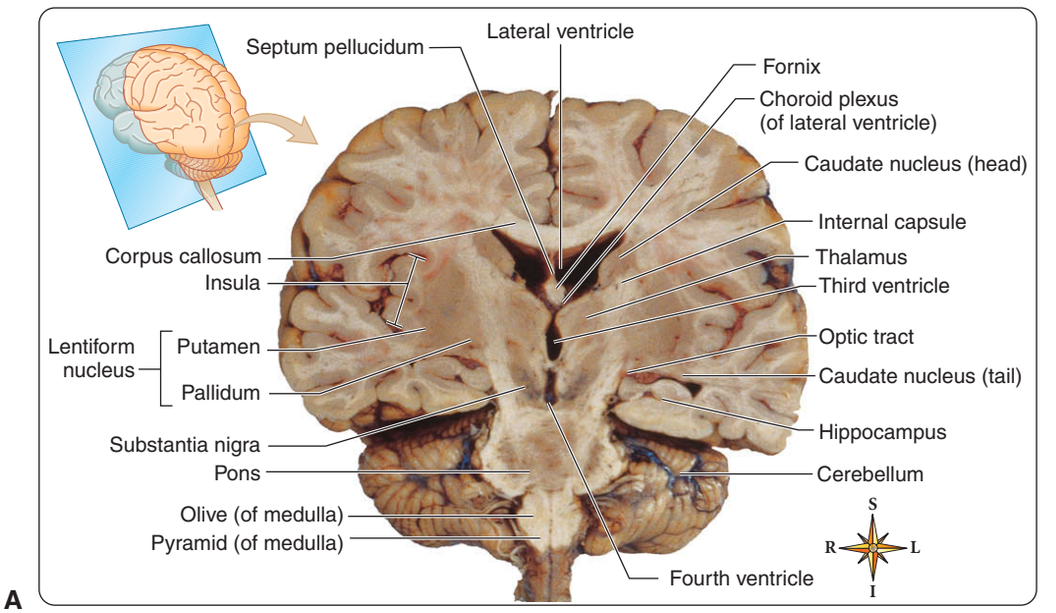
Studying Human Brains

As with any part of the body, the best way to learn the anatomy of the brain is to look at actual specimens. Recall from Chapter 1 (see Figure 1-1, p. 4) that this is the traditional method of learning human anatomy. When cadavers are not available for this purpose, one useful alternative is photographs of well-dissected cadavers.

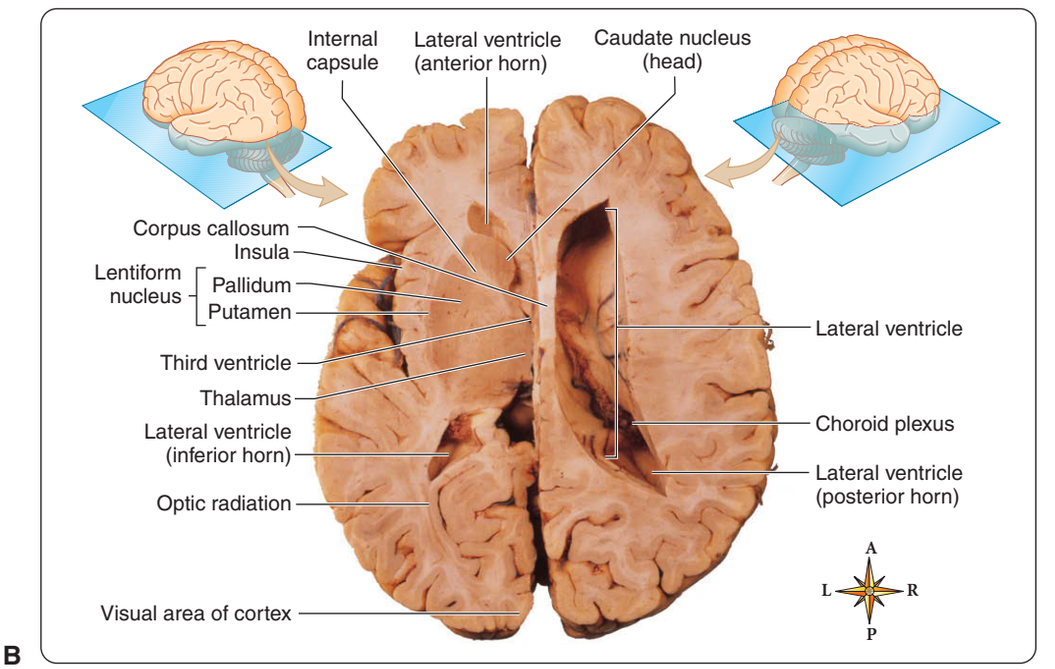
Part *A* of the figure below is an oblique frontal (coronal) section of the human brain, as seen from the front of the subject. This photograph shows details of the internal features of all the major brain divisions. Compare this view of the brain with part *B,* which shows the brain cut on horizontal (transverse) planes at two slightly different levels, as seen from above. Then compare these photographs with those shown in the small atlas that accompanies this book. How does viewing sections in different planes of the brain benefit your understanding of the three-dimensional aspects of brain anatomy? What benefits are there to studying the brains of human cadavers, rather than relying solely on artists' renderings of the brain? Are there any advantages to using artists' renderings of brain anatomy?

Refer to these photographs—and those in the atlas that accompanies this book—often as you study the details of brain anatomy.

Human brain specimens. A, Oblique frontal section. **B,** Horizontal sections (left section is slightly inferior to right section).



A



B

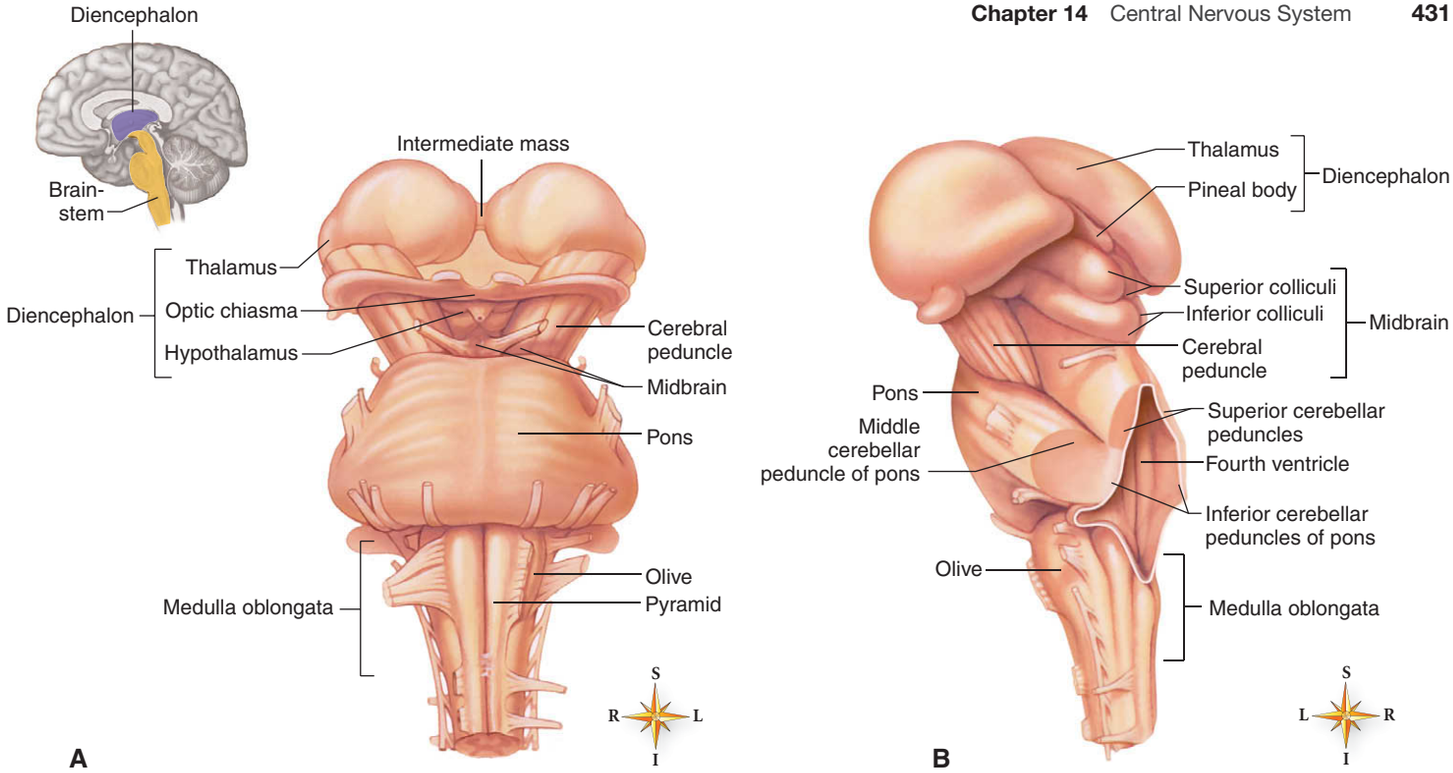


FIGURE 14-10

The brainstem and diencephalon. A, Anterior aspect. **B,** Posterior aspect (shifted slightly to lateral).

MEDULLA OBLONGATA

The medulla oblongata is the part of the brain that attaches to the spinal cord. It is, in fact, an enlarged extension of the spinal cord located just above the foramen magnum. It measures only a few centimeters (about 1 inch) in length and is separated from the pons above by a horizontal groove. It is composed of white matter (projection tracts) and a network of gray and white matter called the **reticular formation** (look ahead to Figure 14-21).

The **pyramids** (Figure 14-10) are two bulges of white matter located on the ventral surface of the medulla. Fibers of the so-called pyramidal tracts form the pyramids.

The **olive** (see Figure 14-10) of the medulla is an oval projection appearing one on each side of the ventral surface of the medulla, lateral to the pyramids.

Located in the medulla's reticular formation are various *nuclei*, or clusters of neuron cell bodies. Some nuclei are called *control centers*—for example, the cardiac, respiratory, and vasomotor control centers (Box 14-4).

PONS

Just above the medulla lies the pons, composed, like the medulla, of white matter and reticular formation. Fibers that run transversely across the pons and through the middle cerebellar peduncles into the cerebellum make up the external white matter of the pons and give it its arching, bridgelike appearance.

MIDBRAIN

The midbrain *(mesencephalon)* is appropriately named. It forms the midsection of the brain, because it lies above the pons and below the cerebrum. Both white matter (tracts) and reticular formation compose the midbrain. Extending divergently through it are two ropelike masses of white matter named **cerebral peduncles** (see Figure 14-10). Tracts in the peduncles conduct impulses between the midbrain and cerebrum. In addition to the cerebral peduncles, another landmark of the midbrain is the **corpora quadrigemina** (literally, "body of fourfold twins"). The corpora quadrigemina are two **inferior colliculi** and two **superior colliculi.** Note the location of the two sets of twin colliculi, or the corpora quadrigemina, in Figure 14-10, *B*. They form the posterior, upper part of the midbrain, the part that lies just above the cerebellum. Certain auditory centers are located in the inferior colliculus. The superior colliculus contains visual centers. Two other midbrain structures are the *red nucleus* and the *substantia nigra*. Each of these consists of clusters of cell bodies of neurons involved in muscular control. The substantia nigra (literally, "black matter") gets its name from the dark pigment in some of its cells.

Box 14-4 | HEALTH matters

Vital Centers

Because the cardiac, vasomotor, and respiratory control centers are essential for survival, they are called the *vital centers.* They serve as the centers for various reflexes controlling heart action, blood vessel diameter, and respiration. Because the medulla contains these centers, it is the most vital part of the entire brain—so vital that injury or disease of the medulla often proves fatal. Blows at the base of the skull and bulbar poliomyelitis, for example, cause death if they interrupt impulse conduction in the vital respiratory centers.

Functions of the Brainstem

The brainstem, like the spinal cord, performs sensory, motor, and reflex functions. The spinothalamic tracts are important sensory tracts that pass through the brainstem on their way to the thalamus in the diencephalon. The fasciculi cuneatus and gracilis and the spinoreticular tracts are sensory tracts whose axons terminate in the gray matter of the brainstem. Corticospinal and reticulospinal tracts are two of the major tracts present in the white matter of the brainstem.

Nuclei in the medulla contain a number of reflex centers. Of first importance are the cardiac, vasomotor (vessel muscle), and respiratory centers. Other centers present in the medulla are for various nonvital reflexes such as vomiting, coughing, sneezing, hiccupping, and swallowing.

The pons contains centers for reflexes mediated by the fifth, sixth, seventh, and eighth cranial nerves. The locations and functions of these peripheral nerves are discussed in Chapter 15. In addition, the pons contains the pneumotaxic centers that help regulate respiration.

The midbrain, like the pons, contains reflex centers for certain cranial nerve reflexes, for example, pupillary reflexes and eye movements, mediated by the third and fourth cranial nerves, respectively.

Structure of the Cerebellum

The **cerebellum** (literally "little brain") is located just below the posterior portion of the cerebrum and is partially covered by it (Figure 14-11). A transverse fissure separates the cerebellum from the cerebrum. The cerebellum is the second largest part of the brain (after the cerebrum) but has more neurons than all the other parts of the nervous system combined! Thus the cerebellum has a lot of "computing power" compared with other parts of the brain.

The cerebrum and cerebellum have several structural characteristics in common. For instance, gray matter makes up the outer portion, or *cortex*, of each. White matter predominates in the interior of each. Look at Figure 14-11, *C*, and find the internal white matter of the cerebellum called the **arbor vitae** (literally "tree of life"). Note the arbor vitae's distinctive pattern, similar to the branches of a tree. Note, too, that the surfaces of both the cerebellum and the cerebrum have numerous grooves *(sulci)* and raised areas *(gyri)*. The gyri of the cerebellum, however, are much more slender and less prominent than those of the cerebrum. These delicate, roughly parallel gyri are also called **folia** (literally "leaves"). Like the cerebrum, the cerebellum consists of two large lateral masses, the left and right *cerebellar hemispheres*, and a central section called the **vermis.**

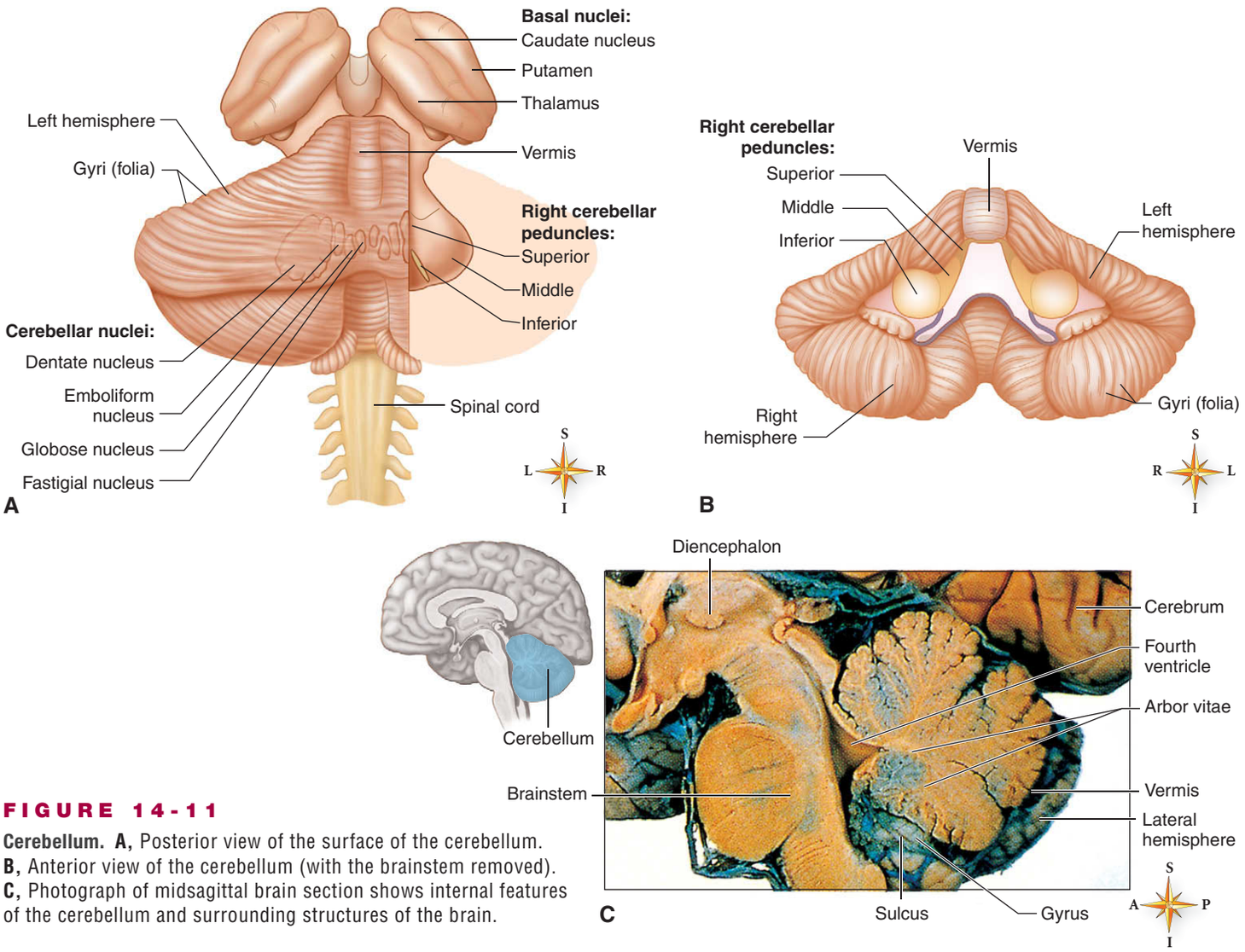


FIGURE 14-11

Cerebellum. A, Posterior view of the surface of the cerebellum. **B,** Anterior view of the cerebellum (with the brainstem removed). **C,** Photograph of midsagittal brain section shows internal features of the cerebellum and surrounding structures of the brain.

The internal white matter of the cerebellum is composed of some short and some long tracts. The shorter tracts conduct impulses from neuron cell bodies located in the cerebellar cortex to neurons whose dendrites and cell bodies compose nuclei located in the interior of the cerebellum. The longer tracts conduct impulses to and from the cerebellum. Fibers of the longer tracts enter or leave the cerebellum by way of its three pairs of peduncles (see Figure 14-11, *B*), as follows:

1. **Inferior cerebellar peduncles:** composed chiefly of tracts into the cerebellum from the medulla and cord (notably spinocerebellar, vestibulocerebellar, and reticulocerebellar tracts)
2. **Middle cerebellar peduncles:** composed almost entirely of tracts into the cerebellum from the pons, that is, pontocerebellar tracts
3. **Superior cerebellar peduncles:** composed principally of tracts from dentate nuclei in the cerebellum through the red nucleus of the midbrain to the thalamus

An important pair of cerebellar nuclei is the **dentate nuclei,** one of which lies in each hemisphere. Tracts connect these nuclei with the thalamus and with motor areas of the cerebral cortex. By means of these tracts, cerebellar impulses influence the motor cortex. Impulses in other tracts enable the motor cortex to influence the cerebellum.

Functions of the Cerebellum

The cerebellum shares similarities with the cerebrum, functionally as well as structurally. The current view of cerebellar function states that the cerebellum performs a variety of different functions that complement or assist the cerebrum, many of which involve the planning and coordination of skeletal muscle activity and maintaining balance in the body.

Coordinated control of muscle action is a function of the upper part of the cerebellum working with the motor control areas of the cerebrum. Normal muscle action involves groups of muscles, the various members of which function together as a unit. In any given action, for example, the prime mover contracts and the antagonist relaxes but then contracts weakly at the proper moment to act as a brake, checking the action of the prime mover. Also, the synergists contract to assist the prime mover, and the fixation muscles of the neighboring joint contract. Through such harmonious, coordinated patterns and group action, normal movements are smooth, steady, and precise as to force, rate, and extent. These patterns, such as the sequence of leg movements needed for walking, are learned and stored in the cerebellum.

Achievement of coordinated movements results from the combined efforts of the cerebrum and cerebellum. Impulses from the cerebrum may trigger the action, but those from the cerebellum plan and coordinate the contractions and relaxations of the various muscles once they have begun. Figure 14-12 shows how the cerebrum and cerebellum work together. Impulses from the motor control areas of the cerebrum travel down the corticospinal tract and, through peripheral nerves, to skeletal muscle tissue. At the same time, the impulses go to the cerebellum. The cerebellum compares the motor commands of the cerebrum with information coming in from sensory receptors in the muscles (proprioception). Using "sensory maps" of the body, the cerebellum compares the intended movement with the actual state of the body and its current position or movement. Impulses then travel from the cerebellum to both the cerebrum and the muscle tissue to adjust or coordinate the movements to produce the intended action.

Interestingly, the cerebellum becomes involved when a person is just thinking about doing some activity, thus "getting ready" for

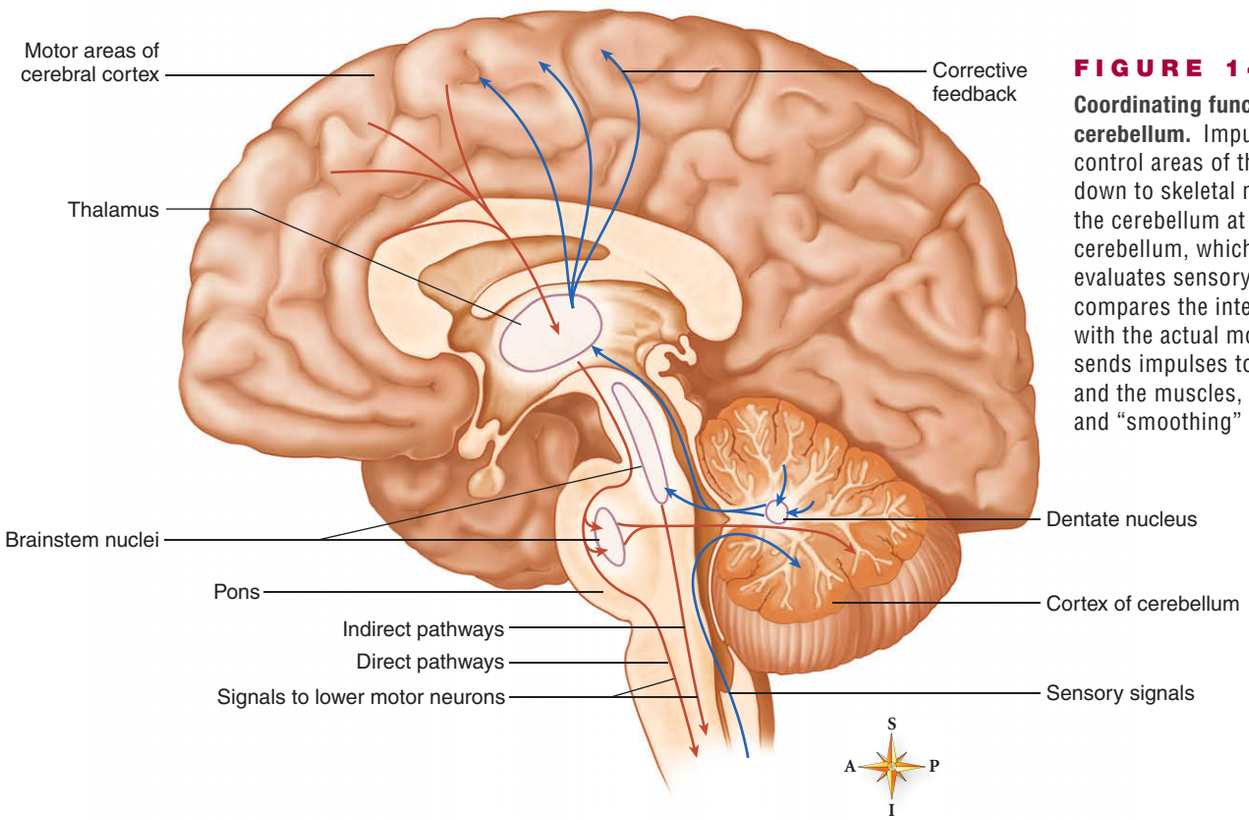


FIGURE 14-12

Coordinating function of the cerebellum. Impulses from the motor control areas of the cerebrum travel down to skeletal muscle tissue and to the cerebellum at the same time. The cerebellum, which also receives and evaluates sensory information, compares the intended movement with the actual movement. It then sends impulses to both the cerebrum and the muscles, thus coordinating and "smoothing" muscle activity.

possible later movement. Some physiologists consider the planning and coordination of movement to be the main functions of the cerebellum.

The cerebellum is also thought to be concerned with both exciting and inhibiting the postural reflexes that help us maintain a stable body position. Sensory impulses from equilibrium (balance) receptors in the ear reach the cerebellum. Using this information, the cerebellum then stimulates or inhibits various muscles to maintain stability of the body.

Not only does the cerebellum work with the cerebrum as a sort of "executive assistant" to coordinate and plan movement and maintain balance—current evidence suggests that the cerebellum is an all-around assistant or planner of a variety of functions normally associated with the cerebrum. In fact, it is becoming clear that the cerebellum coordinates incoming sensory information as much or more than it coordinates outgoing motor information. Cerebellar disease (e.g., abscess, hemorrhage, tumors, trauma) produces certain characteristic symptoms. Predominant among them are ataxia (muscle incoordination), hypotonia, tremors, and disturbances of gait and balance. One example of ataxia is overshooting a mark or stopping before reaching it when trying to touch a given point on the body (finger-to-nose test). Drawling, scanning, and singsong speech are also examples of ataxia. Tremors are particularly pronounced toward the end of the movements and with the exertion of effort. Disturbances of gait and balance vary, depending on the muscle groups involved. The walk, for instance, is often characterized by staggering or lurching and by a clumsy manner of raising the foot too high and bringing it down with a clap. Paralysis does not result from loss of cerebellar function.

To briefly summarize its general functions, the cerebellum:

- Acts with the cerebral cortex to produce skilled movements by planning and coordinating the activities of groups of muscles
- Helps control posture: functions below the level of consciousness to make movements smooth instead of jerky, steady instead of trembling, and efficient and coordinated instead of ineffective, awkward, and uncoordinated
- Controls skeletal muscles to maintain balance
- Coordinates incoming sensory information and acts in other ways to complement and assist various functions of the cerebrum

| QUICK CHECK |

6. Name the three major divisions of the brainstem, and briefly describe the function of each.
7. What are gyri or folia? What are sulci?
8. How does the cerebellum work with the cerebrum to coordinate muscle activity?

Diencephalon

The **diencephalon** (literally, "between brain") is the part of the brain located between the cerebrum and the midbrain (mesencephalon). Although the diencephalon consists of several structures located around the third ventricle, the main ones are the **thalamus** and **hypothalamus.** The diencephalon also includes the **optic chiasma,** the **pineal gland,** and several other small but important structures.

THALAMUS

The **thalamus** is a dumbbell-shaped mass of gray matter made up of many nuclei. As Figures 14-10 and 14-13 show, each *lateral mass* of the thalamus forms one lateral wall of the third ventricle. Extending through the third ventricle, and thus joining the two lateral masses of the thalamus, is the *intermediate mass.* Two important groups of nuclei that make up the thalamus are the *geniculate bodies*, located in the posterior region of each lateral mass. The geniculate bodies play a role in processing auditory and visual input.

Large numbers of axons conduct impulses into the thalamus from the spinal cord, brainstem, cerebellum, basal nuclei, and various parts of the cerebrum. These axons terminate in thalamic nuclei, where they synapse with neurons whose axons conduct impulses out of the thalamus to virtually all areas of the cerebral cortex. Thus the thalamus serves as the major relay station for sensory impulses on their way to the cerebral cortex.

The thalamus performs the following primary functions:

- Plays two parts in the mechanism responsible for sensations
  1. Impulses from appropriate receptors, on reaching the thalamus, produce conscious recognition of the crude, less critical sensations of pain, temperature, and touch
  2. Neurons whose dendrites and cell bodies lie in certain nuclei of the thalamus relay all kinds of sensory impulses, except possibly olfactory, to the cerebrum
- Plays a part in the mechanism responsible for emotions by associating sensory impulses with feelings of pleasantness and unpleasantness
- Plays a part in the arousal or alerting mechanism
- Plays a part in mechanisms that produce complex reflex movements

HYPOTHALAMUS

The **hypothalamus** consists of several structures that lie beneath the thalamus and form the floor of the third ventricle and the lower part of its lateral walls. Prominent among the structures composing the hypothalamus are the *supraoptic nuclei*, the *paraventricular nuclei*, and the *mamillary bodies.* The supraoptic nuclei consist of gray matter located just above and on either side of the *optic chiasma.* The optic chiasma is the X-shaped junction of the optic tracts and optic nerves. The paraventricular nuclei of the hypothalamus are named for their location, which is close to the wall of the third ventricle. The midportion of the hypothalamus gives rise to the **infundibulum,** the stalk leading to the posterior lobe of the *pituitary gland (neurohypophysis).* The posterior part of the hypothalamus consists mainly of the mamillary bodies (see Figure 14-13, *inset*), which are involved with the olfactory sense (smell).

The hypothalamus is a small but functionally important area of the brain. It weighs little more than 7 grams (¼ oz), yet it performs many functions of the greatest importance both for survival

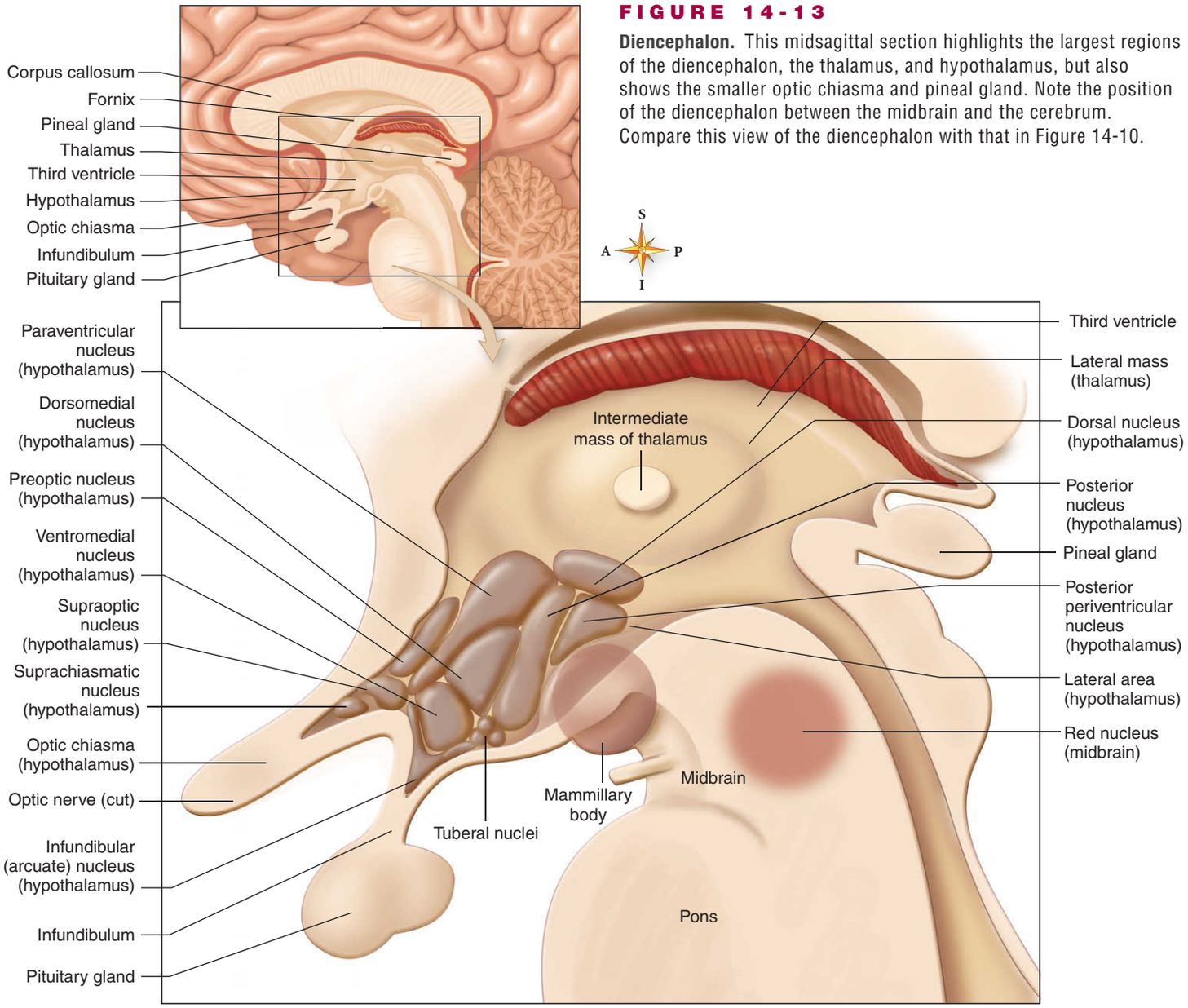


FIGURE 14-13

Diencephalon. This midsagittal section highlights the largest regions of the diencephalon, the thalamus, and hypothalamus, but also shows the smaller optic chiasma and pineal gland. Note the position of the diencephalon between the midbrain and the cerebrum. Compare this view of the diencephalon with that in Figure 14-10.

and for the enjoyment of life. For instance, it functions as a link between the psyche (mind) and the soma (body). It also links the nervous system to the endocrine system. Certain areas of the hypothalamus function as pleasure centers or reward centers for the primary drives such as eating, drinking, and sex. The following list briefly summarizes hypothalamic functions.

- The hypothalamus functions as a higher autonomic center or, rather, as several higher autonomic centers. By this we mean that axons of neurons whose dendrites and cell bodies lie in nuclei of the hypothalamus extend in tracts from the hypothalamus to both parasympathetic and sympathetic centers in the brainstem and cord. Thus impulses from the hypothalamus can simultaneously or successively stimulate or inhibit few or many lower autonomic centers. In other words, the hypothalamus serves as a regulator and coordinator of autonomic activities. It helps control and integrate the responses made by autonomic (visceral) effectors all over the body.
- The hypothalamus functions as the major relay station between the cerebral cortex and lower autonomic centers. Tracts conduct impulses from various centers in the cortex to the hypothalamus. Then, by way of numerous synapses in the hypothalamus, these impulses are relayed to other tracts that conduct them on down to autonomic centers in the brainstem and cord and also to spinal cord somatic centers (anterior horn motor neurons). Thus the hypothalamus functions as the link between the cerebral cortex and lower centers—hence between the psyche and the soma. It provides a crucial part of the route by which emotions can express themselves in changed bodily functions. It is the

all-important relay station in the neural pathways that makes possible the mind's influence over the body—sometimes, unfortunately, even to the profound degree of producing psychosomatic disease. The positive benefits of this mind-body link are the dramatic influences our conscious mind can have in healing the body of various illnesses.

- Neurons in the supraoptic and paraventricular nuclei of the hypothalamus synthesize the hormones released by the posterior pituitary gland (neurohypophysis). Because one of these hormones affects the volume of urine excreted, the hypothalamus plays an indirect but essential role in maintaining water balance (see Chapters 31 and 32).
- Some neurons in the hypothalamus have endocrine functions. Their axons secrete chemicals, *releasing hormones*, into blood, which circulate to the anterior pituitary gland. Releasing hormones control the release of certain anterior pituitary hormones—specifically growth hormone and hormones that control hormone secretion by sex glands, the thyroid gland, and the adrenal cortex (discussed in Chapter 19). Thus indirectly the hypothalamus helps control the functioning of every cell in the body.
- The hypothalamus plays an essential role in maintaining the waking state. Presumably it functions as part of an arousal or alerting mechanism. Clinical evidence of this is that somnolence (sleepiness) characterizes some hypothalamic disorders.
- The hypothalamus functions as a crucial part of the mechanism for regulating appetite and therefore the amount of food intake. Experimental and clinical findings indicate the presence of an "appetite center" in the lateral part of the hypothalamus and a "satiety center" located medially. For example, an animal with an experimental lesion in the ventromedial nucleus of the hypothalamus consumes tremendous amounts of food. Similarly, a human with a tumor in this region of the hypothalamus may eat insatiably and gain an enormous amount of weight.
- The hypothalamus functions as a crucial part of the mechanism for maintaining normal body temperature. Hypothalamus neurons whose fibers connect with autonomic centers for vasoconstriction, dilation, and sweating and with somatic centers for shivering constitute heat-regulating centers. Marked elevation of body temperature often characterizes injuries or other abnormalities of the hypothalamus.

PINEAL GLAND

Although the thalamus and hypothalamus account for most of the tissue that makes up the diencephalon, there are several smaller structures of importance. For example, the *optic chiasma* is a region where the right and left *optic nerves* cross each other before entering the brain—exchanging fibers as they do so. The resulting bundles of fibers are called the *optic tracts*. Various small nuclei just outside the thalamus and hypothalamus, collectively referred to as the **epithalamus**, are also included among the structures of the diencephalon. One of the most intriguing of the epithalamic structures is the *pineal gland* or *pineal body* (formerly known as the *epiphysis*).

As Figures 14-10 and 14-13 show, the pineal gland is located just above the corpora quadrigemina of the midbrain. Its name comes from the fact that it resembles a pine nut.

The functions of the pineal gland are still not completely understood. However, we do know that the tiny pineal gland is an important part of the body's biological clock mechanism. The body's **biological clock** depends partly on the pineal gland varying its secretion of the hormone **melatonin.** Melatonin is a *hormone* because it is a molecule released into the blood to regulate functions elsewhere in the body—a concept we will explore further in Chapters 18 and 19. However, melatonin is in fact simply an altered form of the neurotransmitter serotonin.

As Figure 14-14 shows, changing light levels throughout the day and night (circadian) cycle trigger

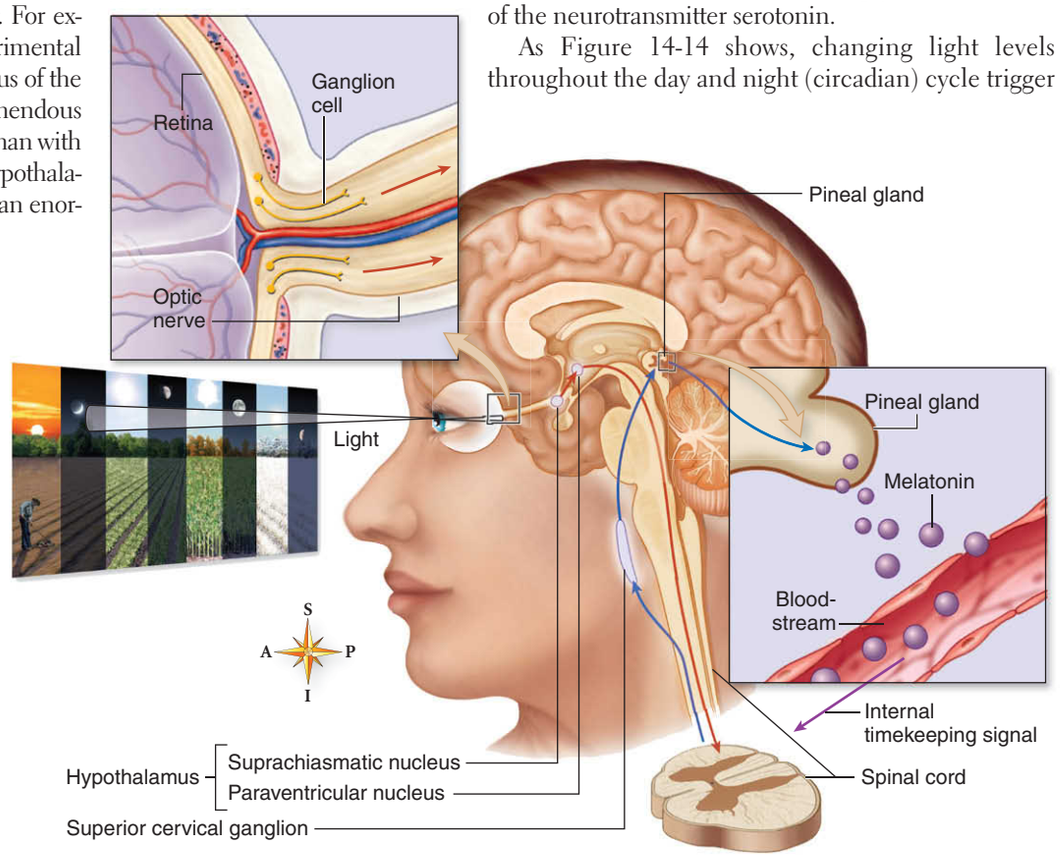


FIGURE 14-14

Role of pineal gland in timekeeping. Changing external levels of light are detected by special receptors in the retina of the eye called *ganglion cells* (see Chapter 17), and the information is relayed to the suprachiasmatic nucleus (SCN) of the hypothalamus. When light levels decrease, signals from the SCN increase, triggering the paraventricular nucleus and a pathway of nervous system signals that eventually result in the release of increased amounts of melatonin from the pineal gland. The changing levels of melatonin throughout the day serve as an internal timekeeping signal.

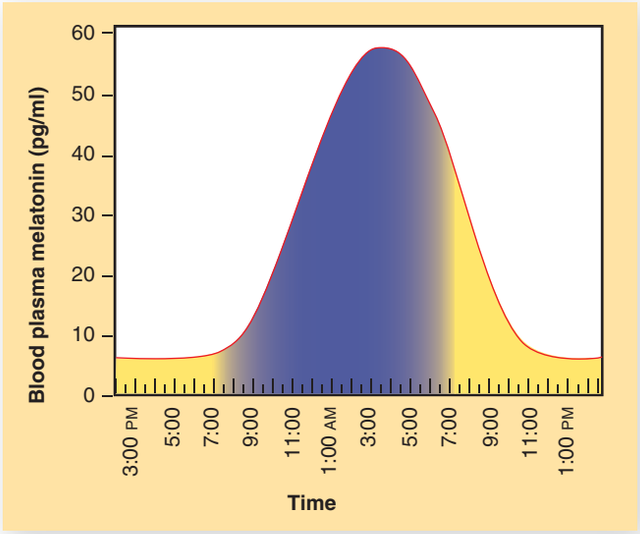


FIGURE 14-15

Melatonin. Graph comparing typical blood melatonin levels throughout the day. Sunlight suppresses melatonin secretion during the day. As the sun goes down, however, melatonin levels begin to rise—dropping again sharply when the sun comes up.

changes in the rate of melatonin secretion. When sunlight levels are high, melatonin secretion decreases (Figure 14-15). When light levels are low, melatonin levels increase proportionally. The changing levels of blood melatonin during the day synchronize various body functions with each other and with external stimuli. This kind of biological clock mechanism is called a daily or *circadian* clock. Melatonin is often called the "timekeeping hormone"—but because high blood levels of melatonin signal the body that it is time to sleep, it is also called the "sleep hormone."

When a person travels to another time zone, or when the seasons change, the altered sunlight patterns cause corresponding time shifts to the melatonin cycle. Likewise, often subtle changes occur in each melatonin cycle depending on how much moonlight (reflected sunlight) is present each evening. Thus the body can sometimes tell what time of the (lunar) month it is—a mechanism that may help regulate the female reproductive cycle.

| QUICK CHECK |

9. What are the two main components of the diencephalon? Where are they located?
10. Name three general functions of the thalamus.
11. Name three general functions of the hypothalamus.
12. What is the pineal gland's primary function?

Structure of the Cerebrum

CEREBRAL CORTEX

The **cerebrum,** the largest and uppermost division of the brain, consists of two halves, the right and left **cerebral hemispheres.** The surface of the cerebrum—called the *cerebral cortex*—is made up of gray matter only 2 to 4 mm (roughly 1/12 to 1/6 inch) thick. But despite its thinness, the cortex has six layers, each composed of millions of axon terminals synapsing with millions of dendrites and cell bodies of other neurons.

If one uses a little imagination, the surface of the cerebral cortex looks like a group of small sausages. Each "sausage" is actually a **convolution,** or gyrus. Names of some of these are the *precentral gyrus*, *postcentral gyrus*, *cingulate gyrus*, and *hippocampal gyrus (hippocampus)*.

Between adjacent gyri lie either shallow grooves called *sulci* or deeper grooves called *fissures* (Box 14-5). Fissures, as well as a few, largely imaginary boundaries, divide each cerebral hemisphere into five *lobes.* Four of the lobes are named for the bones that lie over them: **frontal lobe, parietal lobe, temporal lobe,** and **occipital lobe** (Figure 14-16). A fifth lobe, the **insula** *(Reil island)*, lies hidden from view in the lateral fissure. The lobes are highlighted in Figure 14-16. The insula can also be seen in the photographs in Box 14-3 (p. 430).

Names and locations of prominent cerebral fissures are as follows (see Figure 14-16):

Longitudinal fissure: the deepest groove in the cerebrum; divides the cerebrum into two hemispheres

Central sulcus (Rolando fissure): groove between the frontal and parietal lobes

Lateral fissure (Sylvius fissure): a deep groove between the temporal lobe below and the frontal and parietal lobes above; island of Reil lies deep in the lateral fissure

Parietooccipital sulcus: groove that separates the occipital lobe from the parietal lobe

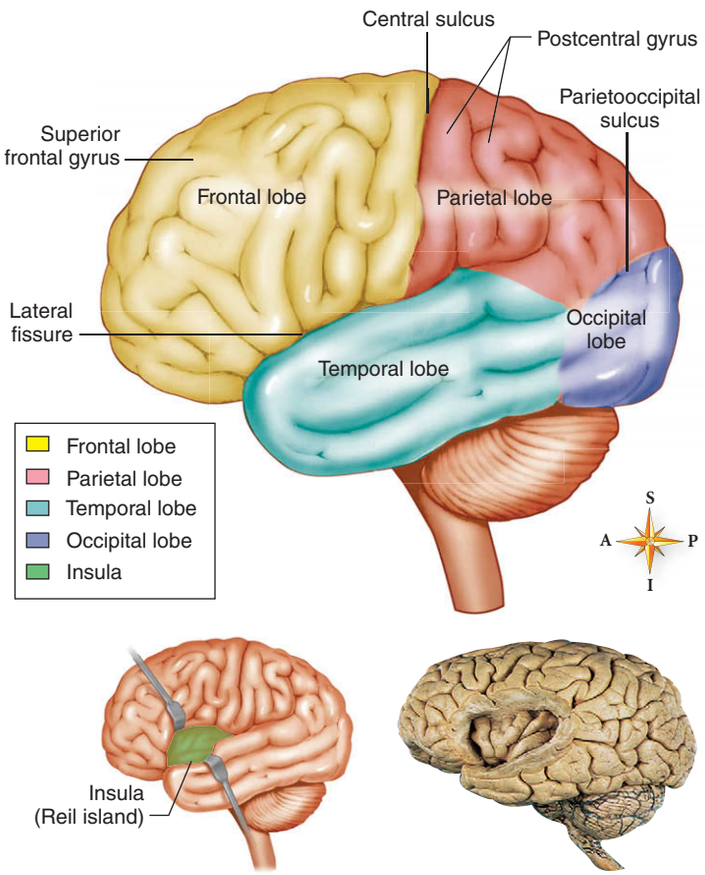


FIGURE 14-16

Left hemisphere of cerebrum, lateral surface. Note the highlighted lobes of the cerebrum.

Box 14-5 | FYI

Brain Wrinkles

One of the first things that people notice about the brain is the very wrinkled appearance of the two largest regions of the brain: the cerebellum and cerebrum (Figure 1). Wrinkling of the skin is associated with aging and degeneration, but the wrinkles in the surfaces of these two brain regions provide great advantages. If you could flatten out the gray matter gyri (folia) of the cerebellar cortex and the gray matter gyri (convolutions) of both cerebral hemispheres, the advantages become clear. As Figure 2 shows, the surface area of these brain structures is much larger than it first appears. The fractal-like wrinkling of these brain surfaces allows more gray matter to be packed into the small space of the cranial cavity than would be the case if the brain were smooth surfaced. Thus many times more "computing power" is available to the cerebellum and cerebrum—enabling them to perform their very complex functions.

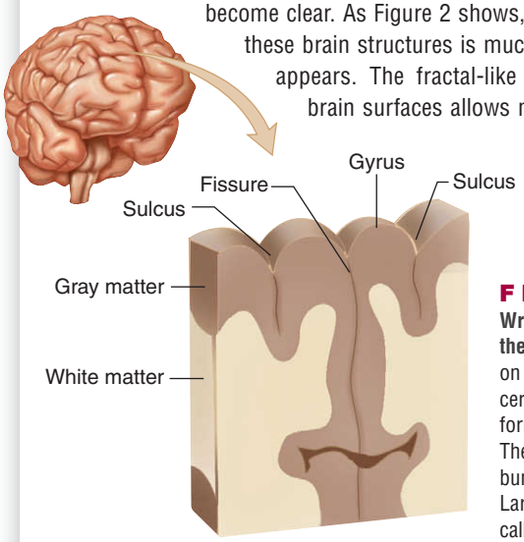


FIGURE 1
Wrinkles and grooves of the brain. Gray matter on the surface of the cerebrum is folded to form bumps or gyri. The valleys between the bumps are called *sulci*. Larger sulci are often called *fissures*.

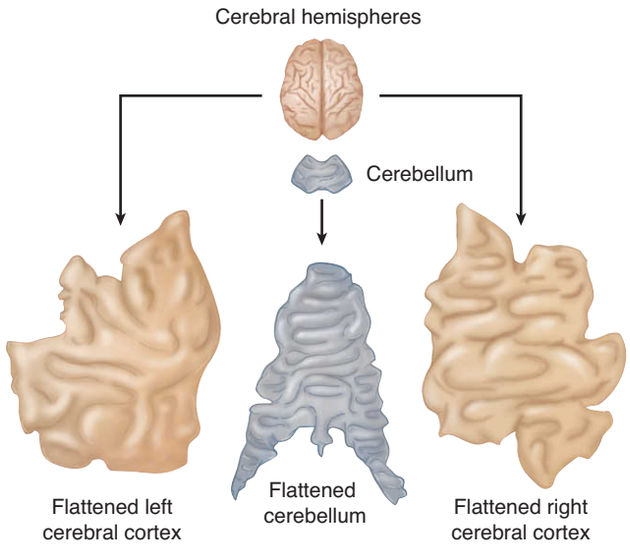


FIGURE 2
Surface area of the cerebellum and cerebrum. The gray matter on the surface of the cerebellum (gray) and the cerebrum (tan) is larger than it first appears because it is highly folded.

CEREBRAL TRACTS AND BASAL NUCLEI

Beneath the cerebral cortex lies the large interior of the cerebrum. It is mostly white matter made up of numerous tracts. Tracts that make up the cerebrum's internal white matter are of three types: projection tracts, association tracts, and commissural tracts (Figure 14-17). *Projection tracts* are extensions of the ascending, or sensory, spinothalamic tracts and descending, or motor, corticospinal tracts. *Association tracts* are the most numerous of cerebral tracts; they extend from one convolution to another in the same hemisphere. *Commissural tracts,* in contrast, extend from a point in one hemisphere to a point in the other hemisphere. Commissural tracts compose the **corpus callosum** (prominent white curved structure seen in Figure 14-9) and the anterior and posterior commissures.

All of the connections within the human cortex to the rest of the brain—the human **connectome**—are currently being mapped out. This massive, international effort hopes to generate better understanding of the complex functions of the human brain.

A few islands of gray matter lie deep inside the white matter of each hemisphere. Collectively these are called **basal nuclei** (or historically, *basal ganglia*). Basal nuclei, seen in Figure 14-18, include the following masses of gray matter in the interior of each cerebral hemisphere:

Caudate nucleus: observe the curving "tail" shape of this basal nucleus

Lentiform nucleus: so named because of its lenslike shape; note in Figure 14-18 that the lentiform nucleus consists of two structures, the putamen and the pallidum; the putamen lies lateral to the pallidum (also called the *globus pallidus*)

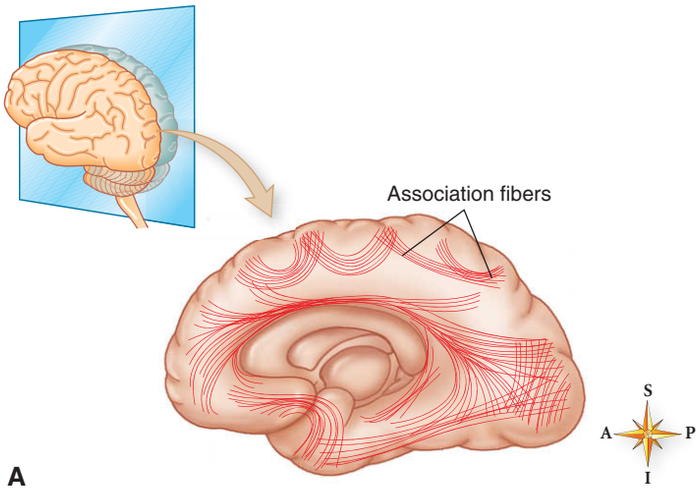
Amygdaloid nucleus: observe the location of this almond-shaped structure at the tip of the caudate nucleus (also called the *amygdala*, literally "almond")

A structure associated with the basal nuclei is the **internal capsule.** It is a large mass of white matter located, as Figure 14-18 shows, between the caudate and lentiform nuclei and between the lentiform nucleus and thalamus. The caudate nucleus, internal capsule, and lentiform nucleus constitute the corpus striatum, a term that means "striped body."

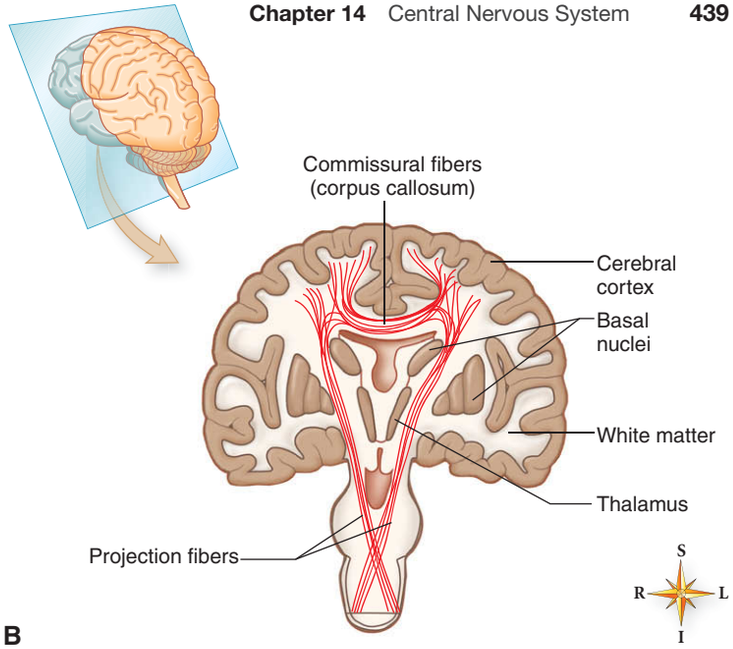
Researchers are still investigating the exact functions of the basal nuclei, but we already know that this part of the cerebrum plays an important role in regulating voluntary motor functions. For example, most of the muscle contractions involved in maintaining posture, walking, and performing other gross or repetitive movements seem to be initiated or modulated in the basal nuclei (Box 14-6). The basal nuclei may also play a role in thinking and learning.

| QUICK CHECK |

13. Name the five lobes that make up each cerebral hemisphere. Where is each located?
14. Name the basal nuclei, and describe where they are located within the cerebrum.



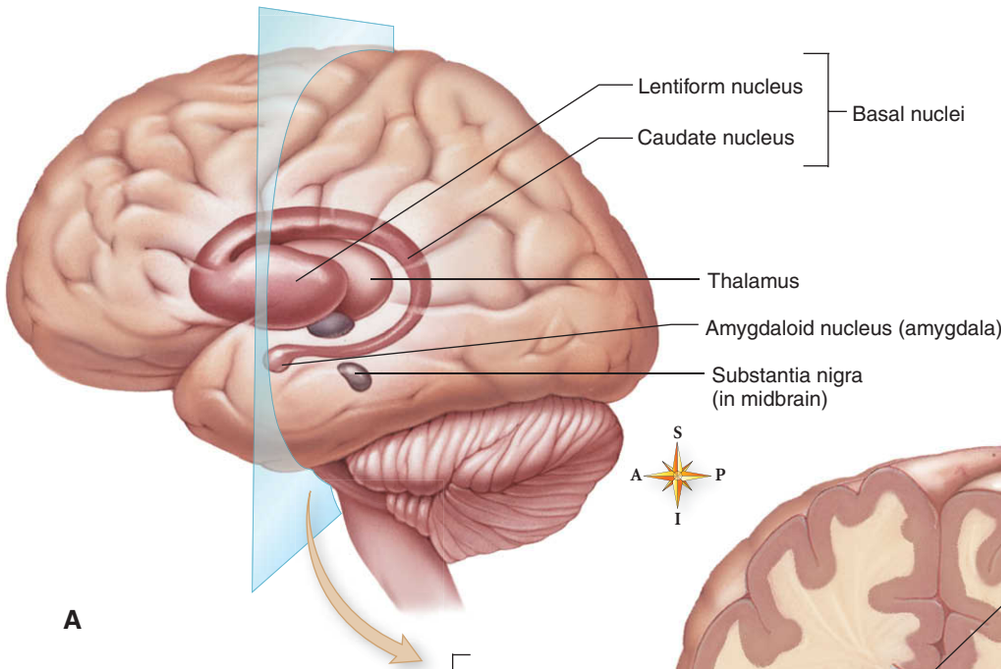
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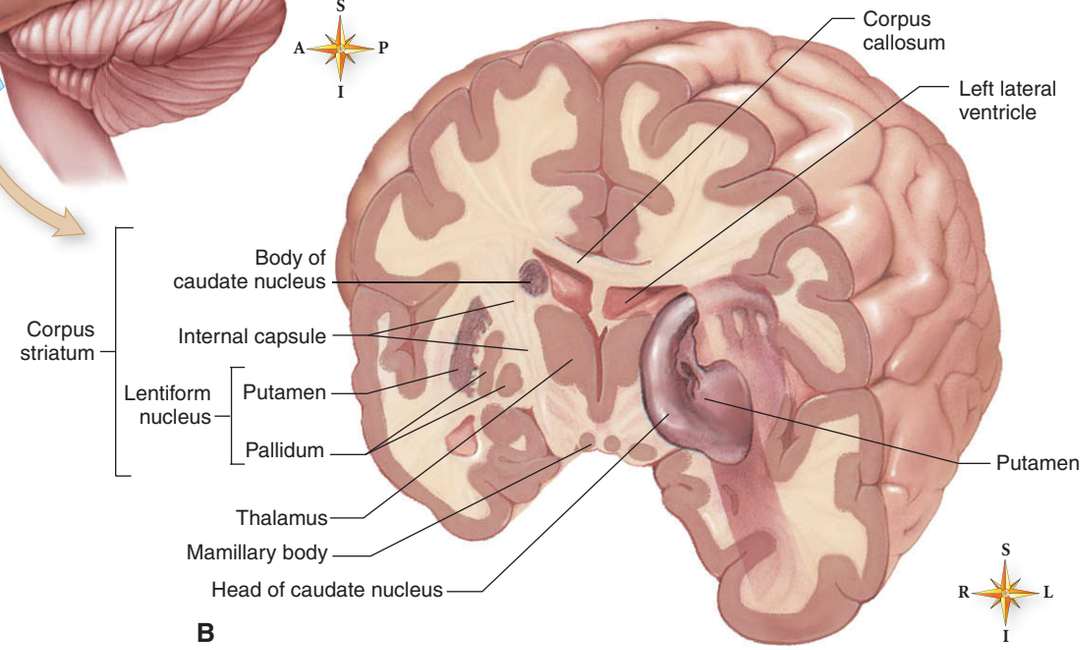
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FIGURE 14-17

Cerebral tracts. A, Lateral perspective, showing various association fibers. **B,** Frontal (coronal) perspective, showing commissural fibers that make up the corpus callosum and the projection fibers that communicate with lower regions of the nervous system.



A



B

FIGURE 14-18

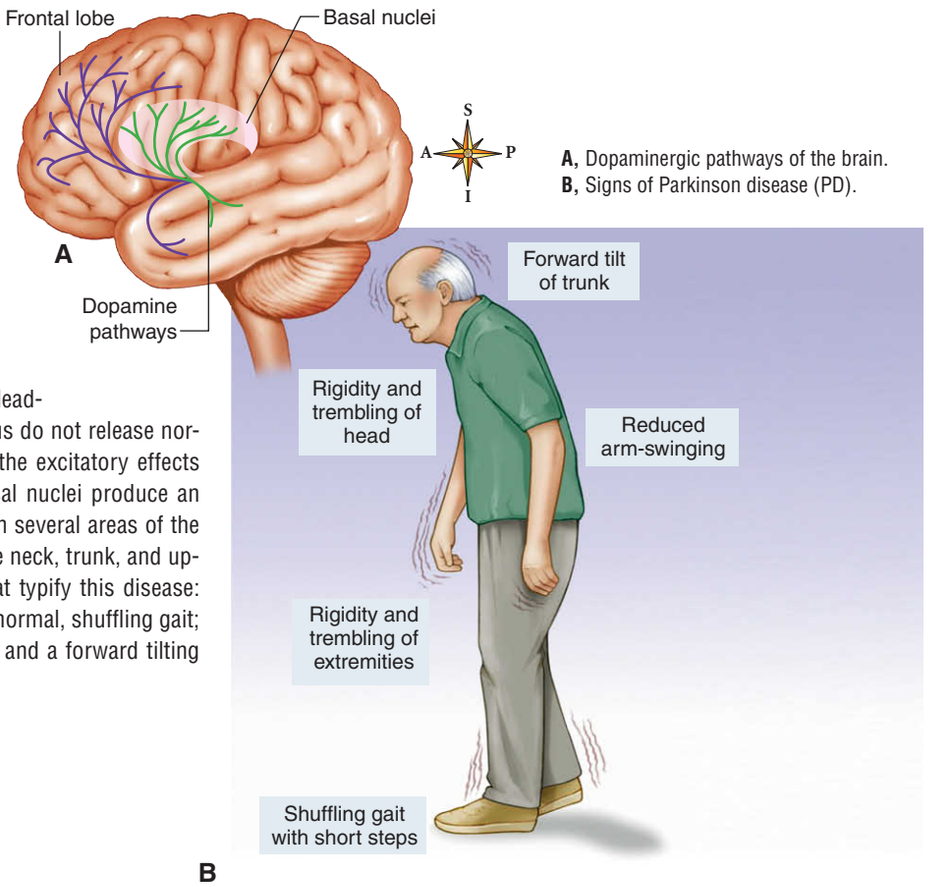
Basal nuclei. A, The basal nuclei seen through the cortex of the left cerebral hemisphere. **B,** The basal nuclei seen in a frontal (coronal) section of the brain.

UNIT 3

Box 14-6 | HEALTH matters

Parkinson Disease

The importance of the basal nuclei in regulating voluntary motor functions is made clear in cases of **Parkinson disease (PD).** Normally, neurons that lead from the substantia nigra to the basal nuclei secrete dopamine. Dopamine inhibits the excitatory effects of acetylcholine produced by other neurons in the basal nuclei. Such inhibition by *dopaminergic* (dopamine-producing) neurons produces a balanced, restrained output of muscle-regulating signals from the basal nuclei. In PD, however, neurons leading from the substantia nigra degenerate and thus do not release normal amounts of dopamine. Without dopamine, the excitatory effects of acetylcholine are not restrained, and the basal nuclei produce an excess of signals that affect voluntary muscles in several areas of the body. Over-stimulation of postural muscles in the neck, trunk, and upper limbs produces the syndrome of effects that typify this disease: rigidity and tremors of the head and limbs; an abnormal, shuffling gait; absence of relaxed arm-swinging while walking; and a forward tilting of the trunk.



A, Dopaminergic pathways of the brain.
B, Signs of Parkinson disease (PD).

Functions of the Cerebral Cortex

FUNCTIONAL AREAS OF THE CORTEX

During the past few decades, research scientists in various fields—neurophysiology, neurosurgery, neuropsychiatry, and others—have added mountains of information to our knowledge about the brain. However, new questions come faster than answers, and a clear, complete understanding of the brain's mechanisms still eludes us. Perhaps it always will. Perhaps the capacity of the human brain falls short of the ability to fully understand its own complexity.

We do know that certain areas of the cortex in each hemisphere of the cerebrum engage predominantly in one particular function—at least on the average. Differences between genders and among individuals of both genders are not uncommon. The fact that many cerebral functions have a typical location is known as the concept of cerebral localization. The fact that localization of function varies from person to person, and even at different times in an individual's life when the brain has sustained damage, is called **cerebral plasticity.**

The function of each region of the cerebral cortex depends on the structures with which it communicates. For example, the postcentral gyrus (Figures 14-19 and 14-20) functions mainly as a general somatic sensory area. It receives impulses from receptors activated by heat, cold, and touch stimuli. The precentral gyrus, on the other hand, functions chiefly as the somatic motor area (see Figures 14-19 and 14-20). Impulses from neurons in this area descend over motor tracts and eventually stimulate somatic effectors, the skeletal muscles. The transverse gyrus of the temporal lobe serves as the primary auditory area. The primary visual areas are in the occipital lobe. It is important to remember that no part of the brain functions alone. Many structures of the central nervous system must function together for any one part of the brain to function normally.

Sometimes, specific functional areas of the cortex are labeled with numbers (1 through 47) called *Brodmann areas (BAs)*. They are named for Korbinian Brodmann, a German neurologist who in 1908 first proposed a numbered map of the cortex based on the organizational pattern of neurons in different regions. We have learned that structure and function are related, so it is no surprise that Brodmann's structural approach has proven to have functional applications.

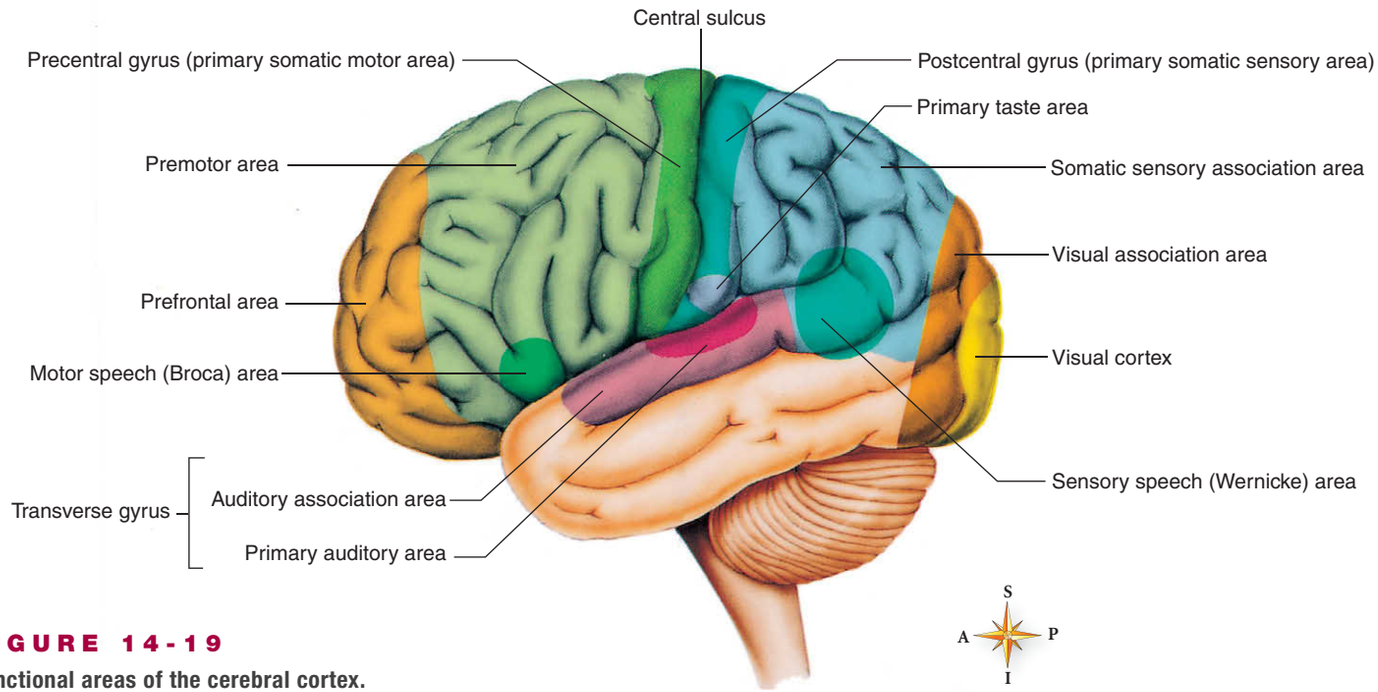


FIGURE 14-19

Functional areas of the cerebral cortex.

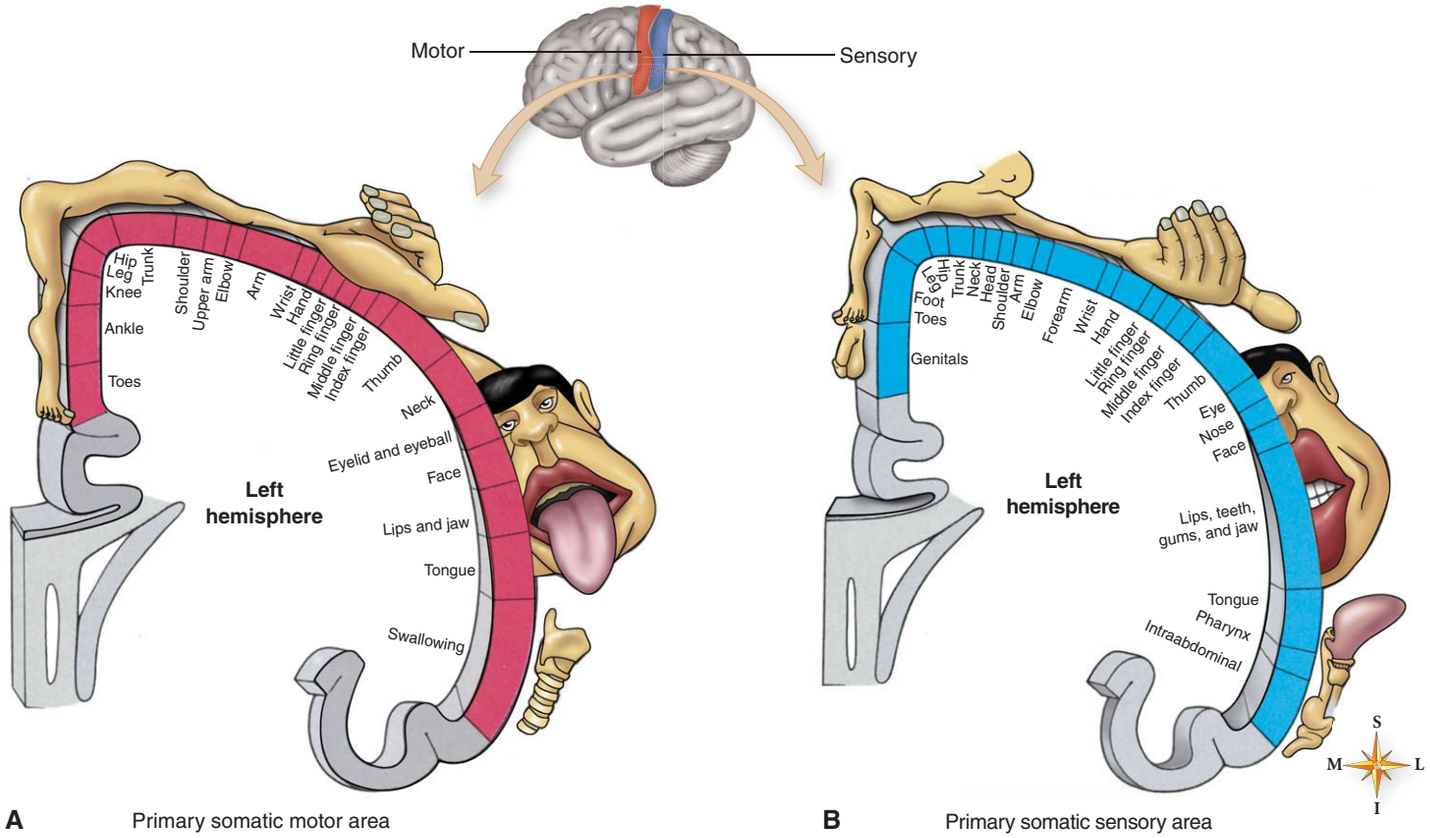


FIGURE 14-20

Primary somatic sensory (A) and motor (B) areas of the cortex. The body parts illustrated here show which parts of the body are "mapped" to specific areas of each cortical area. The exaggerated face indicates that more cortical area is devoted to processing information to and from the many receptors and motor units of the face than for the leg or arm, for example.

UNIT 3

| A&P CONNECT |

Images of the brain that help us understand the relationship between structure and function can be produced in many ways. These brain-imaging techniques can be used to discover new concepts of brain function and also to assess structural and functional problems in individual patients. Box 14-7 describes one important method for visualizing brain activity. Explore other fascinating brain imaging techniques in ***Brain Studies*** online at ***A&P Connect.***

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SENSORY FUNCTIONS OF THE CORTEX

Various areas of the cerebral cortex are essential for normal functioning of the somatic, or "general," senses, as well as the so-called "special" senses. The somatic senses include sensations of touch, pressure, temperature, body position (proprioception), and similar perceptions that do not require complex sensory organs. The special senses include vision, hearing, and other types of perception that require complex sensory organs, for example, the eye and the ear.

As stated earlier, the postcentral gyrus serves as a primary area for the general somatic senses. As Figure 14-20, A, shows, sensory fibers carrying information from receptors in specific parts of the body terminate in specific regions of the somatic sensory area. In

Box 14-7 | DIAGNOSTIC study

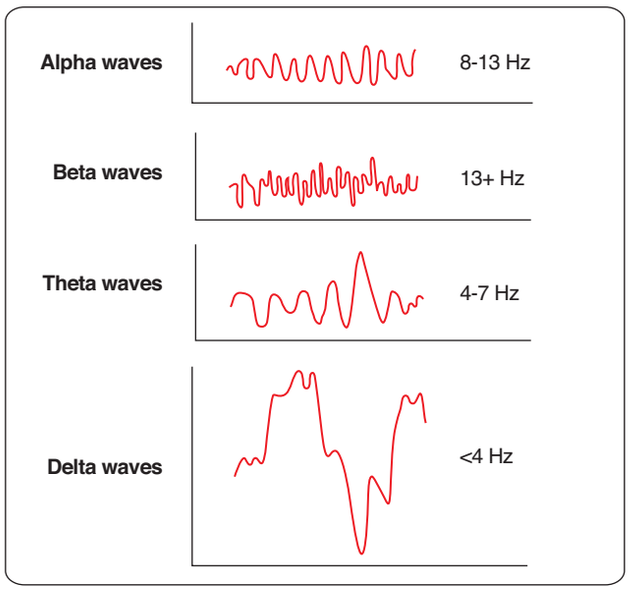
The Electroencephalogram (EEG)

Cerebral activity goes on as long as life itself. Only when life ceases (or moments before) does the cerebrum cease its functioning. Only then do all its neurons stop conducting impulses. Proof of this has come from records of brain electrical potentials known as **electroencephalograms,** or **EEGs.** These records are usually made from data detected by a number of electrodes placed on different regions of the scalp; they are records of wave activity—*brainwaves* (parts *A* and *B* of the figure).

Four types of brainwaves are recognized based on frequency and amplitude of the waves. Frequency, or the number of wave cycles per second, is usually referred to as *hertz* (Hz, from Hertz, a German physicist). Amplitude means voltage. Listed in order of frequency from fastest to slowest, brainwaves are designated as *beta, alpha, theta,* and *delta. Beta waves* have a frequency of more than 13 Hz and a relatively low voltage. *Alpha waves* have a frequency of 8 to 13 Hz and a relatively high voltage. *Theta waves* have both a relatively low frequency—4 to 7 Hz—and a low voltage. *Delta waves* have the slowest frequency—less than 4 Hz—but a high voltage. Brainwaves vary in different regions of the brain, in different states of awareness, and in abnormal conditions of the cerebrum.

Fast, low-voltage beta waves characterize EEGs recorded from the frontal and central regions of the cerebrum when an individual is awake, alert, and attentive, with eyes open. Beta waves predominate when the cerebrum is busiest, that is, when it is engaged with sensory stimulation or mental activities. In short, beta waves are "busy waves." Alpha waves, in contrast, are "relaxed waves." They are moderately fast, relatively high-voltage waves that dominate EEGs recorded from the parietal lobe, occipital lobe, and posterior parts of the temporal lobes when the cerebrum is idling, so to speak. The individual is awake but has eyes closed and is in a relaxed, nonattentive state. This state is sometimes called the "alpha state." When drowsiness descends, moderately slow, low-voltage theta waves appear. Theta waves are "drowsy waves." "Deep sleep waves," on the other hand, are known as delta waves. These slowest brainwaves characterize the deep sleep from which one is not easily aroused. For this reason, deep sleep is referred to as slow-wave sleep.

Physicians use electroencephalograms (EEGs) to help localize areas of brain dysfunction, to identify altered states of consciousness, and often to establish death. Two flat EEG recordings (no brainwaves) taken 24 hours apart in conjunction with no spontaneous respiration and total absence of somatic reflexes are criteria accepted as evidence of brain death.



A



B

The electroencephalogram (EEG). A, Examples of alpha, beta, theta, and delta waves seen on an EEG. **B,** Photograph showing a person undergoing an EEG test. Notice the scalp electrodes that detect voltage fluctuations within the cranium.

other words, the cortex contains a sort of "somatic sensory map" of the body. Areas such as the face and hand have a proportionally larger number of sensory receptors, so their part of the somatic sensory map is larger. Likewise, information regarding vision is mapped in the visual cortex, and auditory information is mapped in the primary auditory area (see Figure 14-19).

The cortex does more than just register separate and simple sensations, however. Information sent to the primary sensory areas is in turn relayed to the various sensory association areas, as well as to other parts of the brain. There the sensory information is compared and evaluated. Eventually, the cortex integrates separate bits of information into whole perceptions.

Suppose, for example, that someone put an ice cube in your hand. You would, of course, see it and sense something cold touching your hand. But also you would probably know that it was an ice cube because you would perceive a total impression compounded of many sensations such as temperature, shape, size, color, weight, texture, and movement and position of your hand and arm.

Discussion of somatic sensory pathways begins on p. 448. The special senses are discussed in Chapter 17.

MOTOR FUNCTIONS OF THE CORTEX

Mechanisms that control voluntary movements are extremely complex and imperfectly understood. It is known, however, that for normal movements to take place, many parts of the nervous system—including certain areas of the cerebral cortex—must function.

The precentral gyrus, that is, the most posterior gyrus of the frontal lobe, constitutes the primary somatic motor area (see Figures 14-19 and 14-20, *B*). A secondary motor area lies in the gyrus immediately anterior to the precentral gyrus. Neurons in the precentral gyrus are said to control individual muscles, especially those that produce movements of distal joints (wrist, hand, finger, ankle, foot, and toe movements). Notice in Figure 14-20 that the primary somatic motor area is mapped according to the specific areas of the body it controls. Neurons in the premotor area just anterior to the precentral gyrus are thought to activate groups of muscles simultaneously.

Motor pathways descending from the cerebrum through the brainstem and spinal cord are discussed on pp. 449–450. Autonomic motor pathways are discussed in Chapter 16.

INTEGRATIVE FUNCTIONS OF THE CORTEX

"Integrative functions" is a murky term. Even more obscure, however, are the neural processes it designates. They consist of all events that take place in the cerebrum between its reception of sensory impulses and its sending out of motor impulses. Integrative functions of the cerebrum include consciousness and mental activities of all kinds. Consciousness, use of language, emotions, and memory are the integrative cerebral functions that we shall discuss—but only briefly.

Consciousness

Consciousness may be defined as a state of awareness of one's self, one's environment, and other humans. Very little is known about the neural mechanisms that produce consciousness. We do know, however, that consciousness depends on excitation of cortical neurons by impulses conducted to them by a network of neurons known as the *reticular activating system*. The **reticular activating system (RAS)** consists of centers in the brainstem's *reticular formation* that receive impulses from the spinal cord and relay them to the thalamus and from the thalamus to all parts of the cerebral cortex (Figure 14-21). Both direct spinal reticular tracts and collateral fibers from the sensory tracts (spinothalamic, lemniscal, auditory, and visual) relay impulses over the reticular activating system to the cortex. Without continual excitation of cortical neurons by reticular activating impulses, an individual is unconscious and cannot be aroused. Here, then, are two current concepts about the reticular activating system: (1) it functions as the arousal or alerting system for the cerebral cortex, and (2) its functioning is crucial for maintaining consciousness. Drugs known to depress the reticular activating system decrease alertness and induce sleep.

Barbiturates, for example, produce these effects. On the other hand, amphetamine, a drug known to stimulate the cerebrum and to enhance alertness and produce wakefulness, probably acts by stimulating the reticular activating system.

Certain variations in the levels or state of consciousness are normal. All of us, for example, experience different levels of wakefulness. At times, we are highly alert and attentive. At other times, we are relaxed and nonattentive. All of us also experience different levels of sleep.

In addition to the various normal states of consciousness, altered states of consciousness also occur under certain conditions. Anesthetic

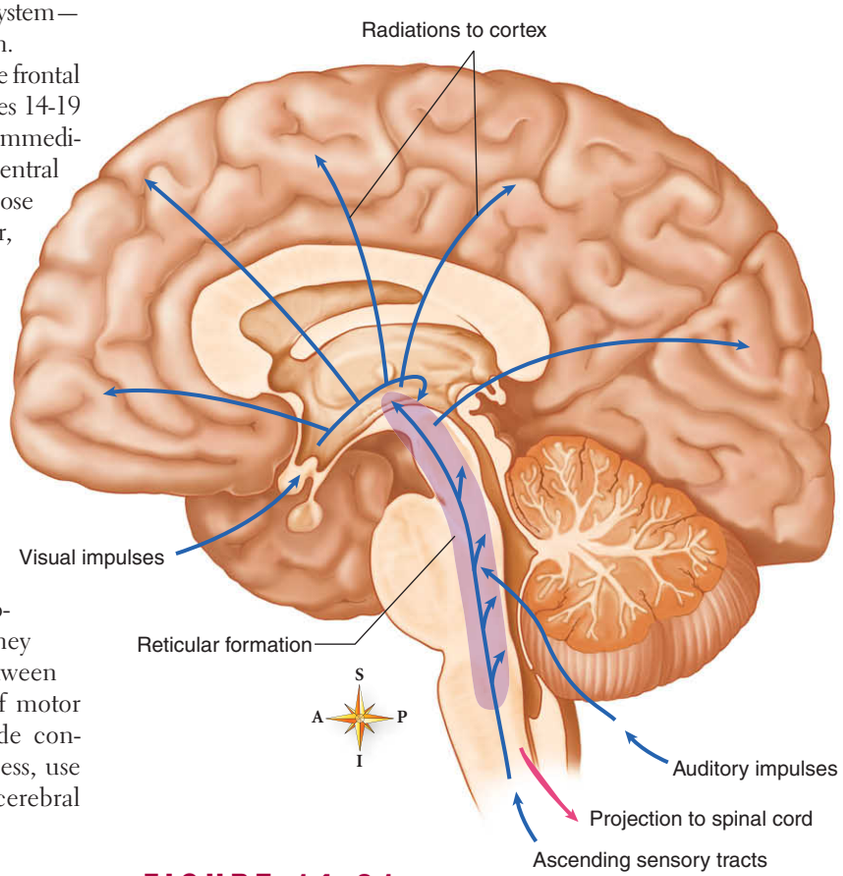


FIGURE 14-21

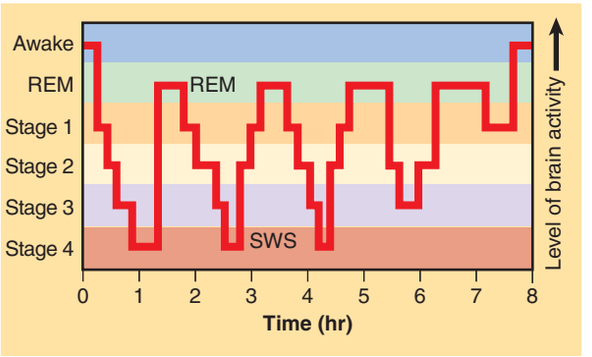
Reticular activating system (RAS). Consists of centers in the brainstem's *reticular formation* plus fibers that conduct to the centers from below and fibers that conduct from the centers to widespread areas of the cerebral cortex. Functioning of the RAS is essential for regulating levels of consciousness.

drugs produce an altered state of consciousness, namely, *anesthesia*. Disease or injury of the brain may produce an altered state called **coma.**

Peoples of various cultures have long been familiar with an altered state called *meditation*. Meditation is a waking state but differs markedly in certain respects from the usual waking state. According to some, meditation is a "higher" or "expanded" level of consciousness. This higher consciousness is accompanied, almost paradoxically, by a high degree of both relaxation and alertness. With training in meditation techniques and practice, an individual can enter the meditative state at will and remain in it for an extended period of time.

| A&P CONNECT |

Sleep is a fascinating and mysterious process that we are just beginning to understand. What we do understand is that sleep involves changes in the level of brain activity, as seen in the figure. Shortly after falling asleep, we fall into a deep **slow-wave sleep (SWS)** characterized by slow electroencephalogram (EEG) waves. Approximately every 90 minutes or so, brain activity increases during a dream stage called **rapid eye movement (REM) sleep.** Learn more about the sleep cycle in ***Sleep*** online at ***A&P Connect.***

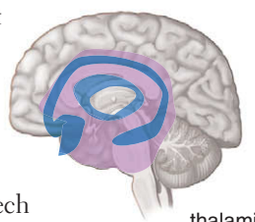


Sleep Stages

evolve

Language

Language functions consist of the ability to speak and write words and the ability to understand spoken and written words. Certain areas in the frontal, parietal, and temporal lobes serve as speech centers—as crucial areas, that is, for language functions. The left cerebral hemisphere contains these areas in about 90% of the population; in the remaining 10%, either the right hemisphere or both hemispheres contain them.



Lesions in speech centers give rise to language defects called *aphasias*. For example, with damage to an area in the inferior gyrus of the frontal lobe (Broca's area, see Figure 14-19), a person becomes unable to articulate words but can still make vocal sounds and understand words heard and read.

Box 14-8 discusses a newly discovered class of neurons that may help us learn and use language.

Box 14-8 | FYI

Mirror Neurons

A special functional class of neurons called *mirror neurons* exist in the cortex. These neurons exhibit action potentials both when we experience something ourselves and also when someone else does. In other words, certain circuits in our cortex become active whether we perform an action or whether we observe someone else doing so—thus enabling the brain to "mirror" the activity of another person's brain. Although much more is yet to be learned about the so-called *mirror-neuron system,* it seems clear that the action of these neurons may explain how humans are able to learn spoken language; interpret complex body language; empathize with the feelings of others; and learn to walk, write, or ride a bicycle.

Emotions

Emotions—both the subjective experiencing of them and the objective expression of them—involve functioning of the cerebrum's **limbic system.** The name *limbic* (Latin for "border or fringe") suggests the shape of the cortical structures that make up the system. They form a curving border around the corpus callosum, the structure that connects the two cerebral hemispheres.

Look now at Figure 14-22. Here on the medial surface of the cerebrum lie most of the structures of the limbic system. They are the cingulate gyrus and the hippocampus (the extension of the hippocampal gyrus that protrudes into the floor of the inferior horn of the lateral ventricle). These limbic system structures have primary connections with various other parts of the brain, notably

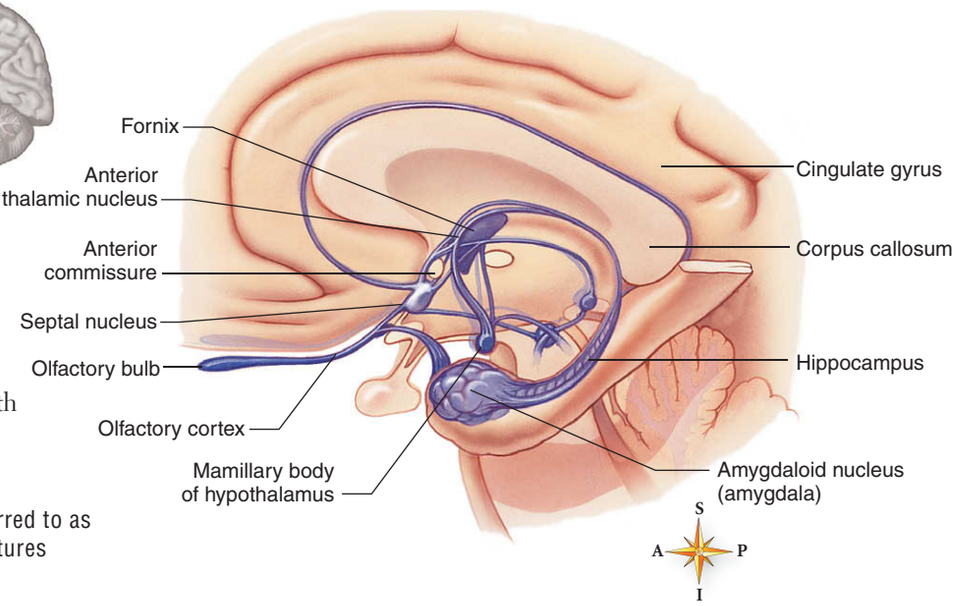


FIGURE 14-22

Structures of the limbic system. Sometimes referred to as "the emotional brain," this network of brain structures functions as we experience emotions.

the thalamus, fornix, septal nucleus, amygdaloid nucleus (the tip of the caudate nucleus, one of the basal nuclei), and the hypothalamus. Some physiologists therefore include these connected structures as parts of the limbic system.

The limbic system (or to use its more descriptive name, the *emotional brain*) functions in some way to make us experience many kinds of emotions—anger, fear, joy, sadness, surprise, and disgust, for example. To bring about the normal expression of emotions, parts of the cerebral cortex other than the limbic system must also function. Considerable evidence exists to indicate that limbic activity without the modulating influence of the other cortical areas may bring on the attacks of abnormal, uncontrollable rage suffered periodically by some unfortunate individuals.

Memory

Memory is one of our major mental activities. The cortex is capable of storing and retrieving both *short-term memory* and *long-term memory*. Short-term memory involves the storage of information over a few seconds or minutes. Short-term memories can be somehow consolidated by the brain and stored as long-term memories that can be retrieved days—or even years—later.

Both short-term memory and long-term memory are functions of many parts of the cerebral cortex, especially of the temporal, parietal, and occipital lobes. Findings by Dr. Wilder Penfield, a noted Canadian neurosurgeon, first gave evidence of this almost 100 years ago. He electrically stimulated the temporal lobes of epileptic patients undergoing brain surgery. They responded, much to his surprise, by recalling in the most minute detail songs and events from their past.

Such long-term memories are believed to consist of some kind of structural changes in the synapses of the cerebral cortex, as you learned in Chapter 13 (see p. 404). Repeated impulse conduction over a given neuronal circuit produces the synaptic change. Two possible changes are an increase in the number of presynaptic axon terminals or an increase in the number of receptor proteins in the postsynaptic neuron's membrane. Other possible changes involve changes in the average concentrations of neurotransmitters at certain synapses or changes in the functions of astrocytes. All of these changes somehow facilitate impulse transmission at the synapses.

More recent data suggests that different kinds of memories may be stored in different ways. Some memories are perhaps stored by way of changes at synapses and some by changes in the neurons themselves. For example, some neurons have been shown to react only when a specific person is seen or mentioned—thus somehow acting as a "recognition neuron" for the particular individual who is recognized.

Many research findings indicate that the cerebrum's limbic system—the "emotional brain"—plays a key role in memory. To mention one role, when the hippocampus (part of the limbic system) is removed, the patient loses the ability to recall new information. Your own personal experience substantiates a relationship between emotion and memory.

| A&P CONNECT |

Have you ever heard someone called "left-brained" or "right-brained" in their approach to work or learning? What does that mean? Find out in ***Specialization of Cerebral Hemispheres*** online at ***A&P Connect.***

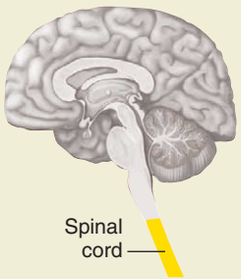
evolve

Table 14-3 briefly summarizes the major structures and functions of the central nervous system. Take a moment now to review it. This will help you reinforce what you have just learned about the CNS before moving on to the last topics of the chapter.

| QUICK CHECK |

15. Where is the primary somatic motor area of the cerebral cortex? Where is the primary somatic sensory area?
16. What does the reticular activating system have to do with alertness?
17. What is the function of the limbic system?

TABLE 14-3 Summary of CNS Structures and Functions

REGION	STRUCTURE*	FUNCTION*
Spinal cord 	Elongated cylinder extending from the brainstem through the foramen magnum of the skull; gray matter interior surrounded by white matter; 31 pairs of spinal nerves attached by dorsal and ventral nerve roots	Integration of simple, subconscious spinal reflexes; conduction of nerve impulses
Gray matter	Numerous synapses and interneurons arranged into anterior, lateral, and posterior gray columns linked by a gray commissure	Integration of spinal reflexes and filtering of information going to higher centers (as in gated pain control)
White matter	Myelinated nerve tracts arranged into anterior, lateral, and posterior white columns (funiculi)	Ascending tracts conduct sensory information to higher CNS centers; descending tracts conduct motor information from higher CNS centers

(continued)

TABLE 14-3 Summary of CNS Structures and Functions *(continued)*

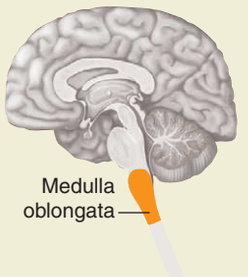
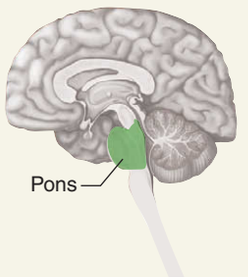
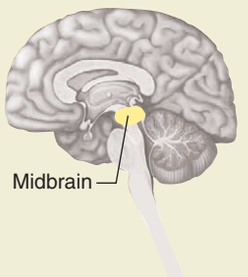
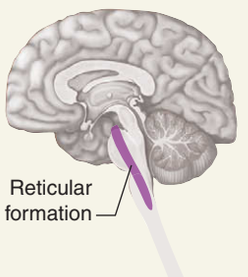
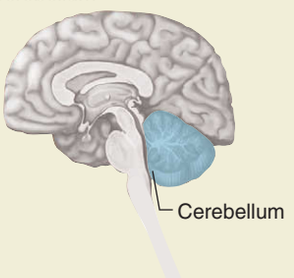
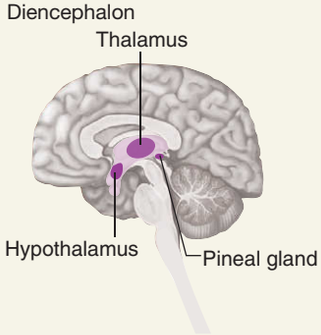
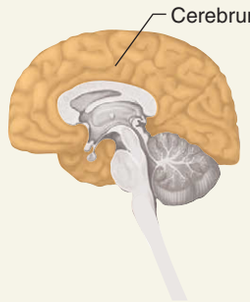
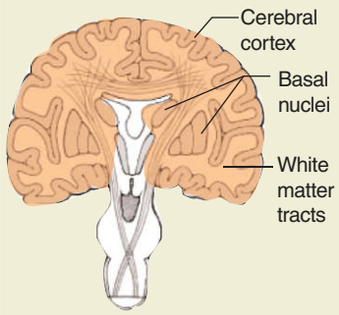
REGION	STRUCTURE*	FUNCTION*
Brainstem	Extends inferiorly from diencephalon to foramen magnum of skull, where it meets the spinal cord; central gray matter nuclei surrounded and connected by white matter tracts; 10 of the 12 pairs of cranial nerves attached here	Subconscious integration of basic vital functions
Medulla oblongata 	Inferior region of brainstem between the spinal cord and the pons	Integration of cardiac, vasomotor (vessel muscle), respiratory, digestive and other reflexes
Pons 	Intermediate region of brainstem between the medulla and the midbrain	Integration of numerous autonomic reflexes mediated by cranial nerves V, VI, VII, and VIII (see Chapters 15, 16) and respiration
Midbrain 	Superior region of the brainstem between the pons and the diencephalon	Integration of numerous cranial nerve reflexes, such as eye movements, pupillary reflex, ear (sound muffling) reflexes
Reticular formation 	Roughly cylindrical network of nerve pathways and centers extending through the brainstem and into the diencephalon	Operates the reticular activating system (RAS) that regulates state of consciousness
Cerebellum 	Roughly spherical structure attached at the posterior of the brainstem; wrinkled gray matter cortex, branched network of white fibers inside (arbor vitae), and several small gray nuclei	Coordinates many functions of cerebrum, including planning and control of skilled movements, posture, balance, coordination of sensory information relating to body position and movement

TABLE 14-3 Summary of CNS Structures and Functions *(continued)*

REGION	STRUCTURE*	FUNCTION*
Diencephalon 	Brain region in the central part of the brain, between the cerebrum and brainstem (midbrain); made up of various gray-matter nuclei	Numerous coordinating and integrating functions
Thalamus	Large ovoid of gray matter, divided into two large lateral masses connected by an intermediate mass	Crude sensations, coordination of sensory information relayed to cerebrum; involved in emotional response to sensory information; involved in arousal; general processing of information to/from cerebrum
Hypothalamus	Numerous gray-matter nuclei clustered below the thalamus	Integration/coordination of many autonomic reflexes, hormonal functions; involved in arousal, appetite, thermoregulation
Pineal gland	Single nucleus of neuroendocrine tissue posterior to the thalamus	Produces melatonin, a timekeeping hormone, as part of the body's biological clock
Cerebrum 	Largest, most superior region of brain; divided into right and left hemispheres, connected by the corpus callosum	Complex processing of sensory and motor information; complex integrative functions
Cerebral cortex 	Highly wrinkled gray-matter surface of the cerebrum; divided into five major lobes per hemisphere; functionally mapped based on concept of localization	Higher-level processing of sensory and motor information, including conscious sensation and motor control; complex integrative functions such as consciousness, language, memory, emotions
Cerebral tracts	White-matter tracts connect various regions of the cortex with each other and with inferior CNS structures	Conduction information between CNS areas to facilitate complex processing and integration
Basal nuclei	Gray-matter nuclei deep in the cerebrum	Integration and regulation of conscious motor control, especially posture, walking, other repetitive movements; possible roles in thinking and learning

*Summary only; see chapter text and figures for detailed descriptions of structure and function.
CNS, Central nervous system.

SOMATIC SENSORY PATHWAYS IN THE CENTRAL NERVOUS SYSTEM

For the cerebral cortex to perform its *sensory* functions, impulses must first be conducted to its sensory areas by way of relays of neurons referred to as *sensory pathways*. Most impulses that reach the sensory areas of the cerebral cortex have traveled over at least three pools of sensory neurons. We shall designate these as *primary sensory neurons*, *secondary sensory neurons*, and *tertiary sensory neurons* (Figure 14-23).

Primary sensory neurons of the relay conduct from the periphery to the central nervous system. Secondary sensory neurons conduct from the cord or brainstem up to the thalamus. Their dendrites and cell bodies are located in spinal cord or brainstem gray matter. Their axons ascend in ascending tracts up the cord, through the brainstem, and terminate in the thalamus. Here they synapse with dendrites or cell bodies of tertiary sensory neurons (see Figure 14-23). Tertiary sensory neurons conduct from the thalamus to the postcentral gyrus of the parietal lobe, the somaticosensory area. Bundles of axons of tertiary sensory neurons form thalamocortical tracts. They extend through the portion of cerebral white matter known as the *internal capsule* to the cerebral cortex (see Figure 14-23).

For the most part, sensory pathways to the cerebral cortex are crossed pathways. This means that each side of the brain registers sensations from the opposite side of the body. Look again at Figure 14-23. The axons that *decussate* (cross from one side to the other) in these sensory pathways are which sensory neurons: primary, secondary, or tertiary? Usually it is the axon of a secondary sensory neuron that decussates at some level in its ascent to the thalamus. Thus general sensations of the right side of the body are predominantly experienced by the left somatic sensory area. General sensations of the left side of the body are predominantly experienced by the right somatic sensory area.

Two sensory pathways conduct impulses that produce sensations of touch and pressure, namely, the *medial lemniscal system* and the *spinothalamic pathway* (see Figure 14-23). The medial lemniscal system consists of the tracts that make up the posterior white columns of the cord (the fasciculi cuneatus and gracilis) plus the *medial lemniscus*, a flat band of white fibers extending through the medulla, pons, and midbrain. (The term *lemniscus* literally means "ribbon," referring to this tract's flattened shape.)

The fibers of the medial lemniscus, like those of the spinothalamic tracts, are axons of secondary sensory neurons. They originate from cell bodies in the medulla, decussate, and then

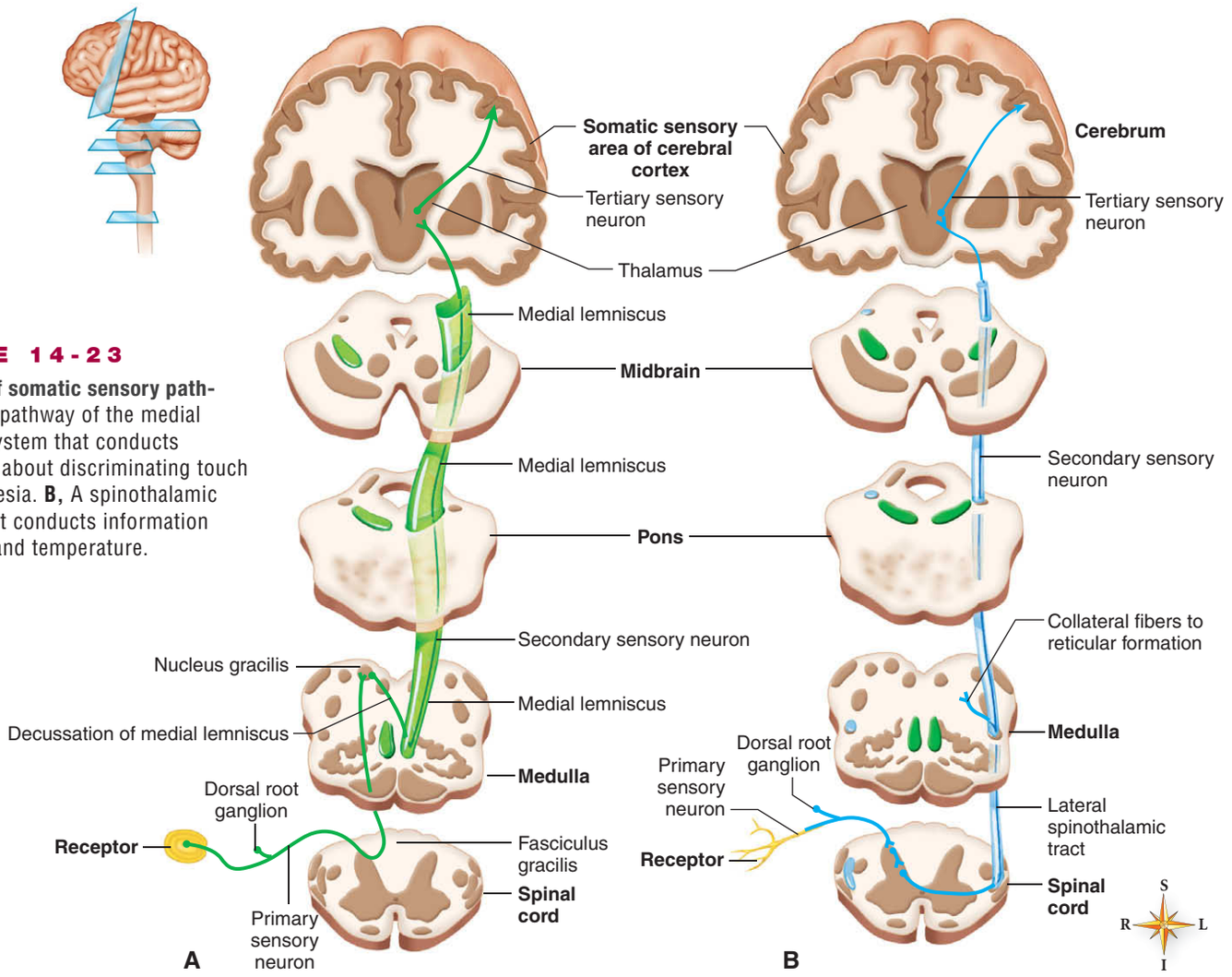


FIGURE 14-23

Examples of somatic sensory pathways. A, A pathway of the medial lemniscal system that conducts information about discriminating touch and kinesthesia. **B,** A spinothalamic pathway that conducts information about pain and temperature.

extend upward to terminate in the thalamus on the opposite side. The function of the medial lemniscal system is to transmit impulses that produce our more discriminating touch and pressure sensations, including *stereognosis* (awareness of an object's size, shape, and texture), precise localization, two-point discrimination, weight discrimination, and sense of vibrations. The sensory pathway for kinesthesia (sense of movement and position of body parts) is also part of the medial lemniscal system.

Crude touch and pressure sensations are functions of the **spinothalamic pathway.** Knowing that something is touching the skin is a crude touch sensation, whereas knowing its precise location, size, shape, or texture involves the discriminating touch sensations of the medial lemniscal system.

| QUICK CHECK |

18. Over how many afferent neurons does somatic sensory information usually pass?
19. Explain why stimuli on the left side of the body are perceived by the right side of the cerebral cortex.

SOMATIC MOTOR PATHWAYS IN THE CENTRAL NERVOUS SYSTEM

For the cerebral cortex to perform its *motor* functions, impulses must be conducted from its motor areas to skeletal muscles by relays of neurons referred to as *somatic motor pathways.* Somatic motor pathways consist of motor neurons that conduct impulses from the central nervous system to somatic effectors, that is, skeletal muscles. Some motor pathways are extremely complex and not at all clearly defined. Others, notably spinal cord reflex arcs, are simple and well established. You read about those in Chapter 13.

Look now at Figure 14-24. From this diagram you can derive a cardinal principle about somatic motor pathways—the *principle of the final common path.* It is this: only one final common path (namely, each single motor neuron from the anterior gray horn of the spinal cord) conducts *impulses* to a specific motor unit within a skeletal muscle. Axons from the anterior gray horn are the only ones that terminate in skeletal muscle cells. This principle of the final common path to skeletal muscles has important practical implications. For example, it means that any condition that makes anterior horn motor neurons unable to conduct impulses also

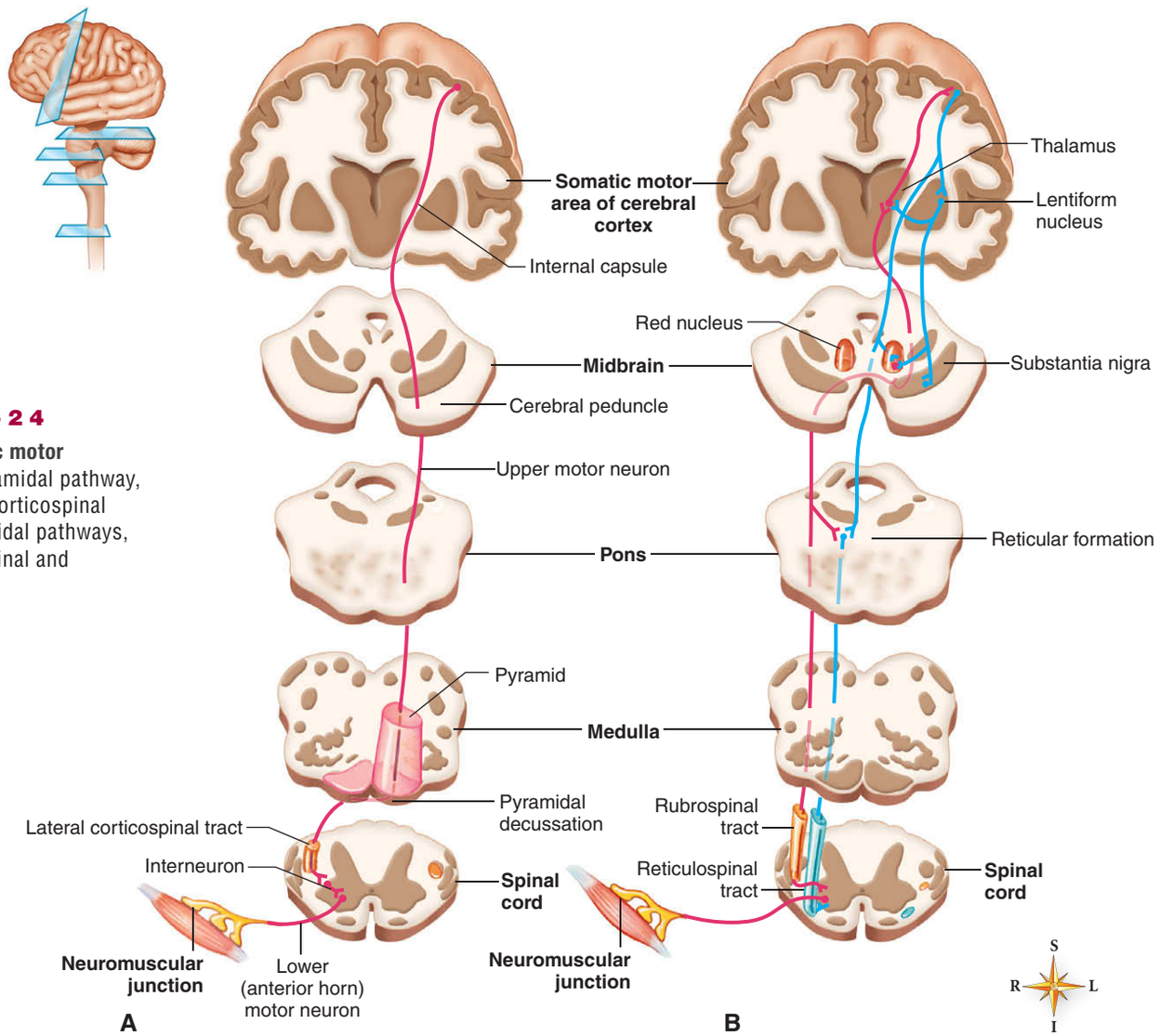


FIGURE 14-24

Examples of somatic motor pathways. A, A pyramidal pathway, through the lateral corticospinal tract. **B,** Extrapyramidal pathways, through the rubrospinal and reticulospinal tracts.

makes skeletal muscle cells supplied by these neurons unable to contract. They cannot be willed to contract nor can they contract reflexively. They are, in short, so flaccid that they are paralyzed. Most well known of the diseases that produce flaccid paralysis by destroying anterior horn motor neurons is *poliomyelitis*. Numerous somatic motor paths conduct impulses from motor areas of the cerebrum down to anterior horn motor neurons at all levels of the cord.

Two methods are used to classify somatic motor pathways—one based on the location of their fibers in the medulla and the other on their influence on the lower motor neurons. The first method divides them into pyramidal and extrapyramidal tracts. The second classifies them as facilitatory and inhibitory tracts.

Pyramidal Tracts

Pyramidal tracts are those whose fibers come together in the medulla to form the pyramids, hence their name (see Figure 14-24, A). Because axons composing the pyramidal tracts originate from neuron cell bodies located in the cerebral cortex, they also bear another name—*corticospinal tracts*. About three fourths of their fibers decussate (cross over from one side to the other) in the medulla. After decussating, they extend down the spinal cord in the crossed corticospinal tract located on the opposite side of the spinal cord in the lateral white column.

About one fourth of the corticospinal fibers do not decussate.

Instead, they extend down the same side of the spinal cord as the cerebral area from which they came. One pair of uncrossed tracts lies in the anterior white columns of the cord, namely, the anterior corticospinal tracts. The other uncrossed corticospinal tracts form part of the lateral corticospinal tracts.

About 60% of corticospinal fibers are axons that arise from neuron cell bodies in the precentral (frontal lobe) region of the cortex. About 40% of corticospinal fibers originate from neuron cell bodies located in postcentral areas of the cortex, areas classified as sensory; now, more accurately, they are often called *sensorimotor areas*.

Relatively few corticospinal tract fibers synapse directly with anterior horn motor neurons. Most of them synapse with interneurons, which in turn synapse with anterior horn motor neurons. All corticospinal fibers conduct impulses that depolarize resting anterior horn motor neurons. The effects of depolarizations occurring rapidly in any one neuron add up, or summate. Each impulse, in other words, depolarizes an anterior horn motor neuron's resting potential a little bit more. If sufficient numbers of impulses impinge rapidly enough on a neuron, its potential reaches the threshold level. At that moment the neuron starts conducting impulses—it is stimulated.

Stimulation of anterior horn motor neurons by corticospinal tract impulses results in stimulation of individual muscle groups (mainly of the hands and feet). Precise control of their contractions is, in short, the function of the corticospinal tracts. Without stimulation of anterior horn motor neurons by impulses over corticospinal fibers, willed movements cannot occur. This means that paralysis results whenever pyramidal corticospinal tract conduction is interrupted. For instance, the paralysis that so often follows **cerebrovascular accidents** (CVAs, or strokes) comes from pyramidal neuron injury—sometimes of their cell bodies in the motor areas, sometimes of their axons in the internal capsule (see Figure 14-24).

Extrapyramidal Tracts

Extrapyramidal tracts are much more complex than pyramidal tracts. They consist of all motor tracts from the brain to the spinal cord anterior horn motor neurons except the corticospinal (pyramidal) tracts. Within the brain, extrapyramidal tracts consist of numerous relays of motor neurons between motor areas of the cortex, basal nuclei, thalamus, cerebellum, and brainstem. In the cord, some of the most important extrapyramidal tracts are the reticulospinal tracts.

Fibers of the *reticulospinal tracts* originate from cell bodies in the reticular formation of the brainstem and terminate in gray matter of the spinal cord, where they synapse with interneurons that synapse with lower (anterior horn) motor neurons. Some reticulospinal tracts function as facilitatory tracts and others as inhibitory tracts. Summation of these opposing influences determines the lower motor neuron's response. It initiates impulse conduction only when facilitatory impulses exceed inhibitory impulses sufficiently to decrease the lower motor neuron's negativity to its threshold level.

Conduction by extrapyramidal tracts plays a crucial part in producing our larger, more automatic movements because extrapyramidal impulses bring about contractions of groups of muscles in sequence or simultaneously. Such muscle action occurs, for example, in swimming and walking and, in fact, in all normal voluntary movements.

Conduction by extrapyramidal tracts plays an important part in our emotional expressions. For instance, most of us smile automatically at things that amuse us and frown at things that irritate us. It is extrapyramidal, not pyramidal, impulses that produce the smiles or frowns.

Axons of many different neurons converge on, that is, synapse with each anterior horn motor neuron (see Figure 14-24). Hence many impulses from diverse sources—some facilitatory and some inhibitory—continually bombard this final common path to skeletal muscles. Together the added, or summated, effect of these opposing influences determines lower motor neuron functioning. Facilitatory impulses reach these cells by way of sensory neurons (whose axons, you will recall, lie in the posterior roots of spinal nerves), pyramidal (corticospinal) tracts, and extrapyramidal facilitatory reticulospinal tracts. Impulses over facilitatory reticulospinal fibers facilitate the lower motor neurons that supply extensor muscles. At the same time, they reciprocally inhibit the lower motor neurons that supply flexor muscles. Hence facilitatory reticulospinal impulses tend to increase the tone of extensor muscles and decrease the tone of flexor muscles.

Inhibitory impulses reach lower motor neurons mainly by way of inhibitory reticulospinal fibers that originate from cell bodies located in the *bulbar inhibitory area* in the medulla. They inhibit the lower motor neurons to extensor muscles (and reciprocally stimulate those to flexor muscles). Hence inhibitory reticulospinal impulses tend to decrease extensor muscle tone and increase flexor muscle tone; note that these effects are opposite from those of facilitatory reticulospinal impulses.

The set of coordinated commands that control the programmed muscle activity mediated by extrapyramidal pathways is often called a **motor program.** Traditionally, the primary somatic motor areas of the cerebral cortex were thought to be the principal organizer of motor programs sent along the extrapyramidal pathway. That view has been replaced by the concept illustrated in Figure 14-25. This newer concept holds that motor programs result from the interaction of several different centers in the brain. Apparently, many voluntary motor programs are organized in the basal nuclei and cerebellum—perhaps in response to a willed command by the cerebral cortex. Impulses that constitute the motor program are then channeled through the thalamus and back to the cortex, specifically to the primary motor area. From there, the motor program is sent down to the inhibitory and facilitatory regions of the brainstem. Signals from the brainstem then continue on down one or more spinal tracts and out to the muscles by way of the lower (anterior horn) motor neurons. All along the way, neural connections among the various motor control centers allow refinement and adjustment of the motor program.

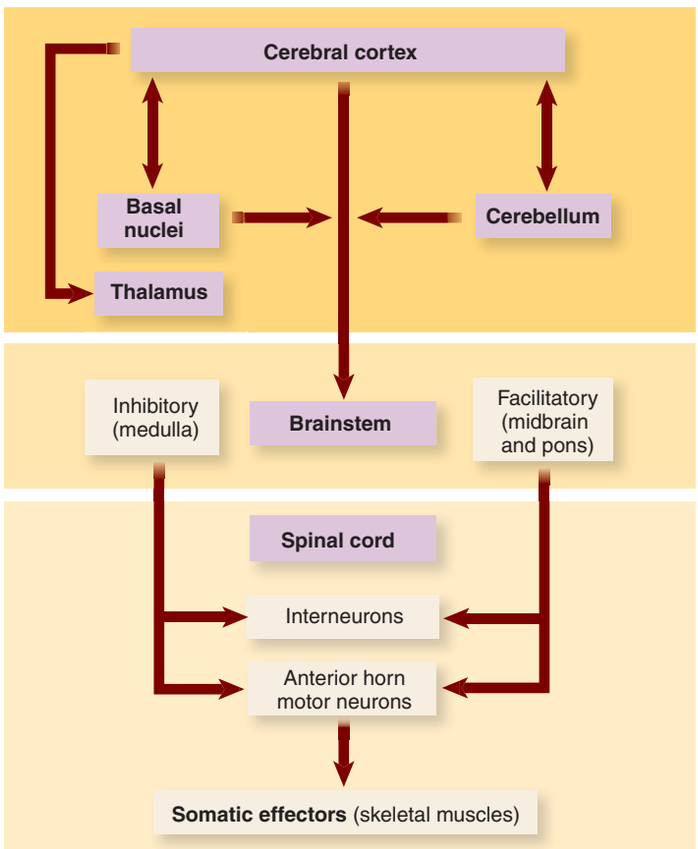


FIGURE 14-25

Concept of extrapyramidal motor control. Programmed movements result from a set of impulses called a *motor program.* The motor program organized in the basal nuclei and cerebellum in response to a command from the cortex is sent back to the primary motor control area of the cortex. From there, it is sent to the brainstem and then on through the spinal cord to the skeletal muscles. All along the motor pathway, the motor program can be refined by various components of this complex pathway.

Box 14-9 | HEALTH matters

Signs of Motor Pathway Injury

Injury of upper motor neurons (those whose axons lie in either pyramidal or extrapyramidal tracts) produces symptoms frequently referred to as "pyramidal signs," notably a spastic type of paralysis, exaggerated deep reflexes, and a positive Babinski reflex (see p. 483). Actually, pyramidal signs result from interruption of both pyramidal and extrapyramidal pathways. The paralysis stems from interruption of pyramidal tracts, whereas the spasticity (rigidity) and exaggerated reflexes come from interruption of inhibitory extrapyramidal pathways.

Injury to lower motor neurons produces symptoms different from those of upper motor neuron injury. Anterior horn cells or lower motor neurons, you will recall, constitute the final common path by which impulses reach skeletal muscles. This means that if they are injured, impulses can no longer reach the skeletal muscles they supply. This, in turn, results in the absence of all reflexes and willed movements produced by contraction of the muscles involved. Unused, the muscles soon lose their normal tone and become soft and flabby (flaccid). In short, absence of reflexes and flaccid paralysis are the chief "lower" motor neuron signs.

If all this sounds complicated and confusing, imagine what it must be like to be a neurobiologist trying to figure out how all this works! In fact, scientists working in this field admit that they have not worked out all the details of the extrapyramidal circuits—or exactly how they control muscle activity. However, the model shown in Figure 14-25 summarizes the current notion that it is a complex, interactive process.

Knowing about all these motor pathways helps us understand and treat injuries and disorders that affect motor functions. Box 14-9 discusses some of the clinical signs of motor pathway injury.

| QUICK CHECK |

20. What is the "principle of final common path" as it pertains to somatic motor pathways?
21. Distinguish between pyramidal and extrapyramidal pathways.

Cycle of LIFE

Central Nervous System

If the most obvious *structural* changes over the life span are the overall growth and then degeneration of the skeleton and other body parts, then the most obvious *functional* changes are the development and then degeneration of the complex integrative capacity of the central nervous system.

Although the development of the brain and spinal cord begins in the womb, further development beyond the time of birth is required. The lack of development of the CNS in a newborn is evidenced by lack of the more complex integrative functions, such as

language, complex memory, comprehension of spatial relationships, and complex motor skills such as walking. As childhood proceeds, one can easily see evidence of the increasing capacity of the CNS for complex function. A child learns to use language, to remember both concrete and abstract ideas, to walk, and even to behave in ways that conform to the norms of society. By the time a person reaches adulthood, most, if not all, of these complex functions have become fully developed. We use them throughout adult life to help us maintain internal stability in an unstable external world.

As we enter very late adulthood, the tissues of the brain and spinal cord may degenerate. If they do degenerate—and they may not—the degree of change varies from one individual to the next. In some cases, the degeneration is profound—or it occurs in a critical part of the brain—and an older person becomes unable to communicate, to walk, or to perform some other complex functions. In many cases, however, the degeneration produces milder effects, such as temporary lapses in memory or fumbling with certain very complex motor tasks. As our understanding of this process increases, we are finding ways to avoid entirely such changes associated with aging.

the BIG picture

The Central Nervous System and the Whole Body

The central nervous system is the ultimate regulator of the entire body. It serves as the anatomical and functional center of the countless feedback loops that maintain the relative constancy of the internal environment. The CNS directly or indirectly regulates, or at least influences, nearly every organ in the body.

The intriguing thing about the way in which the CNS regulates the whole body is that it is able to integrate, or bring together, literally millions of bits of information from all over the body and make sense of it all. The CNS not only makes sense of all this information but also compares it with previously stored memories and makes decisions based on its own conclusions about the data. The complex integrative functions of human language, consciousness, learning, and memory enable us to adapt to situations that less complex organisms could not. Thus our wonderfully complex CNS is essential to our survival.

MECHANISMS of DISEASE

DISORDERS OF THE CENTRAL NERVOUS SYSTEM

Destruction of Brain Tissue

Injury or disease can destroy neurons. A common example is the destruction of neurons of the motor area of the cerebrum that results from a cerebrovascular accident (CVA). A CVA, or *stroke*, is a hemorrhage from or cessation of blood flow through cerebral blood vessels. When this happens, the oxygen supply to portions of the brain is disrupted and neurons cease functioning. If the lack of oxygen is prolonged, the neurons die. If the damage occurs in a motor control area of the brain (see Figures 14-19 and 14-20), a person can no longer voluntarily move the parts of the body controlled by the affected area or areas. Because motor neurons cross over from side to side in the brainstem (see Figure 14-24), flaccid paralysis appears on the side of the body opposite the side of the brain on which the CVA occurred. The term *hemiplegia* refers to paralysis (loss of voluntary muscle control) of one whole side of the body.

One of the most common crippling diseases that appears during childhood, **cerebral palsy,** also results from damage to brain tissue. Cerebral palsy involves permanent, nonprogressive damage to motor control areas of the brain. Such damage is present at birth or occurs shortly after birth and remains throughout life. Possible causes of brain damage include prenatal infections or diseases of the mother; mechanical trauma to the head before, during, or after birth; nerve-damaging poisons; reduced oxygen supply to the brain; and other factors. The resulting impairment to voluntary muscle control can manifest in various ways. Many people with cerebral palsy exhibit **spastic paralysis,** a type of paralysis characterized by involuntary contractions of affected muscles. In cerebral palsy, spastic paralysis often affects one entire side of the body (**hemiplegia**), both legs (**paraplegia**), both legs and one arm (**triplegia**), or all four extremities (**quadriplegia**).

Dementia

Various degenerative diseases can result in destruction of neurons in the brain. This degeneration can progress to adversely affect memory, attention span, intellectual capacity, personality, and motor control. The general term for this syndrome is **dementia.**

Alzheimer disease (AD) is characterized by dementia. Its characteristic lesions develop in the cortex during the middle to late adult years. Exactly what causes dementia-producing lesions to develop in the brains of individuals with Alzheimer disease is not

known. There is strong evidence that this disease has a genetic basis—at least in some families. A current theory is that more than one of the handful of different genes associated with AD has to be abnormal before AD occurs. Other evidence indicates that environmental factors may have a role. Because the exact cause of Alzheimer disease is still not known, development of an effective treatment has proven difficult. Currently, people diagnosed with this disease are treated by helping them maintain their remaining mental abilities and looking after their hygiene, nutrition, and other aspects of personal health management. A few drugs such as memantine HCl (Namenda) and donepezil (Aricept) are available to slow down the progression of AD or lessen the severity of some of the symptoms.

Huntington disease (HD) is an inherited disease characterized by chorea (involuntary, purposeless movements) that progresses to severe dementia and death. The initial symptoms of this disease first appear between ages 30 and 40 years, with death generally occurring by age 55 years. The gene responsible for Huntington disease causes the body to make the protein *huntingtin* incorrectly. In brain cells, the abnormal form of huntingtin apparently clings to molecules too tightly and thus prevents normal function.

Acquired immune deficiency syndrome (AIDS), caused by HIV (human immunodeficiency virus) infection, can also cause dementia. The immune deficiency characteristic of AIDS results from HIV infection of white blood cells that are critical to the proper function of the immune system (see Chapter 24). However, HIV also infects neurons and can cause progressive degeneration of the brain—resulting in dementia.

Diseases caused by prions, pathogenic protein molecules, can also cause dementia. For example, *bovine spongiform encephalopathy*, also known as BSE or "mad cow disease," is a degenerative disease of the central nervous system caused by prions that convert normal proteins of the nervous system into abnormal proteins, causing loss of nervous system function, including dementia. **Variant Creutzfeldt-Jakob disease (vCJD)** is another prion disease that similarly reduces brain function, causing dementia. These diseases have caused alarm occasionally when animal brains (the tissue that carries prions to other organisms) were fed to other animals in the human food chain, increasing the risk of infecting large numbers of humans. The mechanism of prion disease was outlined in Chapter 1, p. 26.

Seizure Disorders

Some of the most common nervous system abnormalities belong to the group of conditions called *seizure disorders*. These disorders are characterized by **seizures**—sudden bursts of abnormal neuron activity that result in temporary changes in brain function. Seizures may be very mild, causing subtle changes in the level of consciousness, motor control, or sensory perception. On the other hand, seizures may be quite severe—resulting in jerky, involuntary muscle contractions called *convulsions* or even unconsciousness.

Recurring or chronic seizure episodes constitute a condition called **epilepsy.** Although some cases of epilepsy can be traced to specific causes such as tumors or chemical imbalances, most epilepsy is idiopathic (of unknown cause). Epilepsy is often treated with anticonvulsive drugs such as *phenobarbital*, *phenytoin*, or *valproic acid* that block neurotransmitters in affected areas of the brain. By thus blocking synaptic transmission, such drugs inhibit the explosive bursts of neuron activity associated with seizures. With proper medication, many people with epilepsy lead normal lives without the fear of experiencing uncontrollable seizures. Even those who have not responded well to drug therapies often have gained some relief from surgeries that cut or destroy areas of the brain prone to severe seizures.

Diagnosis and evaluation of epilepsy or any seizure disorder often rely on **electroencephalography** (see Box 14-7, p. 442). As Figure 14-26 illustrates, a normal EEG shows the moderate rise and fall of voltage in various parts of the brain, but a seizure manifests as an explosive increase in the size and frequency of voltage fluctuations. Different classifications of epilepsy are based on the location or locations and the duration of these changes in brain activity.

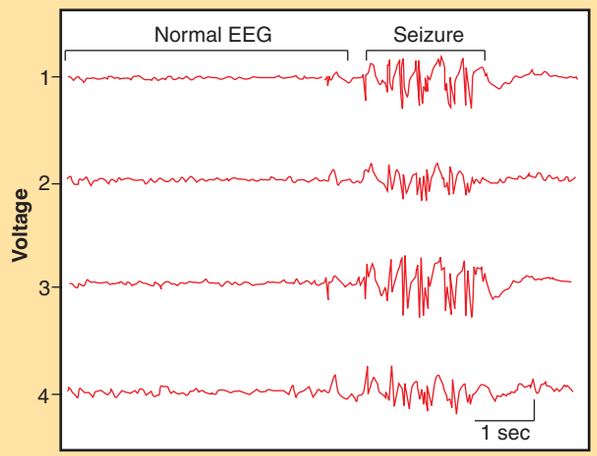


FIGURE 14-26
Electroencephalogram (EEG).

LANGUAGE OF SCIENCE (continued from p. 420)

central sulcus (Rolando fissure)
(SUL-kus [FISH-ur of roh-LAHN-doh])
[*sulcus* **trench**, *Luigi Rolando* **Italian physician**] *pl.,* sulci

cerebellum
(sair-eh-BELL-um)
[*cereb-* **brain**, *-ellum* **small thing**] *pl.,* cerebella or cerebellums

cerebral hemisphere
(seh-REE-bral HEM-i-sfeer)
[*cerebr-* **brain**, *-al* **relating to**, *hemi-* **half**, *-sphere* **globe**]

cerebral peduncle
(seh-REE-bral peh-DUNG-kul)
[*cerebr-* **brain**, *-al* **relating to**, *ped-* **foot**, *-uncl-* **little**]

cerebrospinal fluid (CSF)
(seh-ree-broh-SPY-nal FLOO-id)
[*cerebr-* **brain**, *-spin-* **backbone**, *-al* **relating to**]

cerebrum
(SAIR-eh-brum)
[*cerebrum* **brain**] *pl.,* cerebra or cerebrums

choroid plexus
(KOH-royd PLEK-sus)
[*chorio-* **skin**, *-oid* **like**, *plexus* **network**] *pl.,* plexi or plexuses

connectome
(kon-NEK-tohm)
[*con-* **together**, *-nect-* **bind**, *-ome* **complete set**]

conus medullaris
(KOH-nus MED-yoo-lair-is)
[*conus* **cone**, *medulla* **middle**] *pl.,* coni medullares

convolution
(kon-voh-LOO-shun)
[*con-* **together**, *-volut-* **roll**, *-tion* **process**]

corpora quadrigemina
(KOHR-pohr-ah kwod-ri-JEM-i-nah)
[*corpora* **bodies**, *quadri-* **fourfold**, *-gemina* **twin**]

corpus callosum
(KOHR-pus kah-LOH-sum)
[*corpus* **body**, *callosum* **callous**] *pl.,* corpora callosa

dentate nucleus
(DEN-tayt NOO-klee-us)
[*dent-* **tooth**, *-ate* **of or like**, *nucleus* **nut or kernel**] *pl.,* nuclei

descending tract
[*descend-* **move downward**, *tract-* **trail**]

diencephalon
(dye-en-SEF-ah-lon)
[*di-* **between**, *-en-* **within**, *-cephalon* **head**] *pl.,* diencephala or diencephalons

dorsal (posterior) nerve root
(DOR-sal)
[*dors-* **back**, *-al* **relating to**]

epidural space
(ep-i-DOO-ral)
[*epi-* **upon**, *-dura-* **hard**, *-al* **relating to**]

epithalamus
(ep-i-THAL-ah-mus)
[*epi-* **upon**, *-thalamus* **inner chamber**] *pl.,* epithalami

extrapyramidal tract
(eks-trah-pi-RAH-mi-dal)
[*extra-* **outside**, *-pyramid-* **pyramid**, *-al* **relating to**, *tract-* **trail**]

falx cerebelli
(falks ser-eh-BEL-lee)
[*falx* **sickle**, *cerebelli* **of the cerebellum (small brain)**] *pl.,* falces cerebelli

falx cerebri
(falks SER-eh-bree)
[*falx* **sickle**, *cerebri* **of the cerebrum**] *pl.,* falces cerebri

fasciculus cuneatus
(fah-SIK-yoo-lus KYOO-nee-ay-tus)
[*fasci-* **bundles**, *-iculus* **little**, *cuneatus* **wedgelike**] *pl.,* fasciculi

fasciculus gracilis
(fah-SIK-yoo-lus GRAH-sil-iss)
[*fasci-* **bundles**, *-iculus* **little**, *gracilis* **thin**] *pl.,* fasciculi

filum terminale
(FYE-lum ter-mi-NAL-ee)
[*filum* **thread**, *termin-* **boundary**, *-al* **relating to**] *pl.,* fila terminales

folia
(FOH-lee-ah)
[*folia* **leaves**] *sing.*, **folium**

frontal lobe
(FRON-tal)
[*front-* **forehead**, *-al* **relating to**]

funiculus
(fuh-NIK-yoo-lus)
[*funi-* **rope**, *-icul-* **little**] *pl.,* funiculi

gray column
gray commissure
(KOHM-is-shoor)
[*commissur-* **a joining**]

hypothalamus
(hye-poh-THAL-ah-muss)
[*hypo-* **under or below**, *-thalamus* **inner chamber**] *pl.,* hypothalami

inferior cerebellar peduncle
(SAIR-eh-bell-ar peh-DUNG-kuls)
[*infer-* **lower**, *-or* **quality**, *cerebellar* **relating to the cerebellum (small brain)**, *ped-* **foot**, *-uncl-* **little**]

inferior colliculi
(koh-LIK-yoo-lee)
[*infer-* **lower**, *-or* **quality**, *colli-* **hill**, *-iculus* **small**] *sing.,* **colliculus**

infundibulum
(in-fun-DIB-yoo-lum)
[*infundibulum* **funnel**] *pl.,* infundibula

insula
(IN-soo-lah)
[*insula* **island**] *pl.,* insulae

internal capsule
[*intern-* **inside**, *-al* **relating to**, *caps-* **box**, *-ula* **little**]

lateral corticospinal tract
(LAT-er-al kohr-ti-koh-SPY-nal)
[*later-* **side**, *-al* **relating to**, *cortico-* **bark**, *-spin-* **backbone**, *-al* **relating to**, *tract-* **trail**]

lateral fissure (Sylvius fissure)
(LAT-er-al FISH-ur)
[**FISH-ur of SIL-vi-us**] [*later-* **side**, *-al* **relating to**, *Franciscus Sylvius* **German medical professor**]

lateral spinothalamic tract
(LAT-er-al spy-notha-LAM-ik trakt)
[*later-* **side**, *-al* **relating to**, *spino-* **backbone**, *-thalam-* **inner chamber**, *-ic* **relating to**, *tract-* **trail**]

lentiform nucleus
(LEN-ti-form NOO-klee-us)
[*lent-* **lentil (lens)**, *-form* **shape**, *nucleus* **nut or kernel**] *pl.,* nuclei

limbic system
(LIM-bik)
[*limb-* **edge**, *-ic* **relating to**]

longitudinal fissure
(lon-ji-TOO-dih-nal FISH-ur)
[*longitud-* **length**, *-al* **relating to**]

medulla oblongata
(meh-DUL-ah ob-long-GAH-tah)
[*medulla* **middle**, *oblongata* **oblong**] *pl.,* medullae oblongatae

melatonin
(mel-ah-TOH-nin)
[*mela-* **black**, *-ton-* **tone**, *-in* **substance**]

meninges
(meh-NIN-jeez)
[*mening* **membrane**] *sing.*, **meninx**

midbrain
middle cerebellar peduncle
(SAIR-eh-bell-ar peh-DUNG-kul)
[*cerebell-* **cerebellum (small brain)**, *-ar* **relating to**, *ped-* **foot**, *-uncl* **little**]

motor program
[*mot-* **movement**, *-or* **agent**]

occipital lobe
(ok-SIP-it-al)
[*occipit-* **back of head**, *-al* **relating to**]

olive
optic chiasma
(OP-tik kye-AS-mah)
[*opti-* **vision**, *-ic* **relating to**, *chiasma* **crossed lines**] *pl.,* chiasmata, chiasms, or chiasmas

parietal lobe
(pah-RYE-eh-tal)
[*pariet-* **wall**, *-al* **relating to**]

parietooccipital sulcus
(pah-RYE-eh-toh-ok-SIP-i-tal SUL-kus)
[*parieto-* **wall**, *-occipit-* **back of head**, *-al* **relating to**, *sulcus* **trench**] *pl.,* sulci

pineal gland
(PIN-ee-al)
[*pine-* **pine**, *-al* **relating to**, *gland* **acorn**]

pons
(ponz)
[*pons* **bridge**] *pl.,* pontes

pyramid
(PEER-ah-mid)
pyramidal tract
(pi-RAM-i-dal)
[*pyrami-* **pyramid**, *-al* **relating to**, *tract-* **trail**]

reticular activating system (RAS)
(reh-TIK-yoo-lar)
[*ret-* **net**, *-ic-* **relating to**, *-ul-* **little**, *-ar* **characterized by**]

reticular formation
(reh-TIK-yoo-lar)
[*ret-* **net**, *-ic-* **relating to**, *-ul-* **little**, *-ar* **characterized by**]

reticulospinal tract
(reh-TIK-yoo-loh-SPY-nal)
[*ret-* **net**, *-ic-* **relating to**, *-ul-* **little**, *-spin-* **backbone**, *-al* **relating to**, *tract-* **trail**]

rubrospinal tract
(roo-broh-SPY-nal)
[*rubro-* **red**, *- spin-* **backbone**, *-al* **relating to**, *tract-* **trail**]

spinal nerve
(SPY-nal)
[*spin-* **backbone**, *-al* **relating to**]

spinal tract
(SPY-nal)
[*spin-* **backbone**, *-al* **relating to**, *tract-* **trail**]

spinocerebellar tract
(SPY-no-sair-eh-BELL-ar)
[*spino-* **backbone**, *-cerebell-* **cerebellum (small brain)**, *-ar* **relating to**, *tract-* **trail**]

spinotectal tract
(SPY-no-TEK-tal)
[*spino-* **backbone**, *-tect-* **roof**, *-al* **relating to**, *tract-* **trail**]

spinothalamic pathway
(spy-no-thah-LAM-ik)
[*spino-* **backbone**, *-thalam-* **inner chamber**, *-ic* **relating to**]

subarachnoid space
(sub-ah-RAK-noyd)
[*sub-* **beneath**, *-arachn-* **spider**, *-oid* **like**]

subdural space
(sub-DOO-ral)
[*sub-* **beneath**, *-dura-* **hard or tough**, *-al* **relating to**]

superior cerebellar peduncle
(SAIR-eh-bell-ar peh-DUNG-kuls)
[*super-* **over or above**, *-or* **quality**, *cerebell-* **cerebellum (small brain)**, *-ar* **relating to**, *ped-* **foot**, *-uncl* **little**]

superior colliculi
(koh-LIK-yoo-lee)
[*super-* **over or above**, *-or* **quality**, *colli-* **hill**, *-iculus* **small**] *sing.,* colliculus

tectospinal tract
(tek-toh-SPY-nal)
[*tecto-* **roof**, *-spin-* **backbone**, *-al* **relating to**, *tract-* **trail**]

temporal lobe
(TEM-poh-ral)
[*tempor-* **temple of head**, *-al* **relating to**]

tentorium cerebelli
(ten-TOR-ee-um sair-eh-BEL-lee)
[*tentorium* **tent**, *cerebelli* **of the cerebellum (small brain)**] *pl.,* tentoria cerebelli

thalamus
(THAL-ah-muss)
[*thalamus* **inner chamber**]
pl., thalami

ventral
(anterior) nerve root
(VEN-tral)
[*ventr-* **belly**, *-al* **relating to**]

ventricle
(VEN-tri-kul)
[*ventr-* **belly**, *-icle* **little**]

vermis
(VER-mis)
[*vermis* **worm**] *pl.,* vermes

vestibulospinal tract
(ves-TIB-yoo-loh-SPY-nal)
[*vestibul-* **entrance hall**, *-spino-* **backbone**, *-al* **relating to**, *tract-* **trail**]

LANGUAGE OF MEDICINE

acquired immune deficiency syndrome (AIDS)
(ah-KWYERD IM-yoon deh-FISH-en-see SIN-drohm)
[*syn-* **together**, *-drome* **running or (race)course**]

Alzheimer disease (AD)
(AHLZ-hye-mer)
[*Alois Alzheimer* **German neurologist**]

cerebral palsy
(seh-REE-bral PAWL-zee)
[*cerebr-* **brain**, *-al* **relating to**, *palsy* **paralysis** (*para-* **beyond**, *-lysis* **loosening**)]

cerebral plasticity
(seh-REE-bral plas-TIS-i-tee)
[*cerebr-* **brain**, *-al* **relating to**, *plastic-* **moldable**, *-ity* **state**]

cerebrovascular accident (CVA)
(SAIR-eh-broh-VAS-kyoo-lar)
[*cerebr-* **brain**, *-vas-* **vessel**, *cul-* **little**, *-ar* **relating to**]

coma
(KOH-mah)
[*coma* **deep sleep**]

dementia
(de-MEN-shah)
[*de-* **off**, *-mens-* **mind**, *-ia* **condition of**]

electroencephalogram (EEG)
(eh-lek-troh-en-SEF-ah-loh-gram)
[*electro-* **electricity**, *-en-* **within**, *-cephal-* **head**, *-gram* **drawing**]

electroencephalography
(eh-lek-troh-en-SEF-ah-log-rah-fee)
[*electro-* **electricity**, *-en-* **inside**, *-cephal* **head**, *-graph-* **draw**, *-y* **activity**]

epilepsy
(EP-i-lep-see)
[*epilepsy-* **seizure**]

hemiplegia
(hem-ee-PLEE-jee-ah)
[*hemi-* **half**, *-plegia* **stroke**]

Huntington disease (HD)
(HUN-ting-ton)
[*George S. Huntington* **American physician**]

hydrocephalus
(hye-droh-SEF-ah-lus)
[*hydro-* **water**, *-cephalus* **head**]

lumbar puncture
(LUM-bar)
[*lumb-* **loin**, *-ar* **relating to**]

meningitis
(men-in-JYE-tis)
[*mening-* **membrane**, *-itis* **inflammation**]

pain control area

paraplegia
(pair-ah-PLEE-jee-ah)
[*para-* **beside**, *-plegia* **stroke**]

Parkinson disease (PD)
(PAR-kin-son)
[*James Parkinson* **English physician**]

quadriplegia
(kwod-ri-PLEE-jee-ah)
[*quadri-* **fourfold**, *-plegia* **stroke**]

rapid eye movement (REM) sleep

seizure
(SEE-zhur)

slow-wave sleep (SWS)

spastic paralysis
(SPAS-tik pah-RAL-i-sis)
[*spast-* **pull**, *-ic* **relating to**, *para-* **beyond**, *-lysis* **loosening**]

transcutaneous electrical nerve stimulation (TENS) unit
(trans-kyoo-TAY-nee-us)
[*trans-* **across**, *-cutan-* **skin**, *-ous* **relating to**]

triplegia
(try-PLEE-jee-ah)
[*tri-* **three**, *-plegia* **stroke**]

variant Creutzfeldt-Jakob disease (vCJD)
(KROYTS-felt YAH-kobe)
[*Hans G. Creutzfeldt* **German neurologist**, *Alfons M. Jakob* **German neurologist**]

x-ray photography
[*x* **unknown**, *photo-* **light**, *-graph-* **draw**, *-y* **activity**]

CASE study

After several days of a pounding headache, Polai went to the university clinic, hoping for some aspirin. But after she explained her symptoms, instead of being sent home with aspirin, she was sent to the hospital for a lumbar puncture (also called a *spinal tap*) to determine whether she had contracted meningitis. In this procedure, a needle is inserted into the lumbar region to obtain a sample of cerebrospinal fluid.

1. In what order will the needle pierce the meninges?
   a. Pia mater, arachnoid mater, dura mater
   b. Arachnoid mater, pia mater, dura mater
   c. Dura mater, arachnoid mater, pia mater
   d. Dura mater, pia mater, arachnoid mater

2. Where exactly will the cerebrospinal fluid be drawn from?
   a. Epidural space
   b. Subdural space
   c. Epiarachnoid space
   d. Subarachnoid space

Anyone performing a spinal tap must be extremely careful. If the needle goes past its mark, it could puncture the posterior portion of the spinal cord. One of the tracts in this region is the fasciculi gracilis.

3. The transmission of what type of information would be affected if the fasciculi gracilis were damaged?
   a. Discriminating touch
   b. Crude touch
   c. Voluntary movement
   d. Coordination of posture and balance

One possible (though rare) complication of meningitis (inflammation of the meninges) could be a spread of the bacteria to the cerebellum.

4. Which of the following is NOT a function of the cerebellum?
   a. Coordinates skilled movement
   b. Controls language
   c. Helps control posture
   d. Controls balance

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

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HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

COVERINGS OF THE BRAIN AND SPINAL CORD

A. Two protective coverings (Figure 14-2)
   1. Outer covering is bone; cranial bones encase the brain, and vertebrae encase the spinal cord (Figure 14-1)
   2. Inner covering is the meninges; the meninges of the cord continue inside the spinal cavity beyond the end of the spinal cord

B. Meninges—three membranous layers (Figure 14-3)
   1. Dura mater—strong, white fibrous tissue; outer layer of meninges and inner periosteum of the cranial bones; has three important extensions
      a. Falx cerebri
         (1) Projects downward into the longitudinal fissure between the two cerebral hemispheres
         (2) Dural sinuses—function as veins, collecting blood from brain tissues for return to the heart
         (3) Superior sagittal sinus—one of several dural sinuses
      b. Falx cerebelli—separates the two hemispheres of the cerebellum
      c. Tentorium cerebelli—separates the cerebellum from the cerebrum
   2. Arachnoid mater—delicate, spiderweb-like layer between the dura mater and pia mater
   3. Pia mater—innermost, transparent layer; adheres to the outer surface of the brain and spinal cord; contains blood vessels; beyond the spinal cord, forms a slender filament called *filum terminale*, at level of sacrum, blends with dura mater to form a fibrous cord that disappears into the periosteum of the coccyx
   4. Several spaces exist between and around the meninges
      a. Epidural space—located between the dura mater and inside the bony covering of the spinal cord; contains a supporting cushion of fat and other connective tissues (virtually absent around brain because dura is continuous with periosteum of bone)
      b. Subdural space—located between the dura mater and arachnoid mater; contains lubricating serous fluid
      c. Subarachnoid space—located between the arachnoid and pia mater; contains a significant amount of cerebrospinal fluid (CSF)

CEREBROSPINAL FLUID

A. Functions
   1. Provides a supportive, protective cushion
   2. Reservoir of circulating fluid, which is monitored by the brain to detect changes in the internal environment

B. Fluid spaces
   1. Cerebrospinal fluid—found within the subarachnoid space around the brain and spinal cord and within the cavities and canals of the brain and spinal cord
   2. Ventricles—fluid-filled spaces within the brain; four ventricles within the brain (Figure 14-4)
      a. First and second ventricles (lateral)—one located in each hemisphere of the cerebrum
      b. Third ventricle—thin, vertical pocket of fluid below and medial to the lateral ventricles
      c. Fourth ventricle—tiny, diamond-shaped space where the cerebellum attaches to the back of the brainstem

C. Formation and circulation of cerebrospinal fluid (Figure 14-5)
   1. Occurs by separation of fluid from blood in the choroid plexuses
      a. Fluid from the lateral ventricles seeps through the interventricular foramen (of Monro) into the third ventricle
      b. From the third ventricle, fluid goes through the cerebral aqueduct into the fourth ventricle
      c. From the fourth ventricle, fluid goes to two different areas
         (1) Some fluid flows directly into the central canal of the spinal cord
         (2) Some fluid leaves the fourth ventricle through openings in its roof and goes into the cisterna magna, a space that is continuous with the subarachnoid space
      d. Fluid circulates in the subarachnoid space and then is absorbed into venous blood through the arachnoid villi

SPINAL CORD

A. Structure of the spinal cord (Figure 14-6)
   1. Lies within the spinal cavity and extends from the foramen magnum to the lower border of the first lumbar vertebra
   2. Oval-shaped cylinder that tapers slightly from above downward
   3. Two bulges, one in the cervical region and one in the lumbar region
   4. Anterior median fissure and posterior median sulcus are two deep grooves; anterior fissure is deeper and wider
   5. Nerve roots
      a. Fibers of dorsal nerve root
         (1) Carry sensory information into the spinal canal
         (2) Dorsal root ganglion—cell bodies of unipolar, sensory neurons make up a small region of gray matter in the dorsal nerve root
      b. Fibers of ventral nerve root
         (1) Carry motor information out of the spinal cord
         (2) Cell bodies of multipolar, motor neurons are in the gray matter of the spinal cord
   6. Interneurons are located in the spinal cord's gray matter core
   7. Spinal nerve—a single mixed nerve on each side of the spinal cord where the dorsal and ventral nerve roots join together
   8. Cauda equina—bundle of nerve roots extending (along with the filum terminale) from the conus medullaris (inferior end of spinal cord) (Figure 14-7)
   9. Gray matter
      a. Columns of gray matter extend the length of the cord
      b. Consists predominantly of cell bodies of interneurons and motor neurons
      c. In transverse section, looks like an H with the limbs being called the *anterior*, *posterior*, and *lateral horns of gray matter*; crossbar of H is the *gray commissure*
   10. White matter
      a. Surrounds the gray matter and is subdivided in each half on the cord into three funiculi: anterior, posterior, and lateral white columns
      b. Each funiculus consists of a large bundle of axons divided into tracts
      c. Names of spinal tracts indicate the location of the tract, the structure in which the axons originate, and the structure in which they terminate

B. Functions of the spinal cord
   1. Provides conduction routes to and from the brain
      a. Ascending tracts—conduct impulses up the cord to the brain
      b. Descending tracts—conduct impulses down the cord from the brain
      c. Bundles of axons compose all tracts
      d. Tracts are both structural and functional organizations of nerve fibers
         (1) Structural—all axons of any one tract originate in the same structure and terminate in the same structure
         (2) Functional—all axons that compose one tract serve one general function
      e. Important ascending (sensory) tracts (Figure 14-8)
         (1) Lateral spinothalamic tracts—crude touch, pain, and temperature
         (2) Anterior spinothalamic tracts—crude touch, pressure
         (3) Fasciculi gracilis and cuneatus—discriminating touch and conscious kinesthesia
         (4) Spinocerebellar tracts—subconscious kinesthesia
         (5) Spinotectal—touch related to visual reflexes
      f. Important descending (motor) tracts (Figure 14-8)
         (1) Lateral corticospinal tracts—voluntary movements on opposite side of the body
         (2) Anterior corticospinal tracts—voluntary movements on same side of body
         (3) Reticulospinal tracts—maintain posture during movement

(4) Rubrospinal tracts—transmit impulses that coordinate body movements and maintenance of posture
(5) Tectospinal tracts—head and neck movements during visual reflexes
(6) Vestibulospinal tracts—coordination of posture and balance

g. Spinal cord—reflex center for all spinal reflexes; spinal reflex centers are located in the gray matter of the cord

BRAIN

A. One of the largest organs in the adult body—1.4 kg
1. Almost 100 billion neurons and as many glia
2. Most new neurons are produced before and shortly after birth
3. Synapses are made and broken throughout life

B. Structure of the brainstem (Figures 14-9 and 14-10)
1. Medulla oblongata
a. Lowest part of the brainstem
b. Part of the brain that attaches to spinal cord, located just above the foramen magnum
c. A few centimeters in length and separated from the pons above by a horizontal groove
d. Composed of white matter and a network of gray and white matter called the *reticular formation network*
e. Pyramids—two bulges of white matter located on the ventral side of the medulla; formed by fibers of the pyramidal tracts
f. Olive—oval projection located lateral to the pyramids
g. Nuclei—clusters of neuron cell bodies located in the reticular formation
2. Pons
a. Located above the medulla and below the midbrain
b. Composed of white matter and reticular formation
3. Midbrain
a. Located above the pons and below the cerebrum; forms the midsection of the brain
b. Composed of white tracts and reticular formation
c. Extending divergently through the midbrain are cerebral peduncles; conduct impulses between the midbrain and cerebrum
d. Corpora quadrigemina—landmark in midbrain
(1) Made up of two inferior colliculi and two superior colliculi
(2) Forms the posterior, upper part of the midbrain that lies just above the cerebellum
(3) Inferior colliculus—contains auditory centers
(4) Superior colliculus—contains visual centers
e. Red nucleus and substantia nigra—clusters of cell bodies of neurons involved in muscular control

B. Functions of the brainstem
1. Performs sensory, motor, and reflex functions
2. Spinothalamic tracts—important sensory tracts that pass through the brainstem
3. Fasciculi cuneatus and gracilis and spinoreticular tracts—sensory tracts whose axons terminate in the gray matter of the brainstem
4. Corticospinal and reticulospinal tracts—two of the major tracts present in the white matter of the brainstem
5. Nuclei in medulla—contain reflex centers
a. Of primary importance—cardiac, vasomotor, and respiratory centers
b. Nonvital reflexes—vomiting, coughing, sneezing, and so on
6. Pons—contains reflexes mediated by fifth, sixth, seventh, and eighth cranial nerves and pneumotaxic centers that help regulate respiration
7. Midbrain—contains centers for certain cranial nerve reflexes

C. Structure of the cerebellum (Figure 14-11)
1. Second largest part of the brain—contains more neurons than the rest of the nervous system
2. Located just below the posterior portion of the cerebrum; transverse fissure separates these two parts of the brain
3. Gray matter makes up the cortex, and white matter predominates in the interior
4. Arbor vitae—internal white matter of the cerebellum; distinctive pattern similar to the veins of a leaf
5. Cerebellum has numerous sulci and delicate, parallel gyri (folia)
6. Consists of the cerebellar hemispheres and the vermis
7. Internal white matter—composed of short and long tracts
a. Shorter tracts—conduct impulses from neuron cell bodies located in the cerebellar cortex to neurons whose dendrites and cell bodies compose nuclei located in the interior of the cerebellum
b. Longer tracts—conduct impulses to and from the cerebellum; fibers enter or leave by way of three pairs of peduncles
(1) Inferior cerebellar peduncles—composed chiefly of tracts into the cerebellum from the medulla and cord
(2) Middle cerebellar peduncles—composed almost entirely of tracts into the cerebellum from the pons
(3) Superior cerebellar peduncles—composed principally of tracts from dentate nuclei in the cerebellum through the red nucleus of the midbrain to the thalamus
8. Dentate nuclei
a. Important pair of cerebellar nuclei, one of which is located in each hemisphere
b. Nuclei connected with thalamus and with motor areas of the cerebral cortex by tracts
c. By means of the tracts, cerebellar impulses influence the motor cortex, and the motor cortex influences the cerebellum

D. Functions of the cerebellum
1. Cerebellum compares the motor commands of the cerebrum with the information coming from proprioceptors in the muscle; impulses travel from the cerebellum to both the cerebrum and muscles to coordinate movements to produce the intended action (Figure 14-12)
2. General functions
a. Acts with cerebral cortex to produce skilled movements by coordinating the activities of groups of muscles

b. Controls skeletal muscles to maintain balance
c. Controls posture; operates at subconscious level to smooth movements and make movements efficient and coordinated
d. Processes sensory information; complements and assists various functions of the cerebrum

E. Diencephalon (Figure 14-13)
1. Located between the cerebrum and the midbrain
2. Consists of several structures located around the third ventricle: thalamus, hypothalamus, optic chiasma, pineal gland, and several others
3. Thalamus
a. Dumbbell-shaped mass of gray matter made up of many nuclei
b. Each lateral mass forms one lateral wall of the third ventricle
c. Intermediate mass—extends through the third ventricle and joins the two lateral masses
d. Geniculate bodies—two of the most important groups of nuclei comprising the thalamus; located in posterior region of each lateral mass; play role in processing auditory and visual input
e. Serves as a major relay station for sensory impulses on their way to the cerebral cortex
f. Performs the following primary functions:
(1) Plays two parts in mechanism responsible for sensations
(a) Impulses produce conscious recognition of the crude, less critical sensations of pain, temperature, and touch
(b) Neurons relay all kinds of sensory impulses, except possibly olfactory, to the cerebrum
(2) Plays part in the mechanism responsible for emotions by associating sensory impulses with feeling of pleasantness and unpleasantness
(3) Plays part in arousal mechanism
(4) Plays part in mechanisms that produce complex reflex movements
4. Hypothalamus
a. Consists of several structures that lie beneath the thalamus
b. Forms floor of the third ventricle and lower part of lateral walls
c. Prominent structures found in the hypothalamus
(1) Supraoptic nuclei—gray matter located just above and on either side of the optic chiasma
(2) Paraventricular nuclei—located close to the wall of the third ventricle
(3) Mamillary bodies—posterior part of hypothalamus, involved with olfactory sense
d. Infundibulum—the stalk leading to the posterior lobe of the pituitary gland
e. Small but functionally important area of the brain, performs many functions of greatest importance for survival and enjoyment
f. Links mind and body
g. Links nervous system to endocrine system
h. Summary of hypothalamic functions
(1) Regulator and coordinator of autonomic activities
(2) Major relay station between the cerebral cortex and lower autonomic centers; crucial part of the route by which emotions can express themselves in changed bodily functions
(3) Synthesizes hormones secreted by posterior pituitary and plays an essential role in maintaining water balance
(4) Some neurons function as endocrine glands
(5) Plays crucial role in arousal mechanism
(6) Crucial part of mechanism regulating appetite
(7) Crucial part of mechanism maintaining normal body temperature
5. Pineal gland
a. Located just above the corpora quadrigemina of the midbrain
b. Involved in regulating the body's biological clock (Figure 14-14)
c. Produces melatonin as a "timekeeping hormone"
(1) Melatonin is made from the neurotransmitter serotonin
(2) Melatonin levels increase when sunlight is absent; decrease when sunlight is present, thus regulating the circadian (daily) biological clock (Figure 14-15)
(3) Melatonin is the "sleep hormone"

F. Structure of the cerebrum
1. Cerebral cortex
a. Largest and uppermost division of the brain; consists of right and left cerebral hemispheres; each hemisphere is divided into five lobes (Figure 14-16)
(1) Frontal lobe
(2) Parietal lobe
(3) Temporal lobe
(4) Occipital lobe
(5) Insula (island of Reil)
b. Cerebral cortex—outer surface made up of six layers of gray matter
c. Gyri—convolutions; some are named: precentral gyrus, postcentral gyrus, cingulate gyrus, and hippocampal gyrus
d. Sulci—shallow grooves
e. Fissures—deeper grooves, divide each cerebral hemisphere into lobes; four prominent cerebral fissures
(1) Longitudinal fissure—deepest fissure; divides cerebrum into two hemispheres
(2) Central sulcus (fissure of Rolando)—groove between frontal and parietal lobes
(3) Lateral fissure (fissure of Sylvius)—groove between temporal lobe below and parietal lobes above; island of Reil lies deep in lateral fissure
(4) Parietooccipital sulcus—groove that separates occipital lobe from parietal lobes
2. Cerebral tracts and basal nuclei
a. Cerebral tracts make up cerebrum's white matter; there are three types (Figure 14-17)

(1) Projection tracts—extensions of the sensory spinothalamic tracts and motor corticospinal tracts
(2) Association tracts—most numerous cerebral tracts; extend from one convolution to another in the same hemisphere
(3) Commissural tracts—extend from one convolution to a corresponding convolution in the other hemisphere; compose the corpus callosum and anterior and posterior commissures

b. Connectome—entire network of neural connections in the brain
c. Basal nuclei
(1) Structure—islands of gray matter located deep inside the white matter of each hemisphere (Figure 14-18); include the following:
(a) Caudate nucleus
(b) Lentiform nucleus—consists of putamen and pallidum
(c) Amygdaloid nucleus
(2) Function—regulation of voluntary (conscious) motor control related to posture, walking, and other repetitive movements; possible roles in thinking and learning
d. Corpus striatum—composed of caudate nucleus, internal capsule, and lentiform nucleus

G. Functions of the cerebral cortex
1. Functional areas of the cortex—certain areas of the cerebral cortex engage in predominantly one particular function (Figures 14-19 and 14-20)
a. Postcentral gyrus—mainly general somatic sensory area; receives impulses from receptors activated by heat, cold, and touch stimuli
b. Precentral gyrus—chiefly somatic motor area; impulses from neurons in this area descend over motor tracts and stimulate skeletal muscles
c. Transverse gyrus—primary auditory area
d. Occipital lobe—primary visual areas
2. Sensory functions of the cortex
a. Somatic senses—sensations of touch, pressure, temperature, proprioception, and similar perceptions that require complex sensory organs
b. Cortex contains a "somatic sensory map" of the body
c. Information sent to primary sensory areas is relayed to sensory association areas, as well as to other parts of the brain
d. The sensory information is compared and evaluated, and the cortex integrates separate bits of information into whole perceptions
3. Motor functions of the cortex
a. For normal movements to occur, many parts of the nervous system must function
b. Precentral gyrus—primary somatic motor area; controls individual muscles
c. Secondary motor area—in the gyrus immediately anterior to the precentral gyrus; activates groups of muscles simultaneously
4. Integrative functions of the cortex

H. Consciousness (Figure 14-21)
1. State of awareness of one's self, one's environment, and other humans
2. Depends on excitation of cortical neurons by impulses conducted to them by the reticular activating system
3. Two current concepts about the reticular activating system
a. Functions as the arousal system for the cerebral cortex
b. Its functioning is crucial for maintaining consciousness

I. Language
1. Ability to speak and write words and ability to understand spoken and written words
2. Speech centers—areas in the frontal, parietal, and temporal lobes
3. Left cerebral hemisphere contains speech centers in approximately 90% of the population; in the remaining 10%, contained in either the right hemisphere or both
4. Aphasias—lesions in speech centers

J. Emotions (Figure 14-22)
1. Subjective experiencing and objective expressing of emotions involve functioning of the limbic system
2. Limbic system—also known as the "emotional brain"
a. Most structures of limbic system lie on the medial surface of the cerebrum; they are the cingulate gyrus and hippocampus
b. Have primary connections with other parts of the brain, such as the thalamus, fornix, septal nuclei, amygdaloid nucleus, and hypothalamus

K. Memory
1. One of our major mental activities
2. Cortex is capable of storing and retrieving both short- and long-term memory
3. Temporal, parietal, and occipital lobes are among the areas responsible for short- and long-term memory
4. Structural changes in the neural pathways of the cerebral cortex store long-term memories
5. Limbic system plays a key role in memory

SOMATIC SENSORY PATHWAYS IN THE CENTRAL NERVOUS SYSTEM

A. For the cerebral cortex to perform its sensory functions, impulses must first be conducted to the sensory areas by sensory pathways (Figure 14-23)
B. Three main pools of sensory neurons
1. Primary sensory neurons—conduct impulses from the periphery to the central nervous system
2. Secondary sensory neurons
a. Conduct impulses from the cord or brainstem to the thalamus
b. Dendrites and cell bodies are located in the gray matter of the cord and brainstem
c. Axons ascend in ascending tracts up the cord and through the brainstem, terminating in the thalamus, where they synapse with dendrites or cell bodies of tertiary sensory neurons

3. Tertiary sensory neurons
   a. Conduct impulses from thalamus to the postcentral gyrus of the parietal lobe
   b. Bundle of axons of tertiary sensory neurons form the thalamocortical tracts
   c. Extend through the internal capsule to the cerebral cortex

C. Sensory pathways to the cerebral cortex are crossed
D. Two sensory pathways conduct impulses that produce sensations of touch and pressure
   1. Medial lemniscal system
      a. Consists of tracts that make up the fasciculi cuneatus and gracilis, and the medial lemniscus
      b. Axons of secondary sensory neurons make up medial lemniscus
      c. Functions—transmit impulses that produce discriminating touch and pressure sensations and kinesthesia
   2. Spinothalamic pathway—functions are crude touch and pressure sensations

SOMATIC MOTOR PATHWAYS IN THE CENTRAL NERVOUS SYSTEM

A. Impulse conduction
   1. For the cerebral cortex to perform its motor functions, impulses are conducted from its motor areas to skeletal muscles by somatic motor pathways
   2. Pathways consist of motor neurons that conduct impulses from the central nervous system to skeletal muscles; some motor pathways are extremely complex, and others are very simple
   3. Principle of the final common path—cardinal principle about somatic motor pathways; only one final common path, the motor neuron from the anterior gray horn of the spinal cord, conducts impulses to skeletal muscles
   4. Two methods used to classify somatic motor pathways: pyramidal and extrapyramidal tracts (Figure 14-24)

B. Pyramidal tracts—also known as *corticospinal tracts*
   1. Approximately three quarters of the fibers decussate in the medulla and extend down the cord in the crossed corticospinal tract located on the opposite side of the spinal cord in the lateral white column
   2. Approximately one quarter of the fibers do not decussate but extend down the same side of the spinal cord as the cerebral area from which they came

C. Extrapyramidal tracts—much more complex than pyramidal tracts
   1. Consist of all motor tracts from the brain to the spinal cord anterior horn motor neurons except the corticospinal tracts
   2. Within the brain, consist of numerous relays of motor neurons between motor areas of the cortex, basal nuclei, thalamus, cerebellum, and brainstem
   3. Within the spinal cord, some important tracts are the reticulospinal tracts
   4. Conduction by extrapyramidal tracts plays a crucial part in producing large, automatic movements
   5. Conduction by extrapyramidal tracts plays an important part in emotional expressions
   6. Motor program—set of coordinated commands that control the programmed motor activity mediated by extrapyramidal pathways (Figure 14-25)

CYCLE OF LIFE: CENTRAL NERVOUS SYSTEM

A. Development and degeneration of CNS—most obvious functional change over the life span
B. Development of brain and spinal cord begins in the womb
C. Lack of development in the newborn is evidenced by lack of complex integrative functions
   1. Language
   2. Complex memory
   3. Comprehension of spatial relationships
   4. Complex motor skills
D. Complex functions develop by adulthood
E. Late adulthood—tissues degenerate
   1. Profound degeneration—unable to perform complex functions
   2. Milder degeneration—temporary memory lapse or difficulty with complex motor tasks

THE BIG PICTURE: THE CENTRAL NERVOUS SYSTEM AND THE WHOLE BODY

A. Central nervous system—ultimate regulator of the body; essential to survival
B. Able to integrate bits of information from all over the body, make sense of it, and make decisions

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. What term refers to the membranous covering of the brain and cord? What three layers compose this covering?
2. What are the large fluid-filled spaces within the brain called? How many are there? What do they contain?
3. Describe the formation and circulation of cerebrospinal fluid.
4. Describe the structure and general functions of the spinal cord.
5. List the major components of the brainstem, and identify their general functions.
6. Describe the general functions of the cerebellum.
7. Describe the general functions of the thalamus.
8. Describe the general functions of the hypothalamus.
9. Describe the general functions of the cerebrum.
10. What general functions does the cerebral cortex perform?
11. Define consciousness. Name the normal states, or levels, of consciousness.

12. Name some altered states of consciousness.
13. Identify the following kinds of brainwaves according to their frequency, voltage, and the level of consciousness in which they predominate: alpha, beta, delta, theta.
14. Locate the dendrite, cell body, and axon of primary, secondary, and tertiary sensory neurons.

CRITICAL THINKING QUESTIONS

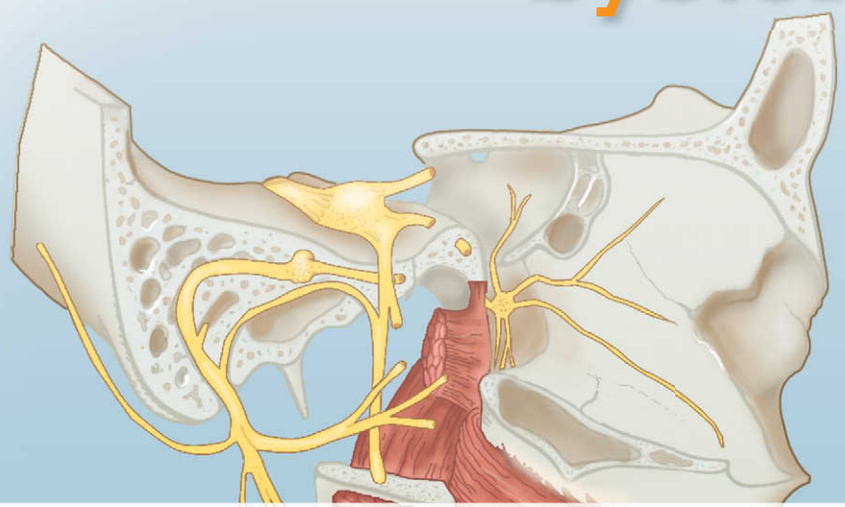


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Explain what the term *reflex center* means. Is an interneuron necessary for a reflex center? Explain your answer.
2. Explain briefly what is meant by the arousal or alerting mechanism.
3. Some people claim meditation has a wide range of benefits. What benefits can be supported by scientific evidence?
4. If a researcher discovered that a substantial reduction in neurotransmitter concentration caused difficulty in forming memory, what theory of memory formation would be refuted?
5. In Chapter 13, an action potential was explained in terms of electrical activity. Explain the process of measuring that activity to differentiate the types of brainwaves.
6. A person having an absence of any reflex and a person having exaggerated deep tendon reflexes are showing signs of different motor pathway injuries. Using these symptoms as the basis, explain the motor pathway that was damaged and what other symptoms each person might have.
7. Compare pyramidal tract and extrapyramidal tract functions.
8. A patient with a brain infection can be diagnosed by culturing cerebrospinal fluid. The greatest concentration of the disease-causing organism can be drawn from the fluid as soon as it leaves the brain at the level of the third or fourth vertebra. Why would this be an unwise place to take the sample? Where would a better location be? Explain your answer.

Peripheral Nervous System

15



CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

Spinal Nerves, 464
- Structure of Spinal Nerves, 466
- Nerve Plexuses, 466
  - Cervical Plexus, 468
  - Brachial Plexus, 468
  - Lumbar Plexus, 468
  - Sacral Plexus and Coccygeal Plexus, 470
- Dermatomes and Myotomes, 471

Cranial Nerves, 473
- Olfactory Nerve (I), 474
- Optic Nerve (II), 474
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- Divisions of the Peripheral Nervous Systems, 481
- Basic Principles of Somatic Motor Pathways, 481
- Somatic Reflexes, 481

The Big Picture: Peripheral Nervous System and the Whole Body, 483

Case Study, 484

LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

abdominal reflex
(ab-DOM-i-nal REE-fleks)
[*abdomin-* **belly,** *-al* **relating to,** *re-* **again,** *-flex* **bend**]

abducens nerve
(ab-DOO-sens)
[*ab-* **away,** *-duc-* **lead,** *-ens* **process**]

accessory nerve
(ak-SES-oh-ree)

acetylcholine (ACh)
(ass-ee-til-KOH-leen)
[*acetyl-* **vinegar,** *-chole-* **bile,** *-ine* **made of**]

ankle jerk reflex
[*re-* **again,** *-flex* **bend**]

autonomic (visceral) reflex
(aw-toh-NOM-ik [VISS-er-al] REE-fleks)
[*auto-* **self,** *-nomo-* **law** *-ic* **relating to,** *viscer-* **internal organ,** *-al* **relating to** *re-* **again,** *-flex* **bend**]

brachial plexus
(BRAY-kee-all PLEK-sus)
[*brachi-* **arm,** *-al* **relating to,** *plexus* **network**] *pl.,* plexi or plexuses

cauda equina
(KAW-dah eh-KWY-nah)
[*cauda* **tail,** *equina* **of a horse**] *pl.,* caudae equinae

cervical plexus
(SER-vih-kal PLEK-sus)
[*cervic-* **neck,** *-al* **relating to,** *plexus* **network**] *pl.,* plexi or plexuses

corneal reflex
(KOR-nee-al REE-fleks)
[*corn-* **horn,** *-al* **relating to,** *re-* **again,** *-flex* **bend**]

cranial nerve
(KRAY-nee-al)
[*crani-* **skull,** *-al* **relating to**]

continued on p. 483

In Chapter 14, you learned about the structure and function of the central nervous system (CNS). In this chapter we explore the nerve pathways that lead to and from the CNS, which together make up the peripheral nervous system (PNS). The PNS is made up of the 31 pairs of spinal nerves that emerge from the spinal cord, the 12 pairs of cranial nerves that emerge from the brain, and all the smaller nerves that branch from these "main" nerves.

Recall from earlier discussions that afferent *fibers carry information into the CNS. Afferent fibers, part of the sensory nervous system, help us maintain homeostasis by sensing changes in our internal or external environment—providing the feedback necessary to keep the body functioning normally. Afferent fibers belonging to the somatic sensory or special sensory nervous system feed back information regarding changes detected by receptors in the skin, skeletal muscles, and special sense organs. Afferent fibers belonging to the autonomic nervous system (ANS) feed back information regarding the effects of autonomic control of the viscera.*

Recall also that efferent *fibers carry information away from the CNS. Efferent fibers may belong to the somatic nervous system (SNS) that regulates skeletal muscles, allowing us to survive by defending ourselves, getting food, or performing other essential tasks. Efferent fibers may, on the other hand, belong to the ANS. Autonomic regulation controls smooth and cardiac muscle and glands in ways that help us maintain homeostasis of the internal environment.*

The first sections of this chapter explore concepts regarding the structure and function of the spinal and cranial nerves. The last portion of the chapter is devoted to discussion of the peripheral elements of the SNS, with an emphasis on efferent (motor) pathways. Chapter 16 then picks up the story, emphasizing efferent pathways of the ANS. Finally, Chapter 17 explores major concepts of sensation via the afferent pathways.

This study of peripheral nerve pathways clarifies and expands the understanding of the nervous system gained in previous chapters. It also serves as a foundation for understanding important clinical applications (Box 15-1).

Box 15-1 | HEALTH matters

Peripheral Neuropathy

The term **peripheral neuropathy** tells you exactly what it signifies: disease of the peripheral nerves. The term is used to designate many different diseases with many different causes—but all involve damage to peripheral nerves. These disorders can also be called *peripheral neuritis.* If many nerves are involved, peripheral neuropathy can also be called *polyneuropathy* or *polyneuritis.* Probably the most common cause of peripheral nerve damage in the United States and Europe is diabetes mellitus (see ***Diabetes Mellitus*** online at ***A&P Connect***), affecting some 17 million people. But additional causes include other metabolic problems such as kidney disease, injuries such as sports mishaps, poisoning as in drug neurotoxicity and alcohol abuse, infections such as in *leprosy (Hansen disease; Mycobacterium leprae)* or shingles (see Box 15-3, p. 472), and genetic mutations such as *Leber hereditary optic neuropathy* (see Chapter 37, p. 1142).

SPINAL NERVES

Thirty-one pairs of **spinal nerves** are connected to the spinal cord. They have no special names but are merely numbered according to the level of the vertebral column at which they emerge from the spinal cavity (Figure 15-1). Although there are only seven cervical vertebrae, there are eight cervical nerve pairs (C1 through C8), twelve thoracic nerve pairs (T1 through T12), five lumbar nerve pairs (L1 through L5), five sacral nerve pairs (S1 through S5), and one coccygeal pair of spinal nerves. The first pair of cervical nerves emerges from the cord in the space above the first cervical vertebra, and the eighth cervical nerve emerges between the last cervical vertebra and the first thoracic vertebra. Thus nerve pair C1 passes between the skull and vertebra C1, nerve pair C2 passes between vertebrae C1 and C2, nerve pair C3 passes between vertebrae C2 and C3, and so on. All the thoracic nerves pass out of the spinal cavity horizontally through the intervertebral foramina below their respective vertebrae.

Lumbar, sacral, and coccygeal nerve roots, on the other hand, descend from their point of origin at the lower end of the spinal

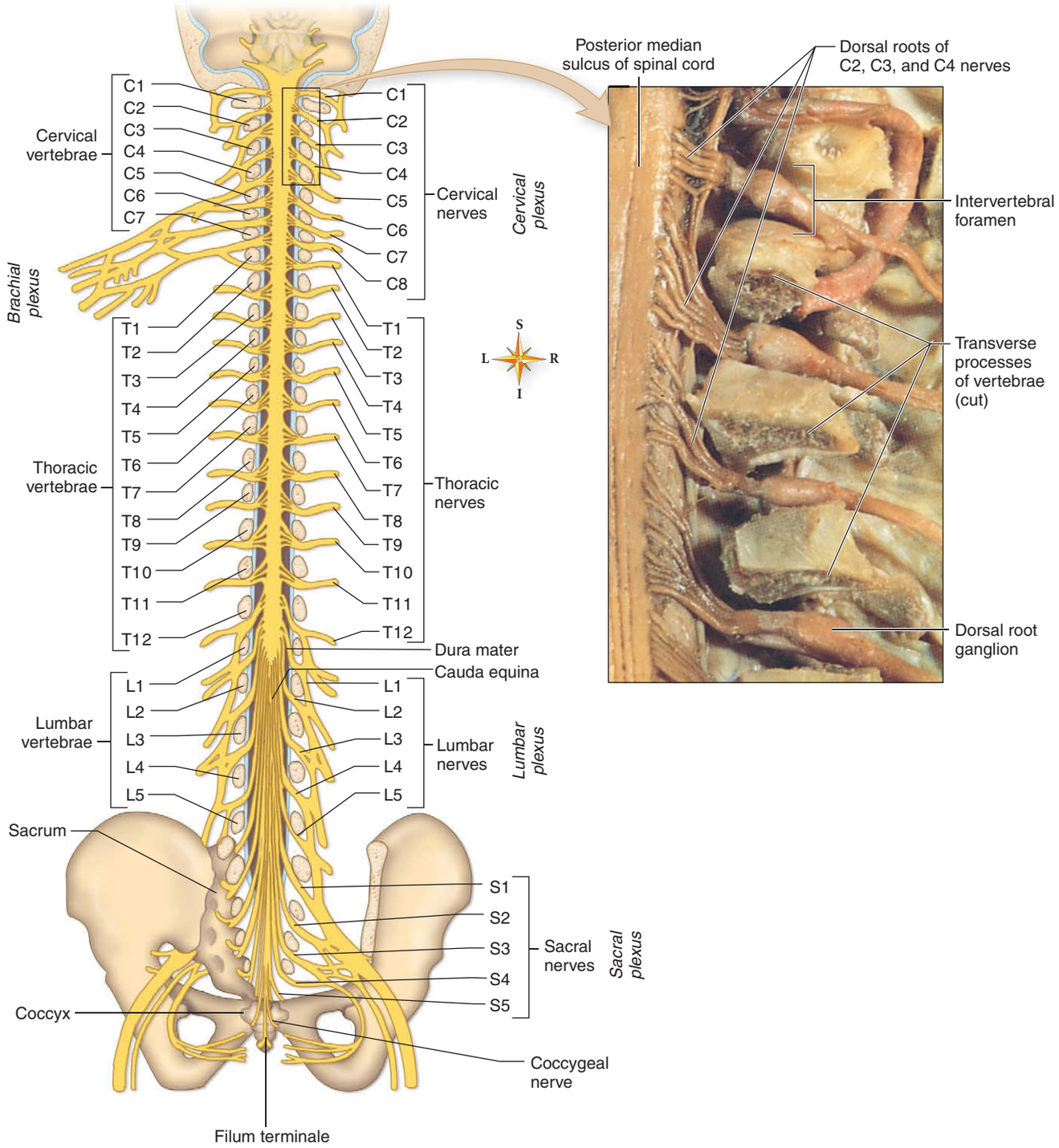


FIGURE 15-1

Spinal nerves. Each of 31 pairs of spinal nerves exits the spinal cavity from the intervertebral foramina. The names of the vertebrae are given on the left and the names of the corresponding spinal nerves on the right. Note that after leaving the spinal cavity, many of the spinal nerves interconnect to form networks called *plexuses.* The inset shows a dissection of the cervical region, showing a posterior view of cervical spinal nerves exiting intervertebral foramina on the right side.

cord (which terminates at the level of the first lumbar vertebra) before reaching the intervertebral foramina of their respective vertebrae, through which the nerves then emerge. This gives the lower end of the cord, with its attached spinal nerve roots, the appearance of a horse's tail. In fact, it bears the name **cauda equina,** which is the Latin equivalent for "horse's tail" (see Figure 15-1).

Structure of Spinal Nerves

Each spinal nerve attaches to the spinal cord by means of two short roots, a **ventral** (anterior) **root** and a **dorsal** (posterior) **root.** The dorsal root of each spinal nerve is easily recognized by a swelling called the dorsal root **ganglion,** or *spinal ganglion* (Figure 15-2). The roots and dorsal ganglia lie within the spinal cavity, as Figure 15-2 shows.

As described in Chapter 14, the ventral root includes motor neurons that carry information from the CNS and toward effectors (muscles and glands). Recall that in each somatic motor pathway, a single motor fiber stretches from the anterior gray horn of the spinal cord, through the ventral root, and on through the spinal nerve toward a skeletal muscle. Autonomic fibers, which also carry motor information toward effectors, may also pass through the ventral root to become part of a spinal nerve. The dorsal root of each spinal nerve includes sensory fibers that carry information from receptors in the peripheral nerves. The dorsal root ganglion contains the cell bodies of the sensory neurons. Because all spinal nerves contain both motor and sensory fibers, they are designated as **mixed nerves.**

Soon after each spinal nerve emerges from the spinal cavity, it forms several large branches, each of which is called a **ramus** (*plural*, rami). As Figure 15-2 shows, each spinal nerve splits into a distinct **dorsal ramus** and **ventral ramus.** The dorsal ramus supplies somatic motor and sensory fibers to several smaller nerves. These smaller nerves, in turn, innervate the muscles and skin of the posterior surface of the head, neck, and trunk. The structure of the ventral ramus is a little more complex. Autonomic motor fibers split away from the ventral ramus, heading toward a ganglion of the *sympathetic chain*. There, some of the autonomic fibers synapse with autonomic neurons that eventually continue on to autonomic effectors by way of *splanchnic nerves* (see Figure 15-2). However, some fibers synapse with autonomic neurons whose fibers rejoin the ventral ramus. The two thin rami formed by this splitting away, then rejoining, of autonomic fibers are together called the *sympathetic rami*. Motor (autonomic and somatic) and sensory fibers of the ventral rami innervate muscles and glands in the extremities (arms and legs) and in the lateral and ventral portions of the neck and trunk.

Nerve Plexuses

The ventral rami of most spinal nerves—all but nerves T2 through T12—subdivide to form complex networks called **plexuses.** As Figure 15-1 shows, there are four major pairs of plexuses: the cervical plexus, the brachial plexus, the lumbar plexus, and the sacral plexus. Table 15-1 summarizes important information about these major plexuses.

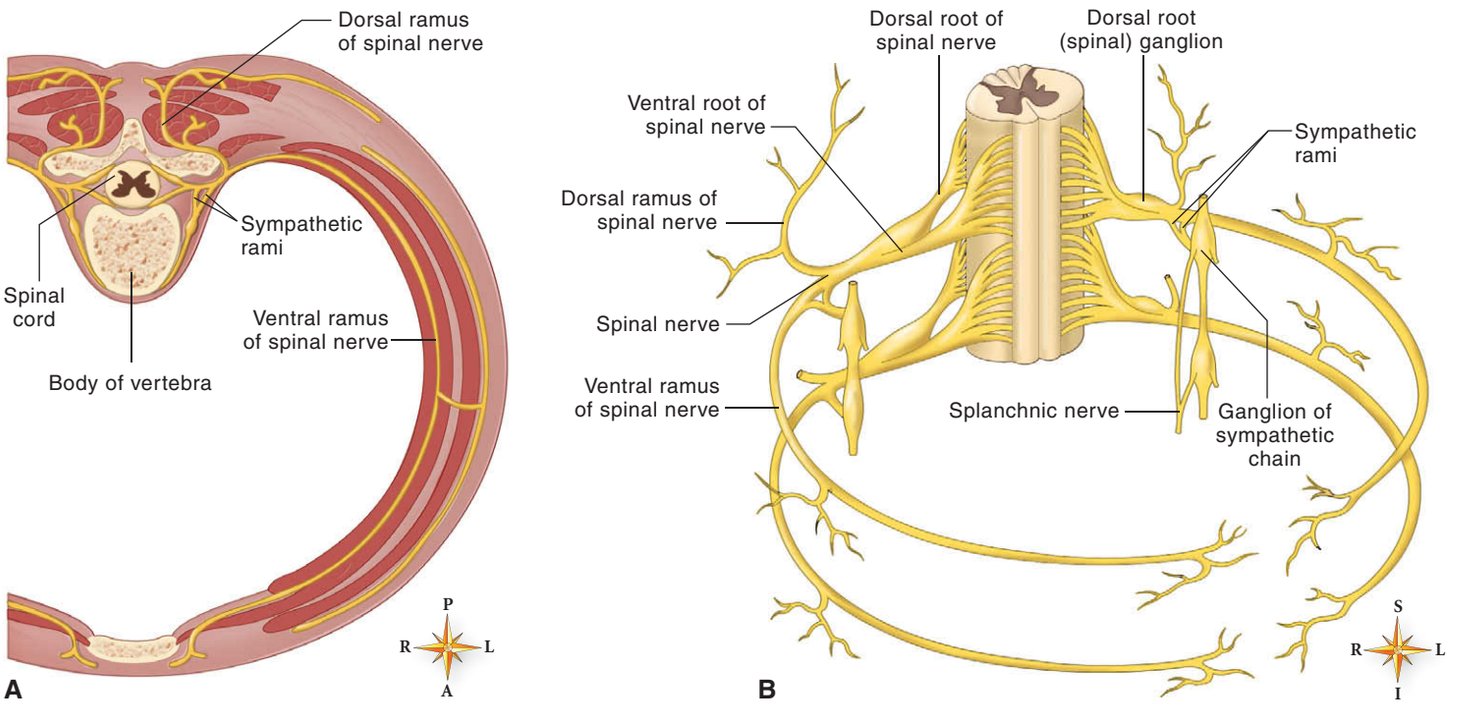


FIGURE 15-2

Rami of the spinal nerves. Note that ventral and dorsal roots join to form a spinal nerve. The spinal nerve then splits into a *dorsal ramus* (plural, *rami*) and *ventral ramus*. The ventral ramus communicates with a chain of sympathetic (autonomic) ganglia by way of a pair of thin sympathetic rami. **A,** Superior view of a pair of thoracic spinal nerves. **B,** Anterior view of several pairs of thoracic spinal nerves.

TABLE 15-1 Spinal Nerves and Peripheral Branches

SPINAL NERVES	PLEXUSES FORMED FROM ANTERIOR RAMI	SPINAL NERVE BRANCHES FROM PLEXUSES		PARTS SUPPLIED
Cervical 1, 2, 3, 4	Cervical plexus	Lesser occipital		Sensory to back of head, front of neck, and upper part of shoulder; motor to numerous neck muscles
		Greater auricular		
		Cutaneous nerve of neck		
		Supraclavicular nerves		
		Branches to muscles		
		Phrenic nerve		Diaphragm
Cervical 5, 6, 7, 8	Brachial plexus	Suprascapular and dorsoscapular		Superficial muscles* of scapula
		Thoracic nerves, medial and lateral branches		Pectoralis major and minor
Thoracic (or Dorsal) 1	No plexus formed; branches run directly to intercostal muscles and skin of thorax	Long thoracic nerve		Serratus anterior
		Thoracodorsal		Latissimus dorsi
2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12		Subscapular		Subscapular and teres major muscles
		Axillary (circumflex)		Deltoid and teres minor muscles and skin over deltoid
		Musculocutaneous		Muscles of front of arm (biceps brachii, coracobrachialis, brachialis) and skin on outer side of forearm
		Ulnar		Flexor carpi ulnaris and part of flexor digitorum profundus; some muscles of hand; sensory to medial side of hand, little finger, and medial half of fourth finger
		Median		Rest of muscles of front of forearm and hand; sensory to skin of palmar surface of thumb, index, and middle fingers
		Radial		Triceps muscle and muscles of back of forearm; sensory to skin of back of forearm and hand
		Medial cutaneous		Sensory to inner surface of arm and forearm
Lumbar 1, 2, 3, 4, 5	Lumbosacral plexus	Iliohypogastric	Sometimes fused	Sensory to anterior abdominal wall
		Ilioinguinal		Sensory to anterior abdominal wall and external genitalia; motor to muscles of abdominal wall
		Genitofemoral		Sensory to skin of external genitalia and inguinal region
		Lateral femoral cutaneous		Sensory to outer side of thigh
Sacral 1, 2, 3, 4, 5		Femoral		Motor to quadriceps, sartorius, and iliacus muscles; sensory to front of thigh and medial side of leg (saphenous nerve)
		Obturator		Motor to adductor muscles of thigh
		Tibial† (medial popliteal)		Motor to muscles of calf of leg; sensory to skin of calf of leg and sole of foot
		Common peroneal (lateral popliteal)		Motor to evertors and dorsiflexors of foot; sensory to lateral surface of leg and dorsal surface of foot
		Nerves to hamstring muscles		Motor to muscles of back of thigh
		Gluteal nerves		Motor to buttock muscles and tensor fasciae latae
		Posterior femoral cutaneous		Sensory to skin of buttocks, posterior surface of thigh, and leg
		Pudendal nerve		Motor to perineal muscles; sensory to skin of perineum
Coccygeal 1	Coccygeal plexus	Anococcygeal nerves		Sensory to skin overlying coccyx

*Although nerves to muscles are considered motor, they do contain some sensory fibers that transmit proprioceptive impulses.
†Sensory fibers from the tibial and peroneal nerves unite to form the medial cutaneous (or sural) nerve that supplies the calf of the leg and the lateral surface of the foot. In the thigh the tibial and common peroneal nerves are usually enclosed in a single sheath to form the *sciatic nerve,* the largest nerve in the body with a width of approximately ¾ inch (2 cm). About two thirds of the way down the posterior part of the thigh, it divides into its component parts. Branches of the sciatic nerve extend into the hamstring muscles.

The term *plexus* is the Latin word for "braid." This is an apt name for a structure in which fibers of several different rami join together to form individual nerves. Each individual nerve that emerges from a plexus contains all the fibers that innervate a particular region of the body. In fact, the destination of each nerve serves as a basis for its name (see Table 15-1). Because spinal nerve fibers are thus rearranged according to their ultimate destination, the plexus reduces the number of nerves needed to supply each body part. And because each body region is innervated by fibers that originate from several adjacent spinal nerves, damage to one spinal nerve does not mean a complete loss of function in any one region.

CERVICAL PLEXUS

The **cervical plexus,** shown in Figure 15-3, is found deep within the neck. Ventral rami of the first four cervical spinal nerves (C1 through C4), along with a branch of the ventral ramus of C5, exchange fibers in the cervical plexus. Individual nerves emerging from this plexus innervate the muscles and skin of the neck, upper shoulders, and part of the head. Also exiting this plexus is the **phrenic nerve,** which innervates the diaphragm (Box 15-2). Two cranial nerves, the accessory nerve (XI) and the hypoglossal nerve (XII), receive small branches that emerge from the cervical plexus.

BRACHIAL PLEXUS

The **brachial plexus,** shown in Figure 15-4, is found deep within the shoulder. It passes from the ventral rami of spinal nerves C5 through T1, beneath the clavicle (collarbone), and toward the arm. Individual nerves that emerge from the brachial plexus innervate the lower part of the shoulder and the entire arm.

LUMBAR PLEXUS

Another spinal nerve plexus is the **lumbar plexus,** which is formed by the intermingling of fibers from the first four lumbar nerves

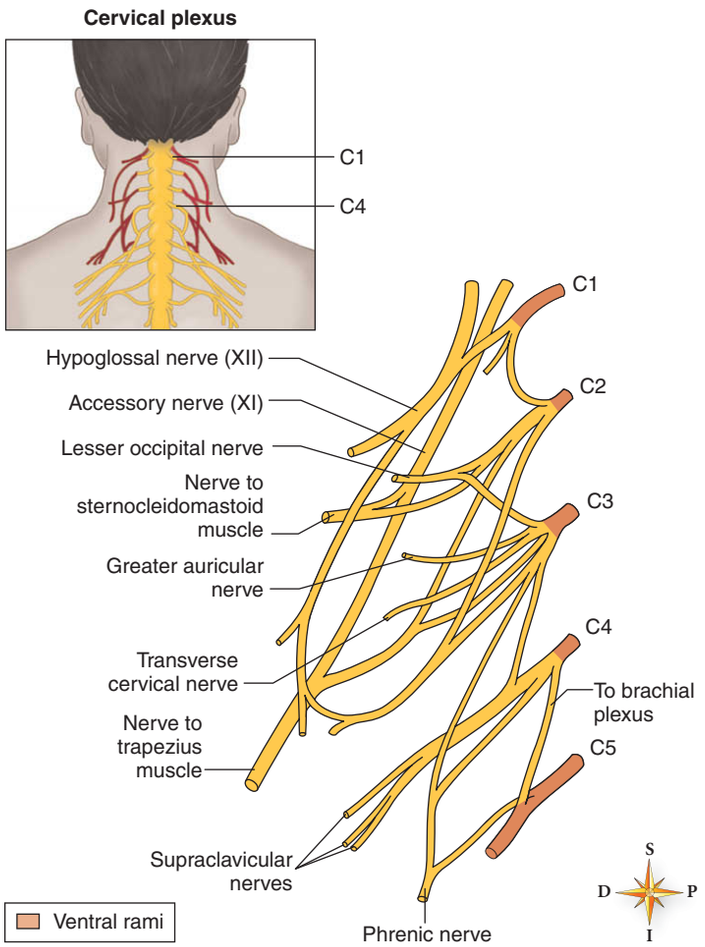


FIGURE 15-3

Cervical plexus. Ventral rami of the first four cervical spinal nerves (C1 through C4) exchange fibers in this plexus found deep within the neck. Notice that some fibers from C5 also enter this plexus to form a portion of the phrenic nerve.

Box 15-2 | HEALTH matters

Phrenic Nerves

The right and left **phrenic nerves,** whose fibers come from the cervical plexus, are of considerable clinical interest because they supply the diaphragm muscle. Contraction of the diaphragm permits inspiration, and relaxation of the diaphragm permits expiration. If the neck is broken in a way that severs or crushes the spinal cord above this level, nerve impulses from the brain can no longer reach the phrenic nerves, and therefore the diaphragm stops contracting. Unless artificial respiration of some kind is provided, the patient dies of respiratory paralysis as a result of the broken neck. Any disease or injury that damages the spinal cord between the third and fifth cervical segments may paralyze the phrenic nerve and, therefore, the diaphragm.

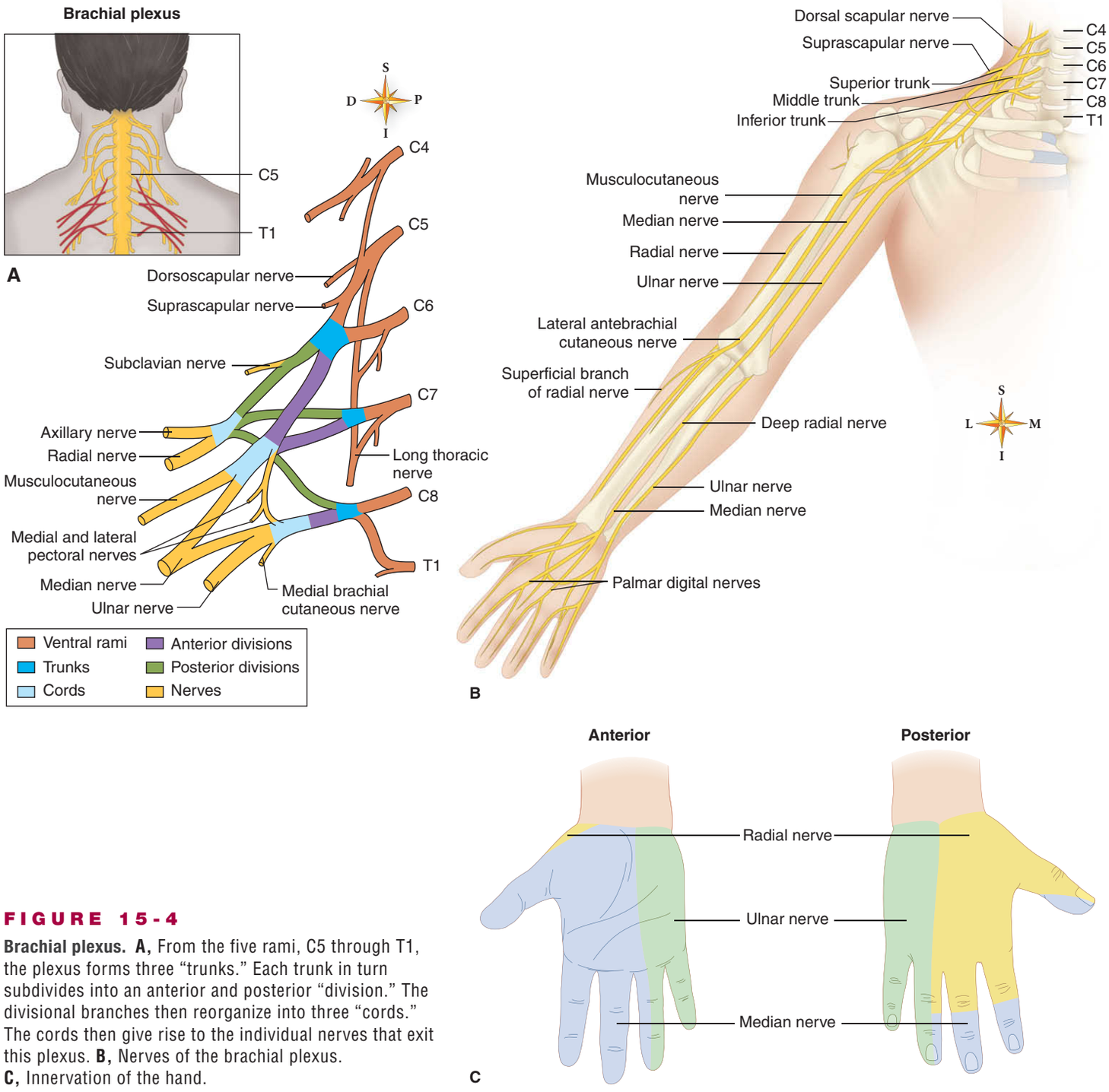


FIGURE 15-4

Brachial plexus. A, From the five rami, C5 through T1, the plexus forms three "trunks." Each trunk in turn subdivides into an anterior and posterior "division." The divisional branches then reorganize into three "cords." The cords then give rise to the individual nerves that exit this plexus. **B,** Nerves of the brachial plexus. **C,** Innervation of the hand.

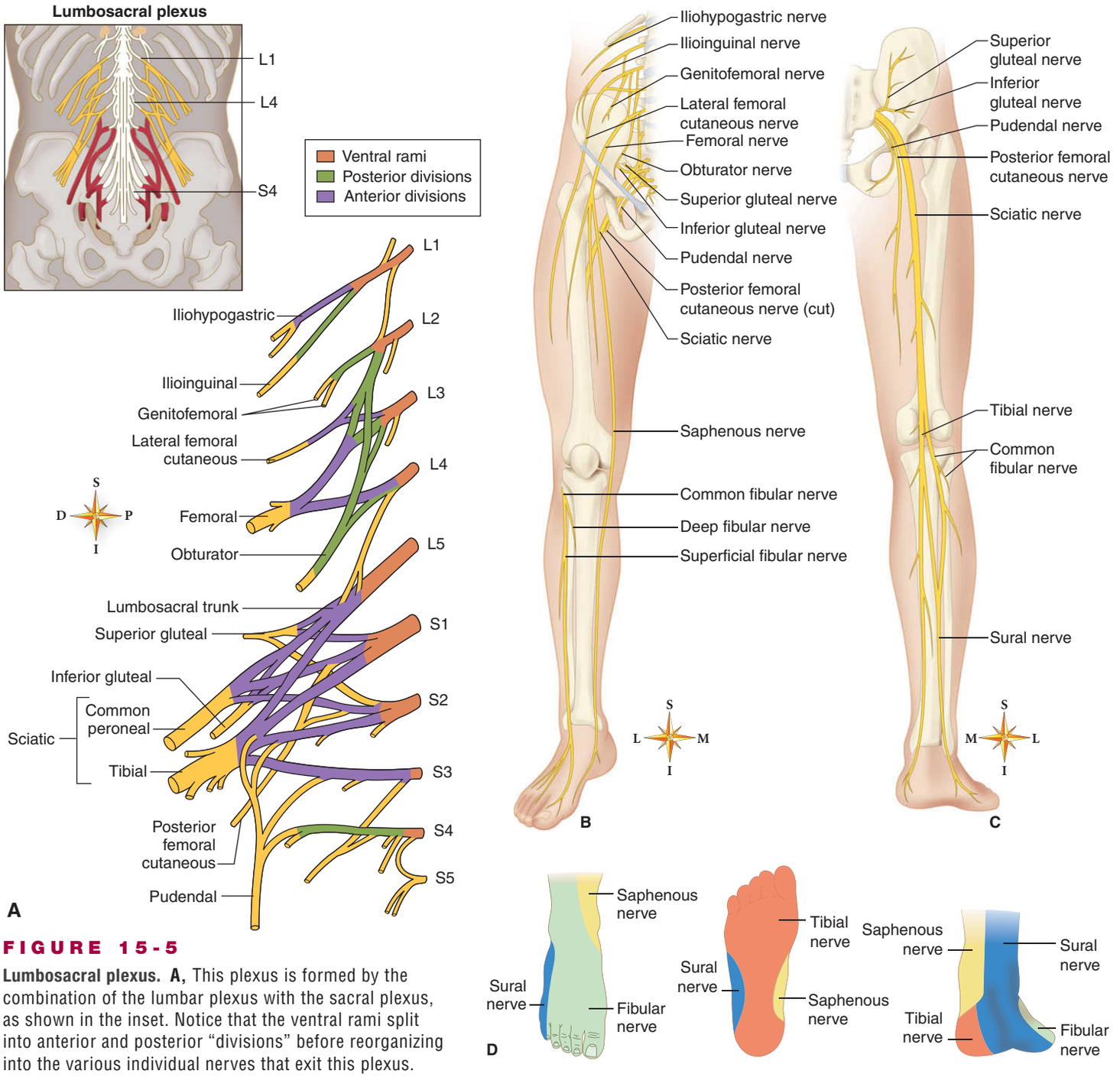


FIGURE 15-5

Lumbosacral plexus. A, This plexus is formed by the combination of the lumbar plexus with the sacral plexus, as shown in the inset. Notice that the ventral rami split into anterior and posterior "divisions" before reorganizing into the various individual nerves that exit this plexus. **B,** Anterior view of lumbosacral plexus nerves. **C,** Posterior view of lumbosacral plexus nerves. **D,** Innervation of the foot and ankle.

(Figure 15-5). This network of nerves is located in the lumbar region of the back near the psoas muscle. The large femoral nerve is one of several nerves emerging from the lumbar plexus. It divides into many branches supplying the thigh and leg.

SACRAL PLEXUS AND COCCYGEAL PLEXUS

Fibers from the fourth and fifth lumbar nerves (L4 and L5) and the first four sacral nerves (S1 through S4) form the **sacral plexus.** It lies in the pelvic cavity on the anterior surface of the piriformis muscle. Because of their close proximity and overlap of fibers, the lumbar and sacral plexuses are often considered together as the *lumbosacral* plexus (see Figure 15-5). Among other nerves that emerge from the sacral plexus are the tibial and common peroneal nerves. In the thigh, they form the largest nerve in the body, the great **sciatic nerve.** It pierces the buttocks and runs down the back of the thigh. Its many branches supply nearly all the skin of the leg, the posterior thigh muscles, and the leg and foot muscles. *Sciatica,* or neuralgia of the sciatic nerve, is a fairly common and very painful condition.

The last sacral spinal nerve (S5), along with a few fibers from S4, joins with the coccygeal nerve to form a small *coccygeal plexus.* Thin anococcygeal nerves arising from this plexus supply the skin that lies over the coccyx bone.

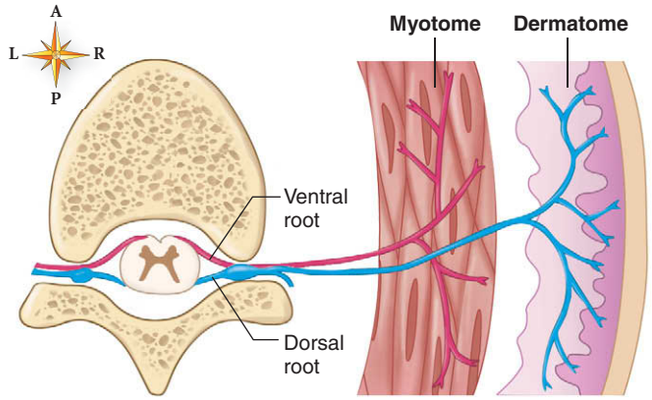


FIGURE 15-6

Segmental distribution of spinal nerves. A dermatome is a region of skin supplied by afferent (sensory) fibers of a given spinal nerve. A myotome is a region of skeletal muscle innervated by efferent (motor) fibers of a given spinal nerve. Spinal nerves at different segments of the spinal cord innervate different sets of dermatomes and myotomes.

Dermatomes and Myotomes

At first glance the distribution of spinal nerves does not appear to follow an ordered arrangement, but detailed mapping of the skin surface has revealed a close relationship between the spinal origin of each spinal nerve and the region of the body it innervates. Knowledge of the segmental arrangement of spinal nerves and the region of the body innervated by each segment has proved useful to health professionals. For instance, one can identify the site of spinal cord or nerve abnormality by locating the corresponding area of the body insensitive to a pinprick. Each skin surface area supplied by sensory fibers of a given spinal nerve is called a **dermatome,** a name that means "skin section" (Figures 15-6 and 15-7).

The body maps in Figure 15-7 show sharp boundaries between sensory dermatomes, but there is actually quite a bit of overlap between adjacent dermatomes. Overlap of dermatomes results from differences in the way various types of sensory receptors are distributed in the skin. Dermatome maps help us to better understand

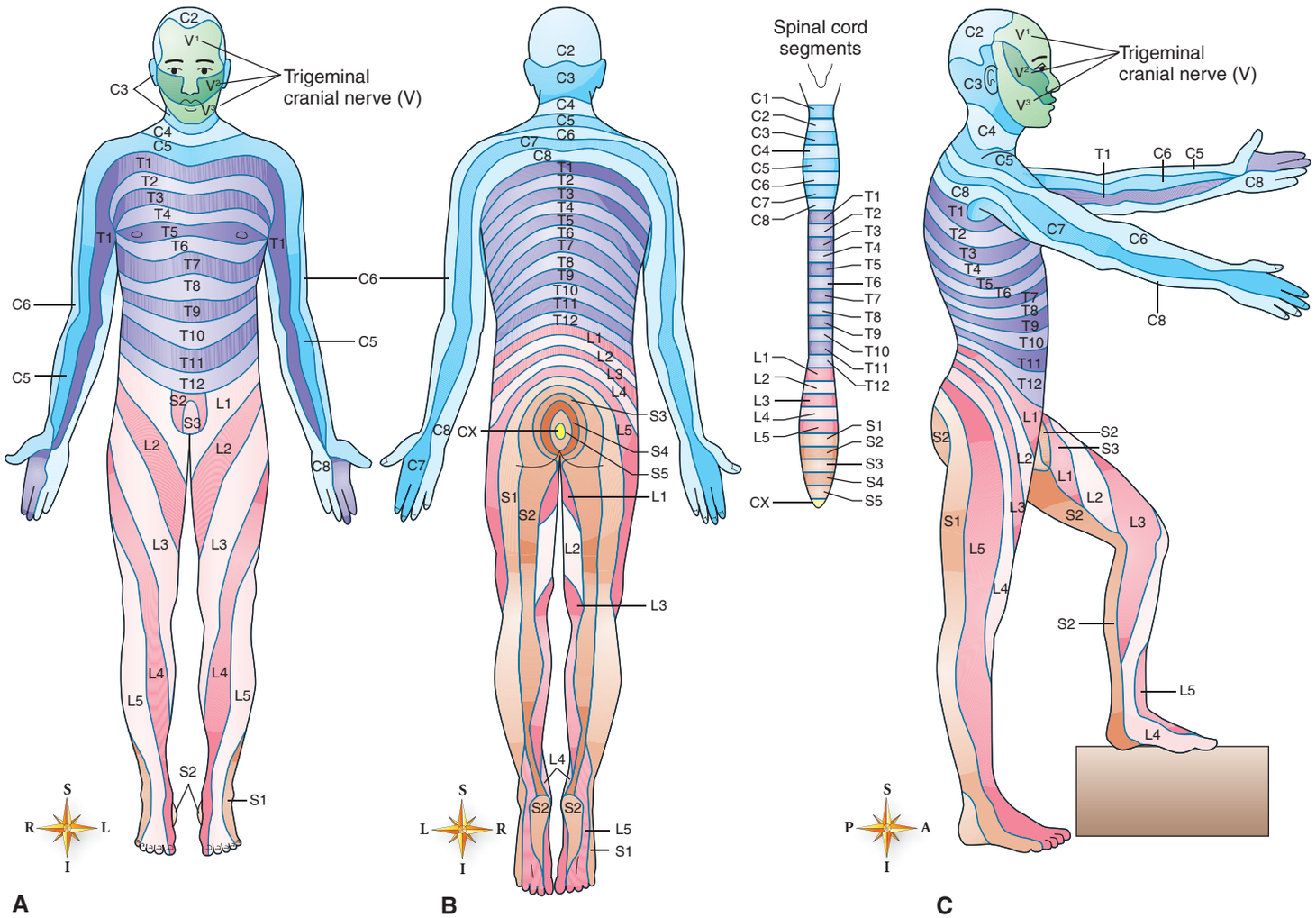


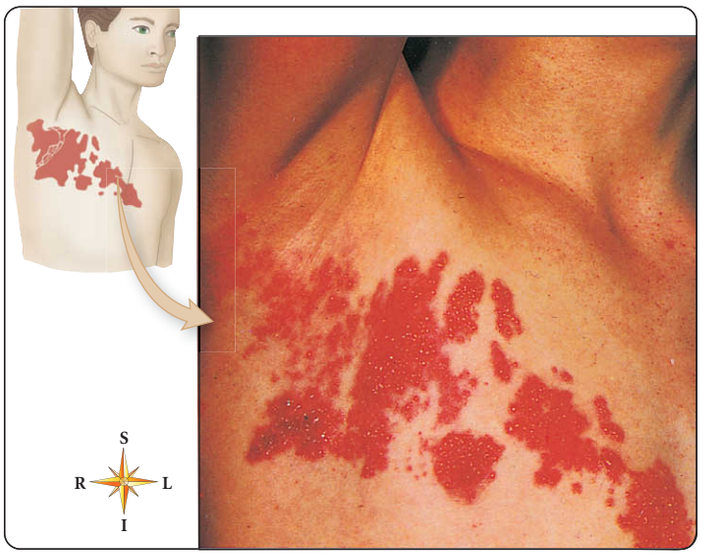
FIGURE 15-7

Dermatome distribution of spinal nerves. **A,** The front of the body's surface. **B,** The back of the body's surface. **C,** The side of the body's surface. The inset shows the segments of the spinal cord connected with each of the spinal nerves associated with the sensory dermatomes shown. *T,* thoracic segments and spinal nerves; *L,* lumbar segments and spinal nerves; *S,* sacral segments and spinal nerves.

Box 15-3 | HEALTH matters

Herpes Zoster

Herpes zoster, or **shingles,** is a unique viral infection that almost always affects the skin of a single dermatome. It is caused by the varicella zoster virus of chickenpox. About 3% of the population will suffer from shingles at some time in their lives. In most cases the disease results from reactivation of the varicella virus. The virus most likely travels through a cutaneous nerve and remains dormant in a dorsal root ganglion for years after an initial episode of chickenpox. If the body's immunological protective mechanism becomes diminished, as in the elderly or as a result of stress, or because of radiation therapy or immunosuppressive drugs, the virus may reactivate. If this occurs, the virus will travel over the sensory nerve to the skin of a single dermatome. The figure shows involvement of dermatome T4 in a 13-year-old boy. The result is a painful eruption of red swollen plaques or vesicles that eventually rupture and crust before clearing in 2 to 3 weeks. In severe cases, extensive inflammation, hemorrhagic blisters, and secondary bacterial infection may lead to permanent scarring. In most cases of shingles, the eruption of vesicles is preceded by 4 to 5 days of preeruptive pain, burning, and itching in the affected dermatome. Unfortunately, an attack of herpes zoster does not confer lasting immunity. Many individuals have three or more episodes in a lifetime.



cutaneous sensation, discussed later in Chapter 17, and also certain conditions that appear on the skin, such as shingles (Box 15-3).

A **myotome** is a skeletal muscle or group of muscles that receives motor axons from a given spinal nerve. There is some overlap among myotomes also. Thus some skeletal muscle organs may be innervated by motor axons from more than one spinal nerve. Figure 15-8 shows examples of how myotomes relate to specific movements of the body.

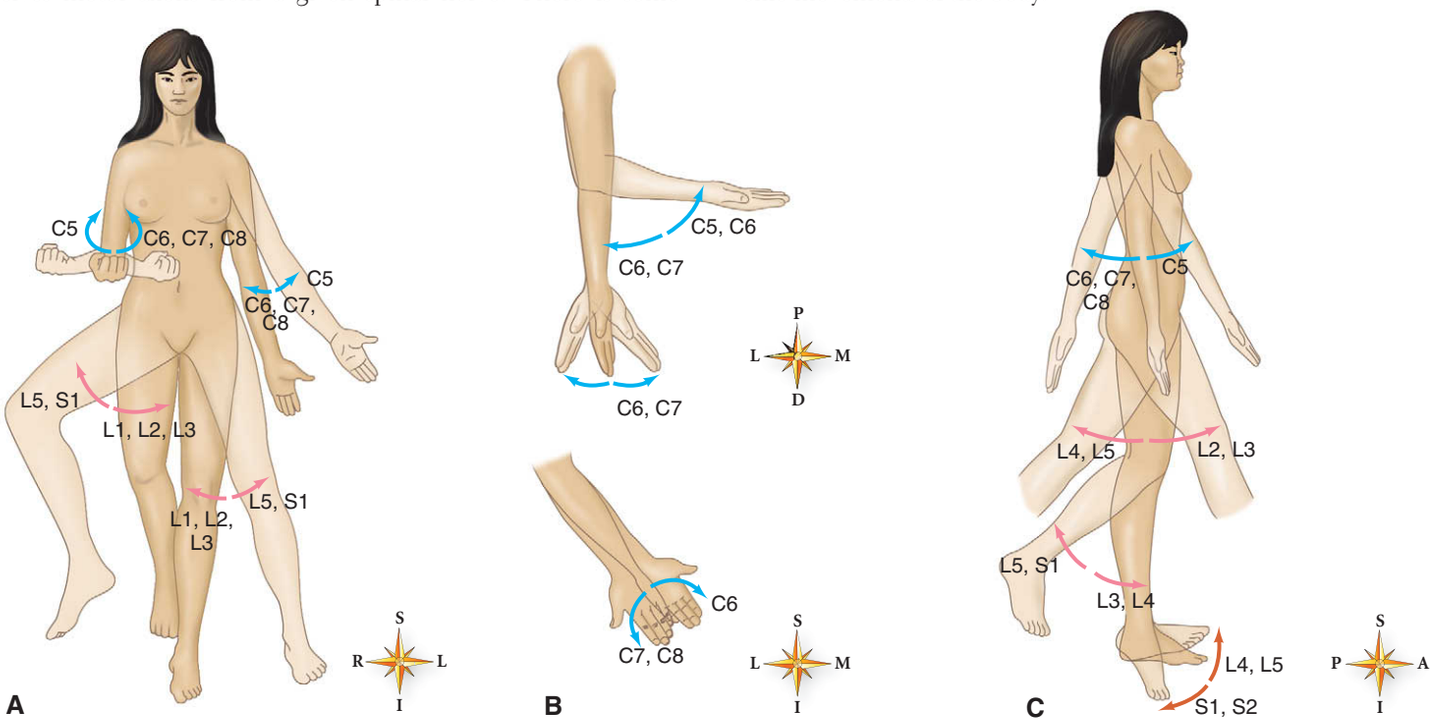


FIGURE 15-8

Myotomes and body movement. Myotomes are skeletal muscles innervated by one or more given spinal nerves. These examples show which spinal nerves innervate the skeletal muscles that produce the movements indicated by the arrows. **A,** Rotation and abduction/adduction of arm and hip. **B,** Flexion/extension of hand and wrist; pronation/supination of hand. **C,** Flexion/extension/hyperextension of arm, hip, knee; dorsiflexion and plantar flexion of foot. *C,* Cervical spinal nerves; *L,* lumbar spinal nerves; *S,* sacral spinal nerves.

CRANIAL NERVES

Twelve pairs of **cranial nerves** connect to the undersurface of the brain (Figure 15-9), mostly on the brainstem. Cranial nerves pass through small foramina (holes) in the cranial cavity of the skull, allowing them to extend to or from their peripheral destinations. Both names and numbers identify the cranial nerves. Their names suggest either their distribution—where they extend to (or from). For example, the optic nerve extends from the eye, carrying visual information. Their numbers indicate the order in which they connect to the brain from anterior to posterior. Roman numerals are most often used for cranial nerves, sometimes with the acronym CN (for "cranial nerve"). For example, the optic nerve is also known as *cranial nerve II* or *CN II*. Less frequently, Arabic numerals are used, as in CN 2.

As with all nerves, cranial nerves are made up of bundles of axons. **Mixed cranial nerves** contain axons of sensory and motor neurons. **Sensory cranial nerves** consist of sensory axons only, and **motor cranial nerves** consist mainly of motor axons. Cranial nerves classified as "motor nerves" contain a small number of sensory fibers. These sensory fibers are *proprioceptive* fibers that carry information regarding tension in the muscles controlled by the motor fibers of the same motor nerve. Table 15-2 lists the name, number, and functional classification of each of the 12 pairs of cranial nerves. Details of the structure and function of each

TABLE 15-2 Names, Numbers, and Functional Classifications of Cranial Nerves

NAME*	NUMBER	FUNCTIONAL CLASSIFICATION†
Olfactory	I	Sensory
Optic	II	Sensory
Oculomotor	III	Motor
Trochlear	IV	Motor
Trigeminal	V	Mixed
Abducens	VI	Motor
Facial	VII	Mixed
Vestibulocochlear	VIII	Sensory
Glossopharyngeal	IX	Mixed
Vagus	X	Mixed
Accessory	XI	Motor
Hypoglossal	XII	Motor

*The first letter of each word in the following sentence correlates with the first letter of the name of each of the cranial nerves, in the correct order, I to XII: **O**n **O**ld **O**lympus' **T**iny **T**ops, **A** **F**riendly **V**iking **G**rew **V**ines **A**nd **H**ops. Many anatomy students find that using this sentence, or one like it, helps in memorizing the names and numbers of the cranial nerves.

†The following sentence is a memory aid for learning the functional classification of each cranial nerve: **S**ome **S**ay '**M**arry **M**oney,' **B**ut **M**y **B**rothers **S**ay '**B**ad **B**usiness, **M**arry **M**oney.' In this sentence, **S** indicates *sensory,* **M** indicates *motor,* and **B** indicates *both* sensory and motor (mixed).

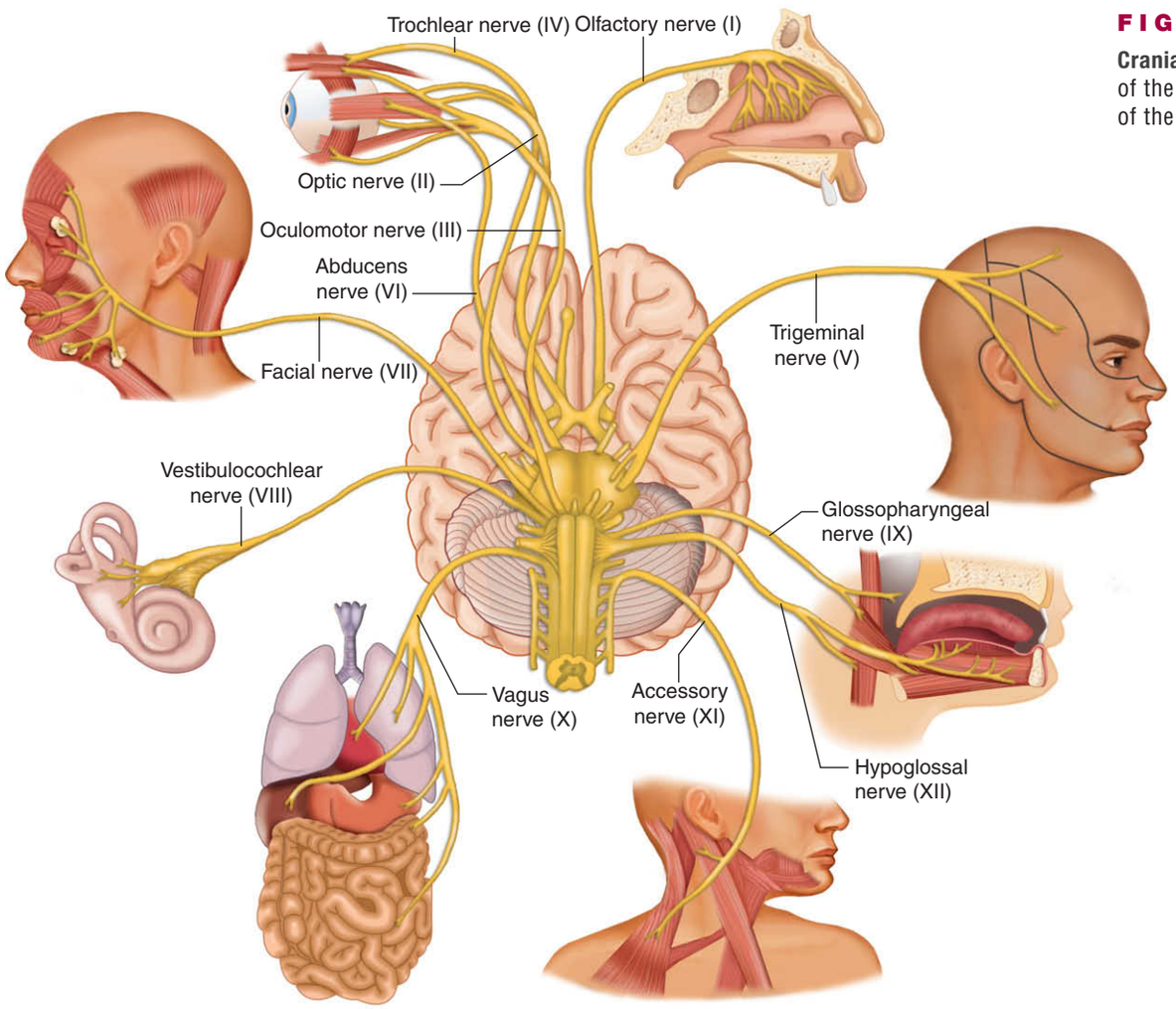


FIGURE 15-9
Cranial nerves. Ventral surface of the brain showing attachment of the cranial nerves.

cranial nerve are described in Table 15-3 and in the paragraphs that follow.

| QUICK CHECK |

1. How many pairs of spinal nerves are there? Can you name them?
2. What is a plexus? Name the four major pairs of plexuses.
3. What is a dermatome? A myotome?

Olfactory Nerve (I)

The **olfactory nerves** are composed of axons of neurons whose dendrites and cell bodies lie in the nasal mucosa, high up along the septum and superior conchae (turbinates). Axons of these neurons form about 20 small bundles of fibers that pierce each cribriform plate and terminate in the olfactory bulbs (see Figure 17-6, p. 514). Here they synapse with the second pool of olfactory neurons, whose axons compose the olfactory tracts. The olfactory nerves carry information about the sense of smell.

| A&P CONNECT |

Although you will not find it in most introductory anatomy texts, there is an additional pair of cranial nerves not found in the classic list of twelve. The **terminal nerve,** or cranial *nerve zero,* is a very thin nerve located near each olfactory nerve. Why is it often missing from the list? Why is it called nerve "zero?" And why are some scientists calling it the "sex nerve?" Check out ***Nerve Zero*** online at ***A&P Connect*** to find out!

evolve

Optic Nerve (II)

Axons from the innermost layer of sensory neurons of the retina compose the second pair of cranial nerves. They are called **optic nerves** because they carry visual information from the eyes to the brain. After entering the cranial cavity through the optic foramina, the two optic nerves unite to form the *optic chiasma*, in which some of the fibers of each nerve cross to the opposite side and continue in the *optic tract* of that side (see Figure 17-31, p. 533). Thus each optic nerve contains fibers only from the retina of the same side, whereas each optic tract has fibers in it from both retinas, an important fact in interpreting certain visual disorders.

Most of the optic tract fibers terminate in the thalamus (in the portion known as the *lateral geniculate nucleus*). From here a new relay of fibers runs to the visual area of the occipital lobe cortex. A few optic tract fibers terminate in the superior colliculi of the midbrain, where they synapse with motor fibers to the external eye muscles (cranial nerves III, IV, VI).

Oculomotor Nerve (III)

Fibers of each **oculomotor nerve** originate from cells in the oculomotor nucleus in the ventral part of the midbrain and extend to the various external eye muscles, with the exception of the superior oblique and the lateral rectus. Autonomic fibers are also present in the oculomotor nerves. They extend to the intrinsic muscles of the eye, which regulate the amount of light entering the eye and aid in focusing on near objects.

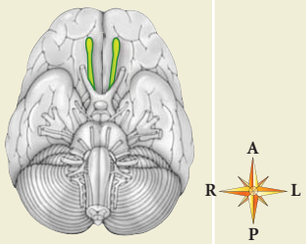
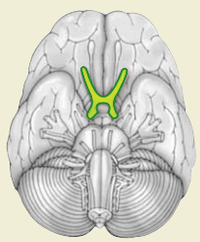
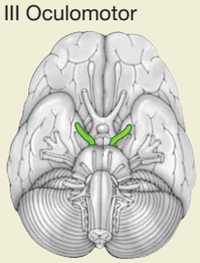
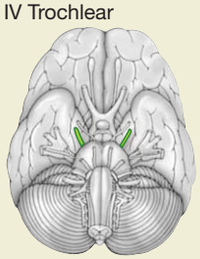
Yet a third group of fibers is found in the third cranial nerves. These are sensory fibers from proprioceptors in the eye muscles.

Trochlear Nerve (IV)

Motor fibers of each **trochlear nerve** have their origin in cells in the midbrain, from which they extend to the superior oblique muscles of the eye. The name *trochlear*, from a Greek word meaning "pulley," refers to the fact that the superior oblique muscles of the eye pass through a pulleylike ligament (see Figure 17-20, p. 526). Afferent fibers from proprioceptors in these muscles are also contained in the trochlear nerves.

TABLE 15-3 Structure and Function of the Cranial Nerves

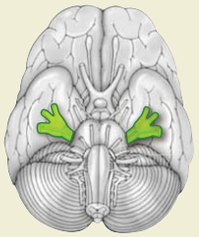
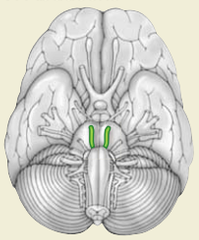
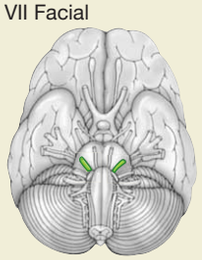
☐ sensory (afferent) ☐ motor (efferent)

	SENSORY FIBERS			MOTOR FIBERS		
NERVE	**RECEPTORS**	**CELL BODIES**	**TERMINATION**	**CELL BODIES**	**TERMINATION**	**FUNCTIONS**
I Olfactory 	Nasal mucosa	Nasal mucosa	Olfactory bulbs (new relay of neurons to olfactory cortex)			Sense of smell
II Optic 	Retina (proprioceptive)	Retina	Nucleus in thalamus (lateral geniculate); some fibers terminate in superior colliculus of midbrain			Vision
III Oculomotor 	External eye muscles except superior oblique and lateral rectus	Trigeminal ganglion	Midbrain (oculomotor nucleus)	Midbrain (oculomotor nucleus)	External eye muscles except superior oblique and lateral rectus; autonomic fibers terminate in ciliary ganglion and then to ciliary and iris muscles	Eye movements, regulation of size of pupil, accommodation (for near vision), proprioception (muscle sense)
IV Trochlear 	Superior oblique (proprioceptive)	Trigeminal ganglion	Midbrain	Midbrain	Superior oblique muscle of eye	Eye movements, proprioception

(continued)

TABLE 15-3 Structure and Function of the Cranial Nerves *(continued)*

□ sensory (afferent) □ motor (efferent)

	SENSORY FIBERS			MOTOR FIBERS		
NERVE	**RECEPTORS**	**CELL BODIES**	**TERMINATION**	**CELL BODIES**	**TERMINATION**	**FUNCTIONS**
V Trigeminal 	Skin and mucosa of head, teeth	Trigeminal ganglion	Pons (sensory nucleus)	Pons (motor nucleus)	Muscles of mastication	Sensations of head and face, chewing movements, proprioception
VI Abducens 	Lateral rectus (proprioceptive)	Trigeminal ganglion	Pons	Pons	Lateral rectus muscle of eye	Abduction of eye, proprioception
VII Facial 	Taste buds of anterior two thirds of tongue	Geniculate ganglion	Medulla (nucleus solitarius)	Pons	Superficial muscles of face and scalp; autonomic fibers to salivary and lacrimal glands	Facial expressions, secretion of saliva and tears, taste

(continued on page 492)

Trigeminal Nerve (V)

The fifth pair of cranial nerves is called **trigeminal nerves** because they each split into three large branches. The name trigeminal means "three pairs." The three branches of each pair are the *ophthalmic nerve*, *maxillary nerve*, and *mandibular nerve* (Figure 15-10).

Sensory neurons in all three branches of the trigeminal nerve carry afferent impulses from the skin and mucosa of the head and from the teeth to cell bodies in the trigeminal ganglion (lodged in the petrous part of the temporal bone). Fibers extend from the ganglion to the main sensory nucleus of the fifth cranial nerve situated in the pons. Some of the sensory pathways carry information from the mouth about the texture and temperature of food. The so-called *trigeminal senses* that contribute to the flavor of foods are discussed further in Chapter 17. Damage to some of the sensory pathways of the trigeminal nerve could lead to trigeminal neuralgia (Box 15-4).

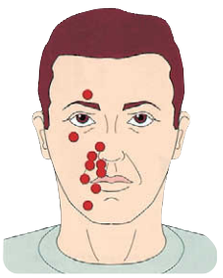
Motor fibers of the trigeminal nerve originate in the trifacial motor nucleus located in the pons just medial to the sensory

Box 15-4 | HEALTH matters

Trigeminal Neuralgia

Compression, inflammation, or degeneration of the fifth cranial nerve, the trigeminal nerve, may result in a condition called **trigeminal neuralgia,** or *tic douloureux* (tic doo-loo-ROO). This condition is characterized by recurring episodes of intense stabbing pain, or *neuralgia,* radiating from the angle of the jaw along a branch of the trigeminal nerve (see the figure).

Treatment with the drug carbamazepine (Tegretol) provides relief in most cases. If drugs do not provide relief, surgical methods may be used. The most drastic method of pain reduction is removal of the trigeminal ganglion on the posterior portion of the nerve (see Figure 15-10). This large ganglion contains the cell bodies of the nerve's afferent fibers. After such an operation, the patient's face, scalp, teeth, and conjunctiva on the side treated show anesthesia (loss of sensation). Therefore, special care, such as wearing protective goggles and irrigating the eye frequently, is prescribed. The patient is also instructed to visit the dentist regularly because he or she can no longer experience a toothache—a warning of diseased teeth.



Pain zones in trigeminal neuralgia.

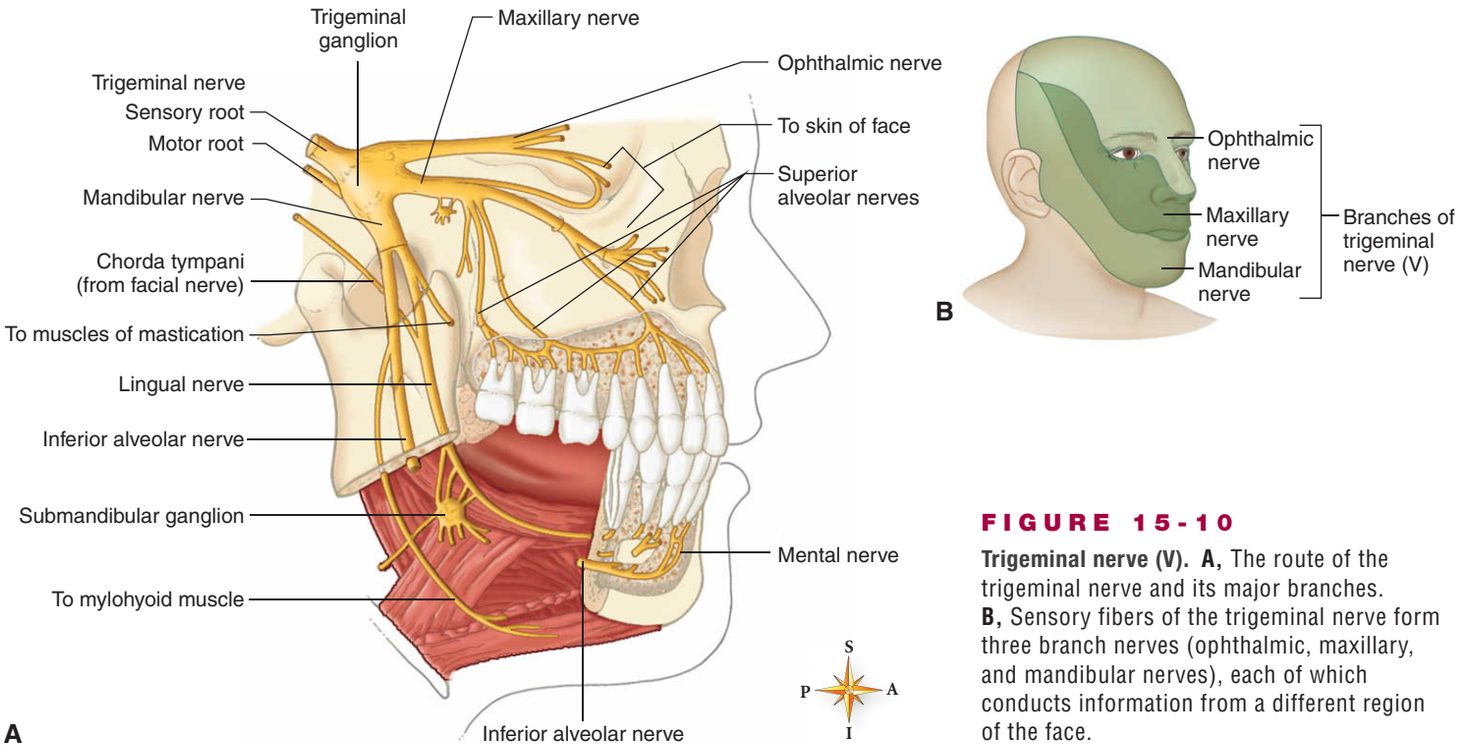


FIGURE 15-10

Trigeminal nerve (V). A, The route of the trigeminal nerve and its major branches. **B,** Sensory fibers of the trigeminal nerve form three branch nerves (ophthalmic, maxillary, and mandibular nerves), each of which conducts information from a different region of the face.

nucleus. These motor fibers run to the muscles of mastication by way of the mandibular nerve.

Abducens Nerve (VI)

Each **abducens nerve** is a motor nerve with fibers originating from a nucleus in the pons in the floor of the fourth ventricle and extending to the lateral rectus muscles of the eyes (see Figure 17-20, p. 526). The lateral rectus muscle *abducts* the eye to which it is attached, hence the name *abducens* for this nerve. The sixth cranial nerve also contains some afferent fibers from proprioceptors in the lateral rectus muscles.

Facial Nerve (VII)

The motor fibers of the **facial nerve** arise from a nucleus in the lower part of the pons, from which they extend by way of several branches to the superficial muscles of the face and scalp (Figure 15-11). Efferent autonomic fibers of the facial nerve extend to the submaxillary and sublingual salivary glands, as well as to the lacrimal (tear) glands. Sensory fibers from the taste buds of the anterior two thirds of the tongue run in the facial nerve to cell bodies in the geniculate ganglion, a small swelling on the facial nerve, where it passes through a canal in the temporal bone. From the ganglion, fibers extend to a nucleus in the medulla.

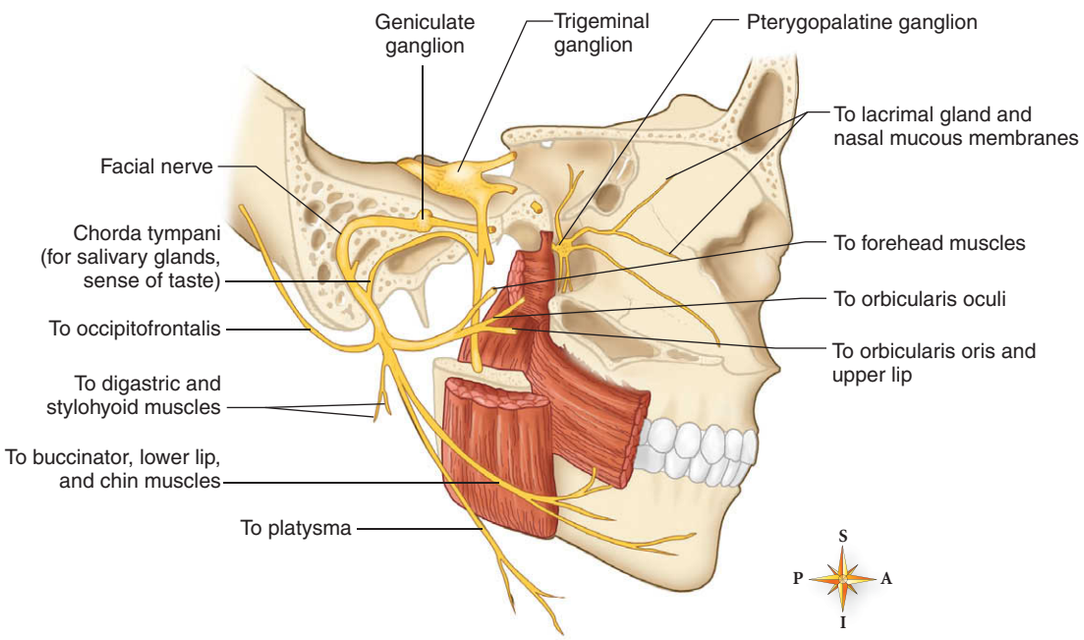
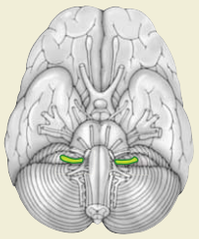
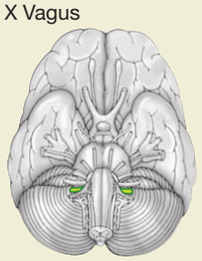


FIGURE 15-11

Facial nerve (VII). Artist's interpretation of the location of the various branches of the facial nerve.

TABLE 15-3 Structure and Function of the Cranial Nerves *(continued)*

□ sensory (afferent) □ motor (efferent)

	SENSORY FIBERS			MOTOR FIBERS		
NERVE	**RECEPTORS**	**CELL BODIES**	**TERMINATION**	**CELL BODIES**	**TERMINATION**	**FUNCTIONS**
VIII Vestibulocochlear						
Vestibular branch	Semicircular canals and vestibule (utricle and saccule)	Vestibular ganglion	Pons and medulla (vestibular nuclei)			Balance or equilibrium sense
Cochlear (auditory) branch	Spiral (Corti) organ in cochlear duct	Spiral ganglion	Pons and medulla (cochlear nuclei)			Hearing
IX Glossopharyngeal 	Pharynx; taste buds and other receptors of posterior one third of tongue	Jugular and petrous ganglia	Medulla (nucleus solitarius)	Medulla (nucleus ambiguus)	Muscles of pharynx	Sensations of tongue, swallowing movements, secretion of saliva, aid in reflex control of blood pressure and respiration
	Carotid sinus and carotid body	Jugular and petrous ganglia	Medulla (respiratory and vasomotor centers)	Medulla at junction of pons (nucleus salivatorius)	Otic ganglion and then to parotid salivary gland	
X Vagus 	Pharynx, larynx, carotid body, thoracic and abdominal viscera	Jugular and nodose ganglia	Medulla (nucleus solitarius), pons (nucleus of fifth cranial nerve)	Medulla (dorsal motor nucleus)	Ganglia of vagal plexus and then to muscles of pharynx, larynx, and autonomic fibers to thoracic and abdominal viscera	Sensations and movements of organs supplied; e.g., slows heart, increases peristalsis, contracts muscles for voice production

(continued on page 480)

Vestibulocochlear Nerve (VIII)

The **vestibulocochlear nerve** has two distinct divisions: the *vestibular nerve* and the *cochlear nerve* (see Figure 17-12, p. 519). Both are sensory.

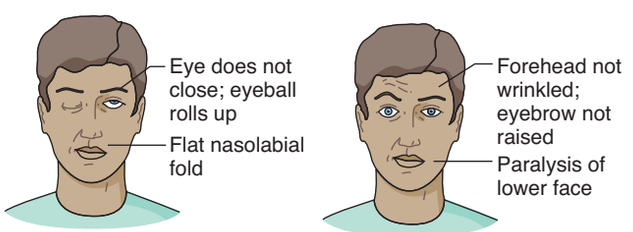
Fibers from the semicircular canals in the inner ear run to the vestibular ganglion (in the internal acoustic meatus). Here, the neurons' cell bodies are located, and from them, fibers extend to the vestibular nuclei in the pons and medulla. Together, these fibers constitute the *vestibular nerve*. Some of its fibers run to the cerebellum. The vestibular nerve transmits impulses that result in sensations of equilibrium.

The *cochlear nerve* consists of peripheral axon fibers starting in the organ of Corti in the cochlea of the inner ear. They have their cell bodies in the spiral ganglion in the cochlea, and their central axon fibers terminate in the cochlear nuclei located between the medulla and pons. Conduction by the cochlear nerve results in sensations of hearing. Damage to this nerve can cause deafness (Box 15-5). Because of its role in hearing, the eighth cranial nerve is sometimes still called the *auditory* or *acoustic* nerve.

Box 15-5 | HEALTH matters

Cranial Nerve Damage

Severe head injuries often damage one or more of the cranial nerves, producing symptoms that reflect loss of the functions mediated by the affected nerve or nerves. For example, injury of the sixth cranial nerve causes the eye to turn in because of paralysis of the abducting muscle of the eye. Injury of the eighth cranial nerve, on the other hand, produces deafness. Injury to the facial nerve results in a poker-faced expression and a drooping of the corner of the mouth from paralysis of the facial muscles.



Signs of damage to the facial nerve (VII).

Glossopharyngeal Nerve (IX)

Both sensory and motor fibers compose the **glossopharyngeal nerve.** This nerve supplies fibers not only to the tongue and pharynx (throat), as its name implies, but also to other structures (Figure 15-12). One is the carotid sinus. The carotid sinus plays an important part in the control of blood pressure. Sensory fibers, with their receptors in the pharynx and posterior one third of the tongue, have their cell bodies in the jugular (superior) and petrous (inferior) ganglia. These are located, respectively, in the jugular foramen and the petrous part of the temporal bone. The ganglia fibers extend to a nucleus in the medulla.

The motor fibers of the ninth cranial nerve originate in another medullary nucleus and run to muscles of the pharynx. Also present in this nerve are autonomic fibers that originate in a nucleus at the junction of the pons and medulla. These fibers run to the otic ganglion, from which postganglionic fibers extend to the parotid gland.

Vagus Nerve (X)

The **vagus nerve** contains both sensory and motor fibers. The name vagus means "wanderer" and aptly describes this nerve with many widely distributed branches. Its sensory fibers supply the pharynx, larynx, trachea, heart, carotid body, lungs, bronchi, esophagus, stomach, small intestine, and gallbladder (Figure 15-13). Cell bodies attached to these sensory fibers lie in the jugular and nodose ganglia, which are located, respectively, in the jugular foramen and just inferior to it on the trunk of the nerve. The sensory axons terminate in the medulla and in the pons. Somatic motor fibers of the vagus travel to the pharynx and larynx (voice box), where they control muscles involved in swallowing.

Most motor fibers of the vagus nerve are autonomic (parasympathetic) fibers. They originate in cells in the medulla and extend to various autonomic ganglia. From there, the fibers run to muscles of the pharynx, larynx, and thoracic and abdominal organs, where they control heart rate and other "visceral" activities.

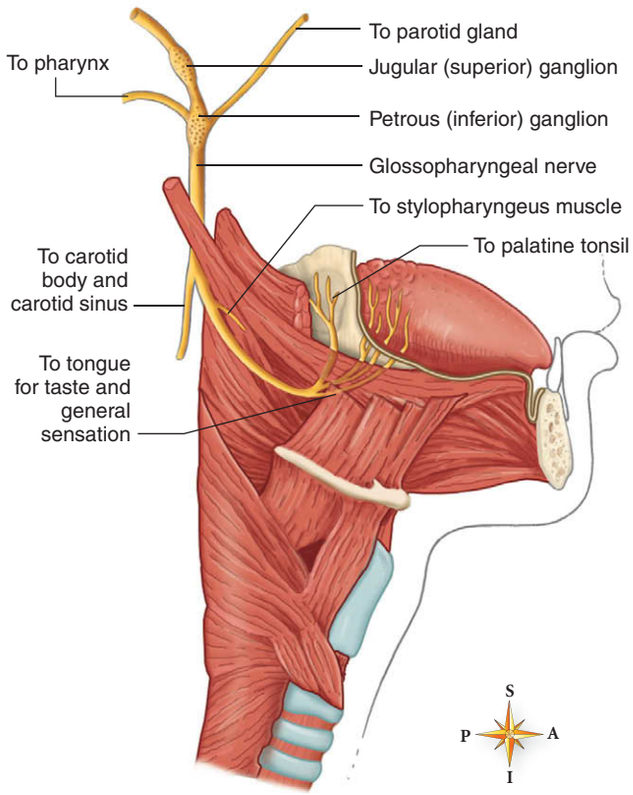


FIGURE 15-12

Glossopharyngeal nerve (IX). As its name implies (*glosso-*, "tongue"; *-pharyng-*, "throat"), the ninth cranial nerve supplies fibers to the tongue and throat. It is a mixed nerve that carries both sensory and motor fibers.

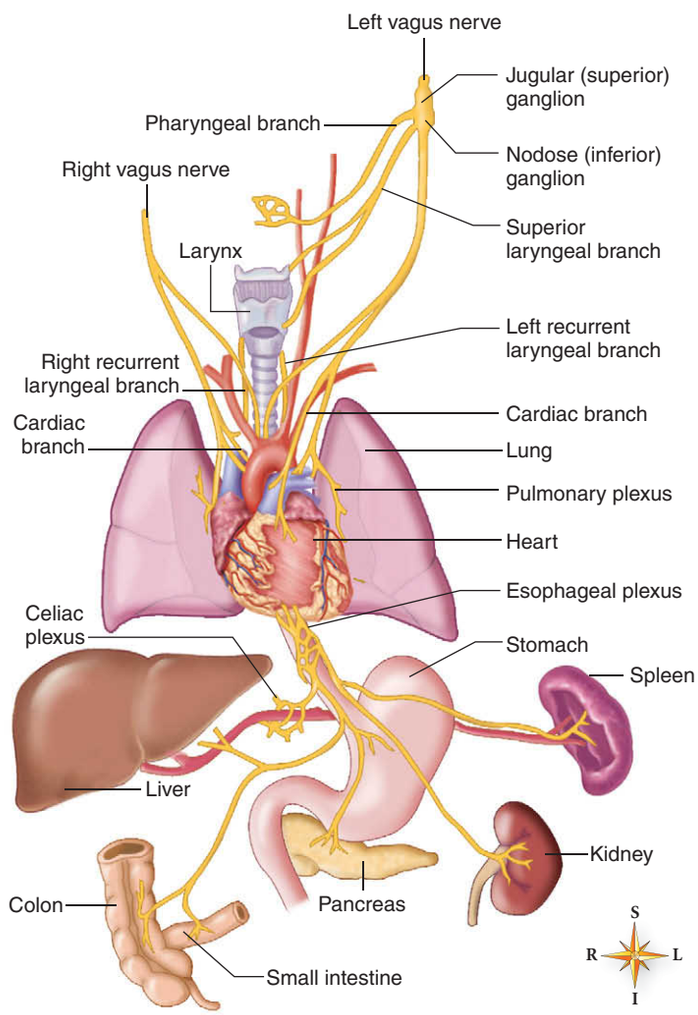
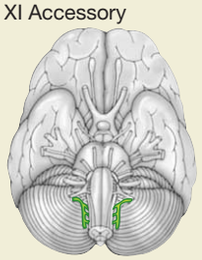
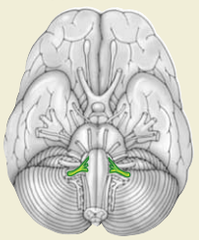


FIGURE 15-13

Vagus nerve (X). The vagus nerve is a mixed cranial nerve with many widely distributed branches—hence the name *vagus,* which is the Latin word for "wanderer."

TABLE 15-3 Structure and Function of the Cranial Nerves *(continued)*

☐ sensory (afferent) ☐ motor (efferent)

	SENSORY FIBERS			MOTOR FIBERS		
NERVE	**RECEPTORS**	**CELL BODIES**	**TERMINATION**	**CELL BODIES**	**TERMINATION**	**FUNCTIONS**
XI Accessory 	Trapezius and sternocleidomastoid (proprioceptive)	Upper, cervical ganglia	Spinal cord	Anterior gray column of first five or six cervical segments of spinal cord	Trapezius and sternocleidomastoid muscle	Shoulder movements, turning movements of head, proprioception
XII Hypoglossal 	Tongue muscles (proprioceptive)	Trigeminal ganglion	Medulla (hypoglossal nucleus)	Medulla (hypoglossal nucleus)	Muscles of tongue and throat	Tongue movements, proprioception

Accessory Nerve (XI)

The **accessory nerve** is a motor nerve historically considered to be an "accessory" to the vagus nerve. In a very few individuals, some of its fibers originate in cells in the medulla and join the fibers of the vagus nerve. However, we now know that in most people, all the fibers of this nerve originate in the upper cervical region (C1-C5) of the spinal cord—and none of the fibers originate in the brain. From there, they extend to the trapezius and sternocleidomastoid muscles (Figure 15-14).

The accessory nerve is still classified as a cranial nerve because it passes into the foramen magnum and then through the cranial cavity, where it exits by way of the jugular foramen. Like the other cranial nerves, this cranial nerve also exits the cranial cavity.

Because of its spinal origin, the eleventh cranial nerve was formerly called the *spinal accessory nerve.*

Hypoglossal Nerve (XII)

Motor fibers with cell bodies in the hypoglossal nucleus of the medulla compose the twelfth cranial nerve. They supply the muscles of the tongue (see Figure 15-9). The **hypoglossal nerve** also contains sensory fibers from proprioceptors in muscles of the tongue. The name *hypoglossal* means "under the tongue."

Table 15-3 summarizes the main facts about the distribution and function of each of the cranial nerve pairs.

| QUICK CHECK |

4. List the names and numbers of the 12 pairs of cranial nerves.
5. Identify the primary function of each pair of cranial nerves.
6. Distinguish between a motor nerve, sensory nerve, and mixed nerve.

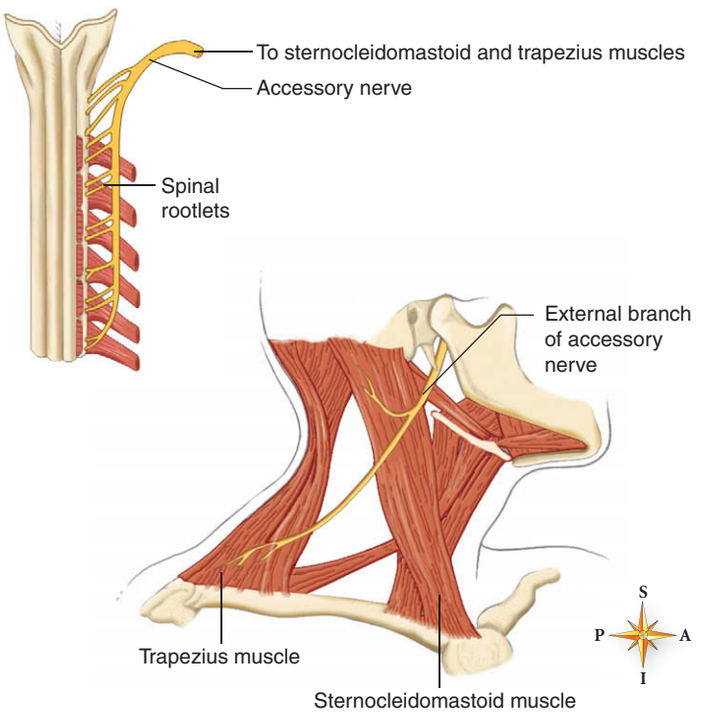


FIGURE 15-14

Accessory nerve (XI). This cranial nerve is an "accessory" to the vagus nerve because some of its fibers join the vagus nerve before traveling on to the viscera, pharynx, and larynx. Fibers that originate in the cervical spinal segments travel through an external nerve branch to the trapezius and sternocleidomastoid muscles of the neck.

SOMATIC MOTOR NERVOUS SYSTEM

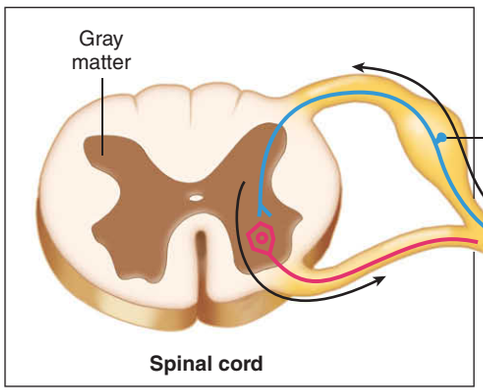
Divisions of the Peripheral Nervous System

Recall from Chapter 13 that the PNS includes all the nervous pathways *outside* the brain and spinal cord (see Figure 13-2, p. 382). Thus the entire PNS includes the fibers present in the cranial nerves, the spinal nerves, and all their individual branches. Although many of these nerves are *mixed nerves*—containing both sensory and motor fibers—it is often convenient to consider the PNS as having two functional divisions: the sensory (afferent) division and the motor (efferent) division. In this chapter, we concentrate on some essential details of the somatic motor division of the PNS—the *somatic motor nervous system*. Then in Chapter 16 we move on to discuss the efferent pathways of the *autonomic nervous system*. Details of the sensory division of the PNS are discussed in Chapter 17.

BASIC PRINCIPLES OF SOMATIC MOTOR PATHWAYS

The somatic motor nervous system includes all the voluntary motor pathways outside the CNS. That is, it involves the peripheral pathways to the skeletal muscles, which are the *somatic effectors*. Recall from Chapter 14 that all these pathways operate according to the principle of *final common path*. This means that all the somatic motor pathways involve a single motor neuron whose axon stretches from the cell body in the CNS all the way to the effector innervated by that neuron. For fibers that originate in the spinal cord, this means that the axon extends from the anterior gray horn, through the ventral nerve root, and out to a skeletal muscle.

Another important principle of somatic motor pathways was mentioned in Chapter 12, when we were discussing the function of skeletal muscles. This principle states that the axon of the last somatic motor neuron—also called the *anterior horn neuron* or *lower motor neuron*—stimulates effector cells by means of the neurotransmitter **acetylcholine.** This fact will have added importance later when we compare the somatic motor nervous system with the ANS.



Because the basic plan of the somatic motor pathways was discussed in Chapter 14, and the effect of acetylcholine on the somatic effectors (skeletal muscles) has already been outlined in Chapter 11, we will end our discussion of the somatic motor division of the PNS with a brief review of the concept of the reflex arc and how it relates to peripheral motor pathways.

SOMATIC REFLEXES

Nature of a Reflex

The action that results from a nerve impulse passing over a reflex arc is called a **reflex** (see Figure 13-10, p. 390). In other words, a reflex is a predictable response to a stimulus. It may or may not be conscious. Usually the term is used to mean only involuntary responses rather than those directly willed. If the center of a reflex arc is in the brain, the response it mediates is called a **cranial reflex.** If the center of a reflex arc is in the spinal cord, the response is called a **spinal reflex.**

A reflex consists of either muscle contraction or glandular secretion.

Somatic reflexes are contractions of skeletal muscles. Impulse conduction over somatic reflex arcs—arcs whose motor neurons are somatic motor neurons (i.e., anterior horn neurons or lower motor neurons)—produces somatic reflexes.

Autonomic (visceral) reflexes consist of contractions of smooth or cardiac muscle or secretion by glands. Visceral reflexes are mediated by impulse conduction over autonomic reflex arcs, the motor neurons of which are autonomic neurons (discussed later).

The following paragraphs describe only somatic reflexes.

Somatic Reflexes of Clinical Importance

Clinical interest in reflexes stems from the fact that they deviate from normal in certain diseases. Therefore the testing of reflexes is a valuable diagnostic aid. The following reflexes are frequently tested: knee jerk, ankle jerk, plantar reflex, corneal reflex, and abdominal reflex.

Knee Jerk Reflex

The **knee jerk reflex,** or *patellar reflex*, is an extension of the leg in response to tapping of the patellar ligament (Figures 15-15 and

FIGURE 15-15

Patellar reflex. Neural pathway involved in the patellar (knee jerk) reflex.

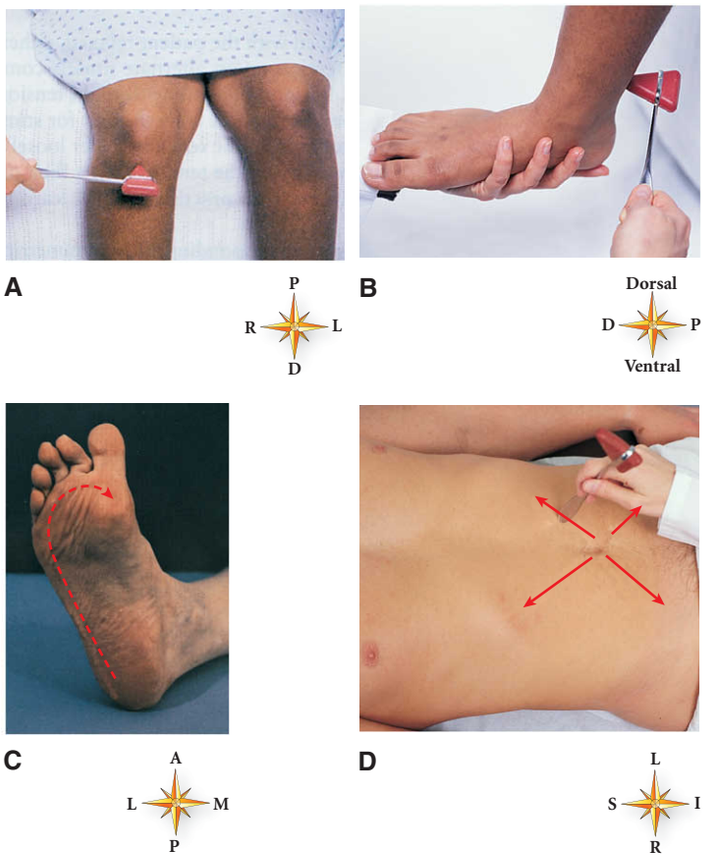


FIGURE 15-16

Common clinical reflex tests. A, Knee jerk reflex. **B,** Ankle jerk reflex. **C,** Plantar reflex showing the Babinski sign (arrow shows path of stimulation along plantar surface). **D,** Abdominal reflexes (one of several ways to test this type of reflex). As an object is moved away from umbilicus and toward the side, the rectus abdominis muscles pull the umbilicus toward the stroked side.

15-16, A). The tap stretches the ligament, pulling on the patella and the tendon of the quadriceps femoris muscles and thereby stimulates muscle spindles (receptors) in the muscle and initiates conduction over the following two-neuron reflex arc:

- Sensory neurons

  Peripheral axon fibers—in femoral and second, third, and fourth lumbar nerves

  Cell bodies—second, third, and fourth lumbar ganglia

  Central axon fibers—in posterior roots of second, third, and fourth lumbar nerves; terminate in these segments of the spinal cord; synapse directly with lower motor neurons

- Reflex center—synapses in anterior gray column between axons of sensory neurons and dendrites and cell bodies of lower motor neurons
- Motor neurons

  Dendrites and cell bodies—in spinal cord anterior gray column

  Axons—in anterior roots of second, third, and fourth lumbar spinal nerves and femoral nerves; terminate in quadriceps femoris muscle

The knee jerk can be classified in various ways as follows:

- As a *spinal cord reflex*—because the center of the reflex arc (which transmits the impulses that activate the muscles producing the knee jerk) lies in the spinal cord gray matter
- As a *segmental reflex*—because impulses that mediate it enter and leave the same segment of the cord
- As an *ipsilateral reflex*—because the impulses that mediate it come from and go to the same side of the body (a *contralateral reflex*, on the other hand, would trigger a response on the opposite side of the body)
- As a *stretch reflex* or *myotatic reflex* (from the Greek *mys-*, "muscle," *-tasis*, "stretching")—because of the kind of stimulation used to evoke it
- As an *extensor reflex*—because it is produced by extensors of the leg (muscles located on the anterior surface of the thigh, which extend the leg)
- As a *deep reflex*—because of the deep location (in muscle) of the receptors stimulated to produce this reflex (as opposed to *superficial reflexes*—those elicited by stimulation of receptors located in the skin or mucosa)

When testing a patient's reflexes, a physician interprets the test results on the basis of what is known about the reflex arcs that must function to produce normal reflexes.

To illustrate, suppose that a patient has been diagnosed as having poliomyelitis. During the examination the physician finds that she cannot elicit the knee jerk when she taps the patient's patellar tendon. She knows that the poliomyelitis virus attacks anterior horn motor neurons. She also knows the information previously related about which spinal cord segments contain the reflex centers for the knee jerk. On the basis of this knowledge, therefore, she deduces that in this patient the poliomyelitis virus has damaged the second, third, and fourth lumbar segments of the spinal cord. Do you think that this patient's leg would be paralyzed, that he would be unable to move it voluntarily? What neurons would not be able to function that must function to produce voluntary contractions?

Ankle Jerk Reflex

Ankle jerk reflex, or *Achilles reflex*, is an extension (plantar flexion) of the foot in response to tapping of the Achilles tendon (Figure 15-16, *B*). As with the knee jerk, it is a tendon reflex and a deep reflex mediated by two-neuron spinal arcs. The centers for the ankle jerk lie in the first and second sacral segments of the cord.

Plantar Reflex

The **plantar reflex** consists of a curling under of all the toes (plantar flexion) plus a slight turning in and flexion of the

anterior part of the foot in response to stimulation of the outer edge of the sole.

The **Babinski sign,** however, is an extension of the great toe, with or without fanning of the other toes, in response to stimulation of the outer margin of the sole of the foot (Figure 15-16, *C*). Normal infants, up until they are about 1½ years old, exhibit this Babinski sign. At about 18 months, corticospinal fibers have become fully myelinated and the Babinski sign becomes suppressed. A Babinski sign after this age is abnormal and is one of the pyramidal signs (see Box 14-9, p. 429). It is interpreted to mean destruction of pyramidal tract (corticospinal) fibers.

Corneal Reflex

The **corneal reflex** is blinking in response to the cornea being touched. It is mediated by reflex arcs with sensory fibers in the ophthalmic branch of the fifth cranial nerve, centers in the pons, and motor fibers in the seventh cranial nerve.

Abdominal Reflex

The **abdominal reflex** occurs when the umbilicus moves in response to stroking the side of the abdomen (Figure 15-16, *D*). It is mediated by arcs with sensory and motor fibers in the ninth to twelfth thoracic spinal nerves and centers in these segments of the cord. It is classified as a superficial reflex. A decrease in this reflex or its absence occurs in lesions involving pyramidal tract upper motor neurons. It can, however, be absent without any pathological condition—in pregnancy, for example.

| QUICK CHECK |

7. What are the somatic effectors?
8. State the principle of final common path as it applies to the somatic motor nervous system.
9. Explain how the knee jerk reflex can be both a stretch reflex and a spinal reflex.

the BIG picture

Peripheral Nervous System and the Whole Body

The peripheral nervous system is made up of all the afferent nervous pathways coming into the CNS and all the efferent pathways going out of the CNS. After reviewing all the major spinal and cranial nerves, including their major branches, we turned our attention to the efferent somatic pathways. The next chapter (16) will continue the story by picking up with the efferent autonomic pathways. We will finally finish the story of the nervous system with the peripheral afferent (sensory) pathways in Chapter 17.

The peripheral motor pathways are simply those nervous pathways that lead from the integrator (CNS) to the effectors. The somatic motor pathways lead to skeletal muscle effectors, allowing them to carry information that regulates how and when our voluntary muscles contract. This allows us to move our skeleton and accomplish many of the tasks that promote survival and make life productive and enjoyable. Somatic motor pathways also control our breathing—a topic we will explore in later chapters. Less obviously—but just as importantly—somatic motor pathways are directly involved in producing heat with our skeletal muscles.

UNIT 3

LANGUAGE OF SCIENCE (continued from p. 463)

cranial reflex
(KRAY-nee-al REE-fleks)
[*crani-* **skull,** *-al* **relating to,** *re-* **again,** *-flex* **bend**]

dermatome
(DER-mah-tohm)
[*derma-* **skin,** *-tome* **cut segment or region**]

dorsal ramus
(DOR-sal RAY-mus)
[*dors-* **the back,** *-al* **relating to,** *ramus* **branch**] *pl.,* rami

dorsal root
(DOR-sal)
[*dors-* **the back,** *-al* **relating to**]

facial nerve
(FAY-shal)
[*faci-* **face,** *-al* **relating to**]

ganglion
(GANG-lee-on)
[*gangli-* **knot,** *-on* **unit**] *pl.,* ganglia

glossopharyngeal nerve
(glos-oh-fah-RIN-jee-al)
[*glosso-* **tongue,** *-pharyng-* **throat,** *-al* **relating to**]

hypoglossal nerve
(hye-poh-GLOS-al)
[*hypo-* **under or below,** *-gloss-* **tongue,** *-al* **relating to**]

knee jerk reflex
[*re-* **again,** *-flex* **bend**]

lumbar plexus
(LUM-bar PLEK-sus)
[*lumb-* **loin,** *-ar* **relating to,** *plexus* **network**] *pl.,* plexi or plexuses

mixed cranial nerve
(KRAY-nee-al)
[*crani-* **skull,** *-al* **relating to**]

mixed nerve
motor cranial nerve
(KRAY-nee-al)
[*mot-* **movement,** *-or* **agent,** *crani-* **skull,** *-al* **relating to**]

myotome
(MY-oh-tohm)
[*myo-* **muscle,** *-tome* **cut segment or region**]

oculomotor nerve
(awk-yoo-loh-MOH-tor)
[*oculo-* **eye,** *mot-* **movement,** *-or* **agent**]

olfactory nerve
(ol-FAK-tor-ee)
[*olfact-* **smell,** *-ory* **relating to**]

optic nerve
(OP-tik)
[*opt-* **vision,** *-ic* **relating to**]

phrenic nerve
(FREN-ik)
[*phren-* **mind,** *-ic* **relating to**]

plantar reflex
(PLAN-tar REE-fleks)
[*planta-* **sole,** *-ar* **relating to,** *re-* **again,** *-flex* **bend**]

plexus
(PLEK-sus)
[*plexus* **network**] *pl.,* plexi or plexuses

LANGUAGE OF SCIENCE (continued from p. 483)

ramus
(RAY-mus)
[*ramus* **branch**] *pl.,* rami

reflex
(REE-fleks)
[*re-* **again,** *-flex* **bend**]

sacral plexus
(SAY-kral PLEK-sus)
[*sacr-* **sacred,** *-al* **relating to,** *plexus* **network**] *pl.,* plexi or plexuses

sciatic nerve
(sye-AT-ik)
[*(i)sci-* **hip joint,** *-atic* **relating to**]

sensory cranial nerve
(SEN-sor-ee KRAY-nee-al)
[*sens-* **feel,** *-ory* **relating to,** *crani-* **skull,** *-al* **relating to**]

somatic reflex
(so-MAH-tik REE-fleks)
[*soma-* **body,** *-ic* **relating to,** *re-* **again,** *-flex* **bend**]

spinal nerve
(SPY-nal)
[*spine-* **backbone,** *-al* **relating to**]

spinal reflex
(SPY-nal REE-fleks)
[*spine-* **backbone,** *-al* **relating to,** *re-* **again,** *-flex* **bend**]

terminal nerve
(TER-mih-nal)
[*termin-* **boundary,** *-al* **relating to**]

trigeminal nerve
(try-JEM-i-nal)
[*tri-* **three,** *-gemina-* **twin or pair,** *-al* **relating to**]

trochlear nerve
(TROK-lee-ar)
[*trochlea-* **pulley,** *-al* **relating to**]

vagus nerve
(VAY-gus)
[*vagus* **wanderer**]

ventral ramus
(VEN-tral RAY-mus)
[*ventr-* **belly,** *-al* **relating to** *ramus* **branch**] *pl.,* rami

ventral root
(VEN-tral root)
[*ventr-* **belly,** *-al* **relating to**]

vestibulocochlear nerve
(ves-TIB-yoo-loh-kok-lee-ar)
[*vestibulo-* **entrance hall,** *-cochle-* **sea shell,** *-ar* **relating to**]

LANGUAGE OF MEDICINE

Babinski sign
(bah-BIN-skee)
[*Joseph F.F. Babinski* **French neurologist**]

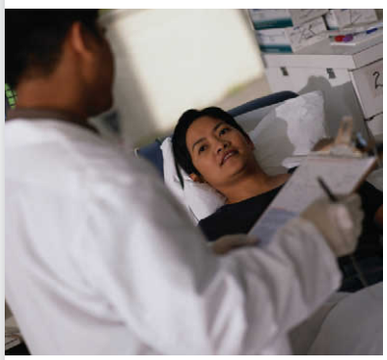
herpes zoster
(HER-peez ZOS-ter)
[*herpe* **creep,** *zoster* **girdle**]

peripheral neuropathy
(peh-RIF-er-al noo-ROP-ah-thee)
[*peri-* **around,** *-phera-* **boundary,** *-al* **relating to,** *neuro-* **nerves,** *-path-* **disease,** *-y* **state**]

shingles
(SHING-guls)
[**from** *cingul-* **girdle**]

trigeminal neuralgia
(try-JEM-i-nal noo-RAL-jee-ah)
[*tri-* **three,** *-gemina-***twins or pair,** *-al* **relating to,** *neur-* **nerves,** *-algia* **pain**]

CASE study



The store was only two blocks away. Tomasina was in such a hurry, and it was so close, she didn't think she really needed to rummage through the garage for her bike helmet. She jumped on her bike and peddled quickly toward the store. From out of nowhere, a car sped by—too close to the side of the road—and clipped Tomasina with the side mirror, knocking her to the ground, banging her head sharply on the curb. When she regained consciousness, Tomasina was in the hospital. She was told some tests would be conducted to see whether her cranial nerves had been affected by the head injury.

1. In one of the tests, Tomasina was asked to stick out her tongue. Which cranial nerve was being tested?
   a. Glossopharyngeal
   b. Hypoglossal
   c. Vagus
   d. Trigeminal
2. In a second test, Tomasina's hearing was evaluated. What cranial nerve is involved in the sense of hearing?
   a. Accessory
   b. Vagus
   c. Vestibulocochlear
   d. Trochlear
3. Tomasina was having difficulty focusing her eyes and following the doctor's finger on command. Which of the following cranial nerves does not control eye movement?
   a. Optic
   b. Oculomotor
   c. Trochlear
   d. Abducens
4. The nurse touched a series of swabs with different tastes to the front portion of Tomasina's tongue—sugar, salt, lemon juice, and dissolved aspirin. Which cranial nerve was the nurse testing?
   a. Glossopharyngeal
   b. Olfactory
   c. Trigeminal
   d. Facial

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

SPINAL NERVES

A. Overview
1. Thirty-one pairs of spinal nerves are connected to the spinal cord (Figure 15-1)
2. No special names; numbered by level of vertebral column at which they emerge from the spinal cavity
   a. Eight cervical nerve pairs (C1 through C8)
   b. Twelve thoracic nerve pairs (T1 through T12)
   c. Five lumbar nerve pairs (L1 through L5)
   d. Five sacral nerve pairs (S1 through S5)
   e. One coccygeal nerve pair
3. Lumbar, sacral, and coccygeal nerve roots descend from point of origin to the lower end of the spinal cord (level of first lumbar vertebra) before reaching the intervertebral foramina of the respective vertebrae, through which the nerves emerge
4. Cauda equina—describes the appearance of the lower end of the spinal cord and its spinal nerves as a horse's tail

B. Structure of spinal nerves
1. Each spinal nerve attaches to spinal cord by a ventral (anterior) root and a dorsal (posterior) root
2. Dorsal root ganglion—swelling in the dorsal root of each spinal nerve
3. All spinal nerves are mixed nerves
4. Ramus
   a. One of several large branches formed after each spinal nerve emerges from the spinal cavity (Figure 15-2)
   b. Dorsal ramus—supplies somatic motor and sensory fibers to smaller nerves that innervate the muscles and skin of the posterior surface of the head, neck, and trunk
   c. Ventral ramus
      (1) Structure is more complex than that of dorsal ramus
      (2) Autonomic motor fibers split from the ventral ramus and head toward a ganglion of the sympathetic chain
      (3) Some autonomic fibers synapse with neurons that continue on to autonomic effectors through splanchnic nerves; others synapse with neurons whose fibers rejoin the ventral ramus
      (4) Sympathetic rami—splitting and rejoining of autonomic fibers
      (5) Motor and sensory fibers innervate muscles and glands in the extremities and lateral and ventral portions of neck and trunk

C. Nerve plexuses
1. Plexuses—complex networks formed by the ventral rami of most spinal nerves (not T2 through T12) subdividing and then joining together to form individual nerves
2. Each individual nerve that emerges contains all the fibers that innervate a particular region of the body
3. In plexuses, spinal nerve fibers are rearranged according to their ultimate destination, reducing the number of nerves needed to supply each body part
4. Four major pairs of plexuses
   a. Cervical plexus (Figure 15-3)
      (1) Located deep within the neck
      (2) Made up of ventral rami of C1 through C4 and a branch of the ventral ramus of C5
      (3) Individual nerves emerging from cervical plexus innervate the muscles and skin of the neck, upper shoulders, and part of the head
      (4) Phrenic nerve exits the cervical plexus and innervates the diaphragm
   b. Brachial plexus (Figure 15-4)
      (1) Located deep within the shoulder
      (2) Made up of ventral rami of C5 through T1
      (3) Individual nerves emerging from brachial plexus innervate the lower part of the shoulder and the entire arm
   c. Lumbar plexus (Figure 15-5)
      (1) Located in the lumbar region of the back in the psoas muscle
      (2) Formed by intermingling fibers of L1 through L4
      (3) Femoral nerve exits the lumbar plexus, divides into many branches, and supplies the thigh and leg
   d. Sacral plexus and coccygeal plexus (Figure 15-5)
      (1) Located in the pelvic cavity in the anterior surface of the piriformis muscle
      (2) Formed by intermingling of fibers from L4 through S4
      (3) Tibial, common peroneal, and sciatic nerves exit the sacral plexus and supply nearly all the skin of the leg, posterior thigh muscles, and leg and foot muscles

D. Dermatomes and myotomes (Figure 15-6)
1. Dermatome—region of skin surface area supplied by afferent (sensory) fibers of a given spinal nerve (Figure 15-7)
2. Myotome—skeletal muscle or muscles supplied by efferent (motor) fibers of a given spinal nerve (Figure 15-8)

CRANIAL NERVES (TABLES 15-2 AND 15-3)

A. Overview
1. Twelve pairs of cranial nerves connect to the brain, mostly the brainstem (Figure 15-9)
2. Identified by name (determined by either distribution or function) or number (order in which they emerge, anterior to posterior) or both
3. Made up of bundles of axons

a. Mixed cranial nerve—axons of sensory and motor neurons
b. Sensory cranial nerve—axons of sensory neurons only
c. Motor cranial nerve—mainly axons of motor neurons and a small number of sensory fibers (proprioceptors)

B. Olfactory nerve (I)
1. Composed of axons of neurons whose dendrites and cell bodies lie in nasal mucosa and terminate in olfactory bulbs
2. Carries information about sense of smell

C. Optic nerve (II)
1. Composed of axons from the innermost layer of sensory neurons of the retina
2. Carries visual information from the eyes to the brain

D. Oculomotor nerve (III)
1. Fibers originate from cells in the oculomotor nucleus and extend to some of the external eye muscles
2. Efferent autonomic fibers are also present, which extend to the intrinsic muscles of the eye to regulate amount of light entering eye and aid focusing on near objects
3. Sensory fibers from proprioceptors in the eye muscles are also present

E. Trochlear nerve (IV)
1. Motor fibers originate in cells of the midbrain and extend to the superior oblique muscles of the eye
2. Also contains afferent fibers from proprioceptors in the superior oblique muscles of the eye

F. Trigeminal nerve (V) (Figure 15-10)
1. Has three branches: ophthalmic nerve, maxillary nerve, and mandibular nerve
2. Sensory neurons carry afferent impulses from skin and mucosa of head and teeth to cell bodies in the trigeminal ganglion
3. Motor fibers originate in trifacial motor nucleus and extend to the muscles of mastication through the mandibular nerve

G. Abducens nerve (VI)
1. Motor nerve with fibers originating from a nucleus in the pons on the floor of the fourth ventricle and extending to the lateral rectus muscles of the eye
2. Contains afferent fibers from proprioceptors in the lateral rectus muscles

H. Facial nerve (VII)
1. Motor fibers originate from a nucleus in lower part of pons and extend to superficial muscles of the face and scalp (Figure 15-11)
2. Autonomic fibers extend to submaxillary and sublingual salivary glands
3. Also contains sensory fibers from taste buds of anterior two thirds of the tongue

I. Vestibulocochlear nerve (VIII)
1. Two distinct divisions that are both sensory: vestibular nerve and cochlear nerve
2. Vestibular nerve fibers originate in the semicircular canals in inner ear and transmit impulses that result in sensations of equilibrium
3. Cochlear nerve fibers originate in the organ of Corti in the cochlea of the inner ear and transmit impulses that result in sensations of hearing

J. Glossopharyngeal nerve (IX)
1. Composed of sensory, motor, and autonomic nerve fibers
2. Supplies fibers to tongue, pharynx, and carotid sinus (Figure 15-12)

K. Vagus nerve (X)
1. Composed of sensory and motor fibers with many widely distributed branches
2. Sensory fibers supply pharynx, larynx, trachea, heart, carotid body, lungs, bronchi, esophagus, stomach, small intestine, and gallbladder (Figure 15-13)
3. Somatic motor fibers innervate the pharynx and larynx and are mostly autonomic fibers

L. Accessory nerve (XI)
1. Motor nerve that was once thought to be an "accessory" to the vagus nerve
2. Innervates the trapezius, and sternocleidomastoid muscles (Figure 15-14)

M. Hypoglossal nerve (XII)
1. Composed of motor and sensory fibers
2. Motor fibers innervate the muscles of the tongue
3. Contains sensory fibers from proprioceptors in muscles of the tongue

SOMATIC MOTOR NERVOUS SYSTEM

A. Two functional divisions of the peripheral nervous system (PNS)
1. Afferent (sensory) division
2. Efferent (motor) division
a. Somatic motor nervous system (SNS)
b. Autonomic nervous system (ANS) efferent pathways; ANS is discussed in Chapter 16

B. Basic principles of somatic motor pathways
1. Somatic nervous system—includes all voluntary motor pathways outside the central nervous system
2. Somatic effectors—skeletal muscles

C. Somatic reflexes
1. Nature of a reflex
a. Reflex—action that results from a nerve impulse passing over a reflex arc; predictable response to a stimulus
(1) Cranial reflex—center of reflex arc is in the brain
(2) Spinal reflex—center of reflex arc is in the spinal cord
b. Reflex consists of either muscle contraction or glandular secretion
(1) Somatic reflex—contraction of skeletal muscles
(2) Autonomic (visceral) reflex—either contraction of smooth or cardiac muscle or secretion by glands
2. Somatic reflexes of clinical importance—reflexes deviate from normal in certain diseases, and reflex testing is a valuable diagnostic aid (Figure 15-16)
a. Knee jerk reflex (also known as *patellar reflex*)—extension of the leg in response to tapping the patellar

ligament; tendon and muscles are stretched, stimulating muscle spindles and initiating conduction over a two-neuron reflex arc (Figure 15-15); may be classified in several different ways
  (1) Spinal cord reflex—center of reflex arc located in spinal cord gray matter
  (2) Segmental reflex—mediating impulses enter and leave at same cord segment
  (3) Ipsilateral reflex—mediating impulses come from and go to the same side of the body
  (4) Stretch or myotatic reflex—result of type of stimulation used to evoke reflex
  (5) Extensor reflex—produced by extensors of the leg
  (6) Deep reflex—result of deep location of receptors stimulated to produce reflex
- b. Ankle jerk reflex (also known as *Achilles reflex*)—extension of the foot in response to tapping the Achilles tendon
  (1) Tendon reflex and deep reflex mediated by two-neuron spinal arcs
  (2) Centers lie in first and second sacral segments of the cord
- c. Plantar reflex—plantar flexion of all toes and a slight turning in and flexion of the anterior part of the foot in response to stimulation of the outer edge of the sole; compare to Babinski sign (below)
  (1) Babinski sign—extension of great toe, with or without fanning of other toes, in response to stimulation of outer margin of sole of foot
  (2) Present in normal infants until approximately 1½ years of age and then becomes suppressed when corticospinal fibers become fully myelinated
  (3) In humans older than 1½ years of age, a positive Babinski reflex is one of the pyramidal signs indicating destruction of corticospinal (pyramidal tract) fibers; compare to the normal adult plantar reflex (above)
- d. Corneal reflex—winking in response to the cornea being touched; mediated by reflex arcs with sensory fibers in the ophthalmic branch of the fifth cranial nerve, centers in the pons, and motor fibers in the seventh cranial nerve
- e. Abdominal reflex—drawing in of the abdominal wall in response to stroking the side of the abdomen; superficial reflex; mediated by arcs with sensory and motor fibers in T9 through T12 and centers in these segments of the cord; decreased or absent reflex may involve lesions of pyramidal tract upper motor neurons

THE BIG PICTURE: THE PERIPHERAL NERVOUS SYSTEM AND THE WHOLE BODY

A. The peripheral nervous system is made of all the afferent nervous pathways coming into the CNS and all the efferent pathways going out of the central nervous system
B. Peripheral efferent (motor) pathways are pathways that lead from the integrator central nervous system to the effectors; allow the central nervous system to communicate regulatory information to the nervous effectors in the body
D. Somatic motor pathways regulate skeletal movements needed for survival, breathing, and heat production

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Identify the direction of the information carried by the ventral root of a spinal nerve.
2. Define mixed nerves.
3. Identify the areas innervated by the individual nerves emerging from the cervical plexus.
4. Explain the concept of a dermatome.
5. Explain the correlation between a myotome and a specific movement of the body.
6. Which cranial nerves transmit impulses that result in vision? In eye movement?
7. Which cranial nerves transmit impulses that result in hearing? In taste sensations?
8. What pathways are found in the somatic motor nervous system?
9. Describe what happens when the fifth cranial nerve is compressed.
10. Describe the condition of shingles.

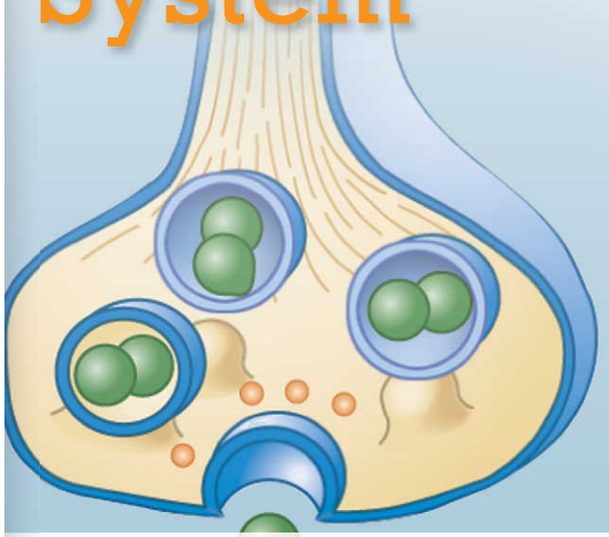
CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Can you distinguish between the reflexes that cause cardiac muscle to react and those that cause skeletal muscles to react?
2. An adult has an extension of the great toe and the fanning of the other toes in response to stimulation of the outer margin of the sole of the foot. Why is this a concern, and where would the problem most likely be?
3. A single reflex can be classified in several ways. What example can you find that would show this? In what ways can this reflex be classified?
4. Can you predict the respiratory consequences of an injury that damaged the spinal cord between the third and fifth cervical segments? What specific mechanism would cause these consequences?

16 Autonomic Nervous System



LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

acetylcholine (ACh)
(ass-ee-til-KOH-leen)
[*acetyl-* **vinegar,** *-chole-* **bile,** *-ine* **made of**]

alpha (α) receptor
(AL-fah ree-SEP-tor)
[*alpha* **first letter of Greek alphabet,** *recept-* **receive,** *-or* **agent**]

autonomic nervous system (ANS)
(aw-toh-NOM-ik)
[*auto-* **self,** *-nomo-* **law,** *-ic* **relating to**]

autonomic (visceral) reflex
(aw-toh-NOM-ik REE-fleks)
[*auto-* **self,** *-nomo-* **law,** *-ic* **relating to,** *re-* **again,** *-flex* **bend**]

beta (β) receptor
(BAY-tah ree-SEP-tor)
[*beta* **second letter of Greek alphabet,** *recept-* **receive,** *-or* **agent**]

collateral ganglion
(koh-LAT-er-al GANG-glee-on)
[*co-* **together,** *-later-* **side,** *-al* **relating to,** *gangli-* **knot,** *-on* **unit**] *pl.,* ganglia

co-transmission
(koh-tranz-MISH-un)
[*co-* **together,** *-trans-* **across,** *-miss-* **send,** *-ion* **process**]

"fight-or-flight" reaction ganglion
(GANG-lee-on)
[*gangli-* **knot,** *-on* **unit**] *pl.,* ganglia

muscarinic (M) receptor
(mus-kah-RIN-ik ree-SEP-tor)
[*musca-* **fly,** *-in-* **substance,** *-ic* **relating to** (**after the toxic mushroom** *A. muscaria*), *recept-* **receive,** *-or* **agent**]

continued on p. 501

CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

Overview of the Autonomic Nervous System, 489
Role of the Autonomic Nervous System, 489
Divisions of the Autonomic Nervous System, 490

Structure of the Autonomic Nervous System, 490
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The Big Picture: Autonomic Nervous System and the Whole Body, 501

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In Chapter 15, we explored the efferent (motor) pathways of the somatic nervous system (SNS) that regulates skeletal muscles, allowing us to survive by defending ourselves, getting food, or performing other essential tasks. This chapter continues the story by exploring the efferent pathways of the autonomic nervous system (ANS).

Autonomic regulation operates below the conscious level to control smooth and cardiac muscle, glands, and other tissues. Such regulation helps us maintain homeostasis of the internal environment and deal with threats to that stability.

OVERVIEW OF THE AUTONOMIC NERVOUS SYSTEM

Role of the Autonomic Nervous System

The **autonomic nervous system (ANS)** is a subdivision of the nervous system that regulates involuntary effectors (Figure 16-1). Because it controls involuntary effectors, we can think of the autonomic system as our system of subconscious regulation of body functions.

It is the ANS that carries efferent signals to the autonomic, or *visceral*, effectors—cardiac muscle, smooth muscle, glandular epithelia, and adipose and other tissues (Box 16-1). Some autonomic pathways connect to the skeletal muscles, which are ordinarily considered somatic effectors. In skeletal muscles, subconscious autonomic stimulation helps prevent fatigue during intense exercise—it does not directly control muscle contractions.

The major functions of the ANS are heartbeat regulation, smooth muscle contraction, glandular secretion, and metabolism regulation in ways that maintain homeostatic balance or respond to threats to that balance. Recall from the previous chapter that **autonomic (visceral) reflexes** can produce these effects over a visceral reflex pathway, which you can see illustrated as a simple reflex arc in Figure 16-1.

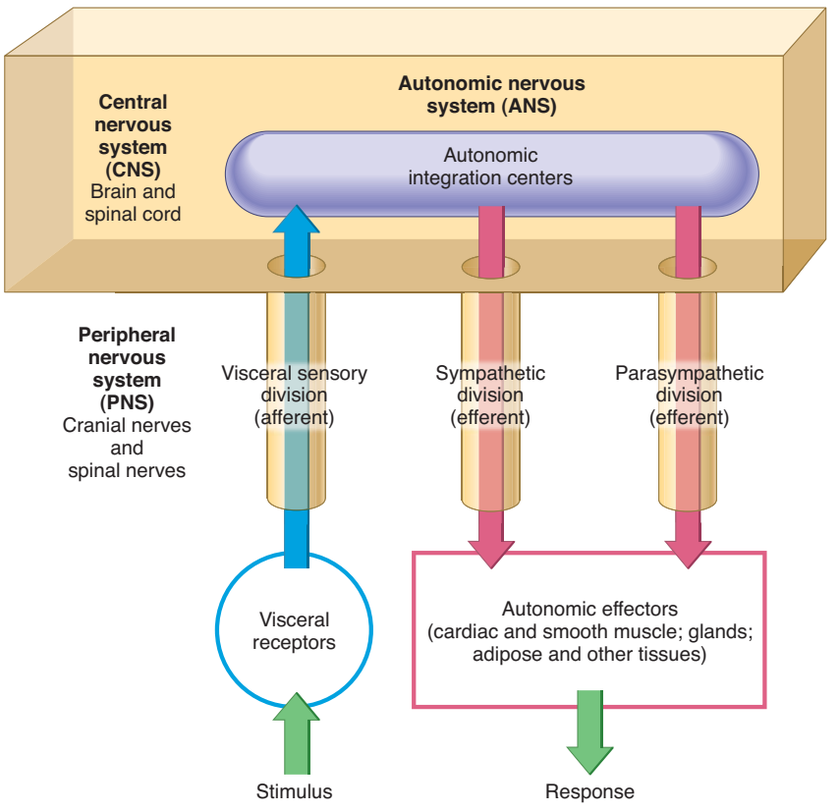


FIGURE 16-1

Organization of the autonomic nervous system. Note the simple arc pattern to information flow in the diagram. Compare to Figure 13-2 on p. 392 to see how this part of the nervous system fits into the big picture of nervous regulation.

Box 16-1 | Autonomic Effector Tissues and Organs

Smooth Muscle

Blood vessels
Bronchial tubes
Stomach
Gallbladder
Intestines
Urinary bladder
Spleen
Eye (iris, ciliary muscles)
Hair follicles

Cardiac Muscle

Heart

Glandular Epithelium

Sweat glands
Lacrimal glands
Digestive glands (salivary, gastric, pancreas, liver)
Adrenal medulla

Other Tissues

Adipose tissue
Kidneys
Skeletal muscle*

*Skeletal muscle is primarily a somatic effector, but sympathetic fibers help regulate contractility of skeletal muscle during intense exercise to avoid fatigue.

Divisions of the Autonomic Nervous System

Although the ANS also includes sensory (afferent) pathways that provide the feedback necessary to regulate effectors, we will emphasize the motor (efferent) pathways in this chapter. Sensory functions as a whole are discussed in the next chapter.

The ANS has two efferent divisions: the **sympathetic division** and the **parasympathetic division.** The sympathetic division consists of neural pathways that are separate from the parasympathetic pathways.

As you can see in Figure 16-2, however, even though the two divisions follow separate pathways, many autonomic effectors are *dually innervated.* That is, many autonomic effectors receive input from both sympathetic and parasympathetic pathways.

In dually innervated effectors, the effects of the two systems are often antagonistic: one inhibits the effector and the other stimulates the effector. This is similar to the antagonistic effects of an accelerator and brake in a vehicle. The opposing influences allow a dually innervated effector to be controlled with remarkable precision. Such antagonism also allows a dually innervated effector to participate in timed events, such as the sexual response, in which effectors must be stimulated and then rapidly inhibited (or vice versa) in a specific timed sequence.

Some autonomic effectors are *singly innervated*, receiving input from only the sympathetic division.

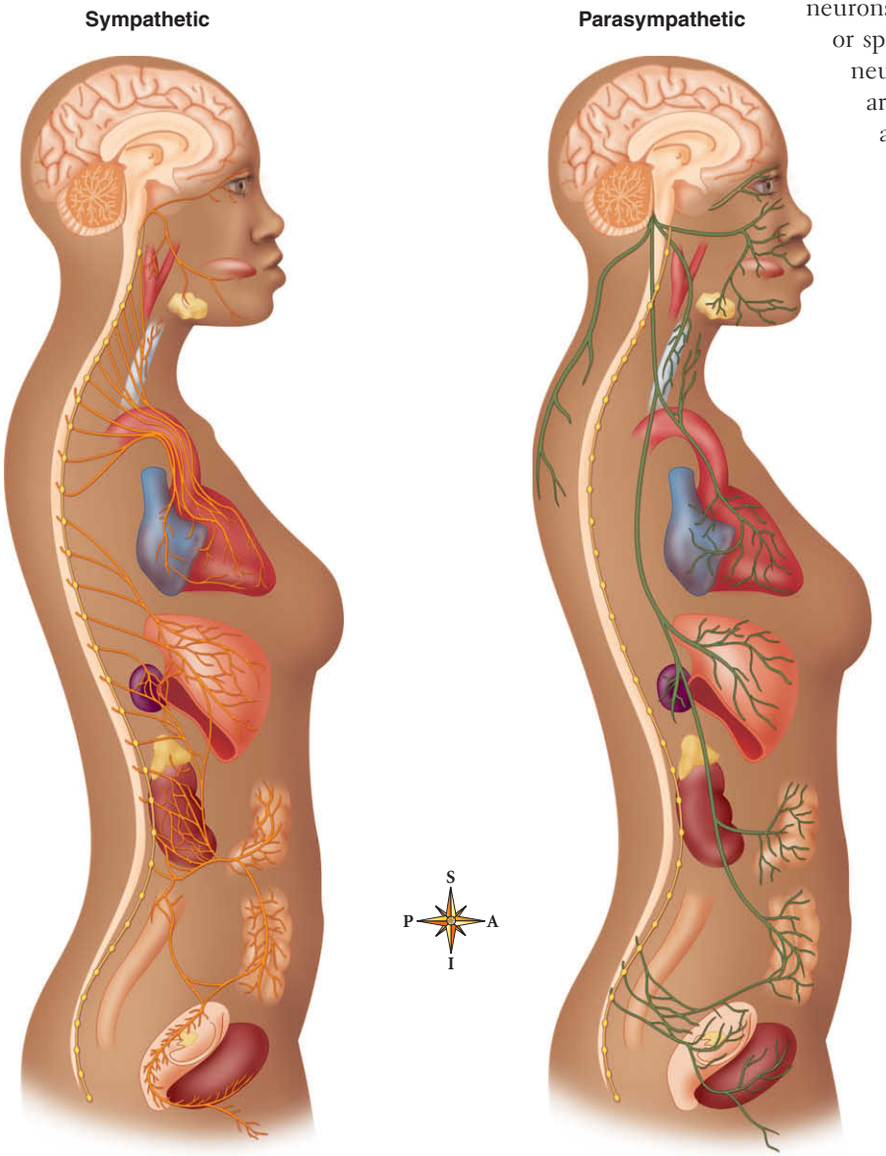


FIGURE 16–2

Divisions of the autonomic nervous system. Note that although the sympathetic pathways are separate from the parasympathetic pathways, most autonomic effectors are innervated by both pathways.

STRUCTURE OF THE AUTONOMIC NERVOUS SYSTEM

Basic Plan of Autonomic Pathways

Each efferent autonomic pathway, whether sympathetic or parasympathetic, is made up of autonomic nerves, ganglia, and plexuses. These structures, in turn, are made up of efferent autonomic neurons. They conduct impulses away from the brainstem or spinal cord to autonomic effectors. As with all efferent neurons, efferent autonomic neurons function in reflex arcs. Thus as with somatic motor regulation, efferent autonomic regulation ultimately depends on feedback from the sensory pathways.

A relay of two autonomic neurons conducts information from the central nervous system (CNS) to the autonomic effectors. The first is called a **preganglionic neuron**—an awkward name but a descriptive one. Preganglionic neurons conduct impulses from the brainstem or spinal cord to an autonomic **ganglion,** locating them *before* the ganglion—thus *pre*ganglionic. Within an autonomic ganglion, the preganglionic neuron synapses with a second efferent neuron. Because this second neuron conducts impulses away from the ganglion and to the effector, it is called the **postganglionic neuron.**

As you can see in Figure 16-3, A, this plan fundamentally differs from the efferent pathways of the somatic motor nervous system. Conduction to somatic effectors requires only one efferent neuron, the somatic motor neuron that originates in the anterior gray horn of the spinal cord. Conduction to autonomic effectors, however, requires a sequence of two efferent neurons from the CNS to the effector. Essential features of the somatic motor pathways and autonomic efferent pathways are further compared and contrasted in Table 16-1.

Structure of the Sympathetic Pathways

SYMPATHETIC PREGANGLIONIC NEURONS

Sympathetic preganglionic neurons begin within the spinal cord. Specifically, they have their dendrites and cell bodies within the lateral gray horns of the thoracic and lumbar segments of the spinal cord (see Figure 16-3, A). For this reason, the sympathetic division has also been called the *thoracolumbar division.*

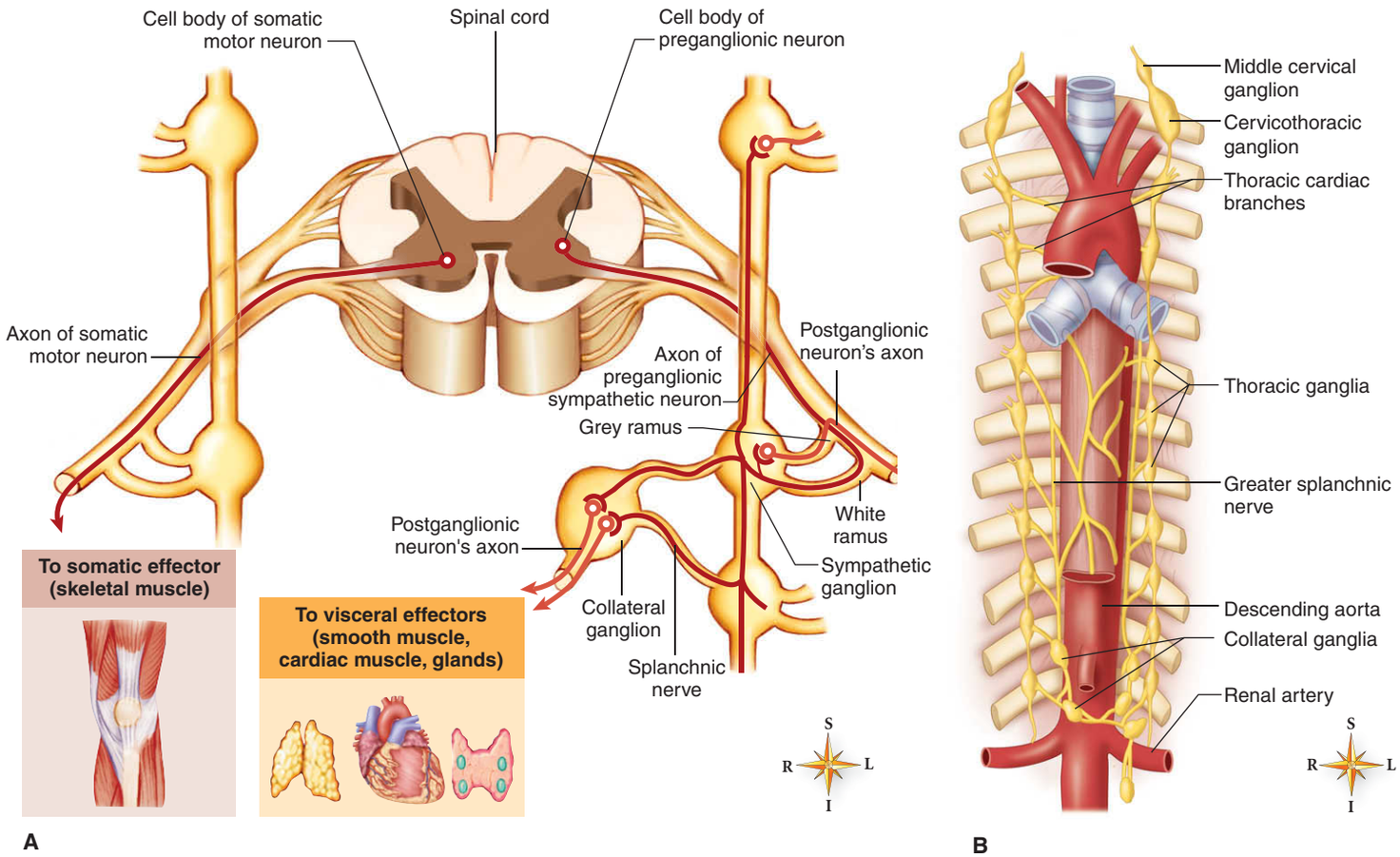


FIGURE 16-3

Diagram of autonomic conduction paths. A, The left side of the diagram shows that one somatic motor neuron conducts impulses all the way from the spinal cord to a somatic effector. Conduction from the spinal cord to any visceral effector, however, requires a relay of at least two autonomic motor neurons—a preganglionic and a postganglionic neuron, shown on the right side of the diagram. **B,** Sketch showing a portion of the left and right sympathetic chain or trunk.

Most of the ganglia of the sympathetic division lie along either side of the anterior surface of the vertebral column (see Figure 14-3, p. 423). Both gray rami and white rami are sympathetic rami. Sympathetic axon collaterals bridge the gap between adjacent ganglia that lie on the same side of the vertebral column. This arrangement forms a structure that resembles a chain of beads (see Figure 16-3, *B*). Thus the linked ganglia are often referred to as the *sympathetic chain ganglia*, or the **sympathetic trunk.**

Each chain runs from the second cervical vertebra in the neck all the way down to the level of the coccyx. There are usually 22 sympathetic chain ganglia on each side of the vertebral column: three cervical, eleven thoracic, four lumbar, and four sacral. Axons of sympathetic preganglionic neurons leave the cord by

TABLE 16-1 Comparison of Somatic Motor and Autonomic Pathways

FEATURE	SOMATIC MOTOR PATHWAYS	AUTONOMIC EFFERENT PATHWAYS
Direction of information flow	Efferent	Efferent
Number of neurons between CNS and effector	One (somatic motor neuron)	Two (preganglionic and postganglionic)
Myelin sheath present	Yes	Preganglionic: yes Postganglionic: no
Location of peripheral fibers	Most cranial nerves and all spinal nerves	Most cranial nerves and all spinal nerves
Effector innervated	Skeletal muscle (voluntary)	Smooth and cardiac muscle, glands, and adipose and other tissues (involuntary)
Neurotransmitter	Acetylcholine	Acetylcholine or norepinephrine

CNS, Central nervous system.

way of the ventral roots of the thoracic and first four lumbar spinal nerves. From there, they split away from other spinal nerve fibers by means of a small branch called the *white ramus*. The white ramus gets its name from the fact that most of the sympathetic preganglionic fibers within it are myelinated axons. Note in Figure 16-3 that the sympathetic preganglionic axon extends through the white ramus to a sympathetic chain ganglion.

If we trace the axon inside the sympathetic chain ganglion, we see that the preganglionic fiber may branch along any of three paths:

1. It can synapse with a sympathetic postganglionic neuron.
2. It can send ascending or descending branches through the sympathetic trunk to synapse with postganglionic neurons in other chain ganglia.
3. It can pass through one or more ganglia without synapsing.

Preganglionic neurons that pass through chain ganglia without synapsing continue on through **splanchnic nerves** to other sympathetic ganglia (see Figures 16-3 and 16-4). These **collateral ganglia,** or *prevertebral ganglia*, are pairs of sympathetic ganglia located a short distance from the spinal cord. The collateral ganglia are named for nearby blood vessels. For example, the *celiac ganglion* (also called the *solar plexus*) is a large ganglion that lies next to the celiac artery just below the diaphragm. Other examples include the *superior mesenteric ganglion* and the *inferior mesenteric ganglion*, each located close to the beginning of an artery of the same name.

Some of the preganglionic fibers that enter the celiac ganglion do not synapse there but continue on to the central portion (medulla) of the *adrenal gland*. Within the adrenal medulla, they synapse with modified postganglionic neurons. These modified postganglionic cells are actually endocrine cells that release hormones (mostly epinephrine) into the bloodstream. These chemical messengers may reach the various sympathetic effectors, where they enhance and prolong the effects of sympathetic stimulation.

SYMPATHETIC POSTGANGLIONIC NEURONS

Most of the sympathetic postganglionic neurons have their dendrites and cell bodies in the sympathetic chain ganglia or collateral ganglia.

Some postganglionic axons return to a spinal nerve by way of a short branch called the *gray ramus*, so named because most postganglionic fibers are unmyelinated (see Figure 16-3). Once in the spinal nerve, the postganglionic fibers are distributed with other nerve fibers to the various sympathetic effectors. On the other hand, some postganglionic fibers are distributed to sympathetic effectors by way of separate autonomic nerves. The course of postganglionic fibers through these autonomic nerves is complex, involving the redistribution of fibers in autonomic plexuses before they reach their respective destinations.

In the sympathetic division, preganglionic neurons are relatively short, and postganglionic neurons are relatively long.

The axon of any one sympathetic preganglionic neuron synapses with many postganglionic neurons, and these frequently terminate in widely separated organs. This anatomical fact partially explains a well-known physiological principle—sympathetic responses are usually widespread, involving many organs—not just one.

| QUICK CHECK |

1. Do autonomic pathways follow the principle of final common path?
2. Why is the sympathetic division of the ANS also known as the *thoracolumbar division?*
3. Describe the path generally taken by an impulse along a sympathetic pathway from the CNS to an autonomic effector.

Structure of the Parasympathetic Pathways

PARASYMPATHETIC PREGANGLIONIC NEURONS

Parasympathetic preganglionic neurons have their cell bodies in nuclei in the brainstem or in the lateral gray columns of the sacral cord. For this reason, the parasympathetic division has also been called the *craniosacral division*.

Axons of parasympathetic preganglionic neurons are contained in cranial nerves III, VII, IX, and X and in some pelvic nerves. They extend a considerable distance before synapsing with postganglionic neurons. For example, at least 75% of all parasympathetic preganglionic fibers travel in the *vagus nerve* (X) for a distance of 30 cm (1 foot) or more before synapsing with postganglionic fibers in **terminal ganglia** near effectors in the chest and abdomen (Figure 16-4 and Table 16-2).

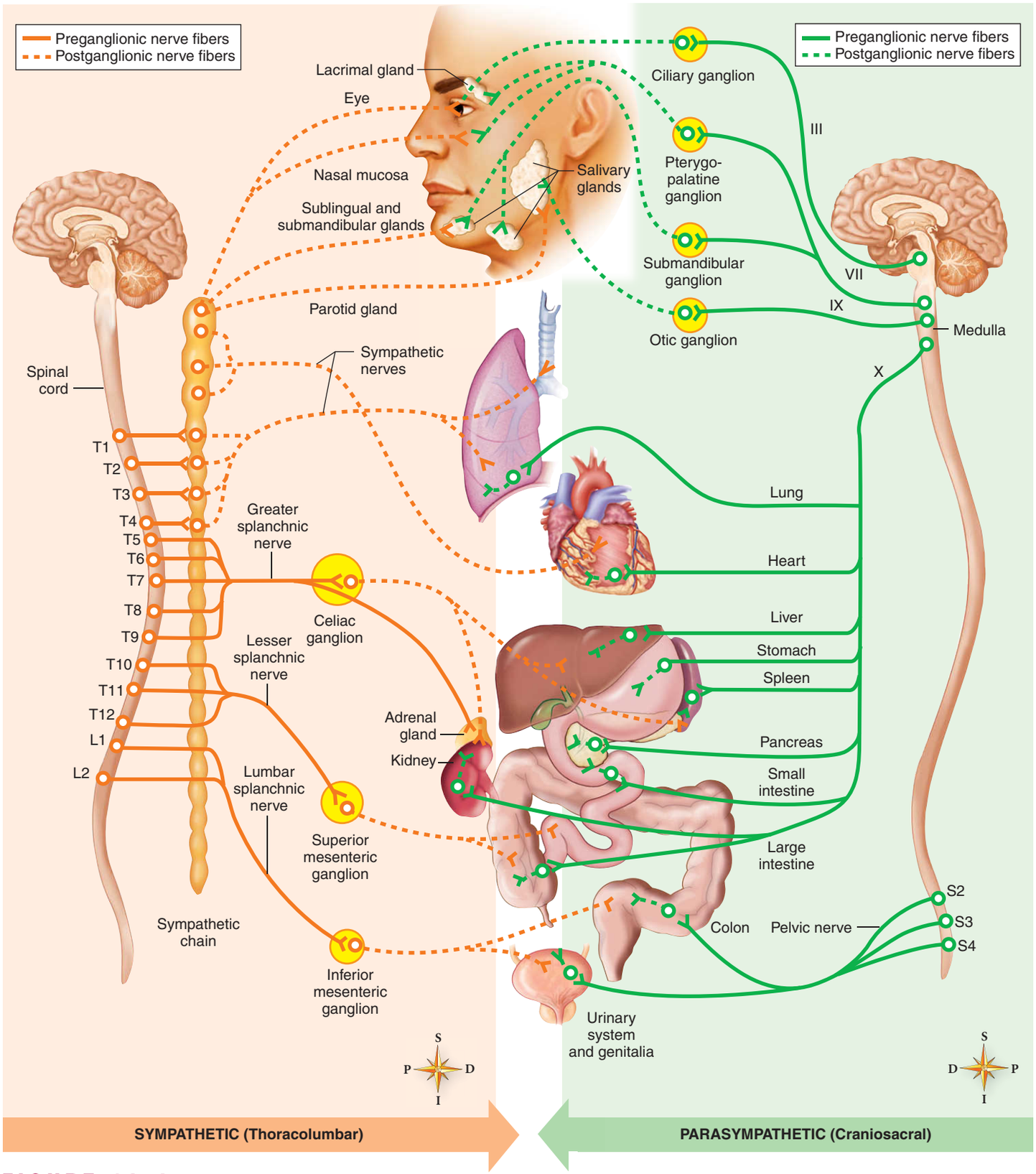


FIGURE 16-4

Major autonomic pathways.

TABLE 16-2 Comparison of Structural Features of the Sympathetic and Parasympathetic Pathways

NEURONS	SYMPATHETIC PATHWAYS	PARASYMPATHETIC PATHWAYS
Preganglionic Neurons		
Dendrites and cell bodies	In lateral gray columns of thoracic and first two or three lumbar segments of spinal cord	In nuclei of brainstem and in lateral gray columns of sacral segments of cord
Axons	In anterior roots of spinal nerves to spinal nerves (thoracic and first four lumbar), to and through white rami to terminate in sympathetic ganglia at various levels or to extend through sympathetic ganglia, to and through splanchnic nerves to terminate in collateral ganglia	From brainstem nuclei through cranial nerve III to ciliary ganglion From nuclei in pons through cranial nerve VII to sphenopalatine or submaxillary ganglion From nuclei in medulla through cranial nerve IX to otic ganglion or through cranial nerves X and XI to cardiac and celiac ganglia, respectively
Distribution	Short fibers from CNS to ganglion	Long fibers from CNS to ganglion
Neurotransmitter	Acetylcholine	Acetylcholine
Ganglia	Sympathetic chain ganglia (22 pairs); collateral ganglia (celiac, superior, inferior mesenteric)	Terminal ganglia (in or near effector)
Postganglionic Neurons		
Dendrites and cell bodies	In sympathetic and collateral ganglia	In parasympathetic ganglia (e.g., ciliary, sphenopalatine, submaxillary, otic, cardiac, celiac) located in or near visceral effector organs
Receptors	Cholinergic (nicotinic)	Cholinergic (nicotinic)
Axons	In autonomic nerves and plexuses that innervate thoracic and abdominal viscera and blood vessels in these cavities In gray rami to spinal nerves, to smooth muscle of skin, blood vessels, and hair follicles, and to sweat glands	In short nerves to various visceral effector organs
Distribution	Long fibers from ganglion to widespread effectors	Short fibers from ganglion to single effector
Neurotransmitter	Norepinephrine (many); acetylcholine (few)	Acetylcholine

CNS, Central nervous system.

PARASYMPATHETIC POSTGANGLIONIC NEURONS

Parasympathetic postganglionic neurons have their dendrites and cell bodies in parasympathetic ganglia. Unlike sympathetic ganglia that lie near the spinal column, parasympathetic ganglia lie near or embedded in autonomic effectors.

For example, note the ciliary ganglion in Figure 16-4. This and the other ganglia shown near it are parasympathetic ganglia located in the skull.

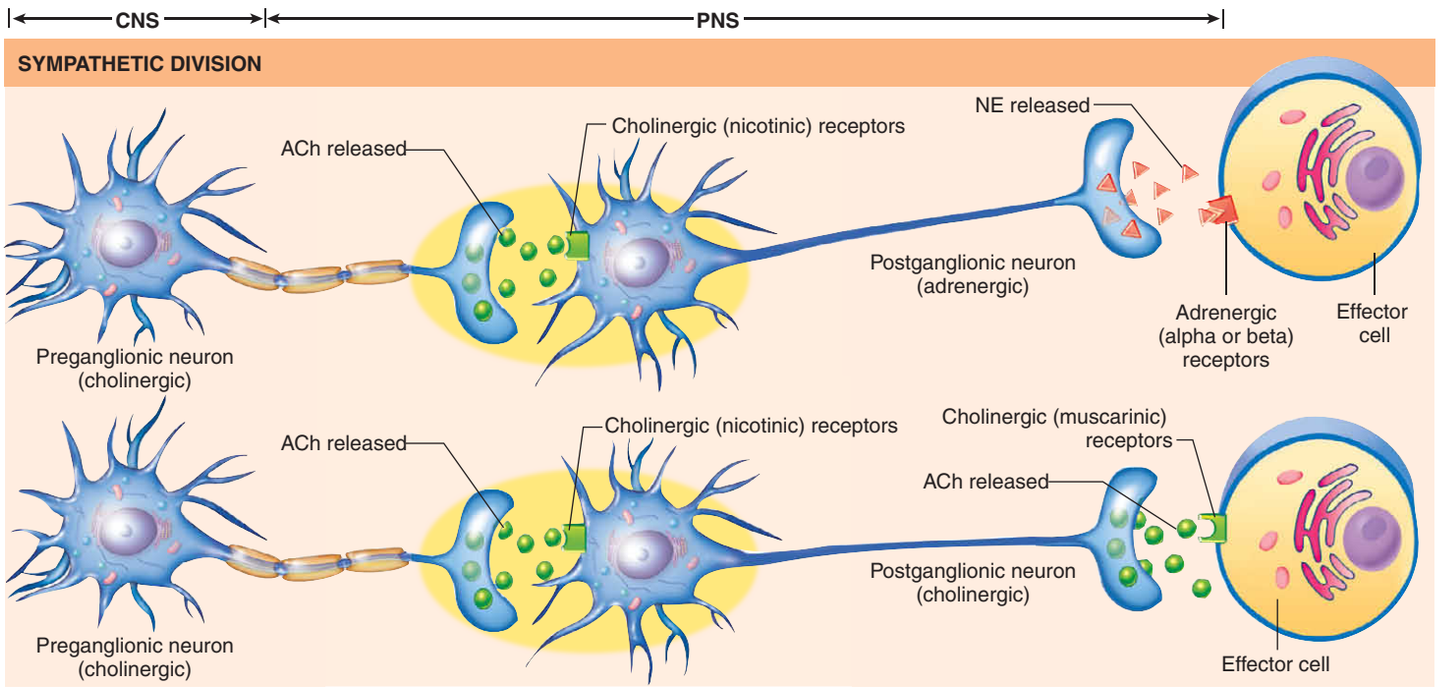
In a parasympathetic ganglion, preganglionic axons synapse with postganglionic neurons that send their short axons into the nearby autonomic effector. A parasympathetic preganglionic neuron therefore usually synapses with postganglionic neurons to a single effector. For this reason, parasympathetic stimulation frequently involves response by only one organ. Sympathetic stimulation, on the other hand, usually evokes responses by numerous organs.

Autonomic Neurotransmitters and Receptors

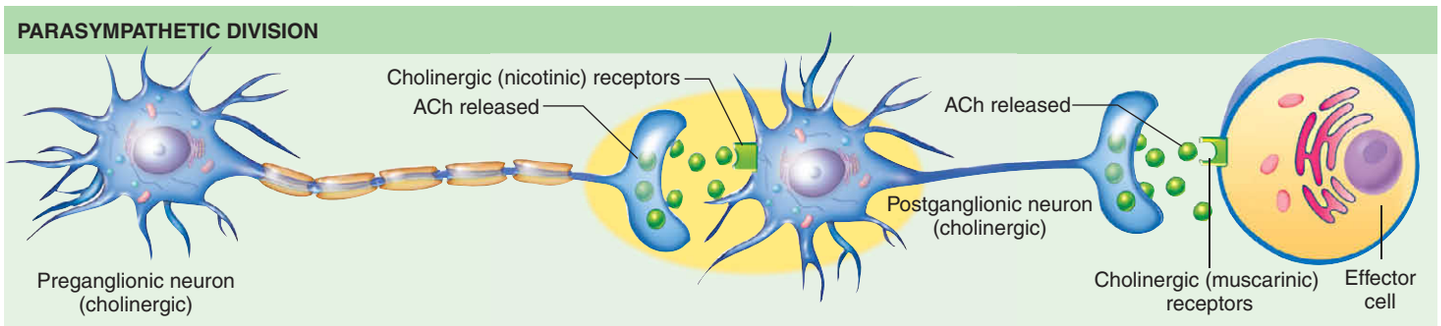
Axon terminals of autonomic neurons release either of two neurotransmitters: **norepinephrine** (**NE**) or **acetylcholine** (**ACh**). Axons that release norepinephrine are known as *adrenergic fibers.* Axons that release acetylcholine are called *cholinergic fibers.* Autonomic cholinergic fibers are the axons of preganglionic sympathetic neurons and of both preganglionic and postganglionic parasympathetic neurons. This leaves the axons of postganglionic sympathetic neurons as the only autonomic adrenergic fibers, and as you can see in Figure 16-5, not all of these are adrenergic. Sympathetic postganglionic axons to sweat glands and some blood vessels are cholinergic fibers.

NOREPINEPHRINE AND ITS RECEPTORS

Norepinephrine affects visceral effectors by first binding to *adrenergic receptors* in their plasma membranes. The adrenergic



A



B

FIGURE 16-5

Locations of neurotransmitters and receptors of the autonomic nervous system. In all pathways, preganglionic fibers are cholinergic, secreting acetylcholine *(ACh),* which stimulates nicotinic receptors in the postganglionic neuron. Most sympathetic postganglionic fibers are adrenergic **(A),** secreting norepinephrine *(NE),* thus stimulating alpha or beta adrenergic receptors. A few sympathetic postganglionic fibers are cholinergic, stimulating muscarinic receptors in effector cells **(B).** All parasympathetic postganglionic fibers are cholinergic **(C),** stimulating muscarinic receptors in effector cells.

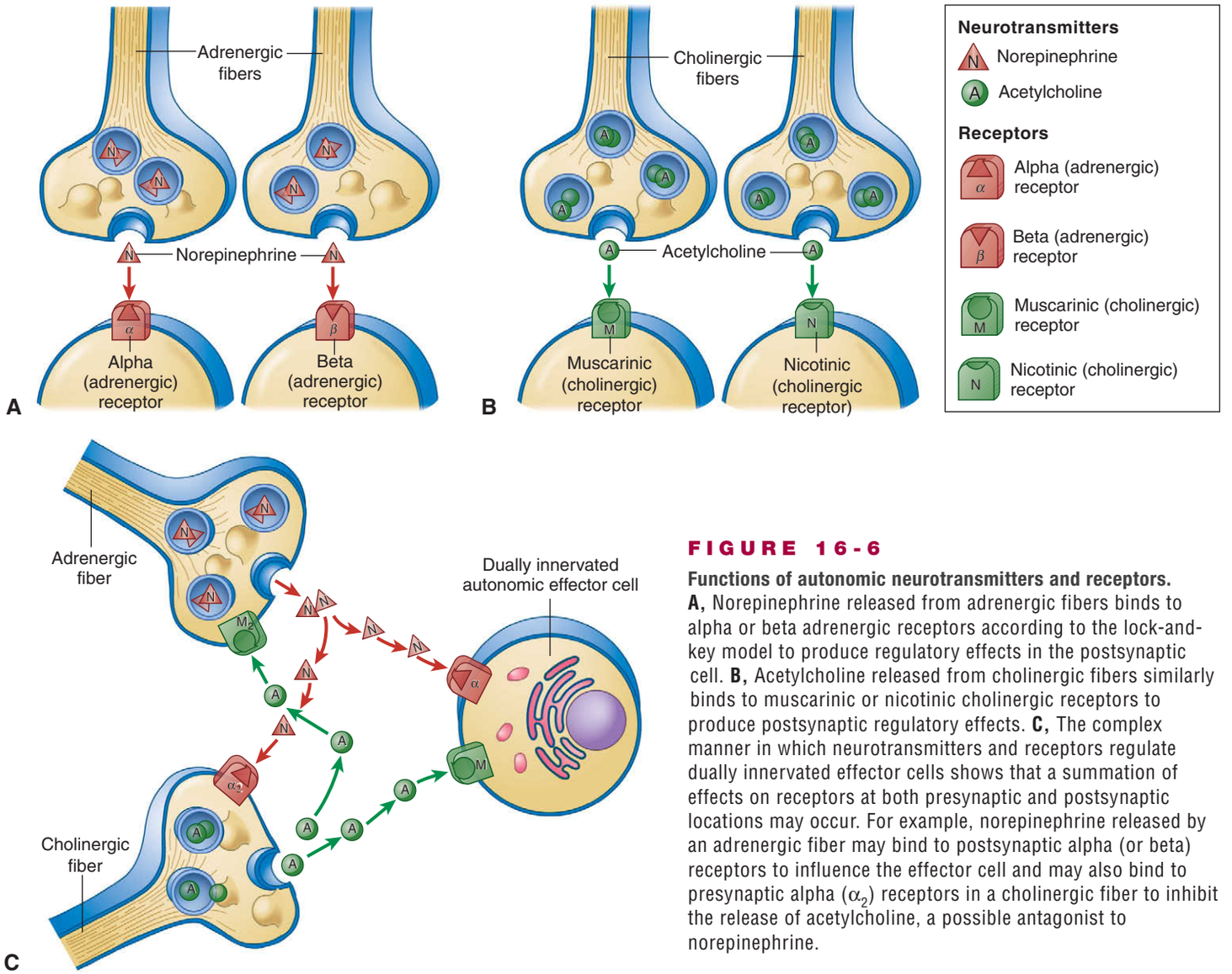


FIGURE 16-6

Functions of autonomic neurotransmitters and receptors. **A,** Norepinephrine released from adrenergic fibers binds to alpha or beta adrenergic receptors according to the lock-and-key model to produce regulatory effects in the postsynaptic cell. **B,** Acetylcholine released from cholinergic fibers similarly binds to muscarinic or nicotinic cholinergic receptors to produce postsynaptic regulatory effects. **C,** The complex manner in which neurotransmitters and receptors regulate dually innervated effector cells shows that a summation of effects on receptors at both presynaptic and postsynaptic locations may occur. For example, norepinephrine released by an adrenergic fiber may bind to postsynaptic alpha (or beta) receptors to influence the effector cell and may also bind to presynaptic alpha (α_2) receptors in a cholinergic fiber to inhibit the release of acetylcholine, a possible antagonist to norepinephrine.

receptors are of two main types, one named **alpha (α) receptors** and the other named **beta (β) receptors** (Figure 16-6, *A*). Different subtypes of alpha and beta receptors, such as alpha-1 (α_1), alpha-2 (α_2), beta-1 (β_1), and beta-2 (β_2), exist among cells that have adrenergic receptors.

The binding of norepinephrine to alpha receptors in the smooth muscle of blood vessels has a stimulating effect on the muscle that causes the vessel to constrict. The binding of norepinephrine to beta receptors in smooth muscle of a different blood vessel produces opposite effects. It inhibits the muscle, causing the vessel to dilate. But the binding of norepinephrine to beta receptors in cardiac muscle has a stimulating effect that results in a faster and stronger heartbeat.

Epinephrine released by the sympathetic postganglionic cells in the adrenal medulla also stimulates the adrenergic receptors, enhancing and prolonging the effects of sympathetic stimulation. Because epinephrine has a greater effect on some beta receptors than norepinephrine, effectors with a large proportion of these beta receptors are more sensitive to epinephrine.

All these facts point to an important principle about nervous regulation: the effect of a neurotransmitter on any postsynaptic cell is determined by the characteristics of the receptor and not by the neurotransmitter itself. This principle has been given due consideration in development of therapies that affect autonomic functions (Box 16-2).

The actions of norepinephrine and epinephrine are terminated in two ways. Most of the neurotransmitter molecules are taken back up by the synaptic knobs of postganglionic neurons, where they are broken down by the enzyme *monoamine oxidase (MAO)*. The remaining neurotransmitter molecules are eventually broken down by another enzyme, *catechol-O-methyl transferase (COMT)*. Both of these mechanisms are very slow compared with the rapid deactivation of acetylcholine by acetylcholinesterase. This fact partly explains why adrenergic effects often linger for some time after stimulation has ceased.

Box 16-2 | HEALTH matters

Beta Blockers

Drugs that bind to beta receptors, and thus block the binding of norepinephrine and epinephrine, are informally called **beta blockers.** Propranolol (Inderal) is one of nearly a dozen beta blockers used to treat irregular heartbeats and hypertension (high blood pressure). Beta blockers achieve their therapeutic effects by preventing the increased rate and strength of the heart's pumping action triggered by sympathetic stimulation. For patients who also have had a previous heart attack (myocardial infarction), these drugs possibly have the added benefit of preventing further attacks.

ACETYLCHOLINE AND ITS RECEPTORS

Acetylcholine binds to *cholinergic receptors.* The two main types of cholinergic receptors are **nicotinic (N) receptors** and **muscarinic (M) receptors** (Figure 16-6, *B*). Nicotinic receptors derive their name from the fact that they were first discovered when nicotine, a drug, was shown to bind to them. Muscarinic receptors are named for the fact that their discovery came about when it was shown that muscarine, a toxin from mushrooms, binds to them. Like the adrenergic receptors, cholinergic receptors have subtypes such as nicotinic-1 (N_1), nicotinic-2 (N_2), muscarinic-1 (M_1), muscarinic-2 (M_2), and muscarinic-3 (M_3).

In the ganglia of both autonomic divisions, acetylcholine binds to nicotinic receptors in the membranes of postganglionic cells. Acetylcholine, released by all parasympathetic postganglionic cells and the few sympathetic postganglionic cells that are cholinergic, binds to muscarinic receptors in the membranes of effector cells. As mentioned previously, the action of acetylcholine is quickly terminated by its being hydrolyzed by the enzyme *acetylcholinesterase.*

Figure 16-6, *C,* shows the complex manner in which neurotransmitters and receptors may function at a synapse with a dually innervated autonomic effector cell. Norepinephrine released from a sympathetic adrenergic fiber binds to alpha (or beta) receptors of the effector cell, producing adrenergic (sympathetic) effects. As the figure also shows, norepinephrine may also bind to alpha (α_2) receptors in the presynaptic membrane of a nearby cholinergic (parasympathetic) fiber. This inhibits that fiber's release of the antagonistic neurotransmitter, acetylcholine. Likewise, acetylcholine released from cholinergic fibers may bind to muscarinic (M_2) receptors in the presynaptic membranes of nearby adrenergic fiber. This inhibits the release of acetylcholine's antagonist, norepinephrine.

Autonomic pathways also use additional neurotransmitters to supplement norepinephrine and acetylcholine, further enhancing the complexity of autonomic regulation (Box 16-3).

Because of this complexity of function, the effector cell can be controlled with great precision by balancing the effects of sympathetic and parasympathetic stimulation in various ways.

| QUICK CHECK |

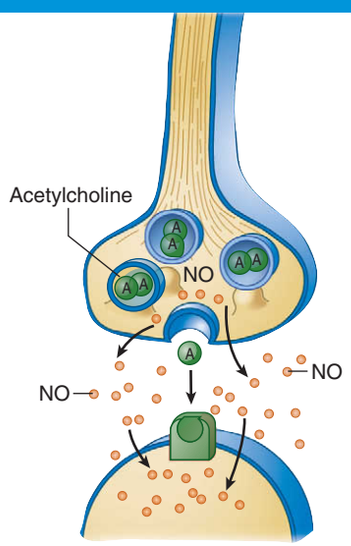
4. Describe the pathway taken by an impulse traveling along a parasympathetic pathway.
5. What is the difference between a cholinergic fiber and an adrenergic fiber? Between a cholinergic receptor and an adrenergic receptor?
6. Name the two major types of cholinergic receptors and the two major types of adrenergic receptors.

Box 16-3 | FYI

Nonadrenergic-Noncholinergic Transmission

Research clearly shows that many neurotransmitters besides norepinephrine and acetylcholine bind to autonomic receptors. Thus a concept of **nonadrenergic-noncholinergic (NANC) transmission** has evolved. Substances that research shows to be involved in NANC transmission across peripheral autonomic synapses include nitric oxide (NO), gamma-aminobutyric acid (GABA), adenosine triphosphate (ATP), neuropeptide Y, vasoactive intestinal peptide (VIP), luteinizing hormone–releasing hormone (LHRH), and others. A theory of autonomic transmission called **co-transmission** states that all or most postganglionic fibers release either norepinephrine or acetylcholine along with NANC transmitters or modulators and that each substance combines with postsynaptic or presynaptic receptors to produce regulatory effects.

Discoveries in autonomic co-transmission have led to a number of therapeutic breakthroughs. One of the better known of these discoveries is the drug sildenafil citrate (Viagra) used to treat **erectile dysfunction** (ED) in males. During the male sexual response, co-transmission of NO in the parasympathetic nerves helps relax smooth muscles in the blood vessels—thus increasing blood flow to the penis. This drug enhances that effect by reducing the natural breakdown of NO in blood vessels of the penis.



Nonadrenergic-noncholinergic (NANC) transmission. In this example, nitric oxide *(NO)* is released from a cholinergic fiber along with acetylcholine *(A).*

FUNCTIONS OF THE AUTONOMIC NERVOUS SYSTEM

Overview of Autonomic Function

The ANS as a whole functions to regulate autonomic effectors in ways that tend to maintain or quickly restore homeostasis. Both sympathetic and parasympathetic divisions are *tonically active*. That is, they continually conduct impulses to autonomic effectors. They often exert opposite, or antagonistic, influences on them. We can call this concept the *principle of autonomic antagonism*.

If sympathetic impulses tend to stimulate an effector, parasympathetic impulses tend to inhibit it. Doubly innervated effectors continually receive both sympathetic and parasympathetic impulses. Summation of the two opposing influences determines the dominating or controlling effect. For example, continual sympathetic impulses to the heart tend to accelerate the heart rate whereas continual parasympathetic impulses tend to slow it. The actual heart rate is determined by whichever influence dominates. To find other examples of autonomic antagonism, examine Table 16-3.

TABLE 16-3 Autonomic Functions

AUTONOMIC EFFECTOR	EFFECT OF SYMPATHETIC STIMULATION (neurotransmitter: norepinephrine unless otherwise stated)	EFFECT OF PARASYMPATHETIC STIMULATION (neurotransmitter: acetylcholine)
Cardiac Muscle	Increased rate and strength of contraction (beta receptors)	Decreased rate and strength of contraction
Smooth Muscle of Blood Vessels		
Skin blood vessels	Constriction (alpha receptors)	No effect
Skeletal muscle blood vessels	Dilation (beta receptors)	No effect
Coronary blood vessels	Constriction (alpha receptors) Dilation (beta receptors)	Dilation
Abdominal blood vessels	Constriction (alpha receptors)	No effect
Blood vessels of external genitalia	Constriction (alpha receptors)	Dilation of blood vessels causing erection
Smooth Muscle of Hollow Organs and Sphincters		
Bronchioles	Relaxation (dilation)	Constriction
Digestive tract, except sphincters	Decreased peristalsis	Increased peristalsis
Sphincters of digestive tract	Contraction	Relaxation
Urinary bladder	Relaxation	Contraction
Urinary sphincters	Contraction	Relaxation
Reproductive ducts	Constriction	Relaxation
Eye		
Iris	Contraction of radial muscle; dilated pupil	Contraction of circular muscle; constricted pupil
Ciliary	Relaxation; accommodates for far vision	Contraction; accommodates for near vision
Hairs (arrector pili muscles)	Contraction produces goose pimples, or piloerection (alpha receptors)	No effect
Glands		
Sweat	Increased sweat (neurotransmitter, acetylcholine)	No effect
Lacrimal	No effect	Increased secretion of tears
Digestive (salivary, gastric, etc.)	Decreased secretion of saliva; not known for others	Increased secretion of saliva
Pancreas, including islets	Decreased secretion	Increased secretion of pancreatic juice and insulin
Liver	Increased glycogenolysis (beta receptors); increased blood sugar level	No effect
Adrenal medulla*	Increased epinephrine secretion	No effect
Adipose	Increased lipolysis	No effect
Skeletal muscle*	During intense exercise, regulates contractility to prevent fatigue (beta receptors)	No effect

*Sympathetic preganglionic axons terminate in contact with secreting cells of the adrenal medulla. Thus the adrenal medulla functions, to quote someone's descriptive phrase, as a "giant sympathetic postganglionic neuron."
**Skeletal muscle is primarily a somatic effector but during intense exercise, subconscious autonomic stimulation also occurs.

The ANS does not function autonomously as its name suggests. It is continually influenced by impulses from the so-called autonomic centers. These are clusters of neurons located at various levels in the brain whose axons conduct impulses directly or indirectly to autonomic preganglionic neurons. Autonomic centers function as a hierarchy in their control of the ANS (Figure 16-7). Highest ranking in the hierarchy are the autonomic centers in the cerebral cortex, for example, in the frontal lobe and limbic system (structures near the medial surface of the cerebrum that form a border around the corpus callosum). Neurons in these centers send impulses to other autonomic centers in the brain, notably in the hypothalamus. Then neurons in the hypothalamus send either stimulating or inhibiting impulses to parasympathetic and sympathetic preganglionic neurons located in the lower autonomic centers of the brainstem and cord.

You may be wondering why the name *autonomic system* was ever chosen if the system is really not autonomous. Originally the term seemed appropriate. The autonomic system seemed to be self-regulating and independent of the rest of the nervous system. Common observations furnished abundant evidence of its independence from cerebral control, from direct control by the will, that is. Later, however, even this was found to be not entirely true. Some rare and startling exceptions were discovered. For example, a man in a brightly lighted amphitheater can change the size of his pupils from small, constricted dots (normal response to bright lights) to widely dilated circles. It is also possible to will the smooth muscle of the hairs on the arms to contract, producing gooseflesh. Box 16-4 discusses how this knowledge can be used in therapy.

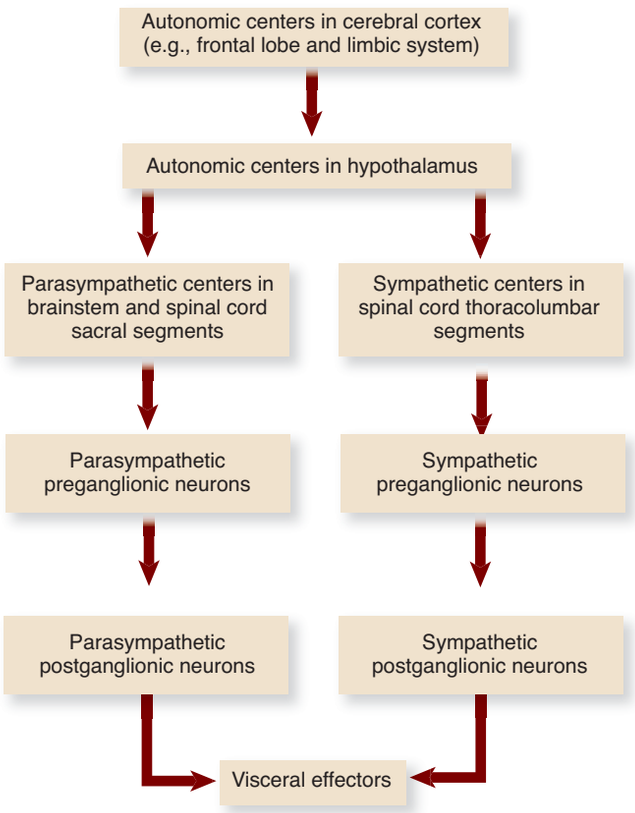


FIGURE 16-7

Central nervous system hierarchy that regulates autonomic functions.

Functions of the Sympathetic Division

Under ordinary, resting conditions the sympathetic division can act to maintain the normal functioning of doubly innervated autonomic effectors. It does this by opposing the effects of parasympathetic impulses to these structures. For example, by counteracting parasympathetic impulses that tend to slow the heart and weaken its beat, sympathetic impulses function to maintain the heartbeat's normal rate and strength.

The sympathetic division also serves another important function under usual conditions. Because only sympathetic fibers innervate the smooth muscle in blood vessel walls, sympathetic impulses function to maintain the normal tone of this muscle. By so doing, the sympathetic system plays a crucial role in maintaining blood pressure under usual conditions.

The major function of the sympathetic division, however, is that it serves as an "emergency" system. When we perceive that the homeostasis of the body might be threatened—that is, when we are under physical or psychological stress—outgoing sympathetic signals increase greatly. In fact, one of the very first steps in the body's complex defense mechanism against stress is a sudden and marked increase in sympathetic activity. This brings about a group of responses that all go on at the same time. Together they make the body ready to expend maximum energy and thus to engage in the maximum muscular exertion needed to deal with the perceived threat—as, for example, in running or fighting. Walter B. Cannon coined the descriptive and now famous phrase the "**fight-or-flight" reaction** as his name for this group of sympathetic responses.

Box 16-4 | FYI

Biofeedback

We now know that individuals can learn to control specific autonomic effectors if two conditions are fulfilled. First, they must be informed that they are achieving the desired response, and second, they must be rewarded for it. Various kinds of **biofeedback** instruments have been developed to provide these conditions. For example, a biofeedback instrument that detects slight temperature changes has been used with patients who suffer from migraine headaches. (Migraine headaches initially involve distention of blood vessels in the head.) The instrument is attached to the hands and emits a high sound each time the blood vessels in the hand dilate. The reward for these patients is a lessening of the migraine pain—presumably because of the shunting of blood away from the head to the hands.

TABLE 16-4 Summary of the Sympathetic "Fight-or-Flight" Reaction

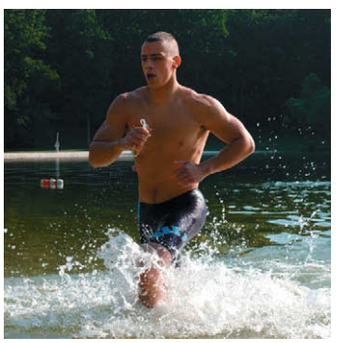
RESPONSE	ROLE IN PROMOTING ENERGY USE BY SKELETAL MUSCLES
Increased heart rate	Increased rate of blood flow, thus increased delivery of oxygen and glucose to skeletal muscles
Increased strength of cardiac muscle contraction	Increased rate of blood flow, thus increased delivery of oxygen and glucose to skeletal muscles
Dilation of coronary vessels of the heart	Increased delivery of oxygen and nutrients to cardiac muscle to sustain increased rate and strength of heart contractions
Dilation of blood vessels in skeletal muscles	Increased delivery of oxygen and nutrients to skeletal muscles
Increased stimulation at neuromuscular junctions and increased ion pump activity in skeletal muscles	Increased availability of ACh at the neuromuscular junction and more efficient restoration of resting ion balance in muscle fibers both reduce fatigue in skeletal muscles
Constriction of blood vessels in digestive and other organs	Shunting of blood to skeletal muscles to increase oxygen and glucose delivery
Contraction of spleen and other blood reservoirs	More blood discharged into general circulation, causing increased delivery of oxygen and glucose to skeletal muscles
Dilation of respiratory airways	Increased loading of oxygen into blood
Increased rate and depth of breathing	Increased loading of oxygen into blood (indirect effect)
Increased sweating	Increased dissipation of heat generated by skeletal muscle activity
Increased conversion of glycogen into glucose	Increased amount of glucose available to skeletal muscles
Increased breakdown of stored fats	Increased amount of fatty acids and glycerol available to skeletal muscles

Read Table 16-4 to find many of the fight-or-flight physiological changes. Some particularly important changes for maximum energy expenditure by skeletal muscles are faster, stronger heartbeat, dilated blood vessels in skeletal muscles, and dilated bronchi. Stimulation of glycogenolysis (breakdown of stored glycogen) and lipolysis (breakdown of stored fat) increases available blood levels of glucose, fatty acids, and related nutrients that can be used for energy in muscle cells. Stimulation of the medulla of each adrenal gland triggers its secretion of epinephrine and some norepinephrine. These hormones reinforce and prolong effects of the norepinephrine released by sympathetic postganglionic fibers. The sympathetic system can also directly affect skeletal muscle function (Box 16-5).

The fight-or-flight reaction is a normal response in times of stress. Without such a response, we might not be able to resist or retreat from something that actually threatens our well-being. However, chronic exposure to stress can lead to dysfunction of sympathetic effectors—and perhaps even to the dysfunction of the ANS itself. Some current concepts regarding the effects of chronic stress are discussed in Chapter 25.

Box 16-5 | SPORTS and FITNESS

Sympathetic Stimulation of Skeletal Muscle



We learned in the previous chapter that skeletal muscles are somatic effectors that respond to acetylcholine from somatic motor neurons by contracting. We learned that such motor control is ordinarily conscious, voluntary control. However, there are sympathetic adrenergic fibers that extend into every skeletal muscle of the body.

For a long time we thought that the sole function of adrenergic fibers in skeletal muscle tissue was to innervate the arterioles and thus regulate blood flow during exercise or stress. Later we found beta receptors in skeletal muscle that also respond during exercise and stress. One adrenergic effect in skeletal muscle fibers is to speed up the sodium-potassium pumps that maintain the ion concentration gradients needed to produce action potentials. These pumps may fail to keep up with the barrage of action potentials during intense exercise and thus produce a temporary inability to contract efficiently—producing physiological fatigue (see Box 12-5 on p. 363).

Adrenergic effects on the somatic motor neurons at the neuromuscular junction during intense exercise can trigger the release of additional acetylcholine and thus also help prevent or overcome fatigue.

Clearly, skeletal muscle contractions are directly controlled by somatic motor stimulation. But sympathetic stimulation can enhance skeletal muscle function to avoid fatigue during intense activity.

Functions of the Parasympathetic Division

The parasympathetic division is the dominant controller of most autonomic effectors most of the time. Under quiet, nonstressful conditions, more impulses reach autonomic effectors by cholinergic parasympathetic fibers than by adrenergic sympathetic fibers. If the sympathetic division dominates during times that require fight-or-flight, then the parasympathetic division dominates during the in-between times of "rest-and-repair."

Acetylcholine, the neurotransmitter of the parasympathetic system, tends to slow the heartbeat but acts to promote digestion and elimination. For example, it stimulates digestive gland secretion. It also increases peristalsis by stimulating the smooth muscle of the digestive tract. Can you identify other parasympathetic effects in Table 16-3?

| QUICK CHECK |

7. What is the principle of autonomic antagonism? Give an example.
8. Name the responses that occur in the fight-or-flight reaction. How does each of these prepare the body to expend a maximum amount of muscular energy?
9. Which division of the ANS is the dominant controller of autonomic effectors when the body is at rest?

the BIG picture

Autonomic Nervous System and the Whole Body

As you know, the main role of the nervous system as a whole is to detect changes in the internal and external environment, to evaluate those changes in terms of their effect on homeostatic balance, and to regulate effectors accordingly. The autonomic efferent pathways lead to the cardiac muscle effectors, smooth muscle effectors, glandular effectors, and other effectors. Such regulation not only helps us maintain our homeostatic balance, it can also react rapidly when that balance is threatened.

Because the autonomic pathways communicate with endocrine glands, endocrine effectors throughout the body can also be regulated through nervous mechanisms. Every major organ of the body is thus influenced, directly or indirectly, by autonomic output. Although the CNS is an overall controller of the major homeostatic functions of the body, the autonomic pathways are the means to exert that control.

UNIT 3

LANGUAGE OF SCIENCE (continued from p. 488)

nicotinic (N) receptor
(NIK-oh-tin-ik ree-SEP-tor)
[*Jean Nicot Villemain* **French diplomat (brought tobacco to France)**, *-in-* **substance**, *-ic* **relating to**, (**after plant genus** *Nicotiana*) *recept-* **receive**, *-or* **agent**]

nonadrenergic-noncholinergic (NANC) transmission
(non-AD-ren-er-jik non-KOHL-iner-jik tranz-MISH-un)
[*non-* **not**, *-ad-* **toward**, *-ren-* **kidney**, *-erg-* **work**, *-ic* **relating to**, *-non-* **not**, *-chole-* **bile**, *-erg-* **work**, *-ic* **relating to**]

norepinephrine (NE)
(nor-ep-i-NEF-rin)
[*nor-* **chemical prefix (unbranched C chain)**, *-epi-* **upon**, *-nephr-* **kidney**, *-ine* **substance**]

parasympathetic division
(pair-ah-sim-pah-THET-ik)
[*para-* **beside**, *-sym-* **together**, *-pathe-* **feel**, *-ic* **relating to**]

postganglionic neuron
(post-gang-glee-ON-ik NOO-ron)
[*post-* **after**, *-ganglion-* **knot**, *-ic* **relating to**, *neuron* **nerve**]

preganglionic neuron
(pree-gang-glee-ON-ik NOO-ron)
[*pre-* **before**, *-ganglion-* **knot**, *-ic* **relating to**, *neuron* **nerve**]

splanchnic nerve
(SPLANK-nik)
[*splanchn-* **internal organ**, *-al* **relating to**]

sympathetic division
(sim-pah-THET-ik)
[*sym-* **together**, *-pathe-* **feel**, *-ic* **relating to**]

sympathetic trunk
(sim-pah-THET-ik)
[*sym-* **together**, *-pathe-* **feel**, *-ic* **relating to**]

terminal ganglion
(TER-mih-nal GANG-glee-on)
[*termin-* **boundary**, *-al* **relating to**, *gangli-* **knot**, *-on* **unit**] *pl.*, ganglia

LANGUAGE OF MEDICINE

beta blocker
(BAY-tah)
[*beta* **second letter of Greek alphabet**]

biofeedback
(bye-oh-FEED-bak)
[*bio-* **life**]

erectile dysfunction (ED)
(eh-REK-tyle dis-FUNK-shun)
[*erect-* **set up**, *-ile* **relating to**, *dys-* **bad or painful**, *-func-* **perform**, *-tion* **process**]

CASE study

Tim was hiking in the Ozark Mountains when he decided to take some time to rest at the top of a bluff with a beautiful view of the river below. Soon he was dozing. After waking from a restful nap, he saw a mountain lion less than a hundred feet from him! The lion was not looking in his direction. In fact, it took no interest in Tim and simply walked away into the thick forest atop the bluff. Despite the restful nap, Tim noticed that his heart was now racing!



1. Which statement is true, given the circumstance in which Tim found himself?
   a. The racing heart resulted from a day of intense exercise including climbing the bluff.
   b. Increased heart rate is abnormal, given that Tim was well rested.
   c. Tim experienced a normal reaction to a threat.
   d. Tim is hallucinating because there are no mountain lions in the Ozarks.
   e. Tim experienced the rest-and-repair response.
2. What triggered Tim's reaction when he saw the mountain lion?
   a. Sympathetic stimulation of the heart
   b. Parasympathetic stimulation of the heart
   c. Somatic motor stimulation of the heart
   d. Both sympathetic and parasympathetic stimulation of the heart
3. What other effect(s) did Tim likely experience besides a rapid heart rate? (choose all that apply)
   a. Increased rate of breathing
   b. Sweating
   c. Slower pulse
   d. Twitching of the ears
   e. Increased digestive activity
4. Which neurotransmitter produced the effects Tim experienced?
   a. Serotonin
   b. Dopamine
   c. Acetylcholine
   d. Norepinephrine
5. Which type of organ was primed for maximum efficiency by Tim's reactions?
   a. Synovial joints
   b. Skeletal muscles
   c. Smooth muscles
   d. Kidneys
   e. Digestive organs
6. Which type of effects did Tim's body experience?
   a. Adrenergic
   b. Dopaminergic
   c. Cholinergic
   d. Anaphylactic

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

OVERVIEW OF THE AUTONOMIC NERVOUS SYSTEM

A. Role of the autonomic nervous system (ANS)
   1. Contains afferent (sensory) and efferent (motor) components (Figure 16-1)
      a. Efferent components of ANS are emphasized in this chapter
      b. Sensory concepts of the ANS are discussed in Chapter 17
   2. Carries fibers to and from the autonomic effectors (Box 16-1)
   3. Major function—to regulate heartbeat, smooth muscle contraction, glandular secretions, and metabolic functions to maintain homeostasic balance and react to threats to that balance

B. Divisions of the autonomic nervous system
   1. Two efferent divisions—sympathetic division and parasympathetic division
   2. Sympathetic division consists of neural pathways that are separate from parasympathetic pathways (Figure 16-2)
   3. Many autonomic effectors are dually innervated, which allows remarkably precise control of effector

STRUCTURE OF THE AUTONOMIC NERVOUS SYSTEM

A. Basic plan of efferent autonomic pathways (Figure 16-3)
   1. Each pathway is made up of autonomic nerves, ganglia, and plexuses, which are made of efferent autonomic neurons
   2. All autonomic neurons function in reflex arcs; called *autonomic reflexes* or *visceral reflexes*
   3. Efferent autonomic regulation ultimately depends on feedback from sensory receptors
   4. Relay of two efferent autonomic neurons conducts information from central nervous system to autonomic effectors
      a. Preganglionic neuron—conducts impulses from the central nervous system to an autonomic ganglion
      b. Postganglionic neuron—efferent neuron with which a preganglionic neuron synapses within autonomic ganglion

B. Structure of the sympathetic pathways
   1. Sympathetic chain ganglia (sympathetic trunk)
      a. Most sympathetic division ganglia lie along either side of the anterior surface of the vertebral column; joined with the other ganglia located on the same side
      b. Each chain runs from the second cervical vertebra to the level of the coccyx
      c. Usually 22 sympathetic chain ganglia on each side of vertebral column: three cervical, eleven thoracic, four lumbar, and four sacral
   2. Thoracolumbar division
      a. Sympathetic preganglionic neurons have dendrite and cell bodies in lateral gray horns of the thoracic and lumbar segments of the spinal cord
      b. Axons leave the cord by way of the ventral roots of the thoracic and first four lumbar spinal nerves; split away from other spinal nerve fibers by means of the white ramus; extend to a sympathetic chain ganglion
   3. Preganglionic fiber may take one of three paths once inside the sympathetic chain ganglion
      a. Synapse with sympathetic postganglionic neuron
      b. Send ascending or descending branches through the sympathetic trunk to synapse with postganglionic neurons in other chain ganglia
      c. Pass through one or more chain ganglia without synapsing
   4. Sympathetic postganglionic neurons
      a. Dendrites and cell bodies are mostly in sympathetic chain ganglia or collateral ganglia
      b. Gray ramus—short branch by which some postganglionic axons return to a spinal nerve
   5. In the sympathetic division, preganglionic neurons are relatively short, and postganglionic neurons are relatively long
   6. Axon of one sympathetic preganglionic neuron synapses with many postganglionic neurons, terminating in widely spread organs (Figure 16-4)

D. Structure of the parasympathetic pathways
   1. Parasympathetic preganglionic neurons—cell bodies are located in nuclei in the brainstem or lateral gray columns of the sacral cord; extend a considerable distance before synapsing with postganglionic neurons
   2. Parasympathetic postganglionic neurons—dendrites and cell bodies are located in parasympathetic ganglia, which are embedded in or near autonomic effectors
   3. Parasympathetic postganglionic neurons synapse with postganglionic neurons that each lead to a single effector (Figure 16-4)

E. Autonomic neurotransmitters and receptors (Figures 16-5 and 16-6)
   1. Axon terminal of autonomic neurons releases either of two neurotransmitters: norepinephrine or acetylcholine
   2. Adrenergic fibers—release norepinephrine; axons of postganglionic sympathetic neurons
   3. Cholinergic fibers—release acetylcholine; axons of preganglionic sympathetic neurons and of preganglionic and postganglionic parasympathetic neurons
   4. Norepinephrine affects visceral effectors by first binding to one of two types of adrenergic receptors in plasma membranes: alpha receptors or beta receptors
      a. Binding of norepinephrine to alpha receptors in smooth muscle of blood vessels is stimulating, causing the vessels to constrict
      b. Binding of norepinephrine to beta receptors in smooth muscle of blood vessels is inhibitory, causing blood vessels to dilate; in cardiac muscle, has stimulating effect
   5. Epinephrine also stimulates adrenergic receptors, enhancing and prolonging effects of sympathetic stimulation
   6. Effect of a neurotransmitter on any postsynaptic cell is determined by characteristics of the receptors, not by the neurotransmitter
   7. Termination of actions of norepinephrine and epinephrine
      a. Monoamine oxidase (MAO)—enzyme that breaks up neurotransmitter molecules taken back up by the synaptic knobs
      b. Catechol-O-methyl transferase (COMT)—enzyme that breaks down the remaining neurotransmitter
   8. Acetylcholine binds to two types of cholinergic receptors: nicotinic receptors and muscarinic receptors
   9. Termination of action of acetylcholine is by the enzyme acetylcholinesterase
   10. Autonomic neurotransmitters and receptors may influence different types of presynaptic and postsynaptic receptors at synapses with dually innervated effectors; this summation of effects increases precision of control

FUNCTIONS OF THE AUTONOMIC NERVOUS SYSTEM

A. Overview of autonomic function
   1. Autonomic nervous system functions to regulate visceral effectors in ways that tend to maintain or quickly restore homeostasis
   2. Sympathetic and parasympathetic divisions are tonically active, often exerting antagonistic influences on visceral effectors

3. Dually innervated effectors continually receive both sympathetic and parasympathetic impulses, and the summation of the two determines the controlling effect

B. Functions of the sympathetic division
   1. Under resting conditions can act to maintain the normal functioning of doubly innervated autonomic effectors
   2. Sympathetic impulses function to maintain normal tone of the smooth muscle in blood vessel walls
   3. Major function of sympathetic division is that it serves as an "emergency" system—the "fight-or-flight" reaction (review Table 16-4)

C. Functions of the parasympathetic division (review Table 16-3)
   1. Dominant controller of most autonomic effectors most of the time
   2. Acetylcholine—slows heartbeat and acts to promote digestion and elimination

THE BIG PICTURE: THE PERIPHERAL NERVOUS SYSTEM AND THE WHOLE BODY

A. The autonomic nervous system maintains homeostatic balance and can react rapidly to threats to that balance

B. Every major organ is influenced, directly or indirectly, by autonomic nervous system output

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Describe an autonomic preganglionic neuron.
2. Identify the paths that a nerve signal may take once it is inside the sympathetic chain ganglion.
3. Differentiate between the sympathetic preganglionic and postganglionic neurons in terms of length.
4. How do parasympathetic ganglia differ from sympathetic ganglia in terms of location?
5. Describe the actions of norepinephrine. How are these actions terminated?
6. Describe the responses caused by acetylcholine release. How are these actions terminated?
7. Name the main types of adrenergic and cholinergic receptors.
8. Which efferent division of the autonomic nervous system is the dominant controller of most autonomic effectors most of the time?

CRITICAL THINKING QUESTIONS

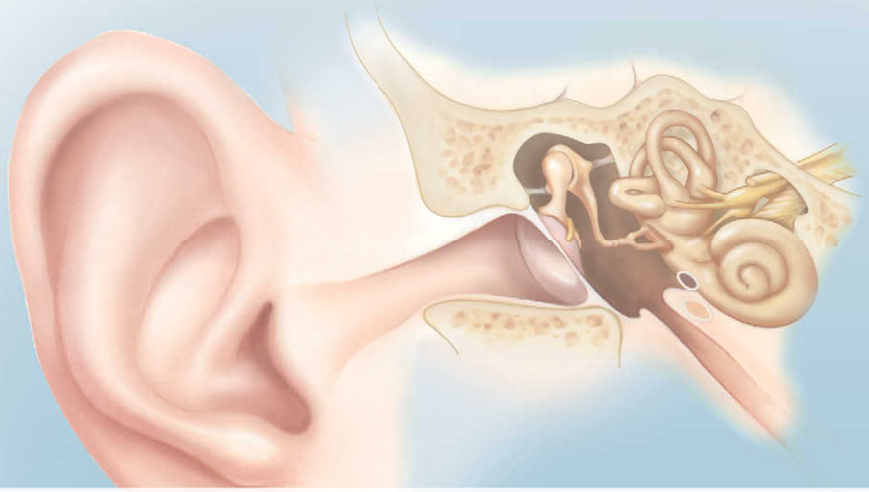


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. What is the distinction between the reflexes that cause cardiac muscle to react and those that cause skeletal muscles to react?
2. Using the control of the speed of a car as an example, explain dual innervation in the autonomic nervous system.
3. What distinguishes the function of autonomic transmitters from that of receptors? How do they regulate dually innervated effector cells?
4. Based on what you know, explain why the autonomic nervous system is not an "automatic" nervous system with little control from the higher brain centers.
5. There are reports of people performing almost superhuman feats of strength when under great stress. Specifically, what is happening in the body that would allow this to happen?
6. The drug propranolol (Inderal) blocks the effect of a portion of the sympathetic nervous system. To what class of drugs does propranolol (Inderal) belong, and what are its therapeutic effects?
7. Can you identify substances (other than acetylcholine and norepinephrine) that respond to receptors for the autonomic nervous system? What name is given to this group of substances, and what is their most likely role?

Sense Organs

17



CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

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LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

accommodation
(ah-kom-oh-DAY-shun)
[*accommoda-* **adjust,** *-ation* **process**]

acute pain
(ah-KYOOT)
[*acut-* **sharp**]

adaptation
(ad-ap-TAY-shun)
[*adapt-* **adjust,** *–tion* **process**]

alpha motor neuron
(AL-fah MOH-tor NOO-ron)
[*alpha (α)* **first letter of Greek alphabet,** *mot-* **movement,** *-or* **agent,** *neuron* **nerve**]

anterior cavity
(an-TEER-ee-or KAV-i-tee)
[*ante-* **front,** *-er-* **more,** *-or* **quality,** *cav-* **hollow,** *-ity* **state**]

auditory
(AW-di-toh-ree)
[*audit-* **hear,** *-ory* **relating to**]

auditory ossicle
(AW-di-toh-ree OS-ik-ul)
[*audit-* **hear,** *-ory* **relating to,** *os-* **bone,** *-icle* **little**]

basal cell
(BAY-sal)
[*bas-* **foundation,** *-al* **relating to,** *cell* **storeroom**]

basilar membrane
(BAYS-i-lar)
[*bas-* **foundation,** *-ar* **relating to,** *membran-* **thin skin**]

bleaching

blind spot

bulboid corpuscle
(BUL-boyd KOR-pus-ul)
[*bulb-* **swollen root,** *-oid* **like,** *corpus-* **body,** *-cle* **little**]

continued on p. 537

The body has millions of sense organs. They fall into two main categories: general sense organs and special sense organs. Of these, by far the most numerous are the general sense organs, or receptors. Receptors function to produce the general, or somatic, senses (e.g., touch, temperature, pain) and to initiate various reflexes necessary for maintaining homeostasis. Special sense organs function to produce the special senses (vision, hearing, balance, taste, smell), and they too initiate reflexes important for homeostasis. In this chapter we begin with a description of receptors and follow with information related to the special senses.

SENSORY RECEPTORS

Sense organs called **sensory receptors** make it possible for the body to respond to stimuli caused by changes occurring in our external or internal environment. This function is crucial to survival. The abilities to see and hear, for example, may provide the necessary warning to help us avoid injury from dangers in our external environment. Internal sensations ranging from pain and pressure to hunger and thirst help us maintain homeostasis of our internal environment.

Receptor Response

The general function of receptors is to respond to stimuli by converting them to nerve impulses. Receptors are often described as the sensitive dendritic endings or "end organs" of sensory neurons. As a rule, different types of receptors respond to different types of stimuli. Heat receptors, for example, do not respond to light or stretch stimuli.

When an adequate stimulus acts on a receptor, a local potential develops in the receptor's membrane. This **receptor potential** is a graded response, graded to the strength of the stimulus (see Chapter 13, p. 395). When a receptor potential reaches a certain threshold, it triggers an action potential in the sensory neuron's axon. These impulses then travel over sensory pathways to the brain and spinal cord, where they are interpreted as a particular **sensation,** such as heat or cold, or they initiate some type of reflex action, such as withdrawal of a limb from a painful stimulus.

Certain sensory impulses terminating in the brainstem may affect so-called "vital sign" reflexes that help regulate heart or respiratory rate. Others may end in the thalamus or cerebral cortex where they trigger imprecise or "crude" sensation awareness (thalamus) or very precise and specific awareness of not only a specific type of sensation but also its exact location and level of intensity (cerebral cortex).

Receptors often exhibit a functional characteristic known as adaptation. **Adaptation** refers to the process by which the magnitude of the receptor potential decreases over time in response to a continuous stimulus (Figure 17-1). As a result, the rate of impulse conduction by the sensory neuron's axon also decreases. So too does the intensity of the resulting sensation. A familiar example of adaptation is feeling the touch of your clothing when you first put it on and then soon not sensing it at all. Touch receptors adapt rapidly. In contrast, the proprioceptors in our muscles, tendons, and joints adapt slowly. As long as stimulation of them continues, they continue sending impulses to the brain.

If we not only remain aware of a particular sensation over time, but also interpret what that sensation means in a larger context, the process is called **perception.** Although we may have no conscious perception of certain sensory inputs, they often play a critical role in maintaining homeostasis. Examples might include our ability to sense and respond to changing levels of blood glucose and carbon dioxide—but not at a conscious level.

Distribution of Receptors

Receptors responsible for the **special senses** of smell, taste, vision, hearing, and equilibrium are grouped into localized areas (such as nasal mucosa or the tongue) or into complex organs such as the eye and ear. The **general sense organs,** on the other hand, consist of microscopic receptors widely distributed throughout the body

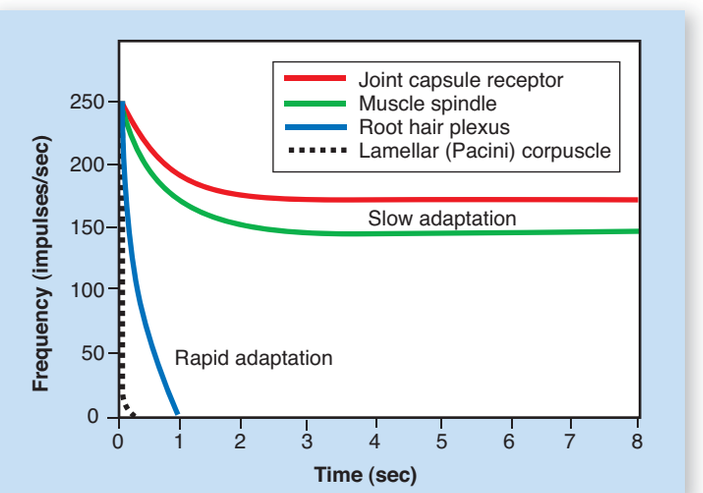


FIGURE 17-1

Adaptation of sensory receptors. In the presence of a continuous stimulus, the rate (frequency) of impulses declines quickly in rapidly adapting receptors of the skin where the initial stimulus, representing a *change,* is valuable information. However, continued sensation from the skin may be distracting. In slow-adapting joint and muscle receptors, the rate of impulses instead declines gradually and levels off to a constant, moderately high level. Thus information about body position is continually sent to the central nervous system. (Specific receptor types are discussed later in this chapter.)

in the skin, mucosa, connective tissues, muscles, tendons, joints, and viscera.

Sensations produced by the receptors of general sense organs are often called the *somatic senses*. The distribution of general sense receptors is not uniform in all areas. In some, it is very dense; in others, it is sparse. The skin covering the fingertips, for instance, contains many more receptors to touch than does the skin on the back. A simple procedure, the **two-point discrimination test,** demonstrates this fact. A subject reports the number of touch points felt when an investigator touches the skin simultaneously with two points of a compass. If the skin on the fingertip is touched with the compass points barely ⅛ inch apart, the subject senses them as two points. If the skin on the back is touched with the compass points this close together, they will be felt as only one point. Unless they are 1 inch or more apart, they cannot be discriminated as two points. Why this difference? Because touch receptors are so densely distributed in the fingertips that two points very close to each other still stimulate two different receptors—they are sensed as two points.

The situation is quite different in the skin on the back. There, touch receptors are so widely scattered that two points have to be at least 1 inch apart to stimulate two receptors and be felt as two points.

CLASSIFICATION OF RECEPTORS

Receptors can be classified according to (1) their location in the body, (2) the particular stimulus that causes them to respond, and (3) their structure.

Classification by Location

Three groups or classes of receptors can be identified by their location:

1. Exteroceptors
2. Viscероceptors (or interoceptors)
3. Proprioceptors

Exteroceptors, as the name implies, are located on or very near the body surface and respond most frequently to stimuli that arise external to the body itself. Receptors in this group are sometimes called *cutaneous receptors* because of their placement in the skin. However, the special sense organs, which are described later in the chapter, are also classified as exteroceptors. Examples of exteroceptors include those that detect pressure, touch, pain, and temperature.

Viscероceptors (interoceptors) are located internally, often within the substance of body organs (viscera), and when stimulated provide information about the internal environment. They are activated by stimuli such as pressure, stretching, and chemical changes that may originate in diverse internal organs, such as the major blood vessels, intestines, and urinary bladder. Viscероceptors are also involved in mediating sensations such as hunger and thirst.

Proprioceptors are a special type of viscероceptor. They are less numerous and generally more specialized than other internally placed receptors, and their location is limited to skeletal muscle, joint capsules, and tendons. Proprioceptors provide us with information about body movement, orientation in space, and muscle stretch.

Activation of two types of proprioceptors, called *tonic* and *phasic* proprioceptors, allows us to orient our body in space and provides us with positional information about specific body parts while at rest or during movement. The firing of the nonadapting tonic proprioceptors allows us to locate, for example, our arm, hand, or foot at rest without having to look. Phasic proprioceptors are rapidly adapting receptors, so they are triggered only when there is a change in position. Phasic proprioceptors therefore permit us to feel the changing position of our body parts during continuous movement.

Classification by Stimulus Detected

Receptors are frequently classified into six categories based on the types of stimuli that activate them:

1. **Mechanoreceptors**—activated by mechanical stimuli that in some way "deform" or change the position of the receptor, resulting in the generation of a receptor potential. Examples include pressure applied to the skin or to blood vessels or pressure caused by stretch or pressure in muscle, tendon, or lung tissue.
2. **Chemoreceptors**—activated by either the amount or the changing concentration of certain chemicals. Our senses of taste and smell depend on chemoreceptors. Some chemoreceptors in the body also detect the concentration of specific chemicals such as carbon dioxide (CO_2) and blood glucose.
3. **Thermoreceptors**—activated by changes in temperature.
4. **Nociceptors**—activated by intense stimuli of any type that results in tissue damage. The cause may be a toxic chemical, intense light, sound, pressure, or heat. The sensation produced is one of pain.
5. **Photoreceptors**—found only in the eye. Photoreceptors respond to light stimuli if the intensity is great enough to generate a receptor potential.
6. **Osmoreceptors**—concentrated in the hypothalamus and sense levels of osmotic pressure in body fluids. They are important in detecting changes in concentration of electrolytes (osmolarity) in extracellular fluids and in stimulating the hypothalamic thirst center.

Classification by Structure

Regardless of their location or how they are activated, the general (somatic) sensory receptors may be classified anatomically as either of the following:

- Free nerve endings
- Encapsulated nerve endings

Refer often to Table 17-1 as you read about the general sensory receptors that are described in the following paragraphs.

FREE NERVE ENDINGS

Free nerve endings are the simplest, most common, and most widely distributed sensory receptors. They are located both on the surface of the body (exteroceptors) and in the deep visceral organs (viscero ceptors). These slender sensory fibers often terminate in small swellings called *dendritic knobs*.

Pain Sensations

The term **nociceptor** is used to describe the free nerve endings that serve as the primary sensory receptors for pain. Nerve fibers that carry pain impulses from nociceptors to the brain can be divided into two types—**acute** or **fast (A) pain** fibers and **chronic** or **slow (B) pain** fibers.

A fibers are concentrated in the skin, mucous membranes, and other superficial areas. Fast pain is sometimes described as a sharp "take your breath away" type of pain associated with superficial injury or trauma. If you have ever slammed your finger while closing a car door you have experienced this type of fast or **somatic pain.**

The type of deep or **visceral pain** that develops more slowly over time and travels over B fibers is often described as dull or aching. It originates in deeper body (visceral) structures and can be severe if caused by conditions such as intestinal obstruction or passage of a kidney stone or gallstone.

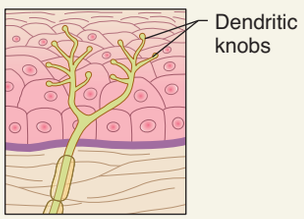
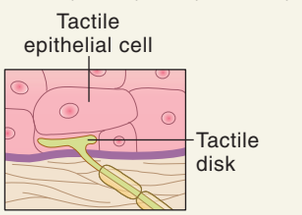
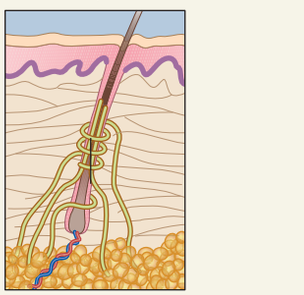
It is important to stress that in responding to powerful stimuli of any kind, including chemical or thermal burns, intense light, sound, or pressure, the generation of a receptor potential in free nerve endings most often results in the sensation of pain—often the first indication of injury or disease.

Brain tissue is unique in that it lacks the type of nociceptors that transmit sensations of pain and is therefore incapable of sensing painful stimuli. Just the opposite is true of many deep visceral organs, in which the presence of free nerve endings makes pain one of the few sensations that can be evoked.

Pain is experienced differently by different people. Many factors cause this—many of which are unknown. Certainly the brain's filtering and processing of sensory information plays a large part. Box 17-1 describes a common phenomenon in which visceral pain is perceived as external pain.

Pain is a "bad news/good news" type of sensation. The bad news, of course, is its relationship to disease and injury. The good news is the important role pain plays in alerting us to threats in our environment. Pain expert Paul Brand often called pain "the

TABLE 17-1 Classification of Somatic Sensory Receptors

BY STRUCTURE	BY LOCATION AND TYPE	BY ACTIVATION STIMULUS	BY SENSATION OR FUNCTION
Free Nerve Endings			
Nociceptor 	Either exteroceptor or visceroceptor—most body tissues	Almost any noxious stimulus; temperature change; mechanical	Pain; temperature; itch; tickle
Tactile (Merkel) disk (meniscus) 	Exteroceptor	Light pressure; mechanical	Discriminative touch
Root hair plexus 	Exteroceptor	Hair movement; mechanical	Sense of "deflection" type of movement of hair

(continued on page 512)

Box 17-1 | FYI

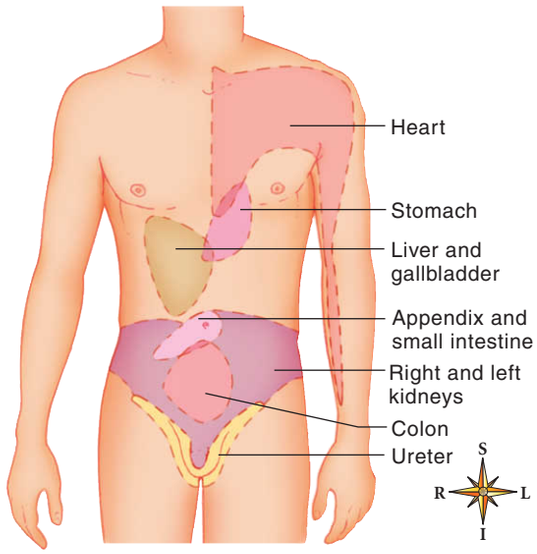
Referred Pain

The stimulation of pain receptors in deep structures may be felt as pain in the skin that lies over the affected organ or in an area of skin on the body surface far removed from the site of disease or injury. **Referred pain** is the term for this phenomenon.

The cause of referred pain is related to a mixing or convergence of sensory nerve impulses from both the diseased organ and the skin in the area of referred pain. For example, pain originating in an organ deep in the abdominal cavity is often interpreted as coming from an area of skin whose sensory fibers enter the same segment of the spinal cord as the sensory fibers from the deep structure.

A classic example is the referred pain often associated with a heart attack. Sensory fibers from the skin on the chest over the heart and from the tissue of the heart itself enter the first to the fifth thoracic spinal cord segments and so do sensory fibers from the skin areas over the left shoulder and inner surface of the left arm. Sensory impulses from all these areas travel to the brain over a common pathway. Thus the brain may feel the pain of a heart attack in the shoulder or arm.

Misinterpretation in the brain in regard to the true location of sensory neurons being stimulated causes referred pain. In clinical medicine, an understanding of referred pain is often an important determinant in whether the correct diagnosis of disease is made (see figure).



gift that nobody wants." Individuals who are unable to adequately sense pain on the body surface tend to have other types of sensory loss as well. They are very much at risk for injury because they lack the ability to sense the "warning signs" that a normally functioning sensory system can provide.

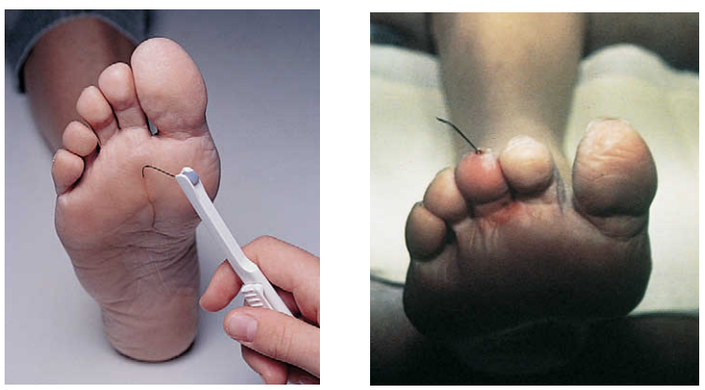
Individuals with uncontrolled or poorly controlled diabetes often lose their ability to sense pain on certain areas of the body surface—especially on the skin of the feet. Other sensations are also frequently diminished or lost over time in diabetics because of nerve damage called **diabetic neuropathy.** For this reason physicians closely monitor the adequacy of cutaneous sensation on the bottom of the foot (Figure 17-2, A). Recognizing early signs of diabetic neuropathy can help prevent later injury. Figure 17-2, *B*, shows a foreign body (a piece of wire) protruding from the tip of the third toe in a diabetic patient. The individual lacked sensation in the feet and only after visually noticing it sought medical attention. This is just one example, but a common one, of a failure of "the gift of pain" to give an appropriate warning of an injury.

In a syndrome called **fibromyalgia (FM),** chronic and widespread musculoskeletal pain is usually accompanied by distress and a variety of other symptoms. The primary mechanism of FM seems to be an abnormal amplification of pain information processed in the central nervous system. However, other mechanisms are also being investigated as contributing factors. The drug *pregabalin (Lyrica)* reduces the pain of FM mainly by blocking calcium channels in the pain-pathway neurons of the spinal cord. Reducing calcium influx, as you probably recall (see Figure 13-27 on p. 402), inhibits the release of pain neurotransmitters.

Temperature Sensations

Free nerve endings called **thermoreceptors** mediate sensations of heat and cold. When small cold or warm probes are used to "map" the skin's sensitivity to temperature, small areas called "receptive fields" about 1 mm across can be identified on the skin surface as being sensitive to *either* cold or warmth, but not both. Research has shown that these receptive fields represent separate *warm receptors* and *cold receptors* that respond to different thermal sensations and are sensitive to a range of relatively hot or cold temperatures. Thermal maps have also shown that thermoreceptors, like other types of cutaneous receptors, are not spread uniformly across the skin surface.

Both types of thermoreceptors undergo rapid adaptation. As a result, the intensity of the warm or cold sensations they initially produce when activated soon fade. We adapt to the heat of a sauna or a cool shower in a short time.



A B

FIGURE 17-2

The importance of cutaneous sensation. A, Using a monofilament to check for sensation on the bottom of the foot. **B,** Foreign body (wire) in the toe of a diabetic patient may not trigger appropriate sensations of pain because of nerve damage (diabetic neuropathy).

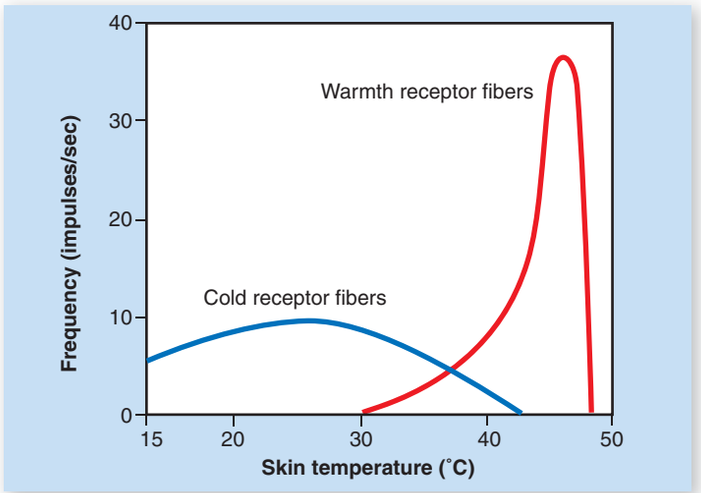


FIGURE 17-3

Range of temperature receptor sensitivity.

Warm receptors, which are located in the dermis, are activated above about 25° C (77° F) and increase their firing rate until the temperature reaches about 46° C (114° F). Figure 17-3 shows the range of temperature receptor sensitivity. Beyond a temperature of about 48° C (118° F) a sensation of burning pain begins.

Cold receptors, which are located in the deepest layer of the epidermis, have a broader temperature response than warm receptors (see Figure 17-3). They are most active between about 10° C (50° F) and 40° C (104° F). Below 10° C the firing of cold receptors decreases dramatically. The falling temperature first acts as a local anesthetic and then activates nociceptors resulting in a sensation of freezing pain. Between temperature extremes the brain senses a particular temperature sensation by integrating sensory inputs from both receptor types.

Tactile Sensations

In addition to their role in mediation of pain and temperature, free nerve endings and slightly modified free nerve endings are also involved in certain tactile sensations.

Skin Movement

Root hair plexuses are rapidly adapting free nerve endings that are activated when very slight skin movement bends or deforms a hair shaft or follicle surrounded by the receptor. When you feel a mosquito "bite," it may not be caused by the piercing of the skin by the mouth of the insect. Instead, it may be the movement of your own skin caused by the mosquito's activity that triggers or stimulates a root hair plexus. In any event, it's a good idea to swat the mosquito!

Itch

The term "itch" is used to describe several different tactile sensations mediated by free nerve endings. Most people would describe it as a sensation that makes you want to scratch. It can vary in intensity from almost imperceptible to intense and disabling. The cause is generally chemical irritation of free nerve endings by inflammatory chemicals, such as bradykinin or histamine. These types of chemicals are often released by injured tissue following insect bites, or during allergic reactions. But itches can also be induced by suggestion, like a yawn. Scientists are just now working out the types of itch that occur in humans and how these itch mechanisms work.

Tickle

Tickle is a unique sensation in that it most often results from tactile stimulation of the skin, not by you, but by someone else. It is mediated by free nerve endings and is a good but somewhat baffling example of how perception can alter the conscious



FIGURE 17-4

Discriminative touch. A, Normally, sensation can be elicited by a light stroke to the skin. **B,** Examples of specific sites used to verify sensation of discriminative touch.

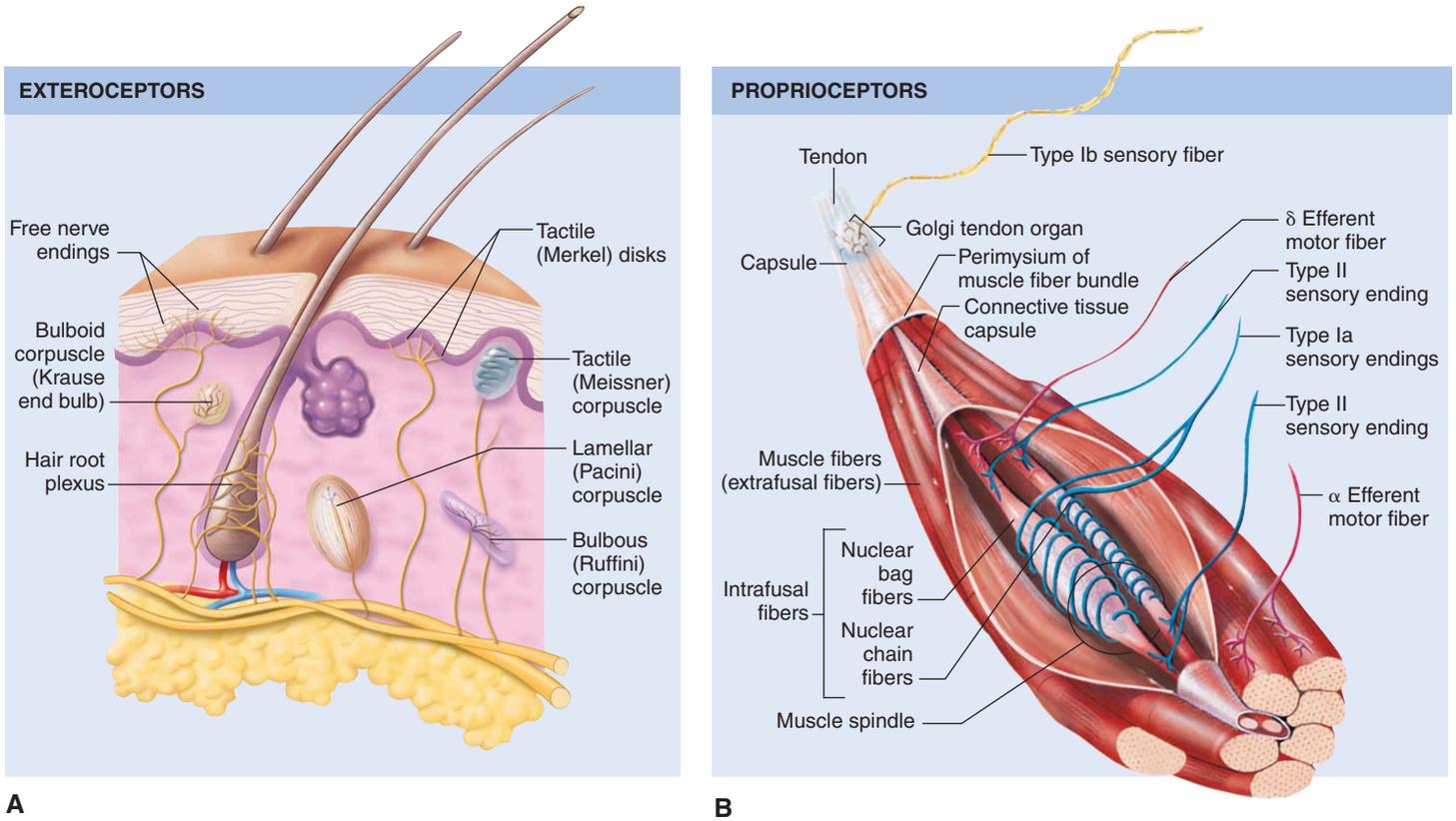
interpretation of a nervous impulse when it reaches the brain. We know that neural pathways in tickle involve both the thalamus and cerebellum before the impulses reach the cerebral cortex. However, the circuits involved in the cerebral cortex and how these circuits interact with neurons in other areas of the brain are not well understood. Obviously, knowing consciously that a particular tactile sensation generally occurs only when you are touched by someone else requires complex nervous system involvement. What begins as a simple receptor potential in a free nerve ending ends in a complex, consciously interpreted tactile sensation.

Discriminative Touch

Discriminative touch, or "light touch," refers to an often very subtle sensation that can be located exactly in certain areas of the skin (Figure 17-4). It is mediated by a flattened or disk-shaped variation of a free nerve ending called a **tactile disk** or *Merkel disk*. It may also be called a *tactile meniscus*. This structure was first described by the German anatomist Friedrich Merkel (1885-1919) when he studied delicate nervous elements near the skin surface.

Structurally, the tactile receptor unit is made up of two cells. One is an epithelial cell called the *tactile epithelial cell*, located in the epidermis of the skin (see Figure 6-4, p. 138). The other cell is a sensory neuron called the *tactile disk*. The tactile epithelial cell is rather stiff and transmits compression of the outer layer of the skin to the tactile disk neuron. The tactile disk is a delicate mechanoreceptor that is not encapsulated and has a superficial placement in the epidermis of the skin (Figure 17-5, A). It is therefore easily "deformed" when pressed by the stiff tactile cell and capable of generating an action potential when exposed to very minimal stimulation. Tactile disks adapt slowly, thus maintaining information flow to the central nervous system for some time.

In addition to discriminative or light touch, the tactile receptor unit is also capable of detecting subtle changes in surface form and contours.

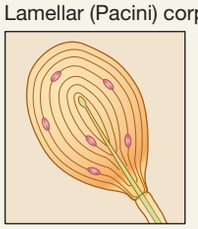
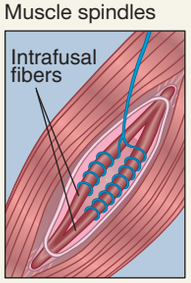
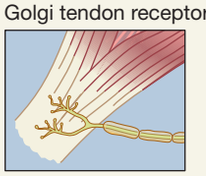


A B

FIGURE 17-5

Somatic sensory receptors.

TABLE 17-1 Classification of Somatic Sensory Receptors *(continued from page 508)*

BY STRUCTURE	BY LOCATION AND TYPE	BY ACTIVATION STIMULUS	BY SENSATION OR FUNCTION
Encapsulated Nerve Endings			
Touch and Pressure Receptors			
Tactile (Meissner) corpuscle 	Exteroceptor; epidermis, hairless skin	Light pressure, mechanical	Touch; low-frequency vibration
Bulboid (Krause) corpuscle 	Exteroceptor; mucous membranes	Mechanical	Touch; low-frequency vibration; textural sensation
Bulbous (Ruffini) corpuscle 	Exteroceptor; dermis of skin	Mechanical	Crude and persistent touch
Lamellar (Pacini) corpuscle 	Exteroceptor; dermis of skin, joint capsules	Deep pressure, mechanical	Deep pressure; high-frequency vibration; stretch
Stretch Receptors			
Muscle spindles 	Interoceptor; skeletal muscle	Stretch; mechanical	Sense of muscle length
Golgi tendon receptors 	Interoceptor; tendon (near muscle tissue)	Force of contraction and tendon stretch; mechanical	Sense of muscle tension

ENCAPSULATED NERVE ENDINGS

The six types of encapsulated nerve endings have in common some type of connective tissue capsule that surrounds their terminal or dendritic end. In addition, most of the encapsulated receptors are primary mechanoreceptors. Thus they are most often activated by a mechanical or "deforming" type of stimulus. Encapsulated receptors vary in size and anatomical characteristics, as well as in numbers and distribution throughout the body (see Table 17-1).

Touch and Pressure Receptors

Tactile corpuscles are encapsulated tactile end organs, also called *Meissner corpuscles*, first described by the German physiologist George Meissner (1829-1905). Note in Figure 17-5, A, and Table 17-1 that they are superficially placed ovoid or egg-shaped mechanoreceptors that are larger than tactile disks. The encapsulated receptor fibers are coiled and enmeshed in connective tissue. They are located in or very close to the dermal papillae in hairless skin areas such as the fingertips, lips, nipples, and genitals.

Although their covering capsule requires slightly more of a "deforming" stimulus to generate an action potential than a tactile (Merkel) disk, they do mediate light touch in addition to textural sensations and low-frequency vibration.

Two important anatomical variants of tactile (Meissner) corpuscles also act as mechanoreceptors. One is called the **bulboid corpuscle** or *Krause end bulb*. Bulboid corpuscles are egg shaped, like tactile corpuscles, but they are somewhat smaller and have fewer and less tightly coiled dendritic endings within their covering capsule. These receptors are more numerous in mucous membranes than in skin and are sometimes called *mucocutaneous corpuscles*. They are involved in touch and low-frequency vibration.

The other variant of the tactile (Meissner) corpuscle is the **bulbous corpuscle,** also known as the *Ruffini corpuscle* (see Figure 17-5, *A*). Although considered to be a variant of the tactile corpuscle, it has a more flattened capsule and is more deeply located in the dermis of the skin. These receptors mediate sensations of crude, heavy, and persistent touch. Because they are slow adapting, they permit the skin of the fingers to remain sensitive to deep pressure for long periods. The ability to grasp an object, such as the steering wheel of a car, for long periods of time and still be able to "sense" its presence between the fingers depends on these receptors.

Lamellar corpuscles (*Pacini corpuscles*) are large mechanoreceptors, which, when sectioned, show thick laminated connective tissue capsules. They are found in the deep dermis of the skin—especially in the hands and feet—and are also numerous in joint capsules throughout the body (see Figure 17-5, *A*). Pacini, or lamellar, corpuscles respond quickly to sensations of deep pressure, high-frequency vibration, and stretch. Although sensitive and quick to respond, these receptors adapt quickly, and the sensations they evoke seldom last for long.

Stretch Receptors

The most important stretch receptors are associated with muscles and tendons and are classified as proprioceptors. Two types of stretch receptors, called **muscle spindles** and **Golgi tendon receptors,** operate to provide the body with information concerning muscle length and the strength of muscle contraction (see Figure 17-5, *B*).

Anatomically, each muscle spindle consists of a discrete grouping of about 5 to 10 modified muscle fibers called *intrafusal fibers*, which are surrounded by a delicate capsule. These fibers have striated ends that are capable of contraction but are devoid of contractile filaments in their central areas where, instead, there are several nuclei surrounded by clear cytoplasm and two types of sensory nerve fibers that are described below. The muscle spindles can be found lying between and parallel to the regular muscle fibers called *extrafusal fibers*. Both ends of each spindle are connected or anchored to connective tissue elements within the muscle mass.

Two types of sensory (afferent) nerve fibers are found encircling the central area of each spindle. Both large-diameter and rapidly conducting type Ia and slower-conducting, small-diameter type II fibers encircle the clear central area of each spindle. When stretching occurs, afferent impulses from these sensory neurons pass to the spinal cord and are relayed to the brain, providing a mechanism to monitor changes in muscle length.

The striated ends of the muscle spindle fibers (intrafusal fibers) are capable of contraction when stimulated by efferent impulses generated in **gamma motor neurons,** whereas regular muscle fibers (extrafusal fibers) are stimulated to contract by efferent impulses generated in **alpha motor neurons.** Both types of neurons are located in the anterior gray horn of the spinal cord.

Muscle spindles are stimulated if the length of a muscle is stretched and exceeds a certain limit. The result of stimulation is a **stretch reflex** that shortens a muscle or muscle group, thus aiding in the maintenance of posture or the positioning of the body or one of its extremities in a way that may be opposed by the force of gravity (see Figure 12-25, p. 366). We do this unconsciously, even though these receptors do contribute to conscious proprioception.

Golgi tendon organs, often called simply *tendon organs*, like muscle spindles, are proprioceptors. They are located at the point of junction between muscle tissue and tendon. Each Golgi tendon organ consists of dendrites *(Golgi tendon receptors)* of afferent (sensory) nerves called *type Ib nerve fibers*, which are associated with bundles of collagen fibers from the tendon and surrounded by a capsule. These sensory organs act in a way opposite that of muscle spindles. Golgi tendon organs are stimulated by excessive stretch of a tendon—as when pulling too great a load for the muscle to bear safely. When the Golgi tendon organ is activated, the skeletal muscle relaxes. This response, called a *Golgi tendon reflex*, protects muscles from tearing internally or pulling away from their tendinous points of attachment to bone because of excessive contractile force.

Table 17-1 summarizes the different types of somatic sense receptors, their locations, and their functions.

| QUICK CHECK |

1. Classify receptors into six groups based on the type of stimuli that activate them.
2. Distinguish between the special and the general, or somatic, senses.
3. Name the three types of sense receptors classified according to location in the body.
4. Name the receptors associated with pain, touch, pressure, and stretch responses.

SENSE OF SMELL

We begin our study of the special senses with olfaction. Olfaction is our sense of smell. It helps us interpret our environment by detecting molecules given off by organisms and substances around us.

Olfactory Receptors

The **olfactory** epithelium consists of yellow-colored **epithelial support cells, basal cells,** and bipolar-type **olfactory sensory neurons.** These neurons, also called *olfactory receptor neurons*, have unique *olfactory cilia*, which touch the surface of the

olfactory epithelium lining the upper surface of the nasal cavity. The olfactory sensory neurons are *chemoreceptors*. They are unique because they are replaced on a regular basis by **basal cells** in the olfactory epithelium.

Receptor potentials are generated in olfactory sensory neurons when gas molecules or chemicals dissolved in the mucus covering the olfactory epithelium (Figure 17-6) bind to protein "*odor receptors*" located in the membrane of the olfactory sensory neurons. Gentle, random movement of the cilia helps "mix" the covering mucus and increases its efficiency as a solvent.

The olfactory epithelium is located in the most superior portion of the nasal cavity (see Figure 17-6). Functionally, this is a poor location because a great deal of inspired air flows around and down the nasal passageways without contacting the protein odorant receptors located in the cell membranes of the olfactory receptor cells. The location of these receptor neurons explains the necessity for sniffing, or drawing air forcefully up into the nose, to smell delicate odors.

The olfactory receptors are extremely sensitive, that is, capable of being stimulated by even very slight odors caused by just a few molecules of a particular chemical. However, rapid adaptation of olfactory sensations in the face of continuous stimulation occurs. It is due to both the inhibition of action potentials by **granule cells** in the olfactory bulbs and by fatigue of odorant receptor function caused by ongoing stimulation of the olfactory sensory neurons.

Although humans have a sense of smell far less keen than many animals, some individuals can distinguish several thousand different odors, and most of us can easily identify at least several hundred. Examples of well-known primary scents include putrid, floral, peppermint, and musky odors. Many odors are combinations of primary scents.

In 2004 U.S. researchers Drs. Linda Buck and Richard Axel received the Nobel Prize in physiology or medicine for their pioneering work that explained for the first time how the sense of smell or olfaction in humans actually "works." Their research identified almost 1000 different types of odorant receptors in the cell membranes of human olfactory sensory neurons. All of them are G-protein–coupled receptors (GPCRs), which we encountered in an earlier chapter (see Figure 13-30 on p. 405).

In a series of sophisticated experiments, they were able to show that by stimulating the entire olfactory epithelium—or specific odorant receptors—or combinations or sequences of these receptor proteins—different odors could be identified. If the receptor proteins are compared to the letters of the alphabet, activation of specific letters, formation of different "words," or word sequences, will cause differing olfactory sensory neurons or groups of neurons to transmit impulses to the brain that are perceived as unique odors.

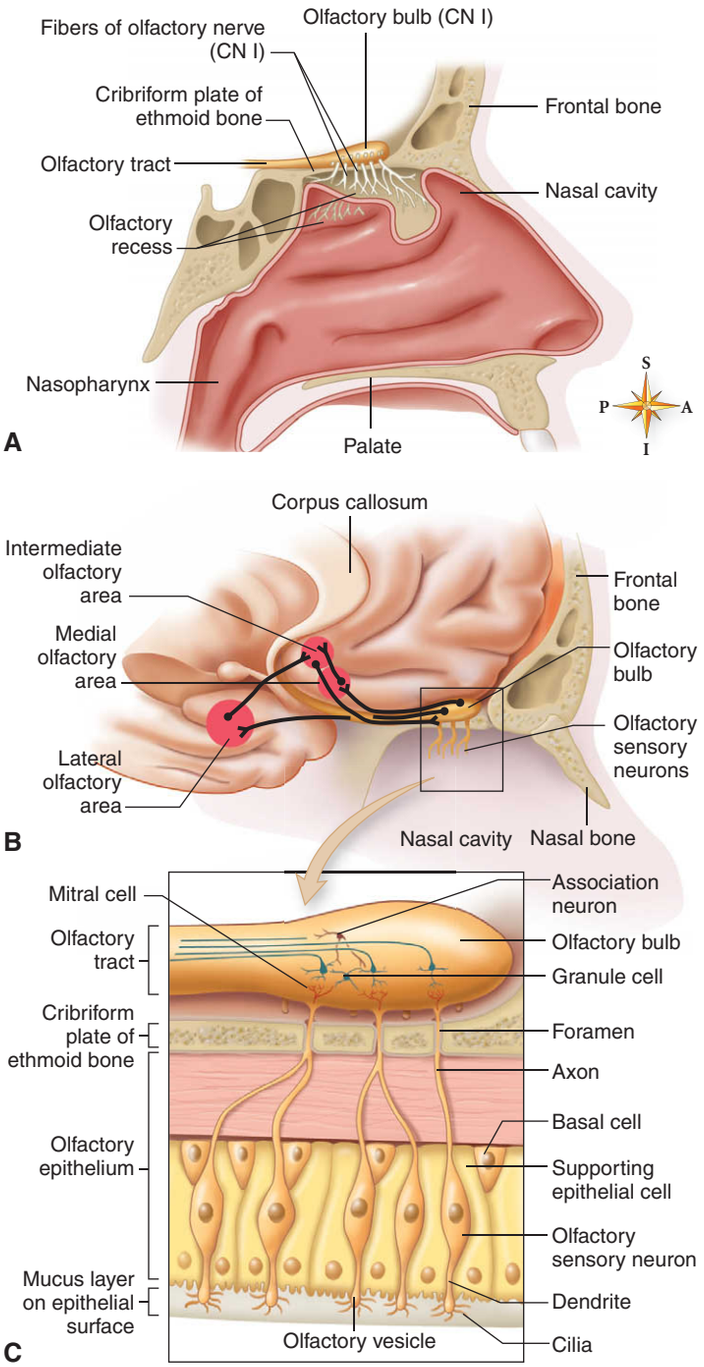


FIGURE 17-6

Olfaction. Location of olfactory epithelium, olfactory bulb, and neural pathways involved in olfaction. **A,** Midsagittal section of the nasal area shows the locations of major olfactory sensory structures. **B,** Major olfactory integration centers of the brain. **C,** Details of the olfactory bulb and olfactory epithelium.

Olfactory Pathway

If the level of odor-producing chemicals dissolved in the mucus surrounding the olfactory cilia reaches a threshold level, a receptor potential and then an action potential will be generated and passed to the olfactory nerves in the olfactory bulb. From there, the impulse passes through the olfactory tract and into the thalamic and olfactory centers of the brain for interpretation, integration, and memory storage.

The sense of smell can create powerful and long-lasting memories. Memories coupled with unique sensory inputs, especially distinctive odors, often persist from early childhood to death. Dental office smells, baby smells, kitchen smells, and new car smells are examples of olfactory "triggers" that often bring back memories of events that occurred years earlier. In addition to the olfactory cortex and thalamic areas of the brain, components of the limbic system, including the cingulate gyrus and hippocampus, play a key role in coupling olfactory sense inputs to both short- and long-term memory.

Not only can specific odors trigger long-term memory, they often allow the individual to recall emotions associated with the recalled experience as well. For example, the smell of an evergreen tree by a 90-year-old man may trigger both the memory of events and the recall of emotions he experienced at Christmas when he was a 9-year-old boy. The mechanism of such a complex association between the detection of a specific odor and recall of the actual emotions and ambiance surrounding a long-term memory remain unknown.

People who suffer from permanent **anosmia,** complete lack of smell, can suffer from serious depression. Apparently, the loss of smell can have more impact on our psychological health than the loss of any other sense.

Our senses of smell and taste are closely related. Note in Figure 17-7 that the neural inputs from both olfactory and gustatory (taste) receptors travel in several common areas of the brain. Ultimately, olfactory sensations are produced in the (smell) sensory cortex located in the temporal lobes, and taste sensations result from stimulation of the (taste) sensory cortex in the parietal lobes.

| A&P CONNECT |

A sense related to olfaction is our ability to detect *pheromones,* or sexual signal molecules, from other people. The receptors for pheromones are just inside our nose, near the olfactory receptors. Find out more about this sexual signaling in ***Pheromones and the Vomeronasal Organ*** online at ***A&P Connect.***

evolve

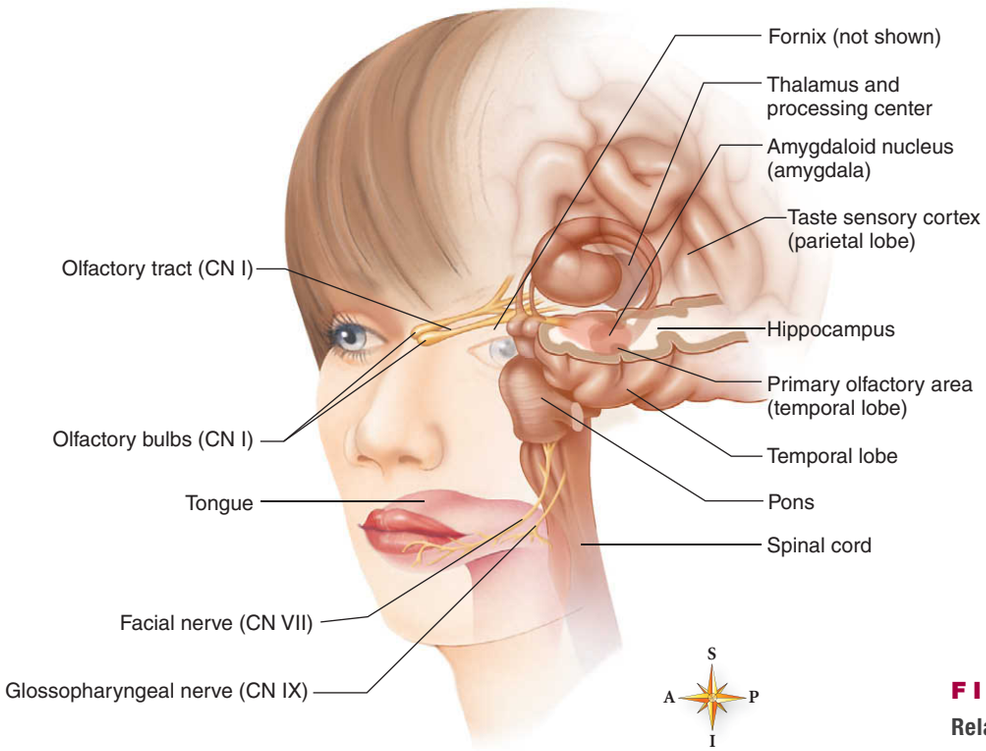


FIGURE 17-7
Relationship of olfactory and gustatory pathways.

UNIT 3

SENSE OF TASTE

Taste Buds

The **taste buds** are the sense organs that respond to **gustatory,** or taste, stimuli. Although a few taste buds are located in the lining of the mouth and on the soft palate, most are associated with small, elevated projections on the tongue, called **papillae** (Figure 17-8, *A* and *B*).

Tongue papillae are classified by their structure:

Fungiform papillae—large, mushroom-shaped bumps found in the anterior two thirds of the tongue surface; each one contains one or a few taste buds

Circumvallate papillae—huge, dome-shaped bumps that form a transverse row near the back of the tongue surface; each one contains thousands of taste buds

Foliate papillae—red, leaflike ridges of mucosa on the lateral edges of the posterior tongue surface; each contains about a hundred or so taste buds

Filiform papillae—bumps with tiny, threadlike projections; these papillae are scattered among the fungiform papillae; they do not contain taste buds but allow us to experience food texture and "feel"

Although the different varieties of papillae are distributed differently across the tongue surface, no regional difference exists in where a particular taste can be detected. For example, the long-held belief that bitter taste was localized at the back of the tongue with its high concentration of circumvallate papillae (see Figure 17-8, *A*) or that sweet taste is detected best at the tip of the tongue is simply not true. No tongue or taste "map" accurately indicates regional areas of particular sensitivity to different tastes. All tastes can be detected in all areas of the tongue that contain taste buds.

Taste buds house the chemoreceptors responsible for taste. They are stimulated by chemicals, called *tastants*, dissolved in the saliva. Each taste bud is like a banana cluster that contains 50 to 125 of these chemoreceptors, called **gustatory cells,** which are surrounded by a supportive epithelial cell capsule. Cilia, here called *gustatory hairs*, extend from each of the gustatory cells and project into an opening called the *taste pore*, which is bathed in saliva (see Figure 17-8, *C*).

The sense of taste depends on the creation of a receptor potential in gustatory cells. Only then can an action potential be generated and a nerve impulse relayed to the brain for interpretation. Generation of a receptor potential begins when G-protein–coupled receptors (GPCRs) or ion channels in the plasma membranes of gustatory hairs bind to taste-producing chemicals (tastants) in the saliva. See Figure 13-30 (p. 405) to review GPCRs and Figure 13-29 (p. 405) to review ion channels acting as receptors. The nature and concentration of the chemicals that bind to either the receptor sites or ion channels determine how fast the receptor potential is generated.

Taste cells appear similar structurally, and all of them can respond at least in some degree to most taste-producing chemicals. Each taste receptor cell, however, responds most effectively to only one of five "primary" taste sensations: sour, sweet, bitter, umami

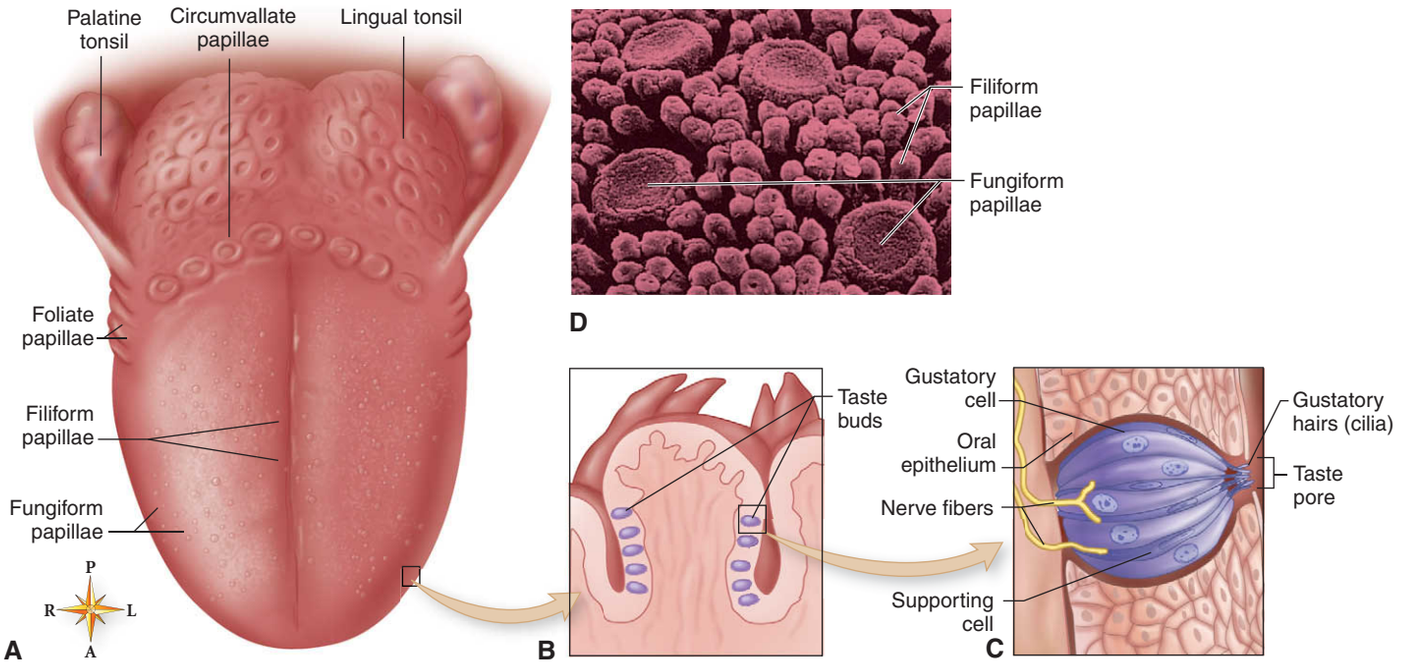


FIGURE 17-8

The tongue. A, Dorsal surface of tongue and adjacent structures. **B,** Section through a papilla with taste buds on the side. **C,** Enlarged view of a section through a taste bud. **D,** Scanning electron micrograph of the tongue surface showing the papillae in detail.

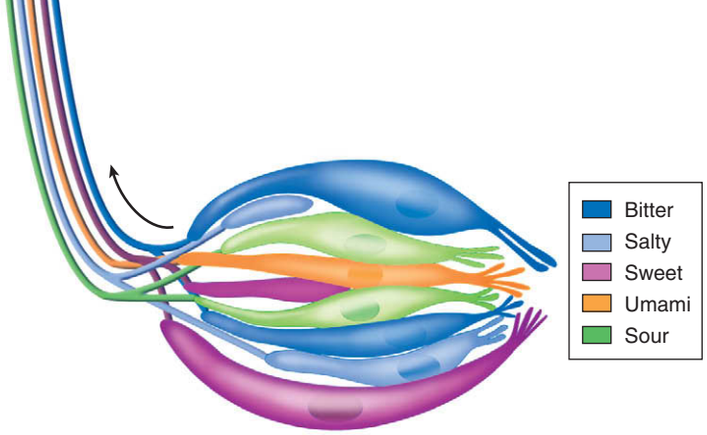


FIGURE 17-9

Taste receptors. The labeled-line model of gustation (taste) holds that each distinct taste has a separate group of taste receptors, with each group sending its impulses along a distinct "line" or neural pathway.

(savory), and salty. The *labeled-line model*, shown in Figure 17-9, holds that our brain can determine which taste we are detecting by the fact that signals from different types of receptors are conducted along different lines or neural pathways. Our ability to experience a larger variety of tastes results from combinations of the five primary sensations.

The exact mechanism by which a chemical tastant binds to a particular receptor site or ion channel on a gustatory hair is unknown. Chemical structure plays a part but is not the only factor involved, because substances that are very different chemically, such as artificial sweeteners, chloroform, and table sugar, produce a sweet taste. Some chemical compounds and specific ions, however, are definitely associated with specific tastes. Sour (H^+) and salty (Na^+) tastes activate ion channels, whereas sweet, umami, and bitter tastes result from stimulation of receptor sites. As chemoreceptors, the taste buds, like olfactory receptors, tend to be quite sensitive initially but fatigue easily. Very low levels of taste-producing chemicals are required to generate a receptor potential. However, adaptation often begins within a few seconds after a taste sensation is first noticed and is generally complete in a few minutes.

The adaptive value of our sense of taste is obvious: taste allows us to chemically test our food before swallowing it. We can then selectively eat salty foods when our body is low in sodium, or avoid foods that contain too much sodium. We can determine which foods are high in sugars when they taste sweet. Foods with a savory, or umami, taste are likely to be high in amino acids. Umami receptors detect *L-glutamate*, a form of the common amino acid *glutamic acid* released from proteins in cooked, fermented, and ripened foods. Bitter tastes, to which we have a natural aversion, signal a variety of toxins and other druglike chemicals such as caffeine that are sometimes present in plants. Research shows that there may be additional taste modalities such as "metallic" taste.

Neural Pathway for Taste

The taste sensation begins with creation of a receptor potential in the gustatory cells of a taste bud. The generation and propagation of an action potential, or nerve impulse, then transmits the sensory input to the brain.

Nerve impulses generated in the anterior two thirds of the tongue travel over the facial (CN VII) nerve, whereas those generated from the posterior one third are conducted by fibers of the glossopharyngeal (CN IX) nerve. A third cranial nerve, the vagus (CN X) nerve, plays a minor role in taste. It contains a few fibers that carry taste sensation from a limited number of taste buds located in the walls of the pharynx and on the epiglottis.

All three cranial nerves carry impulses into the medulla oblongata. The fact that, unlike any other special sense, taste has several different pathways to the brain is evidence that taste information is very important for survival. Once taste information is processed in the medulla, relays then carry the impulses into the thalamus and then into the taste, or gustatory, area of the cerebral cortex in the parietal lobe of the brain (see Figure 17-7).

We generally think of taste in terms of the "primary" sensations of sour, sweet, bitter, umami, and salty (and perhaps metallic). However, touch, texture, and temperature are also involved in taste and whether we sense it as pleasant, neutral, or unpleasant. Take the sensation of *flavor* as an example. Flavor, as the term is normally used, is a combined sense of smell, taste, and the so-called *trigeminal senses* (mediated by CN V) that detect irritants, textures, and other characteristics present in spices and most other foods. As we breathe out as we are chewing or savoring food in the mouth, olfactory receptors are triggered as the same time as receptors in taste buds and the rest of the oral mucosa. This information is integrated in the brain and we sense the combination of smells, tastes, heat (as in pepper), cold (as in mint), and texture as a single, complex flavor experience.

| QUICK CHECK |

5. List the special senses.
6. Discuss how a receptor potential is generated in olfactory cells.
7. Discuss how a receptor potential is generated in gustatory cells.
8. Trace the path of a nervous impulse carrying (1) olfactory and (2) gustatory sense information from its point of origin to that area of the brain where interpretation occurs.
9. List the five "primary" taste sensations.
10. Locate on the tongue where taste buds are detected.

SENSES OF HEARING AND BALANCE: THE EAR

The ear has dual sensory functions. In addition to its role in hearing, it also functions as the sense organ of balance, or equilibrium. The stimulation, or "trigger," responsible for hearing and balance involves activation of mechanoreceptors called *hair cells*. Sound waves and fluid movement are the physical forces that act on hair cells to generate receptor potentials and then nerve impulses, which are eventually perceived in the brain as sound or

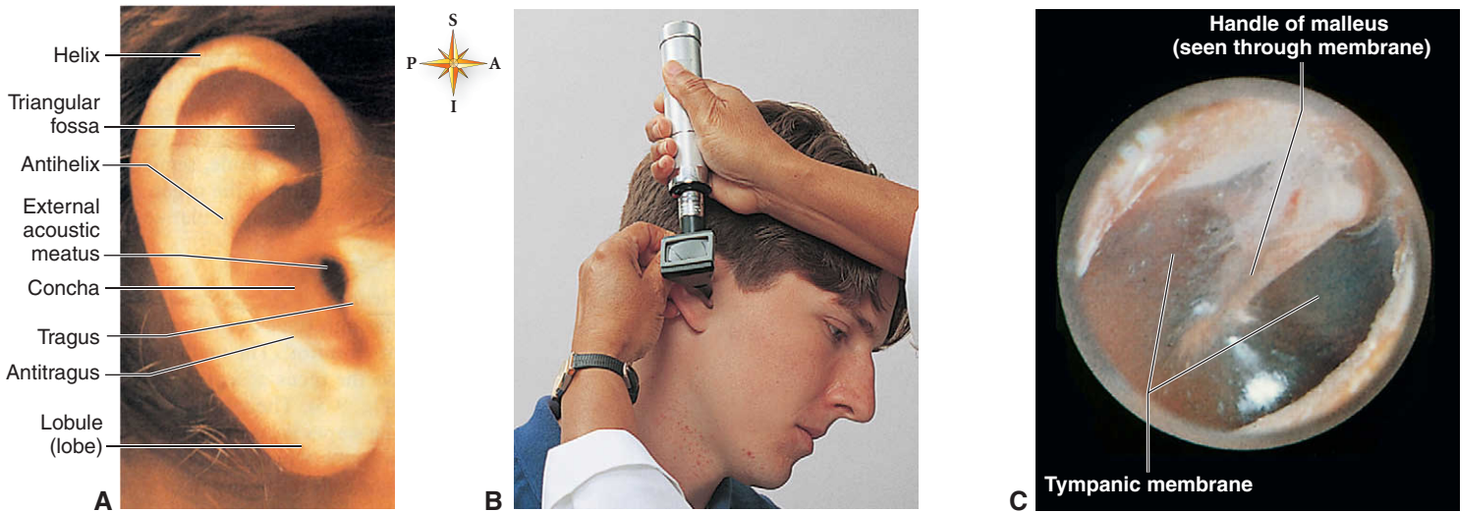


FIGURE 17-10

Examining the external ear, ear canal, and tympanic membrane. **A,** Anatomical structures of the auricle (external ear). **B,** Using a lighted otoscope to view the external ear canal and tympanic membrane. **C,** Note the translucent, pearly-grey appearance of a normal tympanic membrane. The "handle" of the malleus can be seen attaching near the center of the inner surface of the membrane.

balance. The ear is divided into three anatomical parts: **external ear, middle ear,** and **inner ear** (Figures 17-10 and 17-11).

The structures illustrated in Figure 17-11 are not drawn to scale. Instead, the smaller components of the middle and inner ear are enlarged so that they can be more easily identified. In addition, this type of artistic rendering makes it easier to see the anatomical relationships of these tiny elements to one another and to adjacent structures.

External Ear

The external ear has two divisions: the *auricle* or *pinna*, and the *external acoustic meatus* (ear canal). The auricle is the visible appendage on the side of the head surrounding the opening of the external acoustic meatus. A number of anatomical components of the auricle are identified in Figure 17-10.

Because it lies exposed against the bony surface of the skull, the auricle is frequently injured by blunt trauma. Bruising may then cause an accumulation of blood and tissue fluid between the skin and underlying cartilage. If bruising is left untreated, the dramatic swelling of "cauliflower ear" may develop and become permanent. The sun-exposed auricle, especially the tops of the helix, is also a frequent site for development of skin cancer, often squamous cell carcinoma (see Chapter 7).

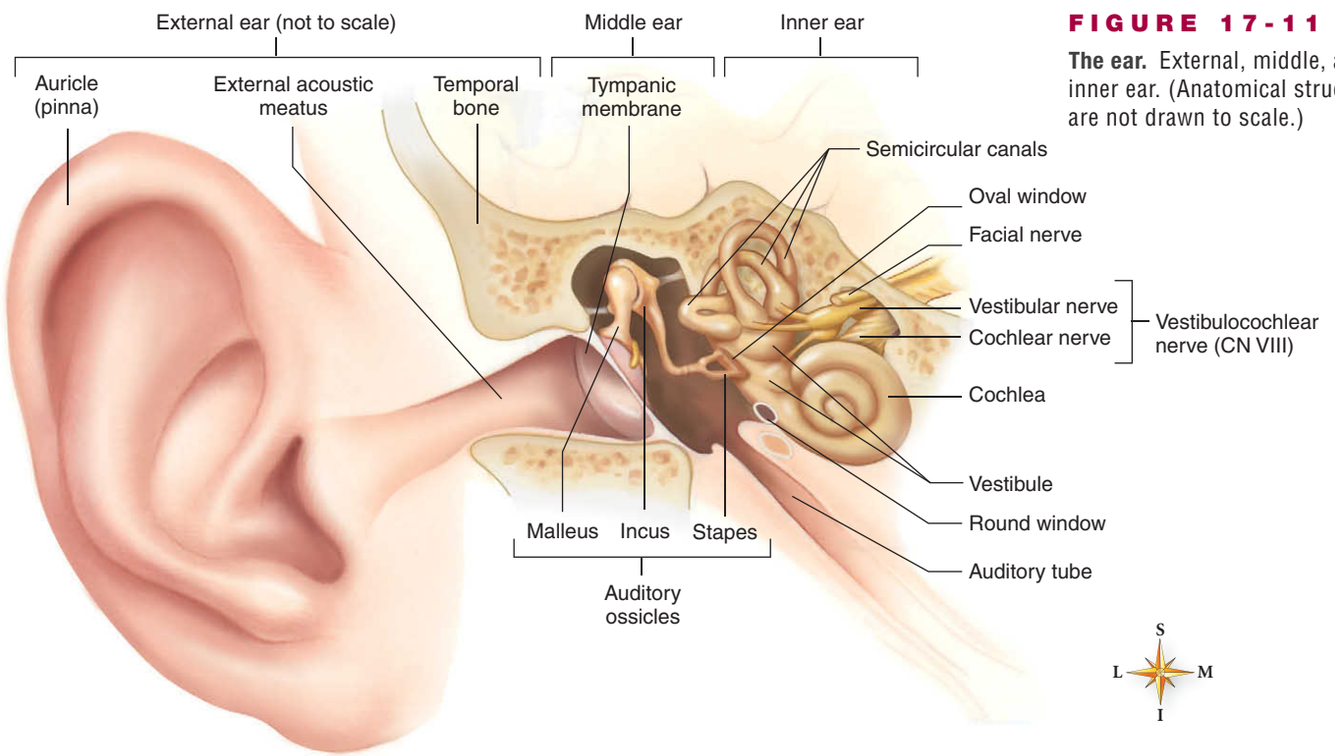


FIGURE 17-11

The ear. External, middle, and inner ear. (Anatomical structures are not drawn to scale.)

The *lobule* or lobe of the auricle is a frequent site of piercing for cosmetic reasons. Piercings of the cartilage in other areas of the auricle carry a higher risk of infection and slower healing because there is a better blood supply in the lobule.

Note in Figure 17-10 that the *tragus* of the auricle is located just in front of the opening to the ear in adults, this canal is about 3 cm long. Initially it slants upward a bit and then curves downward before traveling into the temporal bone in an inward and forward direction. It ends at the **tympanic membrane,** or **eardrum,** which stretches across the inner end of the canal, separating it from the middle ear.

A lighted instrument called an **otoscope** is used to examine the external ear canal and outer surface of the tympanic membrane (see Figure 17-10, *B*). Changes in the appearance of the ear canal and tympanic membrane can provide a skilled observer with a great deal of information. For example, middle ear infection, called **otitis media,** will cause the eardrum to become red and inflamed and to bulge outward into the ear canal as pus and other fluids accumulate in the middle ear (see Mechanisms of Disease, p. 534). Accumulation of the waxlike substance *cerumen*, which is secreted by modified sweat glands in the auditory canal, may cause pain and temporary deafness. It is easily identified during otoscopic examination of the ear canal.

Middle Ear

The middle ear (tympanic cavity), a tiny epithelial-lined cavity hollowed out of the temporal bone, contains the three **auditory ossicles:** the *malleus*, *incus*, and *stapes* (see Figure 17-11). The names of these very small bones describe their shapes (hammer, anvil, stirrup). The "handle" of the malleus is attached to the inner surface of the tympanic membrane, whereas the "head" attaches to the incus, which in turn attaches to the stapes. There are several openings into the middle ear cavity: one from the external acoustic meatus, covered with the tympanic membrane; two into the internal ear, the **oval window** (into which the stapes fits) and the **round window,** which is covered by a membrane; and one into the auditory (eustachian) tube.

Posteriorly the middle ear cavity is continuous with numerous mastoid air spaces in the temporal bone. The clinical importance of these middle ear openings is that they provide routes through which infection can travel. Head colds, for example, especially in children, may lead to middle ear or mastoid infections by way of the nasopharynx-auditory tube, middle ear–mastoid path.

The **auditory,** or **eustachian,** tube is composed partly of bone and partly of cartilage and fibrous tissue and is lined with mucosa. It extends downward, forward, and inward from the middle ear cavity to the nasopharynx, or pharyngotympanic tube (the part of the throat behind the nose). The auditory tube serves a useful function: it makes possible equalization of pressure against inner and outer surfaces of the tympanic membrane and therefore prevents membrane rupture and the discomfort that marked pressure differences produce. The way the auditory tube equalizes tympanic membrane pressure is this: when you swallow or yawn, air spreads rapidly through the open tube. Atmospheric pressure then presses against the inner surface of the tympanic membrane. Because atmospheric pressure is continually exerted against its outer surface, the pressures are equal.

Inner Ear

The inner ear is also called the **labyrinth** because of its complicated shape. It consists of two main parts, a bony labyrinth and, inside this, a membranous labyrinth. The bony labyrinth consists of three parts: the *vestibule*, *cochlea*, and *semicircular canals* (Figure 17-12). The membranous labyrinth consists of the *utricle*

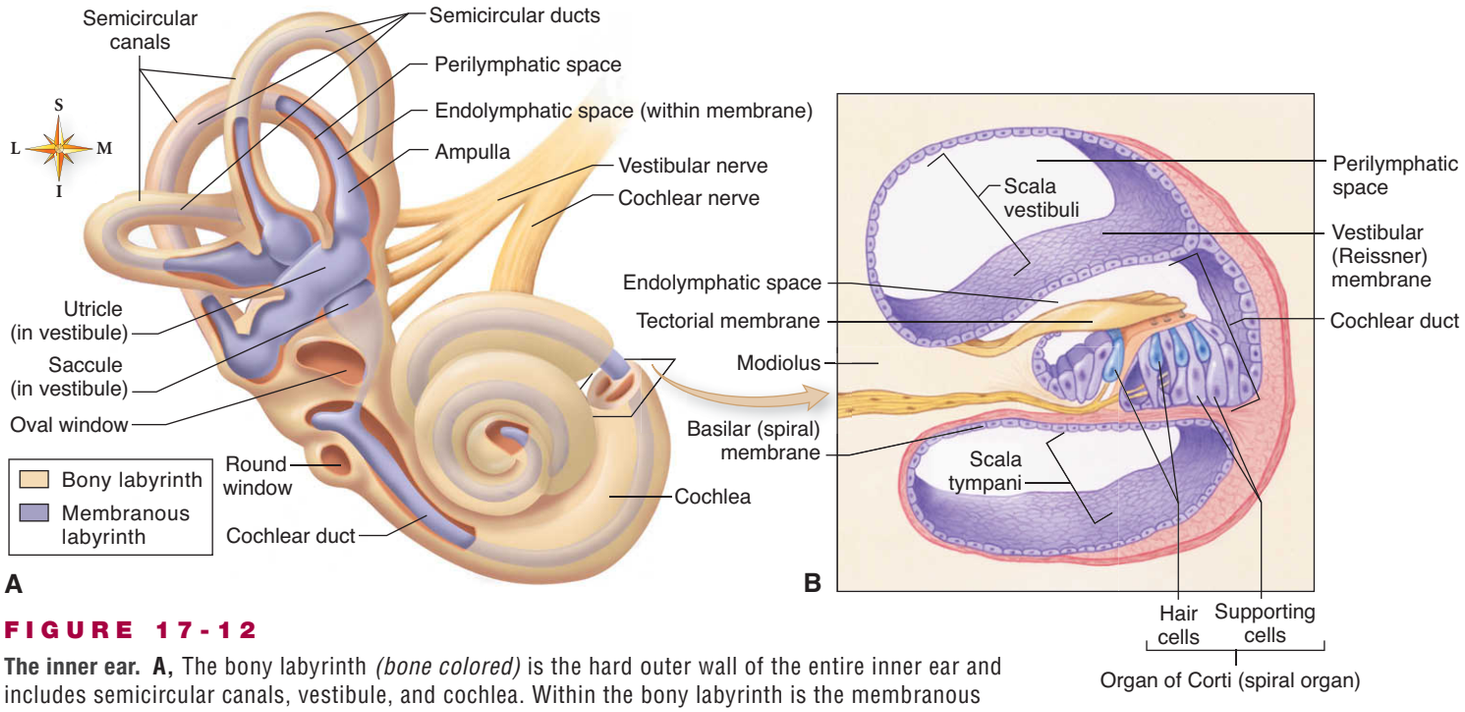


FIGURE 17-12

The inner ear. A, The bony labyrinth *(bone colored)* is the hard outer wall of the entire inner ear and includes semicircular canals, vestibule, and cochlea. Within the bony labyrinth is the membranous labyrinth *(purple),* which is surrounded by perilymph and filled with endolymph. Each ampulla in the vestibule contains a crista ampullaris that detects changes in head position and sends sensory impulses through the vestibular nerve to the brain. **B,** The inset shows a section of the membranous cochlea. Hair cells in the organ of Corti (spiral organ) detect sound and send the information through the cochlear nerve. The vestibular and cochlear nerves join to form the eighth cranial nerve.

and *saccule* inside the vestibule, the *cochlear duct* inside the cochlea, and the membranous *semicircular ducts* inside the bony ones. The vestibule (containing the membranous utricle and saccule) and the semicircular canals (and membranous ducts) are involved in balance; the cochlea (and membranous cochlear duct) is involved in hearing.

The term **endolymph** is used to describe the clear and potassium-rich fluid that fills the membranous labyrinth. **Perilymph,** a fluid similar to cerebrospinal fluid, surrounds the membranous labyrinth and therefore fills the space between this membranous tunnel and its contents and the bony walls that surround it (see Figure 17-12).

COCHLEA AND COCHLEAR DUCT

The word *cochlea*, which means "snail," describes the outer appearance of this part of the bony labyrinth. When sectioned, the cochlea resembles a tube wound spirally around a cone-shaped core of bone, the *modiolus*. The modiolus houses the spiral ganglion, which consists of cell bodies of the first sensory neurons in the auditory relay.

Inside the cochlea lies the membranous *cochlear duct*—the only part of the internal ear concerned with hearing. This structure is shaped like a somewhat triangular tube. It forms a shelf across the inside of the bony cochlea, dividing it into upper and lower sections all along its winding course (see Figure 17-12). The upper section (above the cochlear duct) is called the *scala vestibuli* (vestibular duct), whereas the lower section below the cochlear duct is called the *scala tympani* (tympanic duct). The roof of the cochlear duct is known as the **vestibular membrane** *(Reissner membrane)*. The **basilar membrane** is located on the floor of the cochlear duct. It is also called the *spiral membrane* and is supported by bony and fibrous projections from the wall of the cochlea. Perilymph fills the scala vestibuli and scala tympani, and endolymph fills the cochlear duct.

The hearing sense organ, named the **organ of Corti,** rests on the basilar membrane throughout the entire length of the cochlear duct. The organ of Corti is also called the *spiral organ* because of its spiraling curl within the cochlea. The structure of the organ of Corti consists of supporting cells, as well as important hair cells that project into the endolymph and are topped by an adherent gelatinous membrane called the **tectorial membrane.**

Dendrites of the sensory neurons, whose cell bodies lie in the spiral ganglion in the modiolus, have their beginnings around the bases of the inner row of ciliated hair cells of the organ of Corti. Axons of these neurons extend to form the cochlear nerve (a branch of the eighth cranial nerve) to the brain. They conduct impulses that produce the sensation of hearing.

SENSE OF HEARING

Sound is created by vibrations that may occur in air, fluid, or solid material. When we speak, for example, the vibrating vocal cords create sound waves by producing vibrations in air passing over them.

Numerous terms are used to describe sound waves. The height, or amplitude, of a sound wave determines its perceived loudness, or **volume.** The number of sound waves that occur during a specific time unit (frequency) determines **pitch.** Our ability to hear sound waves depends in part on volume, pitch, and other acoustic properties. Sound waves must be of sufficient amplitude to initiate movement of the tympanic membrane and have a frequency that is capable of stimulating the hair cells in the organ of Corti at some point along the basilar membrane.

The basilar membrane is not the same width and thickness throughout its length. Because of this structural fact, different frequencies of sound will cause the basilar membrane to vibrate and bulge upward at different places along its length. Two bulges are shown in Figure 17-13, *A*.

High-frequency sound waves cause the narrow portion of the basilar membrane near the oval window to vibrate, whereas low frequencies vibrate the membrane near the apex of the cochlea, where it is considerably wider and thicker (Figure 17-13, *B*). This ability of sound waves of differing frequency to vibrate and cause a bulge, or displacement, of the basilar membrane at differing points along its length explains how specific groups of hair cells respond to specific frequencies of sound. When a particular portion of the basilar membrane bulges upward, the cilia on hair cells attached to that particular area are stimulated, and ultimately, sound of a particular pitch is perceived.

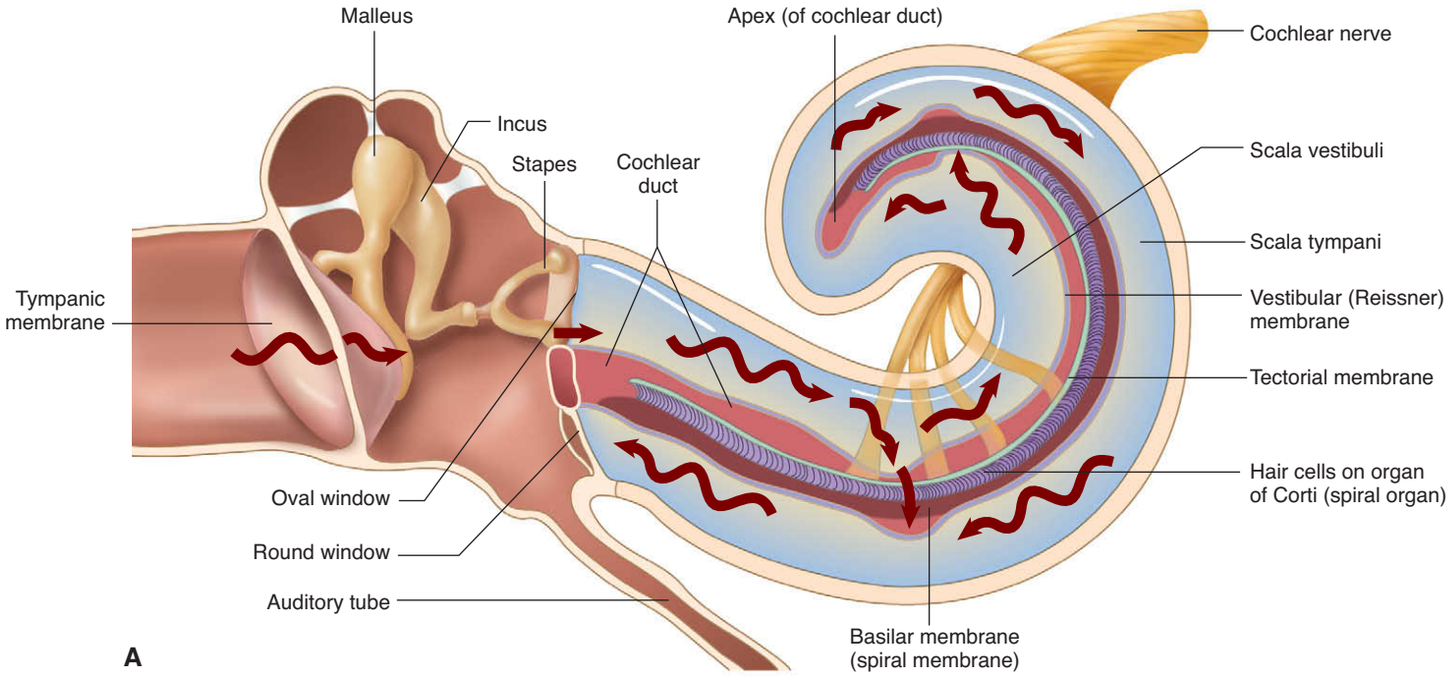
Our perception of different degrees of loudness of the same sound is determined by the amplitude, or movement, of the basilar membrane at any particular point along its length. The higher the upward bulge, the more the cilia on the attached hair cells are bent or stimulated. This causes an increase in perceived loudness. The moving wave of perilymph caused by upward displacement of the basilar membrane is soon dampened as it moves through the cochlea.

Hearing results from stimulation of the auditory area of the cerebral cortex. First, however, sound waves must be projected through air, bone, and fluid to stimulate nerve endings and set up impulse conduction over nerve fibers. Box 17-2 describes a method for artificially detecting sound and stimulating the neural pathways of hearing.

Pathway of Sound Waves

Sound waves in the air enter the external auditory canal with aid from the pinna. At the inner end of the canal, they strike against the tympanic membrane, causing it to vibrate. Vibrations of the tympanic membrane move the malleus, whose handle attaches to the membrane. The head of the malleus attaches to the incus, and the incus attaches to the stapes. So when the malleus vibrates, it moves the incus, which moves the stapes against the oval window into which it fits so precisely. At this point, fluid conduction of sound waves begins. When the stapes moves against the oval window, pressure is exerted inward into the perilymph in the scala vestibuli of the cochlea. This starts a "ripple" in the perilymph that is transmitted through the vestibular membrane (the roof of the cochlear duct) to endolymph inside the duct and then to the organ of Corti and to the basilar membrane that supports the organ of Corti and forms the floor of the cochlear duct. From the basilar membrane the ripple is next transmitted to and through the perilymph in the scala tympani and finally expends itself against the round window—like an ocean wave as it breaks against the shore, but on a much reduced scale.

Figure 17-13 summarizes the steps involved in detecting sound stimuli in the ear.



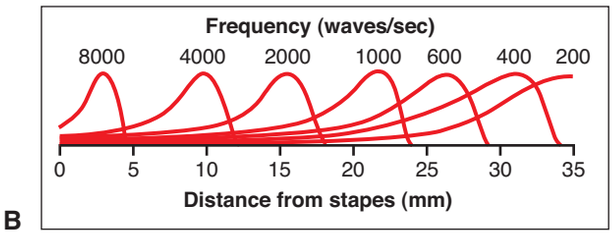


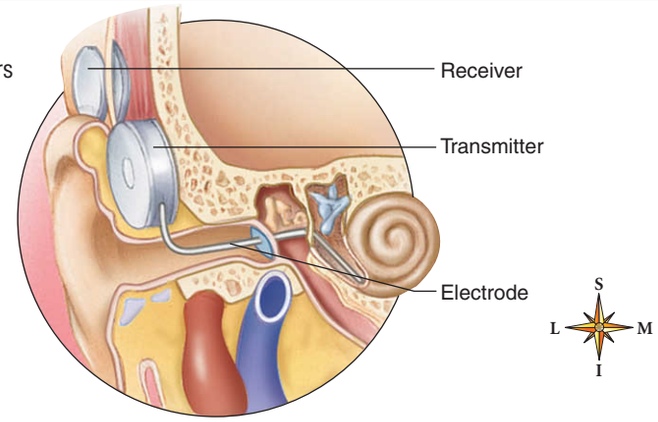
FIGURE 17-13

Effect of sound waves on cochlear structures. A, Sound waves strike the tympanic membrane and cause it to vibrate. This causes the membrane of the oval window to vibrate, which causes the perilymph in the bony labyrinth of the cochlea and the endolymph in the membranous labyrinth of the cochlea, or cochlear duct, to move. This movement of endolymph causes the basilar (spiral) membrane to vibrate, which in turn stimulates hair cells on the organ of Corti (spiral organ) to transmit nerve impulses along the cochlear nerve. Eventually, nerve impulses reach the auditory cortex and are interpreted as sound. **B,** High-frequency (high-pitch) waves stimulate hair cells nearer the stapes (oval window) and low-frequency (low-pitch) waves stimulate hair cells nearer the distal end of the cochlea. The location of peak stimulation of the hair cells allows the brain to interpret the pitch of the sound.

Box 17-2 | HEALTH matters

Cochlear Implants

Electronic devices can help correct some forms of nerve deafness. If the hairs on the organ of Corti (spiral organ) are damaged, nerve deafness results—even if the vestibulocochlear nerve is healthy. A surgically implanted device can improve this form of hearing loss by eliminating the need for the sensory hairs. As you can see in the figure, a transmitter just outside the scalp sends external sound information to a receiver under the scalp (behind the auricle). The receiver translates the information into an electrical code that is relayed down an electrode to the cochlea. The electrode, wired to the organ of Corti, stimulates the vestibulocochlear nerve endings directly. Thus even though the cochlear hair cells are damaged, sound can be perceived.



UNIT 3

Neural Pathway of Hearing

Dendrites of neurons whose cell bodies lie in the spiral ganglion and whose axons make up the cochlear nerve terminate around the bases of the hair cells of the organ of Corti, and the tectorial membrane adheres to their upper surfaces. The movement of the hair cells against the adherent tectorial membrane somehow stimulates these dendrites and initiates impulse conduction by the cochlear nerve to the brainstem. Before reaching the auditory area of the temporal lobe, impulses pass through "relay stations" in nuclei in the medulla, pons, midbrain, and thalamus.

| QUICK CHECK |

11. List the three anatomical divisions of the ear.
12. Identify the three auditory ossicles.
13. Name the divisions of both the membranous and bony labyrinths.
14. Name the specific sense organ responsible for hearing.

VESTIBULE AND SEMICIRCULAR CANALS

The vestibule constitutes the central section of the bony labyrinth. Look again at Figure 17-12, A. Note that the bony labyrinth opens into the oval and round windows from the middle ear, as well as the three semicircular canals of the internal ear. The utricle and saccule are the membranous structures within the vestibule. Both have walls of simple cuboidal epithelium and are filled with endolymph.

Three semicircular canals, each in a plane approximately at right angles to the others, are found in each temporal bone (see Figure 17-12, A). Within the bony semicircular canals and separated from them by perilymph are the membranous semicircular ducts. Each contains endolymph and connects with the utricle inside the bony vestibule. Near its junction with the utricle each canal enlarges into an *ampulla*.

SENSE OF BALANCE

The sense organs involved in the sense of balance, or **equilibrium**, are found in the vestibule and semicircular canals. The sense organs located in the utricle and saccule function in **static equilibrium**—a function needed to sense the position of the head relative to gravity or to sense acceleration or deceleration of the body, such as would occur when seated motionless in a vehicle that was increasing or decreasing in speed. The sense organs associated with the semicircular ducts function in **dynamic equilibrium**—a function needed to maintain balance when the head or body itself is rotated or suddenly moved.

Static Equilibrium

A small patchlike strip of epithelium called the **macula** is found within both the utricle and saccule (Figure 17-14, A). It is sensory

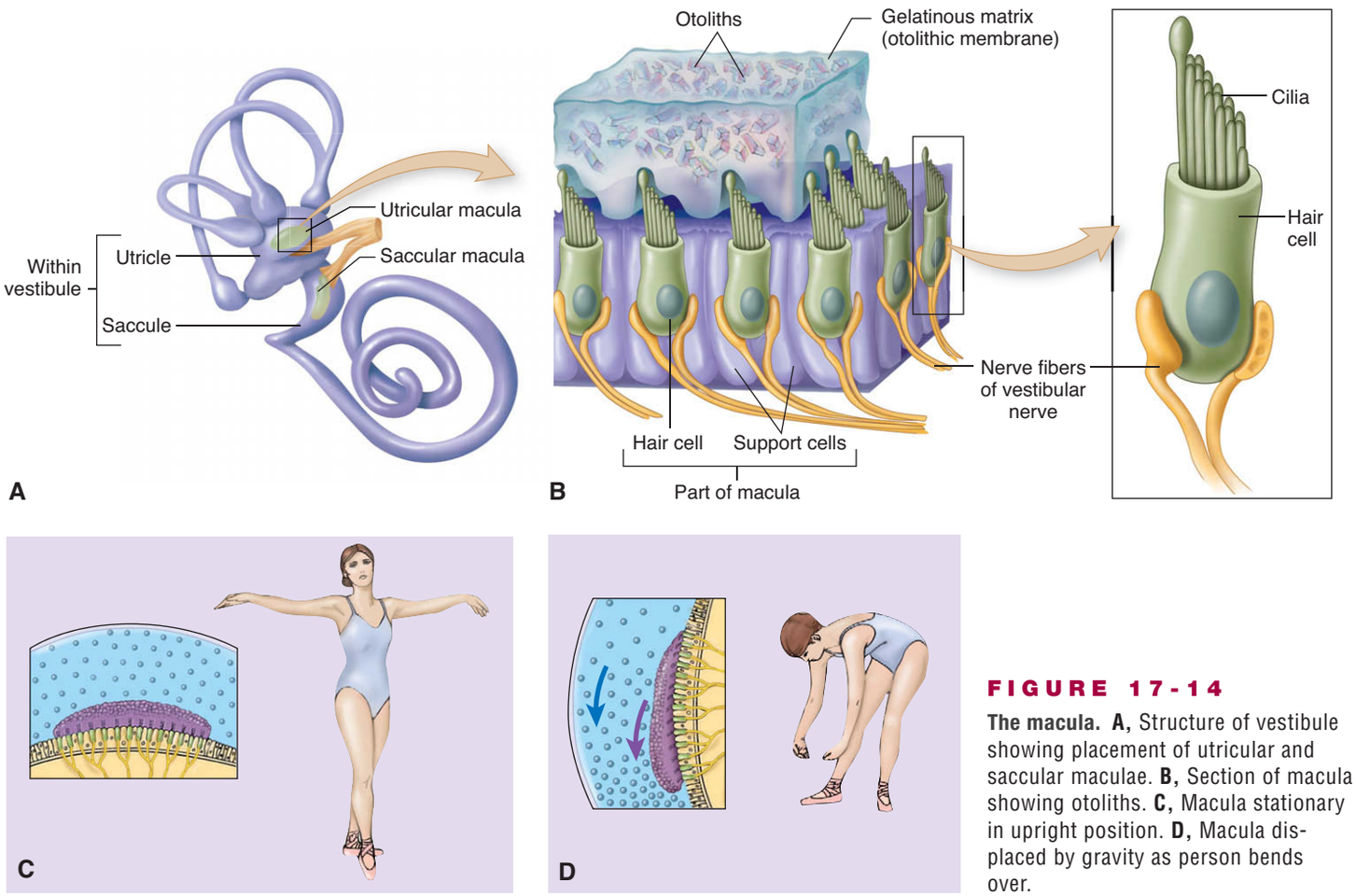


FIGURE 17-14

The macula. A, Structure of vestibule showing placement of utricular and saccular maculae. **B,** Section of macula showing otoliths. **C,** Macula stationary in upright position. **D,** Macula displaced by gravity as person bends over.

epithelium containing receptor hair cells and supporting cells covered with a gelatinous matrix. Movements of the macula provide information related to head position or acceleration. Action potentials are generated by movement of the hair cells, which occurs when the position of the head relative to gravity changes.

Otoliths—tiny "ear stones" composed of protein and calcium carbonate—are located within the matrix of the macula (Figure 17-14, *B*). Now note the relative positions of the utricular and saccular maculae in Figure 17-14, *A*. The two maculae are oriented almost at right angles to each other: the one in the utricle is parallel to the base of the skull, and the one in the saccule is perpendicular.

Changing the position of the head produces a change in the amount of pressure on the otolith-weighted matrix, which, in turn, stimulates the hair cells (Figure 17-14, *C* and *D*). This stimulates the adjacent receptors of the vestibular nerve. Its fibers conduct impulses to the brain that produce a sense of the position of the head and also a sensation of a change in the pull of gravity, for example, a sensation of acceleration.

In addition, stimulation of the macula evokes *righting reflexes*, muscular responses to restore the body and its parts to their normal position when they have been displaced. Impulses from proprioceptors and from the eyes also activate righting reflexes. Interruption of the vestibular, visual, or proprioceptive impulses that initiate these reflexes may cause disturbances of equilibrium, nausea, vomiting, and other symptoms.

Dynamic Equilibrium

Dynamic equilibrium depends on the functioning of the **crista ampullaris,** located in the ampulla of each semicircular duct. It is also called the *ampullary crest*. This unique structure is a form of sensory epithelium that is similar in many ways to the maculae. Each ridgelike crista is dotted with many hair cells, each with their processes embedded in a gelatinous flap called the **cupula** (Figure 17-15, *A* and *B*).

The cupula is not weighted with otoliths and does not respond to the pull of gravity. It serves, instead, much like a float that moves with the flow of endolymph in the semicircular ducts. Like the maculae, the semicircular ducts are placed nearly at right angles to each other. This arrangement enables detection of movement in all directions. As the cupula moves, it bends the hairs

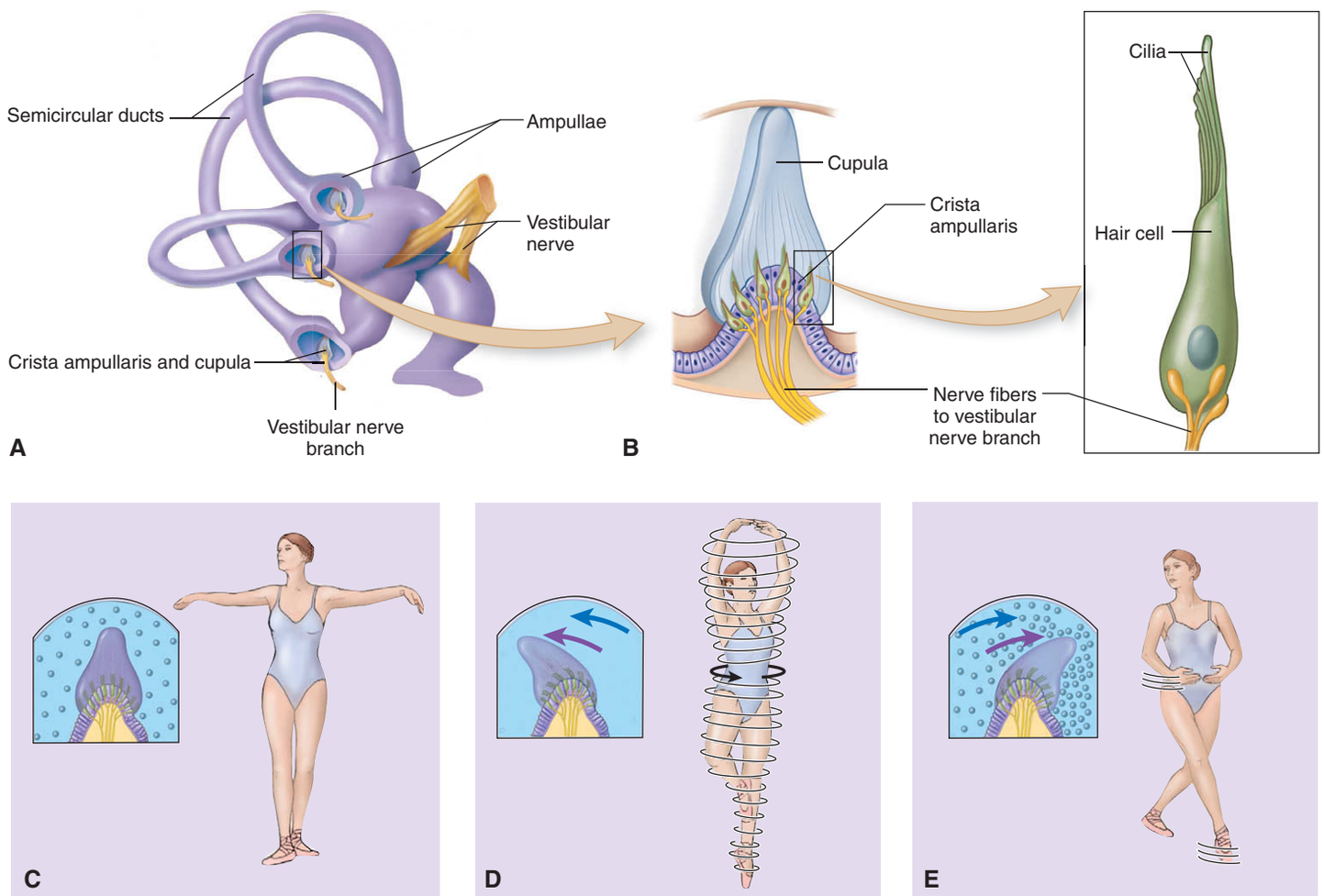


FIGURE 17-15

Structure and function of the crista ampullaris. A, Semicircular ducts showing location of the crista ampullaris in ampullae. **B,** Enlargement of crista ampullaris and cupula. **C,** When a person is at rest, the crista ampullaris does not move. **D** and **E,** As a person begins to spin, the crista ampullaris is displaced by the endolymph in a direction opposite to the direction of spin.

embedded in it, producing first a receptor and then an action potential that passes through the vestibular portion of the eighth cranial nerve to the medulla oblongata and, from there, to other areas of the brain and spinal cord for interpretation, integration, and response.

When a person spins (Figure 17-15, *C* to *E*), the semicircular ducts move with the body, but inertia keeps the endolymph in them from moving at the same rate. The cupula therefore moves in a direction opposite to head movement until after the initial movement stops. Dynamic equilibrium is thus able to detect changes in both the direction and the rate at which movement occurs.

| A&P CONNECT |

Vertigo involves a sensation of one's own body spinning in space or of the external world spinning around the individual. Vertigo can be a frightening and recurring problem often precipitated in affected individuals by sudden changes in body position that may occur when rolling over in bed, bending to pick up an object from the floor, or simply sitting up quickly. This condition is often related to the abnormal displacement of rocks in your head. Really! Want to know more about how "rocks in your head" occurs and how it can be fixed? Check out ***Vertigo and Ear Rocks*** online at ***A&P Connect.***

evolve

VISION: THE EYE

One of the most important sensations involved in maintaining homeostasis is vision, and the eye is the body's sense organ for this important function. Vision is a truly remarkable sensory ability and is used to guide almost all that we do. It allows us to activate and respond to a multitude of warning systems, and provides us with almost constant feedback on various types of form and movement in an ever-changing environment. It is the eye that uses as a stimulus the pervasive nature of light to convert stored photochemical energy into nervous impulses that are ultimately interpreted by the brain as sight.

The study of vision and the visual apparatus is an important area of ongoing research and clinical interest. Clinical **ophthalmology** is a medical practice specialty concerned with pathologic conditions of the eye and the diagnosis and treatment of eye disorders. A number of allied health professionals, including ophthalmic medical technologists, laboratory technicians, and opticians, work closely with ophthalmologists in administrative, research, and clinical environments.

We will first discuss the various structures of the eye and then move on to the ways in which these structures enable the eye to control the amount of light entering it and how the conversion to electrical stimuli actually occurs.

Structure of the Eye

EXTERNAL STRUCTURES

A number of the anatomical structures of the external eye are visible in Figure 17-16 and discussed in the sections that follow. Some of these structures, such as the sclera, iris, and pupil, are structures of the eye itself. Accessory structures of the eye discussed here include the eyebrows, eyelashes, eyelids, and lacrimal apparatus.

Eyebrows and Eyelashes

The eyebrows and eyelashes serve a cosmetic purpose and give some protection against foreign objects entering the eyes. They also help shade the eyes and provide at least minimal protection from direct light. Small glands located at the base of the lashes secrete a lubricating fluid. They frequently become infected, forming a *sty*.

Eyelids

The eyelids, or *palpebrae* (sing., *palpebra*), consist mainly of voluntary muscle and skin, with a border of thick connective tissue at the free edge of each lid, known as the *tarsal plate*. One can feel the tarsal plate as a ridge when turning back the eyelid to remove a foreign object. A lateral and medial angle or *canthus* forms where the superior and inferior eyelids meet. An additional fold of skin over the upper eyelid and medial angle of most infants and toddlers, and many adults, is called an epicanthal fold (Figure 17-16, *B*). The epicanthal fold is especially prominent in many people of Asian descent.

Mucous membrane, called *conjunctiva*, lines each lid (Figure 17-17). It continues over the surface of the eyeball, where it is modified to give transparency. Inflammation of the conjunctiva (conjunctivitis) is a fairly common infection. Because it produces a pinkish discoloration of the eye's surface, it is called *pinkeye* (Figure 17-18).

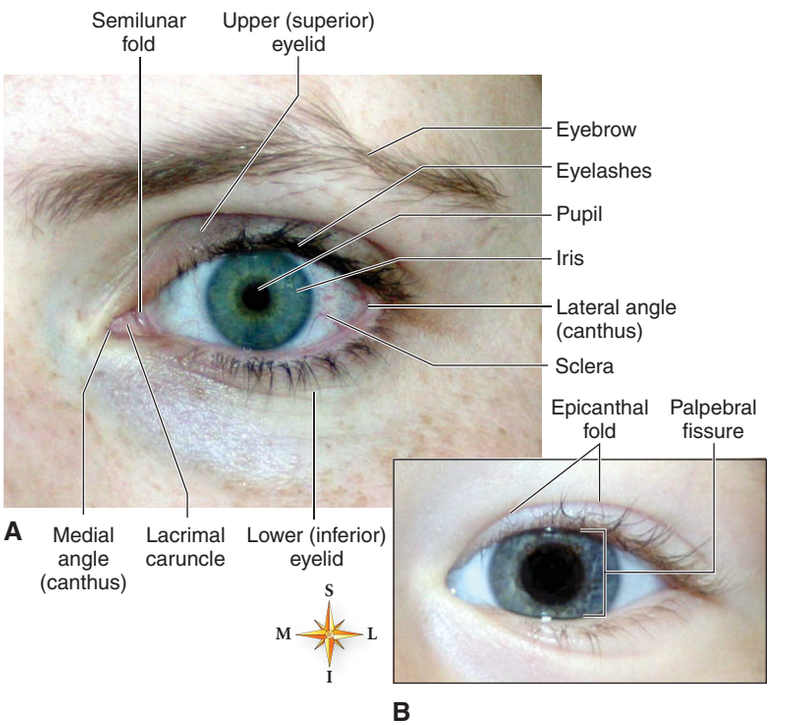


FIGURE 17-16

External eye structures. A, Visible portion of the adult eye and surrounding structures. **B,** Epicanthal fold in a toddler.

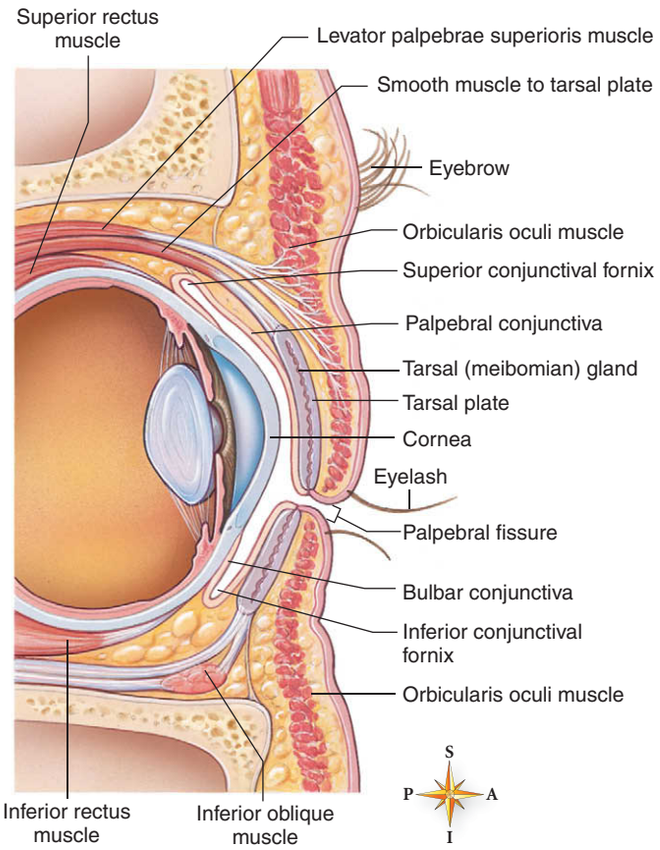


FIGURE 17-17

Accessory structures of the eye. Lateral view with eyelids closed.

The opening between the eyelids bears the technical name of *palpebral fissure*. The height of the fissure determines the apparent size of the eyes. If the eyelids are habitually held wide open, the eyes appear large, although the difference in eyeball size among most adults is not significant. Eyes appear small if the upper eyelids droop. Plastic surgeons can correct this common aging change with an operation called **blepharoplasty.**



FIGURE 17-18

Acute bacterial conjunctivitis. Note the discharge of pus characteristic of this highly contagious infection of the conjunctiva.

Lacrimal Apparatus

The *lacrimal apparatus* consists of the structures that secrete tears and drain them from the surface of the eyeball. They are the lacrimal glands, lacrimal ducts, lacrimal sacs, and nasolacrimal ducts (Figure 17-19).

The *lacrimal glands*, comparable in size and shape to a small almond, are located in a depression of the frontal bone at the upper outer margin of each orbit. Approximately a dozen small ducts lead from each gland, draining the tears onto the conjunctiva at the upper outer corner of the eye.

The *lacrimal canals* are small channels, one above and the other below each *caruncle* (small red body at the inner canthus). They empty into the lacrimal sacs. The openings into the canals are called *puncta* (sing., *punctum*) and can be seen as two small dots at the medial angle (inner canthus) of the eye. The *lacrimal sacs* are located in a groove in the lacrimal bone. The *nasolacrimal ducts* are small tubes that extend from the lacrimal sac into the inferior meatus of the nose.

All the tear ducts are lined with mucous membrane, an extension of the mucosa that lines the nose. When this membrane becomes inflamed and swollen, the nasolacrimal ducts become plugged, causing the tears to overflow from the eyes instead of draining into the nose as they do normally. Hence when we have a common cold, "watery" eyes add to our discomfort.

Muscles of the Eye

Eye muscles are of two types: *extrinsic* and *intrinsic*.

Extrinsic eye muscles are skeletal muscles that attach to the outside of the eyeball and to the bones of the orbit. They move the eyeball in any desired direction and are, of course, voluntary muscles. Four of them are straight muscles, and two are oblique. Their names describe their positions on the eyeball. They are the

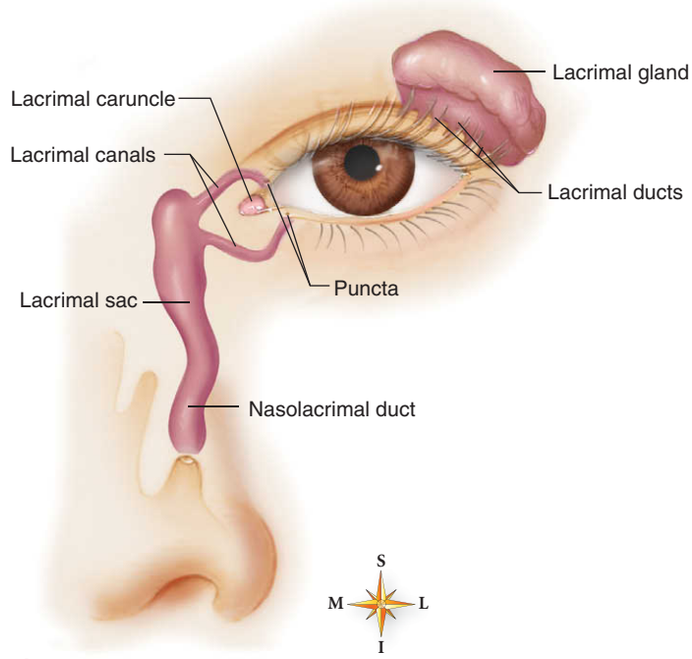


FIGURE 17-19

Lacrimal apparatus. Fluid produced by lacrimal glands (tears) streams across the eye surface, enters the canals, and then passes through the lacrimal sac and nasolacrimal duct to enter the nose.

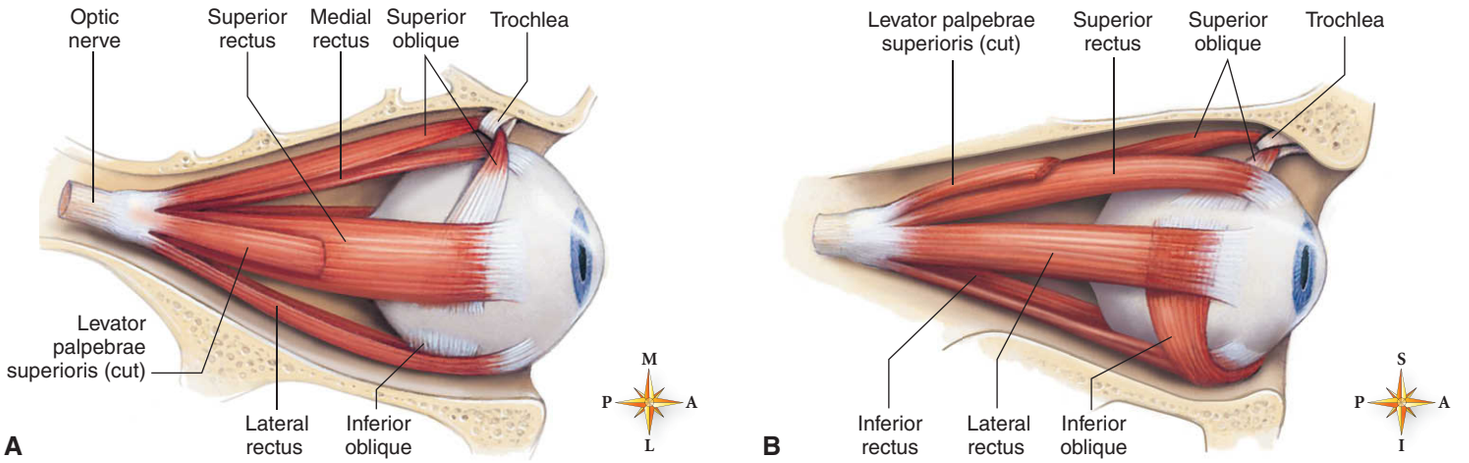


FIGURE 17-20

Extrinsic muscles of the right eye. A, Superior view. **B,** Lateral view.

superior, inferior, medial, and lateral rectus muscles and superior and inferior oblique muscles (Figure 17-20).

Intrinsic eye muscles are smooth, or involuntary, muscles located within the eye. These are called the *iris* and the *ciliary muscles.* Incidentally, the eye is one of only a few organs in the body in which both voluntary and involuntary muscles are found. The iris regulates the size of the pupil. The ciliary muscle controls the shape of the lens. As the ciliary muscle contracts, it releases the suspensory ligament from the backward pull usually exerted on it, and this allows the elastic lens, suspended in the ligament, to bulge, or become more convex. The role of both these muscles in vision is discussed later in this chapter.

LAYERS OF THE EYEBALL

Approximately five sixths of the eyeball, a spherelike globe about 22 to 25 mm in diameter, lies recessed in and is protected by the bony orbit or eye socket. Only the small anterior surface of the eyeball is exposed. Three layers of tissues compose the eyeball. From the outside in, the following three layers of tissues and their component parts or regions form the eyeball.

1. Fibrous layer
   - Sclera
   - Cornea
2. Vascular layer
   - Choroid
   - Ciliary body
   - Iris
3. Inner layer
   - Retina
   - Optic nerve
   - Retinal blood vessels

Refer to Figure 17-21 as you read the following paragraphs.

The anterior portion of the sclera is called the *cornea* and lies over the colored part of the eye, the *iris* (see Figures 17-16 and 17-21). The cornea is transparent, whereas the rest of the sclera is white and opaque, a fact that explains why the visible anterior surface of the sclera is usually spoken of as the "white" of the eye. No blood vessels are found in the cornea or in the lens. Deep within the anterior part of the sclera, at its junction with the cornea, is a ring-shaped *scleral venous sinus*, formerly called the *canal of Schlemm.* Corneas that have lost their transparency can sometimes be transplanted from a donor (Box 17-3).

As noted above, the vascular layer consists of three component parts or regions—the choroid, ciliary body, and iris. This layer is characterized by many blood vessels and a large amount of melanin pigment. Most of this layer, forming the middle and posterior coating just inside the fibrous coat, is the highly pigmented choroid.

Box 17-3 | HEALTH matters

Corneal Transplants

Surgical removal of an opaque or deteriorating cornea and replacement with a donor transplant is a common medical practice. Corneal tissue is avascular; that is, the cornea is free of blood vessels. Therefore corneal tissue is seldom rejected by the body's immune system. Antibodies carried in the blood have no way to reach the transplanted tissue, and therefore long-term success following implant surgery is excellent. The Figure is a photo of a patient with a recent corneal transplant. Note sutures and mild edema.



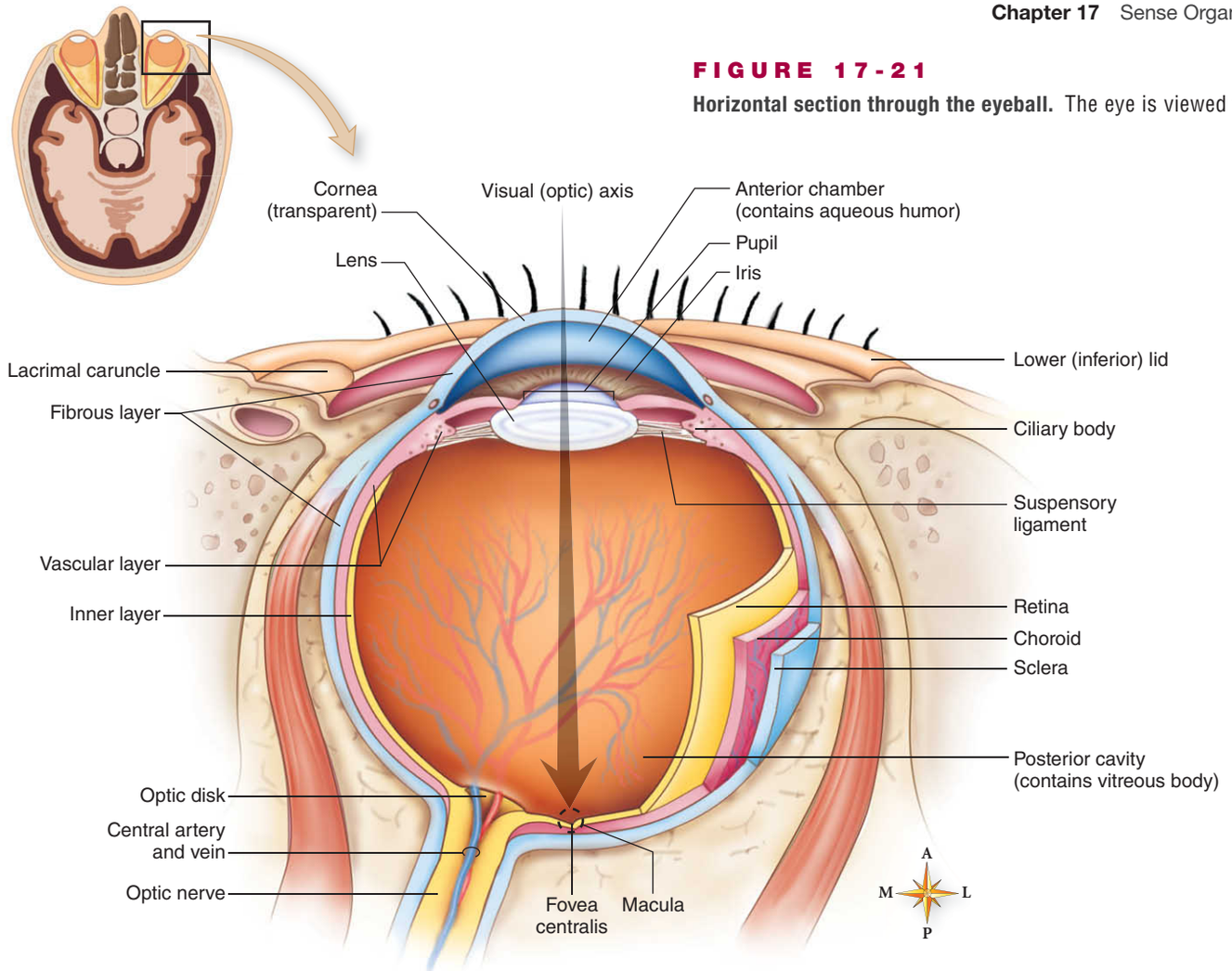


FIGURE 17-21

Horizontal section through the eyeball. The eye is viewed from above.

The **ciliary body** is formed by a thickening of the choroid and fits like a collar into the area between the anterior margin of the retina and the posterior margin of the iris (Figure 17-22). The small *ciliary muscle*, composed of both radial and circular smooth muscle fibers, lies in the anterior part of the ciliary body. Folds in the ciliary body are called *ciliary processes*, and attached to these are the *suspensory ligaments*, which blend with the elastic capsule of the *lens* and hold it suspended in place.

The **iris,** or the colored part of the eye, consists of circular and radial smooth muscle fibers arranged to form a doughnut-shaped structure. It attaches to the ciliary body. The hole-shaped opening in the middle of the iris is the **pupil.** By adjusting the diameter of the opening, the iris acts like the diaphragm of a camera. It controls the amount of light that enters the eye by adjusting the size of the pupil. Eye color is determined by the amount, placement, and type of melanin in the iris—and the reflection of light bouncing off the iris.

In *ocular albinism*, a genetic disorder, there is little or no pigmentation of the vascular layer, and thus light entering the eye passes through this layer and reflects off of the white fibrous coat. This both amplifies the light inside the eye and disrupts the formation of a clear image—often leading to full or partial blindness.

The **retina** is the incomplete innermost coat of the eyeball—incomplete in that it has no anterior portion. Melanin-containing epithelial cells form the layer of the retina next to the choroid coat. This part of the retina is called the *pigmented retina*.

Most of the retina, however, is made up of nervous tissue and is called the *sensory retina*. Three layers of neurons form the basic structure of the sensory retina. Named in the order in which they conduct impulses, these neurons are the *main photoreceptor*

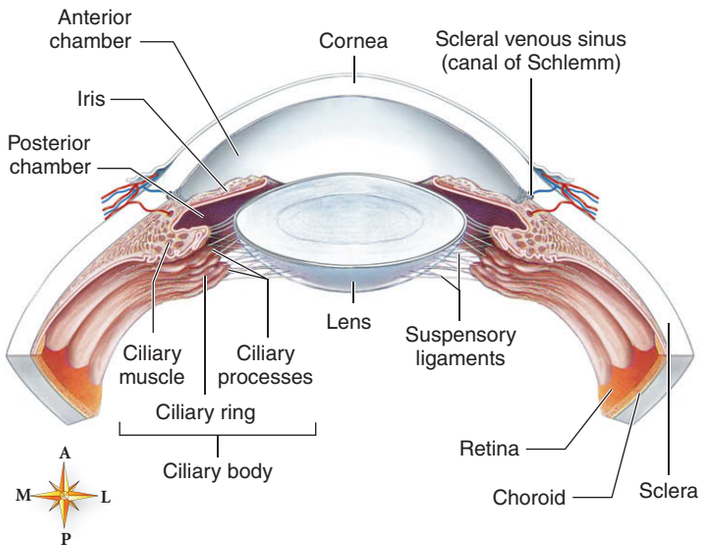


FIGURE 17-22

Lens, cornea, iris, and ciliary body. Note the suspensory ligaments that attach the lens to the ciliary body.

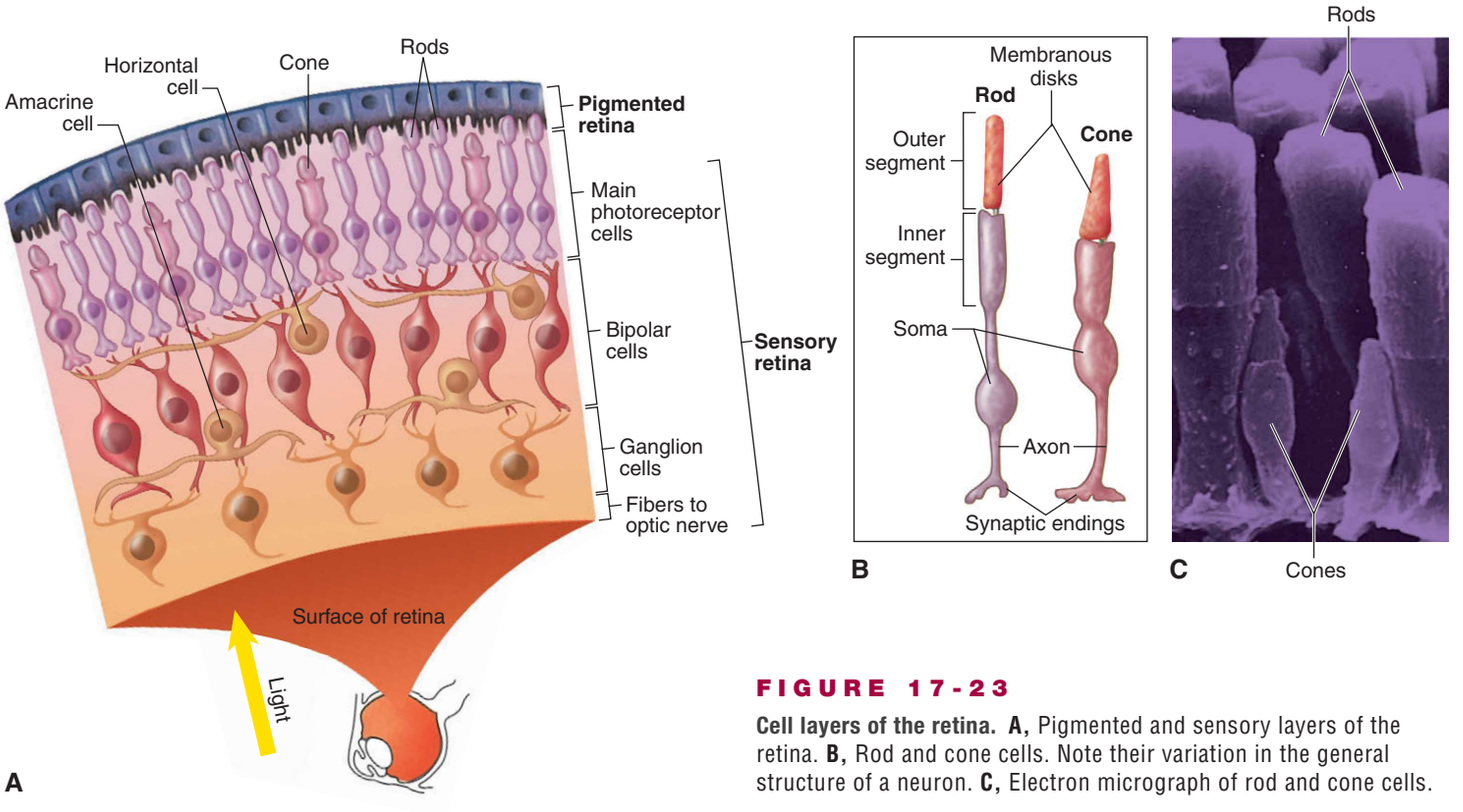


FIGURE 17-23

Cell layers of the retina. A, Pigmented and sensory layers of the retina. **B,** Rod and cone cells. Note their variation in the general structure of a neuron. **C,** Electron micrograph of rod and cone cells.

cells, *bipolar cells*, and *ganglion cells*. Identify each of these in Figure 17-23, *A*. Notice that the main photoreceptor cells are the deepest, then the bipolar cells, then the ganglion cells.

The distal ends of the dendrites of the main photoreceptor neurons have names that describe their shapes. Because some look like tiny rods and others look like cones, they are called **rods** and **cones,** respectively (Figure 17-23, *B* and *C*). Because they are sensitive to light rays, they act as our principal visual receptors. They differ in numbers, distribution, and function. Cones are less numerous than rods and are most densely concentrated in the **fovea centralis,** a small depression in the center of a yellowish area, the **macula lutea,** found near the center of the retina (see Figures 17-21 and 17-24). The macula lutea (Latin) is called simply the *macula* in English. The cones become less and less dense from the fovea outward. Rods, on the other hand, are absent entirely from the fovea and macula and increase in density toward the periphery of the retina. How these anatomical facts relate to rod and cone functions is discussed on pp. 529–530.

The bipolar cells are neurons that receive impulses from the rods and cones and pass these impulses to the ganglion neurons. Notice in Figure 17-23 that a bipolar neuron connects either to one cone or to many rods.

The ganglion neurons collect information from the primary photoreceptor neurons—the rods and cones. But they also act as photoreceptors themselves. Additional sets of neurons allow lateral connections among rods and cones (*horizontal cells*) and among bipolar and ganglion cells (*amacrine cells*). The lateral connecting cells are thought to help us detect patterns of movement.

All the axons of ganglion neurons extend back to a small circular area in the posterior part of the eyeball known as the *optic disk*. This part of the sclera contains perforations through which the fibers emerge from the eyeball as the **optic nerve** (second cranial nerve). The optic disk is also called the **blind spot** because light rays striking this area cannot be seen. Why? Because it contains no rods or cones, only nerve fibers. Box 17-4 shows you how to locate the blind spots in your own eyes.

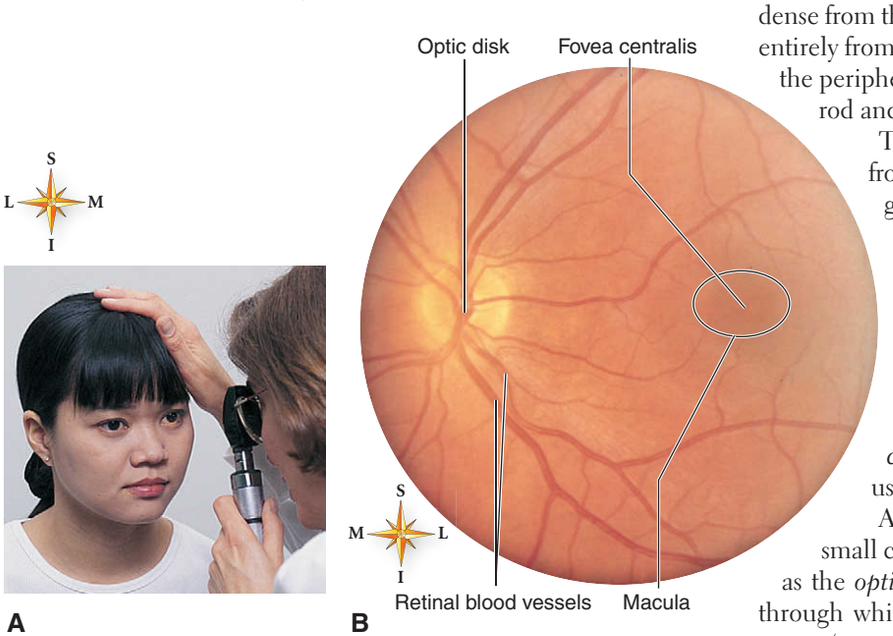


FIGURE 17-24

Examining the eye. A, Using the ophthalmoscope to view the retina. **B,** Ophthalmoscopic view of the retina as seen through the pupil.

Box 17-4 | FYI

Finding Your Blind Spot

Demonstrate the location of the blind spot in your visual field by covering your left eye and looking at the objects below. While staring at the square, begin about 30 cm (12 inches) from objects and slowly bring the figures closer to your eye. At one point, the circle will seem to disappear because its image has fallen on the blind spot.



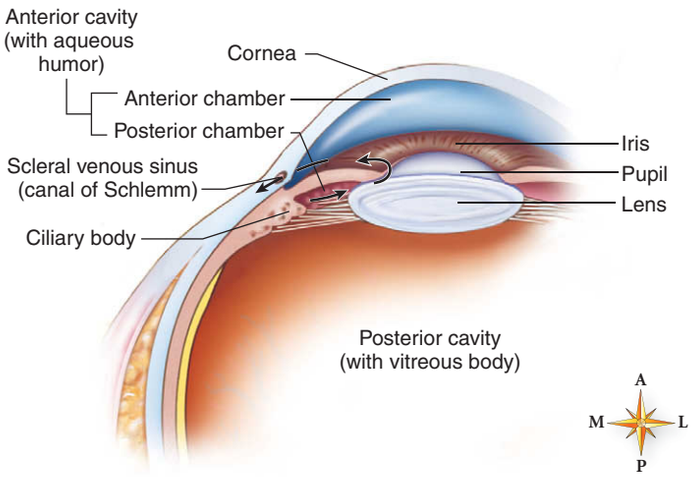


FIGURE 17-25

Formation of aqueous humor. Aqueous humor *(heavy arrows)* is believed to be formed mainly by secretion by the ciliary body into the posterior chamber. It passes into the anterior chamber through the pupil, from which it is drained away by the ring-shaped scleral venous sinus (canal of Schlemm), and finally into the anterior ciliary veins.

Just as an otoscope is used to view the external auditory canal and surface of the tympanic membrane, a lighted **ophthalmoscope** can be used to examine the retinal surface, called the *fundus*, and internal eye structures by viewing them through the pupil (see Figure 17-24, *A* and *B*). This noninvasive technique is a safe and effective aid in the diagnosis of many types of disease (see Mechanisms of Disease, p. 534). Locate the branching network of retinal blood vessels in Figure 17-24, *B*. These vessels supply the retinal tissues and are critical for normal visual function. Diseases such as diabetes mellitus and atherosclerosis can reduce blood flow to these vessels, causing loss of vision.

CAVITIES AND HUMORS

The eyeball is not a solid sphere; rather it contains a large interior space that is divided into two cavities: anterior and posterior.

The **anterior cavity** has two subdivisions, known as the *anterior* and *posterior chambers*. As Figure 17-21 shows, the entire anterior cavity lies in front of the **lens.** The posterior chamber of the anterior cavity consists of the small space directly posterior to the iris but anterior to the lens. And the anterior chamber of the anterior cavity is the space anterior to the iris but posterior to the cornea. *Aqueous humor* fills both chambers of the anterior cavity. This substance is clear and watery and often leaks out when the eye is injured.

The **posterior cavity** of the eyeball is considerably larger than the anterior, because it occupies the entire space posterior to the lens, suspensory ligament, and ciliary body (see Figure 17-21). It contains the *vitreous body*, which is a sac filled with a soft, watery gel. The thick fluid of the vitreous body, along with the aqueous humor, helps maintain sufficient intraocular pressure to prevent the eyeball from collapsing.

Aqueous humor forms from blood in capillaries (located mainly in the ciliary body). The ciliary body actively secretes aqueous humor into the posterior chamber, but passive filtration from capillary blood contributes also to aqueous humor formation. From the posterior chamber, aqueous humor moves from the area between the iris and the lens through the pupil into the anterior chamber. From here, it drains into the scleral venous sinus and moves into small veins (Figure 17-25). Normally, aqueous humor drains out of the anterior chamber at the same rate at which it enters the posterior chamber, so the amount of aqueous humor in the eye remains relatively constant—and so, too, does intraocular pressure. But sometimes something happens to upset this balance, and intraocular pressure increases above the normal level of about 20 to 25 mm Hg. The individual then has the eye disease known as *glaucoma*, which, if untreated, can lead to retinal damage and blindness. Either excess formation or, more often, decreased drainage is seen as an immediate cause of this condition, but underlying causes are unknown (see Mechanisms of Disease, p. 534).

An outline summary of the cavities of the eye appears in Table 17-2. The cavities and lens are not part of the layers of the eyeball.

The Process of Seeing

For vision to occur, the following conditions must be fulfilled: an image must be formed on the retina to stimulate its receptors (rods and cones), and the resulting nerve impulses must be conducted to the visual areas of the cerebral cortex for interpretation.

FORMATION OF RETINAL IMAGE

Four processes focus light rays so that they form a clear image on the retina: *refraction* of the light rays, *accommodation* of the lens, *constriction* of the pupil, and *convergence* of the eyes.

TABLE 17-2 Cavities of the Eye

CAVITY	DIVISIONS	LOCATION	CONTENTS
Anterior	Anterior chamber	Anterior to iris and posterior to cornea	Aqueous humor
	Posterior chamber	Posterior to iris and anterior to lens	Aqueous humor
Posterior	None	Posterior to lens	Vitreous body

Refraction of Light Rays

Refraction is the deflection, or bending, of light rays. It is produced by light rays passing obliquely from one transparent medium into another of different optical density; the more convex the surface of the medium, the greater its refractive power. The refracting media of the eye are the cornea, aqueous humor, lens, and vitreous body. Light rays are bent, or refracted, at the anterior surface of the cornea as they pass from the air into the denser cornea, at the anterior surface of the lens as they pass from the aqueous humor into the denser lens, and at the posterior surface of the lens as they pass from the lens into the less dense gel of the vitreous body.

When an individual goes to an optometrist or ophthalmologist for an eye examination, the doctor performs a "refraction." In other words, by various specially designed methods, the refractory, or light-bending, power of that person's eyes is determined. Tests of visual acuity also rely on a person's ability to refract light properly (Box 17-5).

In a relaxed normal eye, the four refracting media together bend light rays sufficiently to bring to a focus on the retina the parallel rays reflected from an object 20 or more feet (6 m) away. Of course a normal eye can also focus on objects located much nearer than 20 feet (6 m) from the eye. This is accomplished by a mechanism known as *accommodation* (discussed next).

Many eyes, however, show errors of refraction; that is, they are not able to focus the rays on the retina under the stated conditions. Some common errors of refraction that are discussed later in the chapter are nearsightedness (myopia), farsightedness (hyperopia), and astigmatism.

Accommodation for Near Vision

Accommodation for near vision necessitates three changes: (1) increase in the curvature of the lens, (2) constriction of the pupils, and (3) convergence of the two eyes. Light rays from objects 20 or more feet away are practically parallel. The normal eye, as previously noted, refracts such rays sufficiently to focus them clearly on the retina. However, light rays from nearer objects are divergent rather than parallel. So obviously they must be bent more acutely to bring them to a focus on the retina. Accommodation of the lens or, in other words, an increase in its curvature takes place to achieve this greater refraction.

Change in Lens Shape

Contraction of the ciliary muscle pulls the choroid layer closer to the lens (see Figure 17-22). This, in turn, loosens the tension of the suspensory ligaments, allowing the lens to bulge. For near vision, the ciliary muscle is contracted and the lens is bulging. For far vision, however, the ciliary muscle is relaxed and the lens is comparatively flat (Figure 17-26). Continual use of the eyes for near work produces eyestrain because of the prolonged contraction of the ciliary muscle. Some of the strain can be avoided by looking into the distance at intervals while doing close work.

As people grow older, they tend to become farsighted because lenses lose their elasticity and therefore lose their ability to bulge and to accommodate for near vision. This condition is called *presbyopia*.

Constriction of Pupil

The muscles of the iris play an important part in the formation of clear retinal images (Figure 17-27). Part of the accommodation mechanism consists of contraction of the inner circular smooth muscle fibers of the iris as the outer radial fibers relax, which constricts the pupil. Such constriction prevents divergent rays from the object from entering the eye through the periphery of the cornea and lens. Such peripheral rays could not be refracted sufficiently to be brought to a focus on the retina and therefore would cause a blurred image. Constriction of the pupil for near vision is called the *near reflex* of the pupil and occurs simultaneously with accommodation of the lens in near vision.

Box 17-5 | FYI

Visual Acuity

Visual *acuity* is the clearness or sharpness of visual perception. Acuity is affected by our focusing ability, the efficiency of the retina, and the proper function of the visual pathway and processing centers in the brain.

One common way to measure visual acuity for distant vision is to use the familiar test chart on which letters or other objects of various sizes and shapes are printed. The subject is asked to identify the smallest object that he or she can see from a distance of 20 feet (6.1 m). The resulting determination of visual acuity is expressed as a double number such as "20/20." The first number represents the distance (in feet) between the subject and the test chart; the standard is 20. The second number represents the number of feet a person with normal acuity would have to stand to see the same objects clearly. Thus a finding of 20/20 is normal because the subject can see at 20 feet what a person with normal acuity can see at 20 feet. A person with 20/100 vision can see objects at 20 feet that a person with normal vision can see at 100 feet.



Testing for near-vision acuity.

People whose distant-vision acuity is worse than 20/200 after correction are considered to be legally blind. Legal blindness is a designation that is used to identify the severity of a wide variety of visual disorders so that laws that involve visual acuity can be enforced. For example, laws that govern the awarding of driving licenses require that drivers have a minimum level of visual acuity.

The Figure shows a common test for near-vision acuity. A chart or sample of newsprint of different size fonts is held at a distance of 12 to 14 inches and the subject is asked to read it. In both near-vision and distant-vision acuity tests, the subject attempts the test with each eye separately, then both eyes together.

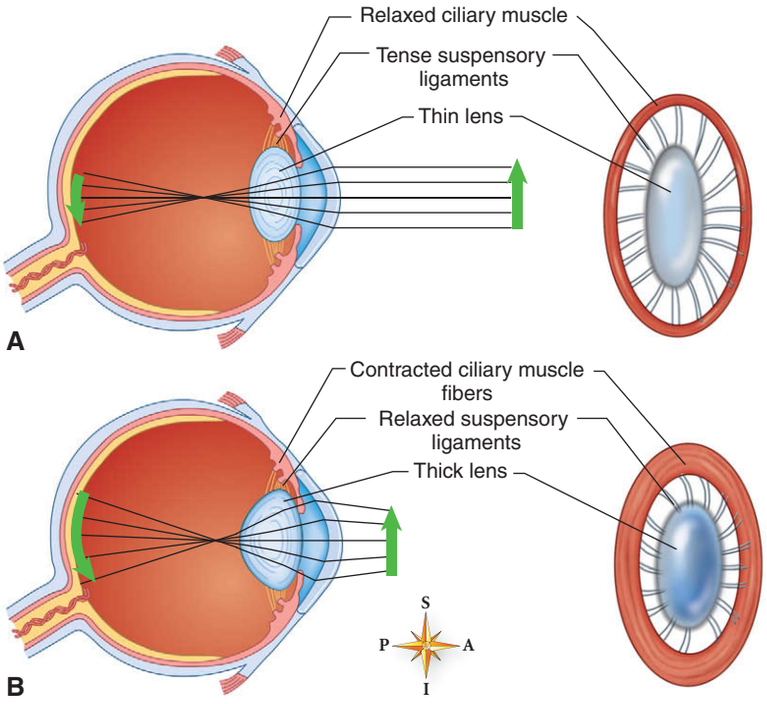


FIGURE 17-26

Accommodation of lens. A, Distant image: the lens is flattened (ciliary muscle relaxed), and the image is focused on the retina. **B,** Close image: the lens is rounded (ciliary muscle contracted), and the image is focused on the retina.

As Figure 17-27 shows, the pupil constricts in bright light (*photopupil reflex* or *pupillary light reflex*) to protect the retina from stimulation that is too intense or too sudden. As the same Figure also shows, relaxation of inner circular fibers and contraction of the outer radial fibers causes dilation of the pupil in dim light. Pupil dilation allows more light to enter and form a more intense image in low-light environments.

Convergence of Eyes

Single binocular vision (seeing only one object instead of two when both eyes are used) occurs when light rays from an object fall on corresponding points of the two retinas. The foveae and all points lying equidistant and in the same direction from the foveae are corresponding points. Whenever the eyeballs move in unison, either with the visual axes parallel (for far objects) or converging on a common point (for near objects), light rays strike corresponding points of the two retinas.

Convergence is the movement of the two eyeballs inward so that their visual axes come together, or converge, at the object viewed. The nearer the object is, the greater the degree of convergence necessary to maintain single vision. A simple procedure demonstrates the fact that single binocular vision results from stimulation of corresponding points on two retinas. Gently press one eyeball out of line while viewing an object. Instead of one object, you will see two. To achieve unified movement of the two eyeballs, a functional balance between the antagonistic extrinsic muscles must exist.

For clear distant vision, the muscles must hold the visual axes of the two eyes parallel. For clear near vision, the muscles must converge the eyes. These conditions cannot be met if, for

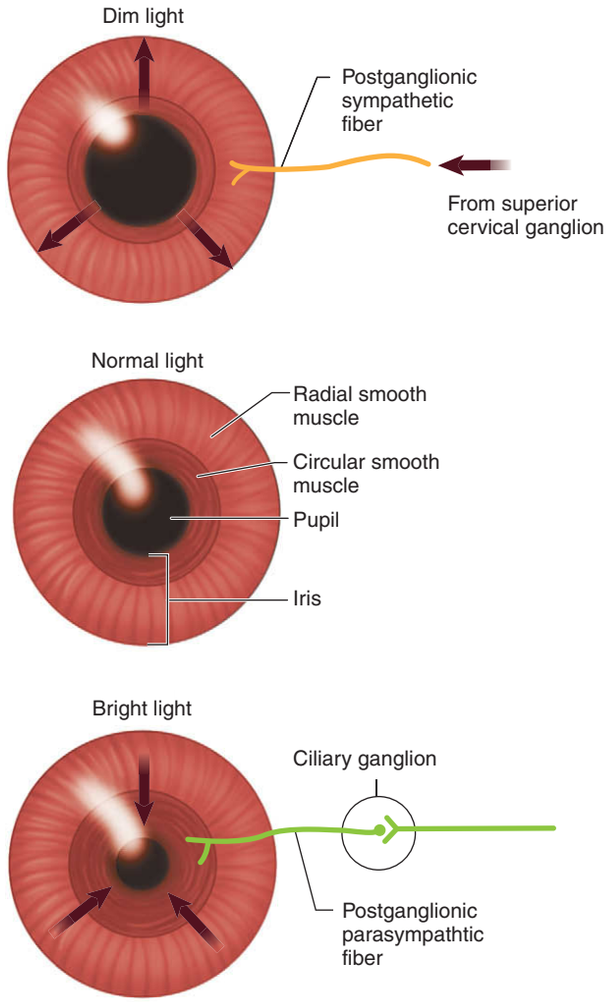


FIGURE 17-27

Constriction and dilation of pupil. Only the muscular part of the iris is shown.

example, the medial rectus muscle of one eye contracts more forcefully than its antagonist, the lateral rectus muscle. That eye is then pulled in toward the nose. The movement of its visual (optic) axis does not coordinate with that of the other eye. Light rays from an object then fall on noncorresponding points of the two retinas, and the object is seen double (**diplopia**). **Strabismus** (cross-eye or squint) is an exaggerated condition that cannot be overcome by neuromuscular effort (Figure 17-28). However, an individual with strabismus usually does not have double vision, as you might expect, because he or she learns to suppress one of the images.



FIGURE 17-28

Strabismus. This child exhibits convergent left eye strabismus.

THE ROLE OF PHOTOPIGMENTS

Rods and cones are our main photoreceptor cells. Both rods and cones contain *photopigments*, or light-sensitive pigmented compounds that are found in the outer (distal) area of both types of photoreceptors near the pigmented retina (see Figure 17-23). Chemically, all photopigments can be broken down into a glycoprotein called **opsin** and a vitamin A derivative called **retinal,** which acts as the light-absorbing portion of all photopigments.

Rods

The single photopigment found in rods is named **rhodopsin.** Rhodopsin is so highly light sensitive that even dim light causes a rapid breakdown of the photopigment into its opsin and retinal components. Light causes retinal to change its shape and the opsin molecule to expand, or open. When opsin and retinal open and separate in the presence of light (a process called **bleaching**), active sites for other chemical reactions are exposed and this triggers a change in the membrane potential of the rod cell (Figure 17-29). This neural membrane signal then travels to the brain for interpretation. Energy is required to bring opsin back to its original shape and reattach retinal to it. Until this occurs, the photopigment remains bleached and is unable to respond to light.

The color of light is measured in wavelengths (usually with the unit nanometer, abbreviated as nm). That is, we perceive different wavelengths of radiant energy (light) as different colors. Figure 17-30 shows that rods are most sensitive to light in the green range of wavelengths, peaking at about 500 nm. However, the brain perceives information from the rods only as intensity of light, not as a color. Thus the rods produce a kind of *monochrome*, or "black-and-white," vision.

Because rods are very sensitive to light, and thus not only become bleached easily but also remain bleached in bright light, they are used only for "dim light" vision.

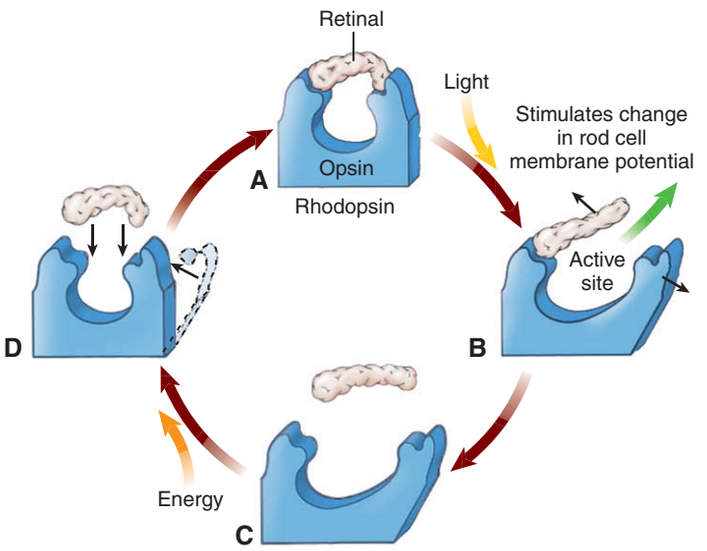


FIGURE 17-29

Rhodopsin cycle. A, Retinal is attached to opsin. **B,** Light causes retinal and opsin to change shape, causing change in rod cell membrane potential. **C,** Retinal separates from opsin (bleaching). **D,** Energy is required to bring opsin back to its original shape and to attach retinal to it.

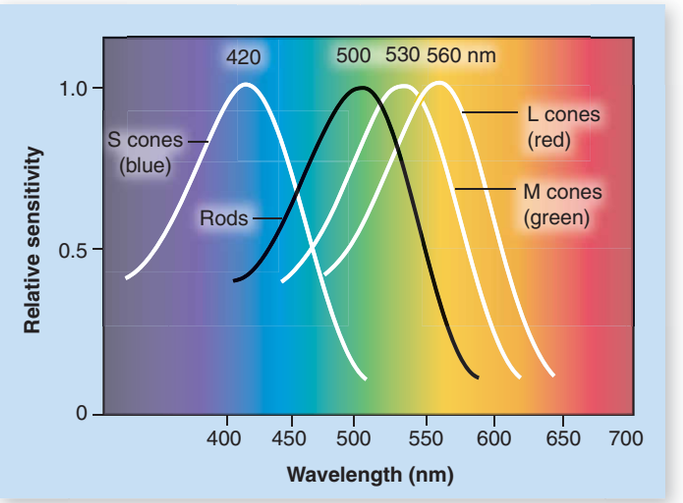


FIGURE 17-30

Color sensitivity of rods and cones. Rods *(black line)* are sensitive only in dim-light conditions in the range of greenish wavelengths—but their information is perceived only as light and dark, not green. Three types of cones *(white lines)* perceive colors in bright-light conditions. Blue (*S,* short-wave) cones are sensitive in the blue range, green (*M,* medium-wave) cones in the green range, and red (*L,* long-wave) cones in the red range. Information from all three cone types is combined to produce a large palette of color perception in the brain.

Cones

Three types of cones are present in the retina. Each contains its own version of the rhodopsin photopigment, different from the rhodopsin found in rod cells. Blue-sensitive cones are sensitive in the blue range of wavelengths (see Figure 17-30) and are often called *S cones* (for "short" wavelengths). Green-sensitive cones are often called *M cones* for "medium" wavelengths. Red-sensitive cones are called *L cones* for "long" wavelengths.

Our perception of a range of colors results from the combined neural input from varying numbers of the three different cone types. Abnormal function in any of the cones disrupts the normal perception of colors—a condition called *color-blindness* (Box 17-6).

Because cone photopigments are less sensitive to light than the rhodopsin in rods, brighter light is necessary for their breakdown. Cones therefore function to produce vision only in bright light.

In addition, cones contribute more than rods to the perception of sharp images. The reason for this difference involves the way in which information generated by the stimulation of rods and cones is "processed" before it reaches the brain. Look again at Figure 17-23. Note that information obtained by the bipolar cells is collated from many rods, whereas bipolar cells tend to synapse with only a single cone receptor. Recall that this property of combining input from several receptors is called *convergence.* The result of convergence is that, although the rods combine their input to make a bipolar cell fire in dimmer light, the brain is unable to determine exactly which rod was stimulated when a given bipolar or ganglion cell fires.

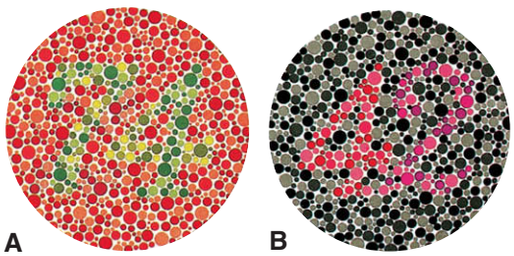
Convergence of impulses from cones is rare. There is almost a one-to-one relationship between cones and the ganglion cells that carry impulses toward the brain. Interpretation by the brain of sharp images is therefore much better as a result of cone stimulation.

Box 17-6 | FYI

Color Blindness

Color blindness, usually an inherited condition, is caused by mistakes in the functioning of the three *photopigments* in the cones. Each photopigment is sensitive to one of the three primary colors of light: green, blue, and red (see Figure 17-30). In many cases, the green-sensitive photopigment is missing or deficient; other times, the red-sensitive photopigment is abnormal. (Dysfunction of the blue-sensitive cone is rare.) Color-blind individuals see colors, but they cannot distinguish between them normally.

Figures such as parts *A* and *B* shown here are often used to screen individuals for color blindness. A person with red-green color blindness cannot see the *74* in part *A* of the figure, whereas a person with normal vision can. To determine which photopigment is deficient, a color-blind person may try a Figure similar to part *B*. Persons with a deficiency of red-sensitive photopigment can distinguish only the *2;* those deficient in green-sensitive photopigment can only see the *4.*



The fovea contains the greatest concentration of cones and is therefore the point of clearest vision in good light. For this reason, when we want to see an object clearly in the daytime, we look directly at it to focus the image on the fovea. But in dim light or darkness, we see an object better if we look slightly to the side of it, thereby focusing the image nearer the periphery of the retina, where the more plentiful rods can collate the lesser amount of light information and generate an image.

Ganglion Cells

Although the rods and cones are the dominant form of photoreceptor cell in the retina, and are entirely responsible for detecting visual images, some ganglion cells are now known to act in an additional visual system. The ganglion photoreceptors contain a photopigment called *melanopsin*. Melanopsin is sensitive to light in the blue range of wavelengths that seem to predominate at dawn and dusk. The light information from this system is not used to form an image but is instead needed to adjust our biological clock—a function involving the pineal body of the brain discussed in Chapter 14 (see Figure 14-14 on p. 424).

NEURAL PATHWAY OF VISION

Fibers that conduct impulses from the rods and cones reach the visual cortex in the occipital lobes by way of the optic nerves, optic chiasma, optic tracts, and optic radiations. "Relay stations" along the way include the superior colliculi and the lateral geniculate nuclei of the thalamus. Look closely at Figure 17-31. Note that each optic nerve contains fibers from only one retina but that the

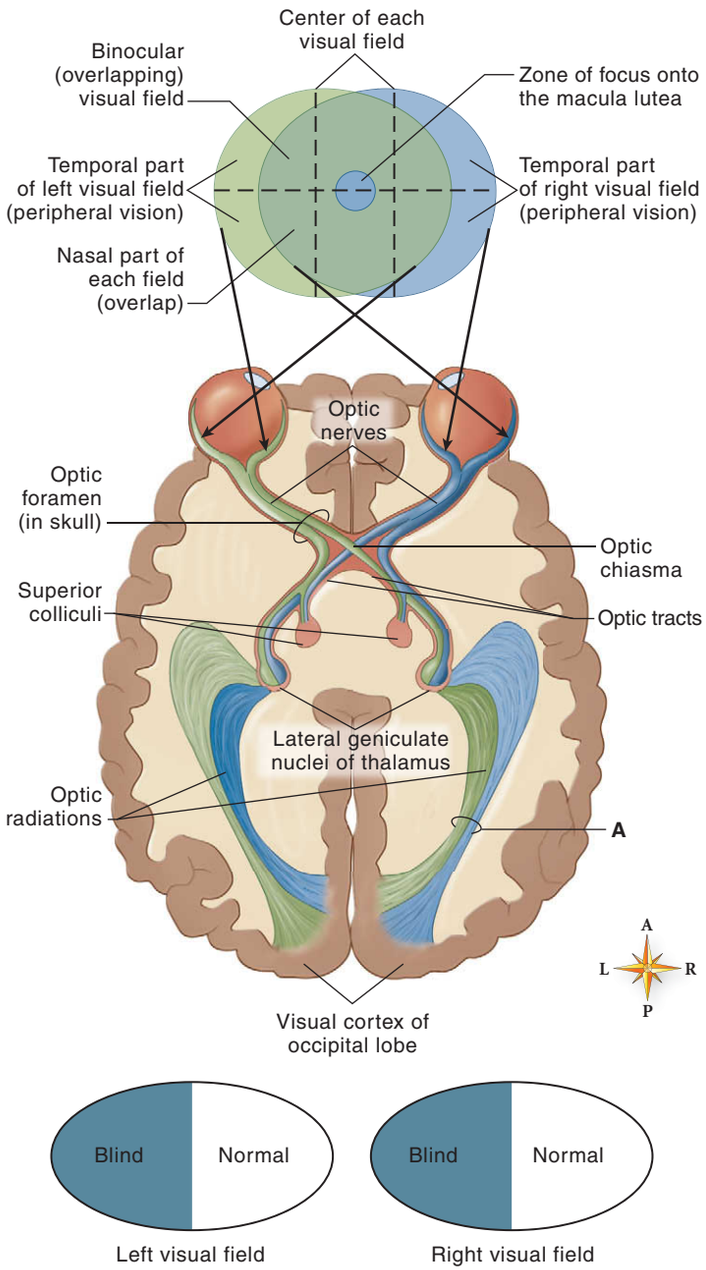


FIGURE 17-31

Visual fields and neural pathways of the eye. Note the structures that make up each pathway: optic nerve, optic chiasma, lateral geniculate body of thalamus, optic radiations, and visual cortex of occipital lobe. Fibers from the nasal portion of each retina cross over to the opposite side at the optic chiasma and terminate in the lateral geniculate nuclei. Location of a lesion in the visual pathway determines the resulting visual defect. Damage at point *A,* for example, would cause blindness in the right nasal and left temporal visual fields, as the ovals beneath indicate. (Trace the visual pathway from point *A* back to the visual field map to see why this is so.) What would be the effect of pressure on the optic chiasma—by a pituitary tumor, for instance? (*Answer:* It would produce blindness in both temporal visual fields. Why? Because it destroys fibers from the nasal side of both retinas.)

optic chiasma contains fibers from the nasal portions of both retinas. Each optic tract also contains fibers from both retinas.

These anatomical facts explain certain peculiar visual abnormalities that sometimes occur. Suppose a person's right optic tract were injured so that it could not conduct impulses—say, at point A in Figure 17-31. This person would be totally blind in neither eye but partially blind in both eyes. Specifically, this person would be blind in the right nasal and left temporal visual fields. Here are the reasons: the right optic tract contains fibers from the right retina's temporal area, the area that sees the right nasal visual field. In addition, the right optic tract contains fibers from the left retina's nasal area, the area that sees the left temporal visual field.

| QUICK CHECK |

15. Name the layers, or coats, of the eyeball.
16. Identify the layers of the retina.
17. Name the four processes that function to focus a clear image on the retina.
18. Outline the steps of the rhodopsin cycle.

Cycle of LIFE

Sense Organs

The ability of the sense organs to respond to stimuli caused by changes in the body's internal or external environment varies during life. Ultimately, all sensory information is acquired through depolarization of sensory nerve endings. Anything that interferes with the generation of a receptor potential or its transmission to and interpretation by areas of the central nervous system influences sensory acuity. Age, disease, structural defects, and lack of maturation all affect our ability to identify and respond to sensory input.

Structure and function response capabilities of the sense organs are related to developmental factors associated with age. For example, a newborn baby has limited sight, hearing, and tactile identification capabilities. As maturation occurs and normal development progresses, the senses become more acute. By late adulthood, presbyopia, progressive hearing loss, and a reduced sense of taste and smell are common.

Some loss of sensory capability in old age is directly related to structural change in receptor cells or other necessary sense organ structures. The lens of the eye becomes harder and less able to change shape, taste buds become less functional, and exteroceptors of all types become less responsive to stimuli because of structural deterioration.

the BIG picture

Sense Organs

Almost invariably, as you study the various organ systems of the body, seeing the "big picture" involves an understanding of how that organ system affects homeostasis. Both the structure and function of the body sense organs illustrate this relationship.

The somatic sense organs are widely distributed throughout the body, and they serve to provide the body with vital information related to both external and internal conditions that affect homeostasis. For example, pain—regardless of cause—is very often the first indicator of homeostatic imbalance. Further, the ability to sense touch, pressure, vibration, stretch, or temperature changes on or in the body before these stimuli reach levels that may cause injury is vital to survival.

The functioning of all the special senses also plays an important homeostatic role. Classic examples include vision and hearing that help us monitor our often hostile external environment and avoid or respond to dangers that might otherwise be life threatening. Also, consider the sensation of thirst. It helps us to regulate our water intake and thus avoid dehydration or the sensation or "craving" for salt, which may signal a dangerous loss of sodium from the body. Other examples include a bitter taste or offensive odor, which are sensations frequently associated with poisonous materials or toxic fumes and thus serve as important defense mechanisms. Take a few minutes to review each of the somatic and special senses by integrating their structure and functions with the "big picture" of homeostasis and survival.

MECHANISMS of DISEASE

DISORDERS OF THE SENSE ORGANS

Disorders of the Ear

Hearing problems can be divided into two basic categories: *conduction impairment* and *nerve impairment*. Conduction impairment refers to the blocking of sound waves as they are conducted through the external and middle ear to the sensory receptors of the inner ear (the conduction pathway). Nerve impairment results in insensitivity to sound because of inherited or acquired nerve damage.

The most obvious cause of conduction impairment is blockage of the external auditory canal. Waxy buildup of cerumen (Figure 17-32, C) commonly blocks conduction of sound toward the tympanic membrane. Foreign objects, tumors, and other matter can block conduction in the external or middle ear. An inherited bone disorder called **otosclerosis** impairs conduction by causing structural irregularities in the stapes. Otosclerosis usually first appears during childhood or early adulthood as **tinnitus,** or "ringing in the ear."

Temporary conduction impairment often results from ear infection, or **otitis.** The structure of the auditory tube, especially its connection with the nasopharynx, makes the middle ear prone to bacterial or viral *otitis media* (Figure 17-32, A). Otitis media often produces swelling and pus formation that block the conduction of sound through the middle ear. Surgical insertion of a *ventilation* or **tympanotomy tube** (Figure 17-32, *B*) is sometimes employed

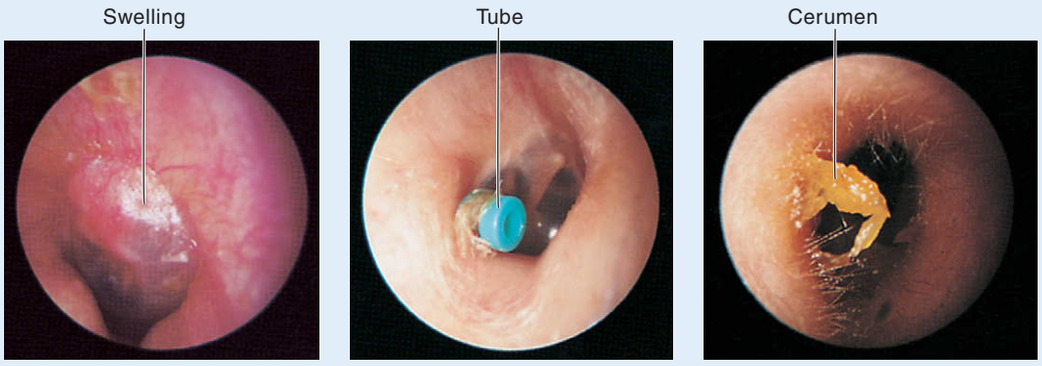


FIGURE 17-32

Disorders of the ear. A, Acute otitis media. Note the red, thickened, and bulging tympanic membrane. **B,** Ventilation or tympanotomy tube ("ear tube"). Inserted to relieve pressure and permit drainage in otitis media. **C,** Cerumen (earwax) in ear canal.

to relieve pressure and permit drainage. Permanent damage to structures of the middle ear occasionally occurs in severe cases.

Hearing loss because of nerve impairment is common in the elderly. Called **presbycusis,** this progressive hearing loss associated with aging results from degeneration of nerve tissue in the ear and the vestibulocochlear nerve. A similar type of hearing loss occurs after chronic exposure to loud noises that damages receptors in the organ of Corti. Because different sound *frequencies* (tones) stimulate different regions of the organ of Corti, hearing impairment is limited to only those frequencies associated with the portion of the organ of Corti that is damaged. For example, the portion of the organ of Corti that degenerates first in presbycusis is normally stimulated by high-frequency sounds. Thus the inability to hear high-pitched sounds is common among older adults.

Two small muscles, the *tensor tympani* and *stapedius*, help prevent damage to hearing caused by prolonged loud noise. The tensor tympani attaches to and limits movement of the eardrum, thus preventing excess displacement caused by prolonged loud sounds.

In addition, the smallest of all body muscles, the stapedius, limits excess movement of the stapes and thus protects the oval window from prolonged noise-related damage. Only protective devices, such as earplugs, can protect hearing from damage caused by very sudden loud noises, such as a gunshot.

Nerve damage can also occur in **Ménière disease,** a chronic inner ear disease of unknown cause. Ménière disease is characterized by tinnitus, progressive nerve deafness, and **vertigo** (sensation of spinning).

Disorders of the Eye

Healthy vision requires three basic processes: formation of an image on the retina (refraction), stimulation of rods and cones, and conduction of nerve impulses to the brain. Malfunction of any of these processes can disrupt normal vision.

Refraction Disorders

Focusing a clear image on the retina is essential for good vision. In the normal eye, light rays enter the eye and are focused into a clear, upside-down image on the retina (Figure 17-33, *A*). The brain can easily right the upside-down image in our conscious perception but cannot correct an image that is not sharply focused. If our eyes are elongated, the image focuses in front of the retina rather than on it. The retina receives only a fuzzy image. This condition, called **myopia** or *nearsightedness*, can be corrected by using concave

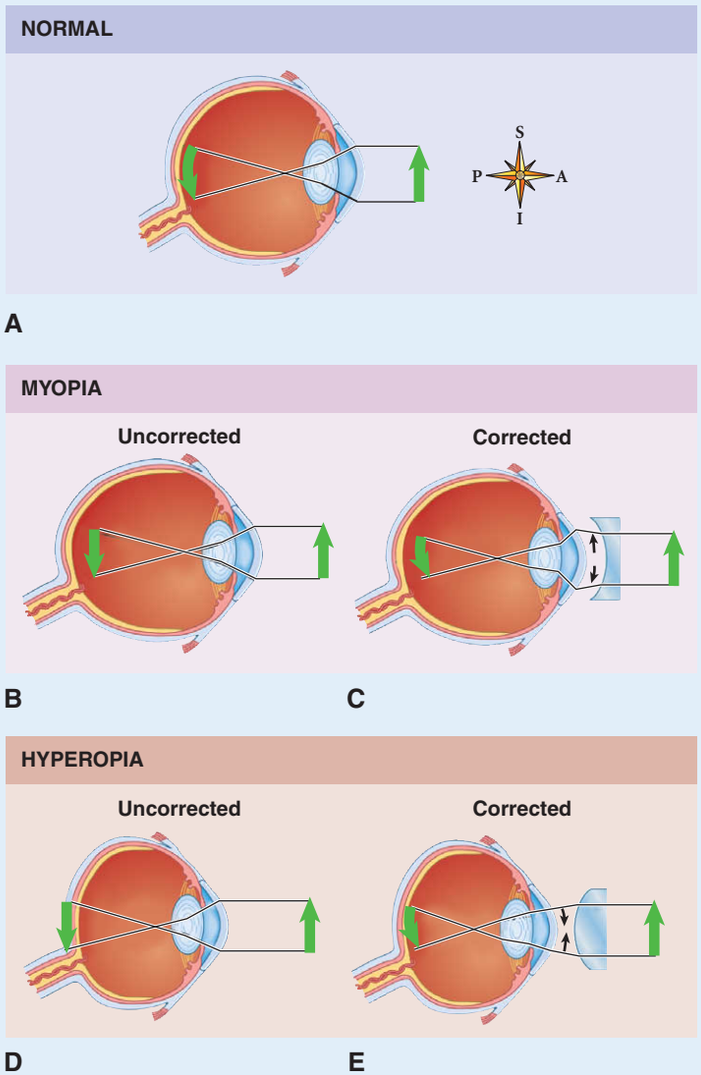


FIGURE 17-33

Correcting refraction disorders. A, Normal eye structure results in a well-focused retinal image. **B,** In myopia, an elongated eyeball causes the image to focus in front of the retina. **C,** An external lens can refocus the image on the retina, correcting the effects of myopia. **D,** In hyperopia, a flattened eyeball causes the image to focus behind the retina. **E,** An external lens can refocus the image on the retina.

(continued)

contact lenses or glasses or by performing refractive eye surgery (Figure 17-33, *B* and *C*). If our eyes are shorter than normal, the image focuses behind the retina, also producing a fuzzy image. This condition, called **hyperopia** or *farsightedness*, can also be corrected by convex lenses or refractive eye surgery (Figure 17-33, *D* and *E*).

| A&P CONNECT |

You have probably heard of eye surgeries such as RK, CK, PRK, or LASIK. But you may have wondered, *what is* a LASIK? Check out ***Refractive Eye Surgery*** online at ***A&P Connect*** to explore the common refractive eye surgeries and how they are done.

evolve

Various other conditions can prevent the formation of a clear image on the retina. For example, the inability to focus the lens properly as we age, or **presbyopia,** has already been mentioned. Older individuals can compensate for presbyopia by using reading glasses when near vision is needed. An irregularity in the curvature of the cornea or lens, a condition called **astigmatism,** can also be corrected with glasses or contact lenses that are formed with the opposite curvature. **Cataracts,** cloudy spots in the eye's lens that develop as we age, may also interfere with focusing (Figure 17-34). Cataracts are especially troublesome in dim light because weak beams of light cannot pass through the cloudy spots the way some brighter light can. This fact accounts for the trouble many older adults have with their night vision.

Infections of the eye also have the potential to impair vision, sometimes permanently. Most eye infections begin in the conjunctiva, producing an inflammation response known as "pink-eye," or **conjunctivitis.** Various pathogens can cause conjunctivitis. For example, the bacterium *Chlamydia trachomatis* that commonly infects the reproductive tract can cause a chronic infection called *chlamydial conjunctivitis*, or **trachoma.** Because *Chlamydia* and other pathogens often inhabit the birth canal, antibiotics are routinely applied to the eyes of newborns to prevent conjunctivitis. Highly contagious *acute bacterial conjunctivitis*, characterized by drainage of a mucous pus, is most commonly caused by bacteria such as *Staphylococcus* and *Haemophilus* (see Figure 17-18, p. 525). Conjunctivitis may produce lesions on the inside of the eyelid that can damage the cornea and thus impair vision. Occasionally infections of the conjunctiva spread to the tissues of the eye proper and cause permanent injury—even total blindness. Besides infection, conjunctivitis may also be caused by allergies. The red, itchy, watery eyes commonly associated with allergic reactions to pollen and other substances result from an allergic inflammatory response of the conjunctiva.



FIGURE 17-34

Cataract. Note the prominent cataract of the left eye.

Disorders of the Retina

Damage to the retina impairs vision because even a well-focused image cannot be perceived if some or all of the light receptors do not function properly. For example, in a condition called **retinal detachment,** part of the retina falls away from the tissue supporting it (Figure 17-35, *A*). This condition may result from aging, eye tumors, or blows to the head—as in a sporting injury. Common warning signs include the sudden appearance of floating spots that may decrease over a period of weeks and odd "flashes of light" that appear when the eye moves. If left untreated, the retina may detach completely and cause total blindness in the affected eye.

Diabetes mellitus, a disorder involving the hormone insulin, may cause a condition known as **diabetic retinopathy**. In this disorder the diabetes causes small hemorrhages in retinal blood vessels that disrupt the oxygen supply to the photoreceptors (Figure 17-35, *B*). The eye responds by building new, but abnormal, vessels that block vision and may cause detachment of the retina. Diabetic retinopathy is one of the leading causes of blindness in the United States. Diabetic retinopathy and other complications of diabetes are often associated with high blood pressure, or *hypertension*, which also causes retinal hemorrhages (Figure 17-35, *C*).

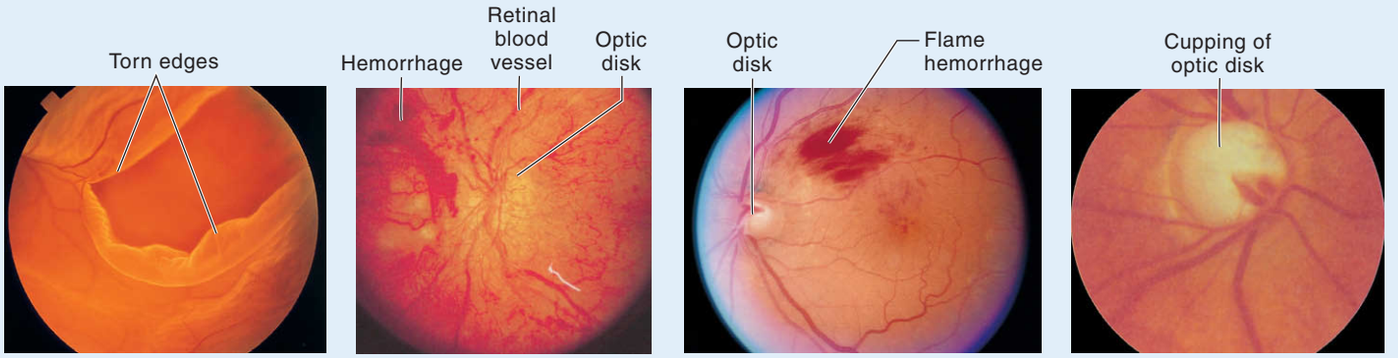


FIGURE 17-35

Retinal pathological conditions. A, Retina tear and detachment. **B,** Diabetic retinopathy. Note the abnormal blood vessels and hemorrhages in the retina caused by diabetes. **C,** Hypertensive retinopathy. Large "flame hemorrhages" in the retina are associated with high blood pressure. **D,** Glaucoma. Note "cupping" of the optic disk caused by increased intraocular pressure. (Compare to normal retina in Figure 17-24 on p. 528.)

Another condition that can damage the retina is **glaucoma.** Recall that glaucoma is excessive *intraocular* (in-trah-AHK-yoo-lar) *pressure* caused by abnormal accumulation of aqueous humor. As fluid pressure against the retina increases above normal, blood flow through the retina slows. Reduced blood flow causes degeneration of the retina and thus leads to loss of vision. Although acute forms of glaucoma can occur, most cases of glaucoma develop slowly over a period of years. This chronic form may not produce any symptoms, especially in its early stages. For this reason, routine eye examinations typically include a screening test for glaucoma. As chronic glaucoma progresses, damage first appears at the edges of the retina—causing a gradual loss of peripheral vision. Blurred vision and headaches may also occur. As the damage becomes more extensive, "halos" are seen around bright lights. If untreated, glaucoma eventually produces total, permanent blindness. One of the most common characteristic early retinal changes associated with glaucoma is swelling or "cupping" of the optic disk (Figure 17-35, *D*).

Degeneration of the retina can cause difficulty seeing at night or in dim light. This condition, called **nyctalopia,** or "night blindness," can also be caused by a deficiency of vitamin A. Recall that vitamin A is needed to make retinal, a component of rhodopsin. A deficiency of rhodopsin impairs the function of rod cells, which are needed for dim light vision.

Disorders of the Visual Pathway

Damage or degeneration in the optic nerve, the brain, or any part of the visual pathway between them, can impair vision. For example, the pressure associated with glaucoma can also damage the optic nerve. Diabetes, already cited as a cause of retina damage, can also cause degeneration of the optic nerve.

Damage to the visual pathway does not always result in total loss of sight. Depending on where the damage occurs, only a part of the visual field may be affected. For example, a certain form of neuritis (nerve inflammation), often associated with multiple sclerosis, can cause loss of only the center of the visual field—a condition called **scotoma.**

A stroke can cause vision impairment when the resulting tissue damage occurs in one of the regions of the brain that processes visual information. For example, damage to an area that processes information about colors may result in a rare condition called **acquired cortical color blindness.** This condition is characterized by difficulty in distinguishing any color—not just one or two colors as in the more common inherited forms of color blindness.

UNIT 3

LANGUAGE OF SCIENCE (continued from p. 505)

bulbous corpuscle
(BUL-bus KOR-pus-ul)
[*bulb-* **swollen root,** *-ous* **relating to,** *corpus-* **body,** *-cle* **little**]

chemoreceptor
(kee-moh-ree-SEP-tor)
[*chemo-* **chemical,** *-recept-* **receive,** *-or* **agent**]

ciliary body
(SIL-ee-air-ee)
[*ciliary* **eyelids or eyelashes**]

circumvallate papillae
(ser-kum-VAL-ayt pah-PIL-ah)
[*circum-* **around,** *-vall-* **post or stake,** *-ate* **relating to,** *papilla* **nipple**] *pl.* papillae

cone

crista ampullaris
(KRIS-tah am-pyoo-LAIR-iss)
[*crista* **ridge,** *ampu-* **flask,** *-ulla-* **little,** *-aris* **relating to**] *pl.,* cristae ampulares

cupula
(KYOO-pyoo-lah)
[*cup-* **tub,** *-ula* **little**] *pl.,* cupulae

dynamic equilibrium
(dye-NAM-ik ee-kwi-LIB-ree-um)
[*dynam-* **power,** *-ic* **relating to,** *equi-* **equal,** *-libr-* **balance**]

eardrum

endolymph
(EN-doh-limf)
[*endo-* **within,** *-lymph* **water**]

epithelial support cell
(ep-i-THEE-lee-al)
[*epi-* **upon,** *-theli* **nipple,** *-al* **relating to**]

equilibrium
(e-kwi-LIB-ree-um)
[*equi-* **equal,** *-libr-* **balance**] *pl.,* equilibria

eustachian
(yoo-STAY-shun)
[*Bartolomeo Eustachio* **Italian anatomist,** *-an* **relating to**]

external ear
[*extern-* **outside,** *-al* **relating to**]

exteroceptor
(eks-ter-oh-SEP-tor)
[*exter-* **outside,** *-cept-* **receive,** *-or* **agent**]

extrinsic eye muscle
(eks-TRIN-sik)
[*extr-* **outside,** *-sic* **beside,** *mus-* **mouse,** *-cle* **small**]

fast (A) pain

filiform papilla
(FIL-ih-form pah-PIL-ah)
[*fili-* **thread,** *-form* **shape,** *papilla* **nipple**] *pl.* papillae

foliate papilla
(FOL-ee-ayt pah-PIL-ah)
[*foli-* **leaf,** *-ate* **relating to,** *papilla* **nipple**] *pl.* papillae

fovea centralis
(FOH-vee-ah sen-TRAL-is)
[*fovea* **pit,** *centralis* **center**] *pl.,* foveae centrales

fungiform papillae
(FUN-jih-form pah-PIL-ah)
[*fungi-* **mushroom,** *-form* **shape,** *papilla* **nipple**] *pl.* papillae

gamma motor neuron
(GAM-mah MOH-tor NOO-roon)
[*gamma (γ)* **third letter of Greek alphabet,** *mot-* **movement,** *-or* **agent,** *neuron* **nerve**]

general sense organ

Golgi tendon organ
(GOL-jee TEN-don OR-gan)
[*Camillo Golgi* **Italian histologist,** *tend-* **pulled tight,** *-on* **unit**]

Golgi tendon receptor
(GOL-jee TEN-don ree-SEP-tor)
[*Camillo Golgi* **Italian histologist,** *-cept-* **receive,** *-or* **agent**]

granule cell
(GRAN-yool)
[*gran-* **grain,** *-ule* **little**]

gustatory
(GUS-tah-tor-ee)
[*gusta-* **taste,** *-ory* **relating to**]

gustatory cell
(GUS-tah-tor-ee sell)
[*gusta-* **taste,** *-ory* **relating to,** *cell* **storeroom**]

inner ear

interoceptor
(in-ter-oh-SEP-tor)
[*inter-* **inward,** *-cept-* **receive,** *-or* **agent**]

intrinsic eye muscle
(in-TRIN-sik)
[*intr-* **within,** *-sic* **beside,** *mus-* **mouse,** *-cle* **small**]

iris
[*iris* **rainbow**]

labyrinth
(LAB-i-rinth)
[*labyrinth* **maze**]

lamellar corpuscle
(lah-MEL-ar KOR-pus-ul)
[*lam-* **plate,** *-ella-* **little,** *-ar* **relating to,** *corpus-* **body,** *-cle* **little**]

lens
(lenz)
[*lens* **lentil**]

macula
(MAK-yoo-lah)
[*macula* **spot**] *pl.,* maculae or maculas

macula lutea
(MAK-yoo-lah LOO-tee-ah)
[*macula* **spot,** *lutea* **yellow**] *pl.,* maculae luteae

mechanoreceptor
(mek-an-oh-ree-SEP-tor)
[*mechano-* **machine (mechanical),** *-cept-* **receive,** *-or* **agent**]

middle ear

muscle spindle
[*mus-* **mouse,** *-cle* **small**]

nociceptor
(noh-see-SEP-tor)
[*noci-* **to harm,** *-cept-* **receive,** *-or* **agent**]

olfactory
(ohl-FAK-tor-ee)
[*olfact-* **smell,** *-ory* **relating to**]

olfactory sensory neuron
(ol-FAK-tor-ee SEN-soree NOO-ron)
[*olfact-* **smell,** *-ory* **relating to,** *neuron* **nerve**]

LANGUAGE OF SCIENCE *(continued from p. 537)*

opsin
(OP-sin)
[*ops-* **vision**, *-in* **substance**]

optic nerve
(OP-tik)
[*opt-* **vision**, *-ic* **relating to**]

organ of Corti
(OR-gan of KOR-tee)
[*Alfonso Corti* **Italian anatomist**]

osmoreceptor
(os-moh-ree-SEP-tor)
[*osmo-* **push (osmosis)**, *-cept-* **receive**, *-or* **agent**]

otolith
(OH-toh-lith)
[*oto-* **ear**, *-lith* **stone**]

oval window

papilla
(pah-PIL-ah)
[*papilla* **nipple**] *pl.,* papillae

perception

perilymph
(PAIR-i-limf)
[*peri-* **around**, *-lymph* **water**]

photoreceptor
(FOH-toh-ree-sep-tor)
[*photo-* **light**, *-cept-* **receive**, *-or* **agent**]

pitch

posterior cavity
(pohs-TEER-ee-or KAV-i-tee)
[*poster-* **behind**, *-or* **quality**, *cav-* **hollow**, *-ity* **state**]

proprioceptor
(proh-pree-oh-SEP-tor)
[*propri-* **one's own**, *-cept-* **receive**, *-or* **agent**]

pupil
(PYOO-pill)
[*pup-* **doll**, *-il* **little**]

receptor potential
(ree-SEP-tor poh-TEN-shal)
[*recept-* **receive**, *-or* **agent**, *potent-* **power**, *-ial* **relating to**]

refraction
(ree-FRAK-shun)
[*refract-* **break apart**, *-tion* **process**]

retina
(RET-i-nah)
[*ret-* **net**, *-ina* **relating to**]

retinal
(RET-i-nal)
[*ret-* **net**, *-ina-* **relating to**, *-al* **relating to**]

rhodopsin
(roh-DOP-sin)
[*rhodo-* **red**, *-ops-* **vision**, *-in* **substance**]

rod

round window

sensation
[*sens-* **feel**, *-ation* **process**]

sensory receptor
(SEN-soh-ree ree-SEP-tor)
[*sens-* **feel**, *-ory* **relating to**, *recept-* **receive**, *-or* **agent**]

slow (B) pain

somatic pain
(so-MAH-tik)
[*soma-* **body**, *-ic* **relating to**]

special sense

static equilibrium
(STAT-ik ee-kwi-LIB-ree-um)
[*stat-* **stand**, *-ic* **relating to**, *equi-* **equal**, *-libr-* **balance**]

stretch reflex
[*re-* **again**, *-flex* **bend**]

tactile corpuscle
(TAK-tyle KOR-pus-ul)
[*tact-* **touch**, *-ile* **relating to**, *corpus-* **body**, *-cle* **little**]

tactile disk
(TAK-tyle)
[*tact-* **touch**, *-ile* **relating to**]

taste bud

tectorial membrane
(tek-TOH-ree-al)
[*tect-* **roof**, *-or-* **quality**, *-al* **relating to**, *membran-* **thin skin**]

thermoreceptor
(ther-moh-ree-SEP-tor)
[*thermo-* **heat**, *-cept-* **receive**, *-or* **agent**]

tympanic membrane
(tim-PAN-ik)
[*tympan-* **drum**, *-ic* **relating to**, *membran-* **thin skin**]

vestibular membrane
(ves-TIB-yoo-lar)
[*vestibule-* **entrance hall**, *-ar* **relating to**, *membran-* **thin skin**]

visceral pain
(VISS-er-al)
[*viscera* **internal organs**]

viscoreceptor
(viss-er-oh-SEP-tor)
[*viscero-* **internal organs**, *-cept-* **receive**, *-or* **agent**]

volume

LANGUAGE OF MEDICINE

acquired cortical color blindness
(ah-KWYERD KOHR-tih-kahl)
[*cortic-* **bark**, *-al* **relating to**]

anosmia
(AN-oz-mee-ah)
[*an-* **without**, *-osm-* **smell**, *-ia* **condition**]

astigmatism
(ah-STIG-mah-tiz-em)
[*a-* **not**, *-stigma-* **point**, *-ism* **condition**]

blepharoplasty
(blef-ar-oh-PLAS-tee)
[*blepharo-* **eyelid or eyelash**, *-plasty* **surgical repair**]

cataracts
(KAT-ah-rakts)
[*cataract* **waterfall**]

chronic pain
[*chron-* **time**, *-ic* **relating to**]

conjunctivitis
(kon-junk-ti-VYE-tis)
[*con-* **together**, *-junct-* **join**, *-iv-* **relating to**, *-itis* **inflammation**]

diabetic neuropathy
(dye-ah-BET-ik nyoo-ROP-ah-thee)
[*diabet-* **siphon**, *-ic* **relating to**, *neuro-* **nerve**, *-path-* **disease**, *-y* **state**]

diabetic retinopathy
(dye-ah-BET-ik ret-in-AH-path-ee)
[*diabet-* **siphon**, *-ic* **relating to**, *ret-* **net**, *-ina* **relating to**, *-path-* **disease**, *-y* **state**]

diplopia
(di-PLOH-pee-ah)
[*di-* **double**, *-op-* **vision**, *-ia* **condition**]

fibromyalgia (FM)
(fye-broh-my-AL-jah)
[*fibr-* **fiber**, *-my-* **muscle**, *-algia* **pain**]

glaucoma
(glaw-KOH-mah)
[*glauco-* **gray or silver**, *-oma* **tumor (growth)**]

hyperopia
(hye-per-OH-pee-ah)
[*hyper-* **excessive or above**, *-op-* **vision**, *-ia* **condition**]

Ménière disease
(men-ee-AIR)
[*Prosper Ménière* **French physician**]

myopia
(my-OH-pee-ah)
[*myops-* **nearsighted**, *-op-* **vision**, *-ia* **condition**]

nyctalopia
(nik-tah-LOH-pee-ah)
[*nyct-* **night**, *-op-* **vision**, *-ia* **condition**]

ophthalmology
(off-thal-MOL-eh-jee)
[*oph-* **eye or vision**, *-thalm-* **inner chamber**, *-o-* **combining form**, *-log-* **words (study of)**, *-y* **activity**]

ophthalmoscope
(off-THAL-mah-skohp)
[*oph-* **eye or vision**, *-thalmo-* **inner chamber**, *-scop-* **see**]

otitis
(oh-TYE-tis)
[*ot-* **ear**, *-itis* **inflammation**]

otitis media
(oh-TYE-tis MEE-dee-ah)
[*ot-* **ear**, *-itis* **inflammation**, *medi-* **middle**, *-al* **relating to**]

otosclerosis
(oh-toh-skleh-ROH-sis)
[*oto-* **ear**, *-sclero-* **hard**, *-sis* **condition**]

otoscope
(OH-toh-skohp)
[*oto-* **ear**, *-scop-* **see**]

presbycusis
(pres-bih-KYOO-sis)
[*presby-* **elderly**, *-cusis* **hearing**]

presbyopia
(pres-bee-OH-pee-ah)
[*presby-* **elderly**, *-op-* **vision**, *-ia* **condition**]

referred pain

retinal detachment
(RET-ih-nal)
[*ret-* **net**, *-ina-* **relating to**, *-al* **relating to**]

scotoma
(skoh-TOH-mah)
[*scoto-* **darkness**, *-oma* **tumor**]

strabismus
(strah-BIS-mus)
[*strab-* **squinting**, *-ismus* **condition**]

tinnitus
(tih-NYE-tus or TIN-nit-us)
[*tinnitis* **a ringing or tinkling**]

trachoma
(trah-KOH-mah)
[*trach-* **rough**, *-oma* **tumor**]

two-point discrimination test

tympanotomy tube
(tim-peh-NOT-eh-mee)
[*tympan-* **drum**, *-tom-* **cut**, *-y* **action**]

vertigo
(VER-ti-go)
[*vertigo* **turning**]

CASE study

Why were the headlights of the oncoming cars so bright, she wondered. Rita flashed her car lights as the next car approached, but when the driver flashed his lights in return, she saw his lights had been on the low setting all along. She noticed too that the street signs were difficult to read tonight. When she got to her daughter's house, Rita was quite relieved to be off the road! Over the years, her vision had always been excellent; not being able to see well was a new experience for her. Her daughter suggested she have her eyes checked as soon as possible.

The next week, as Rita tried to read one of the magazines in the optometrist's waiting room, she found that she could not get the letters to come into focus unless she held the magazine at arm's length—yet another sign of trouble with her eyesight.

1. What could be causing the inability to focus on close objects?
   a. Myopia
   b. Presbyopia
   c. Conjunctivitis
   d. Scotoma

In a few minutes, she heard, "Rita!" The receptionist was calling her back to the examination room.

2. What type of receptors in the ear responded to the receptionist's voice?
   a. Mechanoreceptors
   b. Photoreceptors
   c. Thermoreceptors
   d. Chemoreceptors

As the optometrist leaned closer to get a better look at her eyes, Rita could smell his cologne.

3. What type of receptors are responding to the cologne smell?
   a. Mechanoreceptors
   b. Photoreceptors
   c. Thermoreceptors
   d. Chemoreceptors

When the examination was completed, the optometrist told Rita that the lenses of her eyes had some cloudy spots on them. That would account for the vision problems she had when driving at night.

4. What condition could the spots indicate?
   a. Presbyopia
   b. Glaucoma
   c. Cataracts
   d. Myopia

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

UNIT 3

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

SENSORY RECEPTORS

A. Sensory receptors make it possible for the body to respond to stimuli caused by changes occurring in our internal or external environment
B. Receptor response
   1. General function—responds to stimuli by converting them to nerve impulses
   2. Different types of receptors respond to different stimuli
   3. Receptor potential
      a. The potential that develops when an adequate stimulus acts on a receptor; it is a graded response
      b. When a threshold is reached, an action potential in the sensory neuron's axon is triggered
      c. Impulses travel over sensory pathways to the brain and spinal cord where either they are interpreted as a particular sensation or they initiate a reflex action
   4. Adaptation—a functional characteristic of receptors; receptor potential decreases over time in response to a continuous stimulus, which leads to a decreased rate of impulse conduction and a decreased intensity of sensation (Figure 17-1)
C. Distributions of receptors
   1. Receptors for special senses of smell, taste, vision, hearing, and equilibrium are grouped into localized areas or into complex organs
   2. General sense organs of somatic senses are microscopic receptors widely distributed throughout the body in the skin, mucosa, connective tissue, muscles, tendons, joints, and viscera

CLASSIFICATION OF RECEPTORS (TABLE 17-1)

A. Classification by location
   1. Exteroceptors
      a. On or near body surface
      b. Often called *cutaneous receptors;* examples: pressure, touch, pain, temperature
   2. Visceroceptors (interoceptors)
      a. Located internally—often within body organs, or viscera
      b. Provide body with information about internal environment; examples: pressure, stretch, chemical changes, hunger, thirst
   3. Proprioceptors—special type of visceroceptor
      a. Location limited to skeletal muscle, joint capsules, and tendons

b. Provide information on body movement, orientation in space, and muscle stretch
c. Two types—tonic and phasic proprioceptors provide positional information on body or body parts while at rest or during movement

B. Classification by stimulus detected
1. Mechanoreceptors—activated when "deformed" to generate receptor potential
2. Chemoreceptors—activated by amount or changing concentration of certain chemicals, for example, taste and smell
3. Thermoreceptors—activated by changes in temperature (Figure 17-3)
4. Nociceptors—activated by intense stimuli that may damage tissue; sensation produced in pain (Figure 17-2)
5. Photoreceptors—found only in the eye; respond to light stimuli if the intensity is great enough to generate a receptor potential
6. Osmoreceptors—concentrated in the hypothalamus; activated by changes in concentration of electrolytes (osmolarity) in extracellular fluids.

C. Classification by structure (Figure 17-5): divides sensory receptors into either those with free nerve endings or those with encapsulated nerve endings
1. Free nerve endings
a. Most widely distributed sensory receptor
b. Include both exteroceptors and visceroceptors
c. Called nociceptors—primary receptors for pain
d. Primary receptors for heat and cold
e. Pain sensations
(1) Acute (A) fibers—mediate sharp, intense, localized pain
(2) Chronic (B) fibers—mediate less intense but more persistent dull or aching pain
f. Tactile sensations—skin movement, itch, tickle, discriminative tough
(1) Root hair plexuses
(2) Tactile (Merkel) disks
2. Encapsulated nerve endings—six types; all have connective tissue capsules and are mechanoreceptors
a. Touch and pressure receptors
(1) Tactile corpuscle (Meissner corpuscle), relatively large and superficial in placement; mediates touch and low-frequency vibration; large numbers in hairless skin areas, such as nipples, fingertips, and lips; two anatomical variations of tactile (Meissner) corpuscle
(a) Bulboid corpuscles (Krause end bulbs)—small, with less tightly coiled dendritic endings within their capsule; involved in touch, low-frequency vibrations
(b) Bulbous (Ruffini) corpuscles, have a flattened capsule and are deeply located in the dermis; mediate crude and persistent touch
(2) Lamellar or Pacini corpuscles—large mechanoreceptors that respond quickly to sensations of deep pressure, high-frequency vibration, and stretch; found in deep dermis and in joint capsules—they adapt quickly, and sensations they evoke seldom last for long periods
b. Stretch receptors—two types; operate to provide body with information concerning muscle length and strength of muscle contraction
(1) Muscle spindle—composed of 5 to 10 intrafusal fibers lying between and parallel to regular (extrafusal) muscle fibers
(a) Large-diameter and rapid-conducting type Ia and smaller-diameter and slower-conducting type II afferent fibers carry messages to brain concerning changes in muscle length
(b) If the length of a muscle exceeds a certain limit, a stretch reflex is initiated to shorten the muscle, thus helping to maintain posture
(2) Golgi tendon organs—located at junction between muscle tissue and tendon; made up of encapsulated neuron endings associated with collagen bundles (Figure 17-5)
(a) Type Ib sensory neurons (Golgi tendon receptors) are stimulated by excessive contraction—when stimulated, they cause muscle to *relax*
(b) Golgi tendon reflex protects muscle from tearing internally because of excessive contractile force

SENSE OF SMELL

A. Olfactory receptors
1. Olfactory sense organs consist of epithelial support cells and olfactory sensory neurons (Figure 17-6)
a. Olfactory cilia—located on olfactory sensory neurons that touch the olfactory epithelium lining the upper surface of the nasal cavity
b. Olfactory cells—chemoreceptors; gas molecules or chemicals dissolved in the mucus covering the nasal epithelium stimulate the olfactory cells
c. Olfactory epithelium—located in most superior portion of the nasal cavity
d. Olfactory receptors—extremely sensitive and easily fatigued

B. Olfactory pathway—when the level of odor-producing chemicals reaches a threshold level, the following occurs (Figure 17-7):
1. Receptor potential and then action potential are generated and passed to the olfactory nerves in the olfactory bulb
2. The impulse then passes through the olfactory tract and into the thalamic and olfactory centers of the brain for interpretation, integration, and memory storage

SENSE OF TASTE

A. Taste buds—sense organs that respond to gustatory, or taste, stimuli
1. Associated with papillae
a. Fungiform—large, mushroom shaped; anterior two-thirds of tongue
b. Circumvallate—huge, dome-shaped; form row near back of tongue
c. Foliate—leaflike; lateral edges of posterior tongue

   d. Filiform—threadlike; scattered among fungiform papillae
2. Chemoreceptors that are stimulated by chemicals dissolved in the saliva
3. Gustatory cells—sensory cells in taste buds; gustatory hairs extend from each gustatory cell into the taste pore
4. Sense of taste depends on the creation of a receptor potential in gustatory cells because of taste-producing chemicals in the saliva
5. Taste buds are similar structurally; functionally, each taste bud responds most effectively to one of five primary taste sensations: sour, sweet, bitter, umami, and salty (and perhaps others, such as metallic) (Figure 17-8 and 17-9)
6. Adaptation and sensitivity thresholds differ for each of the primary taste sensations

B. Neural pathway for taste
1. Taste sensation begins with a receptor potential in the gustatory cells of a taste bud; generation and propagation of an action potential then transmits the sensory input to the brain
2. Nerve impulses from the anterior two thirds of the tongue travel over the facial nerve; those from the posterior one third of the tongue travel over the glossopharyngeal nerve; vagus nerve plays a minor role in taste
3. Nerve impulses are carried to the medulla oblongata, relayed into the thalamus, and then relayed into the gustatory area of the cerebral cortex in the parietal lobe of the brain
4. Flavor results from integration of taste, smell, and the trigeminal senses (textures and irritants)

SENSES OF HEARING AND BALANCE: THE EAR

A. External ear—two divisions (Figures 17-10 and 17-11)
1. Auricle, or pinna—the visible portion of the ear
2. External acoustic meatus—tube leading from the auricle into the temporal bone and ending at the tympanic membrane

B. Middle ear (Figure 17-11)
1. Tiny, epithelium-lined cavity hollowed out of the temporal bone
2. Contains three auditory ossicles
   a. Malleus (hammer)—attached to the inner surface of the tympanic membrane
   b. Incus (anvil)—attached to the malleus and stapes
   c. Stapes (stirrup)—attached to the incus
3. Openings into the middle ear cavity
   a. Opening from the external acoustic meatus covered with tympanic membrane
   b. Oval window—opening into inner ear; stapes fits here
   c. Round window—opening into inner ear; covered by a membrane
   d. Opening into the auditory (eustachian) tube

C. Inner ear (Figure 17-12, *A*)
1. Structure of the inner ear
   a. Bony labyrinth—made up of the vestibule, cochlea, and semicircular canals
   b. Membranous labyrinth—made up of utricle and saccule inside the vestibule, cochlear duct inside the cochlea, and membranous semicircular ducts inside the bony semicircular canals
   c. Vestibule and semicircular canal organs are involved with balance
   d. Cochlea—involved with hearing
   e. Endolymph—clear, potassium-rich fluid filling the membranous labyrinth
   f. Perilymph—similar to cerebrospinal fluid, surrounds the membranous labyrinth, filling the space between the membranous tunnel and its contents and the bony walls that surround it

D. Cochlea and cochlear duct (Figure 17-12, *B*)
1. Cochlea—bony labyrinth
2. Modiolus—cone-shaped core of bone that houses the spiral ganglion, which consists of cell bodies of the first sensory neurons in the auditory relay
3. Cochlear duct
   a. Lies inside the cochlea; only part of the internal ear concerned with hearing; contains endolymph
   b. Shaped like a triangular tube
   c. Divides the cochlea into the scala vestibuli, the upper section, and the scala tympani, the lower section; both sections filled with perilymph
   d. Vestibular membrane—the roof of the cochlear duct
   e. Basilar (spiral) membrane—floor of the cochlear duct
   f. Organ of Corti—rests on the basilar membrane; consists of supporting cells and hair cells; also called *spiral organ*
   g. Axons of the neurons that begin around the organ of Corti, extend in the cochlear nerve to the brain to produce the sensation of hearing

E. Sense of hearing
1. Sound is created by vibrations
2. Ability to hear sound waves depends on volume, pitch, and other acoustic properties
3. Sound waves must be of sufficient amplitude to move the tympanic membrane and have a frequency capable of stimulating the hair cells in the organ of Corti (spiral organ) (Figure 17-13, *A*)
4. Basilar membrane width and thickness varies throughout its length
   a. High-frequency sound waves vibrate the narrow portion near the oval window
   b. Low frequencies vibrate the wider, thicker portion near the apex of the cochlea
   c. Each frequency stimulates different hair cells and facilitates perception of different pitches (Figure 17-13, *B*)
   d. Perception of loudness is determined by movement amplitude; the greater the movement, the louder the perceived sound
   e. Hearing results from stimulation of the auditory area of the cerebral cortex
5. Pathway of sound waves (Figure 17-13)
   a. Enter external auditory canal
   b. Strike tympanic membrane, causing vibrations

c. Tympanic vibrations move the malleus, which in turn moves the incus and then the stapes
d. The stapes moves against the oval window, which begins the fluid conduction of sound waves
e. The perilymph in the scala vestibuli of the cochlea begins a "ripple" that is transmitted through the vestibular membrane to the endolymph inside the duct, to the basilar membrane, and then to the organ of Corti
f. From the basilar membrane, the ripple is transmitted through the perilymph in the scala tympani and then expends itself against the round window

6. Neural pathway of hearing
a. A movement of hair cells against the tectorial membrane stimulates the dendrites that terminate around the base of the hair cells and initiates impulse conduction by the cochlear nerve to the brainstem
b. Impulses pass through "relay stations" in the nuclei in the medulla, pons, midbrain, and thalamus before reaching the auditory area of the temporal lobe

F. Vestibule and semicircular canals (Figure 17-12, *A*)
1. Vestibule—the central section of the bony labyrinth; the utricle and saccule are the membranous structures within the vestibule
2. Three semicircular canals—found in each temporal bone
a. Each canal is at a right angle to the other
b. Membranous semicircular ducts, within the canals; each contains endolymph and connects with the utricle
c. Each canal enlarges into an ampulla near junction with utricle

G. Sense of balance
1. Static equilibrium—ability to sense the position of the head relative to gravity or to sense acceleration or deceleration (Figure 17-14)
a. Movements of the maculae, located in both the utricle and saccule almost at right angles to each other, provide information related to head position or acceleration
b. Otoliths are located within the matrix of the macula
c. Changing head position produces a change of pressure on the otolith-weighted matrix, which stimulates the hair cells that in turn stimulate the receptors of the vestibular nerve
d. Vestibular nerve fibers conduct impulses to the brain and produce a sensation of the position of the head and also a sensation of a change in the pull of gravity
e. Righting reflexes—muscular responses to restore the body and its parts to their normal position when they have been displaced; caused by stimuli of the macula and impulses from proprioceptors and from the eyes
2. Dynamic equilibrium—needed to maintain balance when the head or body is rotated or suddenly moved; able to detect changes both in direction and rate at which movement occurs (Figure 17-15)
a. Depends on the functioning of the cristae ampullaris, which are located in the ampulla of each semicircular duct
b. Cupula—gelatinous cap in which the hair cells of each crista are embedded
(1) Does not respond to gravity
(2) Moves with the flow of endolymph in the semicircular ducts
c. Semicircular ducts are arranged at nearly right angles to each other to detect movement in all directions
d. Hair cells bend as cupula moves, producing a receptor potential followed by an action potential
(1) Action potential passes through the vestibular portion of the eighth cranial nerve to the medulla oblongata
(2) Sent next to other areas of the brain and spinal cord for interpretation, integration, and response

VISION: THE EYE

A. Structure of the eye (Figures 17-16 through 17-25)
1. External structures (Figure 17-16 through 17-20)
a. Eyebrows and eyelashes—give some protection against foreign objects entering the eye; cosmetic purposes
b. Eyelids—consist of voluntary muscle and skin with a tarsal plate
(1) Lined with conjunctiva, a mucous membrane
(2) Palpebral fissure—opening between the eyelids
(3) Angle or canthus—where the upper and lower eyelids join
c. Lacrimal apparatus—structures that secrete tears and drain them from the surface of the eyeball (Figure 17-19)
(1) Lacrimal glands—size and shape of a small almond
(a) Located at the upper, outer margin of each orbit
(b) Approximately a dozen small ducts lead from each gland
(c) Drain tears onto the conjunctiva
(2) Lacrimal canals—small channels that empty into lacrimal sacs
(3) Lacrimal sacs—located in a groove in the lacrimal bone
(4) Nasolacrimal ducts—small tubes that extend from the lacrimal sac into the inferior meatus of the nose
2. Muscles of the eye
a. Extrinsic eye muscles (Figure 17-20)—skeletal muscles that attach to the outside of the eyeball and to the bones of the orbit
(1) Named according to their position on the eyeball
(2) Include the superior, inferior, medial, and lateral rectus muscles and superior and inferior oblique muscles
b. Intrinsic eye muscles—smooth muscles located within the eye
(1) Iris—regulates size of pupil
(2) Ciliary muscle—controls shape of lens
3. Layers of the eyeball—three coats of tissues compose the eyeball (Figure 17-21)
a. Fibrous layer—outer coat
(1) Sclera—tough, white, fibrous tissue

(2) Cornea—the transparent anterior portion that lies over the iris; no blood vessels found in the cornea or in the lens
(3) Scleral venous sinus (canal of Schlemm)—ring-shaped venous sinus found deep within the anterior portion of the sclera at its junction with the cornea

b. Vascular layer—middle coat
(1) Contains many blood vessels and a large amount of pigment
(2) Choroid—pigmented membrane lining more than two thirds of the posterior fibrous outer coat
(3) Anterior portion has three different structures (Figure 17-21)
(a) Ciliary body—thickening of choroid, fits between anterior margin of retina and posterior margin of iris; ciliary muscle lies in anterior part of ciliary body; ciliary processes—fold in the ciliary body
(b) Suspensory ligament—attached to the ciliary processes and blends with the elastic capsule of the lens, to hold it in place
(c) Iris—colored part of the eye; consists of circular and radial smooth muscle fibers that form a doughnut-shaped structure; attaches to the ciliary body

c. Inner layer—incomplete innermost coat of the eyeball
(1) Retina—made up of an outer layer of pigmented epithelium (pigmented retina) and an inner layer of nervous tissue (sensory retina) (Figure 17-23)
(2) Three layers of neurons make up the sensory retina
(a) Photoreceptor cells—visual receptors, sensitive to light rays
(i) Rods—absent from the fovea and macula; increased in density toward the periphery of the retina
(ii) Cones—less numerous than rods; most densely concentrated in the fovea centralis in the macula lutea
(b) Bipolar cells
(c) Ganglionic cells—all axons of these neurons extend back to the optic disk; part of the sclera, which contains perforations through which the fibers emerge from the eyeball as the optic nerve
(d) Horizontal and amacrine cells allow lateral connections within the sensory retina
(3) Optic nerve—second cranial nerve (CN II) extends from the eyeball to the brain
(4) Retinal blood vessels—critical to normal visual function (Figure 17-24)

4. Cavities and humors
a. Cavities—eyeball has a large interior space divided into two cavities
(1) Anterior cavity—lies in front of the lens; has two subdivisions
(a) Anterior chamber—space anterior to the iris and posterior to the cornea
(b) Posterior chamber—small space posterior to the iris and anterior to the lens
(2) Posterior cavity—larger than the anterior cavity; occupies all the space posterior to the lens, suspensory ligament, and ciliary body

b. Humors
(1) Aqueous humor—fills both chambers of the anterior cavity; clear, watery fluid that often leaks out when the eye is injured; formed from blood in capillaries located in the ciliary body (Figure 17-25)
(2) Vitreous body—gel-filled sac fills the posterior cavity; helps to maintain sufficient intraocular pressure, with aqueous humor, to give the eyeball its shape

B. The process of seeing
1. Formation of retinal image
a. Refraction of light rays—deflection, or bending, of light rays produced by light rays passing obliquely from one transparent medium into another of different optical density; cornea, aqueous humor, lens, and vitreous body are the refracting media of the eye
b. Accommodation for near vision requires three changes:
(1) Change of lens shape (Figure 17-26)
(a) Increase in curvature of the lens to achieve the greater refraction needed for near vision
(b) Contraction of ciliary muscle reduces tension in suspensory ligaments, allowing lens to bulge to better see near objects
(c) Relaxation of ciliary muscle increases tension in suspensory ligaments, flattening lens for distant vision
(2) Constriction of pupil—muscles of iris are important to formation of a clear retinal image (Figure 17-27)
(a) Pupil constriction prevents divergent rays from object from entering eye through periphery of the cornea and lens
(b) Near reflex—constriction of pupil that occurs with accommodation of the lens in near vision
(c) Photopupil reflex—pupil constricts in bright light
(3) Convergence of eyes—movement of the two eyeballs inward so that their visual axes come together at the object viewed
(a) The closer the object, the greater the degree of convergence necessary to maintain single vision
(b) For convergence to occur, a functional balance between antagonistic extrinsic muscles must exist
(c) Strabismus is abnormal convergence (Figure 17-28)

2. The role of photopigments—light-sensitive pigmented compounds undergo structural changes that result in

generation of nerve impulses, which are interpreted by the brain as sight
   a. Rods—photopigment in rods is rhodopsin
      (1) Highly light sensitive
      (2) Breaks down into opsin and retinal
      (3) Separation of opsin and retinal in the presence of light causes an action potential in rod cells
      (4) Energy is needed to re-form rhodopsin (Figure 17-29)
   b. Cones—three types of cones are present in the retina, with each having a different variation of the rhodopsin photopigment: blue (S) cones, green (M) cones, and red (L) cones
      (1) Perception of a large variety colors results from the combination of signals from different cone types
      (2) Cone pigments are less light sensitive than rhodopsin and need brighter light to break down (Figure 17-30)
   c. Ganglion cells—relay information from rods and cones (by way of bipolar cells) but also relay non-image light information to the body's biological clock; photopigment is melanopsin
3. Neural pathway of vision (Figure 17-31)
   a. Fibers that conduct impulses from the rods and cones reach the visual cortex in the occipital lobes by way of the optic nerves, optic chiasma, optic tracts, and optic radiations
   b. Optic nerve contains fibers from only one retina, but optic chiasma contains fibers from the nasal portion of both retinas; these anatomical facts explain peculiar visual abnormalities that sometimes occur

CYCLE OF LIFE: SENSE ORGANS

A. Sensory information is acquired through depolarization of sensory nerve endings
   1. Age, disease, structural defects, or lack of maturation affects ability to identify and respond
B. Structure and function response capabilities are related to developmental factors associated with age
C. Senses become more acute with maturation
D. Sensory capability loss in old age related to structural change in receptor cells or other sense organ structures

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Define adaptation.
2. Describe each of the following: mechanoreceptors, chemoreceptors, thermoreceptors, nociceptors, photoreceptors.
3. Identify the pathway involved for the production of the sense of smell.
4. What are G-protein–mediated receptor sites?
5. Describe the main features of the middle ear.
6. Name the parts of the bony and membranous labyrinths and describe the relationship of those parts.
7. In what ear structure or structures is the hearing sense organ located? Location of the equilibrium sense organs?
8. What is the name of the hearing sense organ? Of the equilibrium sense organs?
9. Describe the path of sound waves as they enter the ear.
10. Define vertigo. How is vertigo treated?
11. Describe the role of the basilar (spiral) membrane in hearing.
12. What is the difference between static and dynamic equilibrium? Describe the general mechanisms by which each is maintained.
13. Name two involuntary muscles in the eye. Explain their functions.
14. Define the term *refraction*. Name the refractory media of the eye.
15. Explain briefly the mechanism for accommodation for near vision.
16. Name the photopigments present in rods and in cones. Explain their role in vision.
17. Explain why "night blindness" may occur in marked vitamin A deficiency.
18. Describe the phenomenon of referred pain.

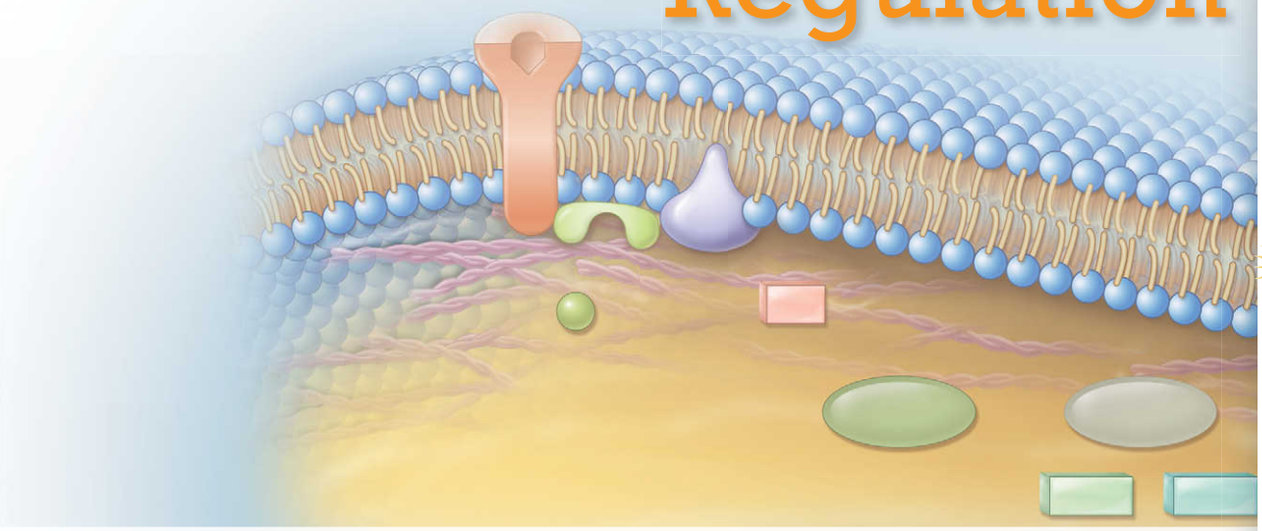
CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. With regard to location, explain the difference between an above-threshold receptor potential and the sensation of that stimulus?
2. Which free nerve ending is able to respond to light touch? Name the free nerve ending that is the most common receptor in the brain.
3. Describe the neural pathways for taste and smell. What would be most likely to stimulate a memory: the taste of apple pie or the smell of apple pie? How can you explain your answer?
4. Identify the three coats of the eye. Include the specific functions of each within your answer.
5. How would you compare and contrast the receptors for vision in dim light and those for vision in bright light?
6. How is sensory response related to age?

18 Endocrine Regulation



CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

Organization of the Endocrine System, 546

Hormones, 547

- Classification of Hormones, 547
  - Steroid Hormones, 548
  - Nonsteroid Hormones, 548
- How Hormones Work, 550
  - General Principles of Hormone Action, 550
  - Mechanism of Steroid Hormone Action, 551
  - Mechanisms of Nonsteroid Hormone Action, 551
  - Regulation of Hormone Secretion, 553
  - Regulation of Target Cell Sensitivity, 555

Prostaglandins, 556

The Big Picture: Endocrine Regulation and the Whole Body, 558

Mechanisms of Disease, 558

LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

amino acid derivative hormone
(ah-MEE-no ASS-id deh-RIV-i-tiv HOR-mohn)
[*amino* **NH$_2$**, *acid* **sour**, *hormon-* **excite**]

anabolic hormone
(an-ah-BOL-ik HOR-mohn)
[*anabol-* **build up**, *-ic* **relating to**, *hormon-* **excite**]

antagonism
(an-TAG-oh-niz-em)
[*ant-* **against**, *-agon-* **struggle**, *-ism* **condition of**]

autocrine hormone
(AW-toh-krin HOR-mohn)
[*auto-* **self**, *-crin-* **secrete** *hormon-* **excite**]

down-regulation

endocrine hormone
(EN-doh-krin HOR-mohn)
[*endo-* **within**, *-crin-* **secrete** *hormon-* **excite**]

G-protein–coupled receptor (GPCR)
(jee-PROH-teen-kup-eld ree-SEP-ter)
[*G* **for guanine nucleotide binding**, *-prote-* **first rank**, *-in* **substance**, *recept-* **receive**, *-or* **agent**]

glycoprotein hormone
(glye-koh-PRO-teen HOR-mohn)
[*glyco-* **sweet (glucose)**, *-prote-* **first rank**, *-in* **substance**, *hormon-* **excite**]

hormone
(HOR-mohn)
[*hormon-* **excite**]

leukotriene
(loo-koh-TRY-een)
[*leuko-* **white**, *-tri-* **three**, *-ene* **chemical**]

mobile-receptor model
(MO-bil-ree-SEP-tor)
[*recept-* **receive**, *-or* **agent**]

continued on p. 559

In the previous chapters we explored important sensory and regulatory mechanisms involving the nervous system. Our study of the regulation of body function continues in this chapter, in which we discuss the regulatory function of the endocrine system. The endocrine system uses signaling molecules called hormones, which are released by glands into the bloodstream and sent throughout the body. These hormones can thus affect any or all tissues of the body. As you learn concepts of hormone function, try to see them as part of an overall system of regulating the body's functions. In the next chapter, we continue the story of endocrine regulation by exploring specific endocrine glands and the hormones they produce.

ORGANIZATION OF THE ENDOCRINE SYSTEM

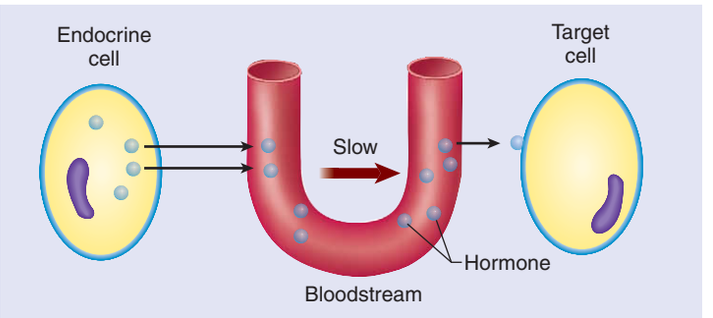
The endocrine system and nervous system both function to achieve and maintain stability of the internal environment. Each system may work alone or in concert with each other as a single **neuroendocrine system,** performing the same general functions within the body: communication, integration, and control.

Both the endocrine system and the nervous system perform their regulatory functions by means of chemical messengers sent to specific cells. In the nervous system, neurons secrete neurotransmitter molecules to signal nearby cells that have the appropriate receptor molecules. In the endocrine system, secreting cells send **hormone** (from the Greek *hormaein*, "to excite") molecules by way of the bloodstream to signal specific **target cells** throughout the body. Tissues and organs that contain endocrine target cells are called *target tissues* and *target organs*, respectively. As with postsynaptic cells, endocrine target cells must have the appropriate receptor to be influenced by the signaling chemical—a process called *signal transduction*. Many cells have receptors for neurotransmitters and hormones, so they can be influenced by both types of chemicals.

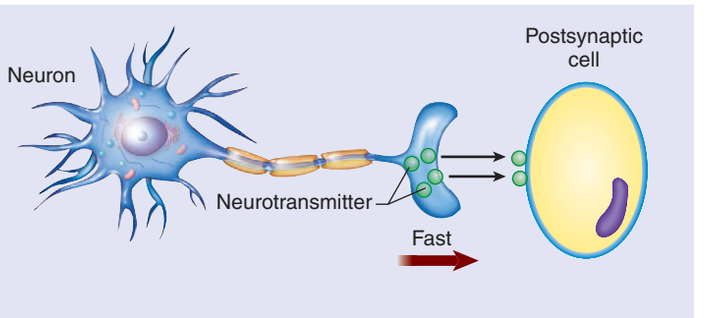
Whereas neurotransmitters are sent over very short distances across a synapse, hormones diffuse into the blood to be carried to nearly every point in the body. The nervous system can directly control only muscles and glands that are innervated with efferent fibers, whereas the endocrine system can regulate most cells in the body. The effects of neurotransmitters are rapid and short lived compared with the effects of hormones, which appear more slowly and last longer. Table 18-1 compares endocrine structure and function with nervous structure and function (Figure 18-1).

TABLE 18-1 Comparison of the Endocrine System and Nervous System

FEATURE	ENDOCRINE SYSTEM	NERVOUS SYSTEM
Overall Function	Regulation of effectors to maintain homeostasis	Regulation of effectors to maintain homeostasis
Control by regulatory feedback loops	Yes (endocrine reflexes)	Yes (nervous reflexes)
Effector tissues	Endocrine effectors: virtually all tissues	Nervous effectors: muscle and glandular tissue only
Effector cells	Target cells (throughout the body)	Postsynaptic cells (in muscle and glandular tissue only)
Chemical Messenger	Hormone	Neurotransmitter
Cells that secrete the chemical messenger	Glandular epithelial cells or neurosecretory cells (modified neurons)	Neurons
Distance traveled (and method of travel) by chemical messenger	Long (by way of circulating blood)	Short (across a microscopic synapse)
Location of receptor in effector cell	On the plasma membrane or within the cell	On the plasma membrane
Characteristics of regulatory effects	Slow to appear, long lasting	Appear rapidly, short lived



A



B

FIGURE 18-1
Mechanisms of endocrine (A) and nervous (B) signals.

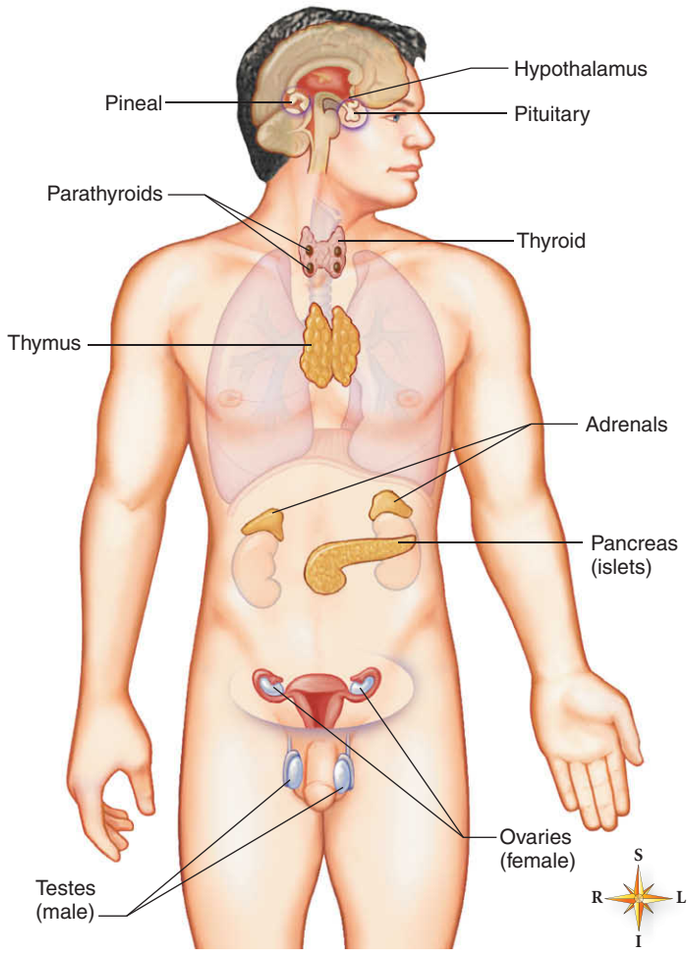


FIGURE 18-2
Locations of some major endocrine glands.

TABLE 18-2 Some of the Major Endocrine Glands

NAME	LOCATION
Hypothalamus	Cranial cavity (brain)
Pituitary gland	Cranial cavity
Pineal gland	Cranial cavity (brain)
Thyroid gland	Neck
Parathyroid glands	Neck
Thymus	Mediastinum
Adrenal glands	Abdominal cavity (retroperitoneal)
Pancreatic islets	Abdominal cavity (pancreas)
Ovaries	Pelvic cavity
Testes	Scrotum
Placenta	Pregnant uterus

Endocrine glands secrete their products, hormones, directly into the blood. Because they do not have ducts, they are often called "ductless glands." This characteristic distinguishes *endocrine glands* from *exocrine glands*, which secrete their products into ducts (see Chapter 6, p. 141). Many endocrine glands are made of glandular epithelium, whose cells manufacture and secrete hormones. However, a few endocrine glands are made of **neurosecretory tissue.** Neurosecretory cells are simply modified neurons that secrete chemical messengers that diffuse into the bloodstream rather than across a synapse. In such cases, the chemical messenger is called a *hormone* rather than a *neurotransmitter.* For example, when norepinephrine is released by neurons, diffuses across a synapse, and binds to an adrenergic receptor in a postsynaptic neuron, we call norepinephrine a *neurotransmitter.* On the other hand, we call norepinephrine a *hormone* when it diffuses into the blood (because no postsynaptic cell is present) and then binds to an adrenergic receptor in a distant target cell.

Glands of the endocrine system are widely scattered throughout the body. New discoveries in *endocrinology* continue to add to the long list of hormone-secreting tissues. However, even the most newly discovered endocrine tissues and their hormones operate according to some basic physiological principles.

In this chapter, we focus our discussion primarily on a few major endocrine glands and their principal hormones. Figure 18-2 and Table 18-2 summarize the names and locations of these representative endocrine glands. After you are familiar with the basic principles of endocrinology and the major examples of glands and their hormones, you will be prepared for additional examples that you will encounter as you continue your study of the human body.

| QUICK CHECK |

1. What is meant by the term *target cell?*
2. Describe how the nervous system and the endocrine system differ in the way they control effectors.

HORMONES

Classification of Hormones

Hormone molecules can be classified in various useful ways. For example, when classified by general function, hormones can be identified as **tropic hormones** (hormones that target other endocrine glands and stimulate their growth and secretion), **sex hormones** (hormones that target reproductive tissues), **anabolic hormones** (hormones that stimulate anabolism in their target cells), and many other functional names. Another useful way to classify hormones is by their chemical structure. Because this method of classifying hormones is so widely used, we will briefly describe it in the following paragraphs.

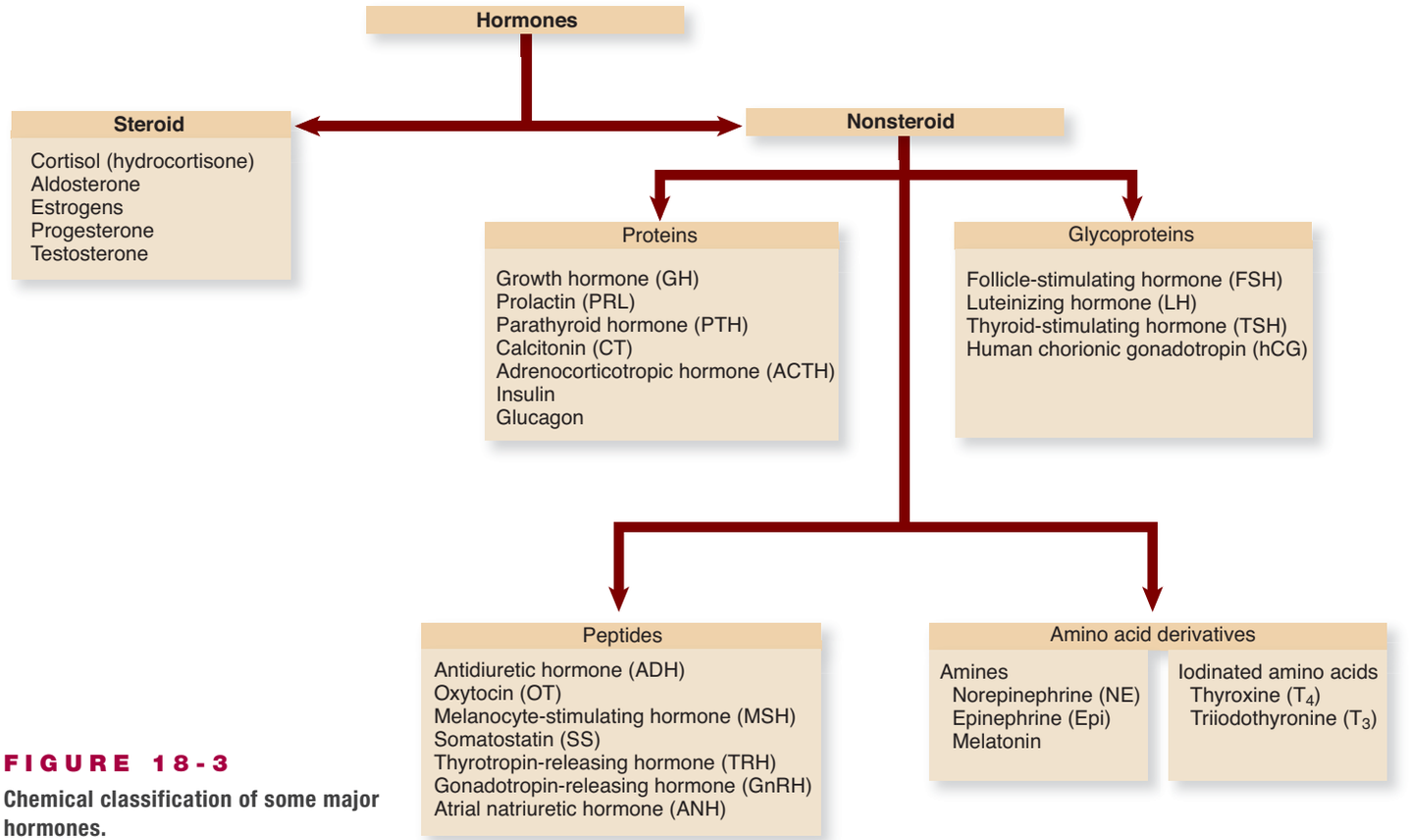


FIGURE 18-3

Chemical classification of some major hormones.

STEROID HORMONES

All of the many hormones secreted by endocrine tissues can be classified simply as **steroid** or **nonsteroid** (Figure 18-3). Steroid hormone molecules are manufactured by endocrine cells from cholesterol, an important type of lipid in the human body (see Chapter 2, p. 50). As Figure 18-4 shows, because all steroid hormones are derived from a common molecule, cholesterol, they have a characteristic chemical group at the core of each molecule. Because steroids are lipid soluble, they can easily pass through the phospholipid plasma membrane of target cells. Figure 18-5 outlines the metabolic pathways used by endocrine cells to convert cholesterol into steroid hormones. Examples of important steroid hormones include cortisol, aldosterone, estrogen, progesterone, and testosterone.

NONSTEROID HORMONES

Most nonsteroid hormones are synthesized primarily from amino acids rather than from cholesterol (Figure 18-6). Some nonsteroid hormones are **protein hormones.** These hormones are long,

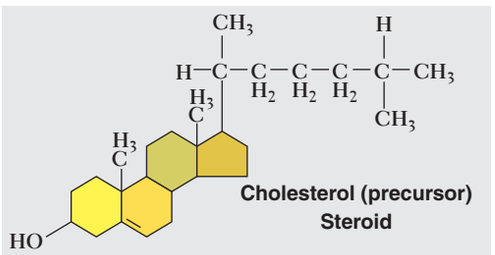
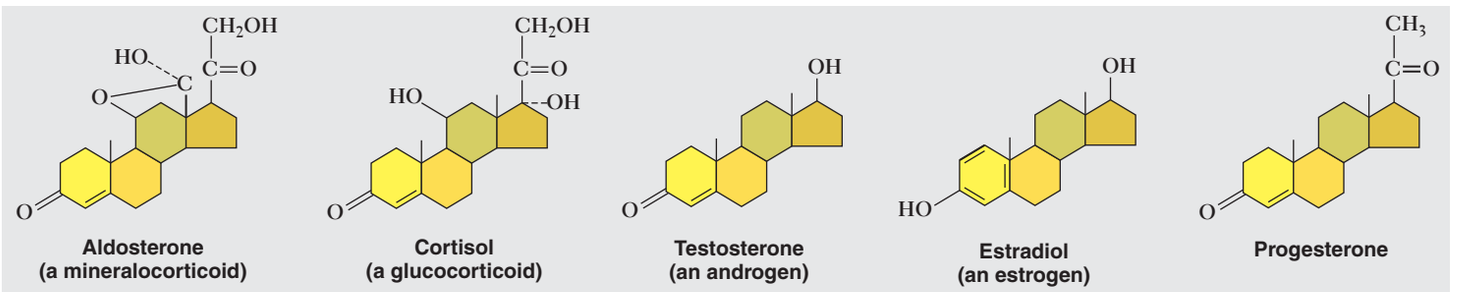


FIGURE 18-4

Steroid hormone structure. As these examples show, steroid hormone molecules are very similar in structure to cholesterol *(top left),* particularly in having a four-ring steroid nucleus at their core. Cholesterol is the precursor molecule from which the steroid hormones are all derived.



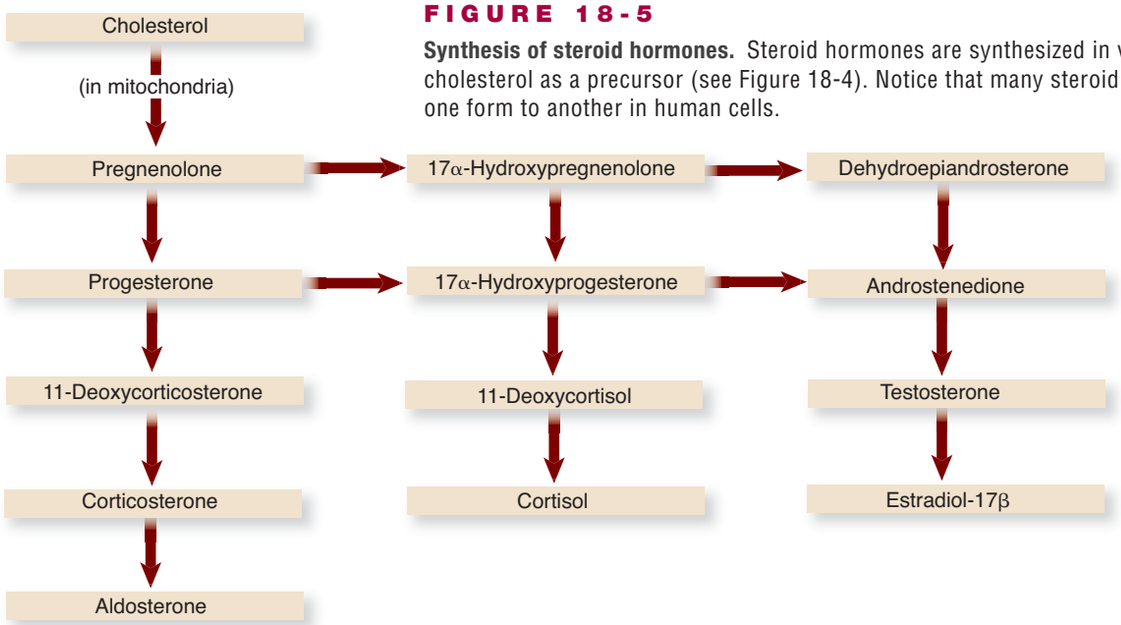


FIGURE 18-5

Synthesis of steroid hormones. Steroid hormones are synthesized in various endocrine tissues using cholesterol as a precursor (see Figure 18-4). Notice that many steroid hormones are converted from one form to another in human cells.

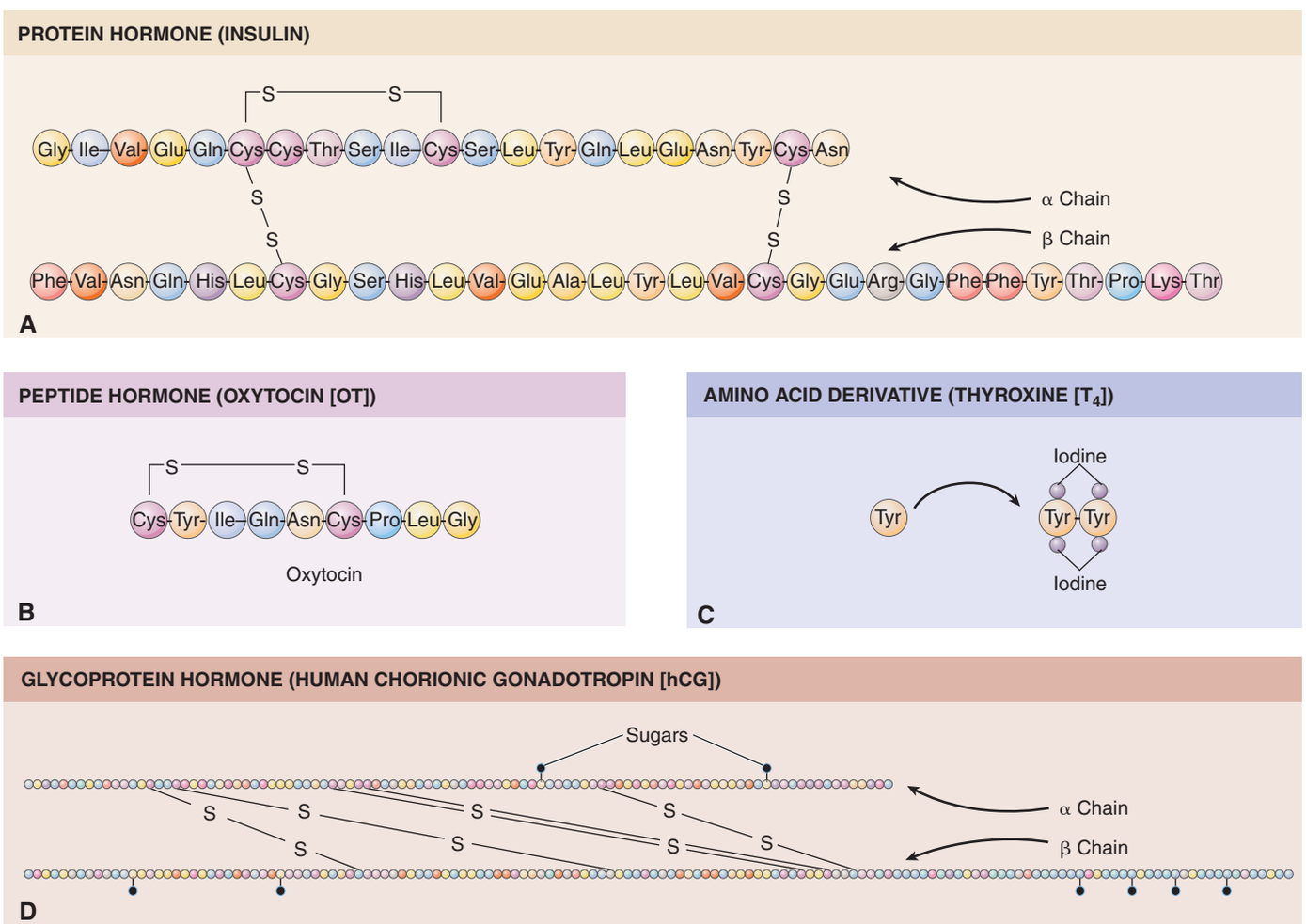


FIGURE 18-6

Nonsteroid hormone structure. **A,** Protein hormone molecules are made of long, folded strands of amino acids. **B,** Peptide hormone molecules are smaller strands of amino acids. **C,** Amino acid derivatives are, as their name implies, derived from a single amino acid. **D,** Glycoprotein hormones are long, folded strands of amino acids with attached sugar groups.

folded chains of amino acids, a structure typical of protein molecules of any sort (see Chapter 2, p. 52). Included among the protein hormones are insulin, parathyroid hormone, and others listed in Figure 18-3. Protein hormones that have carbohydrate groups attached to their amino acid chains are often classified separately as **glycoprotein hormones** (Figure 18-6, *D*).

Another major category of nonsteroid hormones consists of the peptide hormones. **Peptide hormones** such as oxytocin and antidiuretic hormone are smaller than the protein hormones. They are each made of a short chain of amino acids, as Figure 18-6, *B*, shows. Figure 18-3 lists examples of peptide hormones.

Yet another category of nonsteroid hormones consists of the **amino acid derivative hormones.** Each of these hormones is derived from only a single amino acid molecule. There are two major subgroups within this category. One subgroup, the *amine hormones*, is synthesized by modifying a single molecule of an amino acid—either tyrosine or tryptophan. Amine hormones such as epinephrine and norepinephrine are produced by neurosecretory cells (secreted as hormones) and by neurons (secreted as neurotransmitters). Another subgroup of amino acid derivatives produced by the thyroid gland are all synthesized by adding iodine (I) atoms to a tyrosine molecule (Figure 18-6, *C*). Figure 18-3 lists examples of hormones derived from single amino acids.

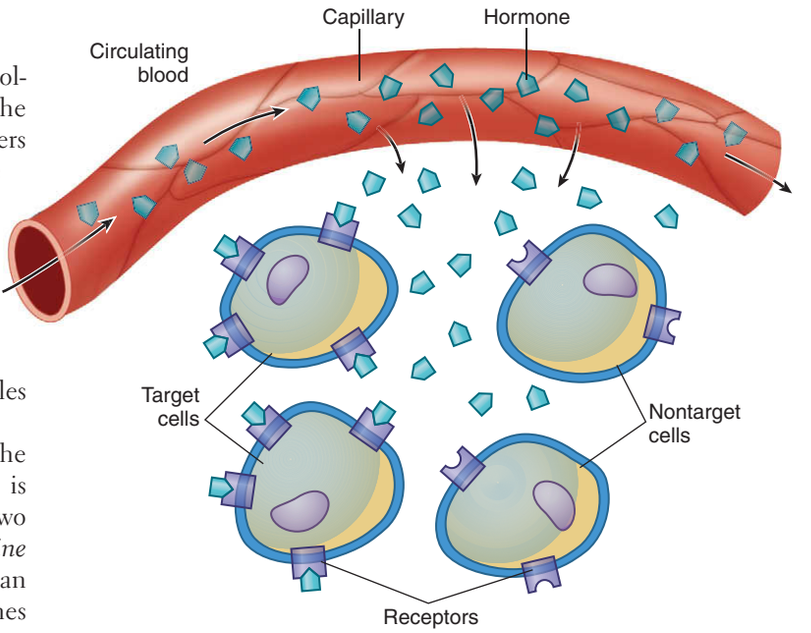


FIGURE 18-7

The target cell concept. A hormone acts only on cells that have receptors specific to that hormone because the shape of the receptor determines which hormone can react with it. This is an example of the lock-and-key model of biochemical reactions.

| QUICK CHECK |

3. How are steroid hormones able to pass through a cell's plasma membrane easily?
4. Name some of the different general types of nonsteroid hormones. Give an example of each.

How Hormones Work

GENERAL PRINCIPLES OF HORMONE ACTION

As previously stated, hormones signal a cell by binding to specific receptors on or in the cell. In a "lock-and-key" mechanism, hormones will bind only to receptor molecules that "fit" them exactly. Any cell with one or more receptors for a particular hormone is said to be a *target* of that hormone (Figure 18-7). Cells usually have many different types of receptors; therefore they are *target cells* of many different hormones.

In a complex process called *signal transduction*, each different hormone-receptor interaction produces different regulatory changes within the target cell. These cellular changes are usually accomplished by altering the chemical reactions within the target cell. For example, some hormone-receptor interactions initiate synthesis of new proteins. Other hormone-receptor interactions trigger the activation or inactivation of certain enzymes and thus affect the metabolic reactions regulated by those enzymes. Still other hormone-receptor interactions regulate cells by opening or closing specific ion channels in the plasma membrane. Specific mechanisms of signal transduction and endocrine effects in target cells are outlined in the next section.

Different hormones may work together to enhance each other's influence on a target cell. In a phenomenon called **synergism,** combinations of hormones have a greater effect on a target cell than the sum of the effects that each would have if acting alone. Combined hormone actions may exhibit instead the phenomenon of **permissiveness.** Permissiveness occurs when a small amount of one hormone allows a second hormone to have its full effect on a target cell; the first hormone "permits" the full action of the second hormone. A common type of combined action of hormones is seen in the phenomenon of **antagonism.** In antagonism, one hormone produces the opposite effect of another hormone. Antagonism between hormones can be used to "fine tune" the activity of target cells with great accuracy, signaling the cell exactly when (and by how much) to increase or decrease a certain cellular process.

Although our discussion is focused on the primary actions of only a few selected hormones, ongoing studies make it clear that hormones usually have many diverse secondary functions in the body. For example, prolactin (PRL) is a hormone with primary actions that regulate milk production (lactation) and reproduction, but it also has about 300 secondary actions in the body. Most secondary effects of hormones modulate, or influence, the activity of other regulatory mechanisms. The primary effect of a hormone, on the other hand, is a more direct regulatory mechanism.

As previously stated, hormones travel to their target cells by way of the circulating bloodstream. This means that all hormones travel throughout the body. Because they affect only their target cells, however, the effects of a particular hormone may be limited to specific tissues in the body. Some hormone molecules are attached to plasma proteins while they are carried along in the bloodstream. Such hormones must free themselves from the plasma protein to leave the blood and combine with their receptors. Because blood carries hormones nearly everywhere in the body, even where there are no target cells, not all hormone molecules produced by endocrine glands actually hit their target. Unused hormones usually are quickly excreted by the kidneys or broken down by metabolic processes.

MECHANISM OF STEROID HORMONE ACTION

Steroid hormones are lipids and thus are not very soluble in blood plasma, which is mostly water. Instead of traveling in the plasma as free molecules, they attach to soluble plasma proteins. As you can see in Figure 18-8, a steroid hormone molecule dissociates from its carrier before approaching the target cell. Because steroid hormones are lipid soluble and thus can pass into cells easily, it is not surprising that many of their receptors are found inside the cell rather than on the surface of the plasma membrane. After a steroid hormone molecule has diffused into its target cell, it passes into the nucleus, where it binds to a mobile-receptor molecule to form a *hormone-receptor complex*. Some hormones must be activated by enzymes before they can bind to their receptors. Because steroid hormone receptors are not attached to the plasma membrane, but seem to move freely in the nucleoplasm, this model of hormone action has been called the **mobile-receptor model,** or the *nuclear-receptor model*.

Once formed, the hormone-receptor complex activates a certain gene sequence to begin transcription of messenger RNA (mRNA) molecules. The newly formed mRNA molecules then move out of the nucleus into the cytosol, where they associate with ribosomes and begin synthesizing protein molecules.

The new protein molecules synthesized by the target cell would not have been made if not for the arrival of the steroid hormone molecule. Steroid hormones regulate cells by regulating their production of certain critical proteins, such as enzymes that control intracellular reactions or integral membrane proteins that alter the permeability of a cell.

This mechanism of steroid hormone action implies several things about the effects of these hormones. For one thing, the more hormone-receptor complexes formed, the more mRNA molecules are transcribed, the more new protein molecules are formed, and thus the greater the magnitude of the regulatory effect. In short, the *amount* of steroid hormone present determines the magnitude of a target cell's response. Also, because transcription and protein synthesis take some time, responses to steroid hormones can be slow—from 45 minutes to several days before the full effect is seen.

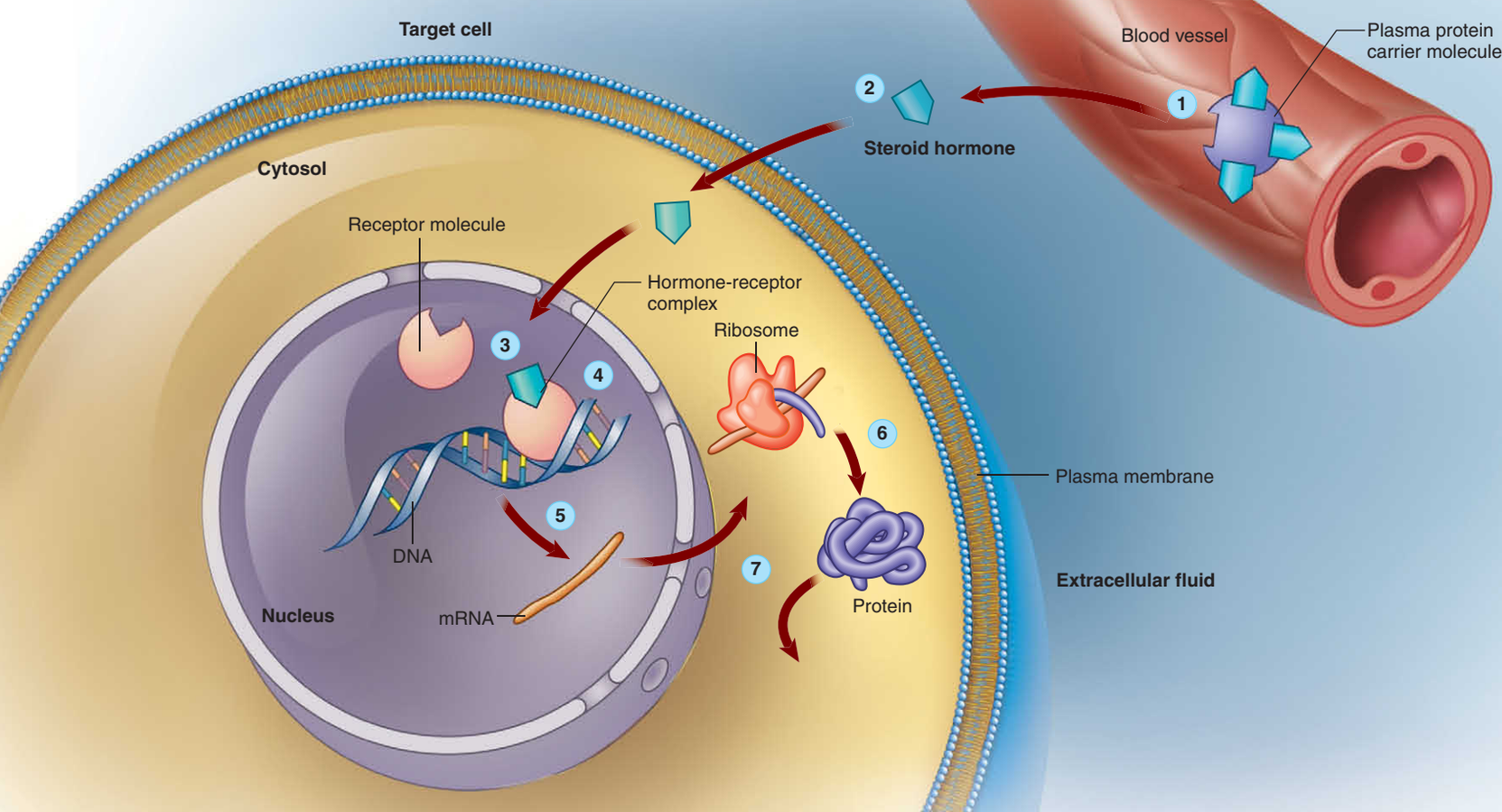
MECHANISMS OF NONSTEROID HORMONE ACTION

The Second Messenger Mechanism

Nonsteroid hormones typically operate according to a mechanism originally called the **second messenger model.** This concept of hormone action—first proposed in the last century by Dr. Earl W. Sutherland—was a milestone in endocrinology for which he received the 1971 Nobel Prize in Medicine or Physiology. According

FIGURE 18-8

Steroid hormone mechanism. According to the mobile-receptor model, lipid-soluble steroid hormone molecules detach from a carrier protein **(1)** and pass through the plasma membrane **(2)**. The hormone molecules then pass into the nucleus where they bind with a mobile receptor to form a hormone-receptor complex **(3)**. This complex then binds to a specific site on a DNA molecule **(4)**, triggering transcription of the genetic information encoded there **(5)**. The resulting mRNA molecule moves to the cytosol, where it associates with a ribosome, initiating synthesis of a new protein **(6)**. This new protein—usually an enzyme or channel protein—produces specific effects in the target cell **(7)**. Some steroid hormones also have additional secondary effects such as influencing signal transduction pathways at the plasma membrane.



to this concept of signal transduction, a nonsteroid hormone molecule acts as a "first messenger," delivering its chemical message to fixed receptors in the target cell's plasma membrane. The "message" is then passed into the cell where a "second messenger" triggers the appropriate cellular changes. This concept of nonsteroid hormone action is also called the *fixed-membrane-receptor model.*

In the example illustrated in Figure 18-9, a nonsteroid hormone can trigger a **G-protein–coupled receptor (GPCR)** embedded in the membrane of a target cell. The activated GPCR causes an integral membrane protein, called the G *protein*, to bind to a nucleotide called *guanosine triphosphate (GTP)*. This in turn activates another membrane protein, *adenyl cyclase*. Adenyl cyclase is an enzyme that promotes the removal of two phosphate groups from adenosine triphosphate (ATP) molecules in the cytosol. The product thus formed is cyclic adenosine monophosphate *(cAMP)*. The cAMP molecule acts as a second messenger within the cell. cAMP activates *protein kinases*, a set of enzymes that activate other types of enzymes. It is this final set of specific enzymes, which are now activated, that catalyze the cellular reactions that characterize the target cell's response. In short, the hormone first messenger binds to a membrane receptor, triggering formation of an intracellular second messenger, which activates a cascade of chemical reactions that produces the target cell's response.

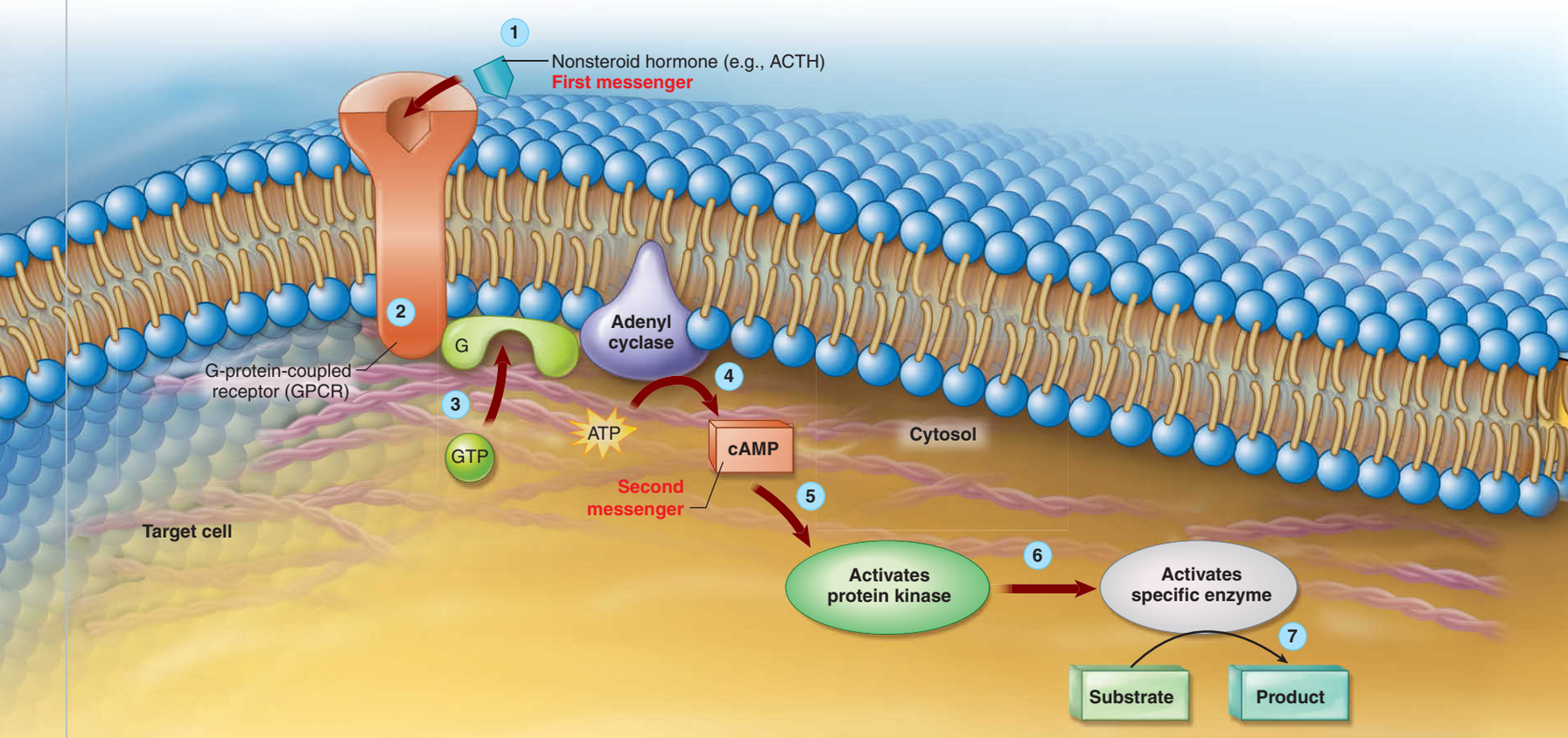
Since the time Sutherland first began his pioneering work, other second messenger systems for signal transduction have been discovered. As a matter of fact, the study of second messenger mechanisms is currently a central area of physiology research. Although many nonsteroid hormones seem to use cAMP as the second messenger, we now know that some hormones use nucleotides such as inositol triphosphate (IP_3) and cyclic guanosine monophosphate (cGMP) as the second messenger.

Still other hormones produce their effects by triggering the opening of calcium (Ca^{++}) channels in the target cell's membranes, as you can see in Figure 18-10. Binding of a hormone to a fixed membrane receptor (GPCR) activates a chain of integral membrane proteins (G protein and phosphatidylinositol 4,5-biphosphate, PIP_2) that in turn trigger the opening of calcium channels in the plasma membrane. Ca^{++} ions that enter the cytosol when the channels open bind to an intracellular molecule called *calmodulin*. The Ca^{++}-calmodulin complex thus formed acts as a second messenger, influencing the enzymes that produce the target cell's response.

Research findings also show that in second messenger systems, the hormone-receptor complexes may be taken into the cell by means of endocytosis. Although the purpose of this may be primarily to break down the complexes and recycle the receptors, the

FIGURE 18-9

Example of a second messenger mechanism. A nonsteroid hormone (first messenger) binds to a fixed G-protein–coupled receptor (GPCR) in the plasma membrane of the target cell **(1)**. The hormone-receptor complex activates the G protein **(2)**. The activated G protein reacts with GTP, which in turn activates the membrane-bound enzyme adenyl cyclase **(3)**. Adenyl cyclase removes phosphates from ATP, converting it to cAMP (second messenger) **(4)**. cAMP activates or inactivates protein kinases **(5)**. Protein kinases activate specific intracellular enzymes **(6)**. These activated enzymes then influence specific cellular reactions, thus producing the target cell's response to the hormone **(7)**. *GTP,* Guanosine triphosphate; *ATP,* adenosine triphosphate; *cAMP,* cyclic adenosine monophosphate.



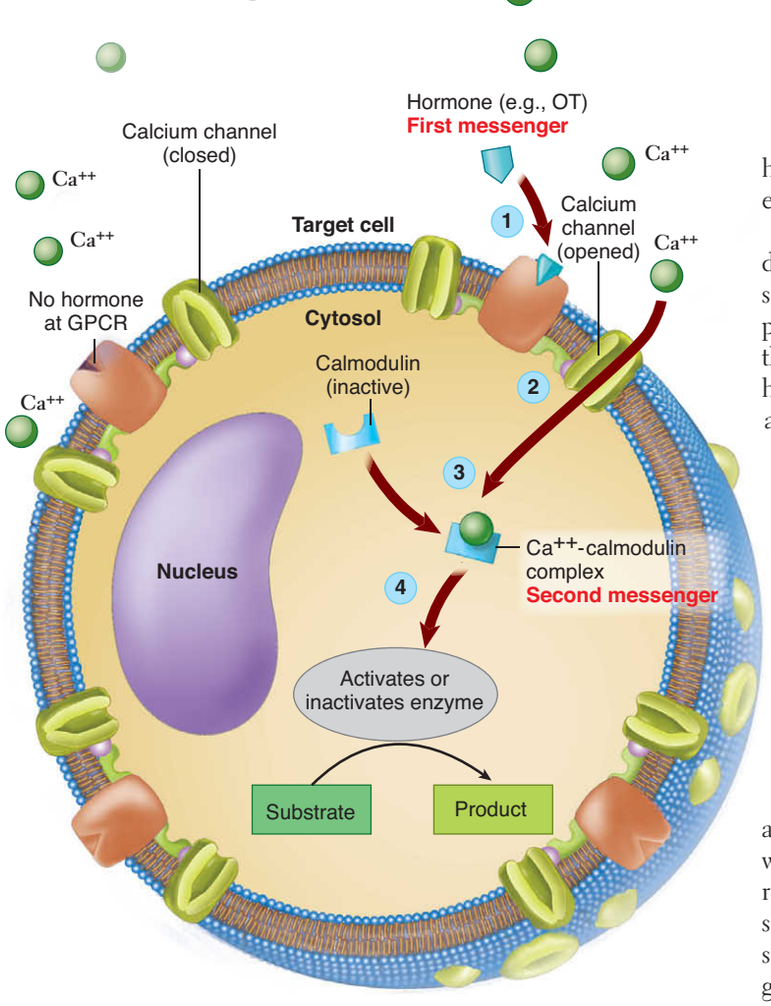


FIGURE 18-10

Calcium-calmodulin as a second messenger. In this example of a second messenger mechanism, a nonsteroid hormone (first messenger) first binds to a fixed receptor (G-protein–coupled receptor, GPCR) in the plasma membrane **(1)**, which activates membrane-bound proteins (G protein and PIP_2) that trigger the opening of calcium channels **(2)**. Calcium ions, which are normally at a higher concentration in the extracellular fluid, diffuse into the cell and bind to a calmodulin molecule **(3)**. The Ca^{++}-calmodulin complex thus formed is a second messenger that binds to an enzyme to produce an allosteric effect that promotes or inhibits the enzyme's regulatory effect in the target cell **(4)**. *PIP_2*, Phosphatidylinositol 4,5-biphosphate.

hormone-receptor complex may continue to have physiological effects after it is taken into the cell.

The second messenger mechanism of signal transduction produces target cell effects that differ from steroid hormone effects in several important ways (Table 18-3). First, the cascade of reactions produced in the second messenger mechanism greatly amplifies the effects of the hormone. Thus the effects of many nonsteroid hormones are disproportionately great when compared with the amount of hormone present. Recall that steroid hormones produce effects in proportion to the amount of hormone present. Also, the second messenger mechanism operates much more quickly than the steroid mechanism. Many nonsteroid hormones produce their full effects within seconds or minutes of initial binding to the target cell receptors—not the hours or days sometimes seen with steroid hormones.

The Nuclear-Receptor Mechanism

Not all nonsteroid hormones operate according to the second messenger model. The notable exception is the pair of thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3). These small iodinated amino acids apparently enter their target cells and bind to receptors already associated with a DNA molecule within the nucleus of the target cell. Formation of a hormone-receptor complex triggers transcription of mRNA and the synthesis of new enzymes in a signal transduction system similar to the steroid mechanism. More information on thyroid hormones is given later in this chapter.

Regulation of Hormone Secretion

The control of hormonal secretion is usually part of a negative feedback loop. Recall from Chapter 1 (see Figure 1-13, p. 22) that negative feedback loops tend to reverse any deviation of the internal environment away from its stable point (the set point value). Rarely, a positive feedback loop controls the secretion of a hormone. Recall that in positive feedback control, deviation from the stable point is exaggerated rather than reversed. Responses that result from the operation of feedback loops within the endocrine system are called *endocrine reflexes*, just as responses to nervous feedback loops (reflex arcs) are called *nervous reflexes*.

TABLE 18-3 Comparison of Steroid and Nonsteroid Hormones

CHARACTERISTIC	STEROID HORMONES*	NONSTEROID HORMONES†
Chemical structure	Lipid	One or more amino acids, sometimes with added sugar groups
Stored in secretory cell	No	Yes; stored in secretory vesicles before release
Interaction with plasma membrane	No; simple diffusion through plasma membrane and into target cell	Yes; binds to specific plasma membrane receptor
Receptor	Mobile receptor in cytoplasm or nucleus	Embedded in plasma membrane
Action	Regulates gene activity (transcription of new proteins that eventually produce effects in the cell)	Triggers signal transduction cascade, producing internal "second messengers" that trigger rapid effects in the target cell
Response time	One hour to several days	Several seconds to a few minutes

*See Box 18-1 on p. 554 for additional emerging concepts of steroid hormone characteristics.
†Some nonsteroid hormones derived from amino acids (e.g., thyroid hormones T_3 and T_4) have gene-activating actions similar to steroid hormones.

Box 18-1 | Rapid Responses to Steroid Hormones

The conventional view of steroid hormone regulation of gene activity states that one or more hours pass before the effects of the hormone reach their peak. Steroid hormones, however, can also produce some rapid effects in target cells—in just seconds or minutes. How is this possible? We now know that additional steroid hormone receptors at the plasma membrane enable many steroid hormones to regulate signal transduction in target cells. That is, steroid hormones have a secondary effect that can change the messages sent by other regulatory molecules, such as other hormones or neurotransmitters.

The emerging view therefore is that steroid hormones produce both slow and rapid effects in target cells. Slow effects result from stimulating the transcription of specific genes in the target cell's nucleus—thus producing new proteins. Rapid effects result from altering signal transduction mechanisms in the plasma membrane of the target cell.

For a moment, let us focus our attention on the specific mechanisms that regulate the release of hormones from endocrine cells (Box 18-1). The simplest mechanism operates when an endocrine cell is sensitive to the physiological changes produced by its target cells (Figure 18-11). For example, parathyroid hormone (PTH) produces responses in its target cells that increase Ca^{++} concentration in the blood. When blood Ca^{++} concentration exceeds the set point value, parathyroid cells sense it and reflexively reduce their output of PTH. Secretion by many endocrine glands is regulated by a hormone produced by another gland. For example, the pituitary gland (specifically, the anterior portion) produces thyroid-stimulating hormone (TSH), which stimulates the thyroid gland to release its hormones. The anterior pituitary responds to changes in the controlled physiological variable and to changes in the blood concentration of hormones secreted by its target gland. Secretion by the anterior pituitary can in turn be regulated by *releasing hormones* or *inhibiting hormones* secreted by the hypothalamus. Hypothalamic secretion is responsive to changes in the controlled variable, as well as changes in the blood concentration of anterior pituitary and target gland hormones. Although the target gland may be able to adjust its own output, the additional controls exerted by long feedback loops involving the anterior pituitary and hypothalamus allow more precise regulation of hormone secretion—and thus more precise regulation of the internal environment.

Another mechanism that may influence the secretion of hormones by a gland is input from the nervous system. For example, secretion by the posterior pituitary is not regulated by releasing hormones but by direct nervous input from the hypothalamus. Likewise, sympathetic nerve impulses that reach the medulla of the adrenal glands trigger the secretion of epinephrine and norepinephrine. Many other glands, including the pancreas, are also influenced to some degree by nervous input. That the nervous system operates with hormonal mechanisms to produce endocrine

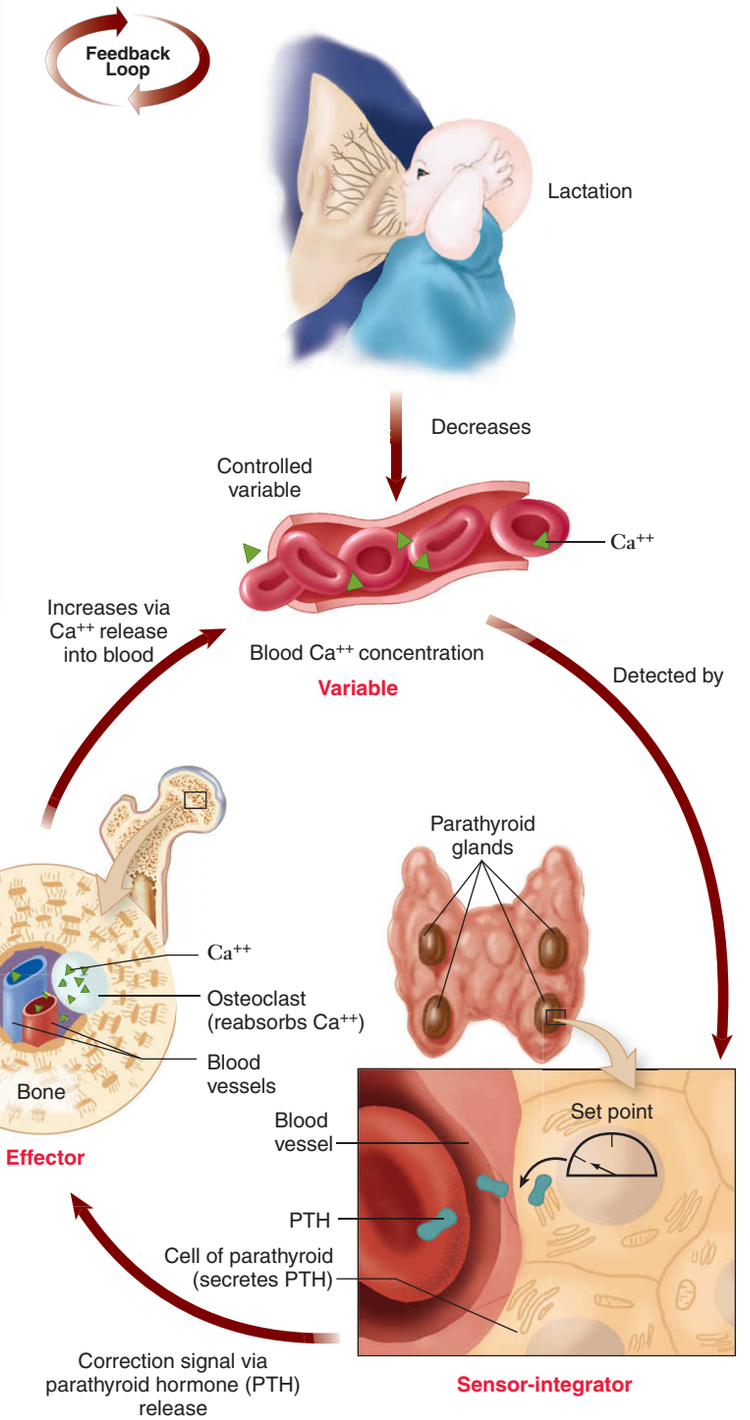


FIGURE 18-11

Endocrine feedback loop. In this example of a short feedback loop, each parathyroid gland is sensitive to changes in the physiological variable its hormone (parathyroid hormone [PTH]) controls—blood calcium (Ca^{++}) concentration. When lactation (milk production) in a breastfeeding woman consumes Ca^{++} and thus lowers blood Ca^{++} concentration, the parathyroids sense the change and respond by increasing their secretion of PTH. PTH stimulates osteoclasts in bone to release more Ca^{++} from storage in bone tissue (among other effects), which increases maternal blood Ca^{++} concentration to the set point level.

reflexes emphasizes the close functional relationship between these two systems.

Although the operation of long feedback loops tends to minimize wide fluctuations in secretion rates, the output of several hormones typically rises and falls dramatically within a short period. For example, the concentration of insulin—a hormone that can correct a rise in blood glucose concentration—increases to a high level just after a meal high in carbohydrates. The level of insulin decreases only after the blood glucose concentration returns to its set point value. Likewise, threatening stimuli can cause a sudden, dramatic increase in the secretion of epinephrine from the adrenal medulla as part of the fight-or-flight response.

Specific examples of feedback control of hormone secretion are given later in this chapter.

Regulation of Target Cell Sensitivity

The sensitivity of a target cell to any particular hormone partly depends on how many receptors for that hormone it has. The more receptors there are, the more sensitive is the target cell. Hormone receptors, as with other cell components, are constantly broken down by the cell and replaced with newly synthesized receptors. This mechanism not only ensures that all cell parts are "new" and working properly, but also provides a method by which the number of receptors can be changed from time to time.

If synthesis of new receptors occurs faster than degradation of old receptors, the target cell will have more receptors and thus be more sensitive to the hormone. This phenomenon, illustrated in Figure 18-12, *A*, is often called **up-regulation** because the number of receptors goes up. If, on the other hand, the rate of receptor degradation exceeds the rate of receptor synthesis, the target cell's number of receptors will decrease (Figure 18-12, *B*). Because the number of receptors, and thus the sensitivity of the target cell, go down, this phenomenon is often called **down-regulation.**

Of course, regulation of signal transduction mechanisms and gene transcription triggered by various hormones can also play a role in adjusting the sensitivity of target cells to a particular hormone at a particular time. For example, one hormone may affect the signal transduction of another hormone, thus inhibiting or enhancing the second hormone's effects (Box 18-2).

Endocrinologists are just now learning the mechanisms that control the process of receptor turnover and signal transduction in the cell and how this affects the functions of the target cell. Information uncovered so far has already led to a better understanding of important and widespread endocrine disorders such as diabetes mellitus.

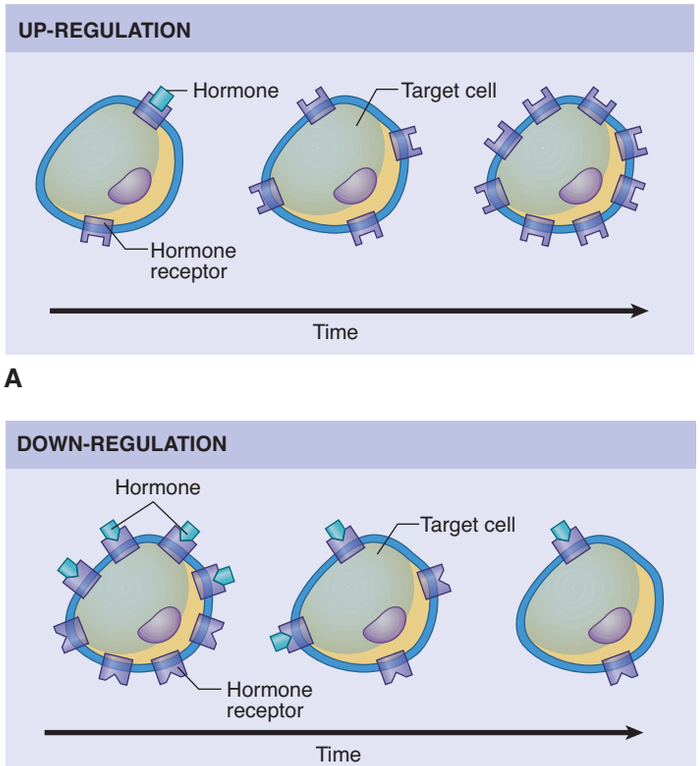


FIGURE 18-12

Regulation of target cell sensitivity. A, Up-regulation. **B,** Down-regulation.

| QUICK CHECK |

5. Name some ways in which hormones can work together to regulate a tissue.
6. Why is the concept of steroid hormone action called the *mobile-receptor model*?
7. Why is the concept of nonsteroid hormone action often called the *second messenger model*? Why is it known as the *fixed-membrane-receptor model*?
8. Name some ways that the secretion of an endocrine cell can be controlled.

Box 18-2 | HEALTH matters

"Too Much or Too Little"

Diseases of the endocrine system are numerous, varied, and sometimes spectacular. Tumors or other abnormalities frequently cause the glands to secrete too much or too little of their hormones. Production of too much hormone by a diseased gland is called **hypersecretion.** If too little hormone is produced, the condition is called **hyposecretion.**

Various endocrine disorders that appear to result from hyposecretion are actually caused by a problem in the target cells. If the usual target cells of a particular hormone have damaged receptors, too few receptors, or some other abnormality, they will not respond to that hormone properly. In other words, lack of target cell response could be a sign of hyposecretion or a sign of target cell insensitivity. *Diabetes mellitus (DM),* for example, can result from insulin hyposecretion or from the target cells' insensitivity to insulin.

Polyendocrine disorders are caused by hypersecretion and/or hyposecretion of more than one hormone. Often, an imbalance of one hormone will lead to an imbalance of other hormones as well.

TABLE 18-4 Prostaglandins and Related Hormones

HORMONE	SOURCE	TARGET	PRINCIPAL ACTION
Prostaglandins (PGs)	Many diverse tissues of the body	Local cells within the source tissue	Diverse local (paracrine/autocrine) effects such as regulation of inflammation, muscle contraction in blood vessels
Thromboxanes (TXs)	Platelets	Other platelets; muscles in blood vessel walls	Increase stickiness of platelets; promote blood clotting; cause constriction of blood vessels
Leukotrienes	Several types of white blood cells (leukocytes)	Local cells of various types	Produce local inflammation triggered by allergens, including constriction of airways (as in asthma) and other inflammatory responses

PROSTAGLANDINS

Before continuing our discussion of endocrine glands and hormones, let us pause a moment to consider the **prostaglandins (PGs)** and related compounds (Table 18-4). The prostaglandins are a unique group of lipid molecules that serve important and widespread integrative functions in the body but do not meet the usual definition of a hormone (Box 18-3).

Prostaglandins are 20-carbon unsaturated fatty acids and contain a 5-carbon ring (Figure 18-13). Prostaglandins are made by cells throughout the body by breaking apart membrane

Box 18-3 | Local Hormones

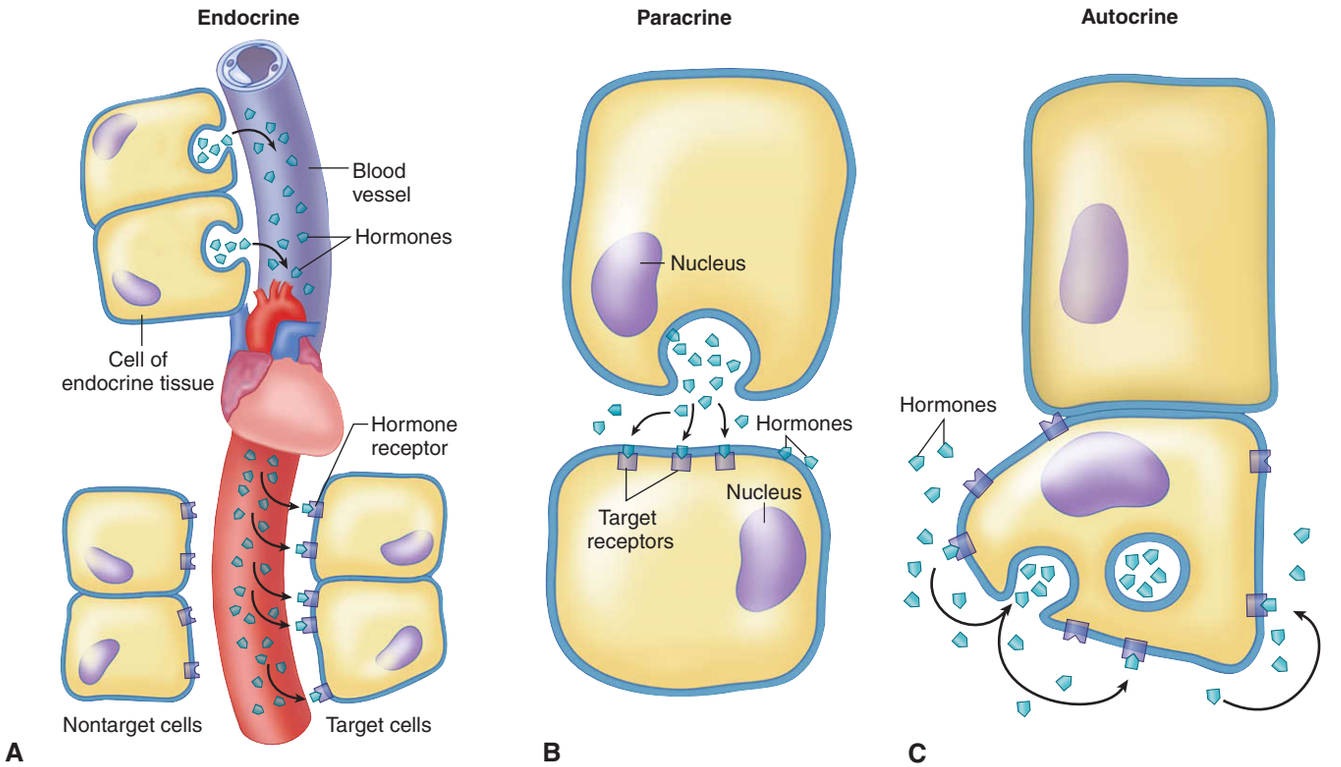
The classical view of hormones is that they are secreted from a tissue into the bloodstream and have their effects in target cells at some distance from their source. This is the standard definition of an **endocrine hormone** (part *A* of figure). That is, hormones have "global" effects in the body.

However, some hormones and related agents have primarily local effects—that is, effects *within* the source tissue. To distinguish classical endocrine hormones from local regulators such as prostaglandins and related compounds, scientists often use more precise terms for "local" hormones. Here are examples of terms used to designate local regulators:

Paracrine hormones—hormones that regulate activity in nearby cells within the same tissue as their source (part *B* of figure)

Autocrine hormones—hormones that regulate activity in the secreting cell itself (part *C* of figure)

To avoid confusion, scientists most often refer only to endocrine hormones simply as "hormones." For local regulators, scientists use general terms such as "tissue hormone" or "local regulator"—or more specific terms such as "paracrine" or "autocrine" factor.



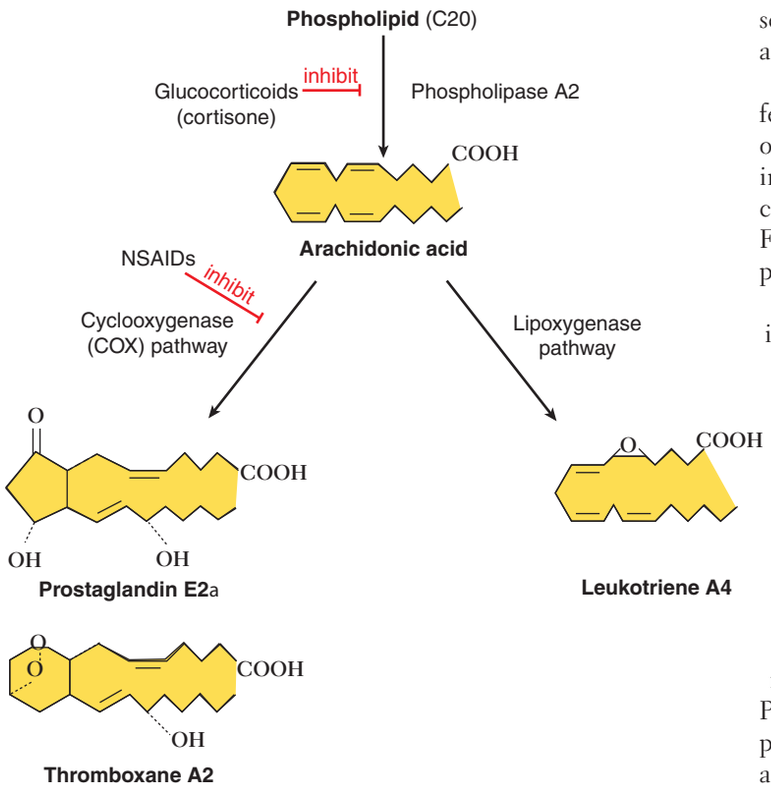


FIGURE 18-13

Formation of prostaglandin and related molecules. Membrane phospholipids containing the 20-carbon fatty acid arachidonic acid are enzymatically broken apart (C20, 20-carbon). Therapeutic use of glucocorticoids such as cortisone can inhibit this pathway, thus reducing the amount (and effects) of any of the resulting regulator molecules. Arachidonic acid is then converted by the COX pathway to either prostaglandins or thromboxanes (*left*). This step can be therapeutically inhibited by NSAIDs (nonsteroidal antiinflammatory drugs). Arachidonic acid may alternatively be converted by the lipoxygenase pathway to a leukotriene. See also Figure 2-24 on p. 51. *COX,* Cyclooxygenase.

phospholipids and using their fatty acid "tails" (specifically, *arachidonic acid*). Box 2-3 on p. 51 discusses one of the enzymes (*cyclooxygenase* or *COX*) used to convert arachidonic acid to prostaglandin.

Although prostaglandins may be secreted directly into the bloodstream, they are rapidly metabolized, so that circulating levels are extremely low. The term *tissue hormone* is appropriate because the secretion is produced in a tissue and diffuses only a short distance to other cells within the same tissue. Whereas typical hormones integrate activities of widely separated organs, prostaglandins tend to integrate activities of neighboring cells.

There are at least 16 different prostaglandins, falling into nine structural classes—prostaglandin A through prostaglandin I. Prostaglandins have been isolated and identified from a variety of tissues. The first prostaglandin was discovered in semen, so it was attributed to the prostate gland (hence the name, prostaglandin). Later, researchers found that the seminal vesicles, not the prostate, secreted the prostaglandin that they had found. Many other tissues are now known to secrete prostaglandins.

As a group, the prostaglandins have diverse physiological effects and are among the most varied and potent of any naturally occurring biological compounds. They are intimately involved in overall endocrine regulation by influencing adenyl cyclase–cAMP interaction within the cell's plasma membrane (see Figure 18-9). Specific biological effects depend on the class of prostaglandin.

Intraarterial infusion of prostaglandins A (PGAs) results in an immediate fall in blood pressure accompanied by an increase in regional blood flow to several areas, including the coronary and renal systems. PGAs apparently produce this effect by causing relaxation of smooth muscle fibers in the walls of certain arteries and arterioles.

Prostaglandins E (PGEs) have an important role in various vascular, metabolic, and gastrointestinal functions. Vascular effects include regulation of red blood cell deformability and platelet aggregation (see Chapter 20). PGEs also have a role in systemic inflammations, such as fever. Common antiinflammatory agents such as aspirin and ibuprofen produce some of their effects by inhibiting PGE synthesis. These drugs act by blocking one or more of the prostaglandin-producing *cyclooxygenase* enzymes such as *COX-1* and *COX-2*, as you may recall from Box 2-3 on p. 51. PGE also regulates hydrochloric acid secretion in the stomach, helping to prevent gastric ulcers.

Prostaglandins F (PGFs) have an especially important role in the reproductive system. They cause uterine muscle contractions, so they have been used to induce labor and thus accelerate delivery of a baby. PGFs also affect intestinal motility and are required for normal peristalsis.

In addition to prostaglandins, various tissues also synthesize other fatty acid compounds that are structurally and functionally similar to prostaglandins (see Figure 18-13). One example is **thromboxane,** a blood regulator important in blood clotting (discussed in Chapter 20). Another important example is a group called the **leukotrienes,** which are regulators of immunity (discussed in Chapter 24). As with prostaglandins, these compounds may also be referred to as "tissue hormones" because of their local, yet potent, regulatory effects.

The potential therapeutic use of prostaglandins and related compounds, which are found in almost every body tissue and are capable of regulating hormone activity on the cellular level, has been described as the most revolutionary development in medicine since the advent of antibiotics. They are likely to play increasingly important roles in the treatment of diverse conditions, such as hypertension, coronary thrombosis, asthma, and ulcers.

| QUICK CHECK |

9. Why are prostaglandins sometimes called *tissue hormones?*
10. Why are prostaglandins considered to be important in clinical applications?

the BIG picture

Endocrine Regulation and the Whole Body

It is important to appreciate the precision of control afforded by the partnership of the two major regulatory systems: the endocrine system and the nervous system. Some of the more important endocrine glands and the actions of their hormones are summarized in the following chapter. However, we have already seen how the hormones interact with each other in functional teams, as well as how their functions complement those of the nervous system. Although there is still much to be learned, we can see that a basic understanding of hormonal regulatory mechanisms is required to fully appreciate the nature of homeostasis in the human organism. As we continue our study of human anatomy and physiology, we will often encounter the critical integrative role played by the endocrine system. Having explored the basic principles of hormonal regulation, we are now ready for the specific examples of important glands and hormones outlined in the next chapter.

MECHANISMS of DISEASE

ENDOCRINE DISORDERS

As we have stated throughout this chapter, endocrine disorders typically result from either elevated or depressed hormone levels (hypersecretion or hyposecretion). At first thought, this may seem very simple and straightforward. In reality, however, nothing could be further from the truth. A variety of specific mechanisms may produce hypersecretion or hyposecretion of hormones. A few of the more well-known mechanisms are briefly explained here.

Mechanisms of Hypersecretion

Excessively high blood concentration of a hormone—or any condition that mimics high hormone levels—is called *hypersecretion.* Specific types of hypersecretion are usually named by placing the prefix *hyper-* in front of the name of the source gland and the suffix *-ism* at the end. For example, hypersecretion of thyroid hormone—no matter what the specific cause—is called **hyperthyroidism.** Hyperthyroidism is not a disease itself but a condition that characterizes several different diseases (e.g., Graves disease, toxic nodular goiter).

Any of several different mechanisms may be responsible for a particular case of hypersecretion. For example, tumors are often responsible for an abnormal proliferation of endocrine cells and the resulting increase in hormone secretion. Pituitary adenomas, for example, are benign tumors that may cause **hyperpituitarism.** As many as one in five people may have pituitary adenomas, but the majority of tumors are microscopic and asymptomatic. Larger tumors may, however, cause hyperpituitarism with possible outcomes of **gigantism** and/or **acromegaly.**

Another cause of hypersecretion is a phenomenon called **autoimmunity.** In autoimmunity, the immune system functions abnormally. In **Graves disease,** for example, autoimmune antibodies against the TSH receptor actually stimulate the receptor and mimic the activity of TSH. As a result, the thyroid gland hypertrophies and excess thyroid hormone is produced.

Another possible cause of hypersecretion of a hormone is a failure of the feedback mechanisms that regulate secretion of a particular hormone. For example, a condition called **primary hyperparathyroidism** is characterized by a failure of the parathyroid gland to adjust its output to compensate for changes in blood calcium levels. Instead, the parathyroid gland seems to operate independently of the normal feedback loop and thus overproduces parathyroid hormone.

Mechanisms of Hyposecretion

Depressed blood hormone levels—or any condition that mimics low hormone levels—is termed *hyposecretion.* Specific types of hyposecretion are named in a manner similar to that in which hypersecretion disorders are named: by the addition of the *hypo-* prefix and the *-ism* suffix. For example, hyposecretion of thyroid hormone is called *hypothyroidism.*

Various different mechanisms have been shown to cause hyposecretion of hormones. For example, although most tumors cause oversecretion of a hormone, they may instead cause a gland to undersecrete its hormone or hormones. Tissue death, perhaps caused by a blockage or other failure of the blood supply, can also cause a gland to reduce its hormonal output. Hypopituitarism (hyposecretion by the anterior pituitary) can occur this way. Still another way in which a gland may reduce its secretion below normal levels is through abnormal operation of regulatory feedback loops. An example of this is in the case of hyposecretion of testosterone and gonadotropic hormones in males who abuse *anabolic steroids.* Men who take testosterone steroids increase their blood concentration of this hormone above set point levels. The body responds to this overabundance by reducing its own output of testosterone (i.e., gonadotropins). This may lead to sterility and other complications.

Abnormalities of immune function may also cause hyposecretion. For example, an autoimmune attack on glandular tissue sometimes has the effect of reducing hormone output. Some endocrinologists theorize that autoimmune destruction of pancreatic islet cells, perhaps in combination with viral and genetic mechanisms, is a culprit in many cases of *type 1 (insulin-dependent) diabetes mellitus (DM)*.

Many types of hyposecretion disorders have been shown to be caused by insensitivity of the target cells to tropic hormones rather than from actual hyposecretion. A few major types of abnormal responses in target cells are as follows:

- An abnormal decrease in the number of hormone receptors
- Abnormal function of hormone receptors, resulting in failure to bind to hormones properly
- Antibodies bind to hormone receptors, thus blocking binding of hormone molecules
- Abnormal metabolic response to the hormone-receptor complex by the target cell
- Failure of the target cell to produce enough second messenger molecules

For example, type 2 (non–insulin-dependent) diabetes mellitus is thought to be caused by target cell abnormalities that render the cells insensitive to insulin.

The next chapter will give several examples of many specific endocrine disorders. Apply the principles you have learned here to determine whether each primarily involves functional hyposecretion or functional hypersecretion of the hormone(s) involved.

UNIT 3

LANGUAGE OF SCIENCE *(continued from p. 545)*

neuroendocrine system
(noo-roh-EN-doh-krin)
[*neuro-* **nerve**, *-endo-* **within**, *-crin-* **secrete**]

neurosecretory tissue
(noo-roh-SEK-reh-tor-ee-TISH-yoo)
[*neuro-* **nerve**, *-secret-* **secretion**, *-ory* **relating to**, *tissu-* **fabric**]

nonsteroid
(nahn-STAYR-oyd)
[*non-* **not**, *-stero-* **solid**, *-oid* **like**]

paracrine hormone
(PAIR-ah-krin HOR-mohn)
[*para-* **beside**, *-crin-* **secrete** *hormon-* **excite**]

peptide hormone
(PEP-tyde HOR-mohn)
[*pept-* **to digest**, *-ide* **chemical**, *hormon-* **excite**]

permissiveness
(per-MISS-iv-ness)

prostaglandin (PG)
(pross-tah-GLAN-din)
[*pro-* **before**, *-stat-* **set or place (prostate)**, *-gland-* **acorn (gland)**, *-in* **substance**]

protein hormone
(PRO-teen HOR-mohn)
[*prote-* **first rank**, *-in* **substance**, *hormon-* **excite**]

second messenger model

sex hormone
(seks HOR-mohn)
[*hormon-* **excite**]

steroid
(STAYR-oyd)
[*stero-* **solid**, *-oid* **like**]

synergism
(SIN-er-jiz-em)
[*syn-* **together**, *-erg-* **work**, *-ism* **condition of**]

target cell
[*cell* **storeroom**]

thromboxane
(throm-BOKS-ayne)
[*thrombo-* **clot**, *-oxa-* **oxygen**, *-ane* **chemical**]

tropic hormone
(TROH-pik HOR-mohn)
[*trop-* **nourish**, *-ic* **relating to**, *hormon-* **excite**]

up-regulation

LANGUAGE OF MEDICINE

acromegaly
(ak-roh-MEG-ah-lee)
[*acro-* **extremities**, *-mega-* **great**, *-aly* **state**]

autoimmunity
(aw-toh-i-MYOO-ni-tee)
[*auto-* **self**, *-immun-* **free**, *-ity* **state**]

gigantism
(jye-GAN-tiz-em)
[*gigant-* **great**, *-ism* **condition**]

Graves disease
(gravz)
[*Robert J. Graves* **Irish physician**]

hyperpituitarism
(hye-per-pih-TYOO-i-tar-iz-em)
[*hyper-* **excessive**, *-pituitar-* **phlegm (pituitary gland)**, *-ism* **condition**]

hypersecretion
(hye-per-seh-KREE-shun)
[*hyper-* **excessive**, *-secret-* **separate**, *-tion* **process**]

hyperthyroidism
(hye-per-THYE-royd-iz-em)
[*hyper-* **excessive**, *-thyr-* **shield (thyroid gland)**, *-oid* **like**, *-ism* **condition**]

hyposecretion
(hye-poh-seh-KREE-shun)
[*hypo-* **under or below**, *-secret-* **separate**, *-tion* **process**]

primary hyperparathyroidism
(hye-per-pair-ah-THY-royd-iz-em)
[*prim-* **first**, *-ary* **relating to**, *hyper-* **excessive**, *-para-* **beside**, *-thyr-* **shield (thyroid)**, *-oid* **like**, *-ism* **condition**]

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

ORGANIZATION OF THE ENDOCRINE SYSTEM

A. The endocrine and nervous systems function to achieve and maintain homeostasis (Table 18-1)
B. When the two systems work together, referred to as the *neuroendocrine system*, they perform the same general functions: communication, integration, and control
C. In the endocrine system, secreting cells send hormone molecules by way of the blood to specific target cells contained in target tissues or target organs
D. Hormones—carried to almost every point in the body; can regulate most cells; effects work more slowly and last longer than those of neurotransmitters
E. Endocrine glands are "ductless glands"; many are made of glandular epithelium whose cells manufacture and secrete hormones; a few endocrine glands are made of neurosecretory tissue
F. Glands of the endocrine system are widely scattered throughout the body (Figure 18-2; Table 18-2)

HORMONES

A. Classification of hormones
  1. Classification by general function
    a. Tropic hormones—hormones that target other endocrine glands and stimulate their growth and secretion
    b. Sex hormones—hormones that target reproductive tissues
    c. Anabolic hormones—hormones that stimulate anabolism in target cells
  2. Classification by chemical structure (Figure 18-3; Table 18-3)
    a. Steroid hormones
    b. Nonsteroid hormones
  3. Steroid hormones (Figure 18-4)
    a. Synthesized from cholesterol (Figure 18-5)
    b. Lipid soluble and can easily pass through the phospholipid plasma membrane of target cells
    c. Examples of steroid hormones: cortisol, aldosterone, estrogen, progesterone, and testosterone
  4. Nonsteroid hormones (Figure 18-6)
    a. Synthesized primarily from amino acids
    b. Protein hormones—long, folded chains of amino acids; e.g., insulin, parathyroid hormone
    c. Glycoprotein hormones—protein hormones with carbohydrate groups attached to the amino acid chain
    d. Peptide hormones—smaller than protein hormones; short chain of amino acids; e.g., oxytocin, antidiuretic hormone (ADH)
    e. Amino acid derivative hormones—each is derived from a single amino acid molecule
      (1) Amine hormones—synthesized by modifying a single molecule of tyrosine or tryptophan; produced by neurosecretory cells and by neurons; e.g., epinephrine, norepinephrine
      (2) Amino acid derivatives produced by the thyroid gland; synthesized by adding iodine to tyrosine
B. How hormones work
  1. General principles of hormone action
    a. Hormones signal a cell by binding to the target cell's specific receptors in a "lock-and-key" mechanism (Figure 18-7)
    b. Different hormone-receptor interactions produce different regulatory changes within the target cell through chemical reactions
    c. Combined hormone actions
      (1) Synergism—combinations of hormones acting together have a greater effect on a target cell than the sum of the effects that each would have if acting alone
      (2) Permissiveness—when a small amount of one hormone allows a second one to have its full effects on a target cell
      (3) Antagonism—one hormone produces the opposite effects of another hormone; used to "fine tune" the activity of target cells with great accuracy
    d. Most hormones have primary effects that directly regulate target cells and many secondary effects that influence or modulate other regulatory mechanisms in target cells
    e. Endocrine glands produce more hormone molecules than actually are needed; the unused hormones are quickly excreted by the kidneys or broken down by metabolic processes
  2. Mechanism of steroid hormone action (Figure 18-8)
    a. Steroid hormones are lipid soluble, and their receptors are normally found in the target cell's cytosol
    b. After a steroid hormone molecule has diffused into the target cell, it binds to a receptor molecule to form a hormone-receptor complex
    c. Mobile-receptor model—the hormone passes into the nucleus, where it binds to a mobile receptor and activates a certain gene sequence to begin transcription of mRNA; newly formed mRNA molecules move into the cytosol, associate with ribosomes, and begin synthesizing protein molecules that produce the effects of the hormone

d. Steroid hormones regulate cells by regulating production of certain critical proteins
e. The amount of steroid hormone present determines the magnitude of a target cell's response
f. Because transcription and protein synthesis take time, responses to steroid hormones are often slow

3. Mechanisms of nonsteroid hormone action
   a. The second messenger mechanism—also known as the *fixed-membrane-receptor model* (Figure 18-9)
      (1) A nonsteroid hormone molecule acts as a "first messenger" and delivers its chemical message to fixed receptors in the target cell's plasma membrane
      (2) The "message" is then passed by way of a G-protein–coupled receptor (GPCR) into the cell where a "second messenger" triggers a G protein, which leads to the appropriate cellular changes
      (3) Second messenger mechanism—produces target cell effects that differ from steroid hormone effects in several important ways
         (a) The effects of the hormone are amplified by the cascade of reactions
         (b) There are a variety of second messenger mechanisms—e.g., IP_3, cGMP, calcium-calmodulin mechanisms (Figure 18-10)
         (c) The second messenger mechanism operates much more quickly than the steroid mechanism
   b. The nuclear-receptor mechanism—small iodinated amino acids (T_4 and T_3) enter the target cell and bind to receptors associated with a DNA molecule in the nucleus; this binding triggers transcription of mRNA and synthesis of new enzymes

C. Regulation of hormone secretion
1. Control of hormonal secretion is usually part of a negative feedback loop and is called *endocrine reflexes* (Figure 18-11)
2. Simplest mechanism—when an endocrine gland is sensitive to the physiological changes produced by its target cells
3. Endocrine gland secretion may also be regulated by a hormone produced by another gland
4. Endocrine gland secretions may be influenced by nervous system input; this fact emphasizes the close functional relationship between the two systems

D. Regulation of target cell sensitivity
1. Sensitivity of target cell depends in part on number of receptors (Figure 18-12)
   a. Up-regulation—increased number of hormone receptors increases sensitivity
   b. Down-regulation—decreased number of hormone receptors decreases sensitivity
2. Sensitivity of target cell may also be regulated by factors that affect signal transcription or gene transcription

PROSTAGLANDINS

A. Unique group of lipid hormones (20-carbon fatty acid with 5-carbon ring) that serve important and widespread integrative functions in the body but do not meet the usual definition of a hormone (Figure 18-13; Table 18-4)
B. Called *tissue hormones* because the secretion is produced in a tissue and diffuses only a short distance to other cells within the same tissue; PGs tend to integrate activities of neighboring cells
C. Many structural classes of prostaglandins have been isolated and identified
1. Prostaglandin A (PGA)—intraarterial infusion resulting in an immediate fall in blood pressure accompanied by an increase in regional blood flow to several areas
2. Prostaglandin E (PGE)—vascular effects: regulation of red blood cell deformability and platelet aggregation; inflammation (which can be blocked with drugs that inhibit PG-producing enzymes such as COX-1 and COX-2); gastrointestinal effects: regulates hydrochloric acid secretion
3. Prostaglandin F (PGF)—especially important in reproductive system, causing uterine contractions; also affects intestinal motility and is required for normal peristalsis

D. Many tissues are known to secrete PGs
E. PGs have diverse physiological effects

THE BIG PICTURE: THE ENDOCRINE SYSTEM AND THE WHOLE BODY

A. Nearly every process in the human organism is kept in balance by the intricate interaction of different nervous and endocrine regulatory chemicals
B. The endocrine system operates with the nervous system to finely adjust the many processes they regulate

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Define the terms *hormone* and *target organ*.
2. Describe the characteristic chemical group found at the core of each steroid hormone.
3. Identify the major categories of nonsteroid hormones.
4. Identify the sequence of events involved in a second messenger mechanism.
5. What is the function of calmodulin?
6. List the classes of prostaglandins. Identify the functions of three of these classes.

CRITICAL THINKING QUESTIONS

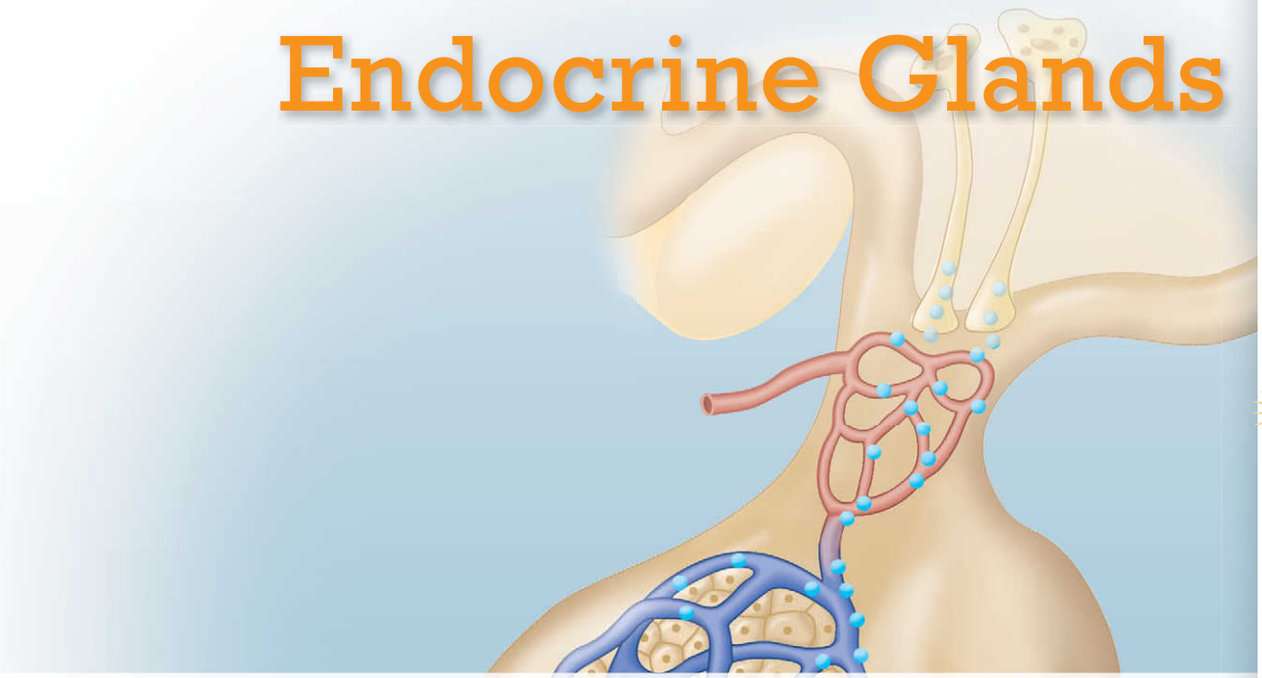


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Driving a car requires rapid response of selected muscles. The regulation of blood sugar level requires regulating almost every cell in the body. Based on the characteristics of each system, explain why driving would be a nervous system function and blood sugar regulation would be an endocrine function.
2. How would you explain the ways in which one hormone interacts with another and its impact on the cell?
3. Compare and contrast the action mechanisms of steroid and nonsteroid hormones.
4. Why are thyroid hormones exceptions to the usual mode of nonsteroid hormone functioning?
5. What examples can you find that apply the concept of a negative feedback loop to the regulation of hormone secretion?

Endocrine Glands

19



CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

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- Adenohypophysis (Anterior Lobe of Pituitary), 564
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The Big Picture: The Endocrine System and the Whole Body, 587

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LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

adenohypophysis
(ad-eh-no-hye-POF-i-sis)
[*adeno-* **gland,** *-hypo-* **under or below,** *-physis* **growth**] *pl.,* adenohypophyses

adrenal cortex
(ah-DREE-nal KOR-teks)
[*ad-* **toward,** *-ren-* **kidney,** *-al* **relating to,** *cortex* **bark**] *pl.,* cortices

adrenal gland
(ah-DREE-nal)
[*ad-* **toward,** *-ren-* **kidney,** *-al* **relating to,** *gland* **acorn**]

adrenal medulla
(ah-DREE-nal meh-DUL-eh)
[*ad-* **toward,** *-ren-* **kidney,** *-al* **relating to,** *medulla* **middle**] *pl.,* medullae or medullas

adrenocorticotropic hormone (ACTH)
(ah-dree-no-kor-teh-koh-TROH-pic HOR-mohn)
[*adreno-* **gland,** *-cortic-* **bark,** *-trop-* **nourish,** *-ic* **relating to,** *hormon-* **excite**]

aldosterone
(AL-doh-steh-rohn or al-DAH-stair-ohn)
[*aldo-* **aldehyde,** *-stero-* **solid or steroid derivative,** *-one* **chemical**]

alpha cell
(AL-fah)
[*alpha* **(α) first letter of Greek alphabet,** *cell* **storeroom**]

angiotensin I
(an-jee-oh-TEN-sin)
[*angio-* **vessel,** *-tens-* **pressure or stretch,** *-in* **substance, I Roman numeral one**]

continued on p. 588

In the previous chapter we outlined the basic mechanisms of endocrine regulation and its partnership with nervous regulation. We learned how hormones released from endocrine glands into the bloodstream can signal target tissues to alter their functions in ways that promote homeostasis. Our study of neuroendocrine regulation of body function continues in this chapter, in which we explore the structure and function of some of the major endocrine glands. By looking at a few of the important glands and their hormones, a clear picture emerges of how endocrine regulation works. As you learn the specific actions of the major hormones, think of them as part of an overall system of regulating the body's functions. In later chapters, we will encounter many of these hormones again as we explore the various body functions they regulate.

PITUITARY GLAND

Structure of the Pituitary Gland

The **pituitary gland** (formerly called the *hypophysis*) is a small but mighty structure. It measures only 1.2 to 1.5 cm (about ½ inch) across. By weight, it is even less impressive—only about 0.5 gram (⅑₀ ounce)! And yet so crucial are the functions of the anterior lobe of the pituitary gland that, in past centuries, it was referred to as the "master gland."

The pituitary gland has a well-protected location within the skull on the ventral surface of the brain (Figure 19-1). It lies in the *pituitary fossa* of the sella turcica and is covered by a portion of the dura mater called the *pituitary diaphragm*. The gland has a stemlike stalk, the **infundibulum,** which connects it to the hypothalamus of the brain.

Although the pituitary looks like one gland, it actually consists of two separate glands—the **adenohypophysis,** or anterior pituitary gland, and the **neurohypophysis,** or posterior pituitary gland. In the embryo, the adenohypophysis develops from an upward projection of the pharynx and is composed of regular endocrine tissue. The neurohypophysis, on the other hand, develops from a downward projection of the brain and is composed of neurosecretory tissue. These histological differences are incorporated into their names—*adeno* means "gland," and *neuro* means "nervous." As you may suspect, the hormones secreted by the adenohypophysis serve very different functions from those released by the neurohypophysis.

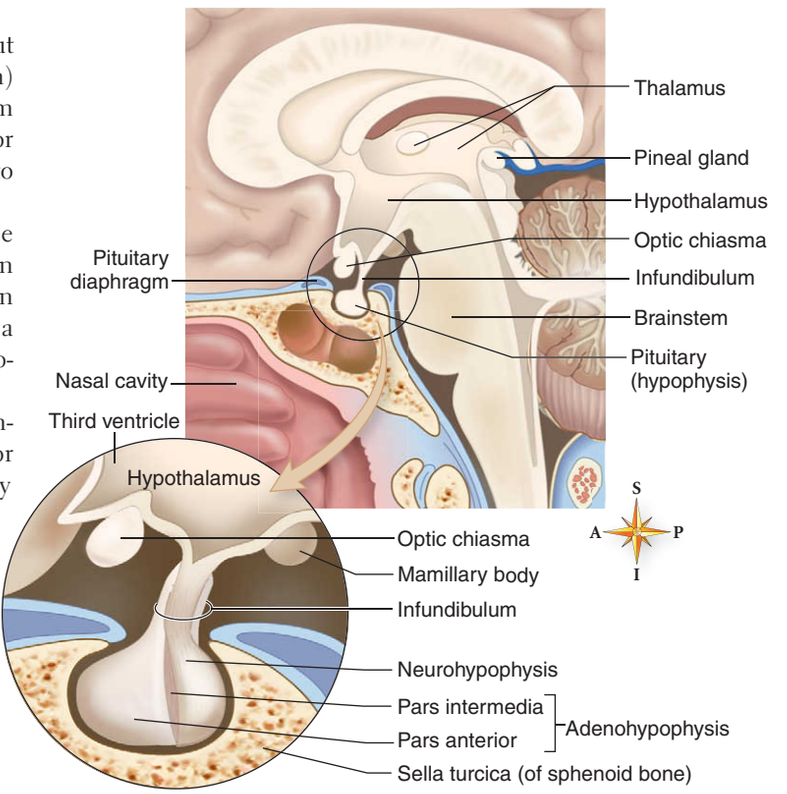


FIGURE 19-1

Location and structure of the pituitary gland. The pituitary gland is located within the sella turcica of the skull's sphenoid bone and is connected to the hypothalamus by a stalklike infundibulum. The infundibulum passes through a gap in the portion of the dura mater that covers the pituitary (the pituitary diaphragm). The inset shows that the pituitary is divided into an anterior portion, the adenohypophysis, and a posterior portion, the neurohypophysis. The adenohypophysis is further subdivided into the pars anterior and pars intermedia. The pars intermedia is almost absent in the adult pituitary.

Adenohypophysis (Anterior Lobe of Pituitary)

The **adenohypophysis,** the anterior portion of the pituitary gland, is divided into two parts—the *pars anterior* and the *pars intermedia*. The pars anterior forms the major portion of the adenohypophysis and is divided from the tiny pars intermedia by a narrow cleft and some connective tissue (see Figure 19-1).

The tissue of the adenohypophysis is composed of irregular clumps of secretory cells supported by fine connective tissue fibers and surrounded by a rich vascular network.

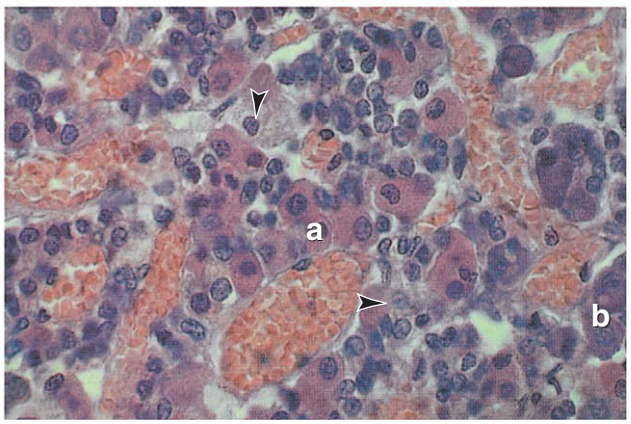


FIGURE 19-2

Histology of the adenohypophysis. In this light micrograph, nonstaining chromophobes are indicated by arrowheads. Examples of hormone-secreting cells are labeled *a* (acidophil) and *b* (basophil).

Traditionally, histologists have identified three types of cells according to their affinity for certain types of stains: *chromophobes* (literally "afraid of color"), *acidophils* ("acid [stain] lovers"), and *basophils* ("base [stain] lovers"). All three types are visible in the photomicrograph shown in Figure 19-2. Currently, however, cells of the adenohypophysis are more often classified by their secretions into five types:

1. **Somatotrophs**—secrete growth hormone (GH)
2. **Corticotrophs**—secrete adrenocorticotropic hormone (ACTH)
3. **Thyrotrophs**—secrete thyroid-stimulating hormone (TSH)
4. **Lactotrophs**—secrete prolactin (PRL)
5. **Gonadotrophs**—secrete luteinizing hormone (LH) and follicle-stimulating hormone (FSH)

Figure 19-3 summarizes the hormones of the adenohypophysis and shows the primary locations of their target cells.

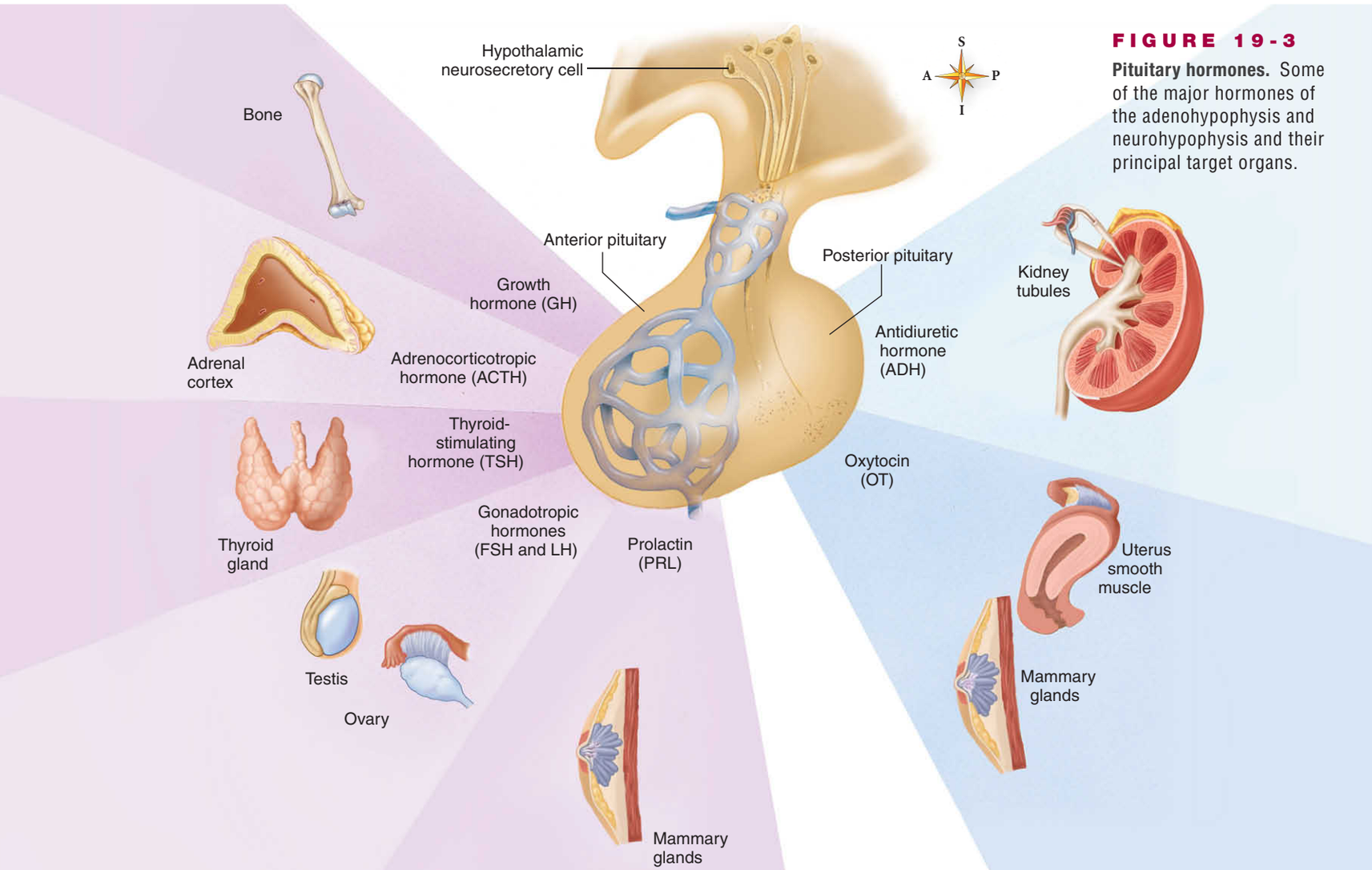


FIGURE 19-3

Pituitary hormones. Some of the major hormones of the adenohypophysis and neurohypophysis and their principal target organs.

GROWTH HORMONE

Growth hormone (GH), or **somatotropin (STH),** promotes bodily growth indirectly by stimulating the liver and other tissues to produce another hormone called *insulin-like growth factor 1 (IGF-1),* which, in turn, produces most of the effects attributed to GH.

One of the functions of the GH, by way of IGF-1, is to accelerate amino acid transport into cells. Rapid entrance of amino acids from the blood into the cells allows protein anabolism within the cells to accelerate. Increased protein anabolism allows an increased rate of growth. GH promotes the growth of bone, muscle, and other tissues (Box 19-1).

Box 19-1 | HEALTH matters

Growth Hormone Abnormalities

Hypersecretion of growth hormone (GH) during the growth years (before ossification of the epiphyseal plates) causes an abnormally rapid rate of skeletal growth. This condition is known as **gigantism** (see figure, *left*). Hypersecretion after skeletal fusion has occurred can result in **acromegaly,** a condition in which cartilage still left in the skeleton continues to form new bone. This abnormal growth may result in a distorted appearance because of the enlargement of the hands, feet, face, jaw (causing separation of the teeth), and other body parts. Overlying soft tissue may also be affected—for instance, the skin often thickens and the pores become more pronounced.

Hyposecretion of GH during growth years may result in stunted body growth, known as **pituitary dwarfism** (see figure, *right*). Formerly, patients were treated only with GH extracted from human tissues. Since 1987, the availability of human GH produced by genetically engineered bacteria has made the treatment obtainable for many more patients. However, continuing concerns have been raised about possible adverse side effects associated with human GH from bacterial sources.



Growth hormone abnormalities. The man on the left exhibits gigantism, and the man on the right exhibits pituitary dwarfism. The two men in the middle are of average height.

In addition to stimulating protein anabolism, GH also stimulates fat metabolism. GH accelerates mobilization of lipids from storage in adipose cells and also speeds up the catabolism of those lipids after they have entered another cell. In this way, GH tends to shift a cell's use of nutrients away from carbohydrate (glucose) catabolism and toward lipid catabolism as an energy source. Because less glucose is then removed from the blood by cells, the blood glucose levels tend to rise. Thus GH is said to have a *hyperglycemic effect.* Insulin (from the pancreas) has the opposite effect—it promotes glucose entry into cells, producing a *hypoglycemic effect.* Therefore GH and insulin function as antagonists. The balance between these two hormones is vital to maintaining a homeostasis of blood glucose levels.

GH affects metabolism in these ways:

- Promotes protein anabolism (growth, tissue repair)
- Promotes lipid mobilization and catabolism
- Indirectly inhibits glucose metabolism
- Indirectly increases blood glucose levels

PROLACTIN

Prolactin (PRL), produced by acidophils in the pars anterior, is also called *lactogenic hormone.* Both names of this hormone suggest its function in "generating" or initiating milk secretion (lactation). During pregnancy, a high level of PRL promotes the development of the breasts in anticipation of milk secretion. At the birth of an infant, PRL in the mother stimulates the mammary glands to begin milk secretion.

Hypersecretion of PRL may cause lactation in nonnursing women, disruption of the menstrual cycle, and impotence in men. **Hyposecretion** of PRL is usually insignificant except in women who want to nurse their children. Milk production cannot be initiated or maintained without PRL.

TROPIC HORMONES

Tropic hormones are hormones that have a stimulating effect on other endocrine glands. These hormones stimulate the development of their target glands and tend to stimulate synthesis and secretion of the target hormone (Box 19-2). Four principal tropic

Box 19-2 | HEALTH matters

Tropic Hormone Abnormalities

Hypersecretion of the tropic hormones may result from a pituitary tumor. The tropic hormones, produced at higher than normal levels, cause hypersecretion in their target glands. This may result in various effects throughout the body. Early hypersecretion of gonadotropins may lead to an abnormally early onset of puberty.

Hyposecretion of tropic hormones often causes their target glands to secrete less than a normal amount of their hormones. This may disrupt reproduction, kidney function, overall metabolism, and other processes.

hormones are produced and secreted by the basophils of the pars anterior:

1. **Thyroid-stimulating hormone (TSH),** or *thyrotropin*, promotes and maintains the growth and development of its target gland—the thyroid. TSH also causes the thyroid gland to secrete thyroid hormone.
2. **Adrenocorticotropic hormone (ACTH),** or *adrenocorticotropin*, promotes and maintains normal growth and development of the cortex of the adrenal gland. ACTH also stimulates the adrenal cortex to synthesize and secrete some of its hormones.
3. **Follicle-stimulating hormone (FSH)** stimulates structures within the ovaries, primary follicles, to grow toward maturity. Each follicle contains a developing egg cell (ovum), which is released from the ovary during ovulation. FSH also stimulates the follicle cells to synthesize and secrete estrogens (female sex hormones). In the male, FSH stimulates the development of the seminiferous tubules of the testes and maintains spermatogenesis (sperm production) by them.
4. **Luteinizing hormone (LH)** stimulates the formation and activity of the corpus luteum of the ovary. The corpus luteum (meaning "yellow body") is the tissue left behind when a follicle ruptures to release its egg during ovulation. The corpus luteum secretes progesterone and estrogens when stimulated by LH. LH also supports FSH in stimulating the maturation of follicles. In males, LH stimulates interstitial cells in the testes to develop and then synthesize and secrete testosterone (the male sex hormone).

FSH and LH are called **gonadotropins** because they stimulate the growth and maintenance of the gonads (ovaries and testes). During childhood the adenohypophysis secretes insignificant amounts of the gonadotropins. A few years before puberty, gonadotropin secretion is gradually increased. Then, suddenly, their secretion spurts, and the gonads are stimulated to develop and begin their normal functions.

In addition to those listed, the adenohypophysis produces many other hormones in small amounts. Many of these are also produced elsewhere in the body. For example, *α-MSH (alpha melanocyte-stimulating hormone)* and other melanocortins discussed in Chapter 7 (see p. 179) are produced in the skin and other tissues, with a relatively insignificant amount also produced in the adenohypophysis.

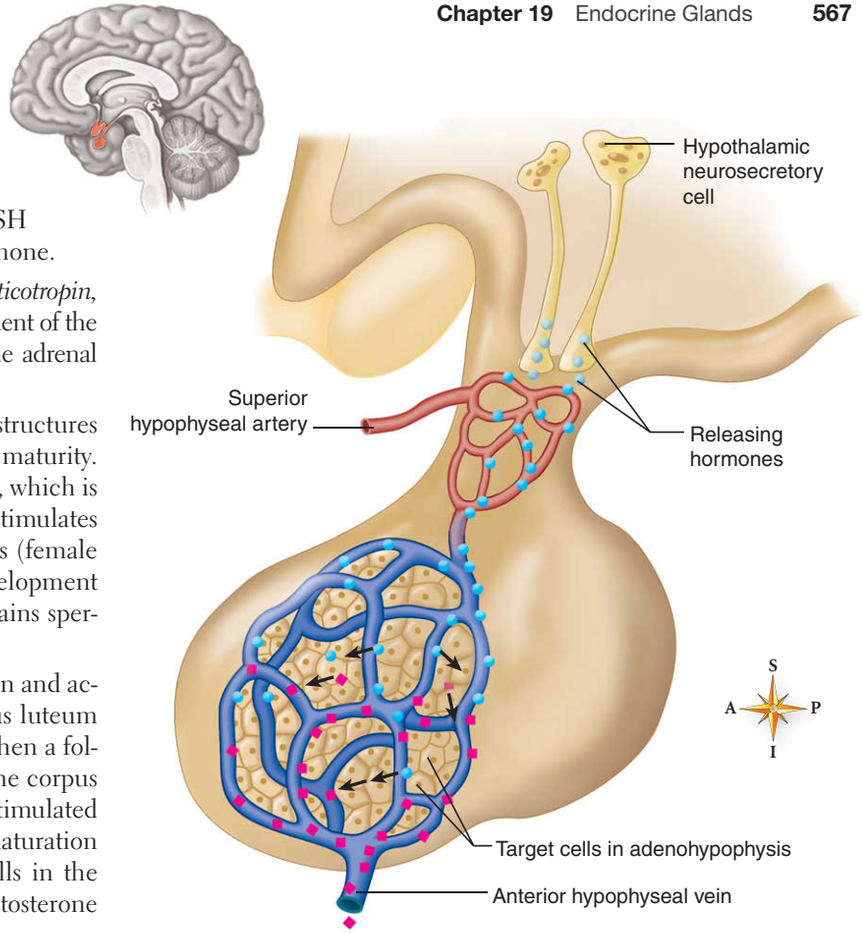


FIGURE 19-4

Hypophyseal portal system. Neurons in the hypothalamus secrete releasing hormones into veins that carry the releasing hormones directly to the vessels of the adenohypophysis, thus bypassing the normal circulatory route.

CONTROL OF SECRETION IN THE ADENOHYPOPHYSIS

The cell bodies of neurons in certain parts of the hypothalamus synthesize chemicals that their axons then secrete into the blood. These chemicals, generally called **releasing hormones,** travel through a complex of small blood vessels called the **hypophyseal portal system** (Figure 19-4). A *portal system* is an arrangement of blood vessels in which blood exiting one tissue is immediately carried to a second tissue before being returned to the heart and lungs for oxygenation and redistribution. The hypophyseal portal system carries blood from the hypothalamus directly to the adenohypophysis, where the target cells of the releasing hormones are located. The advantage of a portal system in the hypophysis is that a small amount of hormone can be delivered directly to its target tissue without the great dilution that would occur in the general circulation. The releasing hormones that arrive in the adenohypophysis by means of this portal system influence the secretion of hormones by acidophils and basophils. In this manner, the hypothalamus directly regulates the secretion of the adenohypophysis. You can see that the supposed "master gland" really has a master of its own—the hypothalamus.

The following is a list of some of the important hormones secreted by the hypothalamus into the hypophyseal portal system:

- Growth hormone–releasing hormone (GHRH)
- Growth hormone–inhibiting hormone (GHIH) (also called somatostatin [SS])
- Corticotropin-releasing hormone (CRH)
- Thyrotropin-releasing hormone (TRH)
- Gonadotropin-releasing hormone (GnRH)
- Prolactin-releasing hormone (PRH)
- Prolactin-inhibiting hormone (PIH)

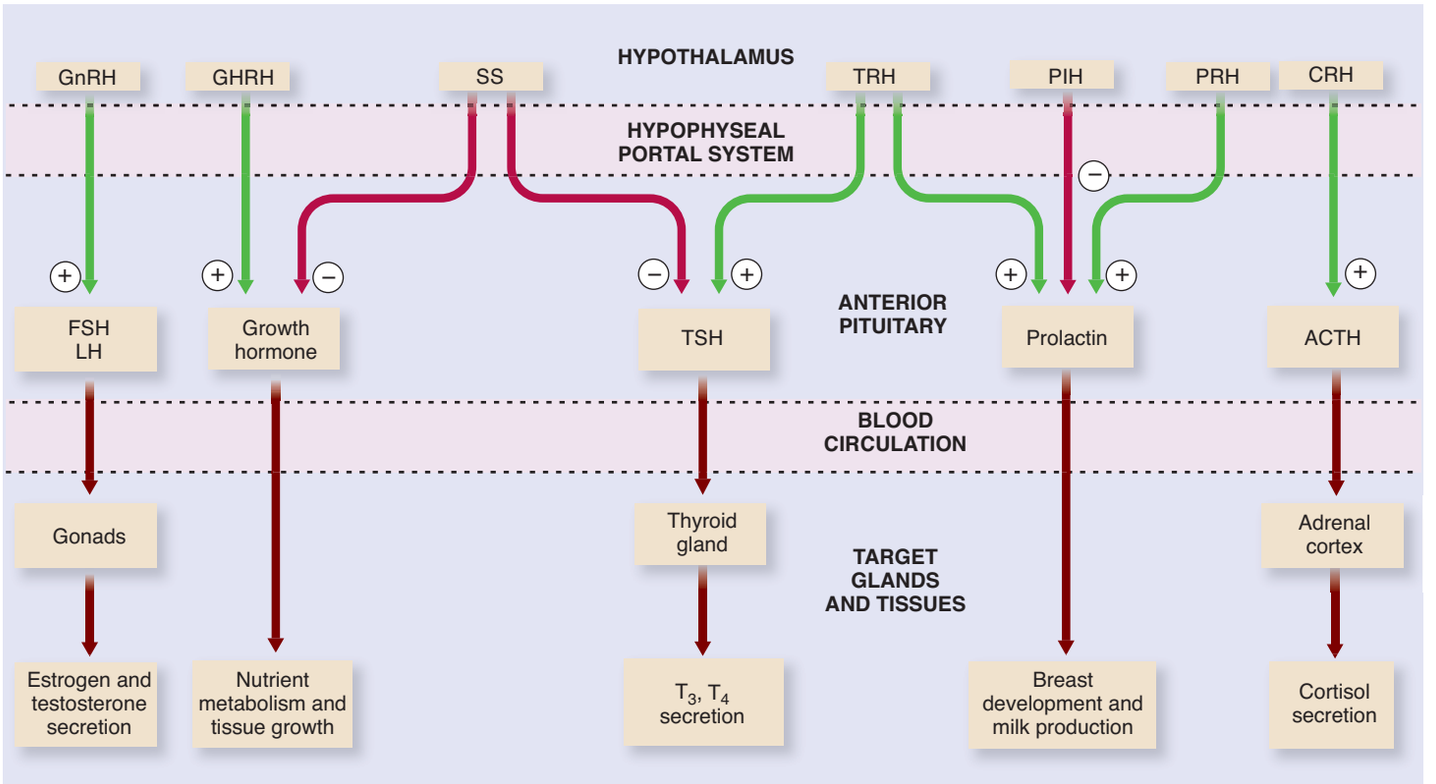


FIGURE 19-5

Action of hypothalamic hormones. Hypothalamic hormones have releasing or inhibiting effects on the various cells of the anterior pituitary, thus regulating anterior pituitary secretion—and thus ultimately regulating the effects of anterior pituitary hormones throughout the body. *GnRH,* Gonadotropin-releasing hormone; *GHRH,* growth hormone–releasing hormone; *SS,* somatostatin; *TRH,* thyroid-releasing hormone; *PIH,* prolactin-inhibiting hormone; *PRH,* prolactin-releasing hormone; *CRH,* corticotropin-releasing hormone; *FSH,* follicle-stimulating hormone; *LH,* luteinizing hormone; *TSH,* thyroid-stimulating hormone; *ACTH,* adrenocorticotropic hormone; T_3, triiodothyronine; T_4, thyroxine.

Figure 19-5 and Table 19-1 list functions of each releasing hormone. Before consulting the figure or table, try to deduce their functions from their names.

Through negative feedback mechanisms, the hypothalamus adjusts the secretions of the adenohypophysis, and the adenohypophysis adjusts the secretions of its target glands, which in turn adjust the activity of their target tissues (Box 19-3). For example, Figure 19-6 shows the negative feedback control of the secretion of TSH and thyroid hormone (T_3 and T_4).

Hormone secretion can occur in pulses or peaks, as we see in a graph of minute by minute variations in GH secretion (Figure 19-7). The peaks result from many somatotroph cells in the pituitary collectively increasing their rate of secretion of GH. Such increases result from pulses in GHRH secretion by the

TABLE 19-1 Hormones of the Hypothalamus

HORMONE	SOURCE	TARGET	PRINCIPAL ACTION
Growth hormone–releasing hormone (GHRH)	Hypothalamus	Adenohypophysis (somatotrophs)	Stimulates secretion (release) of growth hormone
Growth hormone–inhibiting hormone (GHIH), or somatostatin	Hypothalamus	Adenohypophysis (somatotrophs)	Inhibits secretion of growth hormone
Corticotropin-releasing hormone (CRH)	Hypothalamus	Adenohypophysis (corticotrophs)	Stimulates release of adrenocorticotropic hormone (ACTH)
Thyrotropin-releasing hormone (TRH)	Hypothalamus	Adenohypophysis (thyrotrophs)	Stimulates release of thyroid-stimulating hormone (TSH)
Gonadotropin-releasing hormone (GnRH)	Hypothalamus	Adenohypophysis (gonadotrophs)	Stimulates release of gonadotropins (FSH and LH)
Prolactin-releasing hormone (PRH)	Hypothalamus	Adenohypophysis (corticotrophs)	Stimulates secretion of prolactin
Prolactin-inhibiting hormones (PIH)	Hypothalamus	Adenohypophysis (corticotrophs)	Inhibits secretion of prolactin

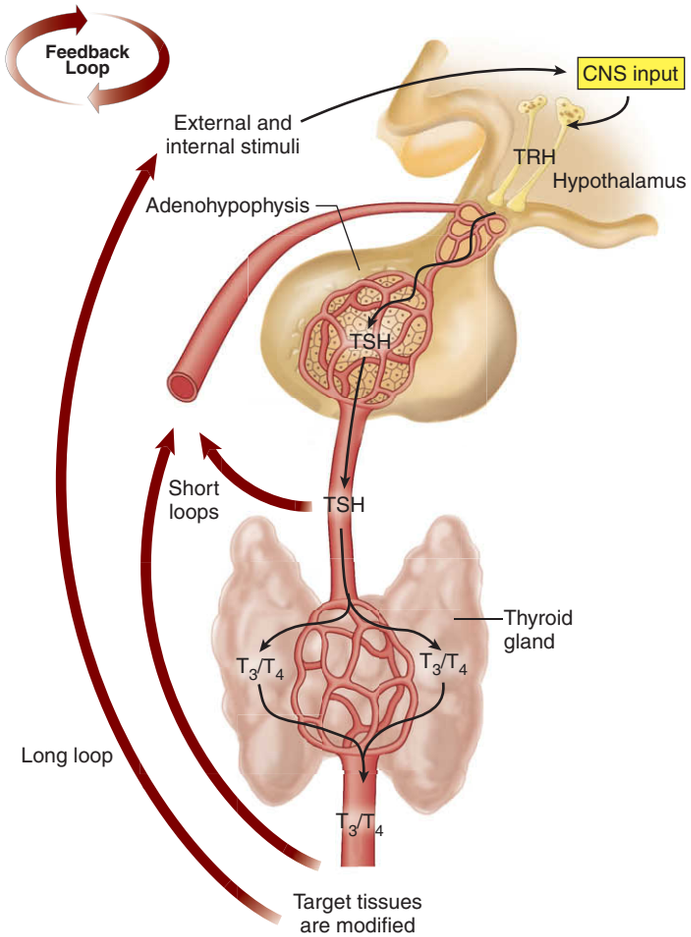


FIGURE 19-6

Negative feedback control by the hypothalamus. In this example, the secretion of thyroid hormone (T_3 and T_4) is regulated by a number of negative feedback loops. A long negative feedback loop *(long red arrow)* allows the central nervous system (CNS) to influence hypothalamic secretion of thyrotropin-releasing hormone (TRH) by nervous feedback from the targets of T_3/T_4 (and from other nerve inputs). The secretion of TRH by the hypothalamus and thyroid-stimulating hormone (TSH) by the adenohypophysis is also influenced by shorter feedback loops *(shorter red arrows),* allowing great precision in the control of this system.

hypothalamus (see Figure 19-5), which are especially large during sleep. Exercise, stress, and high-protein meals can cause an increase in the frequency of these peaks.

Before leaving the subject of control of pituitary secretion, we call your attention to another concept involving the hypothalamus. It functions as an important part of the body's complex machinery for responding to stress situations. For example, in severe pain or intense emotions, the cerebral cortex—especially the limbic area—sends impulses to the hypothalamus. The impulses stimulate the hypothalamus to secrete its releasing hormones into the hypophyseal portal veins. Circulating quickly to the adenohypophysis, they stimulate it to secrete more of its hormones. These in turn stimulate increased activity by the pituitary's target structures. In essence, what the hypothalamus does through its releasing of hormones is to translate nerve impulses into hormone secretion by endocrine glands. Thus the hypothalamus links the nervous system

Box 19-3 | HEALTH matters

Clinical Evidence of Feedback Control

Clinical facts provide interesting evidence about feedback control of hormone secretion by the anterior pituitary gland and its target glands. For instance, patients who have the pituitary gland removed **(hypophysectomy)** surgically or by radiation must be given hormone replacement therapy for the rest of their lives. If not, they will develop thyroid, adrenal cortical, and gonadotropic deficiencies—deficiencies of the anterior pituitary's target gland hormones. Another well-known clinical fact is that estrogen deficiency develops in women between 40 and 50 years of age. By then the ovaries seem to have tired of producing hormones and ovulating each month. They no longer respond to FSH stimulation, so estrogen deficiency develops, brings about menopause, and persists after menopause. What therefore would you deduce is true of the blood concentration of FSH after menopause? Apply the principle that a low concentration of a target gland hormone stimulates tropic hormone secretion by the anterior pituitary gland and you will understand that FSH levels rise, indeed, after menopause.

to the endocrine system. It integrates the activities of these two great integrating systems—particularly, it seems, in times of stress. When survival is threatened, the hypothalamus can take over the adenohypophysis and thus gain control of literally every cell in the body. We discuss stress in more detail in Chapter 25.

The mind-body link provided by the hypothalamus has tremendous implications. It means that the cerebrum can do more than just receive sensory impulses and send out impulses to muscles and glands. It means that our thoughts and emotions—our minds—can,

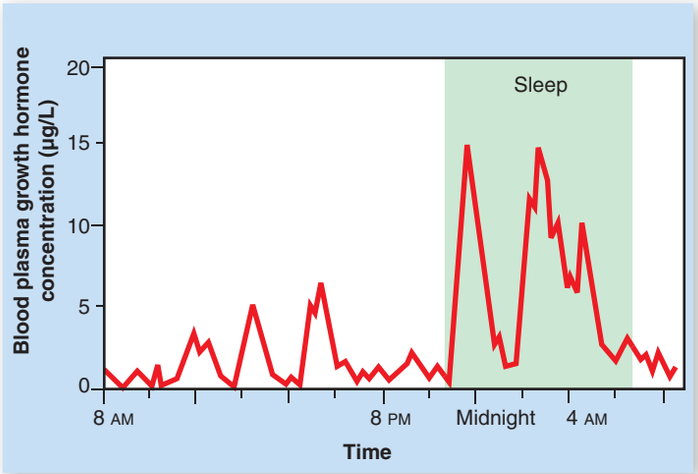


FIGURE 19-7

Secretion of growth hormone (GH). The amount of GH in the blood plasma of a 23-year-old woman was plotted on a graph every 5 minutes over the course of 24 hours. Note that GH fluctuates chaotically minute by minute, with occasional peaks that get larger after she falls asleep. The surges of GH result in part from pulses of GHRH (GH-releasing hormone) from the hypothalamus.

by way of the hypothalamus, influence the functions of all of our billions of cells. In short, the brain has two-way contact with every tissue of the body. Thus the state of the body can influence mental processes, and the state of the mind can affect the functioning of the body. Therefore both psychosomatic (mind influencing the body) and somatopsychic (body influencing the mind) relationships exist between human body systems and the brain.

| QUICK CHECK |

1. What are the two main divisions of the pituitary called? How are they distinguished by location and histology?
2. Name three hormones produced by the adenohypophysis, and give their main functions.
3. What is a tropic hormone? A releasing hormone?

Neurohypophysis (Posterior Lobe of Pituitary)

The **neurohypophysis** serves as a storage and release site for two hormones: **antidiuretic hormone (ADH)** and **oxytocin (OT).** The cells of the neurohypophysis do not themselves make these hormones. Instead, neurons whose bodies are in either the *supra-optic* or the *paraventricular nuclei* of the hypothalamus synthesize them (Figure 19-8).

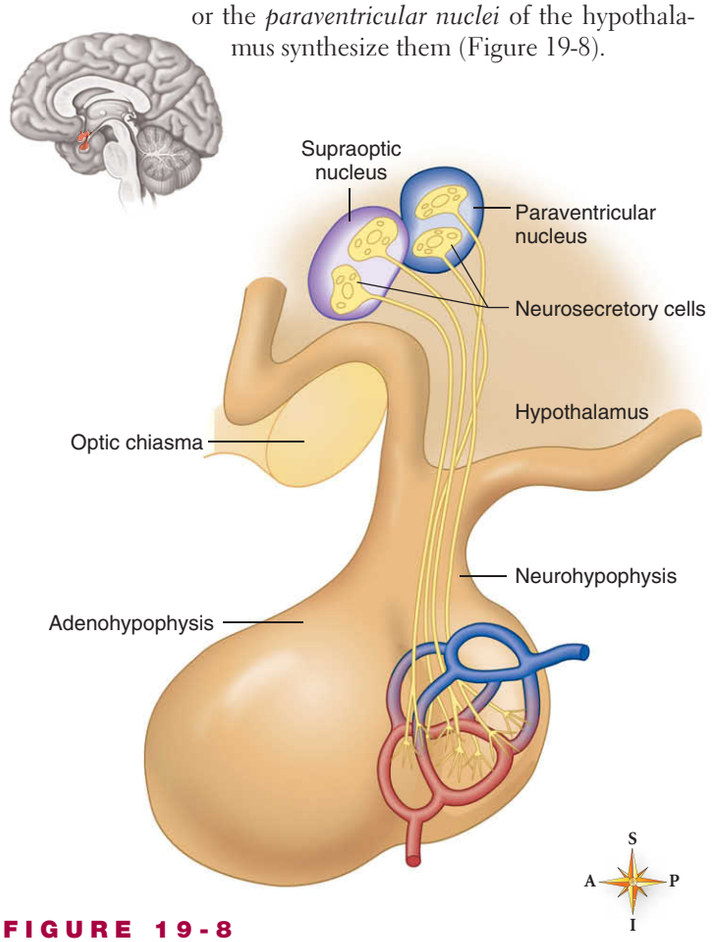


FIGURE 19-8

Relationship of the hypothalamus and neurohypophysis. Neurosecretory cells have their cell bodies in the hypothalamus and their axon terminals in the neurohypophysis. Thus hormones synthesized in the hypothalamus are actually released from the neurohypophysis.

From the cell bodies of these neurons in the hypothalamus, the hormones pass down along axons (in the hypothalamohypophyseal tract) into the neurohypophysis. Instead of the chemical-releasing factors that triggered secretion of hormones from the adenohypophysis, release of ADH and OT into the blood is controlled by nervous stimulation.

ANTIDIURETIC HORMONE

The term *antidiuresis* literally means "opposing the production of a large urine volume." And this is exactly what ADH does—it prevents the formation of a large volume of urine. In preventing large losses of fluid through the excretion of dilute urine, ADH helps the body conserve water. In other words, ADH maintains water balance in the body. When the body dehydrates, the increased osmotic pressure of the blood is detected by special *osmoreceptors* near the supraoptic nucleus. This triggers the release of ADH from the neurohypophysis. ADH causes water to be reabsorbed from the tubules of the kidney and returned to the blood (see Chapter 31). This increases the water content of the blood, restoring the osmotic pressure to its normal lower level.

ADH has many other effects in the body as well. One of the most well known is that ADH stimulates contraction of muscles in the walls of small arteries (blood vessels that supply tissues), thus increasing blood pressure. For that reason, ADH is also known as *vasopressin* (literally, "vessel pressure substance"). Human vasopressin contains the amino acid arginine, unlike the vasopressin of some other organisms, so it is called **arginine vasopressin (AVP).**

Box 19-4 discusses some abnormalities associated with ADH.

OXYTOCIN

Oxytocin has at least two primary actions: it stimulates rhythmic contraction of smooth muscles in the uterus and it causes milk ejection from the breasts of lactating women.

Under the influence of OT, muscle-like *myoepithelial* cells surrounding the milk-storing *alveoli* of the mammary glands squeeze milk into the ducts of the breast. Figure 35-17 on p. 1083 clearly shows the structures involved. This action is very important because milk cannot be removed by suckling unless it has first been ejected into the ducts. Throughout nursing, the mechanical and psychological stimulation of the baby's suckling action triggers the release of more OT. In other words, OT secretion is regulated by a *positive feedback* mechanism: the baby suckles, which increases OT levels, which provides more milk, so the baby continues to suckle, which increases OT levels, and so on.

Box 19-4 | HEALTH matters

Antidiuretic Hormone Abnormalities

Hyposecretion of antidiuretic hormone (ADH) can lead to **diabetes insipidus,** a condition in which the patient produces abnormally large amounts of urine. Drugs such as desmopressin, which mimic ADH, can alleviate this symptom. Studies have shown that ADH may be involved in learning and memory, so investigators are looking into the possibility of administering ADH to reverse the memory loss associated with senility.

OT, together with prolactin, ensures successful nursing. Prolactin prepares the breast for milk production and stimulates cells to produce milk. The milk is not released, however, until OT stimulates its release.

The other major action of OT—its stimulation of uterine contractions—is the source of its name: oxytocin (literally "swift childbirth"). OT stimulates the uterus to strengthen the strong, muscular labor contractions that occur during childbirth. OT secretion is regulated here again by means of a positive feedback mechanism. After they have begun, uterine contractions stimulate stretch receptors in the pelvis, which triggers the release of more OT, which again stretches the pelvic receptors, and so on. Review the diagram in Box 1-3 (p. 23) outlining this positive feedback loop.

The wavelike contractions continue to some degree after childbirth, which helps the uterus expel the placenta and then return to its unstretched shape. Commercial preparations of synthetic OT have been given to stimulate contractions after childbirth to lessen the danger of uterine hemorrhage.

OT rises during sexual arousal in both males and females. The increased OT is related to rhythmic smooth muscle contractions associated with sexual arousal and orgasm.

Interestingly, recent research shows that the smell of OT can increase the feeling of social connection to the person releasing it (perhaps in sweat). This may enhance a strong feeling of trust a newborn has for its mother. The role of oxytocin as a pheromone in social recognition and bonding is still being investigated—possibly leading to a better understanding of *autism* and other disorders that involve disruptions of social bonding.

Important characteristics of the hormones secreted by the pituitary—both the adenohypophysis and the neurohypophysis—are summarized in Table 19-2.

PINEAL GLAND

The **pineal gland,** or *pineal body*, is a tiny (1 cm [about .38 inches]) structure resembling a pine nut (or a large kernel of corn) located on the dorsal aspect of the brain's diencephalon region (see Figure 19-1). It is a member of two body systems because it acts as a part of the nervous system (because it receives and processes nerve stimuli relayed from other parts of the nervous system) and as a part of the endocrine system (because it secretes hormones).

The pineal gland produces small amounts of many different hormones, but the principal hormone is melatonin. As you recall from Chapter 14, melatonin is an altered form of serotonin that acts as a hormone because it is released by neurosecretory cells of the pineal gland into the blood to regulate functions throughout the body. Recall also that melatonin levels rise and fall in a cycle related to the changing levels of sunlight throughout the day—melatonin levels rise when sunlight is absent, triggering sleepiness. Thus the pineal gland and melatonin act as important parts of a person's *biological clock*—the timekeeping mechanism of the body.

Melatonin, whose secretion is inhibited by the presence of sunlight, may also affect a person's mood. This is not surprising, given melatonin's relationship to another mood-altering molecule—serotonin. Serotonin is a precursor of melatonin, making both molecules structurally similar. A mental disorder called *seasonal affective disorder (SAD)*, in which a patient suffers severe depression only in winter (when there are fewer hours of daylight), has been linked to the pineal gland. Patients suffering from this "winter depression" are often advised to expose themselves to special high-intensity lights for several hours each evening during the winter months. Apparently, light stimulates the pineal gland for a longer period, which shifts the phase of melatonin peaks in the bloodstream. For reasons not fully understood, this phase shift often reduces or eliminates

TABLE 19-2 Hormones of the Pituitary Gland

HORMONE	SOURCE	TARGET	PRINCIPAL ACTION
Growth hormone (GH) (somatotropin [STH])	Adenohypophysis (somatotrophs)	General	Promotes growth by stimulating protein anabolism and fat mobilization
Prolactin (PRL) (lactogenic hormone)	Adenohypophysis (lactotrophs)	Mammary glands (alveolar secretory cells)	Promotes milk secretion
Thyroid-stimulating hormone (TSH)*	Adenohypophysis (thyrotrophs)	Thyroid gland	Stimulates development and secretion in the thyroid gland
Adrenocorticotropic hormone (ACTH)*	Adenohypophysis (corticotrophs)	Adrenal cortex	Promotes development and secretion in the adrenal cortex
Follicle-stimulating hormone (FSH)*	Adenohypophysis (gonadotrophs)	Gonads (primary sex organs)	*Female:* promotes development of ovarian follicle; stimulates estrogen secretion *Male:* promotes development of testes; stimulates sperm production
Luteinizing hormone (LH)*	Adenohypophysis (gonadotrophs)	Gonads	*Female:* triggers ovulation; promotes development of corpus luteum *Male:* stimulates production of testosterone
Antidiuretic hormone (ADH), or arginine vasopressin (AVP)	Neurohypophysis	Kidney	Promotes water retention by kidney tubules; raises blood pressure by stimulating muscles in walls of small arteries
Oxytocin (OT)	Neurohypophysis	Uterus and mammary glands	Stimulates uterine contractions; stimulates ejection of milk into ducts of mammary glands; involved in social bonding

*Tropic hormones.

symptoms of depression. Apparently, keeping the body's clock well timed is important for maintaining a healthy mood.

| QUICK CHECK |

4. Where are the hormones of the neurohypophysis manufactured? From which location in the body are they released into the bloodstream?
5. Name the two hormones of the neurohypophysis.
6. How does the pineal gland adjust the body's biological clock?

THYROID GLAND

Structure of the Thyroid Gland

Two large **lateral lobes** and a narrow connecting isthmus make up the **thyroid gland** (Figure 19-9). Often a thin wormlike piece of thyroid tissue, called the *pyramidal lobe*, extends upward from the isthmus. The weight of the gland in the adult is variable, but it is around 30 grams (1 ounce). The thyroid is located in the neck, on the anterior and lateral surfaces of the trachea, just below the larynx.

Thyroid tissue is composed of tiny structural units called **follicles,** the site of thyroid hormone synthesis. Each follicle is a small hollow sphere with a wall of simple cuboidal glandular epithelium (Figure 19-10). The interior is filled with a thick fluid called **thyroid colloid.** The colloid is produced by the cuboidal cells of the follicle wall (**follicular cells**) and contains protein-iodine complexes known as **thyroglobulins**—the precursors of thyroid hormones. Scattered around the outside of the follicles are *parafollicular cells,* which produce a hormone called calcitonin (CT).

Thyroid Hormone

The substance that is often called *thyroid hormone* (TH) is actually two different hormones. The most abundant TH is **tetraiodothyronine (T_4),** or **thyroxine.** The other is called **triiodothyronine (T_3).** One molecule of T_4 contains four iodine atoms, and one molecule of T_3 contains three iodine atoms. After synthesizing a preliminary form of its hormones, the thyroid gland stores considerable amounts of them before secreting them (Figure 19-11). This is unusual because none of the other endocrine glands stores its hormones in another form for later release. T_3 and T_4 form in the colloid of the follicles on globulin molecules, forming thyroglobulin complexes. When they are to be released, T_3 and T_4 detach from the globulin and enter the blood. Once in the bloodstream, however, they attach to plasma proteins, principally a globulin called *thyroid-binding globulin* (TBG) and albumin, and circulate as a hormone-globulin complex. When they near their target cells, T_3 and T_4 detach from the plasma globulin.

Although the thyroid gland releases about 20 times more T_4 than T_3, T_3 is much more potent than T_4 and is considered by physiologists to be the principal thyroid hormone. Why is this? T_4 binds more strongly to plasma globulins than T_3, so T_4 is not removed from the blood by target cells as quickly as T_3. The small amount of T_4 that enters target tissues is usually converted to T_3. Add this to the fact that experiments have shown that T_3 binds more efficiently than T_4 to nuclear receptors in target cells, and the evidence is overwhelming that T_3 is the principal thyroid hormone. Although T_4 may influence target cells to some extent, its major importance is as a precursor to T_3. Such hormone precursors are often called *prohormones.*

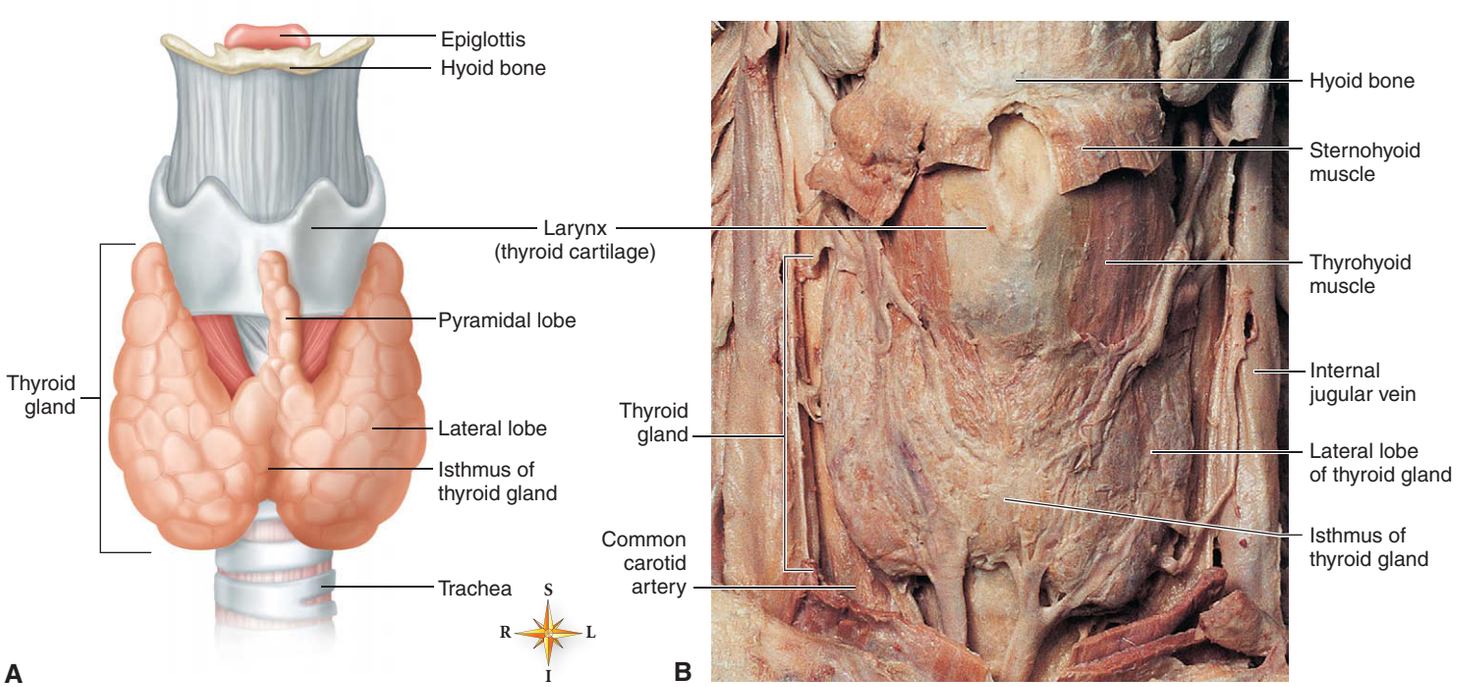


FIGURE 19-9

Thyroid gland. A, In this drawing, the relationship of the thyroid to the larynx (voice box) and to the trachea is easily seen. **B,** In this photo of a dissected cadaver, the location of the thyroid relative to the carotid arteries and jugular veins is seen.

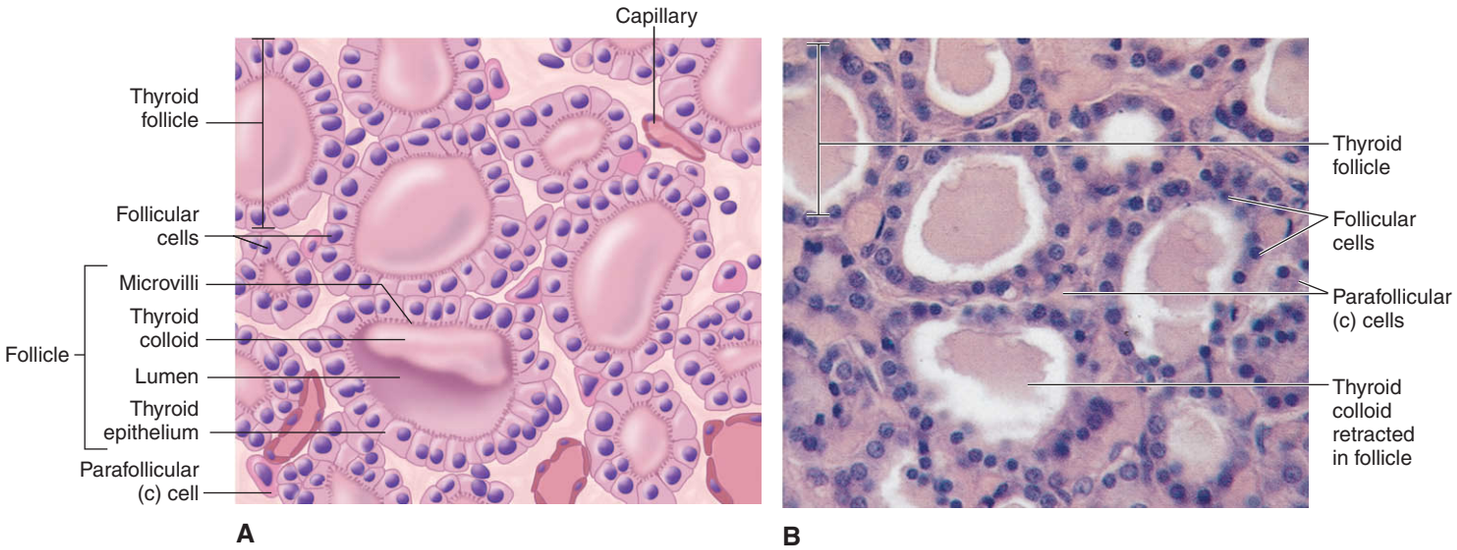
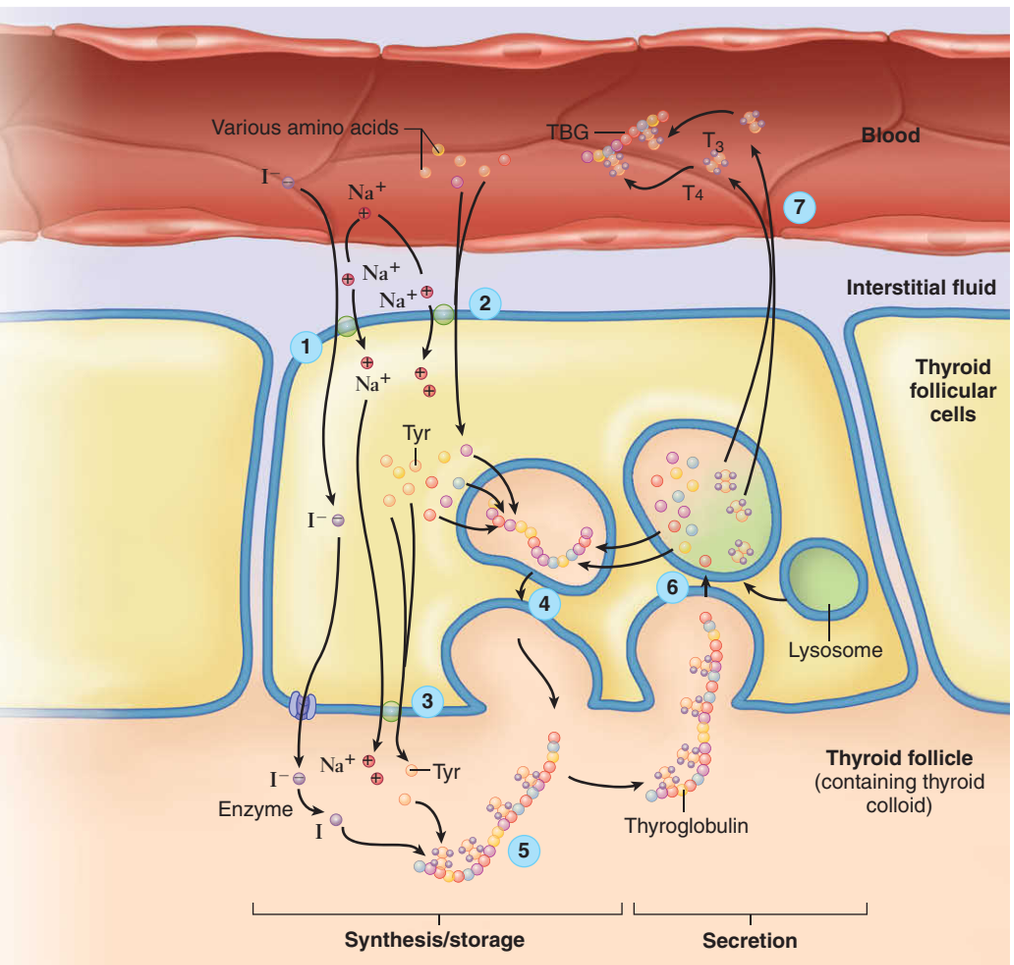


FIGURE 19-10

Thyroid gland tissue. In the drawing **(A)** and the photomicrograph **(B)** note that each of the thyroid follicles is filled with colloid. In the micrograph (×140), the thyroid colloid has separated from the follicular cells during preparation of the specimen.



1. **Step 1.** Iodide ions (I^-) present in the blood enter follicular cells in the thyroid by sodium cotransport (see Box 4-3, p. 96). I^- then moves into the thyroid follicle through an ion channel, after which it is converted to iodine (I).
2. **Step 2.** At the same time, various amino acids (including tyrosine) enter follicular cells by sodium cotransport.
3. **Step 3.** Tyrosine amino acids move into the follicle.
4. **Step 4.** Some of the amino acids form a polypeptide, which is released into the follicle to be used as a structural "backbone" for thyroglobulin.
5. **Step 5.** The iodine (I) and tyrosine (Tyr) molecules are added to the polypeptide backbone to form thyroglobulin.
6. **Step 6.** When needed, thyroglobulin molecules move into follicular cells by endocytosis, where they are digested and thus release "free" T_3 and T_4 molecules.
7. **Step 7.** Thyroid hormones (T_3 and T_4) are secreted into the bloodstream, where they bind to plasma proteins called *thyroid-binding globulins (TBGs)* and travel to other parts of the body.

FIGURE 19-11

Synthesis, storage, and release of thyroid hormone (T_3 and T_4).

UNIT 3

Thyroid hormone helps regulate the metabolic rate of all cells, as well as the processes of cell growth and tissue differentiation (Box 19-5). Because thyroid hormone can potentially interact with any cell in the body, it is said to have a "general" target.

Calcitonin

Besides thyroid hormone (T_3 and T_4), the thyroid gland also produces a hormone called **calcitonin (CT).** You might wonder why some hormones of the thyroid qualify for the name "thyroid hormone," whereas calcitonin does not. The answer lies in the simple fact that for many years, we had no idea that a hormone other than thyroid hormone was produced by the thyroid gland. By the time calcitonin was discovered, and later shown to be made in the thyroid gland, the term *thyroid hormone* was too well established to change it easily.

Produced by *parafollicular cells* (cells associated with the thyroid follicles) called **C cells,** calcitonin influences the processing of calcium by bone cells. Calcitonin apparently controls calcium content of the blood by increasing bone formation by osteoblasts and inhibiting bone breakdown by osteoclasts. This

Box 19-5 | HEALTH matters

Thyroid Hormone Abnormalities

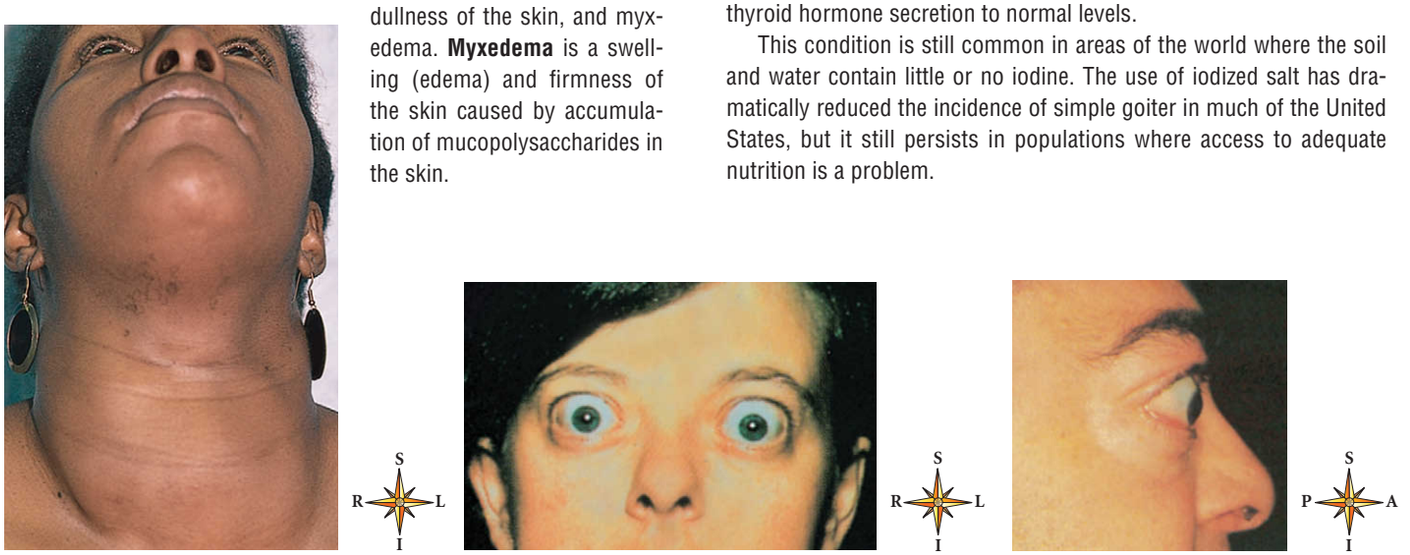
Hypersecretion of thyroid hormone occurs in **Graves disease,** which is thought to be an autoimmune condition. Graves disease patients may suffer from unexplained weight loss, nervousness, increased heart rate, and **exophthalmos** (protrusion of the eyeballs resulting, in part, from edema of tissue at the back of the eye socket; see parts *B* and *C* of the figure).

Hyposecretion of thyroid hormone during growth years may lead to **cretinism,** a condition characterized by a low metabolic rate, retarded growth and sexual development, and possibly mental retardation. People with profound manifestations of this condition are said to have deformed *dwarfism* (as opposed to the proportional dwarfism caused by hyposecretion of growth hormone). Hyposecretion later in life produces a condition characterized by decreased metabolic rate, loss of mental and physical vigor, gain in weight, loss of hair, yellow dullness of the skin, and myxedema. **Myxedema** is a swelling (edema) and firmness of the skin caused by accumulation of mucopolysaccharides in the skin.

In a condition called **simple goiter,** the thyroid enlarges when there is a lack of iodine in the diet (part *A* of figure). This condition is an interesting example of how the feedback control mechanisms illustrated in Figure 19-6 operate.

Because iodine is required for the synthesis of T_3 and T_4, lack of iodine in the diet results in a drop in the production of these hormones. When the reserve (in thyroid colloid) is exhausted, feedback informs the hypothalamus and adenohypophysis of the deficiency. In response, the secretion of thyrotropin-releasing hormone (TRH) and thyroid-stimulating hormone (TSH) increases in an attempt to stimulate the thyroid to produce more thyroid hormone. Because there is no iodine available to do this, the only effect is to increase the size of the thyroid gland. This information feeds back to the hypothalamus and adenohypophysis, and both increase their secretions in response. Thus the thyroid gets larger and larger and larger—all in a futile attempt to increase thyroid hormone secretion to normal levels.

This condition is still common in areas of the world where the soil and water contain little or no iodine. The use of iodized salt has dramatically reduced the incidence of simple goiter in much of the United States, but it still persists in populations where access to adequate nutrition is a problem.



A **B** **C**

Thyroid hormone abnormalities. A, Simple goiter. **B,** Exophthalmos goiter (anterior view). **C,** Exophthalmos goiter (lateral view).

TABLE 19-3 Hormones of the Thyroid and Parathyroid Glands

HORMONE	SOURCE	TARGET	PRINCIPAL ACTION
Triiodothyronine (T_3)	Thyroid gland (follicular cells)	General	Increases rate of metabolism
Tetraiodothyronine (T_4), or thyroxine	Thyroid gland (follicular cells)	General	Increases rate of metabolism (usually converted to T_3 first)
Calcitonin (CT)	Thyroid gland (parafollicular cells)	Bone tissue	Increases calcium storage in bone, lowering blood Ca^{++} levels
Parathyroid hormone (PTH), or parathormone	Parathyroid glands	Bone tissue and kidney	Increases calcium removal from storage in bone and produces the active form of vitamin D in the kidneys, increasing absorption of calcium by intestines and increasing blood Ca^{++} levels

Box 19-6 | FYI

Osteoporosis

Calcitonin contained in nasal spray can be used for the treatment of **osteoporosis.** This treatment is designed especially for patients who are unable to tolerate the more common estrogen replacement therapy. Osteoporosis is a condition that results in brittle and easily fractured bones and is a common disorder affecting millions of postmenopausal women (see Chapter 8, p. 216). The nasal spray delivery mechanism permits easier administration of the drug, called Miacalcin (synthetic calcitonin), to patients suffering from this often crippling disorder. By increasing calcium storage in bone, calcitonin can strengthen weakened bone tissue and help prevent spontaneous fractures, which can occur if the disease is allowed to progress without treatment.

means more calcium is removed from the blood by the osteoblasts, and less calcium is released into the blood by osteoclasts. Calcitonin in humans does not seem to have a great effect—but it may slightly decrease blood calcium levels and promote conservation of hard bone matrix (Box 19-6). Parathyroid hormone, discussed later, is an antagonist to calcitonin, because it has the opposite effect. Together, calcitonin and parathyroid hormone help maintain calcium homeostasis (look ahead to Figure 19-14 on p. 576).

Table 19-3 summarizes hormones of the thyroid gland.

PARATHYROID GLANDS

Structure of the Parathyroid Glands

There are usually four or five **parathyroid glands** embedded in the posterior surface of the thyroid's lateral lobes (Figure 19-12).

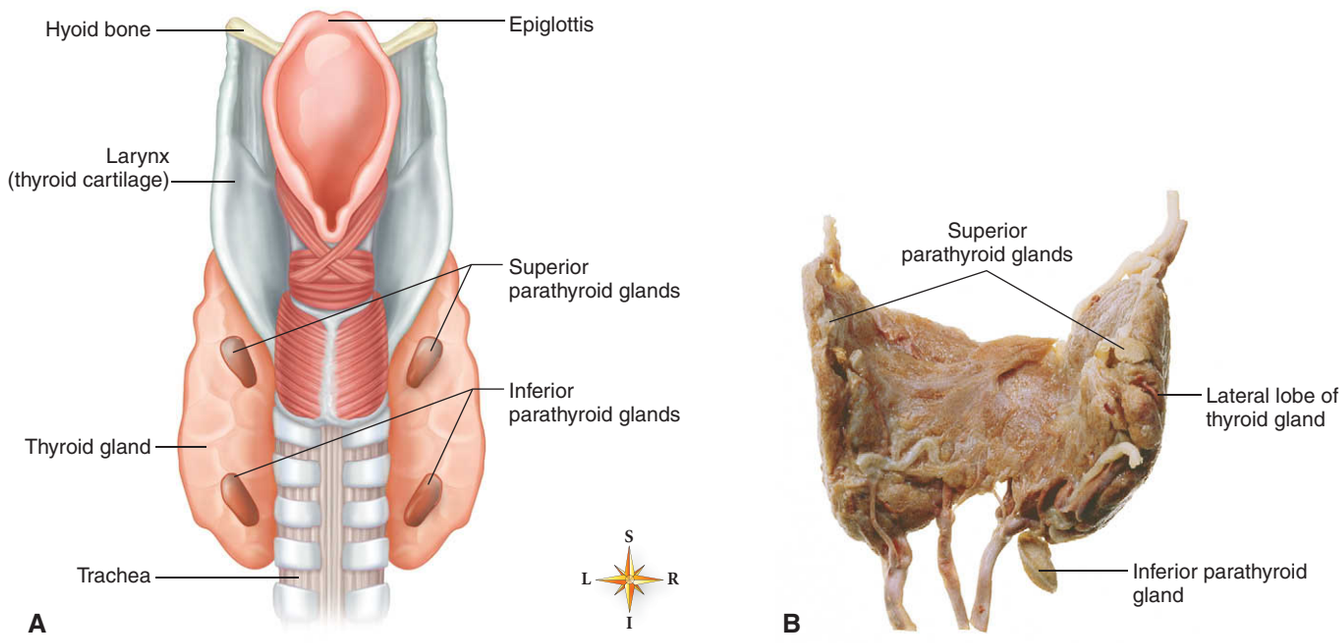


FIGURE 19-12

Parathyroid gland. A, In this drawing from a posterior view, note the relationship of the parathyroid glands to each other, to the thyroid gland, to the larynx (voice box), and to the trachea. **B,** Photo of a cadaver dissection (also from a posterior view) showing several parathyroid glands on the posterior surface of the lateral lobes of an isolated thyroid gland.

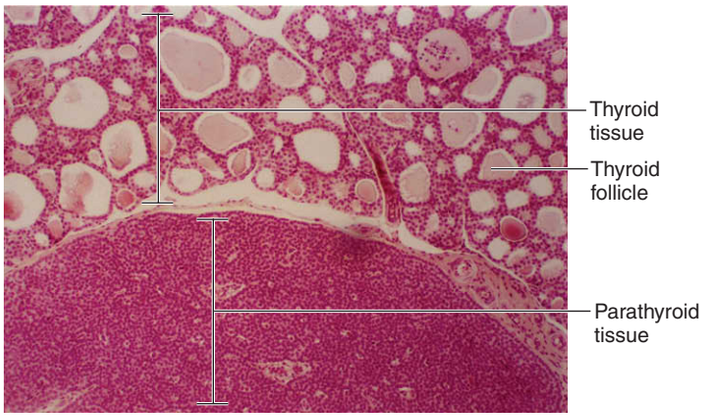


FIGURE 19-13

Parathyroid tissue. This microscopic specimen shows a portion of a parathyroid gland bordered by the surrounding thyroid tissue.

They appear as tiny rounded bodies within thyroid tissue formed by compact, irregular rows of cells (Figure 19-13).

Parathyroid Hormone

The parathyroid glands secrete **parathyroid hormone (PTH),** or *parathormone* (see Table 19-3). PTH is the main hormone the body uses to maintain calcium homeostasis. PTH acts on bone and kidney cells by increasing the release of calcium into the blood. The bone cells are especially affected, causing less new bone to be formed and more old bone to be dissolved, yielding calcium and phosphate. These minerals are then free to move into the blood, elevating blood levels of calcium and phosphate. In the kidney, however, only calcium is reabsorbed from urine into the blood. Under the influence of PTH, phosphate is secreted by kidney cells *out* of the blood and into the urine to be excreted. PTH also increases the body's absorption of calcium from food by activating **vitamin D** *(cholecalciferol)* in the kidney, which then permits Ca^{++} to be transported through intestinal cells and into the blood.

The maintenance of calcium homeostasis, achieved through the interaction of PTH and calcitonin, is very important for healthy survival (Figure 19-14). You learned in Chapter 8 that adequate calcium in the blood is needed to build and maintain a healthy skeleton. Normal neuromuscular excitability, blood clotting, cell membrane permeability, and normal functioning of certain enzymes all depend on the maintenance of normal levels of calcium in the blood. For example, hyposecretion of PTH can lead to hypocalcemia (Box 19-7). Hypocalcemia increases neuromuscular irritability—sometimes so much that it produces muscle spasms and convulsions. Conversely, high blood calcium levels decrease the irritability of muscle and nerve tissue so that constipation, lethargy, and even coma can result.

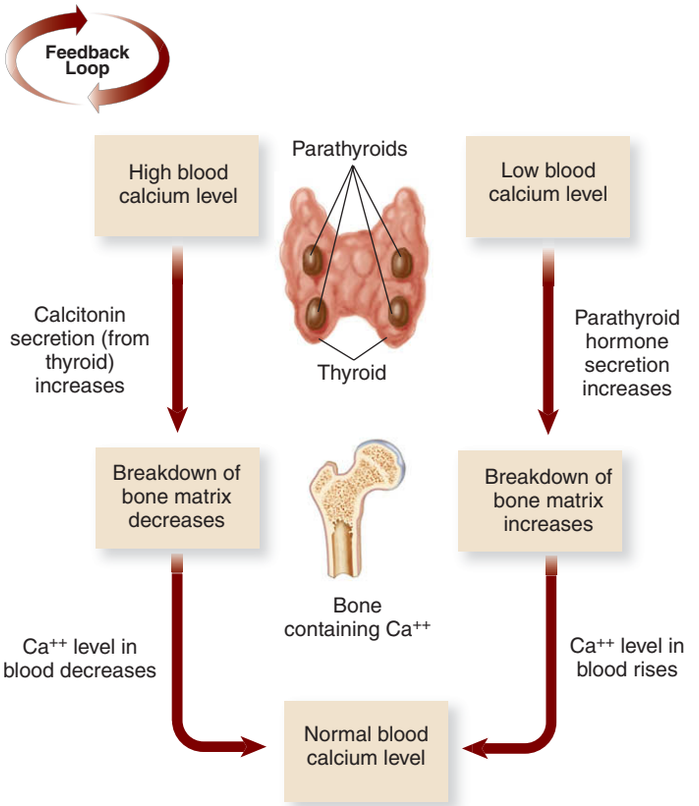


FIGURE 19-14

Regulation of blood calcium levels. Calcitonin and parathyroid hormones have antagonistic (opposite) effects on calcium concentration in the blood. (Also see Figure 18-11.)

| QUICK CHECK |

7. Where is the thyroid located? What does it look like?
8. Thyroid hormone is really two distinct compounds—what are they? Which of the two is considered more physiologically active?
9. How do calcitonin and parathyroid hormone act together to regulate homeostasis of blood calcium concentration?

Box 19-7 | HEALTH matters

Parathyroid Treatments

In cases of hyperparathyroidism, elevated parathyroid hormone (PTH) levels cause increases in blood calcium levels and possible development of osteoporosis and kidney stones. Treatment often involves surgical removal of one or more of the parathyroid glands.

However, knowing just how much parathyroid tissue to remove is a problem for the surgeon. If too much tissue is removed, the resulting drop in PTH below normal limits can result in **hypocalcemia** that requires a lifetime of *PTH replacement therapy.*

A special deep freezing technique permits **cryopreservation,** or frozen storage, of the removed parathyroid tissue for up to 1 year. If too much tissue was removed at the time of surgery, a "banked" portion can be reimplanted (generally below the skin in the forearm) and will function to restore normal blood PTH levels.

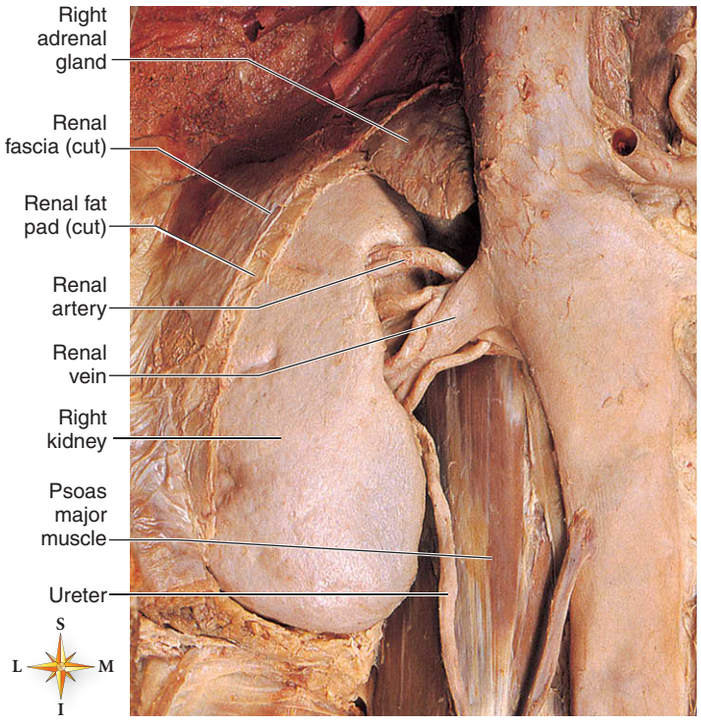


FIGURE 19-15

Location of the adrenal gland. Photograph of a cadaver dissection showing the location of the adrenal gland just superior to the kidney. Note that the adrenal glands are covered by the renal fascia but not the renal fat pad, both of which cover the kidney.

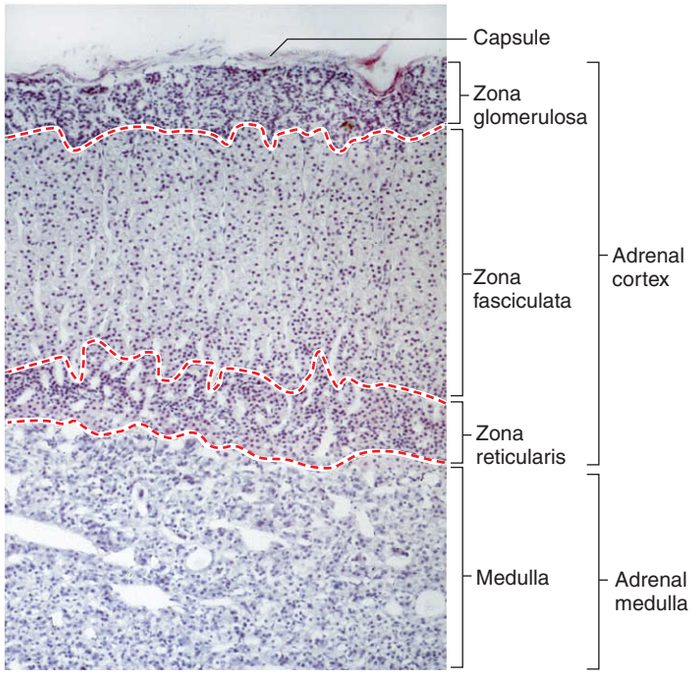


FIGURE 19-17

Adrenal tissue. The major regions of the adrenal gland are shown in a light micrograph of a stained specimen. The cortex is made up of epithelial endocrine tissue, and the medulla is instead made up of neurosecretory tissue. Compare with drawing in Figure 19-16.

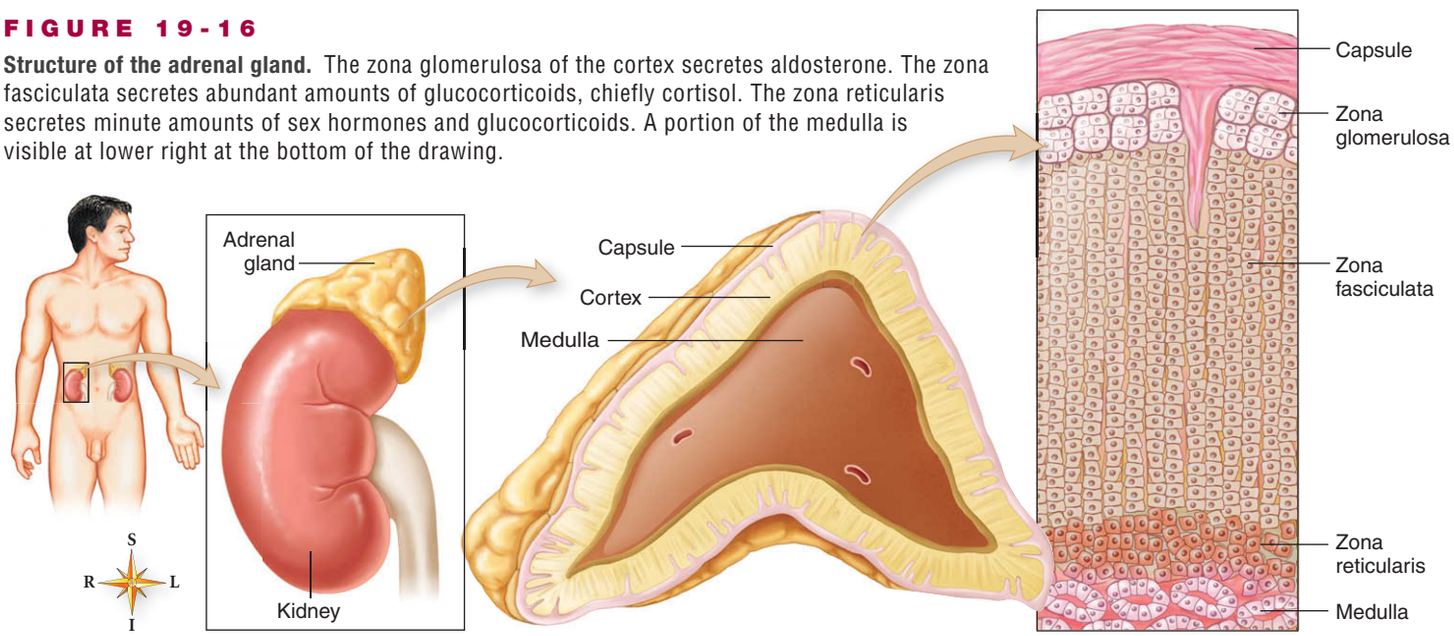
ADRENAL GLANDS

Structure of the Adrenal Glands

The **adrenal glands,** or *suprarenal glands*, are located atop the kidneys, fitting like a cap over these organs (Figure 19-15). The outer portion of the gland is called the **adrenal cortex,** and the inner portion of the gland is called the **adrenal medulla** (Figure 19-16). Even though the adrenal cortex and adrenal medulla are part of the same organ, they have different embryological origins and are structurally and functionally so different that they are often spoken of as if they were separate glands. The adrenal cortex is composed of regular endocrine tissue, but the adrenal medulla is made of neurosecretory tissue (Figure 19-17). As you might guess, each of

FIGURE 19-16

Structure of the adrenal gland. The zona glomerulosa of the cortex secretes aldosterone. The zona fasciculata secretes abundant amounts of glucocorticoids, chiefly cortisol. The zona reticularis secretes minute amounts of sex hormones and glucocorticoids. A portion of the medulla is visible at lower right at the bottom of the drawing.



UNIT 3

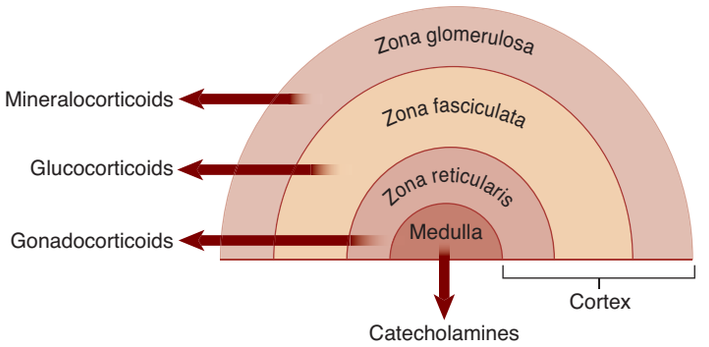


FIGURE 19-18
Adrenal hormones.

these tissues synthesizes and secretes a different set of hormones (Figure 19-18 and Table 19-4).

Adrenal Cortex

The adrenal cortex is composed of three distinct layers, or zones, of secreting cells (see Figures 19-16 to 19-18). Starting with the zone directly under the outer connective tissue capsule of the gland, they are the **zona glomerulosa, zona fasciculata,** and **zona reticularis.** Cells of the outer zone secrete a class of hormones called *mineralocorticoids.* Cells of the middle zone secrete *glucocorticoids.* The inner zone secretes small amounts of *glucocorticoids* and *gonadocorticoids* (sex hormones). All these cortical hormones are steroids, so together they are known as *corticosteroids.*

MINERALOCORTICOIDS

Mineralocorticoids, as their name suggests, have an important role in regulating how mineral salts (electrolytes) are processed in the body. In the human, **aldosterone** is the only physiologically important mineralocorticoid. Its primary function is the maintenance of sodium homeostasis in the blood. Aldosterone accomplishes this by increasing sodium reabsorption in the kidneys. Sodium ions are reabsorbed from the urine back into the blood in exchange for potassium or hydrogen ions. In this way, aldosterone not only adjusts blood sodium levels but also can influence potassium and pH levels in the blood.

Because the reabsorption of sodium ions causes water to also be reabsorbed (partly by triggering the secretion of ADH), aldosterone promotes water retention by the body. Altogether, aldosterone can increase sodium and water retention and promote the loss of potassium and hydrogen ions.

Aldosterone secretion is controlled mainly by the **renin-angiotensin-aldosterone system (RAAS)** and by blood potassium concentration. The RAAS (Figure 19-19) operates as indicated in this sequence of steps:

1. When the incoming blood pressure in the kidneys drops below a certain level, a piece of tissue near the vessels (the *juxtaglomerular apparatus*) secretes *renin* into the blood.
2. **Renin,** an enzyme, causes **angiotensinogen** (a normal constituent of blood) to be converted to *angiotensin I.*
3. **Angiotensin I** circulates to the lungs, where *angiotensin-converting enzyme (ACE)* in the capillaries splits the molecule, forming *angiotensin II.*
4. **Angiotensin II** circulates to the adrenal cortex, where it stimulates the secretion of aldosterone. (Some aldosterone is also synthesized in the heart and blood vessels.)
5. **Aldosterone** causes increased reabsorption of sodium, which causes increased water retention. As water is retained, the volume of blood increases. The increased volume of blood creates higher blood pressure—which then causes the renin-angiotensin-aldosterone system to stop.

The renin-angiotensin-aldosterone system is a negative feedback mechanism that helps maintain homeostasis of blood pressure. One way is to increase the overall volume of blood, a function of aldosterone. Another way is by the action of angiotensin II, which increases the tone of smooth muscle in the wall of arteries—thus increasing arterial blood pressure. A type of drug called an *ACE inhibitor* reduces abnormally high blood pressure by blocking the formation of angiotensin II (see step 3 above) and thus reducing both of these blood-pressure enhancing effects.

GLUCOCORTICOIDS

The chief glucocorticoids secreted by the zona fasciculata of the adrenal cortex are **cortisol** (also called *hydrocortisone*), *cortisone,* and

TABLE 19-4 Hormones of the Adrenal Glands

HORMONE	SOURCE	TARGET	PRINCIPAL ACTION
Aldosterone	Adrenal cortex (zona glomerulosa)	Kidney	Stimulates kidney tubules to conserve sodium, which in turn triggers the release of ADH and the resulting conservation of water by the kidney
Cortisol (hydrocortisone)	Adrenal cortex (zona fasciculata)	General	Influences metabolism of food molecules; in large amounts, it has an antiinflammatory effect
Adrenal androgens	Adrenal cortex (zona reticularis)	Sex organs, other effectors	Exact role uncertain but may support sexual function
Adrenal estrogens	Adrenal cortex (zona reticularis)	Sex organs	Thought to be physiologically insignificant
Epinephrine (Epi) (adrenaline)	Adrenal medulla	Sympathetic effectors	Enhances and prolongs the effects of the sympathetic division of the autonomic nervous system
Norepinephrine (NE)	Adrenal medulla	Sympathetic effectors	Enhances and prolongs the effects of the sympathetic division of the autonomic nervous system

ADH, Antidiuretic hormone.

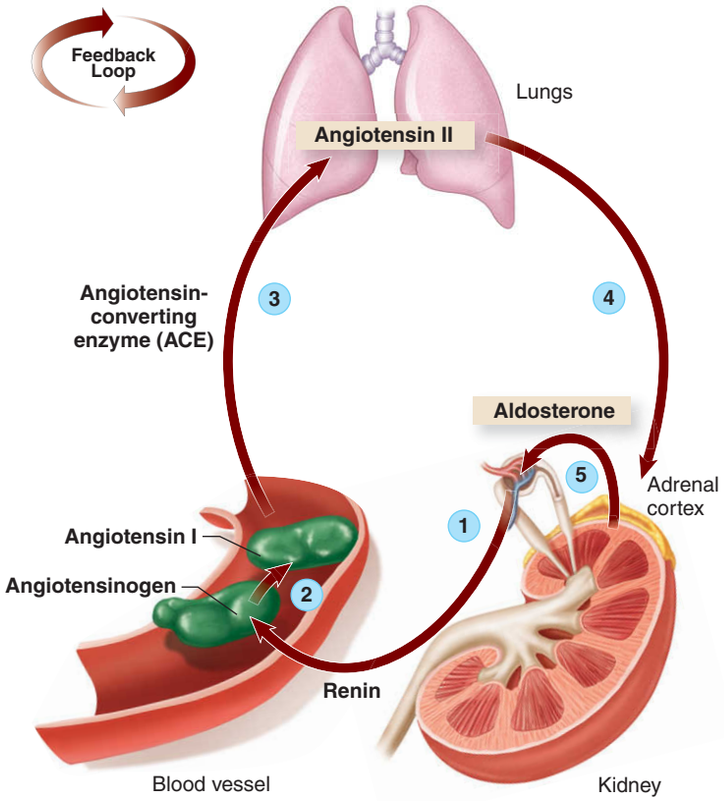


FIGURE 19-19

Renin-angiotensin-aldosterone system (RAAS) for regulating aldosterone secretion. The numbers correspond to the steps outlined in the text.

corticosterone. Of these, only cortisol is secreted in significant quantities in the human. Glucocorticoids affect every cell in the body. Although much remains to be discovered about their precise mechanisms of action, we do know enough to make some generalizations:

- Glucocorticoids accelerate the breakdown of proteins into amino acids (except in liver cells). These "mobilized" amino acids move out of the tissue cells and into the blood. From there, they circulate to the liver cells, where they are changed to glucose in a process called *gluconeogenesis*. A prolonged high blood concentration of glucocorticoids in the blood therefore results in a net loss of tissue proteins ("tissue wasting") and hyperglycemia (high blood glucose). Glucocorticoids are protein mobilizing, gluconeogenic, and hyperglycemic.
- Glucocorticoids tend to accelerate mobilization of both lipids from adipose cells and lipid catabolism by nearly every cell in the body. In other words, glucocorticoids tend to cause a shift from carbohydrate catabolism to lipid catabolism as an energy source. The mobilized lipids may also be used in the liver for gluconeogenesis. This effect contributes to the hyperglycemic effect already observed.
- Glucocorticoids are essential for maintaining a normal blood pressure. Without adequate amounts of glucocorticoids in the blood, the hormones norepinephrine and epinephrine cannot produce their vasoconstricting effect on blood vessels, and blood pressure falls. In other words, glucocorticoids exhibit *permissiveness* in that they permit norepinephrine and epinephrine to have their full effects. When glucocorticoids are present in high concentrations for a prolonged time, they may elevate blood pressure beyond normal (hypertension).
- A high blood concentration of glucocorticoids rather quickly causes a marked decrease in the number of white blood cells called *eosinophils* in the blood (eosinopenia) and marked atrophy of lymphatic tissues. The thymus gland and lymph nodes are particularly affected. This in turn leads to a decrease in the number of lymphocytes and plasma cells in the blood. Because of the decreased number of lymphocytes and plasma cells (antibody-processing cells), antibody formation decreases. Antibody formation is an important part of immunity—the body's defense against infection.
- Normal amounts of glucocorticoids act with epinephrine, a hormone secreted by the adrenal medulla, to bring about normal recovery from injury produced by inflammatory agents. How they act together to bring about this antiinflammatory effect is still uncertain.
- Glucocorticoid secretion increases as part of the stress response. One advantage gained by increased secretion may be the increase in glucose available for skeletal muscles needed in fight-or-flight responses. However, prolonged stress can lead to immune dysfunction, probably as a result of prolonged exposure to high levels of glucocorticoids (see Chapter 25).
- Except during the stress response, glucocorticoid secretion is controlled mainly by means of a negative feedback mechanism that involves ACTH from the adenohypophysis.
- As with many hormones, including all the adrenal cortical hormones, glucocorticoid secretion occurs in pulses and also shows a daily pattern of pulses of different amounts of hormone secretion (Figure 19-20).

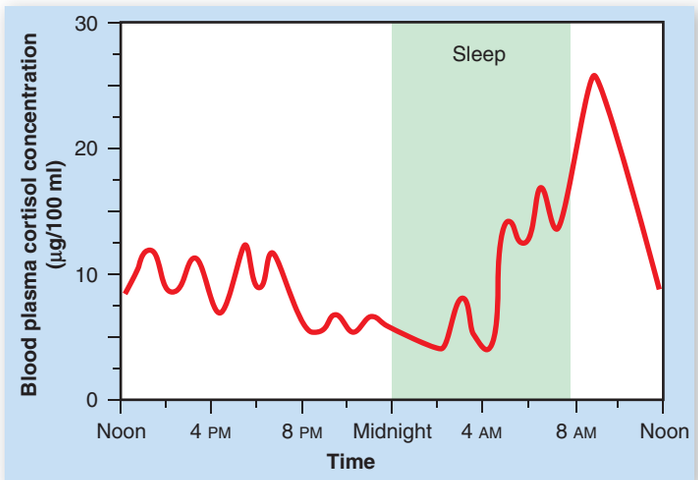


FIGURE 19-20

Secretion of cortisol. As with many hormones, the amount of cortisol secreted into the blood varies chaotically throughout the day. However, pulses of increased hormone secretion occur occasionally with the highest peaks shortly before and after waking. Pulsing secretion (in response to specific conditions in the body) with a daily, or *diurnal,* pattern is seen in many hormones—including all of the adrenal cortical hormones.

GONADOCORTICOIDS

The term *gonadocorticoid* refers to sex hormones that are released from the zona fasciculata and zona reticularis of the adrenal cortex rather than the gonads. The normal adrenal cortex secretes small amounts of male hormones (androgens). Normally, not enough androgen is produced to give women masculine characteristics, but it is sufficient to influence the appearance of pubic and axillary hair in both boys and girls.

Box 19-8 discusses some adrenal cortical hormone disorders.

Adrenal Medulla

The adrenal medulla is composed of neurosecretory tissue, that is, tissue composed of neurons adapted to secrete their products into the blood rather than across a synapse. Actually, the medullary cells are modified versions of sympathetic postganglionic fibers of the autonomic nervous system. They are innervated by sympathetic preganglionic fibers, so that when the sympathetic nervous system is activated (as in the stress response), the medullary cells secrete their hormones directly into the blood.

The adrenal medulla secretes two important hormones, both of which are in the class of nonsteroid hormones called catecholamines. **Epinephrine (Epi),** or *adrenaline*, accounts for about 80% of the medulla's secretion. The other 20% is **norepinephrine** (**NE** or **NR**). You may recall that norepinephrine is also the neurotransmitter produced by postganglionic sympathetic fibers. Sympathetic effectors such as the heart, smooth muscle, and glands have receptors for norepinephrine. Both epinephrine and norepinephrine produced by the adrenal medulla can bind to the receptors of sympathetic effectors to prolong and enhance the effects of sympathetic stimulation by the autonomic nervous system (Figure 19-21).

| QUICK CHECK |

10. Distinguish between the histology of the adrenal cortex and the adrenal medulla.
11. Name some effects of cortisol in the body.
12. How does the function of the adrenal medulla overlap with the function of the autonomic nervous system?

PANCREATIC ISLETS

Structure of the Pancreatic Islets

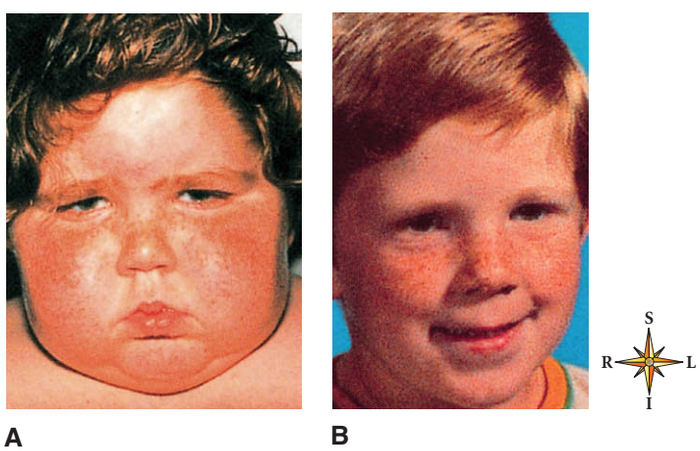
The pancreas is an elongated gland (12 to 15 cm [or about 5 to 6 inches] long) weighing up to 100 grams (3.5 ounces) (Figure 19-22). The "head" of the gland lies in the C-shaped beginning of the small intestine (duodenum), with its body extending horizontally behind the stomach and its tail touching the spleen

The tissue of the pancreas is composed of both endocrine and exocrine tissues. The endocrine portion is made up of scattered,

Box 19-8 | HEALTH matters

Adrenal Cortical Hormone Abnormalities

Hypersecretion of cortisol from the adrenal cortex often produces a collection of symptoms called **Cushing syndrome.** Hypersecretion of glucocorticoids results in a redistribution of body fat. The fatty "moon face" and thin, reddened skin characteristic of Cushing syndrome are shown in part *A* of the figure. Part *B* shows the face of the same boy 4 months after treatment. Hypersecretion of aldosterone, *aldosteronism,* leads to increased water retention and muscle weakness resulting from potassium loss. Hypersecretion of androgens can result from tumors of the adrenal cortex, called *virilizing tumors.* They are so called because the increased blood level of male hormones in women can cause them to acquire male characteristics, such as facial hair. People with Cushing syndrome may suffer from all the symptoms described above.



Cushing syndrome. A, Fatty "moon face" in a boy with Cushing syndrome. **B,** The face of the same boy 4 months after treatment.

Hyposecretion of mineralocorticoids and glucocorticoids, as in **Addison disease,** may lead to a drop in blood sodium and blood glucose, an increase in blood potassium levels, dehydration, and weight loss.

Pharmacological preparations of glucocorticoids have been used for many years to temporarily relieve the symptoms of severe inflammatory conditions such as rheumatoid arthritis. Over-the-counter creams and ointments containing hydrocortisone are widely available for use in treating the pain, itching, swelling, and redness of skin rashes.

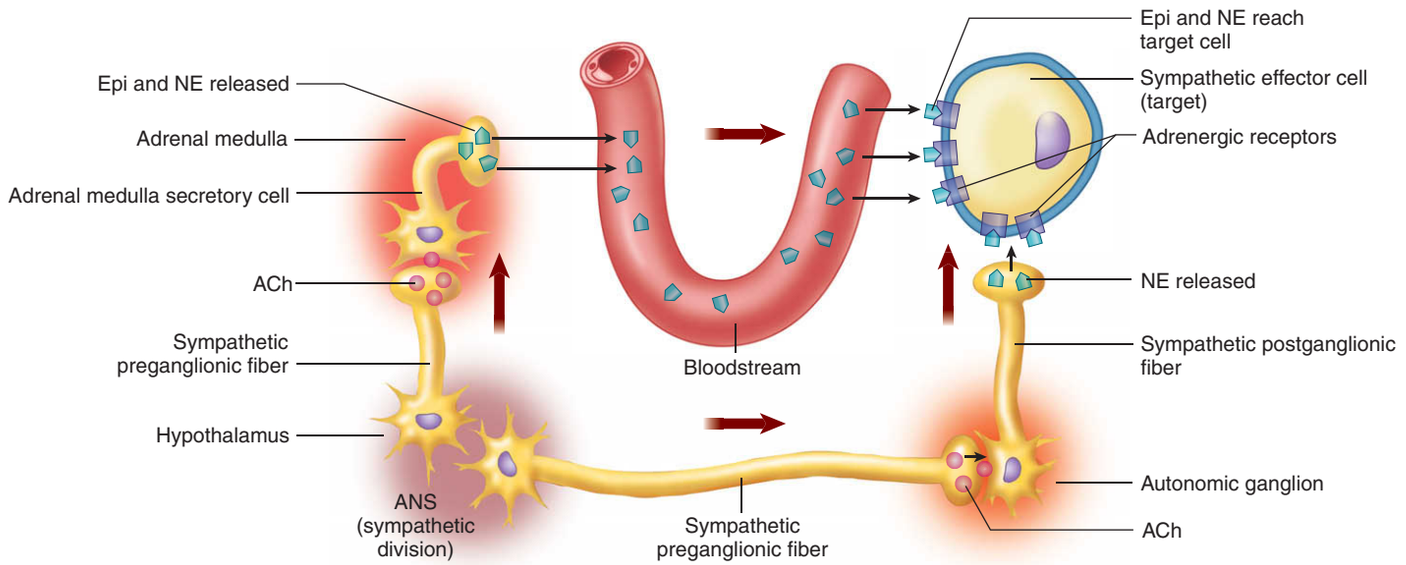


FIGURE 19-21

Combined nervous and endocrine influence on sympathetic effectors. A sympathetic center in the hypothalamus sends efferent impulses through preganglionic fibers. Some preganglionic fibers synapse with postganglionic fibers that deliver norepinephrine *(NE)* across a synapse with the effector cell. Other preganglionic fibers synapse with postganglionic neurosecretory cells in the adrenal medulla. These neurosecretory cells secrete epinephrine *(Epi)* and norepinephrine into the bloodstream, where they travel to the target cells (sympathetic effectors). Compare this figure with Figure 18-1. *ANS,* Autonomic nervous system; *ACh,* acetylcholine.

tiny islands of cells, called **pancreatic islets** *(islets of Langerhans)* that account for only about 2% or 3% of the total mass of the pancreas. These hormone-producing islets are surrounded by cells called *acini*, which secrete a serous fluid containing digestive enzymes into ducts that drain into the small intestine (see Figure 19-22). The digestive roles of the pancreas are discussed in Chapters 28 and 29. For the moment, we will concentrate on the endocrine part of this gland, the pancreatic islets.

Each of the 1 to 2 million pancreatic islets in the pancreas contains a combination of four primary types of endocrine cells, all joined to each other by gap junctions. Each type of cell secretes a different hormone, but the gap junctions may allow for some coordination of these functions as a single secretory unit. One type of pancreatic islet cell is the **alpha cell** (α or *A cell*), which secretes the hormone glucagon. **Beta cells** (β *or B cells*) secrete the hormone insulin; **delta cells** (δ *or D cells*) secrete the hormone somatostatin; **pancreatic polypeptide cells** *(F,* or *PP, cells)* secrete pancreatic polypeptide; and **epsilon cells** (ε *cells*) secrete the hormone ghrelin. Beta cells, which account for about three fourths of all the pancreatic islet cells, are usually found near the center of each islet, whereas cells of the other three types are

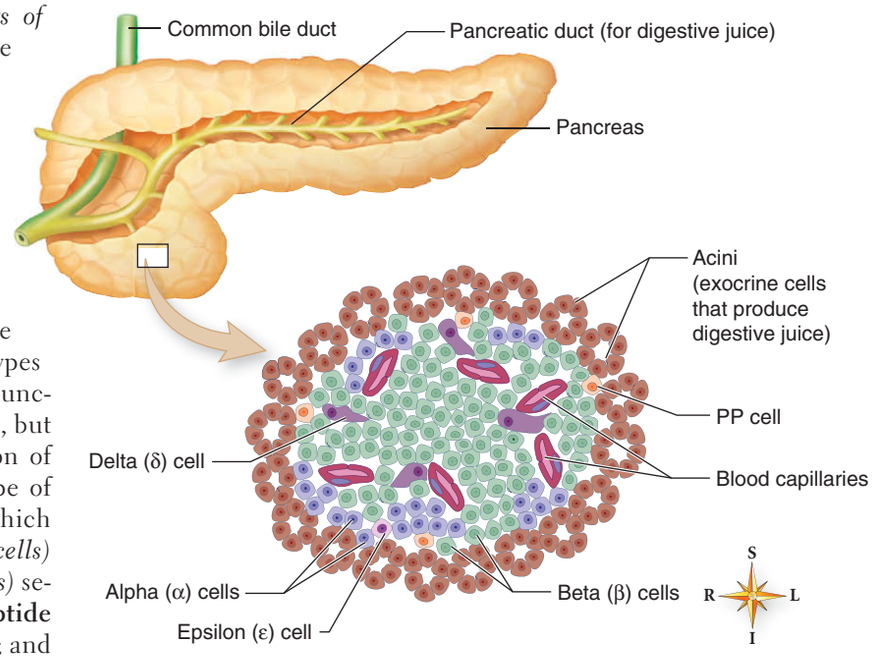


FIGURE 19-22

Pancreas. A pancreatic islet, or hormone-producing area, is evident among the pancreatic cells that produce the pancreatic digestive juice. The pancreatic islets are more abundant in the tail of the pancreas than in the body or head.

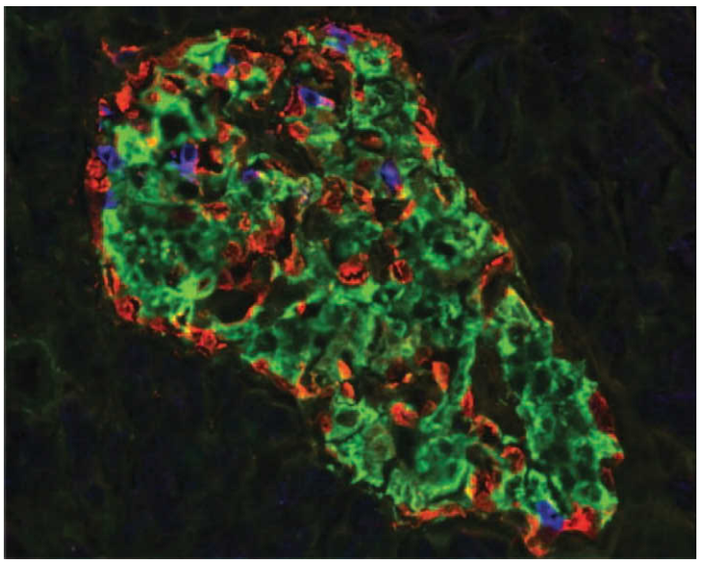


FIGURE 19-23

Cells of the pancreatic islet. A special technique of microscopy, called immunofluorescent staining, allows cells to be distinguished by the different molecules that they contain. Beta cells containing insulin appear green. Alpha cells containing glucagon appear red. Delta cells containing somatostatin appear blue.

more often found in the outer portion. Figure 19-23 shows how the different cell types can be distinguished by the microscope with special staining techniques.

Pancreatic Hormones

The pancreatic islets produce several hormones, the most important of which are described in Table 19-5 and in the following list:

Glucagon, produced by alpha cells, tends to increase blood glucose levels by stimulating the conversion of glycogen to glucose in liver cells. It also stimulates gluconeogenesis (transformation of fatty acids and amino acids into glucose) in liver cells. The glucose produced by way of the breakdown of glycogen and by gluconeogenesis is released into the bloodstream, producing a hyperglycemic effect.

Insulin, produced by beta cells, tends to promote the movement of glucose, amino acids, and fatty acids out of the blood and into tissue cells. Hence insulin tends to lower the blood concentrations of these food molecules and to promote their metabolism by tissue cells. The antagonistic effects that glucagon and insulin have on blood glucose levels are summarized in Figure 19-24 and discussed further in Chapter 30.

Somatostatin, produced by delta cells, may affect many different tissues in the body, but its primary role seems to be in regulating the other endocrine cells of the pancreatic islets. Somatostatin inhibits the secretion of glucagon, insulin, and pancreatic polypeptide. It also inhibits the secretion of growth hormone (somatotropin) from the anterior pituitary.

Pancreatic polypeptide is produced by PP (or F) cells in the periphery of pancreatic islets. Although much is yet to be learned about pancreatic polypeptide, we do know that it influences the digestion and distribution of food molecules to some degree.

Ghrelin (GHRL) is produced in tiny amounts by epsilon cells near the outer boundary of pancreatic islets. It acts by stimulating the hypothalamus to boost appetite. Since it also acts on other body tissues to slow metabolism and reduce fat burning, it may play an important role in contributing to obesity. GHRL is also secreted by the gastric mucosa.

All of the pancreatic hormones work together as a team to maintain a homeostasis of nutrient molecules (glucose, fatty acids, and amino acids). More about their respective roles in overall nutrient metabolism is discussed in Chapter 30.

TABLE 19-5 Hormones of the Pancreatic Islets

HORMONE	SOURCE	TARGET	PRINCIPAL ACTION
Glucagon	Pancreatic islets (alpha [α] cells, or A cells)	General	Promotes movement of glucose from storage and into the blood
Insulin	Pancreatic islets (beta [β] cells, or B cells)	General	Promotes movement of glucose out of the blood and into cells
Somatostatin (SS)	Pancreatic islets (delta [δ] cells, or D cells)	Pancreatic cells and other effectors	Can have general effects in the body, but primary role seems to be regulation of secretion of other pancreatic hormones
Pancreatic polypeptide (PP)	Pancreatic islets (pancreatic polypeptide [PP] or F cells)	Intestinal cells and other effectors	Exact function uncertain but seems to influence absorption in the digestive tract
Ghrelin (GHRL)	Stomach mucosa, pancreatic islets (epsilon [ε] cells)	Hypothalamus; other diverse tissues	Stimulates hypothalamus to boost appetite; affects energy balance in various tissues

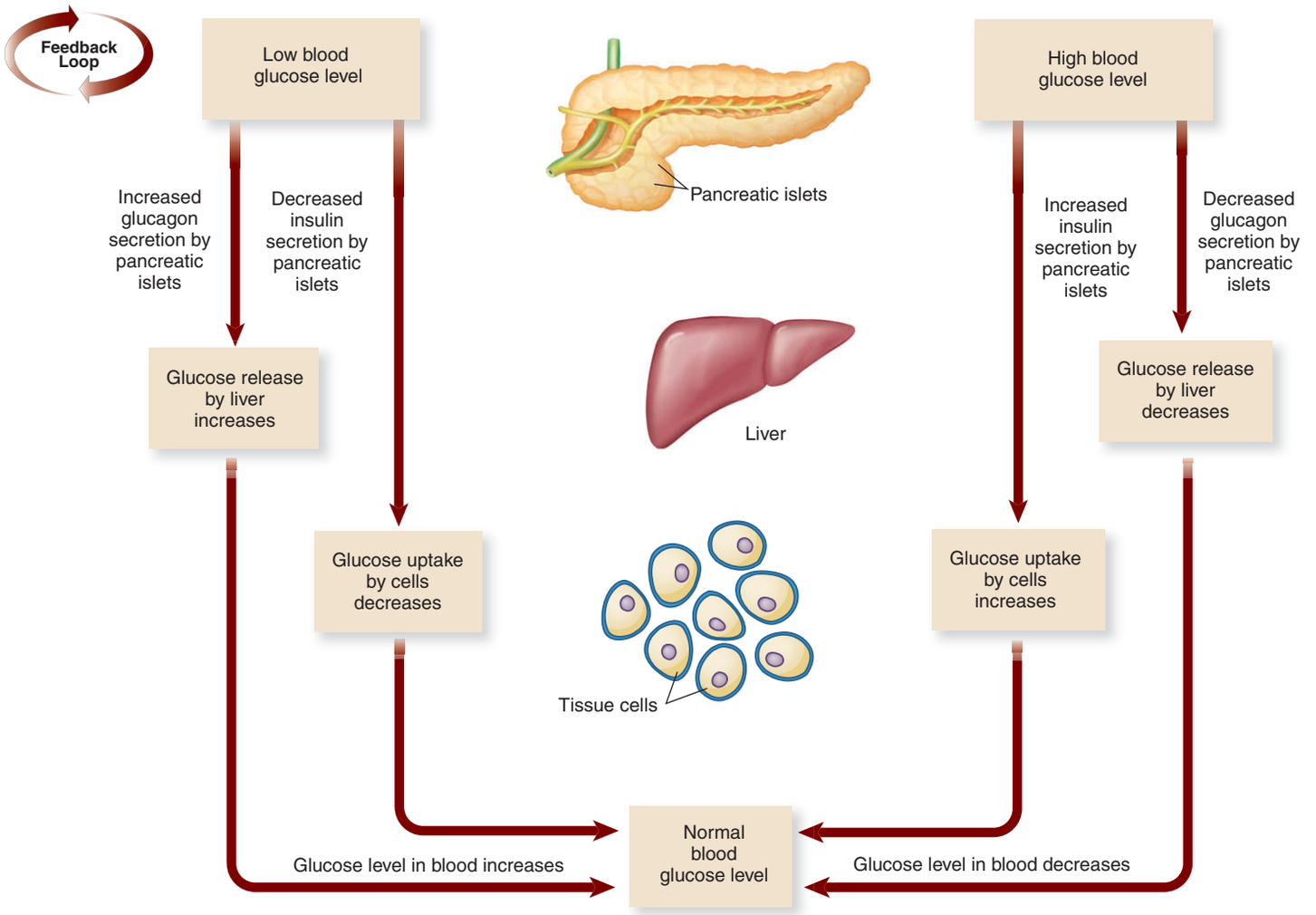


FIGURE 19-24

Regulation of blood glucose levels. Insulin and glucagon, two of the major pancreatic hormones, have antagonistic (opposite) effects on glucose concentration in the blood. Of course, many other hormones, such as GH, cortisol, and others, also influence blood glucose levels.

| A&P CONNECT |

Diabetes mellitus (DM) is one of the most common endocrine disorders. It involves a variety of abnormal effects in the body, all related to either hyposecretion of insulin or a reduction of insulin effects in target cells (or both). For a brief discussion of this disorder, and a chart showing the causes of the common symptoms of DM, check out ***Diabetes Mellitus*** online at ***A&P Connect.***

evolve

| QUICK CHECK |

13. Name two of the four principal hormones secreted by the pancreatic islets.
14. In what way do insulin and glucagon exert antagonistic influences on the concentration of glucose in the blood?

GONADS

Gonads are the primary sex organs in the male (*testes*; singular, *testis*) and in the female (*ovaries*). Each is structured differently, and each produces its own unique set of hormones (Table 19-6).

Testes

The testes are paired organs within a sac of skin called the *scrotum*, which hangs from the groin area of the trunk (see Figure 18-2 on p. 547). They are composed mainly of coils of sperm-producing

TABLE 19-6 Examples of Additional Hormones of the Body

HORMONE	SOURCE	TARGET	PRINCIPAL ACTION
Cholecalciferol (vitamin D_3)	Skin, liver, kidney (in progressive steps)	Intestines, bones, most other tissues	Promotes calcium absorption from food, regulates mineral balance in bones, regulates growth and differentiation of many cell types
Dehydroepiandrosterone (DHEA)	Adrenal gland, testis, ovary, other tissues	Converted to other hormones	Eventually converted to estrogens, testosterone, or both (see Figure 18-5)
Melatonin	Pineal gland	Timekeeping tissues of the nervous system	Helps "set" the biological clock mechanisms of the body by signaling light changes during the day, month, and seasons; may help induce sleep
Testosterone	Testis (small amounts in adrenal and ovary)	Sperm-producing tissues of testis, muscles, other tissues	Stimulates sperm production, stimulates growth and maintenance of male sexual characteristics, promotes muscle growth
Estrogen including estradiol (E_2) and estrone	Ovary and placenta (small amounts in adrenal and testis)	Uterus, breasts, other tissues	Stimulates development of female sexual characteristics, breast development, bone and nervous system maintenance
Progesterone	Ovary and placenta	Uterus, mammary glands, other tissues	Helps maintain proper conditions for pregnancy
Human chorionic gonadotropin (hCG)	Placenta	Ovary	Stimulates secretion of estrogen and progesterone during pregnancy
Human placental lactogens (hPLs)	Placenta	Mammary glands; pancreas and other tissues	Promote development of mammary glands during pregnancy; help regulate energy balance in fetus
Relaxin	Placenta	Uterus and joints	Inhibits uterine contractions during pregnancy and softens pelvic joints to facilitate childbirth
Thymosins and thymopoietins	Thymus gland	Certain lymphocytes (type of white blood cell)	Stimulate development of T lymphocytes, which are involved in immunity
Gastrin	Stomach mucosa	Exocrine glands of stomach	Triggers increased gastric juice secretion
Secretin	Intestinal mucosa	Stomach and pancreas	Increases alkaline secretions of the pancreas and slows emptying of stomach; helps regulate water homeostasis
Cholecystokinin (CCK)	Intestinal mucosa	Gallbladder and pancreas	Triggers the release of bile from gallbladder and enzymes from the pancreas
Atrial natriuretic hormone (ANH) and other atrial natriuretic peptides (ANPs)	Heart muscle	Kidney	Promotes loss of sodium from body into urine, thus promoting water loss from the body and a resulting decrease in blood volume and pressure
Inhibins	Ovary and testis	Hypothalamus Adenohypophysis (anterior pituitary)	Inhibit secretion of GnRH by hypothalamus and FSH by the anterior pituitary, thus helping to regulate the female reproductive cycle
Leptin	Adipose tissue	Hypothalamus; other diverse tissues	Affects energy balance, perhaps as a signal of how much fat is stored; affects various immune, neuroendocrine, and developmental functions throughout body
Resistin	Adipose tissue and macrophages	Liver and other tissues	Reduces sensitivity to insulin (a pancreatic islet hormone), thus increasing blood glucose levels
Insulin-like growth factor 1 (IGF-1)	Liver, kidney, and other tissues	Bone, muscle, and other tissues	Secreted in response to growth hormone (GH) IGF-1 carries out many of the functions attributed to GH



Box 19-9 | SPORTS and FITNESS

Steroid Abuse

Some steroid hormones are called **anabolic steroids** because they stimulate the building of large molecules (anabolism). Specifically, they stimulate the building of proteins in muscle and bone. Steroids such as testosterone and its synthetic derivatives may be abused by athletes and others who want to increase their muscle size, strength, or performance. The anabolic effects of the hormones increase the mass and strength of skeletal muscles.

Unfortunately, steroid abuse has other consequences. Prolonged use of testosterone will cause a negative feedback response of the adenohypophysis: gonadotropin levels will drop in response to high blood levels of testosterone. This may lead to atrophy of the testes and, possibly, permanent sterility. Many other adverse effects, including behavioral abnormalities, are known to result from steroid abuse.

seminiferous tubules with a scattering of endocrine *interstitial cells* found in areas between the tubules. These interstitial cells produce androgens (male sex hormones); the principal androgen is **testosterone.** Testosterone is responsible for the growth and maintenance of male sexual characteristics and for sperm production (Box 19-9). Testosterone secretion is regulated principally by gonadotropin (especially LH) levels in the blood.

Ovaries

Ovaries are a set of paired glands in the pelvis (see Figure 18-2 on p. 547) that produce several types of sex hormones, including those described briefly in the following list:

Estrogens, including estradiol and estrone, are steroid hormones secreted by the cells of the ovarian follicles that promote the development and maintenance of female sexual characteristics. With other hormones, they are responsible for breast development and the proper sequence of events in the female reproductive cycle (menstrual cycle). More details of their function are discussed in Chapter 35.

Progesterone is a hormone whose name, which means "pregnancy-promoting steroid," indicates its chief function. Secreted by the corpus luteum (the tissue left behind after the rupture of a follicle during ovulation), progesterone (along with estrogen) maintains the lining of the uterus necessary for successful pregnancy (gestation). This hormone, along with others, is discussed in detail in Chapter 35.

Regulation of ovarian hormone secretion is complex, to say the least, but basically depends on the changing levels of follicle-stimulating hormone (FSH) and LH (gonadotropins) from the adenohypophysis.

PLACENTA

Another reproductive tissue that functions as an important endocrine gland is the placenta. The **placenta,** the tissue that forms on the lining of the uterus as an interface between the circulatory systems of the mother and developing child, serves as a temporary endocrine gland.

The placenta produces **human chorionic gonadotropin (hCG).** This hormone is called "chorionic" because it is secreted by the chorion, a fetal tissue component of the placenta. It is called "gonadotropin" because, as with the gonadotropins of the adenohypophysis, it stimulates development and hormone secretion by maternal ovarian tissues. Chorionic gonadotropin secretion is high during the early part of pregnancy and serves as a signal to the mother's gonads to maintain the uterine lining rather than allow it to degenerate and fall away (as in menstruation).

The discovery of hCG many years ago led to the development of early pregnancy tests. The high levels of hCG in the urine of women who are in the early part of their pregnancies can be detected through several means. The most familiar test involves the use of an over-the-counter kit that tests for hCG in urine by means of an antigen-antibody reaction that can be easily interpreted.

As the placenta develops past the first trimester (3 months) of pregnancy, its production of hCG drops as its production of estrogens and progesterone increases. The placenta therefore more or less takes over the job of ovaries in producing these hormones necessary for a successful pregnancy.

The placenta also produces additional estrogen and progesterone during pregnancy, as well as several other hormones (see Table 19-6). These include **human placental lactogen (hPL)** and **relaxin.**

More about how placental hormones work is discussed in Chapter 36.

THYMUS

The **thymus** is a gland in the mediastinum, just beneath the sternum (see Figure 18-2 on p. 547). It is large in children until puberty, when it begins to atrophy. It continues to atrophy throughout adulthood, so that by the time an individual reaches old age, the gland is but a vestige of fat and fibrous tissue.

The anatomy of the thymus is described in Chapter 23.

Although it is considered to be primarily a lymphatic organ (see Chapter 23), the hormones **thymosin** and **thymopoietin** have been isolated from thymus tissue and are considered to be largely responsible for its endocrine activity (see Table 19-6). Thymosin and thymopoietin actually refer to two entire families of peptides that together have a critical role in the development of the immune system. Specifically, thymosin and thymopoietin are thought to stimulate the production of special lymphocytes involved in the immune response called *T cells.* The role of T cells in the immune system is discussed in Chapter 24.

GASTRIC AND INTESTINAL MUCOSA

The mucous lining of the gastrointestinal (GI) tract, like the pancreas, contains cells that produce both endocrine and exocrine secretions (see Table 19-6).

GI hormones such as **gastrin, secretin,** and **cholecystokinin (CCK)** have important regulatory roles in coordinating the secretory and motor activities involved in the digestive process. For example, secretin is released when acids make contact with the intestinal mucosa. Secretin carried by the blood triggers its target cells in the stomach to reduce acid secretion. Secretin also triggers its target cells in the pancreas to release an alkaline fluid, and it acts with CCK to trigger the pancreas to release digestive enzymes. CCK triggers the gallbladder to release more bile, which helps break up fat droplets. In effect, secretin and CCK are signals from the intestine to other parts of the digestive system that promote an effective coordination of GI functions.

The appetite-boosting hormone *ghrelin (GHRL)* is secreted by endocrine cells in the gastric mucosa as well as in the pancreatic islets.

Chapter 29 describes the hormonal control of digestion in the stomach and small intestine in more detail (see Table 29-5, p. 920).

HEART

The heart is another organ with a secondary endocrine role. Although the heart's main function is to pump blood, a specific area in its wall contains some hormone-producing cells. These cells produce several peptide hormones (see Table 19-6). This group of hormones is collectively called *atrial natriuretic peptide (ANP)*, and the principal hormone of the group is called **atrial natriuretic hormone (ANH).**

The name of ANH reveals much about its role in the body. The term *atrial* refers to the fact that ANH is secreted by cells in an upper chamber of the heart called an *atrium*. Atrial cells increase their secretion of ANH in response to an increase in the stretch of the atrial wall caused by abnormally high blood volume or blood pressure. The term *natriuretic* refers to the fact that its principal effect is to promote the loss of sodium (Latin, *natrium*) from the body by means of the urine. When sodium is thus lost from the internal environment, water follows. Water loss results in a decrease in blood volume (and thus a decrease in blood pressure). We can then state that the primary effect of ANH is to oppose increases in blood volume or blood pressure. We can also state that ANH is an antagonist to ADH and aldosterone.

ANH is also known by several other names, including *atrial natriuretic factor (ANF)*, *atrial natriuretic peptide*, and simply, *atrial peptide*.

OTHER ENDOCRINE GLANDS AND HORMONES

In this chapter, we have outlined the structure and function of only a few of the more central endocrine glands. And we have discussed only a few of their principal hormones. Many of the glands we have discussed in this chapter produce many more hormones, all of which are important to normal body function. For example, the ovaries produce the hormone **inhibin**—a glycoprotein hormone that helps to regulate FSH levels in women. And many hormones have additional effects besides the principal effects listed in this chapter (see Box 18-1, p. 554).

Many other tissues throughout the body produce hormones—perhaps all tissues in the body produce hormones. For example, adipose tissue has been shown to secrete **leptin,** a protein hormone that plays a role in energy balance, regulation of immunity and neuroendocrine function, and development. Another hormone secreted by adipose tissue and macrophages—*resistin*—reduces sensitivity to insulin and thus raises blood glucose levels. Table 19-6 summarizes a few additional examples of hormones that you are likely to encounter in your studies.

It is neither within the scope of this chapter—nor within the scope of this book—to discuss every known human hormone. Such a discussion would be longer than this *whole* book is now! Having had this brief preview, however, you will now be prepared for additional examples that you will encounter as you continue your study of the human body.

| QUICK CHECK |

15. What are the major hormones secreted by reproductive tissues (gonads and the placenta)?
16. Which gland produces a hormone that regulates the development of cells important to the immune system?
17. Secretin was the first substance in the body to be identified as a hormone. What structure produces secretin?
18. Which type of body tissue produces the hormone *leptin?*



Cycle of LIFE

Endocrine System

Endocrine regulation of body processes first begins during early development in the womb. By the time a baby is born, many of the hormones are already at work influencing the activity of target cells throughout the body. As a matter of fact, it is a hormonal signal from the fetus to the mother that signals the onset of labor and delivery. Many of the basic hormones are active from birth, but most of the hormones related to reproductive functions are not produced or secreted until puberty. Secretion of male reproductive hormones follows the same pattern as most nonreproductive hormones: continuous secretion from puberty until a slight tapering off occurs in late adulthood. The secretion of female reproductive hormones such as estrogens also declines late in life, but more suddenly and completely—often during or just at the end of middle adulthood.

the BIG picture

The Endocrine System and the Whole Body

In the previous chapter we identified the precision of control afforded by the partnership of the two major regulatory systems: the endocrine system and the nervous system. In this chapter we have encountered many examples of this partnership.

The neuroendocrine system is able to finely adjust the availability and processing of nutrients through a diverse array of mechanisms: growth hormone, thyroid hormone, cortisol, epinephrine, somatostatin, autonomic nervous regulation, and so on. The absorption, storage, and transport of calcium ions are kept in balance by the antagonistic actions of calcitonin and parathyroid hormone (and its effects on vitamin D). Reproductive ability is triggered, developed, maintained, and timed by the complex interaction of the nervous system with follicle-stimulating hormone, luteinizing hormone, estrogen, progesterone, testosterone, chorionic gonadotropin, prolactin, oxytocin, and melatonin. Nearly every process in the human organism is kept in balance by the incredibly complex, but precise, interaction of all these different nervous and endocrine regulatory chemicals.

In this chapter, we have also seen the many different structures and regulatory mechanisms that make up the endocrine system. Some of the more important hormones and their characteristics are summarized in tables throughout the chapter. As we continue our study of human anatomy and physiology, we will often encounter these hormones and the critical integrative role played by the endocrine system.

MECHANISMS of DISEASE

ENDOCRINE DISORDERS

In chapter 18 (see p. 546) we stated that nearly all endocrine disorders are caused by abnormal hormonal effects in target tissues. This could result from hypersecretion or hyposecretion of hormones. Or it could result from oversensitivity or undersensitivity in the target tissues, which can produce effects similar to hyper- or hyposecretion of hormones. Throughout this chapter, we have seen examples of many such disorders. Table 19-7 summarizes some important examples of endocrine disorders.

TABLE 19-7 Examples of Endocrine Conditions

CONDITION	MECHANISM	DESCRIPTION
Acromegaly	Hypersecretion of growth hormone (GH) during adulthood	Chronic metabolic disorder characterized by gradual enlargement or elongation of facial bones and extremities
Addison disease	Hyposecretion of adrenal cortical hormones (adrenal cortical insufficiency)	Caused by tuberculosis, autoimmunity, or other factors, this life-threatening condition is characterized by weakness, anorexia, weight loss, nausea, irritability, decreased cold tolerance, dehydration, increased skin pigmentation, and emotional disturbance; it may lead to an acute phase (adrenal crisis) characterized by circulatory shock
Aldosteronism	Hypersecretion of aldosterone	Often caused by adrenal hyperplasia, this condition is characterized by sodium retention and potassium loss—producing Conn syndrome: severe muscle weakness, hypertension (high blood pressure), kidney dysfunction, cardiac problems
Cretinism	Hyposecretion of thyroid hormone during early development	Congenital condition characterized by dwarfism, retarded mental development, facial puffiness, dry skin, umbilical hernia, lack of muscle coordination
Cushing disease	Hypersecretion of adrenocorticotropic hormone (ACTH)	Caused by adenoma of the anterior pituitary; increased ACTH causes hypersecretion of adrenal cortical hormones, producing *Cushing syndrome*
Cushing syndrome	Hypersecretion (or injection) of glucocorticoids	Metabolic disorder characterized by fat deposits on upper back, striated pad of fat on chest and abdomen, rounded "moon" face, muscular atrophy, edema, hypokalemia (low blood potassium level), possible abnormal skin pigmentation; occurs in Cushing disease
Diabetes insipidus	Hyposecretion of (or insensitivity to) antidiuretic hormone (ADH)	Metabolic disorder characterized by extreme polyuria (excessive urination) and polydipsia (excessive thirst) because of a decrease in the kidney's retention of water
Gestational diabetes mellitus (GDM)	Temporary decrease in blood levels of insulin during pregnancy	Carbohydrate-metabolism disorder occurring in some pregnant women; characterized by polydipsia, polyuria, overeating, weight loss, fatigue, irritability
Gigantism	Hypersecretion of GH before age 25 years	Condition characterized by extreme skeletal size caused by excess protein anabolism during skeletal development

(continued)

TABLE 19-7 Examples of Endocrine Conditions *(continued)*

CONDITION	MECHANISM	DESCRIPTION
Graves disease	Hypersecretion of thyroid hormone	Inherited, possibly autoimmune disease characterized by hyperthyroidism, exophthalmos (protruding eyes)
Hashimoto disease	Autoimmune damage to thyroid causing hyposecretion of thyroid hormone	Enlargement of thyroid (goiter) is sometimes accompanied by hypothyroidism, typically occurring between ages 30 and 50 years; 20 times more common in females than males
Hyperparathyroidism	Hypersecretion of parathyroid hormone (PTH)	Condition characterized by increased reabsorption of calcium from bone tissue and kidneys and increased absorption by the gastrointestinal tract; produces hypercalcemia, resulting in confusion, anorexia, abdominal pain, muscle pain, and fatigue, possibly progressing to circulatory shock, kidney failure, death
Hyperthyroidism (adult)	Hypersecretion of thyroid hormone	Condition characterized by nervousness, tremor, weight loss, excessive hunger, fatigue, heat intolerance, heart arrhythmia, and diarrhea; caused by a general acceleration of body function
Hypothyroidism (adult)	Hyposecretion of thyroid hormone	Condition characterized by sluggishness, weight gain, skin dryness, constipation, arthritis, and general slowing of body function; may lead to myxedema, coma, or death if untreated
Insulin shock	Hypersecretion (or overdose injection) of insulin, decreased food intake, excessive exercise	Hypoglycemic (low blood glucose) shock characterized by nervousness, sweating and chills, irritability, hunger, and pallor—progressing to convulsion, coma, and death if untreated
Myxedema	Extreme hyposecretion of thyroid hormone during adulthood	Severe form of adult hypothyroidism characterized by edema of the face and extremities; often progressing to coma and death
Osteoporosis	Hyposecretion of estrogen in postmenopausal women	Bone disorder characterized by loss of minerals and collagen from bone matrix, producing holes or porosities that weaken the skeleton
Pituitary dwarfism	Hyposecretion of GH before age 25 years	Condition characterized by reduced skeletal size caused by decreased protein anabolism during skeletal development
Simple goiter	Lack of iodine in diet	Enlargement of thyroid tissue results from the inability of the thyroid to make thyroid hormone because of a lack of iodine; a positive feedback situation develops in which low thyroid hormone levels trigger hypersecretion of thyroid-stimulating hormone (TSH) by pituitary—which stimulates thyroid growth
Sterility	Hyposecretion of sex hormones	Loss of reproductive function
Type 1 diabetes mellitus	Hyposecretion of insulin	Inherited condition with sudden childhood onset characterized by polydipsia, polyuria, overeating, weight loss, fatigue, and irritability, resulting from the inability of cells to secure and metabolize carbohydrates
Type 2 diabetes mellitus	Insensitivity of target cells to insulin	Carbohydrate-metabolism disorder with slow adulthood onset thought to be caused by a combination of genetic and environmental factors and characterized by polydipsia, polyuria, overeating, weight loss, fatigue, irritability
Winter (seasonal) depression	Hypersecretion of (or hypersensitivity to) melatonin	Abnormal emotional state characterized by sadness and melancholy resulting from exaggerated melatonin effects; melatonin levels are inhibited by sunlight so they increase when day length decreases during winter

LANGUAGE OF SCIENCE *(continued from p. 563)*

angiotensin II
(an-jee-oh-TEN-sin)
[*angio-* **vessel**, *-tens-* **pressure or stretch**, *-in* **substance**, *II* **Roman numeral two**]

angiotensinogen
(an-jee-oh-TEN-sin-oh-jen)
[*angio-* **vessel**, *-tens-* **pressure or stretch**, *-in-* **substance**, *-gen* **produce**]

antidiuretic hormone (ADH)
(an-tee-dye-yoo-RET-ik HOR-mohn)
[*anti-* **against**, *-dia-* **through**, *-uret-* **urination**, *-ic* **relating to**, *hormon-* **excite**]

arginine vasopressin (AVP)
(AHR-jih-neen vas-oh-PRES-in)
[*arginine* **type of amino acid**, *vas-* **vessel**, *-press-* **pressure**, *-in* **substance**]

atrial natriuretic hormone (ANH)
(AY-tree-al nay-tree-yoo-RET-ik HOR-mohn)
[*atria-* **entrance courtyard (atrium of heart)**, *-al* **relating to**, *natri-* **natrium (sodium)**, *-uret-* **urination**, *-ic* **relating to**, *hormon-* **excite**]

beta cell
(BAY-tah)
[*beta (β)* **second letter of Greek alphabet**, *cell* **storeroom**]

C cell
[*C* **for calcitonin**, *cell* **storeroom**]

calcitonin (CT)
(kal-sih-TOH-nin)
[*calci-* **lime (calcium)**, *-ton-* **tone**, *-in* **substance**]

cholecystokinin (CCK)
(koh-lee-sis-toh-KYE-nin)
[*chole-* **bile**, *-cyst-* **bag**, *-kin-* **movement**, *-in* **substance**]

corticotroph
(kohr-tih-koh-TROHF)
[*cortic-* **bark**, *-troph* **nourish**]

cortisol
(KOHR-tih-sol)
[*cortis-* **bark**, *-ol* **alcohol**]

delta cell
[*delta* (*δ*) **fourth letter of Greek alphabet**, *cell* **storeroom**]

epinephrine (Epi)
(ep-i-NEF-rin)
[*epi-* **upon**; *-nephr-* **kidney**, *-ine* **substance**]

epsilon cell
(EP-sih-lon)
[*epsilon* (*ε*) **fifth letter of Greek alphabet**, *cell* **storeroom**]

estrogen
(ES-troh-jen)
[*estro-* **frenzy**, *-gen* **produce**]

follicle
(FOL-lih-kul)
[*foll-* **bag**, *-icle* **little**]

follicle-stimulating hormone (FSH)
(FOL-lih-kul-STIM-yoo-lay-ting HOR-mohn)
[*foll-* **bag**, *-icle-* **little**, *hormon-* **excite**]

follicular cell
(foh-LIK-yoo-lar)
[*foll-* **bag**, *-icul-* **small**, *-ar* **relating to**, *cell* **storeroom**]

gastrin
(GAS-trin)
[*gastr-* **stomach**, *-in* **substance**]

ghrelin (GHRL)
(GRAY-lin)
[*ghrel-* **grow (also acronym for growth hormone releasing peptide)**, *-in* **substance**]

glucagon
(GLOO-kah-gon)
[*gluc-* **glucose**, *-agon* **drive**]

gonad
(GO-nad)
[*gon-* **offspring**, *-ad* **relating to**]

gonadotroph
(go-NAD-oh-trohf)
[*gon-* **offspring**, *-ad-* **relating to**, *-troph* **nourish**]

gonadotropin
(go-nah-doh-TROH-pin)
[*gon-* **offspring**, *-ad-* **relating to**, *-trop-* **nourish**, *-in* **substance**]

growth hormone (GH)
(HOR-mohn)
[*hormon-* **excite**]

human chorionic gonadotropin (hCG)
(KOH-rion-ik go-na-doh-TROH-pin)
[*chorion-* **skin**, *-ic* **relating to**, *gon-* **offspring**, *-ad-* **relating to**, *-trop-* **nourish**, *-in* **substance**]

human placental lactogen (hPL)
(plah-SEN-tal lak-TOH-jen)
[*placenta* **flat cake**, *-al* **relating to**, *lacto-* **milk**, *-gen* **produce**]

hypophyseal portal system
(hye-poh-FIZ-ee-al POR-tal)
[*hypo-* **under or below**, *-physis-* **growth**, *-al* **relating to**, *portal* **doorway**]

infundibulum
(in-fun-DIB-yoo-lum)
[*infundibulum* **funnel**]

inhibin
(in-HIB-in)
[*inhib-* **inhibit**, *-in* **substance**]

insulin
(IN-suh-lin)
[*insul-* **island**, *-in* **substance**]

lactotroph
(lak-toh-TROHF)
[*lacto-* **milk**, *-troph* **nourish**]

lateral lobe
(LAT-er-all)
[*later-* **side**, *-al* **relating to**]

leptin
(LEP-tin)
[*lept-* **thin**, *-in* **substance**]

luteinizing hormone (LH)
(loo-tee-in-EYE-zing HOR-mohn)
[*lute-* **yellow**, *-in-* **substance**, *-iz-* **to cause**, *hormon-* **excite**]

neurohypophysis
(noo-roh-hye-POF-i-sis)
[*neuro-* **nerve**, *-hypo-* **under or below**, *-physis* **growth**]
pl., neurohypophyses

norepinephrine (NE or NR)
(nor-ep-i-NEF-rin)
[*nor-* **chemical prefix (unbranched C chain)**, *-epi-* **upon**, *-nephr-* **kidney**, *-ine* **substance**]

oxytocin (OT)
(ahk-see-TOH-sin)
[*oxy-* **oxygen**, *-toc-* **birth**, *-in* **substance**]

pancreatic islet
(pan-kree-AT-ik eye-let)
[*pan-* **all**, *-creat-* **flesh**, *-ic* **relating to**, *isl-* **island**, *-et* **little**]

pancreatic polypeptide cell
(pan-kree-AT-ik pol-ee-PEP-tyde)
[*pan-* **all**, *-creat-* **flesh**, *-ic* **relating to**, *poly-* **many**, *-pept-* **to digest**, *-ide* **chemical**, *cell* **storeroom**]

parathyroid gland
(pair-ah-THYE-royd)
[*para-* **beside**, *-thyr-* **shield**, *-oid* **like**, *gland* **acorn**]

parathyroid hormone (PTH)
(pair-ah-THYE-royd HOR-mohn)
[*para-* **besides**, *-thyr-* **shield**, *-oid* **like**, *hormon-* **excite**]

pineal gland
(PIN-ee-al)
[*pine-* **pine**, *-al* **relating to**, *gland* **acorn**]

pituitary gland
(pih-TOO-i-tair-ee)
[*pituit-* **phlegm**, *-ary* **relating to**, *gland* **acorn**]

placenta
(plah-SEN-tah)
[*placenta* **flat cake**] *pl.,* placentae or placentas

progesterone
(proh-JES-ter-ohn)
[*pro-* **provide for**, *-gester-* **bearing (pregnancy)**, *-stero-* **solid or steroid derivative**, *-one* **chemical**]

prolactin (PRL)
(proh-LAK-tin)
[*pro-* **provide for**, *-lact-* **milk**, *-in* **substance**]

relaxin
(reh-LAK-sin)
[*relax-* **relaxation**, *-in* **substance**]

releasing hormone
(ree-LEE-sing HOR-mohn)
[*hormon-* **excite**]

renin
(REE-nin)
[*ren-* **kidney**, *-in* **substance**]

renin-angiotensin-aldosterone system (RAAS)
(REE-nin-an-jee-oh-TEN-sin-al-DAH-stair-ohn)
[*ren-* **kidney**, *-in* **substance**, *angio-* **vessel**, *-tens-* **pressure or stretch**, *-in* **substance**, *aldo-* **aldehyde**, *-stero-* **solid or steroid derivative**, *-one* **chemical**]

secretin
(seh-KREE-tin)
[*secret-* **secretion**, *-in* **substance**]

sex hormone
(HOR-mohn)
[*hormon-* **excite**]

somatostatin
(soh-mah-toh-STAT-in)
[*soma-* **body**, *-stat-* **stand**, *-in* **substance**]

somatotroph
(soh-mah-toh-TROHF)
[*soma-* **body**, *-troph* **nourish**]

somatotropin (STH)
(soh-mah-toh-TROH-pin)
[*soma-* **body**, *-trop-* **nourish**, *-in* **substance**]

testosterone
(tes-TOS-teh-rohn)
[*testo-* **witness (testis)**, *-stero-* **solid or steroid derivative**, *-one* **chemical**]

tetraiodothyronine (T_4)
(tet-rah-eye-oh-doh-THY-roh-neen)
[*tetra-* **four**, *-iodo-* **violet (iodine)**, *-thyro-* **shield (thyroid gland)**, *-ine* **chemical**]

thymopoietin
(thy-moh-POY-eh-tin)
[*thymo-* **thymus gland**, *-poiet-* **make**, *-in* **substance**]

thymosin
(THY-moh-sin)
[*thymos-* **thyme flower (thymus gland)**, *-in* **substance**]

thymus
(THY-mus)
[*thymus* **thyme flower**]

thyroglobulin
(thy-roh-GLOB-yoo-lin)
[*thyro-* **shield (thyroid gland)**, *-glob-* **ball**, *-ul-* **small**, *-in* **substance**]

thyroid colloid
(THY-royd KOL-oyd)
[*thyro-* **shield (thyroid gland)**, *-oid* **like**, *coll-* **glue**, *-oid* **like**]

thyroid gland
(THY-royd)
[*thyro-* **shield**, *-oid* **like**, *gland* **acorn**]

thyroid-stimulating hormone (TSH)
(THY-royd STIM-yoo-lay-ting HOR-mohn)
[*thyro-* **shield**, *-oid* **like**, *hormon-* **excite**]

LANGUAGE OF SCIENCE (continued from p. 589)

thyrotroph
(thy-roh-TROHF)
[*thyro-* **shield (thyroid gland),** *-troph* **nourish**]

thyroxine
(thy-ROK-sin)
[*thyro-* **shield (thyroid gland),** *-ox-* **oxygen,** *-ine* **chemical**]

triiodothyronine (T3)
(try-eye-oh-doh-THY-rohneen)
[*tri-* **three,** *-iodo-* **violet (iodine),** *-thyro-* **shield (thyroid gland),** *-nine* **chemical**]

tropic hormone
(TROH-pik HOR-mohn)
[*trop-* **nourish,** *-ic* **relating to,** *hormon-* **excite**]

vitamin D
(VYE-tah-min D)
[*vit-* **life,** *-amine* **chemical group**]

zona fasciculata
(ZOH-nah fas-sic-yoo-LAY-tah)
[*zona* **belt,** *fasiculata* **having little bundles**] *pl.,* zonae fasciculatae

zona glomerulosa
(ZOH-nah gloh-mair-yoo-LOH-sah)
[*zona* **belt,** *glomerulosa* **having small balls**] *pl.,* zonae glomerulosae

zona reticularis
(ZOH-nah reh-tik-yoo-LAIR-is)
[*zona* **belt,** *reticularis* **having little nets**] *pl.,* zonae reticulares

LANGUAGE OF MEDICINE

acromegaly
(ak-roh-MEG-ah-lee)
[*acro-* **extremities,** *-mega-* **great,** *-aly* **state**]

Addison disease
(AD-i-son)
[*Thomas Addison* **English physician**]

anabolic steroid
(an-ah-BOL-ik STAYR-oyd)
[*anabol-* **build up,** *-ic* **relating to,** *stero-* **solid,** *-oid* **like**]

chiropractic
(kye-roh-PRAK-tik)
[*chiro-* **hand,** *-practic* **practical**]

cretinism
(KREE-tin-iz-em)
[*cretin-* **idiot,** *-ism* **condition**]

cryopreservation
(krye-oh-prez-er-VAY-shun)
[*cryo-* **cold,** *-preserv-* **to keep,** *-tion* **process**]

Cushing syndrome
(KOOSH-ing SIN-drohm)
[*Harvey W. Cushing* **American neurosurgeon,** *syn-* **together,** *-drome* **running or (race)course**]

diabetes insipidus
(dye-ah-BEE-teez in-SIP-i-dus)
[*diabetes* **siphon,** *insipidus* **without zest**]

diabetes mellitus
(dye-ah-BEE-teez MELL-i-tus)
[*diabetes* **siphon,** *mellitus* **honey sweet**]

exophthalmos
(ek-soff-THAL-mus)
[*ex-* **outside,** *-oph-* **eye,** *-thalm-* **inner chamber,** *-ic* **relating to**]

gigantism
(jye-GAN-tiz-em)
[*gigant-* **great,** *-ism* **condition**]

Graves disease
(gravz)
[*Robert J. Graves* **Irish physician**]

hypersecretion
(hyp-per-seh-KREE-shun)
[*hyper-* **excessive,** *-secret-* **separate,** *-tion* **process**]

hypocalcemia
(hye-poh-kal-SEE-mee-ah)
[*hypo-* **under or below,** *-calc-* **lime (calcium),** *-emia* **blood condition**]

hypophysectomy
(hye-poff-i-SEK-toh-mee)
[*hypo-* **under or below,** *-phys-* **growth,** *-ec-* **out,** *-tom-* **cut,** *-y* **action**]

hyposecretion
(hye-poh-seh-KREE-shun)
[*hypo-* **under or below,** *-secret-* **separate,** *-tion* **process**]

kinesiopathology
(kih-nee-see-oh-PATH-ol-oh-jee)
[*kines-* **movement,** *-path-* **disease,** *-o-* **combining form,** *-log-* **words (study of),** *-y* **activity**]

myopathology
(mye-oh-PATH-ol-oh-jee)
[*myo-* **muscle,** *-path-* **disease,** *-o-* **combining form,** *-log-* **words (study of),** *-y* **activity**]

myxedema
(mik-seh-DEE-mah)
[*myx-* **mucus,** *-edema* **swelling**]

osteoporosis
(os-tee-oh-poh-ROH-sis)
[*osteo-* **bone,** *-poros-* **passage,** *-osis* **condition**]

pituitary dwarfism
(pih-TOO-i-tair-ee DWARF-iz-em)
[*pituita-* **phlegm,** *-ism* **condition**]

simple goiter
(GOY-ter)
[**from** *gutter* **throat**]

CASE study

"Why are you so grumpy lately?" Sharon was the third person to ask that in the past week. When she stopped to think about it, Cara realized that she had been getting angry at what should be minor issues. "I just need to get more sleep," she thought. But that didn't really make sense either. She'd been getting about 9 hours of sleep each night, but could still barely keep her eyes open during dinner. Her annual check-up was coming up in a few days. She would ask her doctor about it then.

At the doctor's office, Cara filled out the usual paperwork, checking off symptoms that she had recently noted: fatigue, increased urination, irritability, back ache.

1. Increased urination is a symptom associated with which endocrine disorder?
   a. Diabetes mellitus
   b. Acromegaly
   c. Hyperthyroidism
   d. Cretinism

The nurse called Cara in to take her vital signs and weight. Cara was surprised to see that she had gained several pounds because her arms felt so thin. Her blood pressure was much higher than usual too. "How long have you had that cut on your hand?" the nurse asked. Cara

CASE study *(continued)*

replied that she had cut her hand about 3 days before. She was a little concerned because it wasn't healing very quickly.

2. Which hormone alteration could possibly cause weight gain (in the trunk area), increased blood pressure, and slowed healing?
   a. Insulin
   b. Cortisol
   c. Thyroid hormone
   d. Testosterone
3. Which condition would you choose as a diagnosis?
   a. Addison disease
   b. Graves disease
   c. Hashimoto disease
   d. Cushing syndrome
4. One of the most common causes of Cara's condition is a tumor in the anterior pituitary gland. If this is the case for Cara, what will her blood levels show?
   a. Increased CRH; increased ACTH; increased cortisol
   b. Increased CRH; decreased ACTH; increased cortisol
   c. Decreased CRH; increased ACTH; increased cortisol
   d. Decreased CRH; decreased ACTH; increased cortisol

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook, **A&P Connect,** and other resources.*

CAREER choices



Mark Alderman, BS, DC

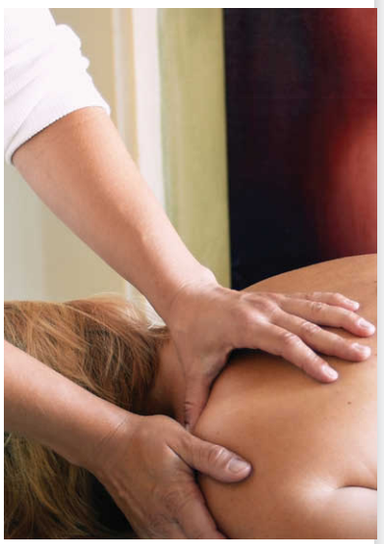
Chiropractor

Chiropractic is a holistic approach to health and illness (the absence of health), recognizing the body's inherent ability to heal itself during times of physical, mental, and environmental stress. I chose to be a Doctor of Chiropractic because I like the mind-body connection concept. I believe health comes from within, not from outside the body with potions and pills. Many chiropractic and medical studies have proven the effectiveness of chiropractic care. I was an athlete with many biomechanical problems, and traditional approaches did not help. Eventually I tried chiropractic, and it worked! Great thinkers such as Hippocrates wrote, "Look well to the spine for the cause of disease." Thomas Edison said, "The doctor of the future will give no medicines, but will interest his patients in the care of the human frame, in diet, and the cause and prevention of disease." I chose to practice in a small-town setting, in a suburb of Philadelphia called Media, Pennsylvania.

D.D. Palmer founded chiropractic back in 1885 in Davenport, Iowa. Chiropractic now enjoys worldwide acceptance by medical professionals. Chiropractic is the second largest health care profession in the world. Currently, there are more than 65,000 chiropractors worldwide. I feel chiropractic will continue to grow and be even further accepted as long as people understand that health does not come from a bottle or a pill but from within.

The reward of chiropractic is quite clear—it helps patients return to their optimum potential for health. Chiropractic is not a treatment for disease. The purpose of the chiropractic adjustment is to allow the inborn intelligence within the body to be more fully expressed. When the innate (inborn) intelligence within the body is fully expressed, the body functions at its maximum potential for health and healing. To see this occur is the biggest reward for me!

Chiropractors use anatomy and physiology in everyday practice. We use the five components of subluxation that affect the physiology of the body. **Kinesiopathology** deals with the biomechanics, *neuropathology* deals with the nerves, **myopathology** deals with the muscles, *histopathology* deals with the cells, and finally, we use the biochemical system. Chiropractic is concerned with the relationship of the spinal column and the musculoskeletal structures of the body to the nervous system. Proper alignment of the spinal column is essential for optimum health because the spine acts as a "switchboard" for the nervous system. When there is nerve interference caused by misalignment in the spine, known as subluxation, pain can occur, and the body's natural defenses are diminished. The chiropractor adjusts the spinal joints to remove subluxation and restore normal nerve function.



The education of the chiropractor is long and challenging. First you must go to undergraduate school to obtain a bachelor of science (B.S.) degree. Then you attend chiropractic school for another 4 years (8 years is a big commitment!). To receive a Doctor of Chiropractic, you have to take four national boards and a state board in the state in which you wish to practice.

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

PITUITARY GLAND

A. Structure of the pituitary gland
   1. Formerly known as *hypophysis*
   2. Size: 1.2 to 1.5 cm (about 1.2 inches) across; weight: 0.5 gram (1.60 ounce)
   3. Located on the ventral surface of the brain within the skull (Figure 19-1)
   4. Infundibulum—stemlike stalk that connects pituitary to the hypothalamus
   5. Made up of two separate glands, the adenohypophysis (anterior pituitary gland) and the neurohypophysis (posterior pituitary gland)

B. Adenohypophysis (anterior lobe of pituitary)
   1. Divided into two parts
      a. Pars anterior—forms the major portion of the adenohypophysis
      b. Pars intermedia
   2. Tissue composed of irregular clumps of secretory cells supported by fine connective tissue fibers and surrounded by a rich vascular network
   3. Three types of cells can be identified according to their affinity for certain stains (Figure 19-2)
      a. Chromophobes—do not stain
      b. Acidophils—stain with acid stains
      c. Basophils—stain with basic stains
   4. Five functional types of secretory cells exist
      a. Somatotrophs—secrete GH
      b. Corticotrophs—secrete ACTH
      c. Thyrotrophs—secrete TSH
      d. Lactotrophs—secrete prolactin (PRL)
      e. Gonadotrophs—secrete LH and FSH
   5. Growth hormone (GH) (Figure 19-3; Table 19-2)
      a. Also known as somatotropin (STH)
      b. Promotes growth of bone, muscle, and other tissues by accelerating amino acid transport into the cells
      c. Stimulates fat metabolism by mobilizing lipids from storage in adipose cells and speeding up catabolism of the lipids after they have entered another cell
      d. GH tends to shift cell chemistry away from glucose catabolism and toward lipid catabolism as an energy source; this leads to increased blood glucose levels
      e. GH functions as an insulin antagonist and is vital to maintaining homeostasis of blood glucose levels
   6. Prolactin (PRL; Table 19-2)
      a. Produced by acidophils in the pars anterior
      b. Also known as *lactogenic hormone*
      c. During pregnancy, PRL promotes development of the breasts, anticipating milk secretion; after the baby is born, PRL stimulates the mother's mammary glands to produce milk
   7. Tropic hormones—hormones that have a stimulating effect on other endocrine glands; four principal tropic hormones are produced and secreted by the basophils of the pars anterior (Table 19-2)
      a. Thyroid-stimulating hormone (TSH), or thyrotropin—promotes and maintains the growth and development of the thyroid; also causes the thyroid to secrete its hormones
      b. Adrenocorticotropic hormone (ACTH), or adrenocorticotropin—promotes and maintains normal growth and development of the cortex of the adrenal gland; also stimulates the adrenal cortex to secrete some of its hormones
      c. Follicle-stimulating hormone (FSH)—in the female, stimulates primary follicles to grow toward maturity; also stimulates the follicle cells to secrete estrogens; in the male, FSH stimulates the development of the seminiferous tubules of the testes and maintains spermatogenesis
      d. Luteinizing hormone (LH)—in the female, stimulates the formation and activity of the corpus luteum of the ovary; corpus luteum secretes progesterone and estrogens when stimulated by LH; LH also supports FSH in stimulating maturation of follicles; in the male, LH stimulates interstitial cells in the testes to develop and secrete testosterone; FSH and LH are called *gonadotropins* because they stimulate the growth and maintenance of the gonads
   8. Control of secretion in the adenohypophysis
      a. Hypothalamus secretes releasing hormones into the blood, which are then carried to the hypophyseal portal system (Figure 19-5; Table 19-1)
      b. Hypophyseal portal system carries blood from the hypothalamus directly to the adenohypophysis, where the target cells of the releasing hormones are located (Figure 19-4)
      c. Releasing hormones influence the secretion of hormones by acidophils and basophils
      d. Through negative feedback, the hypothalamus adjusts the secretions of the adenohypophysis, which then adjusts the secretions of the target glands that in turn adjust the activity of their target tissues (Figure 19-6)
      e. Minute-by-minute variations in hormone secretion can exhibit occasional large peaks, caused by pulse in releasing hormone secretion by the hypothalamus (Figure 19-7)
      f. In stress, the hypothalamus translates nerve impulses into hormone secretions by endocrine glands, basically creating a mind-body link

C. Neurohypophysis (posterior lobe of pituitary)
   1. Serves as storage and release site for antidiuretic hormone (ADH) and oxytocin (OT), which are synthesized in the hypothalamus (Figure 19-8; Table 19-2)
   2. Release of ADH and OT into the blood is controlled by nervous stimulation

3. Antidiuretic hormone (ADH)
   a. Prevents the formation of a large volume of urine, thereby helping the body conserve water
   b. Causes a portion of each tubule in the kidney to reabsorb water from the urine it is forming
   c. Dehydration triggers the release of ADH
   d. Also called arginine vasopressin (AVP) because it stimulates a rise in blood pressure, partly by increasing contraction in small arteries
4. Oxytocin (OT)—has at least two primary actions
   a. Causes milk ejection from the lactating breast; regulated by positive feedback mechanism; PRL cooperates with oxytocin
   b. Stimulates contraction of uterine muscles that occurs during and after childbirth; regulated by positive feedback mechanism
   c. Involved in sexual arousal and social bonding

PINEAL GLAND

A. Tiny, pine cone–shaped structure located on the dorsal aspect of the brain's diencephalons
B. Member of the nervous system because it receives visual stimuli and also a member of the endocrine system because it secretes hormones
C. Pineal gland supports the body's biological clock
D. Principal pineal secretion is melatonin (Table 19-6)

THYROID GLAND

A. Structure of the thyroid gland
   1. Made up of two large lateral lobes and a narrow connecting isthmus (Figure 19-9)
   2. A thin, wormlike projection of thyroid tissue often extends upward from the isthmus
   3. Weight of the thyroid in an adult is approximately 30 grams (1 ounce)
   4. Located in the neck, on the anterior and lateral surfaces of the trachea, just below the larynx
   5. Composed of follicles (Figure 19-10)
      a. Small, hollow spheres
      b. Filled with thyroid colloid that contains thyroglobulins
B. Thyroid hormone (Figure 19-11; Table 19-3)
   1. Actually two different hormones
      a. Tetraiodothyronine (T_4), or thyroxine—contains four iodine atoms; approximately 20 times more abundant than T_3; major importance is as a precursor to T_3
      b. Triiodothyronine (T_3)—contains three iodine atoms; considered to be the principal thyroid hormone; T_3 binds efficiently to nuclear receptors in target cells
   2. Thyroid gland stores considerable amounts of a preliminary form of its hormones *before* secreting them
   3. Before being stored in the colloid of follicles, T_3 and T_4 are attached to globulin molecules, forming thyroglobin complexes
   4. Before release, T_3 and T_4 detach from globulin and enter the bloodstream
   5. Once in the blood, T_3 and T_4 attach to a plasma protein called *thyroid-binding globulins (TBGs)* and travel as a hormone-globulin complex
   6. T_3 and, to a lesser extent, T_4 detach from plasma globulin as they near the target cells
   7. Thyroid hormone—helps regulate the metabolic rate of all cells and cell growth and tissue differentiation; it is said to have a "general" target
C. Calcitonin (CT) (Table 19-3)
   1. Produced by thyroid gland in the parafollicular cells
   2. In humans, CT may subtly influence the processing of calcium by bone cells by decreasing blood calcium levels and promoting conservation of hard bone matrix
   3. Parathyroid hormone acts as antagonist to calcitonin to maintain calcium homeostasis

PARATHYROID GLANDS

A. Structure of the parathyroid glands
   1. Four or five parathyroid glands embedded in the posterior surface of the thyroid's lateral lobes (Figure 19-12)
   2. Tiny, rounded bodies within thyroid tissue formed by compact, irregular rows of cells (Figure 19-13)
B. Parathyroid hormone (PTH) (Table 19-3)
   1. PTH is an antagonist to calcitonin and is the primary hormone to maintain calcium homeostasis (Figure 19-14)
   2. PTH acts on bone and kidney
      a. Causes more bone to be dissolved, yielding calcium and phosphate, which enters the bloodstream
      b. Causes phosphate to be secreted by the kidney cells into the urine to be excreted
      c. Causes increased intestinal absorption of calcium by stimulating the kidney to produce active vitamin D, which increases calcium absorption in gut

ADRENAL GLANDS

A. Structure of the adrenal glands
   1. Located on top of the kidneys, fitting like caps (Figure 19-15)
   2. Made up of two portions (Figure 19-16; Table 19-4)
      a. Adrenal cortex—composed of endocrine tissue (Figure 19-17)
      b. Adrenal medulla—composed of neurosecretory tissue
B. Adrenal cortex—all cortical hormones are steroids and known as *corticosteroids* (Figure 19-18)
   1. Composed of three distinct layers of secreting cells
      a. Zona glomerulosa—outermost layer, directly under the outer connective tissue capsule of the adrenal gland; secretes mineralocorticoids
      b. Zona fasciculata—middle layer; secretes glucocorticoids
      c. Zona reticularis—inner layer; secretes small amounts of glucocorticoids and gonadocorticoids
   2. Mineralocorticoids
      a. Have an important role in the regulatory process of sodium in the body

b. Aldosterone
(1) Only physiologically important mineralocorticoid in the human; primary function is maintenance of sodium homeostasis in the blood by increasing sodium reabsorption in the kidneys
(2) Aldosterone also increases water retention and promotes the loss of potassium and hydrogen ions
(3) Aldosterone secretion is controlled by the renin-angiotensin-aldosterone system (RAAS) and by blood potassium concentration (Figure 19-19)

3. Glucocorticoids
a. Main glucocorticoids secreted by the zona fasciculata are cortisol, cortisone, and corticosterone, with cortisol the only one secreted in significant quantities
b. Affect every cell in the body
c. Are protein mobilizing, gluconeogenic, and hyperglycemic
d. Tend to cause a shift from carbohydrate catabolism to lipid catabolism as an energy source
e. Essential for maintaining normal blood pressure by aiding norepinephrine and epinephrine to have their full effect, causing vasoconstriction
f. High blood concentration causes eosinopenia and marked atrophy of lymphatic tissues
g. Act with epinephrine to bring about normal recovery from injury produced by inflammatory agents
h. Secretion increases in response to stress
i. Except during stress response, secretion is mainly controlled by a negative feedback mechanism involving ACTH from the adenohypophysis
j. Secretion is characterized by several large pulses of increased hormone levels throughout the day—the largest occurring just before waking (Figure 19-20)

4. Gonadocorticoids—sex hormones (androgens) that are released from the adrenal cortex

C. Adrenal medulla
1. Neurosecretory tissue—tissue composed of neurons that secrete their products into the blood
2. Adrenal medulla secretes two important hormones—epinephrine and norepinephrine; they are part of the class of nonsteroid hormones called *catecholamines*
3. Both hormones bind to the receptors of sympathetic effectors to prolong and enhance the effects of sympathetic stimulation by the ANS (Figure 19-21)

PANCREATIC ISLETS

A. Structure of the pancreatic islets (Figure 19-22)
1. Elongated gland, weighing approximately 100 grams (3.5 ounces); its head lies in the duodenum, extends horizontally behind the stomach, and, then, touches the spleen
2. Composed of endocrine and exocrine tissues
a. Pancreatic islets (islets of Langerhans)—endocrine portion
b. Acini—exocrine portion—secretes a serous fluid containing digestive enzymes into ducts draining into the small intestine
3. Pancreatic islets—each islet contains five primary types of endocrine cells joined by gap junctions (Figure 19-23)
a. Alpha cells (A cells)—secrete glucagon
b. Beta cells (B cells)—secrete insulin; account for up to 75% of all pancreatic islet cells
c. Delta cells (D cells)—secrete somatostatin
d. Pancreatic polypeptide cells (F, or PP, cells)—secrete pancreatic polypeptide
e. Epsilon cells (ε cells)—secrete ghrelin

B. Pancreatic hormones (Table 19-5)—work as a team to maintain homeostasis of food molecules (Figure 19-24)
1. Glucagon—produced by alpha cells; tends to increase blood glucose levels; stimulates gluconeogenesis in liver cells
2. Insulin—produced by beta cells; lowers blood concentration of glucose, amino acids, and fatty acids and promotes their metabolism by tissue cells
3. Somatostatin—produced by delta cells; primary role is regulating the other endocrine cells of the pancreatic islets
4. Pancreatic polypeptide—produced by F (PP) cells; influences the digestion and distribution of food molecules to some degree
5. Ghrelin (GHRL)—hormone secreted by epsilon cells at periphery of pancreatic islets; stimulates hypothalamus to boost appetite; slows metabolism and fat burning; may contribute to obesity

GONADS

A. Testes (Figure 18-2; Table 19-6)
1. Paired organs within the scrotum in the male
2. Composed of seminiferous tubules and a scattering of interstitial cells
3. Testosterone is produced by the interstitial cells and responsible for the growth and maintenance of male sexual characteristics
4. Testosterone secretion is mainly regulated by gonadotropin levels in the blood

B. Ovaries (Figure 18-2; Table 19-6)
1. Primary sex organs in the female
2. Set of paired glands in the pelvis that produce several types of sex hormones
a. Estrogens—steroid hormones secreted by ovarian follicles; promote development and maintenance of female sexual characteristics
b. Progesterone—secreted by corpus luteum; maintains the lining of the uterus necessary for successful pregnancy
c. Ovarian hormone secretion depends on the changing levels of FSH and LH from the adenohypophysis

PLACENTA

A. Tissues that form on the lining of the uterus as a connection between the circulatory systems of the mother and developing child
B. Serves as a temporary endocrine gland that produces human chorionic gonadotropin, estrogens, and progesterone (Table 19-6)

THYMUS

A. Gland located in the mediastinum just beneath the sternum (Figure 18-2)
B. Thymus is large in children, begins to atrophy at puberty, and by old age, is a vestige of fat and fibrous tissue
C. Considered to be primarily a lymphatic organ, but the hormone thymosin has been isolated from thymus tissue (Table 19-6)
D. Thymosin—stimulates development of T cells

GASTRIC AND INTESTINAL MUCOSA

A. The mucous lining of the GI tract contains cells that produce both endocrine and exocrine secretions (Table 19-6)
B. GI hormones, such as gastrin, secretin, and cholecystokinin (CCK), play regulatory roles in coordinating the secretory and motor activities involved in the digestive process
C. Ghrelin (GHRL)—appetite-boosting hormone secreted by endocrine cells in gastric mucosa as well as in pancreatic islets

HEART

A. The heart has a secondary endocrine role
B. Hormone-producing cells produce several atrial natriuretic peptides (ANPs), including atrial natriuretic hormone (ANH) (Table 19-6)
C. ANH's primary effect is to oppose increases in blood volume or blood pressure; also an antagonist to ADH and aldosterone

OTHER ENDOCRINE GLANDS AND ORGANS

A. Major endocrine glands produce more hormones than are outlined in this book (e.g., inhibin secreted by the ovaries) (Table 19-6)
B. Many tissues (perhaps all tissues) produce hormones, most of which are beyond the scope of this book (e.g., leptin and resistin secreted by adipose tissue).

CYCLE OF LIFE: ENDOCRINE SYSTEM

A. Endocrine regulation begins in the womb
B. Many active hormones are active from birth—evidence that a hormonal signal from fetus to mother signals the onset of labor
C. Hormones related to reproduction begin at puberty
D. Secretion of male reproductive hormones—continuous production from puberty, slight decline in late adulthood
E. Secretion of female reproductive hormones declines suddenly and completely in middle adulthood

THE BIG PICTURE: THE ENDOCRINE SYSTEM AND THE WHOLE BODY

A. The endocrine system operates with the nervous system to finely adjust the many processes they regulate
B. Neuroendocrine system adjusts nutrient supply
C. Calcitonin, parathyroid hormone, and vitamin D balance calcium ion use
D. The nervous system and hormones regulate reproduction

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Name the two subdivisions of the adenohypophysis.
2. Discuss and identify, by staining tendency and relative percentages, the cell types present in the anterior pituitary gland.
3. Discuss the functions of growth hormone.
4. What effect does growth hormone have on blood glucose concentration? Fat mobilization and catabolism? Protein anabolism?
5. List the four tropic hormones secreted by the basophils of the anterior pituitary gland. Which of the tropic hormones are also called *gonadotropins?*
6. How does antidiuretic hormone act to alter urine volume?
7. Describe the positive feedback associated with oxytocin.
8. Discuss the synthesis and storage of thyroxine and triiodothyronine. How are they transported in the blood?
9. Discuss the functions of parathyroid hormone.
10. List the hormones produced by each "zone" of the adrenal cortex, and describe the actions of these hormones.
11. Discuss the normal function of hormones produced by the adrenal medulla.
12. Identify the hormones produced by each of the cell types in the pancreatic islets.
13. Identify the "pregnancy-promoting" hormone.
14. Where is human chorionic gonadotropin produced? What does it do?
15. Describe the role of atrial natriuretic hormone.
16. Identify the conditions resulting from both hypersecretion and hyposecretion of growth hormone during growth years.
17. Describe the face of a patient with Cushing syndrome.
18. How does exercise affect diabetes mellitus?

CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. What examples can you find that apply the concept of a negative feedback loop to the regulation of hormone secretion?
2. A hyposecretion of which hormone would make it difficult for a mother to nurse her child? How would you summarize the effects of this hormone?
3. Why do you think the hypothalamus can be called the "mind-body link"?
4. How would you explain the hormonal interaction that helps maintain the set point value for the glucose in the blood?
5. Explain how the cell is able to become more or less sensitive to a specific hormone.
6. What is the relationship between increased blood level concentrations of FSH and menopause?
7. A lack of iodine in the diet will cause a simple goiter. Describe the feedback loop that will cause its formation.
8. A friend of yours is considering the use of anabolic steroids. Based on what you know of their effects, how would you explain why using these steroids could be harmful?

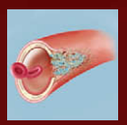
Unit Four

Transportation and Defense

The chapters in Unit Four are concerned with transportation, how the body defends itself, and stress. Blood (Chapter 20), a complex fluid tissue, is discussed and the text explains how blood serves to transport respiratory gases and key nutrients to cells and carry away wastes. The body's blood fills the cardiovascular system (Chapters 21 and 22) and is moved through a closed pathway, or circuit, of vessels by the pumping action of the heart.

The elements of the lymphatic system (Chapter 23) provide an open pathway for return of fluid and proteins from the interstitial spaces and for fats, which are absorbed from the intestine into the general circulation. The lymphatic system is also involved in immunity or resistance to disease and in the removal and destruction of dead red blood cells. The immune system is more fully discussed in Chapter 24. Elements of the immune system provide a multilayered defense mechanism, involving both phagocytic cells and defensive proteins called *antibodies.* Stress—and the body's frequently maladaptive response to it—is discussed in Chapter 25.

SEEING THE BIG PICTURE



20 Blood, 598



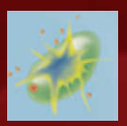
21 Anatomy of the Cardiovascular System, 629



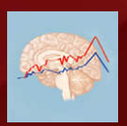
22 Physiology of the Cardiovascular System, 681



23 Lymphatic System, 722

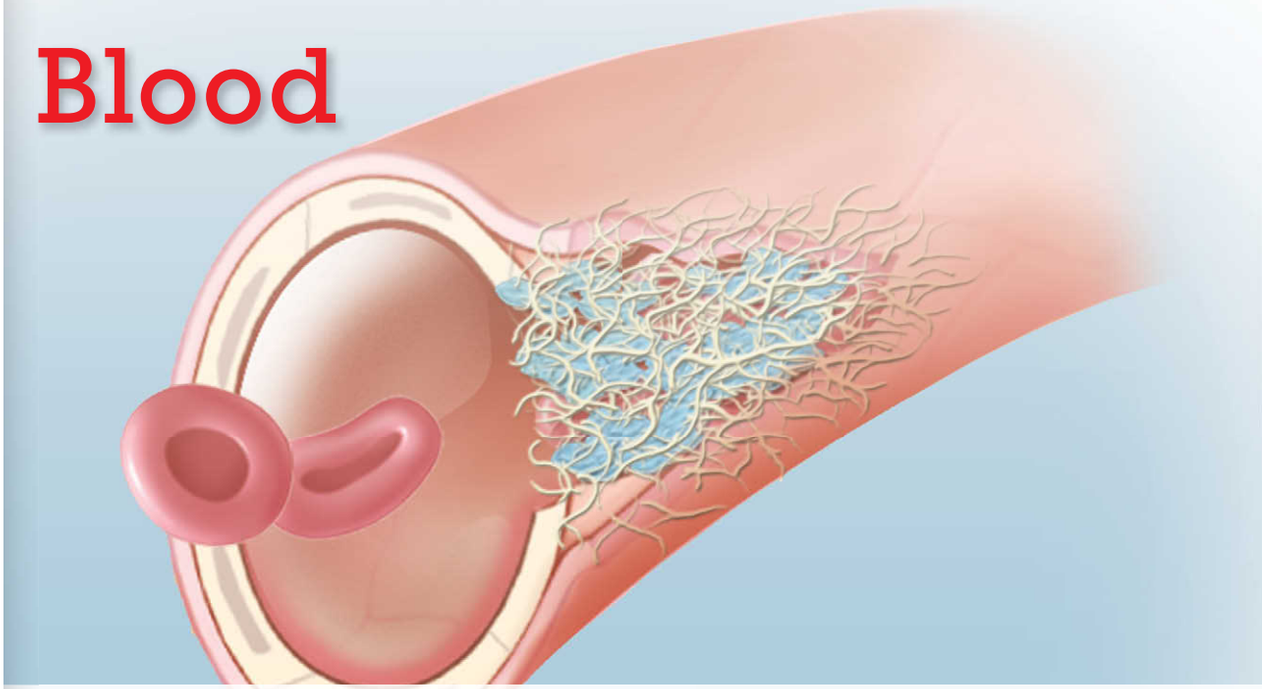


24 Immune System, 745



25 Stress, 782

20 Blood



LANGUAGE OF SCIENCE

HINT *Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.*

adult stem cell

agranulocyte
(ah-GRAN-yoo-loh-syte)
[*a-* **without**, *-gran-* **grain**, *-ul-* **little**]

antibody
(AN-ti-bod-ee)
[*anti-* **against**]

antigen
(AN-ti-jen)
[*anti-* **against**, *-gen* **produce**]

basophil
(BAY-so-fil)
[*bas-* **foundation**, *-phil* **love**]

basophilic erythroblast
(BAY-so-fil-ik eh-rith-roh-BLAST)
[*bas-* **foundation**, *-phil-* **love**, *-ic* **relating to**, *erythro-* **red**, *-blast* **bud**]

bicarbonate ion
(bye-KAR-boh-nayte EYE-on)
[*bi-* **twice**, *-carbo-* **coal**, *-ate* **oxygen**]

blood clotting

blood serum
(SEER-um)
[*serum* **watery fluid**] *pl.,* sera

buffy coat

carbonic anhydrase (CA)
(kar-BON-ik an-HYE-drays)
[*carbo-* **coal**, *-ic* **relating to**, *a-* **without**, *-hydr-* **water**, *-ase* **enzyme**]

chemotaxis
(kee-moh-TAK-sis)
[*chemo-* **chemical**, *-taxis* **movement or reaction**]

diapedesis
(dye-ah-peh-DEE-sis)
[*dia-* **apart or through**, *-pedesis* **oozing**]

electrolyte
(eh-LEK-troh-lyte)
[*electro-* **electricity**, *-lyt-* **loosening**]

continued on p. 623

CHAPTER OUTLINE

HINT *Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.*

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- Blood Volume, 599

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  - Function of Red Blood Cells, 601
  - Hemoglobin, 602
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Four chapters in this unit deal with transportation, one of the body's vital functions. Homeostasis of the internal environment—and therefore survival itself—depend on continual transportation to and from body cells. This chapter discusses the major transportation fluid, blood. Chapters 21 and 22 consider the major transportation system, the cardiovascular system, and Chapter 23 explains a supplementary drainage system, the lymphatic system.

COMPOSITION OF BLOOD

Blood is much more than the simple liquid it seems to be. It consists of not only a fluid but also cells, including *thrombocytes (platelets)*. The fluid portion of blood, that is, the **plasma,** is one of the three major body fluids (interstitial and intracellular fluids are the other two). As explained below, the quantity of whole blood found in the body (blood volume) is often expressed as a percent of total body weight. However, the measurement of the plasma and formed elements is generally expressed as a percent of the *whole blood volume*. Using these measurement criteria, whole blood constitutes about 8% of total body weight, plasma accounts for 55%, and the formed elements account for about 45% of the total blood volume (Figure 20-1). The term **formed elements** is used to designate the various kinds of blood cells that are normally present in blood.

Blood is a complex transport medium that performs vital pickup and delivery services for the body. It picks up food and oxygen from the digestive and respiratory systems and delivers them to cells while also picking up wastes from cells for delivery to excretory organs. Blood also transports hormones, enzymes, buffers, and various other biochemical substances that serve important functions. Blood serves another critical function. It is the keystone of the body's heat-regulating mechanism. Certain physical properties of blood make it especially effective in this role. Its high specific heat and conductivity enable this unique fluid to absorb large quantities of heat without an appreciable increase in its own temperature and to transfer this absorbed heat from the core of the body to its surface, where the heat can be more readily dissipated (see Figure 7-15, p. 183).

Blood Volume

How much blood does the body contain? The answer is about 8% of total body weight in average-sized adults. In a healthy young female, that amounts to about 4 to 5 liters and in a male about 5 to 6 liters. In addition to gender differences, blood volume varies with age, body composition, and method of measurement. A *unit* of blood is the amount (0.45 liter or just under 1 pint) that is collected from a blood donor for transfusion purposes. It constitutes about 10% of total blood volume in many adults.

Blood volume can be determined using direct methods or indirect methods of measurement. *Direct* measurement of total blood volume can be accomplished only by complete removal of all blood from an experimental animal. In humans, *indirect* methods of measurement that employ "tagging" of red blood cells or plasma components with radioisotopes are used. The principle is simply to introduce a known amount of radioisotope into the circulation, allow the material to be distributed uniformly

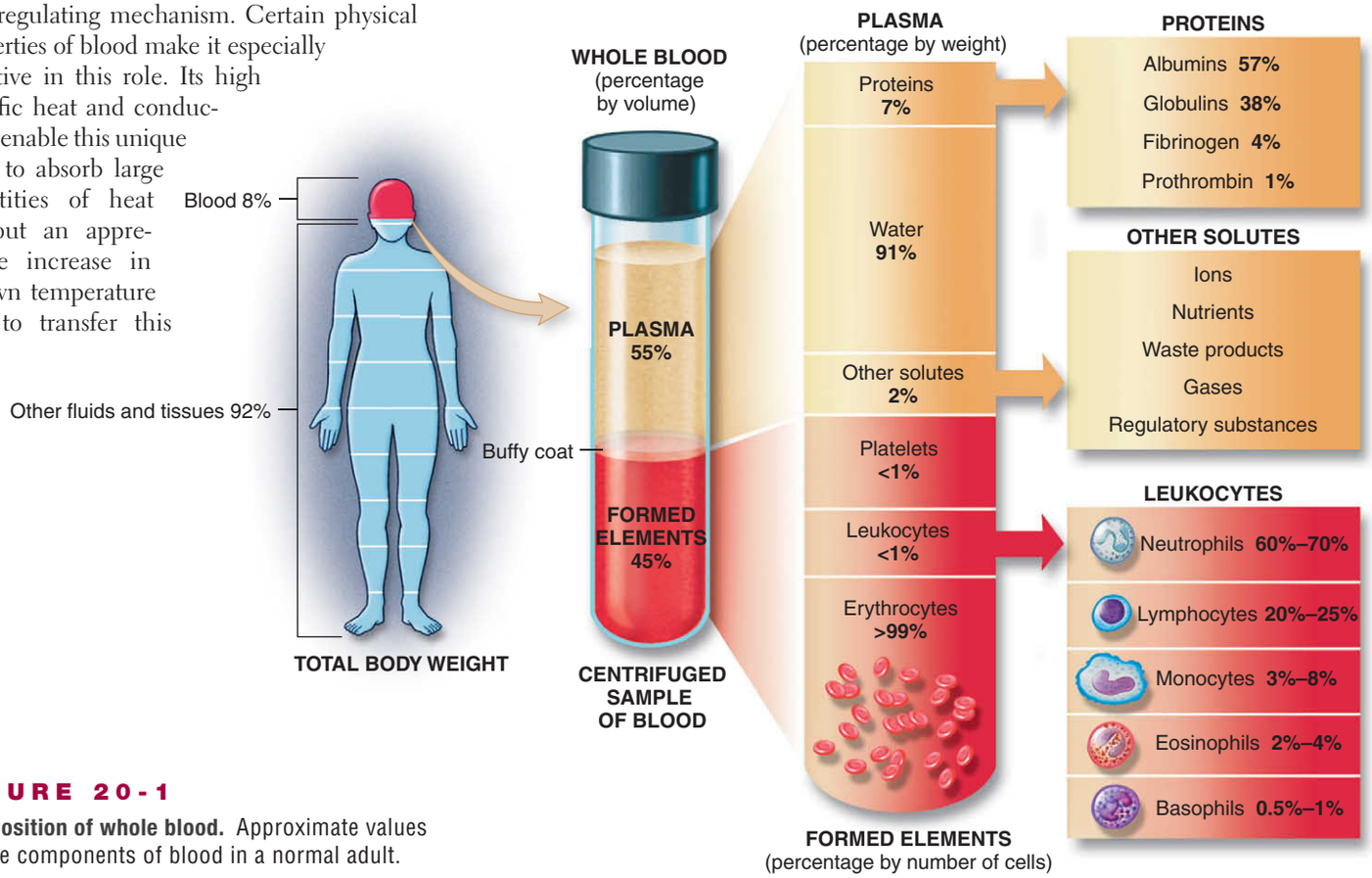


FIGURE 20-1

Composition of whole blood. Approximate values for the components of blood in a normal adult.

throughout the blood, and then analyze its concentration in a representative blood sample. Having an accurate measurement is important in replacing blood lost because of hemorrhage or in treating other serious conditions such as shock.

One of the chief variables influencing normal blood volume is the amount of body fat. Blood volume per kilogram of body weight varies inversely with the amount of excess body fat. This means that the less fat there is in your body, the more blood you have per kilogram of your body weight. Because females normally have a higher percent of body fat than males, they have less blood per kilogram of body weight and therefore a lower blood volume.

FORMED ELEMENTS OF BLOOD

Figure 20-2 illustrates the formed elements of blood. They are as follows:

- Red blood cells (RBCs) (erythrocytes)
- White blood cells (WBCs) (leukocytes)
- Platelets (thrombocytes)

Plasma, when separated from "whole blood," is a clear straw-colored fluid that consists of about 90% water and 10% solutes. *Blood transfusions* most often involve three major blood components—plasma, platelets, and red blood cells. In the United States, red blood cells constitute about 13.5 million transfusions compared with 1.75 million transfusions of platelets and 3.5 million transfusions of plasma each year.

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Blood transfusions are an important therapeutic tool. Learn more about blood transfusions, blood banking, and even *artificial* blood in ***Blood Transfusions*** online at ***A&P Connect.***

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If a tube of whole blood, that is, plasma and formed elements, is allowed to stand or is spun in a centrifuge, separation will occur. The term **packed cell volume (PCV),** or **hematocrit** (hee-MAT-oh-krit),

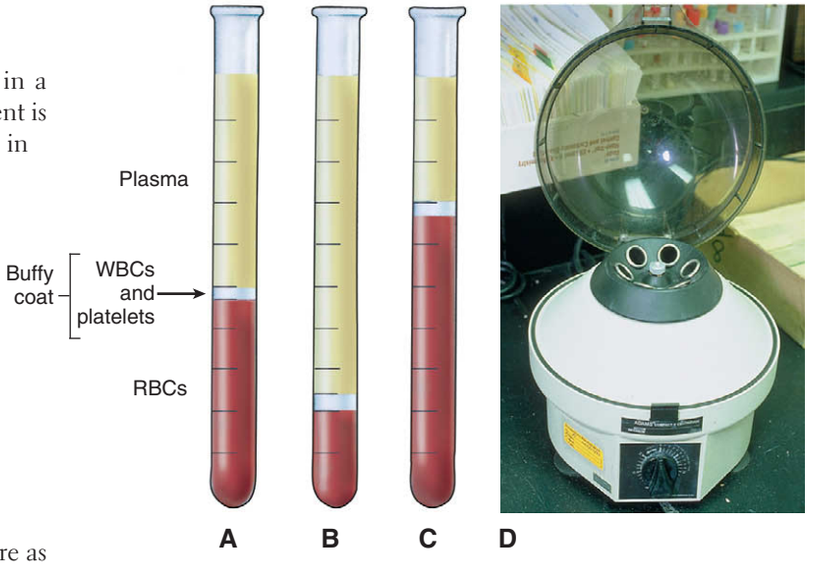


FIGURE 20-3

Hematocrit tubes showing normal blood, anemia, and polycythemia. Note the buffy coat located between the packed RBCs and the plasma. **A,** A normal percent of red blood cells. **B,** Anemia (a low percent of red blood cells). **C,** Polycythemia (a high percent of red blood cells). **D,** Centrifuge used to spin tubes of whole blood and thereby separate blood solids from plasma.

is used to describe the volume percent of red blood cells (RBCs) in whole blood. In Figure 20-3, *A*, a sample of normal whole blood has been separated by spinning in a centrifuge so that the formed elements are forced to the bottom. The percentage of plasma is about 55% of the total sample, whereas the packed cell volume, or hematocrit, is 45%. A hematocrit of 45% means that in every 100 ml of whole blood there are 45 ml of RBCs and 55 ml of fluid plasma.

Normally the average hematocrit for a man is about 45% (40% to 54%, normal range) and for a woman about 42% (38% to 47%, normal range). Conditions that result in decreased RBC numbers (Figure 20-3, *B*) are called **anemias** and are characterized by a reduced hematocrit value. Healthy individuals who live and work in high altitudes often have elevated RBC numbers and hematocrit values (Figure 20-3, *C*). The condition is called **physiological polycythemia** (from word parts meaning "condition of many blood cells").

Box 20-1 describes another clinical blood test that involves separating RBCs from plasma.

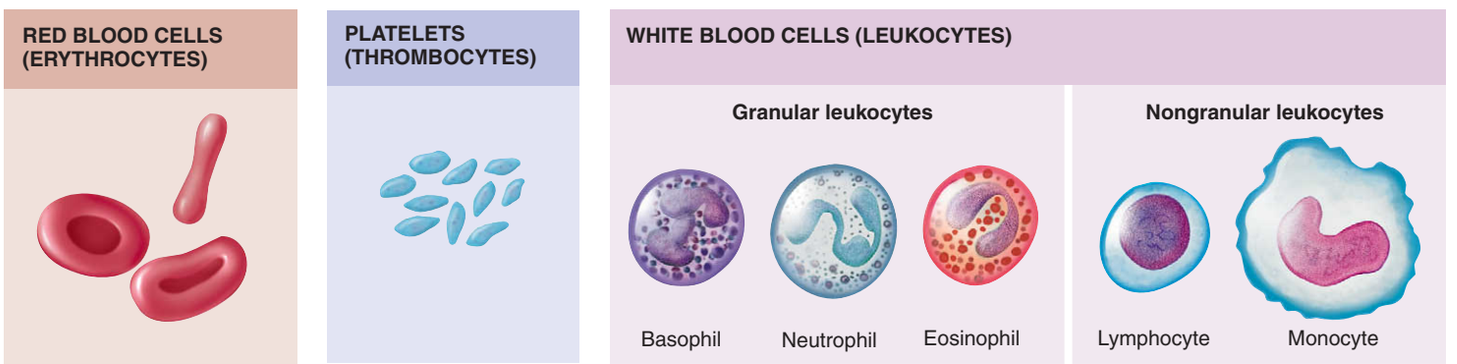


FIGURE 20-2

The formed elements of blood. Red blood cells (erythrocytes), white blood cells (leukocytes), and platelets (thrombocytes) constitute the formed elements of blood.

Box 20-1 | DIAGNOSTIC study

Erythrocyte Sedimentation Rate

If a tube of anticoagulated blood from a healthy individual is allowed to stand upright for an hour, gravity will cause sedimentation of the formed elements leaving a layer of clear plasma about 15 mm thick on top of the tube. The rate of fall in 1 hour is called the **erythrocyte sedimentation rate,** or **ESR.**

In individuals suffering from some type of inflammatory process, the clear layer on top of the ESR tube at the end of an hour is often over 40 mm thick. The increased ESR is due to the liver secreting into the circulation a number of large proteins that assist the body in responding to the inflammation. In addition to their large size and high molecular weight, these proteins also cause RBCs to "cluster," thus effectively increasing blood density. The result is an elevated ESR. The ESR is a "nonspecific" medical test because an increase will occur as a result of many different inflammatory conditions. Although the test cannot identify a specific disease, it is widely used by clinicians because it is a safe, easily performed, and cost-effective procedure that provides useful information early in the diagnostic process. For example, it is often used to make an initial determination concerning the possibility of inflammation as the cause of nonspecific complaints such as generalized fatigue, or weakness. If the presence of an inflammatory process is confirmed by an elevated ESR, more specific diagnostic tests can be used to identify the cause.

White blood cells (WBCs), or leukocytes, and platelets make up less than 1% of blood volume. Note in Figure 20-3 that a thin white layer of leukocytes and platelets, called the **buffy coat,** is present at the interface between the packed red cells and plasma.

| QUICK CHECK |

1. Name the fluid portion of whole blood.
2. What constitutes the formed elements of blood?
3. What factors influence blood volume?
4. Identify the component percentages of the normal hematocrit.

Red Blood Cells (Erythrocytes)

A normal, mature RBC has no nucleus and is only about 7.5 µm in diameter. More than 1500 of them could be placed side by side in a 1 cm space. Before the cell reaches maturity and enters the bloodstream from the bone marrow, the nucleus is extruded. As you can see in Figure 20-4, normal, mature RBCs are shaped like tiny biconcave disks.

The mature **erythrocyte** is also unique in that it does not contain ribosomes, mitochondria, and other organelles typical of most body cells. Instead, the primary component of each RBC is the red protein pigment, **hemoglobin.** It accounts for more than one third of the cell volume and is critically important to its primary function.

The depression on each flat surface of the cell results in a thin center and thicker edges. This unique shape of the RBC gives it a very large surface area relative to its volume. The shape of erythrocytes can passively change as they forcibly pass through blood capillaries that often are smaller than the typical 7.5 µm diameter of an erythrocyte.

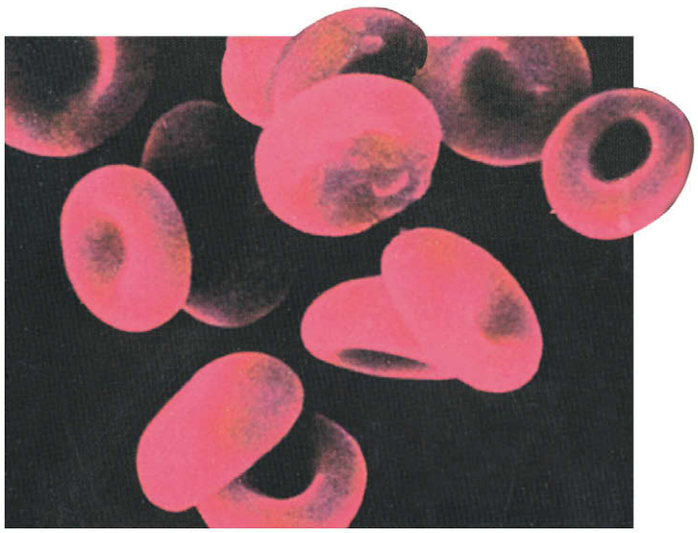


FIGURE 20-4

Erythrocytes. Color-enhanced scanning electron micrograph shows normal erythrocytes.

The flexibility of RBC shape is possible because of the presence of stretchable fibers composed of a unique protein called *spectrin.* These fibers, which are part of the cytoskeleton, adhere to the inside of the erythrocyte plasma membrane. It is the presence of flexible spectrin fibers that permits the plasma membrane surrounding the RBC to accommodate change from a more typical biconcave shape to a smaller cup-shaped cell size and then back to its normal size and appearance when deforming pressures are no longer being applied to the surface of the plasma membrane. This ability to change shape is necessary for the survival of RBCs, which are under almost constant mechanical shearing and bursting strains as they pass through the capillary system. In addition, the degree of cell deformity that is possible influences the speed of blood flow in the microcirculation.

RBCs are the most numerous of the formed elements in the blood. In men, RBC counts average about 5,500,000 per cubic millimeter (mm^3) of blood; in women, 4,800,000/mm^3. Gender differences in RBC numbers may be influenced by the stimulating effect of the male sex hormone testosterone on RBC production. RBC numbers in females are normally lower than those in males.

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To explore the normal values for a variety of blood constituents, including RBC values, scan the list in ***Clinical and Laboratory Values*** online at ***A&P Connect.***

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FUNCTION OF RED BLOOD CELLS

RBCs play a critical role in the transport of oxygen and carbon dioxide in the body. Chapter 27 includes a detailed discussion of how oxygen is transported from air in the lungs to the body

cells and how carbon dioxide moves from body cells to the lungs for removal. Both of these functions depend on hemoglobin. In addition to hemoglobin, the presence of an enzyme, **carbonic anhydrase (CA),** in RBCs catalyzes a reaction that joins carbon dioxide and water to form carbonic acid. Dissociation of the acid then generates **bicarbonate ions** (HCO_3^-) and hydrogen ions (H^+), which diffuse out of the RBCs. Because carbon dioxide (CO_2) is chemically incorporated into the newly formed bicarbonate ions, it can be transported in this new form in the blood plasma until it is excreted from the body. Bicarbonate ions also have an important role in maintaining normal blood pH levels (see Chapter 33).

Considered together, the total surface area of all the RBCs in an adult is enormous. It provides an area larger than a football field for the exchange of respiratory gases between hemoglobin found in circulating erythrocytes and interstitial fluid that bathes the body cells. This is an excellent example of the relationship between form and function.

HEMOGLOBIN

Packed within each RBC are an estimated 200 to 300 million molecules of hemoglobin, which make up about 95% of the dry weight of each cell. Each hemoglobin molecule is composed of four protein chains. Each chain, called a **globin,** is bound to a red pigment, identified in Figure 20-5, as a **heme** group. Each heme group contains one iron atom. Therefore one hemoglobin molecule contains four iron atoms. This structural fact enables one hemoglobin molecule to unite with four oxygen molecules to form *oxyhemoglobin* (a reversible reaction). Hemoglobin can also combine with carbon dioxide to form *carbaminohemoglobin* (also reversible). But in this reaction the structure of the globin part of the hemoglobin molecule, rather than its heme part, makes the combining possible.

A man's blood usually contains more hemoglobin than a woman's. In most normal men, 100 ml of blood contains 14 to 16 grams of hemoglobin. The normal hemoglobin content of a woman's blood is a little less—specifically, in the range of 12 to 14 grams/100 ml. Recall that testosterone in the male tends to stimulate erythrocyte production and cause an increase in RBC numbers. Increased levels of hemoglobin in males are directly related to increased erythrocyte numbers.

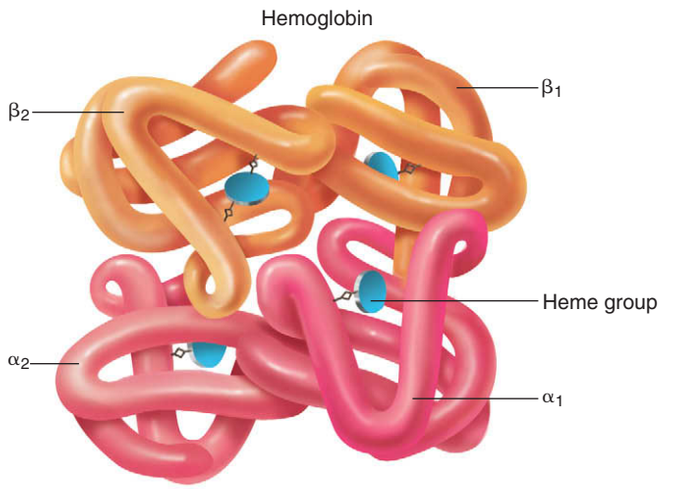


FIGURE 20-5

Hemoglobin. Four protein chains (globins), each with a heme group, form a hemoglobin molecule. Each heme contains one iron atom.

An adult who has a hemoglobin content of less than 10 grams/100 ml of blood is diagnosed as having **anemia.** If you dissect the word parts, you see that *anemia* literally means "lack of blood." The term *anemia* also may be used to describe a reduction in the number or volume of functional RBCs in a given unit of whole blood. Anemias are classified according to the size and hemoglobin content of RBCs. Box 20-2 describes a type of anemia that results from production of an abnormal type of hemoglobin.

FORMATION OF RED BLOOD CELLS

The entire process of RBC formation is called **erythropoiesis.** In the adult, erythrocytes begin their maturation sequence in the red bone marrow from nucleated cells known as **hematopoietic stem cells,** or adult blood-forming stem cells. *Adult stem cells* are cells that have the ability to maintain a constant population of newly differentiating cells of a specific type. These adult blood-forming stem cells divide by mitosis; some of the daughter cells remain as undifferentiated adult stem cells, whereas others go through several stages of development to become erythrocytes. Figure 20-6 shows

Box 20-2 | FYI

Sickle cell anemia.



Sickle cell anemia.

Sickle cell anemia is a severe, sometimes fatal, hereditary disease that is characterized by an abnormal type of hemoglobin. A person who inherits only one defective gene develops a form of the disease called *sickle cell trait,* in which red blood cells contain a small proportion of a hemoglobin type that is less soluble than normal. This hemoglobin forms solid crystals when the blood oxygen level is low, causing distortion and fragility of the red blood cell. If two defective genes are inherited (one from each parent), more of the defective hemoglobin is produced, and the distortion of red blood cells becomes severe. In the United States, about 1 in every 500 African-American and 1 in every 1000 Hispanic newborns are affected each year. In these individuals, the distorted red blood cell membranes can be damaged by drastic changes in shape. Red blood cells damaged in this way tend to stick to vessel walls, and if a blood vessel in the brain is affected, a stroke may occur because of the decrease in blood flow velocity or blockage of blood flow.

Stroke is one of the most devastating problems associated with sickle cell anemia in children and will affect about 10% of the 2500 youngsters who have the disease in the United States. Studies have shown that frequent blood transfusions in addition to standard care can dramatically reduce the risk of stroke in many children suffering from sickle cell anemia. Recent advances in bone marrow transplants in children and hemopoietic stem cell transplants in adults show the promise of long-term reversal of the effects of sickle cell anemia.

The illustration shows the characteristic shape of a red cell containing the abnormal hemoglobin.

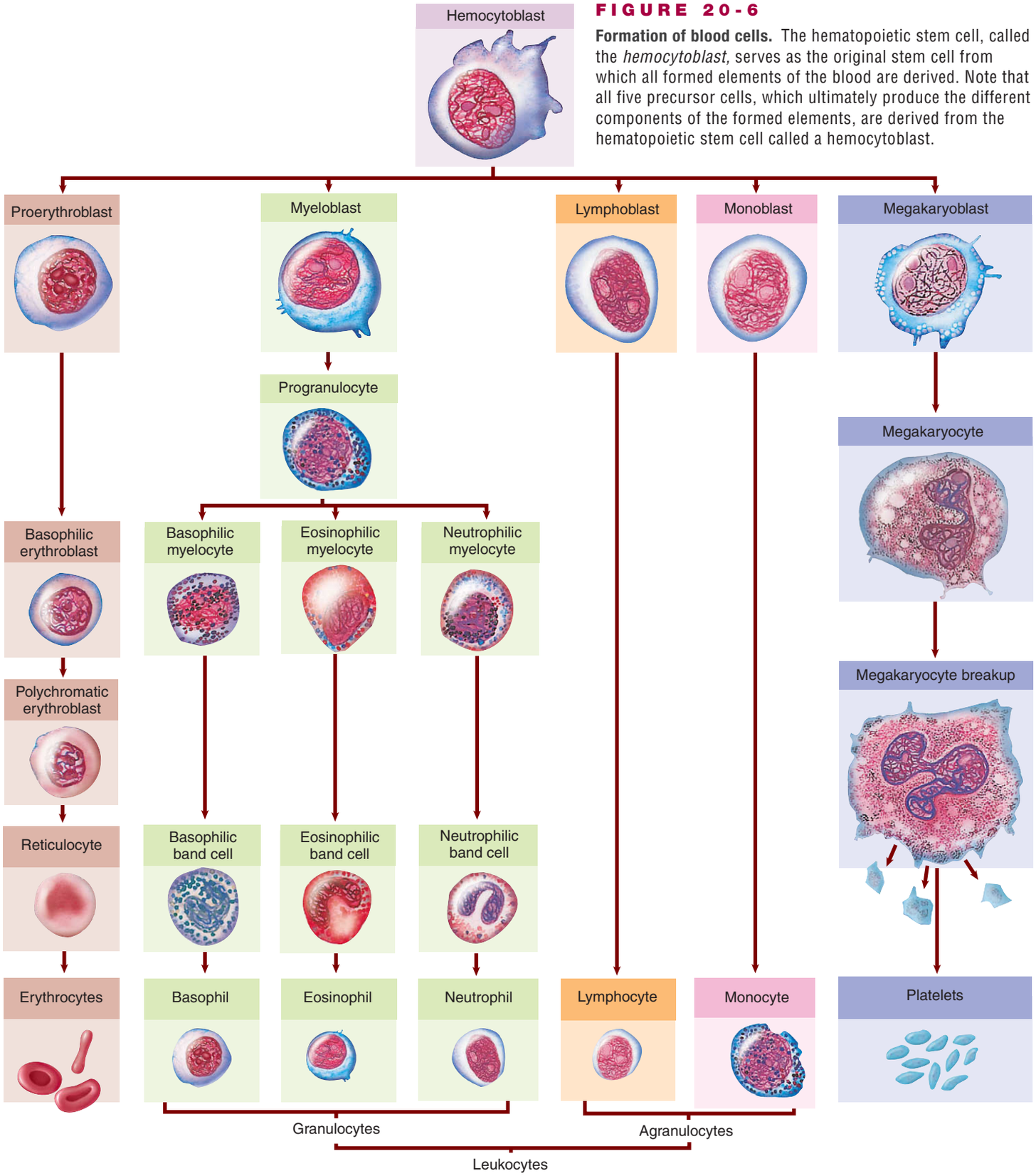


FIGURE 20-6

Formation of blood cells. The hematopoietic stem cell, called the *hemocytoblast,* serves as the original stem cell from which all formed elements of the blood are derived. Note that all five precursor cells, which ultimately produce the different components of the formed elements, are derived from the hematopoietic stem cell called a hemocytoblast.

the developmental stages that can be identified as transformation from the immature forms to the mature red blood cell occurs. The entire maturation process requires about 4 days and proceeds from step to step by gradual transition. Just what influences direct **embryonic stem cells** (found in the embryo and in umbilical cord blood) to develop into a specific type of **adult stem cell** (e.g., hematopoietic stem cells) and then eventually differentiate into a specific cell type, such as an RBC, is a topic of intense research.

As you can see in Figure 20-6, all blood cells are derived from hematopoietic stem cells. In RBCs, differentiation begins with the appearance of **proerythroblasts.** Mitotic divisions then produce

basophilic erythroblasts. The next maturation division produces **polychromatic erythroblasts,** which produce hemoglobin. These cells subsequently lose their nuclei and become **reticulocytes.** Once released into the circulating blood, reticulocytes lose their delicate reticulum and become mature erythrocytes in about 24 to 36 hours. Note in Figure 20-6 that overall cell size decreases as the maturation sequence progresses.

RBCs are formed and destroyed at a breathtaking rate. Every day of our adult lives we produce more than 200 billion RBCs to replace an equal number destroyed during that brief time. Because in health the number of RBCs remains relatively constant, efficient homeostatic mechanisms must operate to balance the number of cells formed against the number destroyed.

The rate of RBC production soon speeds up if blood oxygen levels reaching the tissues decrease. Oxygen deficiency increases RBC numbers by increasing the secretion of a glycoprotein hormone named **erythropoietin** (eh-RITH-roh-POY-eh-tin), or **EPO.** An inactive form of this hormone, called an *erythropoietinogen*, is released into the blood primarily from the liver on an ongoing basis. If oxygen levels decrease, the kidneys release increasing amounts of erythropoietin, which in turn stimulates bone marrow to accelerate its production of red blood cells. With increasing numbers of RBCs, oxygen delivery to tissues increases, and less erythropoietin is produced, and consequently less is available to stimulate RBC production in the red bone marrow. Figure 20-7 shows how erythropoietin production is controlled by a negative feedback loop that is activated by decreasing oxygen concentration in the tissues.

Box 20-3 discusses practices that boost RBC numbers artificially.

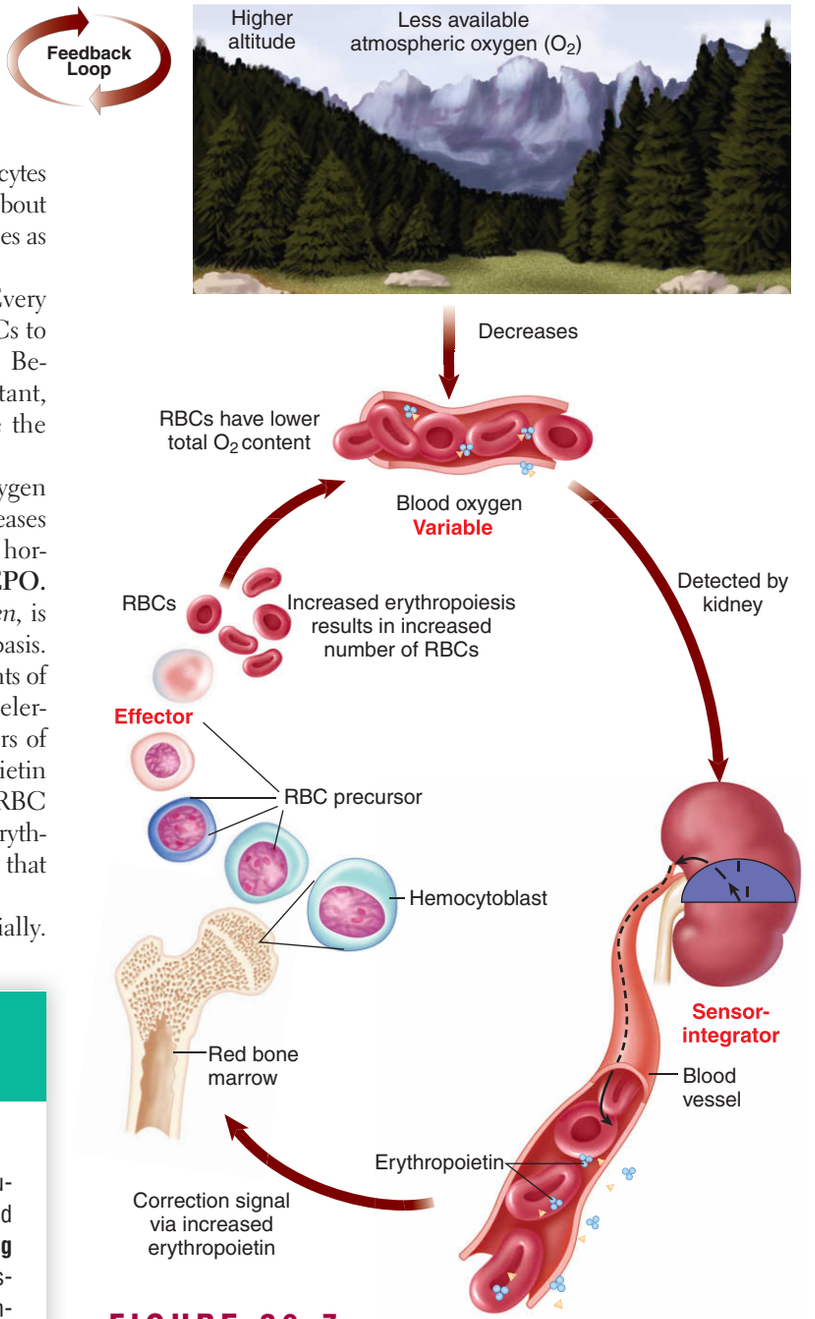


FIGURE 20-7

Erythropoiesis. In response to decreased blood oxygen, the kidneys release erythropoietin, which stimulates erythrocyte production in the red bone marrow.

Box 20-3 | SPORTS and FITNESS

Blood Doping

Reports that some Olympic and other elite athletes employ transfusions of their own blood to improve performance have surfaced repeatedly in the past 20 years. The practice—called **blood doping** or **blood boosting**—is intended to increase oxygen delivery to muscles. A few weeks before competition, blood is drawn from the athlete and the red blood cells (RBCs) are separated and frozen. Just before competition, the RBCs are thawed and injected. Theoretically, infused RBCs and elevation of hemoglobin levels after transfusion should increase oxygen consumption and muscle performance during exercise. In practice, however, the advantage appears to be minimal. All blood transfusions carry some risk, and unnecessary or questionably indicated transfusions are medically unacceptable.

In addition to blood transfusions, injection of substances that increase RBC levels in an attempt to improve athletic performance has also been condemned by leading authorities in the area of sports medicine and by athletic organizations around the world. "Doping" with either the naturally occurring hormone erythropoietin (EPO) or with synthetic drugs that have similar biological effects—such as Epogen and Procrit—can result in devastating medical outcomes. For example, EPO abuse can produce dangerously high blood pressure that may lead to a heart attack or stroke.

DESTRUCTION OF RED BLOOD CELLS

The life span of RBCs circulating in the bloodstream averages about 105 to 120 days. They often break apart, or fragment, in the capillaries as they age. Macrophage cells in the lining of blood vessels, particularly in the liver and spleen, phagocytose (ingest and destroy) the aged, abnormal, or fragmented red blood cells (Figure 20-8). The process results in breakdown of hemoglobin, with the release of amino acids, iron, and the pigment bilirubin. Iron is returned to the bone marrow for use in synthesis of new hemoglobin, and bilirubin is transported to the liver, where it is excreted into the intestine as part of bile. Amino acids, released

from the globin portion of the degraded hemoglobin molecule, are used by the body for energy or for synthesis of new proteins.

For the RBC homeostatic mechanism to succeed in maintaining a normal number of RBCs, the bone marrow must function adequately. To do this the blood must supply it with adequate amounts of several substances with which to form the new red blood cells—vitamin B_{12}, iron, and amino acids, for example, and also copper and cobalt to serve as catalysts. In addition, the gastric mucosa must provide some unidentified intrinsic factor necessary for absorption of vitamin B_{12} (also called **extrinsic factor** because it derives from external sources in foods and is not synthesized by the body; vitamin B_{12} is also called the **antianemic principle**).

| QUICK CHECK |

5. Name the red pigment found in RBCs, and list the normal range (in grams per 100 ml of blood) for women and men.
6. Trace the formation of an erythrocyte from stem cell precursor to a mature and circulating RBC.
7. Explain the negative feedback loop that controls erythropoiesis.
8. Discuss the destruction of RBCs in the body.

White Blood Cells (Leukocytes)

White blood cells, or **leukocytes,** do not contain pigments and thus these transparent cells appear white when collected together—just like clear snowflakes that appear white when grouped together. Because they are colorless WBCs can be seen easily under a microscope only when stained. Five general types of WBCS can be classified according to their staining characteristics, including the presence or absence of stained granules in their cytoplasm.

Granulocytes include the three WBCs that have large granules in their cytoplasm. They are named according to their cytoplasmic staining properties:

1. Neutrophils
2. Eosinophils
3. Basophils

Agranulocytes (WBCs without stained cytoplasmic granules) include the following:

1. Lymphocytes
2. Monocytes

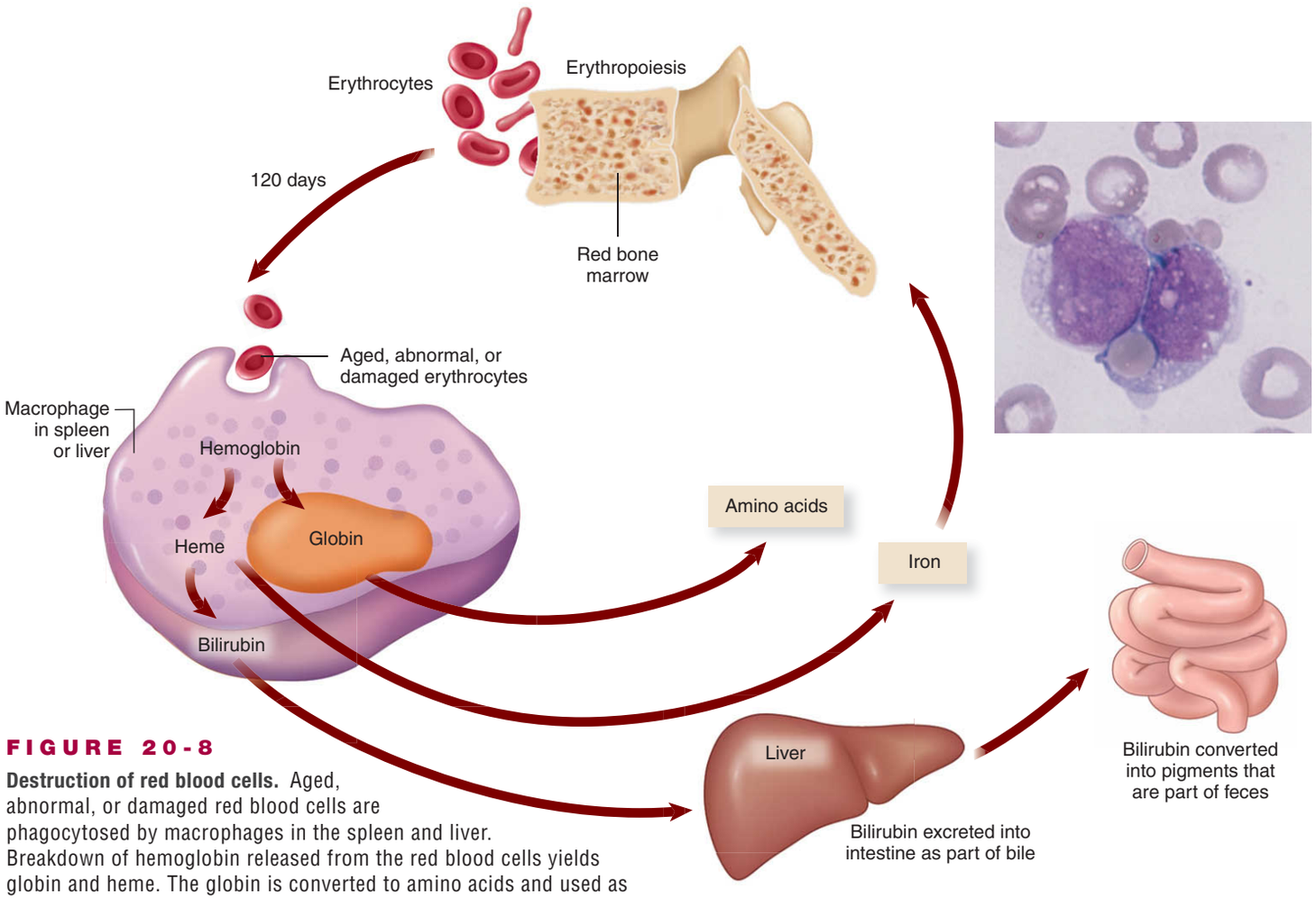


FIGURE 20-8

Destruction of red blood cells. Aged, abnormal, or damaged red blood cells are phagocytosed by macrophages in the spleen and liver. Breakdown of hemoglobin released from the red blood cells yields globin and heme. The globin is converted to amino acids and used as an energy source or for protein synthesis. Note that the released heme is further degraded into iron, which may be stored or used immediately to produce both new hemoglobin and bilirubin; the bilirubin is ultimately excreted in the bile. Photo inset shows phagocytosis of erythrocytes by macrophages in the liver.

WBCs have nuclei and are generally larger in size than RBCs. Table 20-1 illustrates the formed elements, provides a brief description of each cell type, and lists life span and primary functions. In Chapter 24 we more fully explore many of the defensive functions of leukocytes.

GRANULOCYTES

Neutrophils

Neutrophils (Figure 20-9) take their name from the fact that their cytoplasmic granules stain a very light purple with neutral dyes. The granules in these cells are small and numerous and tend to give the cytoplasm a coarse appearance. Because their nuclei have two, three, or more lobes, neutrophils are also called **polymorphonuclear leukocytes** or, to avoid that tongue twister, simply *polys*.

Neutrophil numbers average about 65% of the total WBC count in a normal blood sample. These leukocytes are highly mobile, active phagocytic cells that can migrate out of blood vessels and enter the tissue spaces. The process is called **diapedesis.** The cytoplasmic granules in neutrophils contain powerful lysosomes, the organelles with digestive-like enzymes that are capable of destroying bacterial cells.

Bacterial infections that produce an inflammatory response cause the release of chemicals from damaged cells that attract neutrophils and other phagocytic WBCs to the infection site. The process, called **chemotaxis,** helps the body concentrate phagocytic cells at focal points of infection.

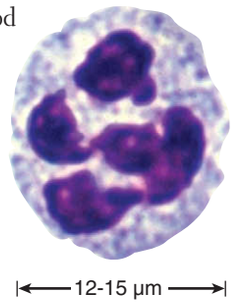
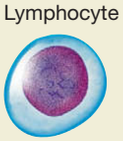


FIGURE 20-9
Neutrophil.

TABLE 20-1 Classes of Blood Cells

CELL TYPE	DESCRIPTION	FUNCTION	LIFE SPAN
Erythrocyte 	7 μm in diameter; concave disk shape; entire cell stains pale pink; no nucleus	Transportation of respiratory gases (O_2 and CO_2)	105–120 days
Neutrophil 	12-15 μm in diameter; spherical shape; multilobed nucleus; small, pink-purple–staining cytoplasmic granules	Cellular defense—phagocytosis of small pathogenic microorganisms	Hours to 3 days
Basophil 	11-14 μm in diameter; spherical shape; generally two-lobed nucleus; large purple-staining cytoplasmic granules	Secretes heparin (anticoagulant) and histamine (important in inflammatory response)	Hours to 3 days
Eosinophil 	10-12 μm in diameter; spherical shape; generally two-lobed nucleus; large, orange-red–staining cytoplasmic granule	Cellular defense—some phagocytosis; chemical attack of large pathogenic microorganisms (such as protozoa) and parasitic worms; helps regulate allergic reactions and other inflammatory responses	10–12 days
Lymphocyte 	6-9 μm in diameter; spherical shape; round (single-lobed) nucleus; small lymphocytes have scant cytoplasm	Humoral defense—secretes antibodies; involved in immune system response and regulation	Days to years
Monocyte 	12-17 μm in diameter; spherical shape; nucleus generally kidney-bean or horseshoe shaped with convoluted surface; ample cytoplasm often "steel blue" in color	Capable of migrating out of the blood to enter tissue spaces as a macrophage—an aggressive phagocytic cell capable of ingesting bacteria, cellular debris, and cancerous cells	Months
Platelet 	2-5 μm in diameter; irregularly shaped fragments; cytoplasm contains very small, pink-staining granules	Releases clot-activating substances and helps in formation of actual blood clot by forming platelet "plugs"	7–10 days

Eosinophils

Eosinophils (Figure 20-10) contain cytoplasmic granules that are large, are numerous, and stain orange with acid dyes such as eosin. Their nuclei generally have two lobes. Normally, eosinophils account for about 2% to 5% of circulating WBCs. They are also numerous in mucous membranes such as the lining of the respiratory and digestive tracts.

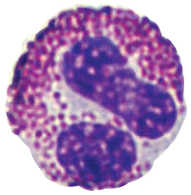


FIGURE 20-10
Eosinophil.

Although eosinophils are weak phagocytes, their major role is the release of chemicals from their granules. These immune chemicals include cell toxins and many regulators of the body's immune response. Perhaps their most important overall functions involve protection against infections caused by parasitic worms and involvement in regulating allergic reactions such as asthma.

Basophils

Basophils (Figure 20-11) have relatively large, but sparse, cytoplasmic granules that stain a dark purple with basic dyes. They are the least numerous of the WBCs, numbering only 0.5% to 1% of the total leukocyte count. Basophils are both motile and capable of diapedesis. They exhibit S-shaped, but indistinct, nuclei. The cytoplasmic granules of these WBCs contain *histamine* (an inflammatory chemical) and *heparin* (an anticoagulant).

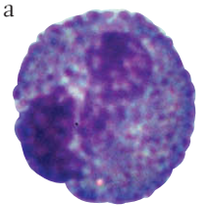


FIGURE 20-11
Basophil.

AGRANULOCYTES

Lymphocytes

Lymphocytes (Figure 20-12) found in the blood are the smallest of the leukocytes, averaging about 6 to 9 μm in diameter. They have large, spherical nuclei surrounded by a very limited amount of pale blue–staining cytoplasm. Next to neutrophils, lymphocytes are the most numerous WBCs. They account for about 25% of all the leukocyte population. Two types of lymphocytes, called *T lymphocytes* and *B lymphocytes*, have important roles in immunity. T lymphocytes function by directly attacking an infected or cancerous cell, whereas B lymphocytes produce antibodies against specific antigens. Activated B lymphocytes are also called *plasma cells*. The functions of both types of lymphocytes are fully discussed in Chapter 24.

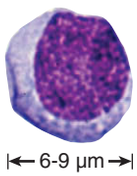


FIGURE 20-12
Lymphocyte.

Monocytes

Monocytes (Figure 20-13) are the largest of the leukocytes. They have dark, kidney bean–shaped nuclei surrounded by large quantities of distinctive blue-gray cytoplasm. Monocytes are motile and highly phagocytic cells capable of engulfing large bacterial organisms and viral-infected cells.

WHITE BLOOD CELL NUMBERS

One cubic millimeter of normal blood usually contains about 5000 to 9000 leukocytes, with different percentages of each type. Because these numbers change in certain abnormal conditions, they have clinical significance. In acute appendicitis, for example, the percentage of neutrophils increases and so, too, does the total WBC count. In fact, these characteristic changes may be the deciding points for surgery.

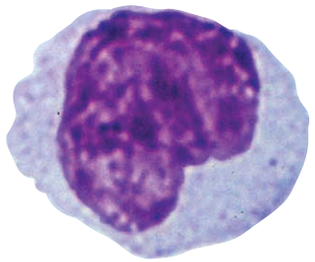


FIGURE 20-13
Monocyte.

An overall decrease in the number of WBCs is called **leukopenia.** An increase in the number of WBCs is **leukocytosis.**

A special type of white blood cell count called a **differential WBC count** reveals more information than simply the total number of all of the different types of WBCs in a blood sample. In a differential WBC count, a component test in the CBC or *complete blood count* (Box 20-4), the *proportions* of each type of white blood cell are reported as percentages of the total WBC count. Normal percentages are shown in Table 20-2. A lab technician may count

Box 20-4 | DIAGNOSTIC study

Complete Blood Cell Count

One of the most useful and frequently performed clinical blood tests is called the **complete blood cell count** or simply the **CBC.** The CBC is a collection of tests whose results, when interpreted as a whole, can yield an enormous amount of information regarding a person's health. Standard red blood cell, white blood cell, and thrombocyte counts, the differential white blood cell count, hematocrit, hemoglobin content, and other characteristics of the formed elements are usually included in this battery of tests.

TABLE 20-2 Differential Count of White Blood Cells

	DIFFERENTIAL COUNT*	
CLASS	NORMAL RANGE (%)	TYPICAL VALUE (%)†
Neutrophils	65-75	65
Lymphocytes (large and small)	20-25	25
Monocytes	3-8	6
Eosinophils	2-5	3
Basophils	½-1	1
TOTAL	100	100

*In any differential count the sum of the percentages of the different kinds of white blood cells (WBCs) must, of course, total 100%.
†The following mnemonic phrase may help you remember percent values in decreasing order by class of WBC: "**N**ever **L**et **M**onkeys **E**at **B**ananas."

the first 100 WBCs seen in a blood smear under a microscope to estimate the percentage of each type of WBC, but often this is done using advanced image-recognition computer technology (Figure 20-14).

Because all disorders do not affect each WBC type the same way, the differential WBC count is a valuable diagnostic tool. For example, although some parasite infestations do not cause an increase in the total WBC count, they often do cause an increase in the proportion of eosinophils that are present. The reason? This type of WBC specializes in defending against parasites (see Table 20-1).

FORMATION OF WHITE BLOOD CELLS

The hematopoietic stem cell serves as the precursor of not only the erythrocytes but also the leukocytes and platelets in blood. Figure 20-6, p. 603, shows the maturation sequence that results in formation of the granular and the agranular leukocytes from the undifferentiated hematopoietic stem cell (hemocytoblast).

Neutrophils, eosinophils, basophils, and a few lymphocytes and monocytes originate, as do erythrocytes, in red bone marrow (myeloid tissue). Most lymphocytes and monocytes derive from hematopoietic adult stem cells in lymphatic tissue. Although many lymphocytes are found in bone marrow, presumably most are formed in lymphatic tissues and carried to the bone marrow by the bloodstream.

Myeloid tissue (bone marrow) and lymphatic tissue together constitute the hematopoietic, or blood cell–forming, tissues of the body. Red bone marrow is myeloid tissue that actually produces blood cells. Its red color comes from the red blood cells it contains. Yellow marrow, on the other hand, is yellow because it stores a considerable amount of fat. It is not active in the business of blood cell formation as long as it remains yellow. Sometimes, however, it becomes active and then red in color when an extreme and prolonged need for red blood cell production occurs.

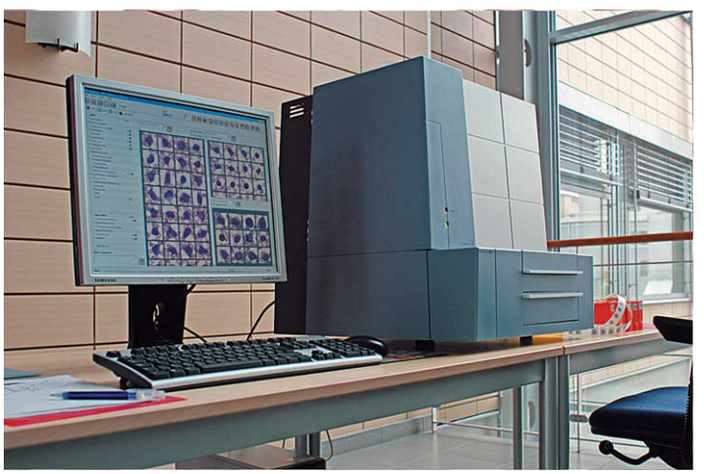


FIGURE 20-14

Differential WBC count. Automated microscope systems use advanced image-recognition technology to identify and count different WBC types in blood smear samples and produce the differential WBC count.

Platelets

To compare **platelets** with other blood cells in terms of appearance and size, see Figure 20-2. In circulating blood, platelets are small, nearly colorless bodies that usually appear as irregular spindles or oval disks about 2 to 4 μm in diameter.

Three important physical properties of platelets—namely, agglutination, adhesiveness, and aggregation—make attempts at classification on the basis of size or shape in dry blood smears all but impossible. As soon as blood is removed from a vessel, the platelets adhere to each other and to every surface they contact; in so doing, they assume various shapes and irregular forms.

Platelet counts in adults average about 250,000/mm^3 of blood. A range of 150,000 to 400,000/mm^3 is considered normal. Newborn infants often show reduced counts, but these rise gradually to reach normal adult values at about 3 months of age. There are no differences between the sexes in platelet count.

FUNCTIONS OF PLATELETS

Platelets play an important role in both **hemostasis** (from the Greek *stasis*, "a standing") and **blood clotting,** or **coagulation.** The two functions, although interrelated, are separate and distinct. Hemostasis refers to the stoppage of blood *flow* and may occur as an end result of any one of several body defense mechanisms. The role that platelets play in the operation of the blood-clotting mechanism is discussed on pp. 614–617.

Within 1 to 5 seconds after injury to a blood capillary, platelets will adhere to the damaged lining of the vessel and to each other to form a hemostatic **platelet plug** that helps stop the flow of blood into the tissues.

The formation of a temporary platelet plug is an important step in hemostasis. It generally follows vascular spasm, which is caused by constriction of smooth muscle fibers in the wall of damaged blood vessels. Vascular spasm can cause temporary closure of a damaged vessel and lessen blood loss until the platelet plug and subsequent coagulation effectively stop the hemorrhage.

The formation of a platelet plug results when platelets undergo a change caused by an encounter with a damaged capillary wall, or with underlying connective tissue fibers. The transformation results in the creation of *sticky platelets*, which bind to underlying tissues and each other. In addition to forming a physical plug at the site of injury, sticky platelets secrete several chemicals, including adenosine diphosphate (ADP), thromboxane, and a fatty acid (arachidonic acid), that are involved in the coagulation process. When released, these substances affect both local blood flow (by vasoconstriction) and platelet aggregation at the site of injury. If the injury is extensive, the blood-clotting mechanism is activated to assist in hemostasis.

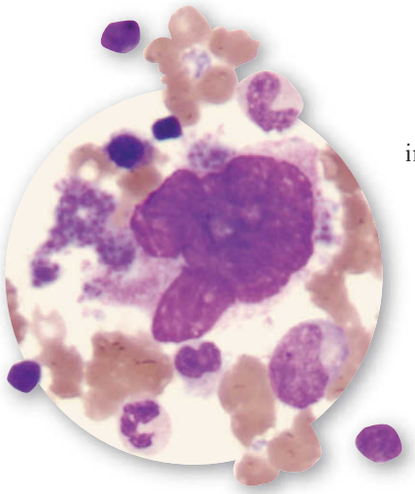


FIGURE 20-15

Megakaryocyte. Note the large size of the cell and multinucleated nucleus. This bone marrow smear also shows a number of WBCs scattered among more numerous RBCs.

Platelet plugs are extremely important in controlling so-called microhemorrhages, which may involve a break in a single capillary. Failure to arrest hemorrhage from these very minor but numerous and widespread capillary breaks can result in life-threatening blood loss.

Platelet plugs are also believed to be involved in causing intermittent arterial microvascular occlusion in certain types of peripheral vascular disease (see Box 20-5, p. 617).

FORMATION AND LIFE SPAN OF PLATELETS

Formation of platelets, sometimes called *thrombocytes*, is referred to as **thrombopoiesis.** It begins with stimulation of precursor cells called megakaryoblasts (see Figure 20-6), and is controlled by the hormone *thrombopoietin*. Mature megakaryocytes are huge cells (20 to 100 mm) with large nuclei containing as many as 20 lobes (Figure 20-15). They often have a bizarre shape. The cytoplasm of a stained specimen is blue to pink in color, is abundant, and contains a variable number of very fine granules. Mature megakaryocytes are largely confined to red bone marrow although some are located in the lungs and, to a lesser extent, the spleen. Between 2000 and more than 3000 platelets are released when the irregular cytoplasmic membrane surrounding the mature megakaryocyte ruptures. The resulting platelets have a limiting plasma membrane but, like RBCs, no nucleus. Platelets have a short life span, an average of about 7 days.

BLOOD TYPES (BLOOD GROUPS)

In 1902, the Austrian pathologist Karl Landsteiner announced his discovery of blood types, one of the most important medical discoveries of the time. The term *blood type* refers to the type of cell markers or antigens present on RBC membranes. (The concept of **antigens** and **antibodies** is discussed in detail in Chapter 24.) Landsteiner discovered the most important blood antigens: A and B. The presence or absence of these antigens determines a person's blood type in the ABO system. In 1940, Landsteiner found that a group of six Rh (or D) antigens previously found in rhesus monkeys was also found in humans. Continuing research by Landsteiner and others revealed nearly two dozen additional blood antigens that vary from person to person.

The fact that not everyone has the same blood antigens is very important. This means that our immune system may "attack" donated blood cells (from a transfusion) if they have antigens different than our own. Antigens A, B, and Rh are the most important blood antigens as far as transfusions and newborn survival are concerned. The other blood antigens are less important clinically but may still cause occasional problems.

Why do different people have different antigens on their RBCs? We do not have a complete answer to that question, but their presence or absence probably gives some biological advantage related to conditions within different human populations. For example, an antigen called *Duffy* (after the patient in whom it was first discovered) is often missing in populations that have lived with the threat of malaria for many generations. The Duffy antigen is used by the malaria parasite to enter RBCs, so its absence protects a person against developing malaria. However, we know very little about functions of the other antigens.

The term *agglutinins* is often used to describe the antibodies dissolved in plasma that react with specific blood group antigens or *agglutinogens*. We use the terms agglutinin and agglutinogen because when they combine and react, they cause the RBCs to clump together or agglutinate. It is the specific agglutinogens or antigens on red cell membranes that characterize the different ABO blood groups, which are described in the following paragraphs.

When a blood transfusion occurs, great care must be taken to prevent a mixture of agglutinogens (antigens) and agglutinins (antibodies) that would result in the agglutination of the donor and recipient blood—a potentially fatal event known as a **transfusion reaction.** Clinical laboratory tests, called *blood typing* and *cross-matching*, ensure the proper identification of blood group antigens and antibodies in both donor and recipient blood and demonstrate the lack of an agglutination reaction when they are mixed together.

The ABO System

Every person's blood belongs to one of the four ABO blood types (or groups). Blood types are named according to the antigens present (agglutinogens) on RBC membranes. Here, then, are the four ABO blood types:

1. Type A—antigen A on RBCs
2. Type B—antigen B on RBCs
3. Type AB—both antigen A and antigen B on RBCs
4. Type O—neither antigen A nor antigen B on RBCs

Blood plasma may or may not contain antibodies (agglutinins) that can react with red blood cell antigens A or B. An important principle related to this is that plasma never contains antibodies against the antigens present on its own red blood cells—for obvious reasons. If it did, the antibody would react with the antigen and thereby destroy the RBCs. However (and this is an equally important principle), plasma does contain antibodies against antigen

A or antigen B if they are *not* present on its RBCs. So by applying these two principles, we can deduce the following: In type A blood, antigen A is present on its RBCs; therefore its plasma contains no anti-A antibodies but does contain anti-B antibodies. In type B blood, antigen-B is present on its RBCs; therefore its plasma contains no anti-B antibodies but does contain anti-A antibodies (Figure 20-16).

Note in Figure 20-17, *A*, that type A blood donated to a type A recipient does not cause an agglutination transfusion reaction because the antiB antibodies in the recipient do not combine with the A antigens in the donated blood. However, type A blood donated to a type B recipient causes an agglutination reaction because the anti-A antibodies in the recipient combine with the A antigens in the donated blood (Figure 20-17, *B*). Figure 20-18 shows the results of different combinations of donor and recipient blood.

Because type O blood does not contain either antigen A or B, it has been referred to as *universal donor* blood, a term that implies that it can safely be given to any recipient. This, however, is not true because the recipient's plasma may contain agglutinins other than anti-A or anti-B antibodies. For this reason the recipient's and the donor's blood—even if it is type O—should be cross-matched; that is, mixed and observed for agglutination of the donor's red blood cells.

Universal recipient (type AB) blood contains neither anti-A nor anti-B antibodies, so it cannot agglutinate type A or type B donor red blood cells. This does not mean, however, that any type of donor blood may be safely given to an individual who has type AB blood without first cross-matching. Other agglutinins may be present in the so-called universal recipient blood and may clump unidentified antigens (agglutinogens) in the donor's blood.

Improperly typed and cross-matched blood given during a blood transfusion can cause a *transfusion reaction* in the recipient. Depending on the response of the recipient's immune system and the amount of mismatched blood given, such a reaction may range from mild to severe to life threatening. As the host antibodies attack the donor RBCs, the RBCs are broken apart—a process called *hemolysis*. Hemoglobin is thus released into the blood stream, which (if severe) may overload the kidney and cause kidney failure. Signs of this type of transfusion reaction include fever, difficulty breathing, and pink urine.

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The Rh System

The term *Rh-positive blood* means that an Rh (or D) antigen is present on its RBCs. *Rh-negative blood*, on the other hand, is blood whose red cells have no Rh antigens present on them.

Blood does not normally contain anti-Rh antibodies. However, anti-Rh antibodies can appear in the blood of an Rh-negative person, provided Rh-positive RBCs have at some time entered the bloodstream. One way this can happen is by giving an Rh-negative person a transfusion of Rh-positive blood. In a short time, the person's body makes anti-Rh antibodies, and these remain in the blood. The other way in which Rh-positive RBCs can enter the bloodstream of an Rh-negative individual can happen only to a woman during pregnancy. In this fact lies the danger for a baby born to an Rh-negative mother and

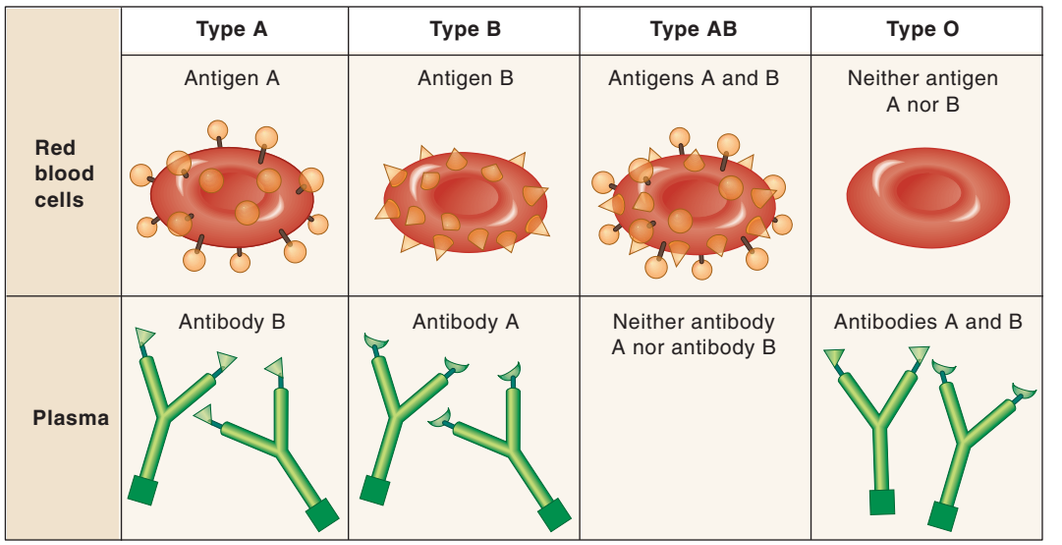


FIGURE 20-16

ABO blood types. Note that antigens characteristic of each blood type are bound to the surface of RBCs. The antibodies of each blood type are found in the plasma and exhibit unique structural features that permit agglutination to occur if exposure to the appropriate antigen occurs.

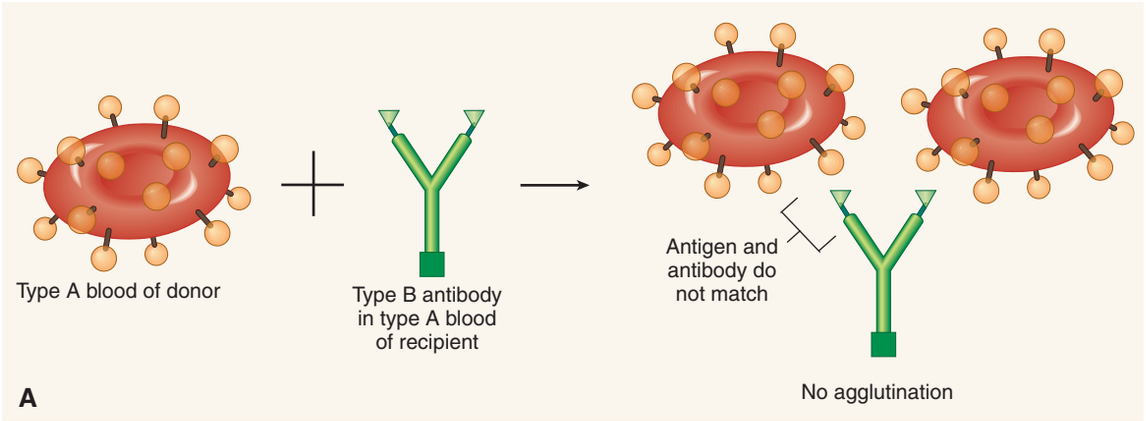


FIGURE 20-17

Agglutination. A, When mixing of donor and recipient blood of the same type *(A)* occurs, there is no agglutination because only anti-B antibodies are present. **B,** If type A donor blood is mixed with type B recipient blood, agglutination will occur because of the presence of anti-A antibodies in the type B recipient blood.

Recipient's blood		Reactions with donor's blood			
RBC antigens	Plasma antibodies	Donor type O	Donor type A	Donor type B	Donor type AB
None (Type O)	Anti-A Anti-B				
A (Type A)	Anti-B				
B (Type B)	Anti-A				
AB (Type AB)	(None)				

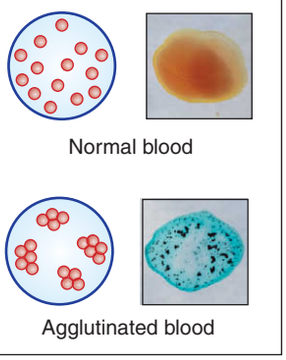


FIGURE 20-18

Results of (cross-matching) different combinations (types) of donor and recipient blood. The left columns show the antigen and antibody characteristics that define the recipient's blood type, and the top row shows the donor's blood type. Cross-matching identifies either a compatible combination of donor-recipient blood (no agglutination) or an incompatible combination (agglutinated blood). Photo inset shows drops of blood showing appearance of agglutinated and non-agglutinated red blood cells.

an Rh-positive father. If the baby inherits the Rh-positive trait from the father, the Rh factor on the RBCs may stimulate the mother's body to form anti-Rh antibodies. Then, if she later carries another Rh-positive fetus, the fetus may develop a disease called **erythroblastosis fetalis,** a hemolytic condition caused by the mother's Rh antibodies reacting with the baby's Rh-positive cells (Figure 20-19).

All Rh-negative mothers who carry an Rh-positive baby should be treated with an anti-Rh antibody marketed under the name RhoGAM (and others). RhoGAM stops the mother's body from forming anti-Rh antibodies and thus prevents the possibility of harm to the next Rh-positive baby she may have. Briefly, the only people who can ever have anti-Rh antibodies in their plasma are Rh-negative men or women who have been transfused with Rh-positive blood or Rh-negative women who have carried an Rh-positive fetus.

Table 20-3 summarizes the ABO and Rh blood types, including the frequency of each in the general population—that is, the human population as a whole. Of course the frequency of these and other blood types may be different within a family or ethnic group based on regional differences in the human gene pool.

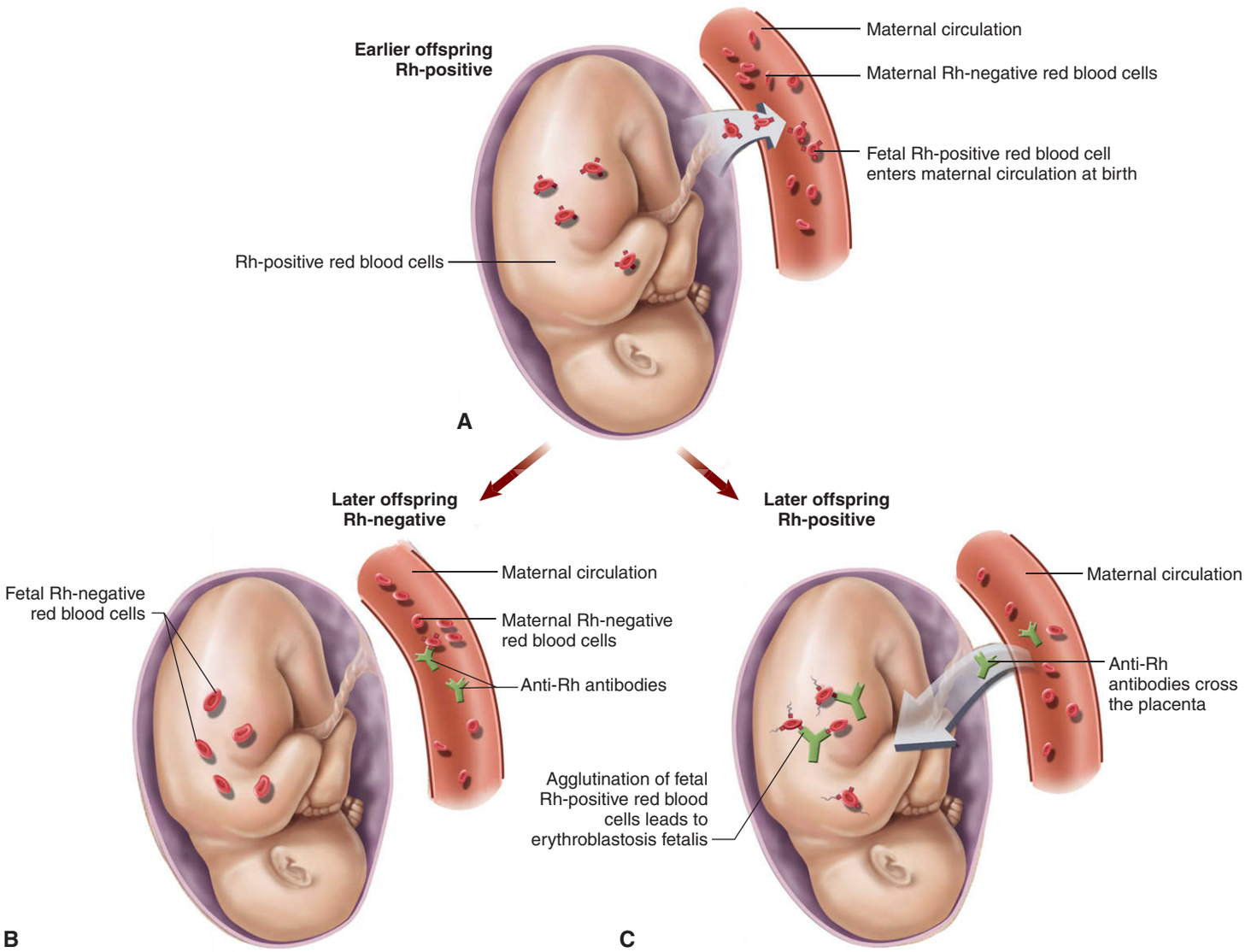


FIGURE 20-19

Erythroblastosis fetalis. A, Rh-positive blood cells enter the mother's bloodstream during delivery of an Rh-positive baby. If not treated, the mother's body will produce anti-Rh antibodies. **B,** A later pregnancy involving an Rh-negative baby is normal because there are no Rh antigens in the baby's blood. **C,** A later pregnancy involving an Rh-positive baby may result in erythroblastosis fetalis. Anti-Rh antibodies enter the baby's blood supply and cause agglutination of RBCs with the Rh antigen.

TABLE 20-3 Blood Typing

BLOOD TYPE (ABO AND RH)	ANTIGENS PRESENT*	ANTIBODIES PRESENT*	PERCENT OF GENERAL POPULATION
O+	Rh	anti-A, anti-B	35%
O–†	None	anti-A, anti-B, anti-Rh?	7%
A+	A, Rh	anti-B	35%
A–	A	anti-B, anti-Rh?	7%
B+	B, Rh	anti-A	8%
B–	B	anti-A, anti-Rh?	2%
AB+‡	A, B, Rh	None	4%
AB–	A, B	anti-Rh?	2%

Adapted from Pagana KD, Pagana TJ: *Mosby's manual of diagnostic and laboratory tests,* ed 4, St Louis, 2010, Mosby.
*Anti-Rh antibodies *may* be present, depending on exposure to Rh antigens.
†Universal donor.
‡Universal recipient.

BLOOD PLASMA

Plasma is the liquid part of blood—whole blood minus formed elements (Figure 20-20). In the laboratory, whole blood that has not clotted is centrifuged to form plasma. This consists of a rapid whirling process that hurls the blood cells to the bottom of the centrifuge tube. A clear, straw-colored fluid—blood plasma—lies above the cells.

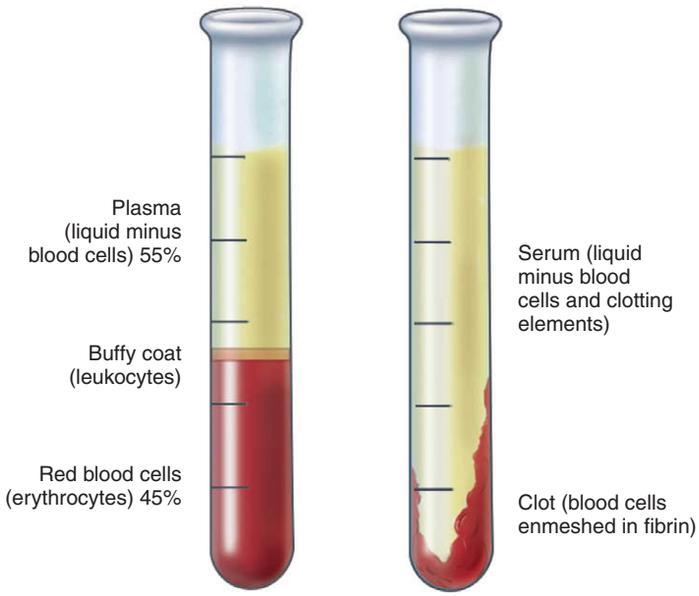


FIGURE 20-20

Difference between blood plasma and blood serum. Plasma is whole blood minus cells. Serum is whole blood minus the clotting elements. Plasma is prepared by centrifuging anticoagulated blood. Serum is prepared by allowing blood to clot.

Plasma consists of 90% water and 10% solutes. By far the largest quantity of these solutes is proteins; normally, they constitute about 6% to 8% of the plasma. Proteins such as factor VIII regulate blood clotting; and others such as gamma globulins, which are important in treating weakened immune systems, and albumin, a blood volume expander, are common transfusion products. Other solutes present in much smaller amounts in plasma are nutrient substances (principally glucose, amino acids, and lipids), compounds formed by metabolism (e.g., urea, uric acid, creatinine, and lactic acid), respiratory gases (oxygen and carbon dioxide), and regulatory substances (hormones, enzymes, and certain other substances).

Some solutes present in blood plasma are true solutes, or crystalloids. Others are colloids. *Crystalloids* are solute particles less than 1 nm in diameter (e.g., ions, glucose, and other small molecules). *Colloids* are solute particles from 1 to about 100 nm in diameter (e.g., proteins of all types). Blood solutes also may be classified as **electrolytes** (molecules that ionize in solution) or **nonelectrolytes**—examples: proteins and inorganic salts are electrolytes; glucose and lipids are nonelectrolytes.

The proteins in blood plasma consist of three main kinds of compounds: *albumins*, *globulins*, and clotting proteins, principally *fibrinogen*. Measuring the amounts of these compounds reveals that 100 ml of plasma contains a total of approximately 6 to 8 grams of protein. Albumins constitute about 55% of this total, globulins about 38%, and fibrinogen about 7%.

Plasma proteins are crucially important substances. Fibrinogen, for instance, and a clotting protein named prothrombin have key roles in the blood-clotting mechanism. Globulins function as essential components of the immunity mechanism. Many modified globulins, called gamma globulins, serve important roles as circulating antibodies (see also immunoglobulins, Chapter 24). All plasma proteins contribute to the maintenance of normal blood viscosity, blood osmotic pressure, and blood volume. Therefore plasma proteins have an essential part in maintaining normal circulation.

Synthesis of plasma proteins occurs in liver cells. They form all kinds of plasma proteins, except some of the gamma globulin antibodies synthesized by plasma cells. Plasma cells are a type of lymphocyte (WBC). Cancer of plasma cells, called *multiple myeloma*, results in production of an abnormal myeloma antibody—a gamma globulin—that results in numerous and very serious disease symptoms (see Mechanisms of Disease, p. 619).

BLOOD CLOTTING (COAGULATION)

The primary purpose of blood coagulation is obvious—to plug ruptured vessels to stop bleeding and prevent loss of a vital body fluid. Recall that this process is called *hemostasis*. A secondary and less well known function of the hemostasis mechanism is to help in defending us against infection. In an injury, bacteria may find an opportunity to invade our tissues. However, a blood clot will hopefully trap and bind enough of them to prevent such an invasion.

Mechanism of Blood Clotting

Because of the function of coagulation, the mechanism for producing it must be swift and sure when needed, such as when a vessel is cut or ruptured. Equally important, however, coagulation needs to be prevented from happening when it is not needed because clots can plug up vessels that must stay open if cells are to receive blood's life-sustaining cargo of oxygen.

What makes blood coagulate? Over many years a host of investigators have searched for the answer to this question. They have tried to find out what events make up the coagulation mechanism and what sets it in operation. They have succeeded in gathering an abundance of relevant information, but questions about this complicated and important process still outnumber answers.

The blood-clotting mechanism involves a series of chemical reactions that takes place in a definite and rapid sequence resulting in a net of fibers that traps red blood cells (Figure 20-21, *B*).

The so-called classic theory of coagulation was advanced in 1905 and dominated research efforts in this complex area for almost 50 years. It continues as the basis of our current understanding of coagulation. This theory has now been expanded and assumes (1) the interaction of numerous coagulation factors in the presence of calcium ions and (2) that the interaction between the components occurs in three stages.

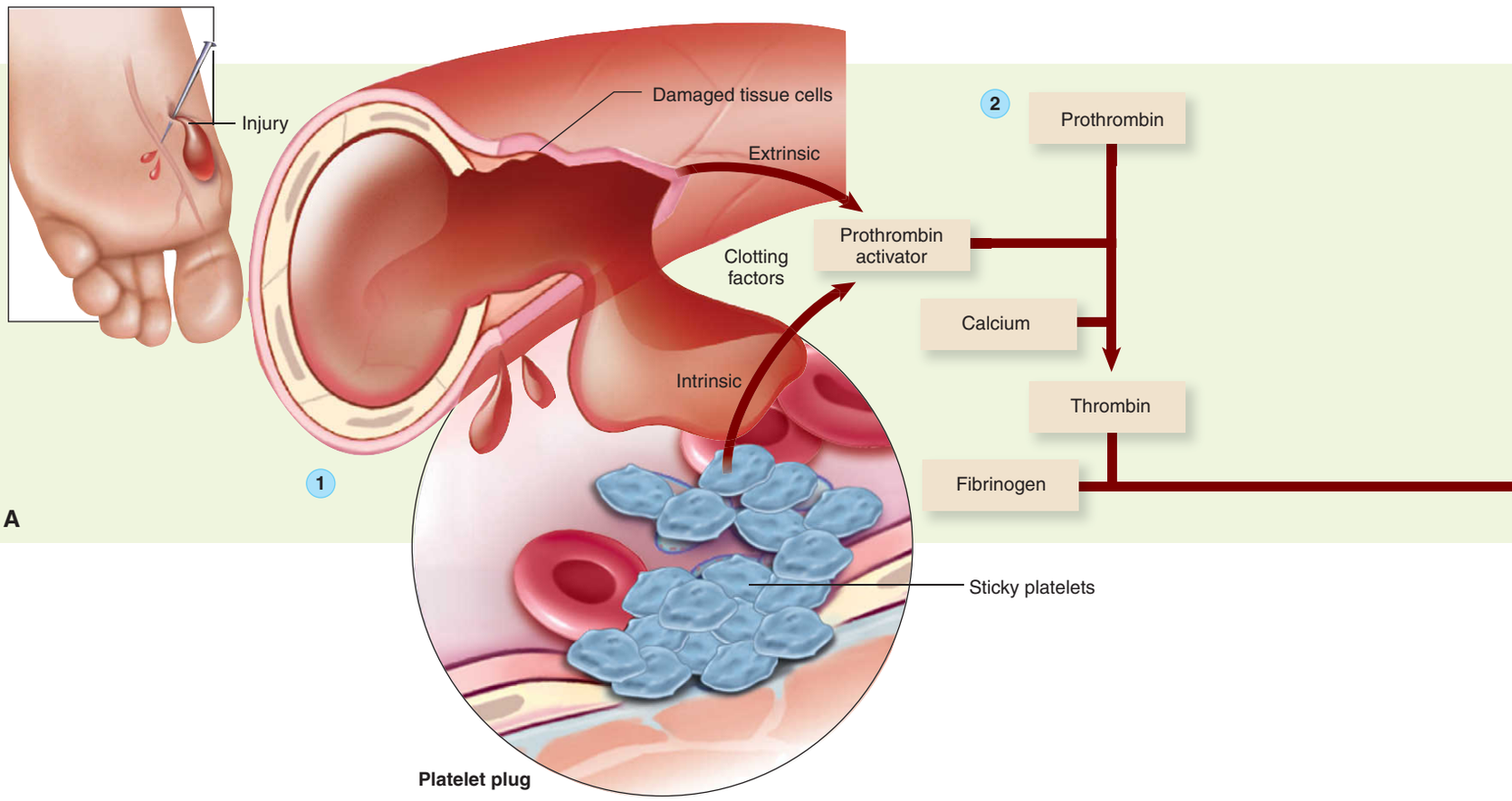
Scientists working more than a century ago discovered that four components were critical to coagulation:

1. Prothrombin
2. Thrombin
3. Fibrinogen
4. Fibrin

These early studies in coagulation research suggested that interactions between these components occurred in what we now

FIGURE 20-21

Blood-clotting mechanism. A, The complex clotting mechanism can be distilled into three basic steps: *(1)* release of clotting factors from both injured tissue cells and sticky platelets at the injury site (which form temporary platelet plug); *(2)* series of chemical reactions that eventually result in the formation of thrombin; and *(3)* formation of fibrin and trapping of blood cells to form a clot. **B,** Photo inset is a colorized electron micrograph showing RBCs and platelets *(blue)* entrapped in a fibrin *(yellow)* mesh during clot formation.



designate as stage 2 and stage 3 of the blood-clotting process, which are simplified and illustrated in Figure 20-21:

Stage 2:

$$\text{Prothrombin} \xrightarrow[Ca^{++}]{\text{Prothrombin activator}} \text{Thrombin}$$

Stage 3:

$$\text{Fibrinogen} \xrightarrow[Ca^{++}]{\text{Thrombin}} \text{Fibrin}$$

It is interesting that basic reaction stages 2 and 3 have been modified only by the action of a host of additional coagulation factors discovered in recent decades (Table 20-4). In addition, the

TABLE 20-4 Coagulation Factors—Standard Nomenclature and Synonyms

FACTOR	COMMON SYNONYM(S)
Factor I	Fibrinogen
Factor II	Prothrombin
Factor III	Thromboplastin
	Thrombokinase
Factor IV (now obsolete)	(Calcium)
Factor V	Proaccelerin
	Labile factor
Factor VI (now obsolete)	(Activated Factor V)
Factor VII	Serum prothrombin conversion accelerator (SPCA)
Factor VIII	Antihemophilic globulin (AHG)
	Antihemophilic factor (AHF)
Factor IX	Plasma thromboplastin component (PTC), Christmas factor
Factor X	Stuart factor
Factor XI	Plasma thromboplastin antecedent (PTA)
Factor XII	Hageman factor
Factor XIII	Fibrin-stabilizing factor

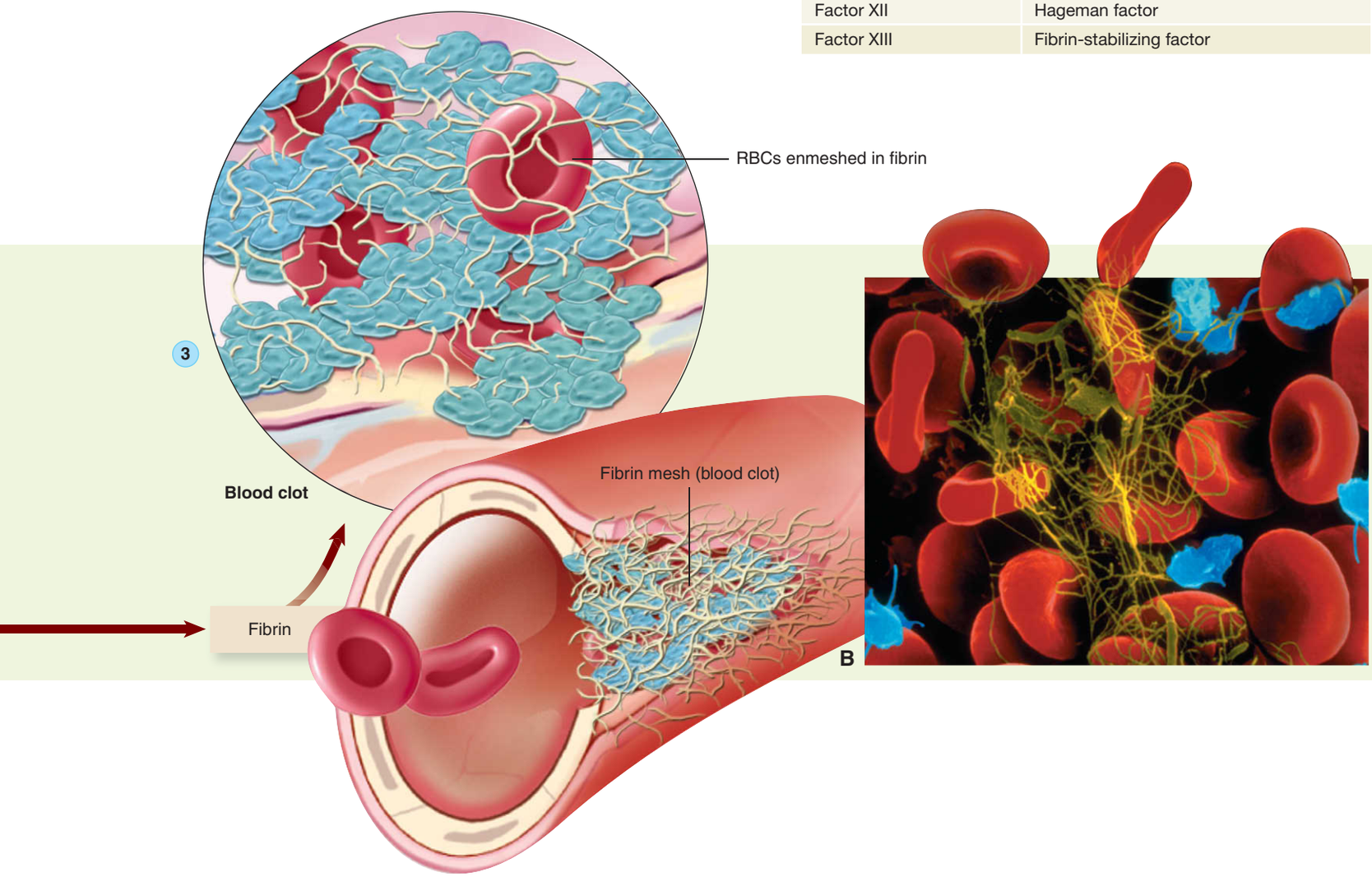
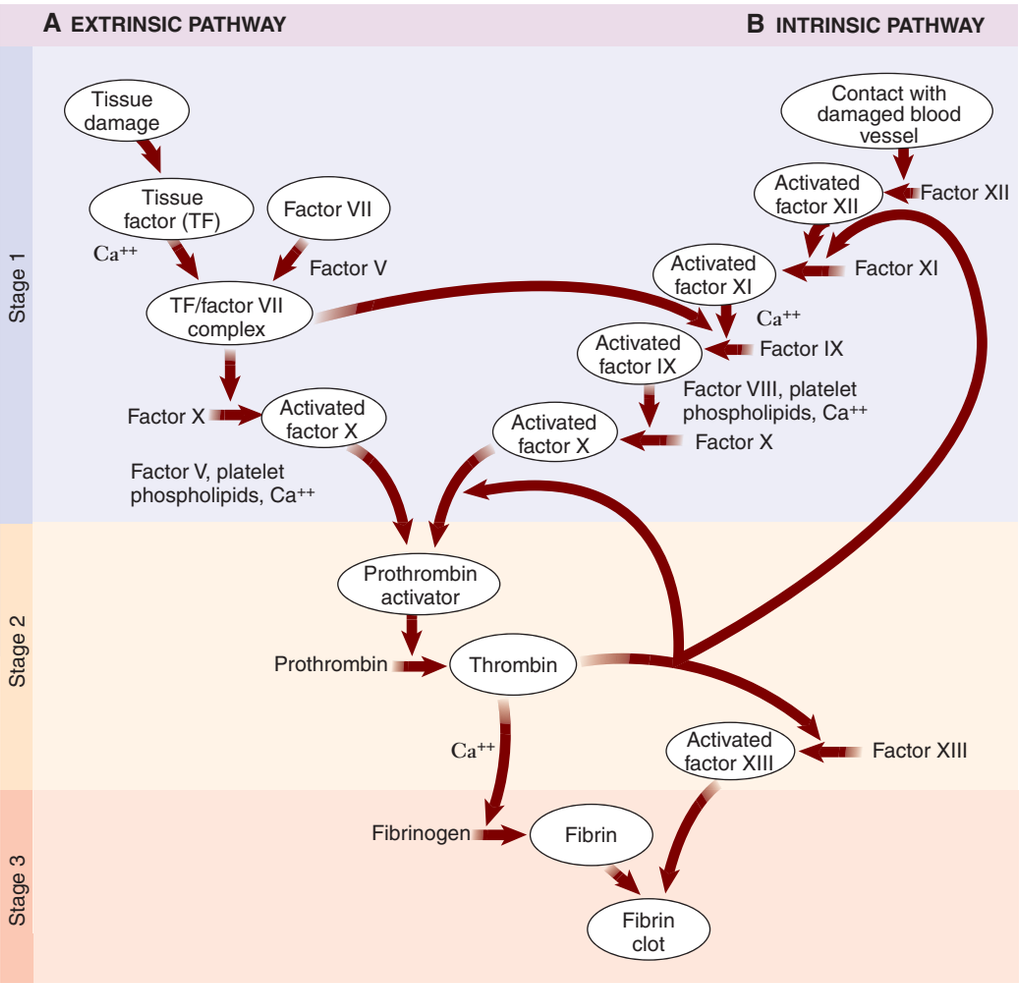


FIGURE 20-22

Clot formation. A, Extrinsic clotting pathway. *Stage 1:* Damaged tissue releases tissue factor, which with factor VII and calcium ions activates factor X. Activated factor X, factor V, phospholipids, and calcium ions form prothrombin activator (prothrombinase). *Stage 2:* Prothrombin is converted to thrombin by prothrombin activator. *Stage 3:* Fibrinogen is converted to fibrin by thrombin. Fibrin forms a clot. **B,** Intrinsic clotting pathway. *Stage 1:* Damaged vessels cause activation of factor XII. Activated factor XII activates factor XI, which activates factor IX. Factor IX, along with factor VIII and platelet phospholipids, activates factor X. Activated factor X, factor V, phospholipids, and calcium ions form prothrombin activator. Stages 2 and 3 take the same course as the extrinsic clotting pathway.



source of prothrombin activator at the end of stage 1 of the current coagulation theory mechanism is now used to divide this stage into *intrinsic* and *extrinsic* systems.

The three stages of coagulation described in the following paragraphs are illustrated in Figure 20-22.

Stage 1 of the clotting mechanism can be divided into two separate mechanisms called the **extrinsic clotting pathways** and **intrinsic clotting pathways.** In both pathways a sequential series of chemical reactions called a *clotting cascade* precedes the formation of prothrombin activator. This substance is the catalyst needed for conversion of prothrombin to thrombin in stage 2 of the clotting process (see Figure 20-22).

EXTRINSIC PATHWAY

In the extrinsic pathway, chemicals released from damaged tissues that are outside or extrinsic to the blood trigger the cascade of events that ultimately result in formation of prothrombin activator. Initially, tissue damage results in release of a mixture of lipoproteins and phospholipids called *tissue factor* or *factor III*. In the coordinated series of chemical reactions that follow, this factor, in the presence of calcium ions, factor V, and factor VII, forms a complex that in turn activates factor X and produces prothrombin activator (see Figure 20-22, A).

INTRINSIC PATHWAY

The intrinsic pathway involves a series of reactions that begin with factors normally present, or intrinsic to, the blood. Damage to the endothelial lining of blood vessels exposes collagen fibers, which in turn causes the activation of a number of coagulation factors present in plasma. When activated in this manner, factor XII (Hageman factor) then causes factor XI to activate factor IX. Sticky platelets participate in the intrinsic pathway by releasing a phospholipid called *platelet factor VIII*. This substance activates factor X, which then produces the prothrombin activator (prothrombinase) (see Figure 20-22, *B*).

STAGES 2 AND 3

Regardless of the pathway involved, after prothrombin activator is produced, stages 2 and 3 of the blood-clotting mechanism are initiated and a clot will form. Thrombin formed in stage 2 accelerates in stage 3 conversion of the soluble plasma protein fibrinogen to insoluble fibrin. The stage 3 polymerization of fibrin strands into a fibrin clot is accelerated by the presence of activated factor XIII. Fibrin appears in blood as fine threads all tangled together. Blood cells catch in the entanglement, and because most of the cells are RBCs, clotted blood has a red color. Note that several of the clotting factors require calcium ions as a co-factor. This explains the need

Box 20-5 | HEALTH matters

Anticoagulant and Antiplatelet Drug Treatments

Many types of drugs are now available to physicians that help prevent thrombosis and embolism. If an individual is at risk for thrombus formation, the selection of a so-called targeted or rational drug treatment may depend on the location in the vascular system in which the clots may form. Research has shown that venous thrombi consist mainly of fibrin and red blood cells, whereas arterial thrombi consist mainly of platelet aggregates. This information provides a theoretic basis for selecting different types of drug treatment for conditions caused by either venous or arterial thrombi.

For example, **anticoagulant drugs** such as aspirin, heparin, and warfarin (Coumadin) should be more effective in prevention of venous thrombi, and drugs that decrease the tendency for platelets to become sticky and form aggregates **(antiplatelet drugs)** should be more effective in preventing arterial thrombi.

A daily low dose of aspirin inhibits the COX-1 enzyme, thus blocking production of the platelet inhibitor thromboxane (see Figure 18-13 on p. 548). Daily low-dose (81 mg) aspirin therapy prevents thrombosis that can trigger a myocardial infarction (MI). A larger dose of aspirin taken during an MI can lessen its severity. Heparin is a naturally occurring "blood thinner" that can be used to prevent excessive clotting. Heparin inhibits the conversion of prothrombin to thrombin, preventing the formation of a thrombus. Warfarin (Coumadin), an oral anticoagulant, is also frequently used to prevent excessive clotting. It blocks the stimulating effect of vitamin K on the liver, and consequently the liver cells make less prothrombin. The prothrombin content soon falls low enough to prevent abnormal clotting.

Despite anticoagulant drugs being called "blood thinners," they do not really dilute the blood. They instead make blood less likely to clot and more likely to flow easily, just as adding "paint thinner" to paint prevents clumping and promotes the smooth flow of paint.

A number of antiplatelet drugs, such as cilostazol (Pletal) and ticlopidine (Ticlid), exert effects by inhibiting an enzyme called *phosphodiesterase,* which is involved in platelet aggregation activity. The mechanism of action of these drugs may explain why a condition such as **intermittent claudication,** which involves cramplike pain in the calves after walking that is caused by occasional arterial microvascular blockages by platelet plugs, often responds well to antiplatelet but not to anticoagulant drug therapy.

Another popular antiplatelet drug is clopidogrel (Plavix), which exerts its antiplatelet action by blocking adenosine diphosphate (ADP) receptors on the platelet membranes. This drug is used to prevent arterial clots that may cause an MI or stroke.

for the presence of adequate calcium levels in the blood for normal clotting to occur. The pale yellowish liquid left after a clot forms is **blood serum.** How do you think serum differs from plasma? What is plasma? To check your answers, see Figure 20-20.

Liver cells synthesize both prothrombin and fibrinogen as they do almost all other plasma proteins. For the liver to synthesize prothrombin at a normal rate, blood must contain an adequate amount of vitamin K. Vitamin K is absorbed into the blood from the intestine. Some foods contain this vitamin, but it is also synthesized in the intestine by certain bacteria (not present for a time in newborn infants). Because vitamin K is fat soluble, its absorption requires bile. Therefore if the bile ducts become obstructed and bile cannot enter the intestine, a vitamin K deficiency develops. The liver cannot then produce prothrombin at its normal rate, and the blood's prothrombin concentration soon falls below normal. A prothrombin deficiency gives rise to a bleeding tendency. As a preoperative safeguard, therefore, patients with obstructive jaundice are generally given some kind of vitamin K preparation.

Conditions That Oppose Clotting

Although blood clotting goes on continuously and concurrently with clot dissolution (fibrinolysis), several conditions operate to oppose clot formation in intact vessels. Most important by far is the perfectly smooth surface of the normal endothelial lining of blood vessels. Platelets do not adhere to healthy endothelium; consequently, they do not activate and release platelet factors into the blood. Therefore the blood-clotting mechanism does not begin in normal vessels.

As an additional deterrent to clotting, blood contains certain substances called *antithrombins.* The name suggests their function—they oppose (inactivate) thrombin. Thus antithrombins prevent thrombin from converting fibrinogen to fibrin. **Heparin,** a natural constituent of blood, acts as an antithrombin. It was first prepared from liver (hence its name), but other organs also contain heparin. Injections of heparin are used to prevent clots from forming in vessels. *Coumarin* compounds such as *warfarin* (Coumadin) impair the liver's use of vitamin K and thereby slow its synthesis of prothrombin and factors VII, IX, and X. Indirectly, therefore, coumarin compounds retard coagulation. Direct thrombin inhibitors such as dabigatron (Pradaxa) can be administered orally to prevent clotting. Citrates keep donor blood from clotting before transfusion. Aspirin and other drugs, such as clopidogrel (Plavix) or cilostazol (Pletal), that inhibit platelet aggregation also inhibit coagulation (Box 20-5).

Conditions That Hasten Clotting

Two conditions particularly favor thrombus formation: a rough spot in the endothelium (blood vessel lining) and abnormally slow blood flow. Atherosclerosis, for example, is associated with an increased tendency toward **thrombosis**, the abnormal formation of clots. It is endothelial rough spots in the form of plaques of accumulated cholesterol lipid material that could trigger abnormal clot formation. Body immobility, on the other hand, may lead to thrombosis

Box 20-6 | HEALTH matters

Clinical Methods of Hastening Clotting

One way of treating excessive bleeding is to speed up the blood-clotting mechanism. This can be accomplished by increasing any of the substances essential for clotting, for example:

- Applying a rough surface such as gauze or gently squeezing the tissues around a cut vessel causes more platelets to activate and release more platelet factors. This in turn accelerates the first of the clotting reactions.
- Applying purified thrombin (in the form of sprays or impregnated gelatin sponges that can be left in a wound) accelerates the third stage.
- Applying cold compresses, which causes vasoconstriction and slows blood flow, can stop some superficial bleeding.
- Applying new types of hemostatic materials made with shrimp shells (HemCon), purified algae derivatives (MDRH), or mineral dust (QuickClot), which incorporate a variety of mechanisms, can promote blood clotting of wounds by providing large surface areas to stimulate platelet stickiness and release of clotting factors.

because blood flow slows down as movements decrease. Incidentally, this fact is one of the major reasons why physicians insist that bed patients must either move or be moved frequently.

Once started, a clot tends to grow. Platelets enmeshed in the fibrin threads activate, releasing more thromboplastin, which, in turn, causes more clotting, which enmeshes more platelets, and so on, in a vicious circle. Clot-retarding substances have proved valuable for retarding this process. Box 20-6 discusses some methods for therapeutically hastening clotting to stop bleeding.

Clot Dissolution

The physiological mechanism that dissolves clots is known as **fibrinolysis** (Figure 20-23). Evidence indicates that the two opposing processes of clot formation and fibrinolysis go on continuously. Normal blood contains an inactive plasma protein called *plasminogen* that can be activated by several substances released from damaged cells. These converting substances include thrombin, factor XII, tissue plasminogen activator (t-PA), and lysosomal enzymes. Plasmin hydrolyzes fibrin strands and dissolves the clot (see Figure 20-23).

In today's clinical practice, several different kinds of proteins are used to dissolve blood clots that are causing an acute medical crisis. These are enzymes that generate plasmin when injected into patients. Streptokinase (SK) is a plasminogen-activating factor made by certain *Streptococci* bacteria. It and recombinant t-PA can be used to dissolve clots in the large arteries of the heart, which, when blocked, can result in myocardial infarction (heart attack). In addition, t-PA has been recognized as a promising drug for the early treatment of strokes. If given within the first 6 hours after a clot forms in a cerebral vessel, it can often improve blood flow and greatly reduce the serious after-effects of a stroke.

The fact that streptococcal bacteria can form blood-dissolving factors such as SK is an important one. Recall that a secondary function of blood clotting is to trap bacteria that attempt to enter our tissues. To make their attack more effective, many bacteria such as *Streptococcus* (strep), *Staphylococcus* (staph), *Escherichia coli* (*E. coli*), and others, release anticlotting agents to overcome our defenses. Such agents often activate plasminogen and thus disrupt formation of the initial blood clot. Some bacterial agents instead bind fibrinogen to disrupt normal clotting.

| QUICK CHECK |

9. List the granulocytic and agranulocytic leukocytes.
10. List the normal percentages of the different WBCs in a differential count.
11. List the four ABO blood groups, and identify the antigens and antibodies (if any) associated with each.
12. Identify the two basic coagulation steps.

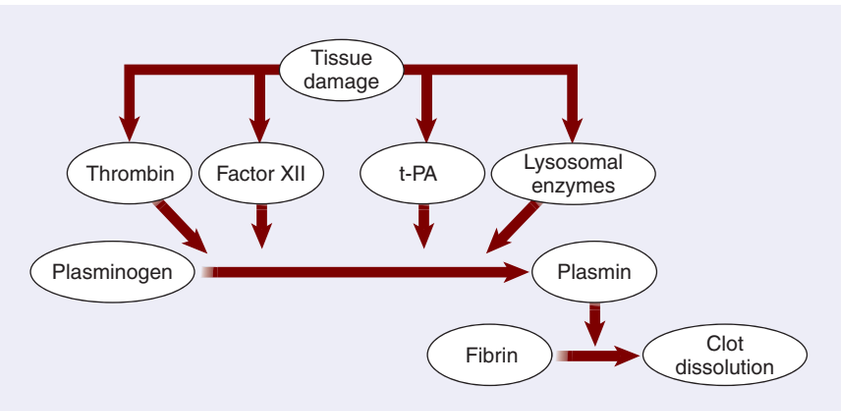


FIGURE 20-23

Fibrinolysis. Dissolution of a clot by fibrinolysis is triggered by the same events as those producing the clot but operates at a slower rate. Plasminogen is converted into the active enzyme plasmin by thrombin, factor XII, tissue plasminogen activator *(t-PA),* and lysosomal enzymes. Plasmin hydrolyzes fibrin strands and dissolves the clot.

the BIG picture

Blood and the Whole Body

In every chapter of this book we have referred to the notion that the whole body's function is geared toward maintaining stability of the internal fluid environment—that is, *homeostasis.* The fluid that makes up the internal environment in which cells are bathed—the fluid that must be kept stable—includes the plasma of the blood. As a matter of fact, it is the blood plasma that transports substances, and even heat, around the internal environment so that all body tissues are linked together. The various tissues of the body are linked by the plasma, which flows back and forth between any two points served by blood vessels. This, of course, means that substances such as nutrients, wastes, dissolved gases, water, antibodies, and hormones can be transported between almost any two points in the body.

Blood tissue is not just plasma, however. It contains the *formed elements*—the blood cells and platelets. The RBCs participate in the mechanisms that permit the efficient transport of the gases oxygen and carbon dioxide. WBCs are important in the defense mechanisms of the whole body. Their presence in blood ensures that they are available to all parts of the body, all of the time, to fight cancer, resist infectious agents, and clean up injured tissues. Platelets provide mechanisms for preventing loss of the fluid that constitutes our internal environment.

All other organs and systems of the body rely on blood to perform their many functions. No organ or system can maintain proper levels of nutrients, dissolved gases, or water without direct or indirect help from the blood. On the other hand, many other systems help blood do its job. For example, the respiratory system excretes carbon dioxide from the blood and picks up oxygen. Organs of the digestive system pick up nutrients, remove some toxins, and dispose of old blood cells. The endocrine system regulates the production of blood cells and the water content of the plasma. Besides removing toxic wastes such as urea, the urinary system has a vital role in maintaining homeostasis of plasma water concentration and pH.

Of course, blood is useless unless it continually and rapidly flows around the whole body—and continues to transport, defend, and maintain balance. The next several chapters outline the structures and functions that make this possible. Chapters 21 and 22 discuss the plan of the blood circulation and how adequate blood flow is maintained. Chapter 23 discusses the role of the lymphatic system in maintaining the fluid balance of the blood. Chapters 24 and 25 deal with the defensive mechanisms of blood and other tissues. As a matter of fact, most of the remaining chapters feature the role of blood in maintaining stability of the whole body.

MECHANISMS of DISEASE

BLOOD DISORDERS

Most blood diseases are disorders of the formed elements. Thus it is not surprising that the basic mechanism of many blood diseases is the failure of the blood-producing myeloid and lymphatic tissues to properly form blood cells. In many cases, this failure is the result of damage by drugs, toxic chemicals, or radiation. In other cases, it results from an inherited defect or even cancer.

If bone marrow failure is the suspected cause of a particular blood disorder, a sample of myeloid tissue may be drawn into a syringe. The bone marrow is obtained from inside the pelvic bone (iliac crest) or the sternum. This procedure, called **aspiration biopsy cytology** (ABC), allows examination of the tissue that may help confirm or reject a tentative diagnosis. If the bone marrow is severely damaged, the choice of a **bone marrow transplant** may be offered to the patient. In this procedure, myeloid tissue from a compatible donor is introduced into the recipient intravenously. If the recipient's immune system does not reject the new tissue, which is always a danger in this type of tissue transplant, the donor cells may establish a colony of new, healthy tissue in the bone marrow. In some cases, infusion of healthy marrow follows total body irradiation. This treatment destroys the diseased marrow, permitting the new tissue to grow.

Red Blood Cell Disorders

Anemia

The term **anemia** is used to describe different disease conditions caused by an inability of the blood to carry sufficient oxygen to the body cells. Anemias can result from inadequate numbers of RBCs or a deficiency of oxygen-carrying hemoglobin. Thus anemia can occur if the hemoglobin in RBCs is inadequate, even if normal numbers of RBCs are present.

Anemia Resulting from Changes in RBC Number

Anemias caused by an actual change in the number of RBCs can occur if blood is lost by hemorrhage, as with accidents or bleeding ulcers or if the blood-forming tissues cannot maintain normal numbers of blood cells. Such failures occur because of cancer, chemotherapy treatment, radiation (x-ray) damage, and certain types of infections. If bone marrow produces an excess of RBCs, the result is a condition called **polycythemia**. The blood in individuals suffering from this condition may contain so many RBCs that it may become too thick to flow properly.

One type of anemia characterized by an abnormally low number of red blood cells is **aplastic anemia.** Although idiopathic forms of this disease occur, most cases result from destruction of bone marrow by drugs, toxic chemicals, or radiation. Less commonly, aplastic anemia results from bone marrow destruction by cancer. Because tissues that produce other formed elements are also affected, aplastic anemia is usually accompanied by a decreased number of WBCs and platelets. Bone marrow transplants have been successful in treating some cases of aplastic anemia.

Pernicious anemia is another disorder characterized by a low number of RBCs. Pernicious anemia sometimes results from a dietary deficiency of vitamin B_{12}. Vitamin B_{12} is used in the formation of new RBCs in the bone marrow. In many cases, pernicious anemia results from the failure of the stomach lining to produce *intrinsic factor*—the substance that allows vitamin B_{12} to be absorbed. Pernicious anemia can be fatal if not successfully treated. One method of treatment involves intramuscular injections of vitamin B_{12}.

Folate deficiency anemia is similar to pernicious anemia because it also causes a decrease in the RBC count resulting from a vitamin deficiency. In this condition, it is *folic acid* (vitamin B_9) that is deficient. Folic acid deficiencies are common among individuals with alcoholism and other malnourished individuals. Treatment for folate deficiency **acute anemia** involves taking vitamin supplements until a balanced diet can be restored.

Of course, a significant reduction in the number of RBCs can occur as a result of blood loss**. Blood loss anemia** often occurs after hemorrhages associated with trauma, extensive surgeries, or other situations involving a sudden loss of blood. **Anemia of chronic disease** can be a serious complication of chronic inflammatory diseases and cancer; the cause is often unknown.

Changes in Hemoglobin

The amount and quality of hemoglobin within RBCs are just as important as the number of RBCs. In hemoglobin disorders, RBCs are sometimes classified as **hyperchromic** (abnormally high hemoglobin content) or hypochromic (abnormally low hemoglobin content).

Iron (Fe) is a critical component of the hemoglobin molecule, forming the central core of each heme group (see Figure 20-5). Without adequate iron in the diet, the body cannot manufacture enough hemoglobin. The result is **iron deficiency anemia**—a worldwide medical problem. Although the body carefully protects its iron reserves, they may be depleted through hemorrhage, increased requirements such as wound healing or pregnancy, or low intake. Unfortunately, iron deficiency is the most common nutritional deficiency in the world. The tragic result is that an estimated 10% of the population in some developed countries and up to 50% in developing countries suffers from iron deficiency anemia. Oral administration of iron-containing compounds, such as ferrous sulfate or ferrous gluconate, is very effective in treating the basic iron deficiency seen in the disease. Figure 20-24 shows a peripheral blood smear from an individual suffering from iron deficiency anemia. The numbers of RBCs are only slightly below normal. Note, however, that the cells are small and appear pale (hypochromic) because of the reduction in hemoglobin content.

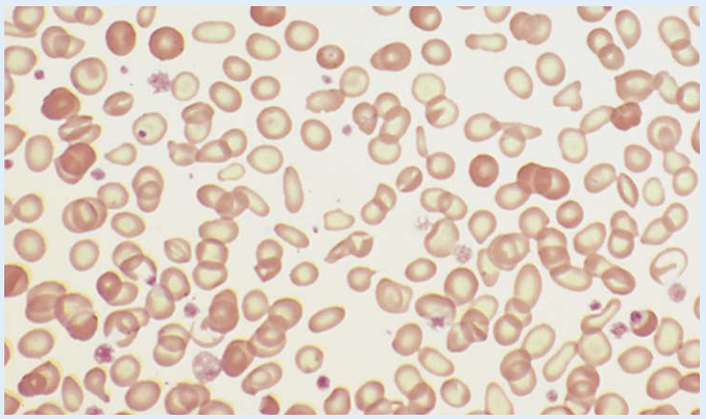


FIGURE 20-24

Iron deficiency anemia. Note the small, pale (hypochromic) red blood cells (RBCs). Lack of adequate color in the RBCs is due to reduced hemoglobin content.

The term **hemolytic anemia** applies to any of a variety of inherited blood disorders characterized by abnormal types of hemoglobin. The term *hemolytic* means "relating to blood breakage" and emphasizes the fact that abnormal hemoglobin often causes red blood cells to become distorted and easily broken. An example of a hemolytic anemia is **sickle cell anemia.** Another type of hemolytic anemia is **thalassemia**. As with sickle cell anemia, thalassemia is an inherited disorder, with both a mild and a severe form (*thalassemia minor* and *thalassemia major*).

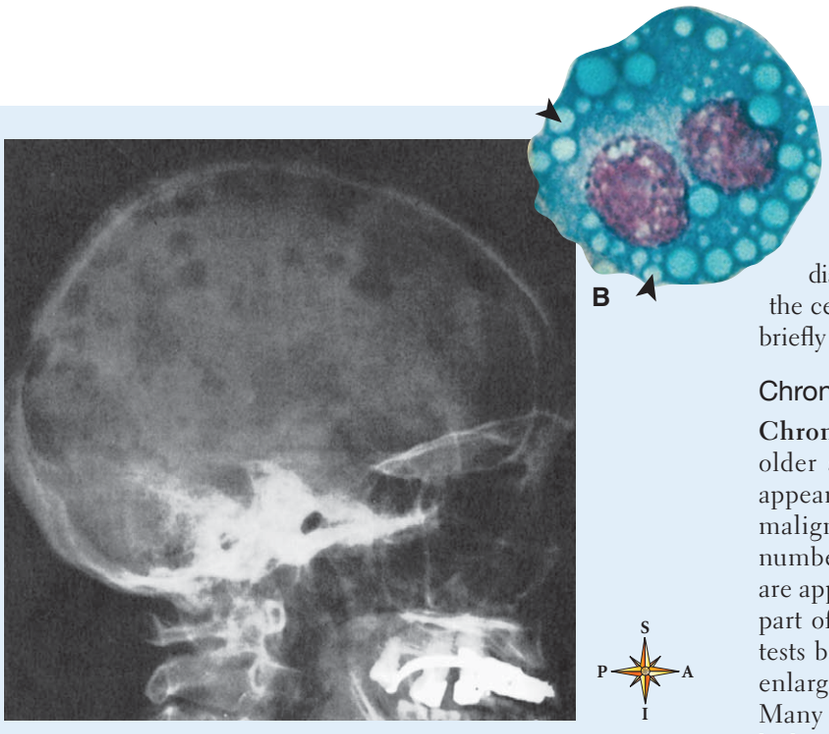
White Blood Cell Disorders

The term **leukopenia** refers to an abnormally low WBC count (less than 5000 cells/mm^3 of blood). Various disease conditions may affect the immune system and decrease the amount of circulating WBCs. Acquired immunodeficiency syndrome, or AIDS, results in marked leukopenia. **Leukocytosis** refers to an abnormally high WBC count. It is a much more common problem than leukopenia, is seen in most types of leukemia, and almost always accompanies bacterial infections.

Two major groups of disease conditions constitute a majority of WBC and blood-related cancers, or malignant neoplasms. **Lymphoid neoplasms** arise from lymphoid precursor cells that normally produce B lymphocytes, T lymphocytes, or their descendent cell types. **Myeloid neoplasms** appear as a result of malignant transformation of myeloid stem or precursor cells that normally produce granulocytic WBCs, monocytes, RBCs, and platelets.

Multiple Myeloma

Multiple myeloma is cancer of antibody-secreting B lymphocytes called *plasma cells* (Figure 20-25, *B*). It is one of the most common and one of the most deadly forms of blood-related cancers in people older than 65 years of age. The cancerous transformation of plasma cells results in impairment of bone marrow function, production of defective antibodies, recurrent infections (from neutropenia), anemia, and the painful destruction and fracture



A B

FIGURE 20-25

Multiple myeloma. A, x ray of skull showing "honeycomb" or "punched-out" appearance of bones caused by defective antibodies from plasma cells. Normal skull bones would instead have a more uniform (less mottled) appearance in an x ray. **B,** Malignant plasma cell. Vesicles *(arrowheads)* contain defective antibodies.

of bones in the skull and throughout the skeletal system. The x-ray photo in Figure 20-25, *A*, shows the typical "honeycomb" or "punched-out" defects in skull bones caused by the defective myeloma antibody.

Leukemia

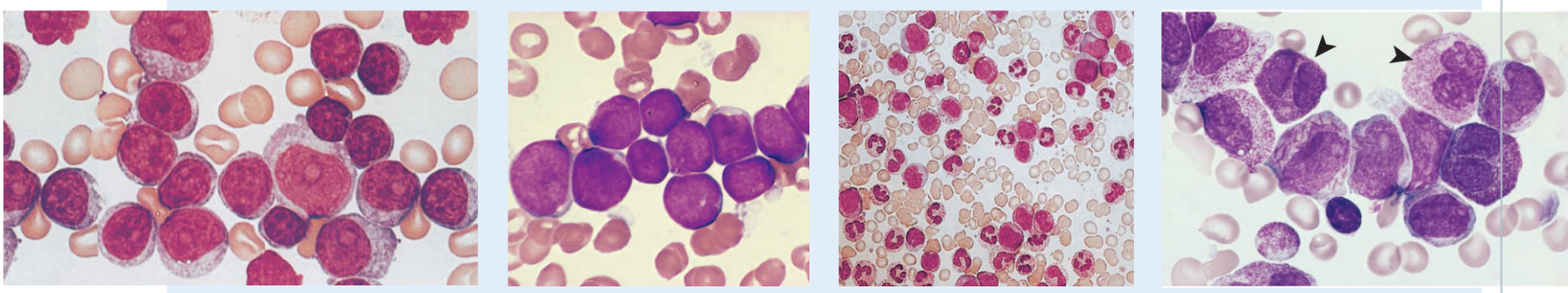
Leukemia is the term used to describe a number of blood cancers affecting the WBCs. In almost every form of leukemia, marked leukocytosis occurs. Leukocyte counts in excess of 100,000/mm^3 in circulating blood are common. The different types of leukemia are identified as either *acute* or *chronic*, based on how quickly symptoms appear after the disease begins, and as *lymphocytic* or *myeloid*, depending on the cell type involved. Four of the most common leukemias are briefly described here.

Chronic Lymphocytic Leukemia (CLL)

Chronic lymphocytic leukemia (CLL) most often affects older adults. Average age of onset is about 65 years, and it appears more often in men than women. In those with CLL, malignant precursor B lymphocytes are produced in great numbers (Figure 20-26, *A*). Early in the disease few symptoms are apparent, and many patients are diagnosed inadvertently as part of a routine physical examination when results of blood tests become available. When symptoms such as lymph node enlargement and fatigue do appear, they are often quite mild. Many patients with CLL live many years after diagnosis with little or no treatment.

Acute Lymphocytic Leukemia (ALL)

Acute lymphocytic leukemia (ALL) is primarily a disease of children and constitutes the most common form of "blood cancer" in children between 3 and 7 years of age (Figure 20-26, *B*). Fully 80% of all children who develop leukemia have this form of the disease. Although always a serious condition, it is highly curable in children but less so when it occurs in adults. As the name implies, onset of the disease is sudden. Symptoms include fever, bone pain, and increased rates of infection. Cancerous cells crowd out other bone marrow cells and decrease the production of RBCs and platelets as well as other nonmalignant lymphocyte cells. Anemia and swelling of lymph nodes, spleen, and liver are common symptoms. Treatment may involve chemotherapy, irradiation, and bone marrow or stem cell transplants.



A B C D

FIGURE 20-26

Types of leukemia. A, Chronic lymphocytic leukemia (CLL)—peripheral blood smear showing large numbers of diseased B lymphocytes. **B,** Acute lymphocytic leukemia (ALL)—appearance of B lymphocytes in ALL. **C,** Chronic myeloid leukemia (CML)—note severe granulocytic leukocytosis. **D,** Acute myeloid leukemia (AML)—note large numbers of myelocytic precursor cells *(arrowheads)*.

Chronic Myeloid Leukemia (CML)

Chronic myeloid leukemia (CML) accounts for about 20% of all cases of leukemia and occurs most often in adults between 25 and 60 years of age. CML results from cancerous transformation of granulocytic (neutrophil, eosinophil, and basophil) precursor cells in the bone marrow. Onset is slow, and once the disease is established, it progresses slowly. Diagnosis is often made by discovery of marked elevations of granulocytic WBCs in peripheral blood (Figure 20-26, *C*) and by extreme spleen enlargement. The drug imatinib (Gleevec) specifically seeks out and blocks the flawed signals in CML cancer cells that cause runaway proliferation (Box 20-7).

Acute Myeloid Leukemia (AML)

Acute myeloid leukemia (AML) is caused by pathologic transformation of myeloid stem cells (Figure 20-26, *D*). It accounts for 80% of all cases of acute leukemia in adults and 20% of acute leukemia cases in children. Onset is sudden, and once symptoms appear the disease progresses rapidly. The most common symptoms include anemia and fatigue, recurrent infections, bone and joint pain, and spongy bleeding gums. The prognosis of AML is poor, with only about 50% of children and 30% of adults achieving long-term survival. However, advances in bone marrow and stem cell transplantation have increased cure rates in selected patients.

Infectious Mononucleosis

Infectious mononucleosis is a common noncancerous WBC disorder appearing most often in adolescents and young adults between 15 and 25 years of age. It is caused by a virus found in the saliva of infected individuals. Leukocytosis is common early in the disease with total WBC counts averaging between 12,000 and 18,000/mm^3. More than 60% of the leukocytes can be identified in a differential WBC count as large, *atypical* (abnormal) lymphocytes that have abundant cytoplasm and a large nucleus (Figure 20-27). Symptoms vary greatly, but, in addition to the leukocytosis and atypical lymphocytes seen in peripheral blood, fever, sore throat, rash, severe fatigue, and enlargement of lymph nodes and the spleen are common findings. Infectious "mono" is generally self-limited and resolves without complications in about 4 to 6 weeks, although fatigue may last for longer periods.

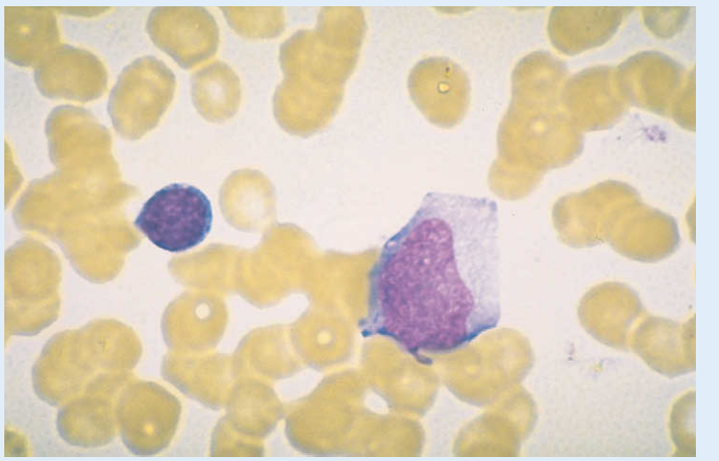


FIGURE 20-27

Infectious mononucleosis. The cell on the left is a typical small lymphocyte with the nucleus almost filling the cell. The larger atypical lymphocyte on the right has much more cytoplasm and a larger nucleus.

Box 20-7 | HEALTH matters

Treating Chronic Myeloid Leukemia

Scientists have known for a number of years now that a pathologic transformation of the gene that controls the production of an intracellular protein called *tyrosine kinase* is associated with development of **chronic myeloid leukemia (CML)**—a common and deadly form of blood cancer.

One type of treatment for CML is a tyrosine kinase **signal transduction inhibitor** drug called imatinib (Gleevec). It acts by seeking out and breaking up the signal transduction between the abnormal tyrosine kinase being produced and the specific receptor sites for this enzyme on the CML cancer cells that send the signal causing runaway proliferation. It is a "rational" drug that acts to treat CML at the molecular level. By doing so, it blocks some of the most serious functional effects of the genetic flaw that causes the disease—not just the symptoms resulting from expression of the genetic defect.

Clotting Disorders

Unfortunately, clots sometimes form in unbroken blood vessels of the heart, brain, lungs, or other organs—a dreaded thing because clots may produce sudden death by shutting off the blood supply to a vital organ. When a clot stays in the place where it formed, it is called a **thrombus**, and the condition itself is spoken of as **thrombosis**. If all or part of a clot dislodges and circulates through the bloodstream, it is called an, and the condition is called an **embolism**.

Thrombosis and embolism cause most myocardial infarctions (MIs or "heart attacks") and cerebrovascular accidents (CVAs or "strokes"), making them the leading cause of death in developed countries. Box 20-5 on p. 617 discusses various therapies to prevent the dangers of thrombus formation.

Hemophilia is an X-linked inherited disorder that affects 1 in every 10,000 males worldwide. It results from a failure to produce one or more plasma proteins responsible for blood clotting—a process illustrated in Figure 20-21. Thus hemophilia is characterized by a relative inability to form blood clots. Because minor blood vessel injuries are common in ordinary life, hemophilia can be a life-threatening condition. The most common form is called *hemophilia* A. It is caused by

absence of factor VIII protein and affects more than 300,000 people around the world.

Historically, factor VIII was obtained by plasma fractionation. This method cannot meet demand given the shortage of available donated blood. Currently, recombinant methods are used to produce enough recombinant antihemophilic factor VIII (rAHF) to meet the therapeutic needs of the world's hemophiliac population. Increasing amounts are needed to meet the larger quantities required as adolescent patients mature and as physicians prescribe more factor VIII to prevent as well as to treat bleeding episodes. The blood's ability to clot can be determined by tests such as prothrombin time (PT), discussed in Box 20-8, which help monitor the success of antihemophilia therapies.

A more common type of clotting disorder results from a decrease in the platelet count—a condition called **thrombocytopenia.** This condition is characterized by bleeding from many small blood vessels throughout the body, most visibly in the skin and mucous membranes. If the number of thrombocytes falls to 20,000/mm^3 or less (normal range is 150,000 to 400,000/mm^3), catastrophic bleeding may occur. Although a number of different mechanisms can result in thrombocytopenia, the usual cause is bone marrow destruction by drugs or an immune system disease, chemicals, radiation, or cancer. Drugs may cause thrombocytopenia as a side effect. In such cases, stopping the drug usually solves the problem.

Box 20-8 | HEALTH matters

Prothrombin Time

A laboratory test called the *prothrombin time (PT)* is often used to assess the body's ability to form blood clots. This can be useful to find the cause of abnormal bruising or bleeding, regulate dosage of anticoagulant drugs (see Box 20-5 on p. 617), check levels of clotting factors, or assess liver function (where prothrombin is produced).

In this test, thromboplastin (a blood clotting factor) and calcium are added simultaneously to a tube of the patient's plasma and a tube containing a normal control solution, and the time required for clot formation in both tubes is determined.

A patient prothrombin time in excess of the standard control value (11 to 12.5 seconds) indicates reduced clotting. Unfortunately, PT test results may vary between different clinical laboratories. Variability is often caused by differing techniques or differences in the sensitivity of reagents used. To minimize the effects of these and other variables and standardize the results of anticoagulation testing, a system called the *INR* (abbreviation for *International Normalized Ratio*) has been developed. PT is reported in seconds. The INR is a mathematical calculation and is reported as a number. An INR of 0.8 to 1.2 is considered normal—and values above the normal range indicate reduced clotting ability.

LANGUAGE OF SCIENCE (continued from p. 597)

embryonic stem cell
(em-bree-ON-ik)
[*em-* **in**, *-bryo-* **fill to bursting**, *-ic* **relating to**]

eosinophil
(ee-oh-SIN-oh-fil)
[*eosin-* **reddish color**, *-phil* **love**]

erythrocyte
(eh-RITH-roh-syte)
[*erythro-* **red**, *-cyte* **cell**]

erythropoiesis
(eh-rith-roh-poy-EE-sis)
[*erythro-* **red**, *-poiesis* **making**]

erythropoietin (EPO)
(eh-RITH-roh-POY-eh-tin)
[*erythro-* **red**, *-poiet-* **make**, *-in* **substance**]

extrinsic clotting pathway
(eks-TRIN-sik)
[*extr-* **outside**, *-sic* **beside**]

extrinsic factor
(eks-TRIN-sik)
[*extr-* **outside**, *-sic* **beside**]

fibrinolysis
(fye-brin-OL-i-sis)
[*fibr-* **fiber**, *-lysis* **loosening**]

formed element

globin
(GLOH-bin)
[*glob-* **ball**, *-in* **substance**]

granulocyte
(GRAN-yoo-loh-syte)
[*gran-* **grain**, *-ul-* **little**, *-cyte* **cell**]

hematopoietic stem cell
(hee-mah-toh-poy-ET-ik)
[*hem-* **blood**, *-poiesis* **making**]

heme
(heem)
[*hem-* **blood**]

hemoglobin
(hee-moh-GLOH-bin)
[*hem-* **blood**, *-globus* **ball**]

heparin
(HEP-ah-rin)
[*hepar-* **liver**, *-in* **substance**]

intrinsic clotting pathway
(in-TRIN-sik)
[*intr-* **within**, *-sic* **beside**]

leukocyte
(LOO-koh-syte)
[*leuko-* **white**, *-cyte* **cell**]

lymphocyte
(LIM-foh-syte)
[*lymph-* **water** (**lymphatic system**), *-cyte* **cell**]

monocyte
(MON-oh-syte)
[*mono-* **single**, *-cyte* **cell**]

neutrophil
(NOO-troh-fil)
[*neuter-* **neither**, *-phil* **love**]

nonelectrolyte
(non-ee-LEK-troh-lyte)
[*non-* **not**, *-electro-* **electricity**, *-lyt-* **loosening**]

plasma
(PLAZ-mah)
[*plasma* **substance**]

platelet
(PLAYT-let)
[*plate-* **flat**, *-let* **small**]

platelet plug
(PLAYT-let)
[*plate-* **flat**, *-let* **small**]

polychromatic erythroblast
(pahl-ee-kroh-MAT-ik ee-RITH-roh-blast)
[*poly-* **many**, *-chrom-* **color**, *-ic* **relating to**, *erythro-* **red**, *-blast* **bud**]

polymorphonuclear leukocyte
(pahl-ee-mohr-foh-NYOO-klee-er LOO-koh-syte)
[*poly-* **many**, *-morph-* **form**, *-nucle-* **nut or kernel**, *-ar* **relating to**, *leuko-* **white**, *-cyte* **cell**]

proerythroblast
(proh-eh-rith-roh-BLAST)
[*pro-* **first**, *-erythro-* **red**, *-blast* **bud**]

reticulocyte
(reh-TIK-yoo-loh-syte)
[*ret-* **net**, *-ic-* **relating to**, *-ul-* **little**, *-cyte* **cell**]

thrombopoiesis
(throm-boh-poy-EE-sis)
[*thromb-* **clot**, *-poiesis* **making**]

thrombus
(THROM-bus)
[*thrombus* **clot**] *pl.*, thrombi

LANGUAGE OF MEDICINE *(continued from p. 623)*

acute anemia
(ah-KYOOT ah-NEE-mee-ah)
[*acu-* **sharp**, *an-* **without**, *-emia* **blood condition**]

acute lymphocytic leukemia (ALL)
(ah-KYOOT LIM-foh-sit-ik loo-KEE-mee-ah)
[*acu-* **sharp**, *lymph-* **water (lymphatic system)**, *-cyt-* **cell**, *-ic* **relating to**, *leuk-* **white**, *-emia* **blood condition**]

acute myeloid leukemia (AML)
(ah-KYOOT MY-eh-loyd loo-KEE-me-ah)
[*acu-* **sharp**, *myel-* **marrow**, *-oid* **like**, *leuk-* **white**, *-emia* **blood condition**]

anemia
(ah-NEE-me-ah)
[*an-* **without**, *-emia* **blood condition**]

anemia of chronic disease
(ah-NEE-mee-ah KRON-ik)
[*an-* **without**, *-emia* **blood condition**, *chron-* **time**, *-ic* **relating to**]

antianemic principle
(an-tee-an-NEE-mik)
[*anti-* **against**, *-an-* **without**, *-emia-* **blood condition**, *-ic* **relating to**]

anticoagulant drug
(an-tee-koh-AG-yoo-lant)
[*anti-* **against**, *-coagul-* **curdle**, *-ant* **agent**]

antiplatelet drug
(an-tee-PLAYT-let)
[*anti-* **against**, *-plate-* **flat**, *-let* **small**]

aplastic anemia
(a-PLAS-tik ah-NEE-mee-ah)
[*a-* **without**, *-plast-* **form**, *-ic* **relating to**, *a-* **without**, *-nemia* **condition of red blood cell deficiency**]

aspiration biopsy cytology
(ass-pih-RAY-shen BYE-op-see SYE-TOL-oh-jee)
[*a-* **act of**, *-spir-* **breathe**, *-ation* **process**, *bio-* **life**, *-ops-* **view**, *-y* **act of**, *cyt-* **cell**, *-o-* **combining form**, *-log-* **words (study of)**, *-y* **activity**]

blood boosting
blood doping

blood loss anemia
(ah-NEE-mee-ah)
[*an-* **without**, *-emia* **blood condition**]

bone marrow transplant
chronic lymphocytic leukemia (CLL)
(KRON-ik LIM-foh-sit-ik loo-KEE-mee-ah)
[*chron-* **time**, *-ic* **relating to**, *lymph-* **water (lymphatic system)**, *-cyte* **cell**, *leuk-* **white**, *-emia* **blood condition**]

chronic myeloid leukemia (CML)
(KRON-ik MY-eh-loyd loo-KEE-mee-ah)
[*chron-* **time**, *-ic* **relating to**, *myel* **bone marrow**, *leuk-* **white**, *-emia* **blood condition**]

coagulation
(koh-ag-yoo-LAY-shen)
[*coagul-* **curdle**, *-ation* **process**]

complete blood cell count (CBC)
differential white blood cell count
(dif-er-EN-shal)

embolism
(EM-boh-liz-em)
[*embol-* **plug**, *-ism* **condition**]

embolus
(EM-boh-lus)
[*embolus* **plug**]

erythroblastosis fetalis
(eh-rith-roh-blas-TOH-sis feh-TAL-is)
[*erythro-* **red**, *-blast-* **bud**, *-osis* **condition**]

erythrocyte sedimentation rate (ESR)
(eh-RITH-roh-syte sed-i-men-TAY-shen)
[*erythro-* **red**, *-cyte* **cell**]

folate deficiency anemia
(FOH-layt deh-FISH-en-see ah-NEE-mee-ah)
[*fol-* **leaf**, *-ate* **relating to**, *an-* **without**, *-emia* **blood condition**]

hematocrit
(hee-MAT-oh-krit)
[*hemato-* **blood**, *-crit* **separate**]

hemolytic anemia
(hee-moh-LIT-ik ah-NEE-mee-ah)
[*hemo-* **blood**, *-lyt-* **loosen**, **-ic relating to**, *an-* **without**, *-emia* **blood condition**]

hemophilia
(hee-moh-FIL-ee-ah)
[*hemo-* **blood**, *-phil-* **love**, *-ia* **condition**]

hemostasis
(hee-moh-STAY-sis)
[*hemo-* **blood**, *-stasis* **standing**]

hyperchromic
(hye-per-KROH-mik)
[*hyper-* **excessive**, *-chrom-* **color**, *-ic* **relating to**]

infectious mononucleosis
(in-FEK-shuss mah-noh-noo-klee-OH-sis)
[*infect-* **stain**, *-ous* **relating to**, *mono-* **single**, *-nucle-* **nut**, *-osis* **condition**]

intermittent claudication
(in-ter-MIT-tent klaw-dih-KAY-shen)
[*inter-* **between**, *-mitt-* **send**, *claudica-* **limping**, *-ation* **process**]

iron deficiency anemia
(deh-FISH-en-see ah-NEE-mee-ah)
[*an-* **without**, *-emia* **blood condition**]

leukemia
(loo-KEE-mee-ah)
[*leuk-* **white**, *-emia* **blood condition**]

leukocytosis
(loo-koh-SYE-toh-sis)
[*leuko-* **white**, *-cyt-* **cell**, *-osis* **condition**]

leukopenia
(loo-koh-PEE-nee-ah)
[*leuko-* **white**, *-penia* **lack**]

lymphoid neoplasm
(LIM-foyd NEE-oh-plaz-em)
[*lymph-* **water (lymphatic system)**, *-oid* **like**, *neo-* **new**, *-plasm* **substance**]

multiple myeloma
(my-eh-LOH-mah)
[*myel-* **marrow**, *-oma* **tumor**]

myeloid neoplasm
(MY-eh-loyd NEE-oh-plaz-em)
[*myel-* **marrow**, *-oid* **like**, *neo-* **new**, *-plasm* **substance**]

packed cell volume (PCV)
pernicious anemia
(per-NISH-us ah-NEE-mee-ah)
[*pernici-* **destruction**, *-ous* **relating to**, *an-* **without**, *-emia* **blood condition**]

physiological polycythemia
(fiz-ee-oh-LOJ-i-kal pol-ee-sye-THEE-mee-ah)
[*physi-* **nature**, *-o-* **combining form**, *-log-* **words (study of)**, *-y* **activity**, *poly-* **many**, *-cyt-* **cell**, *-emia* **blood condition**]

polycythemia
(pahl-ee-sye-THEE-mee-ah)
[*poly-* **many**, *-cyt-* **cell**, *-emia* **blood condition**]

sickle cell anemia
(SIK-ul sell ah-NEE-mee-ah)
[*sickle* **crescent**, *cell* **storeroom**, *an-* **without**, *-emia* **blood condition**]

signal transduction inhibitor
(SIG-nal tranz-DUK-shen in-HIB-ih-tor)
[*trans-* **across**, *-duc-* **transfer**, *-tion* **process**, *inhibit-* **prevent**, *-or* **agent**]

thalassemia
(thal-ah-SEE-mee-ah)
[*thalass-* **sea**, *-emia* **blood condition**]

thrombocytopenia
(throm-boh-sye-toh-PEE-nee-ah)
[*thrombo-* **clot**, *-cyto-* **cell**, *-penia* **lack**]

thrombosis
(throm-BOH-sis)
[*thrombo-* **clot**, *-osis* **condition**]

transfusion reaction
[*trans-* **across**, *-fus-* **pour**, *-sion* **process**]

CASE study



Duncan was slicing a bagel to put in the toaster. When the microwave beeped, he glanced in that direction, taking his eyes off the bagel for a split second. In that split second, the knife slipped and cut deeply into his finger. Immediately blood started spurting out of the damaged blood vessels.

Duncan grabbed a towel and wrapped it tightly around the cut, while holding his hand above his heart.

1. What is the main component of the blood coming out of Duncan's finger?
   a. Erythrocytes
   b. Leukocytes
   c. Plasma
   d. Thrombocytes

Because of the damage to his blood vessels, Duncan's body will immediately start the blood clotting process.

2. What's the first step in hemostasis (stopping bleeding)?
   a. Vascular spasm
   b. Platelet plug
   c. Coagulation
   d. Leukocytic plug

3. What is the last step in clot formation?
   a. Fibrinogen converted to fibrin
   b. Prothrombin converted to thrombin
   c. Profibrin converted to fibrin
   d. Factor VIII converted to factor IX

4. If Duncan were missing factor VIII, what condition would he have?
   a. Thrombocytopenia
   b. Pernicious anemia
   c. Polycythemia
   d. Hemophilia

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

COMPOSITION OF BLOOD

A. Introduction (Figure 20-1)
   1. Blood—made up of plasma and formed elements
   2. Blood—complex transport medium that performs vital pickup and delivery services for the body
   3. Blood—keystone of body's heat-regulating mechanism

B. Blood volume
   1. Young adult male has approximately 5 liters of blood
   2. Blood volume varies according to age, body type, sex, and method of measurement

FORMED ELEMENTS OF BLOOD

A. Red blood cells (RBCs; erythrocytes)
   1. Description of mature RBCs (Figure 20-4)
      a. Have no nucleus and shaped like tiny biconcave disks
      b. Do not contain ribosomes, mitochondria, and other organelles typical of most body cells
      c. Primary component is hemoglobin
      d. Most numerous of the formed elements
   2. Function of RBCs
      a. RBCs' critical role in the transport of oxygen and carbon dioxide depends on hemoglobin
      b. Carbonic anhydrase (CA)—enzyme in RBCs that catalyzes a reaction that joins carbon dioxide and water to form carbonic acid
      c. Carbonic acid—dissociates and generates bicarbonate ions, which diffuse out of the RBC and serve to transport carbon dioxide in the blood plasma
   3. Hemoglobin (Figure 20-5)
      a. Within each RBC are approximately 200 to 300 million molecules of hemoglobin

b. Hemoglobin is made up of four globin chains, with each attached to a heme group
c. Hemoglobin is able to unite with four oxygen molecules to form oxyhemoglobin to allow RBCs to transport oxygen where it is needed
d. A male has a greater amount of hemoglobin than a female
e. Anemia—a decrease in number or volume of functional RBCs in a given unit of whole blood

4. Formation of RBCs (review Figures 20-6 and 20-7)
a. Erythropoiesis—entire process of RBC formation
b. RBC formation begins in the red bone marrow as hematopoietic stem cells and goes through several stages of development to become erythrocytes; entire maturation process requires approximately 4 days
c. RBCs are created and destroyed at approximately 200 billion per day in an adult; homeostatic mechanisms operate to balance the number of cells formed against the number of cells destroyed

5. Destruction of RBCs (Figure 20-8)
a. Life span of a circulating RBC averages 105 to 120 days
b. Macrophage cells phagocytose the aged, abnormal, or fragmented RBCs
c. Hemoglobin is broken down, and amino acids, iron, and bilirubin are released

B. White blood cells (leukocytes; WBCs) (review Table 20-1)
1. Granulocytes
a. Neutrophils (review Figure 20-9)—make up approximately 65% of total WBC count in a normal blood sample; highly mobile and very active phagocytic cells; capable of diapedesis; cytoplasmic granules contain lysosomes
b. Eosinophils (review Figure 20-10)—account for 2% to 5% of circulating WBCs; numerous in mucous lining of respiratory and digestive tracts; weak phagocytes; release chemicals of immunity; provide protection against infections caused by parasitic worms and help regulate allergic reactions
c. Basophils (review Figure 20-11)—account for only 0.5% to 1% of circulating WBCs; motile and capable of diapedesis; cytoplasmic granules contain histamine and heparin

2. Agranulocytes (Figures 20-12 and 20-13)
a. Lymphocytes—smallest of the WBCs; second most numerous WBC; account for approximately 25% of circulating WBCs; T lymphocytes and B lymphocytes have an important role in immunity—T lymphocytes directly attack an infected or cancerous cell, and B lymphocytes produce antibodies against specific antigens
b. Monocytes—largest leukocytes; mobile and highly phagocytic cells

3. WBC numbers—1 mm^3 of normal blood usually contains 5000 to 9000 leukocytes, with different percentages for each type; WBC numbers have clinical significance because they change with certain abnormal conditions (Figure 20-14)

4. Formation of WBCs (review Figure 20-6)
a. Granular and agranular leukocytes mature from the undifferentiated hematopoietic stem cell
b. Neutrophils, eosinophils, basophils, and a few lymphocytes and monocytes originate in red bone marrow; most lymphocytes and monocytes develop from hematopoietic stem cells in lymphatic tissue

C. Platelets (review Figure 20-2)
1. Structure
a. In circulating blood, platelets are small, pale bodies that appear as irregular spindles or oval disks
b. Three important properties are agglutination, adhesiveness, and aggregation
c. Platelet counts in adults average 250,000/mm^3 of blood; normal range is 150,000 to 400,000/mm^3

2. Functions of platelets
a. Important role in hemostasis and blood coagulation; secondary role in defending against bacterial attacks
b. Hemostasis—refers to stoppage of blood flow; however, if injury is extensive, the blood-clotting mechanism is activated to assist

3. Platelet plug formation
a. Platelets adhere to damaged endothelial lining and to each other 1 to 5 seconds after injury to vessel wall, forming a platelet plug
b. Temporary platelet plug is an important step in hemostasis
c. "Sticky platelets" form physical plug and secrete several chemicals involved in the coagulation process

4. Formation and life span of platelets (average of 7 days)—formed in red bone marrow, lungs, and spleen by fragmentation of megakaryocytes

BLOOD TYPES (BLOOD GROUPS)

A. The ABO system (Figures 20-16 to 20-18)
1. Every person's blood belongs to one of four ABO blood groups
2. Named according to antigens present on RBC membranes
a. Type A—antigen A on RBCs
b. Type B—antigen B on RBCs
c. Type AB—both antigen A and antigen B on RBCs; known as universal recipient
d. Type O—neither antigen A nor antigen B on RBCs; known as universal donor

B. The Rh system (Figure 20-19)
1. Rh-positive blood—Rh antigen is present on the RBCs
2. Rh-negative—RBCs have no Rh antigen present
3. Anti-Rh antibodies are not normally present in blood; anti-Rh antibodies can appear in Rh-negative blood if it has come in contact with Rh-positive RBCs

BLOOD PLASMA

A. Plasma—liquid part of blood; clear, straw-colored fluid; made up of 90% water and 10% solutes (Figure 20-20)
B. Solutes—6% to 8% of plasma solutes are proteins, consisting of three main compounds
   1. Albumins—help maintain osmotic balance of the blood
   2. Globulins—essential component of the immunity mechanism
   3. Fibrinogen—key role in blood clotting
C. Plasma proteins have an essential role in maintaining normal blood circulation

BLOOD CLOTTING (COAGULATION)

A. Mechanism of blood clotting—goal of coagulation is to stop bleeding and prevent loss of vital body fluid in a swift and sure method; the classic theory (Figure 20-21) is as follows:
   1. Classic theory of coagulation advanced in 1905; identified four components critical to coagulation
      a. Prothrombin
      b. Thrombin
      c. Fibrinogen
      d. Fibrin
   2. Current explanation of coagulation involves three stages (Figure 20-22)
      a. Stage 1—production of thromboplastin activator by *either* of the following:
         (1) Chemicals released from damaged tissues (extrinsic pathway)
         (2) Chemicals present in the blood (intrinsic pathway)
      b. Stage II—conversion of prothrombin to thrombin
      c. Stage III—conversion of fibrinogen to fibrin and production of fibrin clot
B. Conditions that oppose clotting
   1. Clot formation in intact vessels is opposed
   2. Several factors oppose clotting
      a. Perfectly smooth surface of the normal endothelial lining of blood vessels does not allow platelets to adhere
      b. Antithrombins—substances in the blood that oppose or inactivate thrombin; prevent thrombin from converting fibrinogen to fibrin; for example, heparin
C. Conditions that hasten clotting
   1. Rough spot in the endothelium
   2. Abnormally slow blood flow
D. Clot dissolution (Figure 20-23)
   1. Fibrinolysis—physiological mechanism that dissolves the clot once it has formed
   2. Plasmin—enzyme in the blood that catalyzes the hydrolysis of fibrin, causing it to dissolve; it is activated by chemicals released from damaged cells and acts slowly to dissolve the clot
   3. Substances that generate plasmin can be used as a therapy to dissolve blood clots

THE BIG PICTURE: BLOOD AND THE WHOLE BODY

A. Blood plasma transports substances, including heat, around the body, linking all body tissues together
B. Blood tissue contains formed elements—blood cells and platelets
   1. RBCs assist in the transport of oxygen and carbon dioxide
   2. WBCs assist in the defense mechanisms of the whole body
   3. Platelets prevent loss of the fluid that constitutes the internal environment
C. Blood is needed by all organs and body systems to function properly, just as many body systems aid the functions of blood.
D. Blood is useless to the body unless it continues to flow around the body and performs its functions of transport, defense, and balance (or homeostasis).

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. What are the formed elements of blood?
2. What is the function of carbonic anhydrase?
3. Describe the structure of hemoglobin.
4. How does the structure of hemoglobin allow it to combine with oxygen?
5. Discuss the steps involved in erythropoiesis.
6. What is the average life span of a circulating red blood cell?
7. How are granulocytes similar to agranulocytes? How do they differ?
8. Define the term *chemotaxis*.
9. List the important physical properties of platelets.
10. Explain what is meant by *type AB blood*. Explain Rh-negative blood.
11. Which organ is responsible for the synthesis of most plasma proteins?
12. What is the normal plasma protein concentration?
13. What are some functions served by plasma proteins?
14. Describe the role of platelets in hemostasis and blood clotting.
15. What triggers blood clotting?
16. Identify factors that oppose blood clotting. Do the same for factors that hasten blood clotting.
17. Describe the physiological mechanism that dissolves clots.
18. Describe the hemoglobin in a person with sickle cell trait.
19. List and describe three blood disorders.

CRITICAL THINKING QUESTIONS

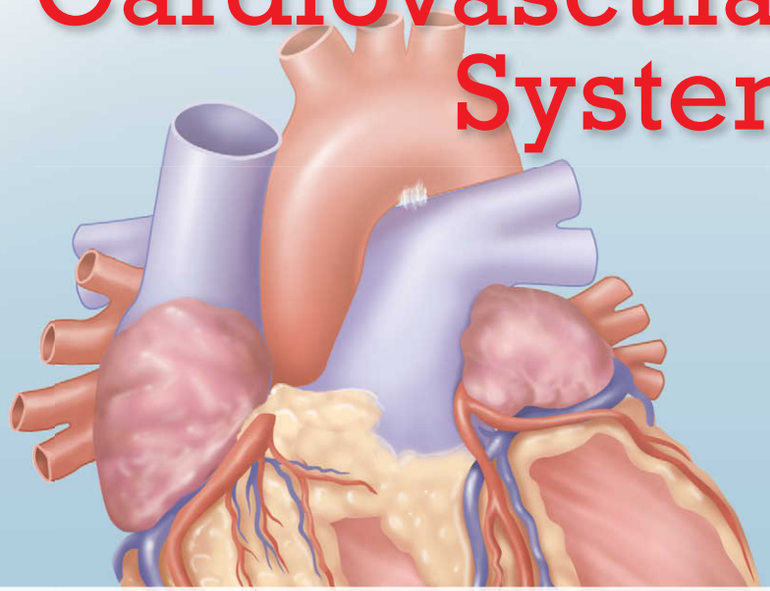


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. A modern hospital laboratory has machines that can automatically do blood cell counts based on the size of cells. If the lab technician did not want to count erythrocytes, for what size range would the machine be set? What white blood cells would be missed? What would be the classes, functions, and life spans of the white blood cells that were counted?
2. A friend received a report detailing the laboratory results related to his recent physical examination and noted that his hematocrit was below normal. Because he knows you are taking anatomy and physiology, he has come to you for an explanation. Based on what you know, explain to him what a hematocrit value is, how it is determined, and what value would put him below normal.
3. You are a medical examiner and are asked to determine the cause of death of a body brought to the morgue. You find a very large agglutination (not a clot) in a major vein. Based on this, what judgment would you make regarding the cause of death?
4. Suppose a person had a thyroid disorder that caused the production of calcitonin to be many times higher than it should be. Elaborate on why a possible side effect of this condition might be a very slow blood-clotting time.
5. A patient comes into the emergency room with severe bleeding. What can be done to speed the formation of a clot?
6. Some athletes, seeking a competitive edge, may resort to blood doping. How would you explain blood doping? What information would you use to discourage athletes from participating in the practice of blood doping?
7. How would you summarize the condition *erythroblastosis fetalis*?

Anatomy of the Cardiovascular System

21



CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

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- Location of the Heart, 630
- Size and Shape of the Heart, 630
- Coverings of the Heart, 634
  - Structure of the Heart Coverings, 634
  - Function of the Heart Coverings, 634
- Structure of the Heart, 635
  - Wall of the Heart, 635
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  - Valves of the Heart, 638
  - Blood Supply of Heart Tissue, 640
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Blood Vessel Types, 642
- Arteries, 642
- Capillaries, 644
- Veins, 645
- Structure of Blood Vessels, 645
  - Components of the Blood Vessel Wall, 645
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Major Blood Vessels, 647
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The Big Picture: Cardiovascular Anatomy and the Whole Body, 669

Mechanisms of Disease, 669

Case Study, 676

LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

abdominal aorta
(ab-DOM-i-nal ay-OR-tah)
[*abdomin-* **belly,** *-al* **relating to** *aort-* **lifted,** *-a* **thing**] *pl.,* aortae or aortas

accessory hemiazygos vein
(ak-SES-oh-ree hem-EE-ah-ZYE-gos)
[*hemi-* **half,** *-a-* **without,** *-zygo-* **union or yoke**]

anastomosis
(ah-nas-toh-MOH-sis)
[*ana-* **anew,** *-stomo-* **mouth,** *-osis* **condition**] *pl.,* anastomoses

angiogenesis
(an-jee-oh-JEN-es-is)
[*angi-* **vessel** *-genesis* **origin**]

angiography
(an-jee-AH-graf-ee)
[*angi-* **vessel,** *-graph-* **draw,** *-y* **process**]

anterior tibial vein
(an-TEER-ee-or TIB-ee-al)
[*ante-* **front,** *-er-* **more,** *-or* **quality,** *tibia* **shin bone,** *-al* **relating to**]

aorta
(ay-OR-tah)
[*aort-* **lifted,** *-a* **thing**] *pl.,* aortae or aortas

aortic arch
(ay-OR-tik)
[*aort-* **lifted,** *-ic* **relating to**]

arterial anastomosis
(ar-TEER-ee-al ahnas-toh-MOH-sis)
[*arteria-* **vessel,** *-al* **relating to,** *ana-* **anew,** *-stomo-* **mouth,** *-osis* **condition**]
pl., anastomoses

arteriole
(ar-TEER-ee-ohl)
[*arteri-* **vessel,** *-ole* **little**]

continued on p. 674

The cardiovascular system is sometimes called simply the circulatory system. *It consists of the heart, which is a muscular pumping device, and a closed system of vessels called* arteries, capillaries, *and* veins. *As the name implies, blood contained in the circulatory system is pumped by the heart around a closed circle or circuit of vessels as it passes again and again through the various circulations of the body (see p. 648).*

As in the adult, survival of the developing embryo depends on the circulation of blood to maintain homeostasis and a favorable cellular environment. In response to this need, the cardiovascular system makes its appearance early in development and reaches a functional state long before any other major organ system. Incredible as it seems, the heart begins to beat regularly early in the fourth week after fertilization.

HEART

Location of the Heart

The human heart is a four-chambered muscular organ, shaped and sized roughly like a person's closed fist (Figure 21-1). It lies in the mediastinum, or middle region of the thorax, just behind the body of the sternum between the points of attachment of the second through the sixth ribs. Approximately two thirds of the heart's mass is to the left of the midline of the body, and one third is to the right (Figure 21-2).

Posteriorly the heart rests against the bodies of the fifth to the eighth thoracic vertebrae. Because of its placement between the sternum in front and the bodies of the thoracic vertebrae behind, it can be compressed by application of pressure to the lower portion of the body of the sternum using the heel of the hand (Figure 21-2, *E*). Rhythmic compression of the heart in this way can maintain blood flow in cases of cardiac arrest and, if combined with effective artificial respiration, the resulting procedure, called *cardiopulmonary resuscitation* (CPR), can be life saving.

The anatomical position of the heart in the thoracic cavity is shown in Figure 21-2. The lower border of the heart, which forms a blunt point known as the *apex*, lies on the diaphragm, pointing toward the left. To count the apical beat, one must place a stethoscope directly over the apex, that is, in the space between the fifth and sixth ribs (fifth intercostal space) on a line with the midpoint of the left clavicle.

The upper border of the heart, that is, its base, lies just below the second rib. The boundaries, which indicate its size, have considerable clinical importance, because a marked increase in heart size accompanies certain types of heart disease. Therefore, when diagnosing heart disorders, the physician charts the boundaries of the heart. The "normal" boundaries of the heart are, however, influenced by factors such as age, body build, and state of contraction.

Size and Shape of the Heart

At birth the heart is said to be transverse (wide) in type and appears large in proportion to the diameter of the chest cavity. In the infant, it is 1/130 of the total body weight compared with about 1/300 in the adult. Between puberty and 25 years of age the heart attains its adult shape and weight—about 310 grams is average for the male and 225 grams for the female.

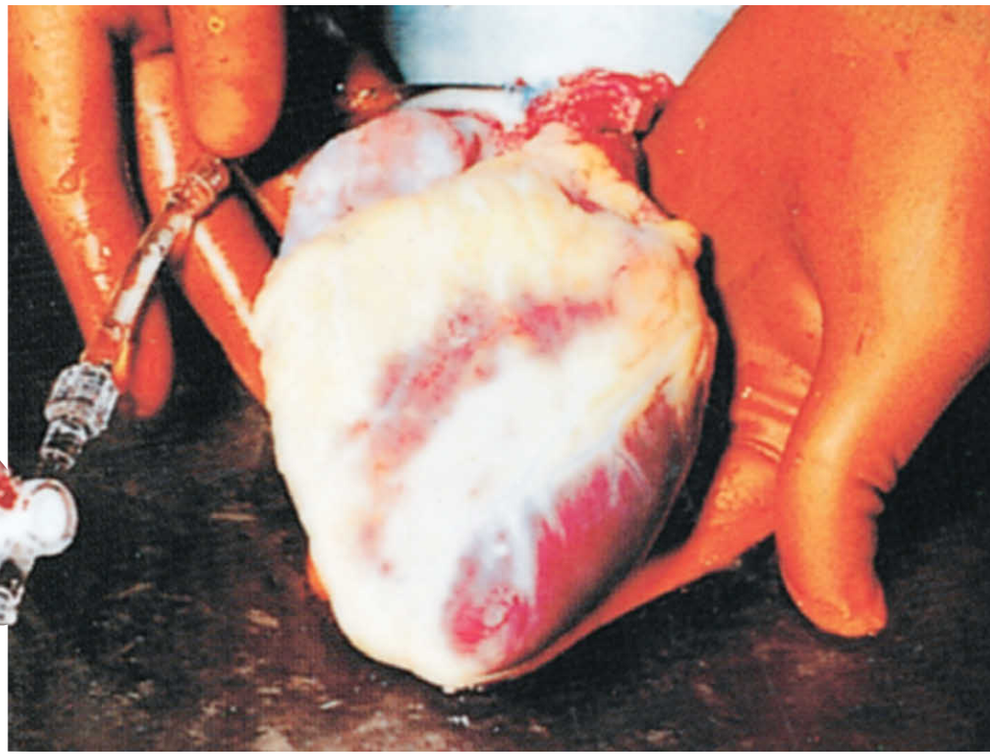


FIGURE 21-1

Appearance of the heart. This photograph shows a living human heart prepared for transplantation into a patient. Note its size relative to the hands that are holding it.

In the adult the shape of the heart tends to resemble that of the chest. In tall, thin individuals the heart is frequently described as elongated, whereas in short, stocky individuals it has greater width and is described as transverse. In individuals of average height and weight it is neither long nor transverse but somewhat intermediate between the two. Its approximate dimensions are 12 cm (4¾ inches) long, 9 cm (3½ inches) wide, and 6 cm (2½ inches) deep. Figure 21-3 shows details of the heart and great vessels in external views.

| QUICK CHECK |

1. In anatomical terms, where is the heart located?
2. Describe the shape of the heart.
3. When does the heart attain its adult shape and weight?

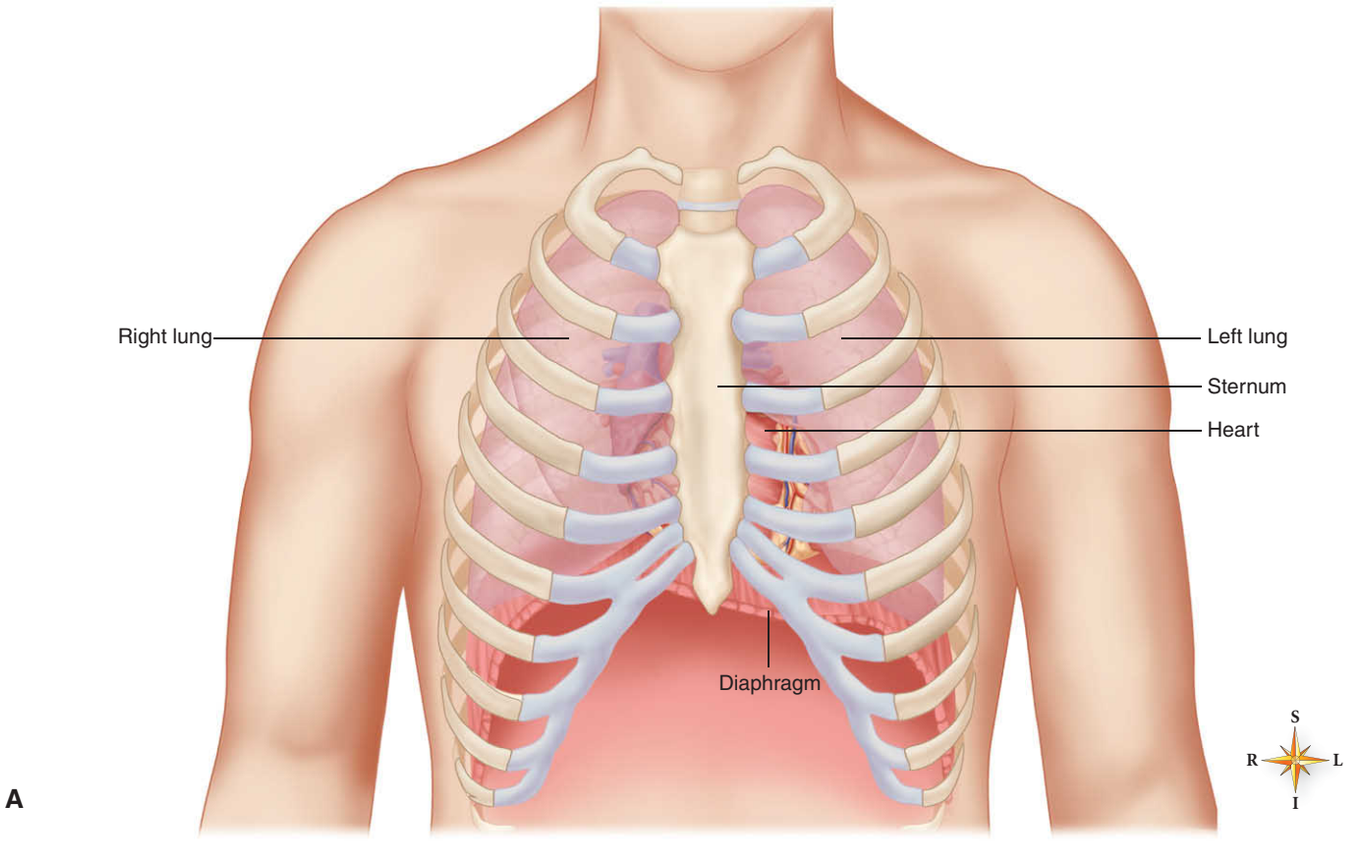
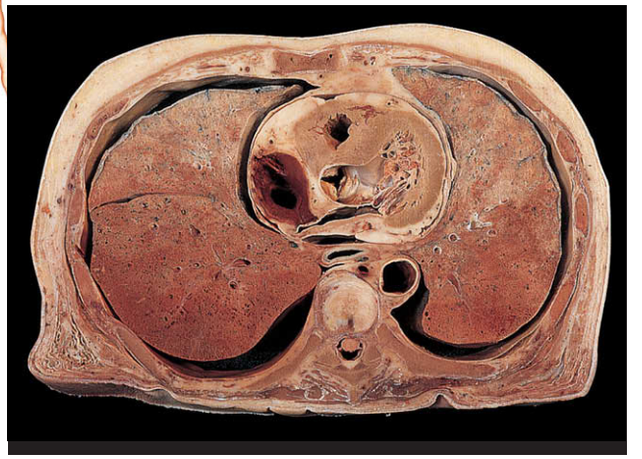


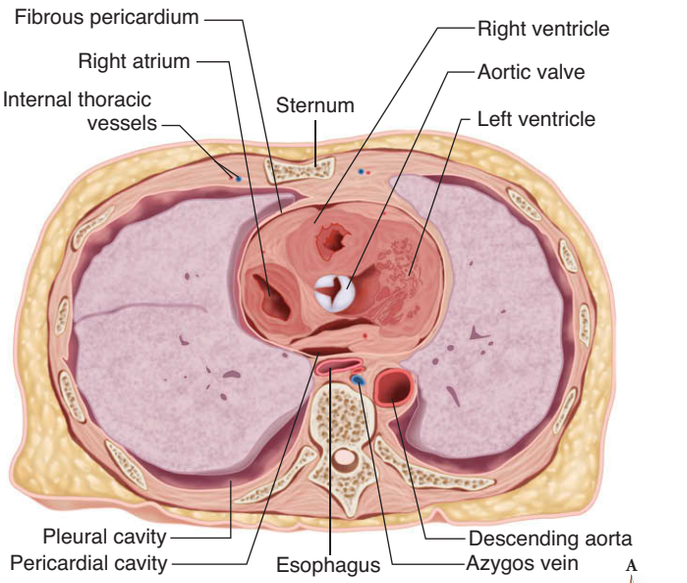
FIGURE 21-2

Location of the heart. A, Heart in mediastinum showing relationship to lungs and other anterior thoracic structures. **B,** Anterior view of isolated heart and lungs. Portions of the parietal pleura and pericardium have been removed. **C,** Detail of heart resting on diaphragm with pericardial sac opened.

(continued)



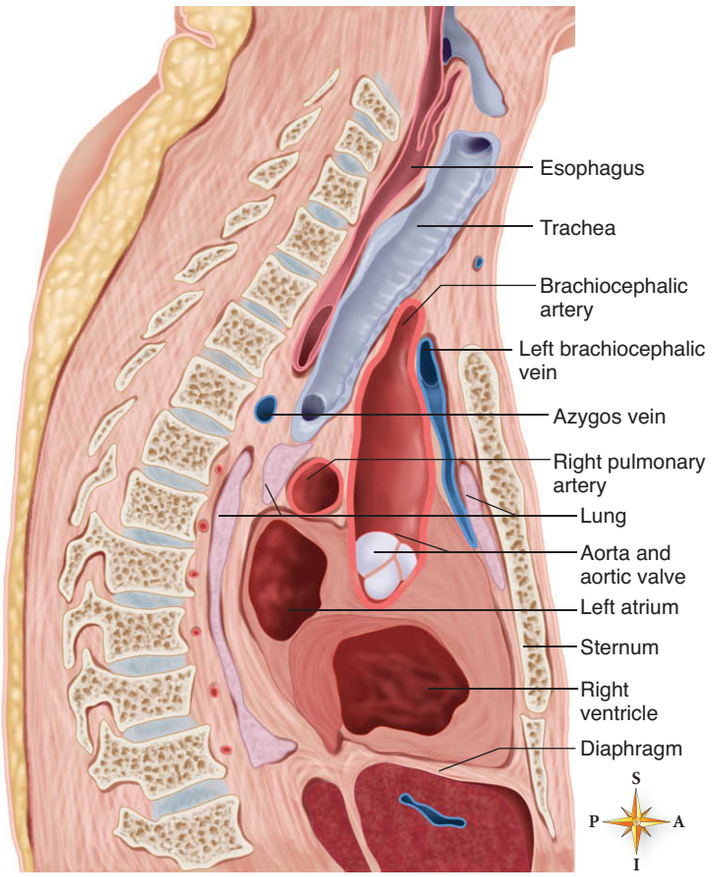




D



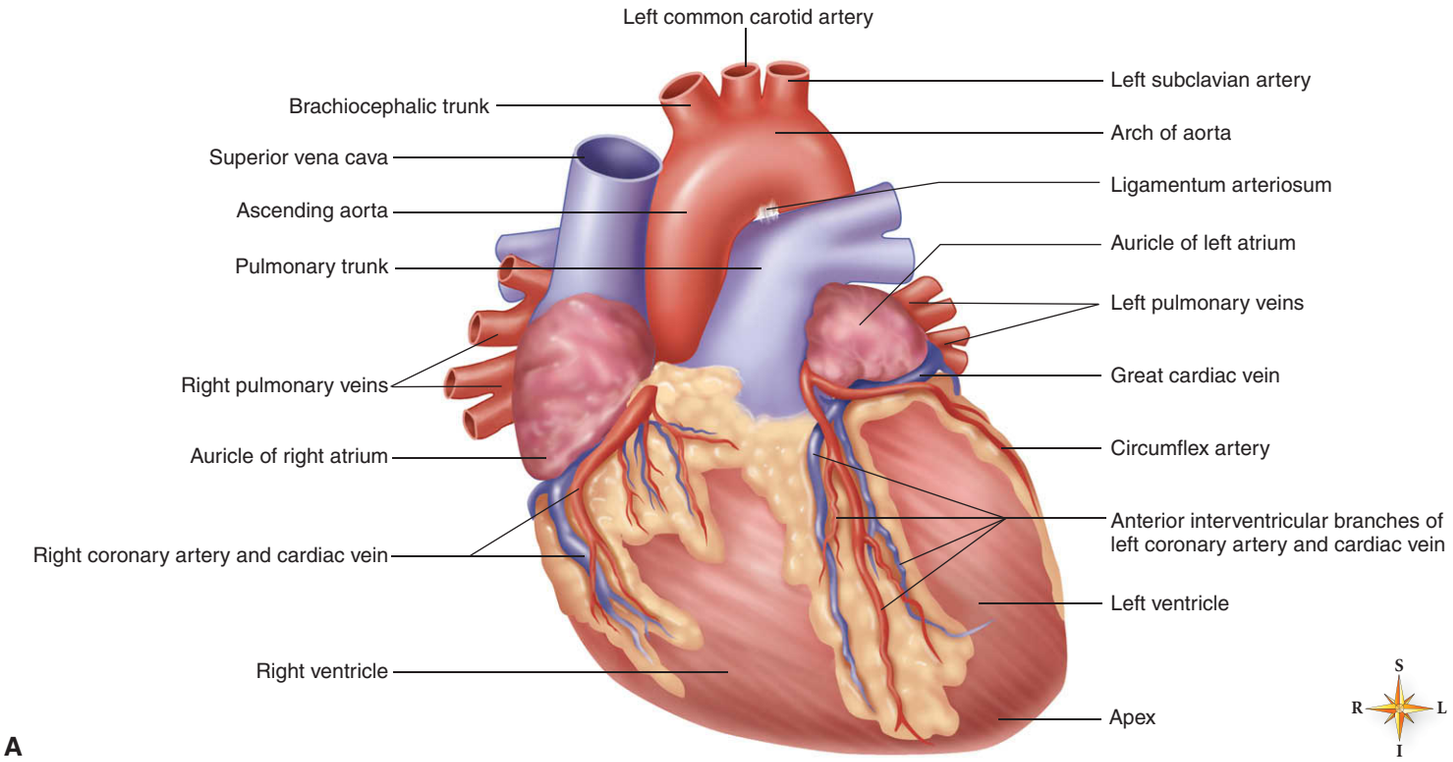




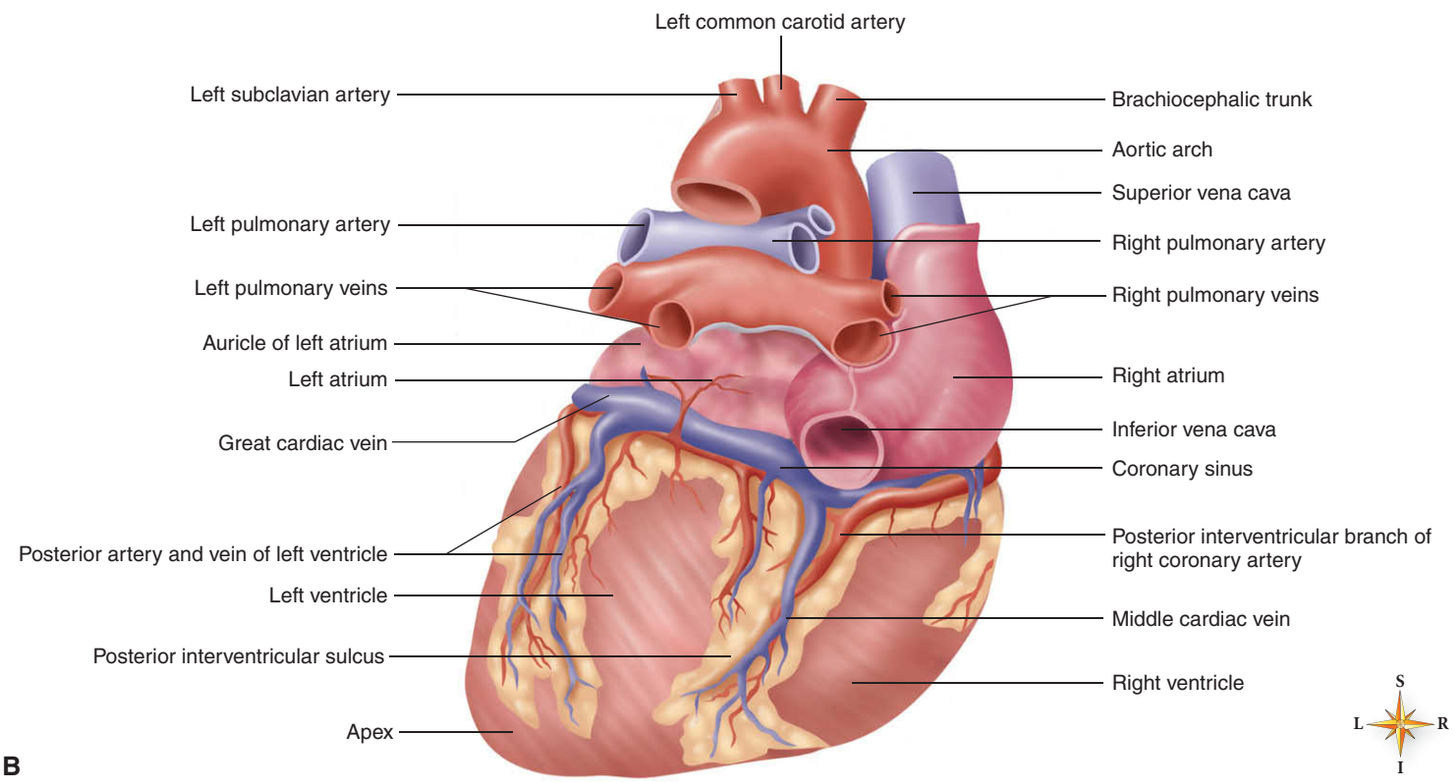
E

FIGURE 21-2

Location of the heart (continued). D, Transverse section of cadaver specimen and color drawing of thoracic structures at the level of the sixth thoracic vertebra. Inferior aspect. **E,** Midline sagittal section of cadaver specimen and color drawing showing thorax structures. Note the placement of the heart between the sternum in front and thoracic vertebrae behind—a fact that explains how CPR compressions can squeeze the heart to keep blood flowing.



A



B

FIGURE 21-3

The heart and great vessels. A, Anterior view. **B,** Posterior view.

Coverings of the Heart

STRUCTURE OF THE HEART COVERINGS

The heart has its own special covering, a loose-fitting inextensible sac called the **pericardium.** The pericardial sac, with the heart removed, can be seen in Figure 21-4. The pericardium consists of two parts: a fibrous portion and a serous portion (Figure 21-5). The sac itself is made of tough white fibrous tissue but is lined with smooth, moist serous membrane—the parietal layer of the serous pericardium. The same kind of membrane covers the entire outer surface of the heart. This covering layer is known as the *visceral layer* of the serous pericardium or the **epicardium.** The fibrous sac attaches to the large blood vessels emerging from the top of the heart but not to the heart itself (see Figure 21-4). Therefore it fits loosely around the heart, with a slight space between the visceral layer adhering to the heart and the parietal layer adhering to the inside of the fibrous sac. This space is called the **pericardial space.** It contains 10 to 15 ml of **pericardial fluid**, a lubricating fluid secreted by the serous membrane.

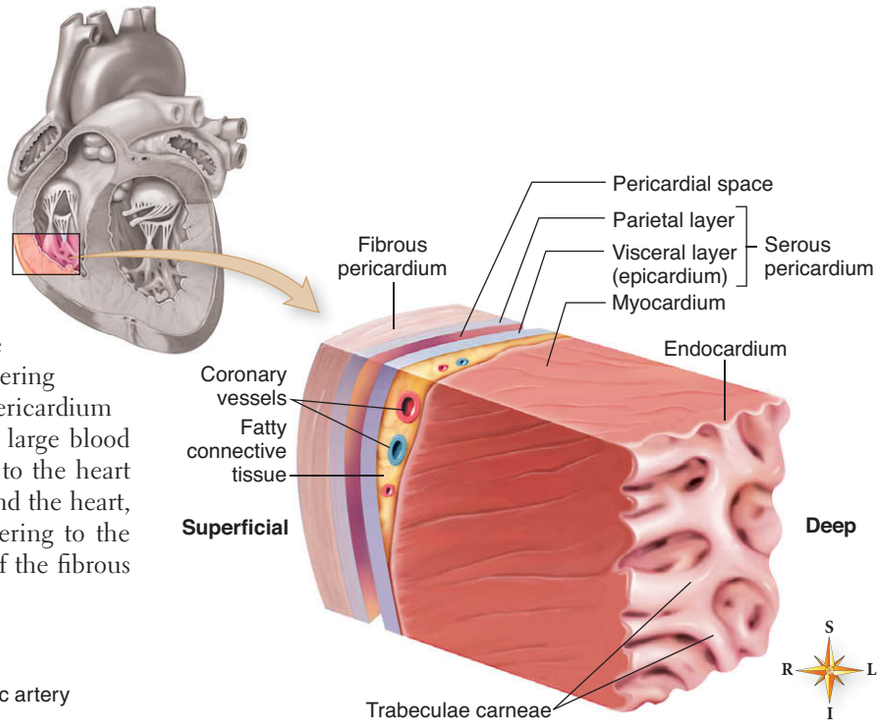


FIGURE 21-5

Wall of the heart. The cutout section of the heart wall shows the outer fibrous pericardium and the parietal and visceral layers of the serous pericardium (with the pericardial space between them). Note that a layer of fatty connective tissue is located between the visceral layer of the serous pericardium (epicardium) and the myocardium. Note also that the endocardium covers beamlike projections of myocardial muscle tissue, called *trabeculae carneae.*

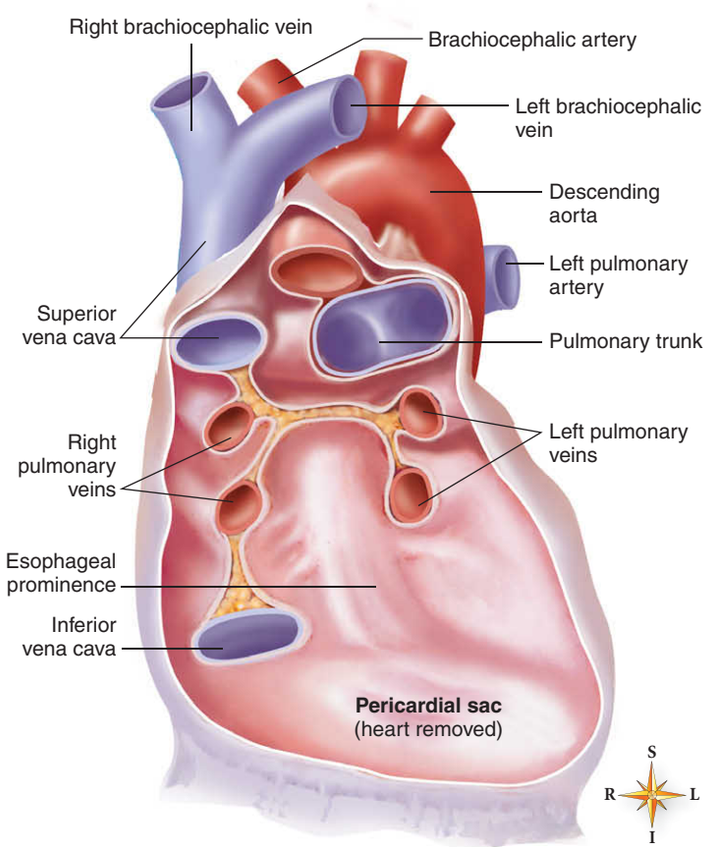


FIGURE 21-4

Pericardium. Frontal view diagram showing cut pericardial sac with heart removed. Notice that the pericardial sac attaches to the large vessels that enter and exit the heart, not to the heart itself. For a different view of the pericardium, see Figure 21-2, *C.*

Fibrous pericardium—tough, loose-fitting, and inelastic sac around the heart

Serous pericardium—consisting of two layers

1. *Parietal layer*—lining inside the fibrous pericardium
2. *Visceral layer (epicardium)*—adhering to the outside of the heart; between visceral and parietal layers is a space, the pericardial space, that contains a few drops of pericardial fluid

FUNCTION OF THE HEART COVERINGS

The fibrous pericardial sac with its smooth, well-lubricated lining provides protection against friction. The heart moves easily in this loose-fitting jacket with no danger of irritation from friction between the two surfaces, as long as the serous pericardium remains normal and continues to produce lubricating serous fluid.

Structure of the Heart

WALL OF THE HEART

Three distinct layers of tissue make up the heart wall (see Figure 21-5) in both the atria and the ventricles: the epicardium, myocardium, and endocardium.

Epicardium

The outer layer of the heart wall is called the **epicardium,** a name that literally means "on the heart." The epicardium is actually the visceral layer of the serous pericardium already described. In other words, the same structure has two different names: epicardium and serous pericardium.

Myocardium

The bulk of the heart wall is the thick, contractile, middle layer of specially constructed and arranged cardiac muscle cells called the **myocardium.** The minute structure of cardiac muscle has been described in Chapters 5 and 12. Review Table 6-7 on p. 152 for a brief overview of cardiac muscle.

Recall that cardiac muscle tissue is composed of many branching cells that are joined into a continuous mass by end-to-end junctions called *intercalated disks* (see Figure 6-35 on p. 153). Because each intercalated disk includes many gap junctions, large areas of cardiac muscle are electrically coupled into a single functional unit called a *syncytium* (meaning "joined cells"). Figure 13-23 on p. 400 shows how such electrical connections work. Because they form an electrically coupled syncytium, cardiac muscle cells can pass an action potential from fiber to fiber along a large area of the heart wall—thus stimulating contraction in each muscle fiber of the syncytium.

Another advantage of the linked structure of myocardial cells is that the cardiac fibers form a continuous sheet of muscle that wraps entirely around the cavities within the heart. Thus the encircling myocardium can compress the heart cavities, and the blood within them, with great force.

Recall also that cardiac muscles are *autorhythmic*, meaning that they can contract on their own in a slow, steady rhythm. As we explained in Chapter 12, cardiac muscle cells cannot summate contractions to produce tetanus and thus do not fatigue—a useful characteristic for muscle tissue that must maintain a continuous cycle of alternating contraction and relaxation for the entire span of life. Because the muscular myocardium can contract powerfully and rhythmically, without fatigue, the heart is an efficient and dependable pump for blood.

If the myocardium is damaged, as it may be in a "heart attack" or myocardial infarction (MI), then it will not pump as efficiently—which may quickly lead to death if the damage is severe. Such damage can be diagnosed by analyzing cardiac marker molecules released into the blood by damaged cardiac muscle fibers (Box 21-1).

Box 21-1 | DIAGNOSTIC study

Cardiac Marker Studies

When the heart muscle is damaged, molecules contained within the muscle cells are released into the bloodstream, causing increased plasma levels of these molecules. Blood tests (see figure) for these "marker" molecules are useful in confirming a *myocardial infarction (MI),* or "heart attack." The **troponins test** is very sensitive and is often the first choice in determining whether damage to the cardiac muscle has occurred. The two types of markers measured by this test are *cardiac-derived troponin I (cTnI) and troponin T (cTnT).* These troponins often increase to 20-fold their normal level within a few hours of an MI and remain high for several days.



A cardiac enzyme called *creatine kinase (CK)* is also often used as a cardiac marker. The ratio of the MB type of creatine kinase, or *CK-MB,* to standard CK increases within a few hours after an MI. The total CK/CK-MB released helps determine the size of the infarct. The CK-MB test is often used to confirm an MI when the results of the troponins test are confusing.

Cardiac marker determinations are also useful in observing the course of a myocardial infarction once it has occurred and in detecting an extension of it.

C-reactive protein (CRP) is a well-known blood marker for inflammation. Research has now confirmed that elevated levels of this blood protein are highly suggestive of either active cardiac disease (including MI) or early stages of progressive risk factor development. Many cardiologists are now measuring C-reactive protein levels in their heart patients as often as they check blood lipid levels or follow other known risk factors. The intent is to actively treat the disease before it becomes symptomatic or a heart attack actually occurs (also see Box 20-1 on erythrocyte sedimentation rate, p. 601).

Endocardium

The lining of the interior of the myocardial wall is a delicate layer known as the **endocardium.** The endocardium is made of a type of tissue called endothelial tissue, or simply **endothelium.** Endothelium lines the heart (where it is called the *endocardium*) and continues on to line all of the blood vessels. Endothelium is a specialized type of simple squamous epithelium.

Note in Figure 21-5 that the endocardium covers beamlike projections of myocardial tissue. These muscular projections are called *trabeculae carneae* (meaning "fleshy beams") and help to add force to the inward contraction of the heart wall.

Inward folds or pockets formed by the endocardium and supporting connective tissue make up the flaps or cusps of the major heart valves. These valves ensure the one-way flow of blood through the chambers of the heart, thus enabling the heart to act as a pump.

CHAMBERS OF THE HEART

The interior of the heart is divided into four cavities, or heart chambers (Figure 21-6). The two upper chambers are called *atria* (singular, *atrium*), and the two lower chambers are called *ventricles.* The left chambers are separated from the right chambers by an extension of the heart wall called the *septum.*

Atria

The two superior chambers of the heart—the **atria**—are separated into left and right chambers by the *interatrial septum.* Atria are often called the "receiving chambers" because they receive blood from vessels called *veins.* **Veins** are the large blood vessels that return blood from various tissues to the heart so that the blood can be pumped out to tissues again.

Figure 21-7 shows how the atria alternately relax and contract to receive blood, then push it into the lower chambers. Because the atria need not generate great pressure to move blood such a small distance, the myocardial wall of each atrium is not very thick.

If you look at Figures 21-2, C, and 21-3, A, you will notice that part of each atrium is labeled as an *auricle.* The term *auricle* (meaning "little ear") refers to the earlike flap protruding from each atrium. Thus the auricles are *part of* the atria. The terms *auricles* and *atria* should not be used synonymously.

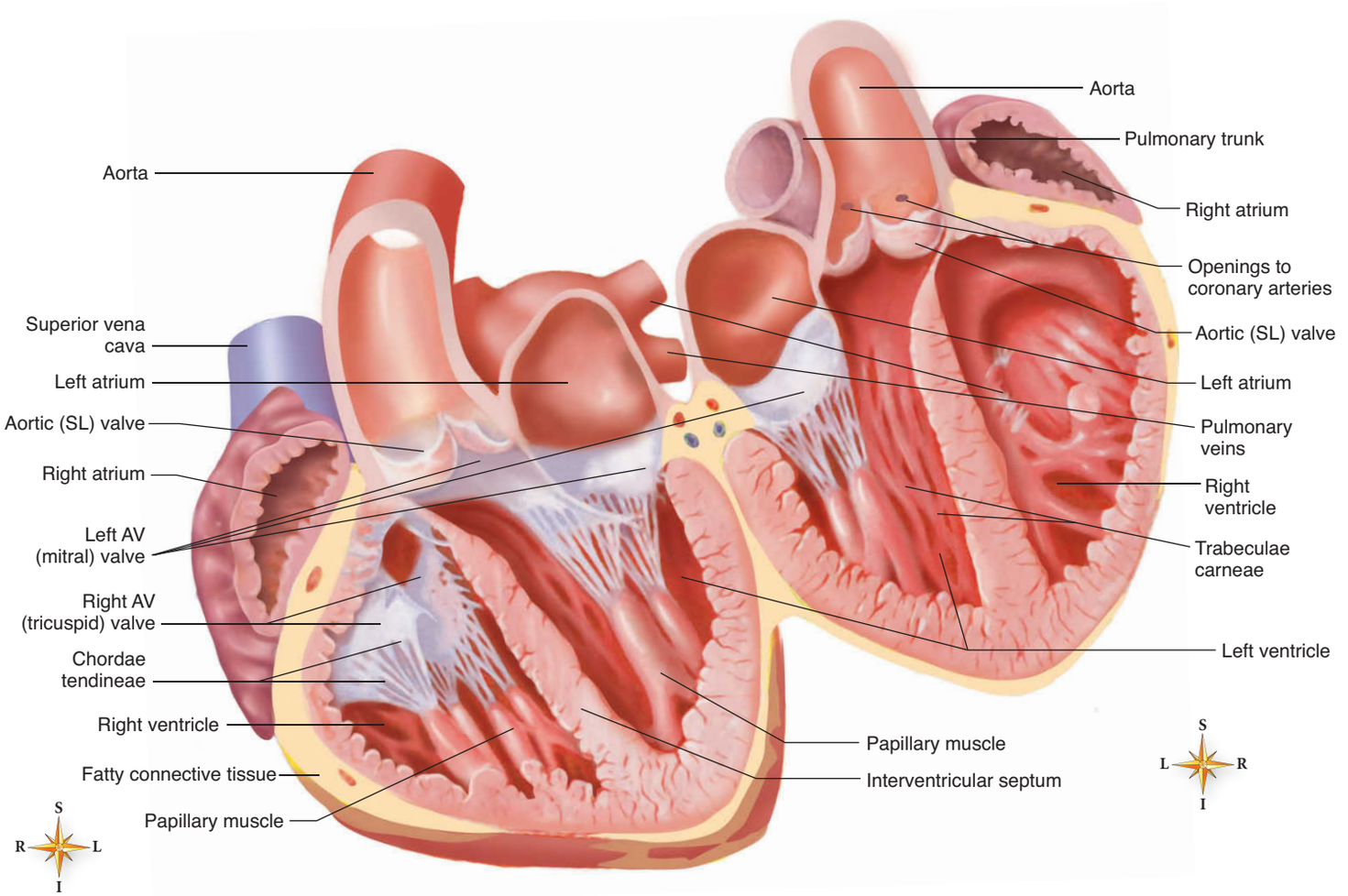


FIGURE 21-6

Interior of the heart. This illustration shows the heart as it would appear if it were cut along a frontal plane and opened like a book. The front portion of the heart lies to the reader's right; the back portion of the heart lies to the reader's left. (Note each portion has a separate anatomical rosette to facilitate orientation.) The four chambers of the heart—two atria and two ventricles—are easily seen. *AV,* Atrioventricular; *SL,* semilunar.

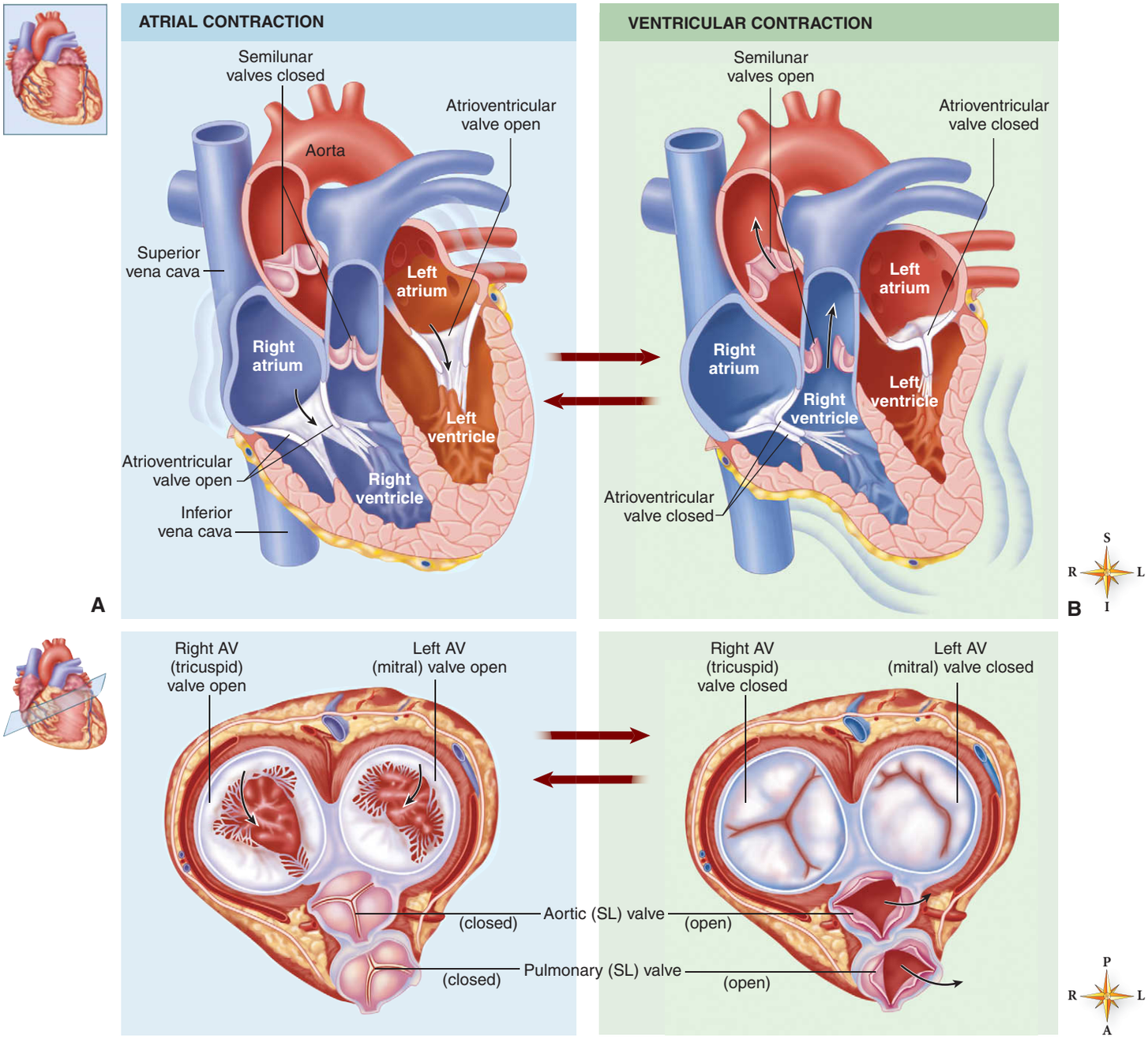


FIGURE 21-7

Chambers and valves of the heart. A, During atrial contraction cardiac muscle in the atrial wall contracts, forcing blood through the atrioventricular (AV) valves and into the ventricles. Bottom illustration shows superior view of all four valves, with semilunar (SL) valves closed and AV valves open. **B,** During ventricular contraction that follows, the AV valves close and the blood is forced out of the ventricles through the SL valves and into the arteries. Bottom illustration shows superior view of SL valves open and AV valves closed.

Ventricles

The **ventricles** are the two lower chambers of the heart. The ventricles are separated into left and right chambers by the *interventricular septum*. Because the ventricles receive blood from the atria and pump blood out of the heart into arteries, the ventricles are considered to be the primary "pumping chambers" of the heart.

Because more force is needed to pump blood a farther distance from the ventricles than from the atria, the myocardium of each ventricle is thicker than the myocardium of either atrium. The myocardium of the left ventricle is thicker than that of the right ventricle because the left ventricle pushes blood through most vessels of the body, whereas the right ventricle pushes blood only

through the nearby pulmonary vessels that serve the gas exchange tissues of the lungs.

The pumping action of the heart chambers is summarized in Figure 21-7 and described further in Chapter 22.

VALVES OF THE HEART

The heart valves are structures that permit the flow of blood in one direction only—allowing the heart to act as a pump that forces the continuous flow of blood in one direction.

Four valves are of importance to the normal functioning of the heart (Figure 21-8; see Figure 21-7). Because they guard the openings between the atria and the ventricles, two of the valves are called the **atrioventricular (AV) valves.** The atrioventricular valves have pointed leaflets or flaps called *cusps* and are therefore also called **cuspid valves.** The other two heart valves, the heart's **semilunar (SL) valves,** are located where the trunk of the pulmonary artery joins the right ventricle (pulmonary valve) and where the aorta joins the left ventricle (aortic valve).

Atrioventricular Valves

The atrioventricular valve regulating flow through the right atrioventricular opening consists of three flaps (cusps) of endocardium. The free edge of each flap is anchored to the *papillary muscles* of the right ventricle by several *tendinous cords* that are more often called **chordae tendineae.**

Because the right atrioventricular valve has three flaps or cusps, it is also called the **tricuspid valve.** The valve that guards the left atrioventricular opening is similar in structure to the right atrioventricular valve, except that it has only two flaps and is therefore also called the **bicuspid valve.** Most commonly, however, the left AV valve is called the **mitral valve**—a name it gets from its resemblance to the miter, a double-cusp hat worn by bishops.

The construction of both atrioventricular valves allows blood to flow from the atria into the ventricles but prevents it from flowing back up into the atria from the ventricles. When ventricles are relaxed, blood can flow through the AV valve from the atrium by simply pushing the flimsy valve cusps aside, into the ventricle.

Ventricular contraction forces the blood in the ventricles hard against the valve flaps, closing the valves. The papillary muscles contract along with the rest of the ventricular myocardium, thus pulling on the edges of the cusps by way of the chordae tendineae. By holding the edges of the cusps firmly during ventricular contraction, the chordae tendinae prevent the edges of the flaps from bending backwards and allowing blood to flow back into the atria. The harder the ventricular myocardium contracts, the more strongly it pushes against the AV valve—and the more strongly the papillary muscles pull on the chordae tendineae to hold the AV valves shut. This mechanism thus prevents backflow, no matter how strongly the heart ventricles contract. Keeping the AV valves closed during ventricular contraction ensures the movement of the blood upward into the pulmonary trunk and aorta as the ventricles contract (see Figure 21-7).

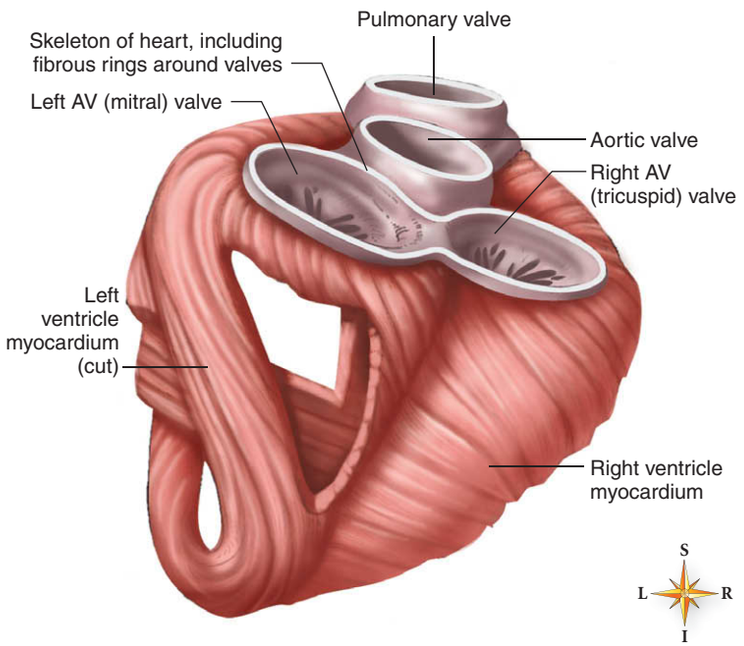


FIGURE 21-8

Skeleton of the heart. This posterior view shows part of the ventricular myocardium with the heart valves still attached. The rim of each heart valve is supported by a fibrous structure, called the skeleton of the heart, that encircles all four valves.

Semilunar Valves

The *semilunar (SL) valves* of the heart consist of pocket-like flaps (leaflets) extending inward from the lining of the trunk of the pulmonary artery and aorta. Semilunar, which literally means "half moon," refers to the crescent shape of the valve cusps visible in a frontal section of the heart.

The semilunar valve at the entrance of the pulmonary trunk is called the *pulmonary valve*. The semilunar valve at the entrance of the aorta is called the *aortic valve*. When the pulmonary and aortic valves are closed, as in Figures 21-7, *A*, blood fills the spaces between the leaflets and the vessel wall. Each leaflet then looks like a tiny, filled bucket. Inflowing blood smoothes the leaflets against the blood vessel walls, collapsing the buckets and thereby opening the valves (see Figures 21-7, *B*). Closure of the semilunar valves, as of the atrioventricular valves, simultaneously prevents backflow and ensures forward flow of blood in places where there would otherwise be considerable backflow.

Whereas the atrioventricular valves prevent blood from flowing back up into the atria from the ventricles, the semilunar valves prevent it from flowing back down into the ventricles from the aorta and pulmonary trunk.

Skeleton of the Heart

Figure 21-8 shows the fibrous structure that is often called the *skeleton of the heart*. It is a set of connected rings that serve as a semirigid support for the heart valves (on the inside of the rings) and for the attachment of cardiac muscle of the myocardium (on the outside of the rings).

The skeleton of the heart also serves as an electrical barrier between the myocardium of the atria and the myocardium of the ventricles. This arrangement allows the ventricles to contract separately from the atria, thus ensuring effective pumping of blood.

Surface Projection

When listening to the sounds of the heart on the body surface, as with a stethoscope, one must have an idea of the relationship between the valves of the heart and the surface of the thorax. Figure 21-9 indicates the surface relationship of the four heart valves and other features of the heart. It is important to remember, however, that considerable variation within the normal range makes a precise "surface projection" outline of the heart's structure on the chest wall difficult.

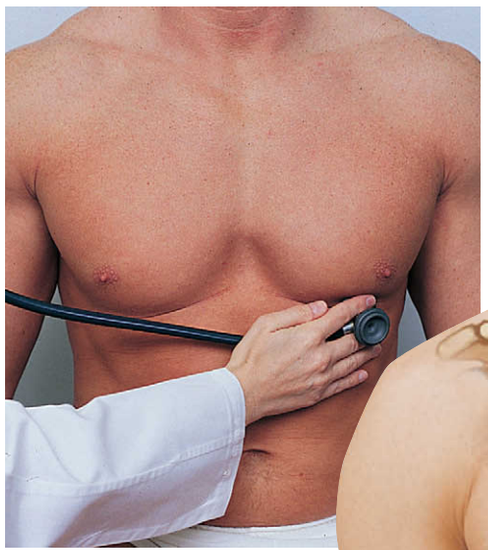
Flow of Blood Through the Heart

To understand the functional anatomy of the heart and the rest of the cardiovascular system, one should be able to trace the flow of blood through the heart. As we take you through one complete pass through the right side of the heart, then the left side of the heart, trace the path of blood flow with your finger, using Figure 21-7. We can trace the path of blood flow through the right side of the heart by beginning in the right atrium. From the right atrium, blood flows through the right atrioventricular (tricuspid) valve into the right ventricle. From the right ventricle, blood flows through the pulmonary semilunar valve into the first portion of the pulmonary artery, the pulmonary trunk. The pulmonary trunk branches to form the left and right pulmonary arteries, which conduct blood to the gas exchange tissues of the lung. From there, blood flows through pulmonary veins into the left atrium.

We can begin to trace the path of blood flow through the left side of the heart from the left atrium. From the left atrium, blood flows through the left atrioventricular (mitral) valve into the left ventricle. From the left ventricle, blood flows through the aortic semilunar valve into the aorta. Branches of the aorta supply all the tissues of the body except the gas-exchange tissues of the lungs. Blood leaving the head, neck, and upper extremities empties into the superior vena cava. Blood leaving the lower body empties into the inferior vena cava. Both large vessels conduct blood into the right atrium, bringing us back to the point where we began.

| A&P CONNECT |

Modern sound-wave technology allows us to visualize the action of the heart valves and the flow of blood through the chambers and great vessels of the heart using sound waves—the same technology often used to visualize fetuses developing within the womb. Learn how this technology is used and see the images it produces in ***Echocardiography*** online at ***A&P Connect.***



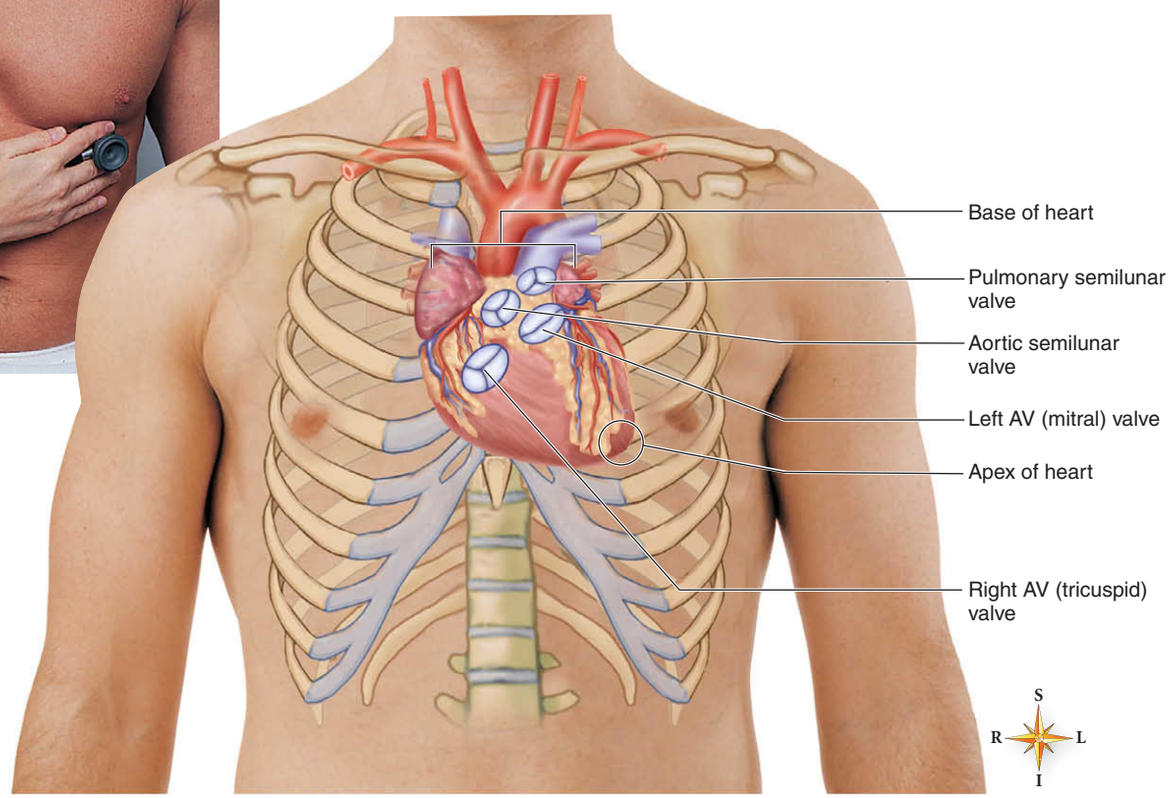


FIGURE 21-9

Relation of the heart to the anterior wall of the thorax. Valves of the heart are projected on the anterior thoracic wall. *AV,* Atrioventricular. The inset shows the use of a stethoscope to listen to heart sounds made by the closing of the valves.

| QUICK CHECK |

4. Name the layers of tissues that make up the pericardium.
5. What is the function of the pericardium?
6. Name the three layers of tissue that make up the wall of the heart. What is the function of each layer?
7. Name the four chambers of the heart and the valves associated with them.
8. How do atrioventricular valves differ from semilunar valves?

BLOOD SUPPLY OF HEART TISSUE

Coronary Arteries

Myocardial cells receive blood by way of two small vessels, the right and left **coronary arteries**. *Coronary* means "crown"—an apt name when you visualize the position of the left and right coronary arteries encircling the myocardium, much as a crown encircles the head (Figure 21-10, *A*). Because the openings into these vitally important vessels lie behind leaflets of the aortic semilunar valve, they come off the aorta at its very beginning and are its first branches.

Figure 21-10, *B*, shows that the placement of the openings of the coronary arteries behind the leaflets or flaps of the aortic valve permits an unusual and necessary method of arterial filling. Ordinarily, arteries that branch from the aorta fill during ventricular contraction when the great force of ventricular pressure pushes blood into the arteries. However, the coronary arteries are squeezed during ventricular contraction and could not fill during this time. Because the coronary artery openings are placed behind the leaflets of the aortic valve, blood flow is diverted from these openings during ventricular contraction when the valve leaflets are against the wall of the aorta. During ventricular relaxation, when the coronary arteries expand somewhat, blood flow is diverted into the coronary artery openings by the closing of the aortic valve—allowing the coronary arteries to fill.

Both right and left coronary arteries have two main branches, as shown in Figures 21-10 and 21-11.

More than one-half million Americans die every year from coronary disease, and another 3.5 million or more are estimated to suffer some degree of incapacitation. Knowledge about the distribution of coronary artery branches therefore has great practical importance. Here, then, are some principles related to the heart's own blood supply that are worth noting:

- Both ventricles receive their blood supply from branches of the right and left coronary arteries.
- Each atrium, in contrast, receives blood only from a small branch of the corresponding coronary artery.
- The most abundant blood supply goes to the myocardium of the left ventricle—an appropriate amount—because the left ventricle does the most work and so needs the most oxygen and nutrients delivered to it.
- The right coronary artery is dominant in about 50% of all hearts; the left coronary artery is dominant in about 20%; and in about 30%, neither right nor left coronary artery dominates.

Another fact about the heart's own blood supply—one of life-and-death importance—is that only a few connections, or anastomoses, exist between the larger branches of the coronary arteries. An **anastomosis** consists of one or more branches from the proximal part of an artery to a more distal part of itself or of another artery. Thus anastomoses provide detours in which arterial blood

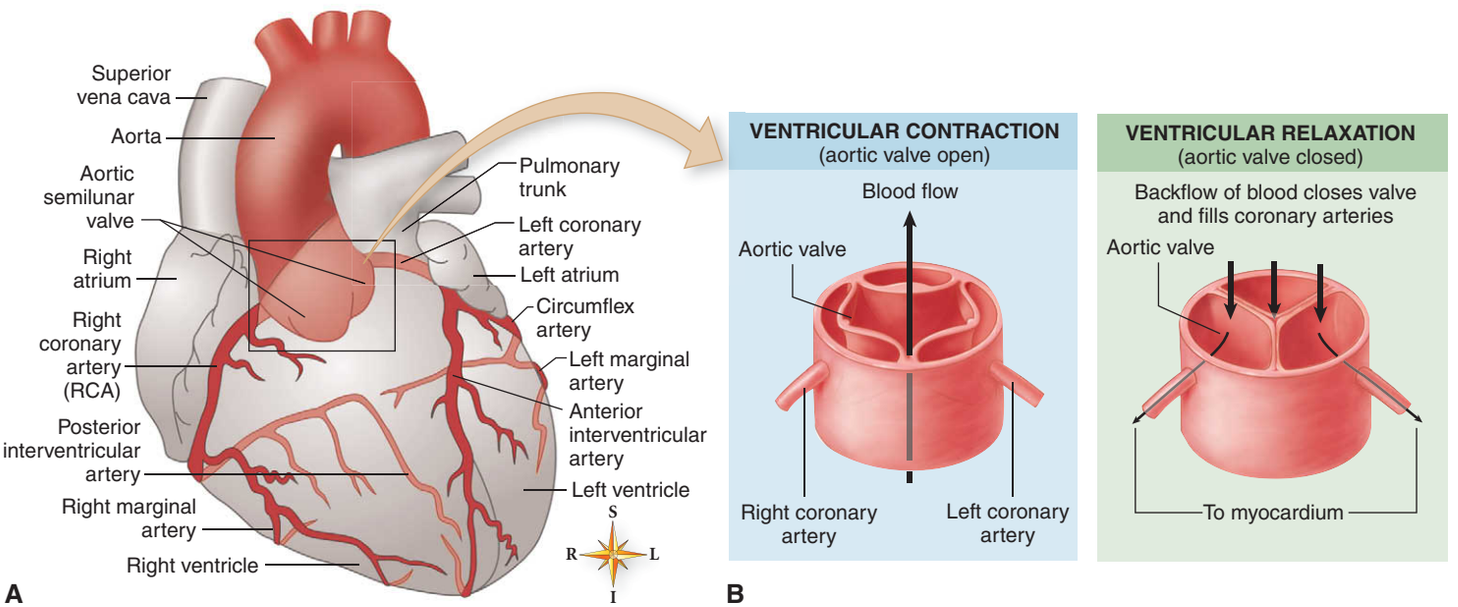


FIGURE 21-10

Coronary arteries. A, Diagram showing the major coronary arteries (anterior view). Clinicians often refer to the interventricular arteries as *descending* arteries. Thus a cardiologist would refer to the *left anterior descending (LAD) artery* and an anatomist would refer to the same vessel as the *anterior interventricular artery.* **B,** The unusual placement of the coronary artery opening behind the leaflets of the aortic valve allows the coronary arteries to fill during ventricular relaxation.

can travel if the main route becomes obstructed. In short, they provide collateral circulation to a part. This explains why the scarcity of anastomoses between larger coronary arteries looms so large as a threat to life.

If, for example, a blood clot plugs one of the larger coronary artery branches, as it frequently does in coronary thrombosis or embolism, too little or possibly no blood at all can reach some of the heart muscle cells. They become ischemic, in other words. Deprived of oxygen, metabolic function is impaired and cell survival is threatened. **Myocardial infarction (MI)**—death of ischemic heart muscle cells—soon results.

Another anatomical fact, however, brightens the picture somewhat: although few anastomoses exist between the larger coronary arteries, many anastomoses do exist between the very small arterial vessels in the heart. Given time, new anastomoses between the very small coronary arteries develop and provide collateral circulation to ischemic areas. Several surgical procedures have been devised to aid this process (see Mechanisms of Disease, p. 669).

Box 21-2 discusses a method for visualizing blood channels through the coronary arteries.

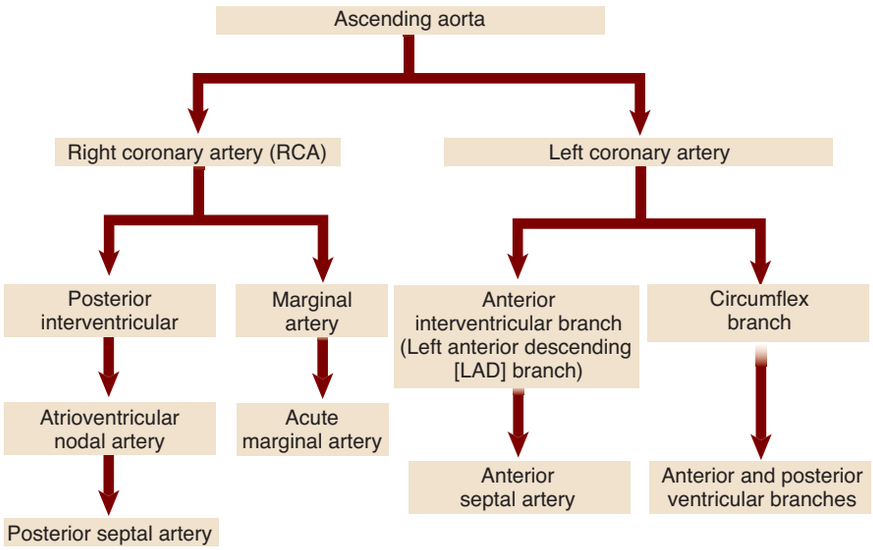


FIGURE 21-11

Blood flow through the coronary arteries. Blood leaves the ascending aorta and flows through the myocardium of the heart. Compare to Figure 21-10.

Cardiac Veins

After blood has passed through **capillary** networks in the myocardium, it enters a series of cardiac veins before draining into the right atrium through a common venous channel called the *coronary sinus.* Several veins that collect blood from a small area of the right ventricle do not end in the coronary sinus but instead drain directly into the right atrium. As a rule, the cardiac veins

Box 21-2 | DIAGNOSTIC study

Angiography

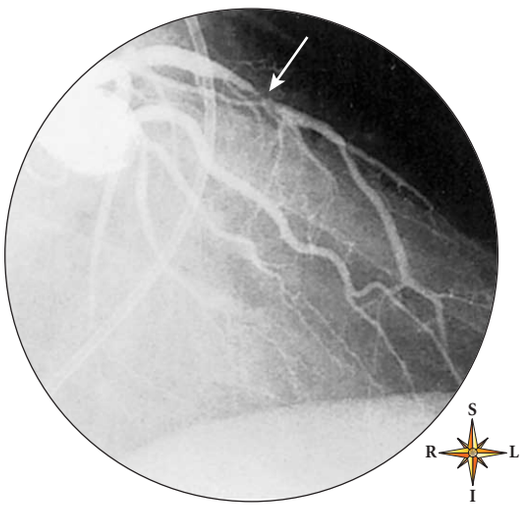
A special type of radiography called **angiography** (an-jee-AH-gra-fee) is often used to visualize arteries. A radiopaque dye—a substance that cannot be penetrated by x rays—is injected into an artery to better visualize vessels that would otherwise be invisible in a radiograph. This dye is often called *contrast medium.*

Sometimes the dye is released through a long, thin tube called a catheter—a procedure called *catheterization.* The catheter can be pushed through arteries until its tip is in just the right location to release the dye. As the dye begins to circulate, an *angiogram* (radiograph) will show the outline of the arteries as clearly as if they were made of bone or other dense material (see figure).

An angiogram of an artery is often called an *arteriogram.* An angiogram of veins can be called a *venogram* or *phlebogram.*

| A&P CONNECT |

To learn more about radiography, check out ***Medical Imaging of the Body*** online at ***A&P Connect. Cardiac Nuclear Scanning*** is also used to assess blood flow in coronary vessels. Read all about it at ***A&P Connect.***



Widow Maker. Coronary arteriogram of the coronary arteries shows a narrowing *(arrow)* of the channel in the left anterior descending (LAD) artery of the heart. Partial or complete occlusion of the LAD coronary artery is sometimes called the "widow maker" because complete occlusion of this artery results in a massive heart attack and sudden death—often occuring in men in their 50s.

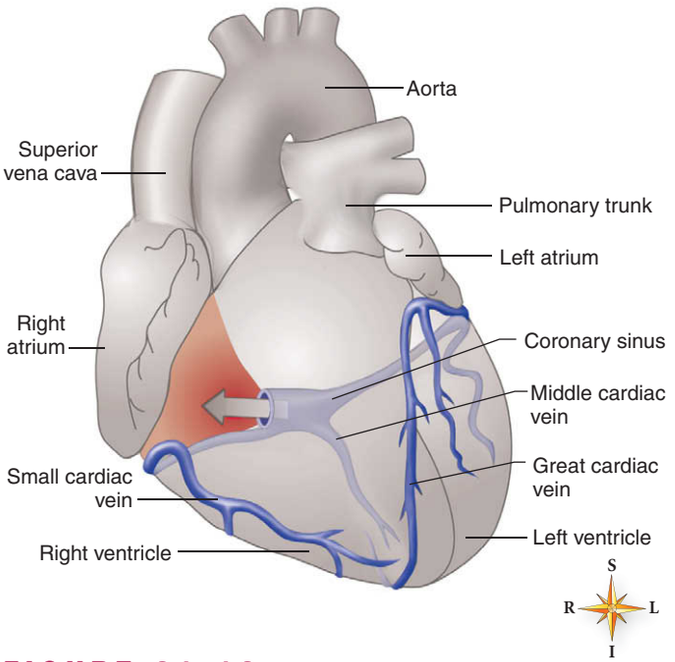


FIGURE 21-12

Coronary veins. Diagram showing the major veins of the coronary circulation (anterior view). Vessels near the anterior surface are more darkly colored than vessels of the posterior surface seen through the heart.

(Figure 21-12) follow a course that closely parallels that of the coronary arteries.

NERVE SUPPLY OF THE HEART

The myocardium is autorhythmic and can thus produce its own action potentials without the influence of afferent nerve signals. To coordinate effective self-activation, the heart has a system of myocardial fibers specialized for rapid electrical conduction along a pathway extending from the top to the bottom of the heart. The myocardial structures that generate and conduct action potentials are called the *conduction system of the heart*. The structure and function of this important system are discussed in Chapter 22.

Although the heart can generate its own rhythm of impulses (action potentials) and thus generate its own pumping contractions, the body sometimes has need to increase or decrease that rhythm. For example, when you increase the use of skeletal muscles and thus use oxygen more rapidly, your heart must increase its rate of pumping to keep the blood oxygen level near the set point. So it is no surprise that the heart receives efferent (motor) nerves that permit such regulation of the contractions of the heart.

Both divisions of the autonomic nervous system send fibers to the heart. Sympathetic fibers (contained in the middle, superior, and inferior cardiac nerves) and parasympathetic fibers (in branches of the vagus nerve) combine to form cardiac plexuses located close to the arch of the aorta. From the cardiac plexuses, fibers accompany the right and left coronary arteries to enter the heart. Here most of the fibers terminate in the *sinoatrial (SA) node* near the junction of the superior vena cava and right atrial wall. The SA node acts as the heart's *pacemaker* and is part of the heart's own conduction system, a concept we explore in Chapter 22 (see Figure 22-2 on p. 683).

However, some of the fibers end in the *atrioventricular (AV) node* (another part of the heart's conduction system) and in the atrial myocardium. A few parasympathetic fibers extend to the ventricular part of the heart's conduction system. Because they increase the heart rate by stimulating the heart's built-in pacemaker, sympathetic nerves to the heart are also called *accelerator nerves*. Vagus fibers to the heart instead serve as *inhibitory* or *depressor nerves*.

| QUICK CHECK |

9. Briefly describe the general structure and the function of the coronary circulation.
10. Why is an understanding of the coronary circulation so critical to understanding major types of heart disease?
11. What is meant by the term *conduction system of the heart*?
12. What is a myocardial infarction?

BLOOD VESSEL TYPES

There are nearly 100,000 km—more than 60,000 miles—of vessels carrying blood through your body right now. These vessels developed through the complex process of **angiogenesis** (*angi* means "vessel") that begins during embryonic development and continues through the lifespan. As scientists work out how angiogenesis is guided by chemical signals, they also develop new therapies to promote angiogenesis after tissue injury and to inhibit the accelerated angiogenesis in tumors that allows them to spread as cancer.

You have already been introduced to the different roles that blood vessels play in the body: *arteries* conduct blood away from the heart, *capillaries* conduct blood through tissues and permit exchange of materials, and *veins* conduct blood back toward the heart. In the following sections, we explore a few important details of blood vessel anatomy.

Arteries

An **artery** is a vessel that carries blood away from the heart. There are several types of arteries in the cardiovascular system.

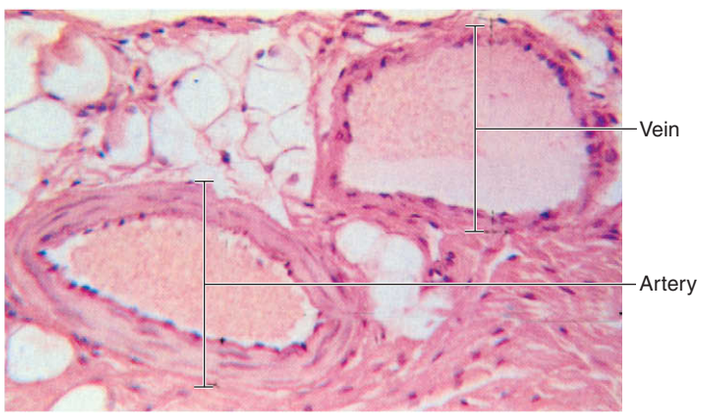


FIGURE 21-13

Artery and vein. Light micrograph of a cross section of similar-sized artery *(left)* and vein *(right)*. Notice the thick muscular wall of the artery as compared to the thin-walled vein.

Elastic arteries (also called *conducting arteries*) are the largest in the body and include the aorta and some of its major branches. As the name implies, elastic arteries can stretch without causing injury to accommodate the surge of blood that is forced into them when the ventricles contract and then recoil when the ventricles relax.

Muscular arteries (also called *distributing arteries*) carry blood farther away from the heart to specific organs and areas of the body. They are smaller in diameter than elastic arteries. However, the muscular layer in the wall of these vessels is proportionately thicker. Because of the thick muscle layer, muscular arteries have a thicker vessel wall than similar-sized veins (Figure 21-13). Like elastic arteries, muscular arteries are given names. Examples include the brachial, gastric, and superior mesenteric arteries.

Arterioles, also called *resistance vessels*, are the smallest arteries. Figure 21-14 shows the structure of arterioles in comparison to muscular and elastic arteries. Arterioles are not named individually, but as a group, they are critically important in regulating blood flow throughout the body. They function in this way by variable contraction of smooth muscle in their walls, which in turn increases resistance to blood flow and helps regulate blood

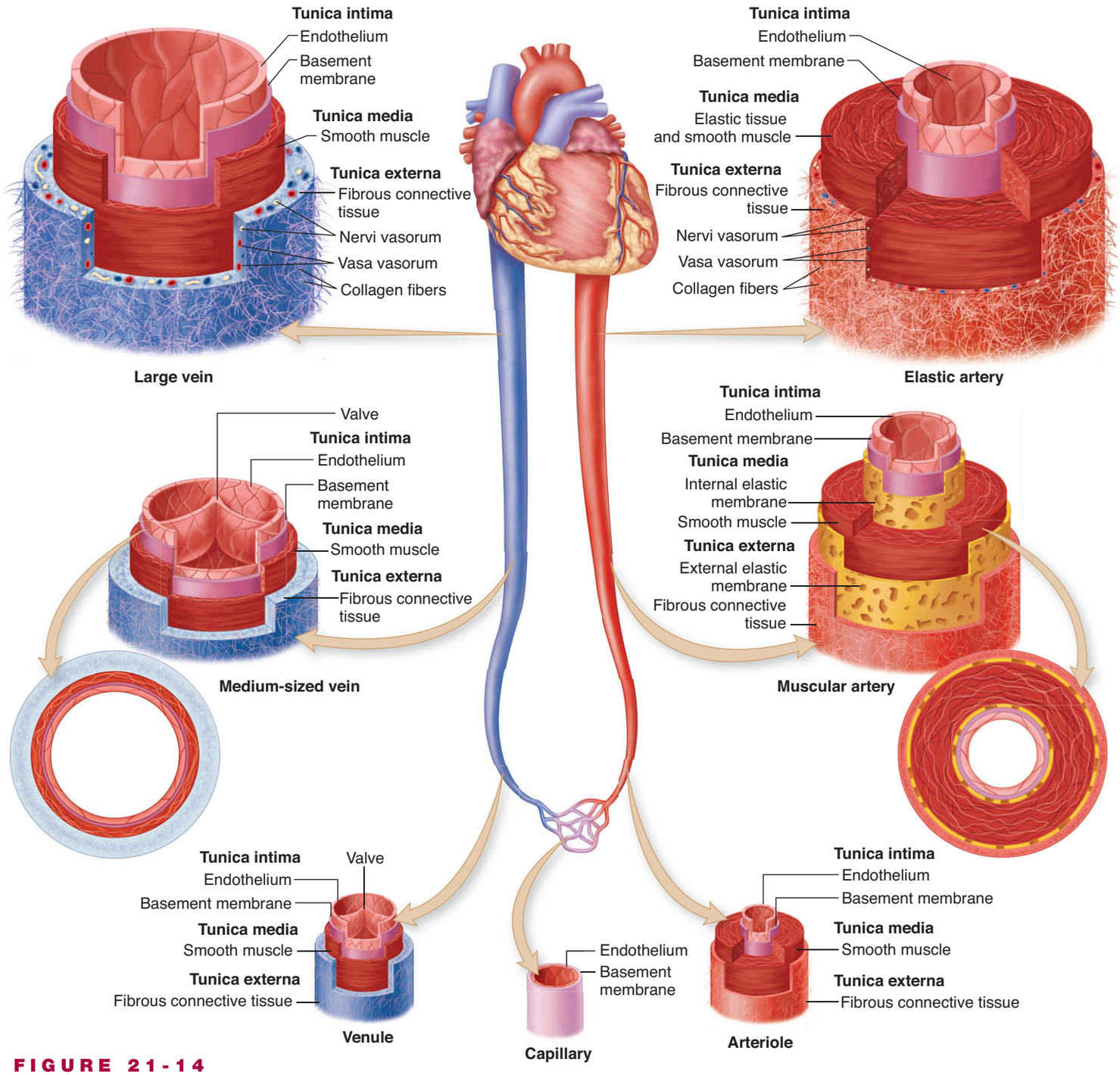


FIGURE 21-14

Structure of blood vessels. The tunica externa of the veins are color-coded blue and the arteries red.

pressure as well as determine the quantity of blood that enters a particular organ. The concept of flow resistance and its relationship to blood vessel diameter are discussed further in Chapter 22.

Metarteriole is the term used to describe the short connecting vessel that connects a true arteriole with the proximal end of between 20 and 100 capillaries and then extends through the capillary bed (Figure 21-15). The proximal ends of metarterioles are encircled by special "regulatory valves"—smooth muscle cells called *precapillary sphincters*. Because each precapillary sphincter wraps around the entrance to a capillary, it can relax or contract to increase or decrease blood flow into specific capillary networks. The distal end of a metarteriole is devoid of precapillary sphincters and is called a *thoroughfare channel*. It is possible for blood passing directly through a metarteriole into a thoroughfare channel to bypass the intervening capillary bed. After birth all arteries except the pulmonary artery and its branches carry oxygenated blood.

Capillaries

Capillaries are the microscopic vessels that carry blood from arterioles to venules. Blood flow through the arterioles, venules, and capillaries is called the *microcirculation* (see Figure 21-15). Transfer of nutrients and other vital substances between blood and tissue cells occurs at or very near a capillary—in so-called capillary beds or networks. It is for this reason that capillaries are sometimes known as the *primary exchange vessels* of the cardiovascular system. So vital is this function that no cell in the body is far removed from a capillary.

Although capillaries are small in size, the number of them in the body is estimated to be in excess of 1 billion. They are not, however, uniformly distributed. Some body tissues, such as liver or cardiac muscle, have high metabolic rates and require large numbers of capillary vessels. Other tissues, such as cartilage and epithelium, are avascular and lack capillary networks altogether.

True capillaries receive blood flowing out of metarterioles or other small arterioles. Precapillary sphincters regulate the volume of inflow of blood and its rate of passage through a true capillary. If the sphincter is "open," blood flows into the capillary; and if the sphincter is closed or partially closed, blood flow into the capillary bed decreases (see Figure 21-15). Capillaries are often categorized into three groups by the ease of passage of substances through their walls or by structural differences that affect their permeability.

Continuous capillaries have a continuous lining of endothelial cells with only small openings called *intercellular clefts* between them (Figure 21-16). This type of capillary is typically found in skeletal muscle, lung, and many types of connective tissue. **Fenestrated capillaries** also have intercellular clefts between their lining endothelial cells. But, in addition, they also have small "holes" or fenestrations through the plasma membrane of the endothelial cell itself. This unique structural adaptation allows for special function. Understanding the anatomy of these tiny vessels will be helpful in understanding the function of a number of major organs, such as the kidneys and small intestines, discussed later in the text.

Sinusoid is the term used to describe a type of capillary that has a much larger lumen and more winding or tortuous course than other capillary vessels. The basement membrane that completely covers other capillaries is either absent or incomplete in sinusoids. In addition, the fenestrations present both between and within the endothelial lining cells are much larger than in other capillary types. The result is great porosity. Because of this structural

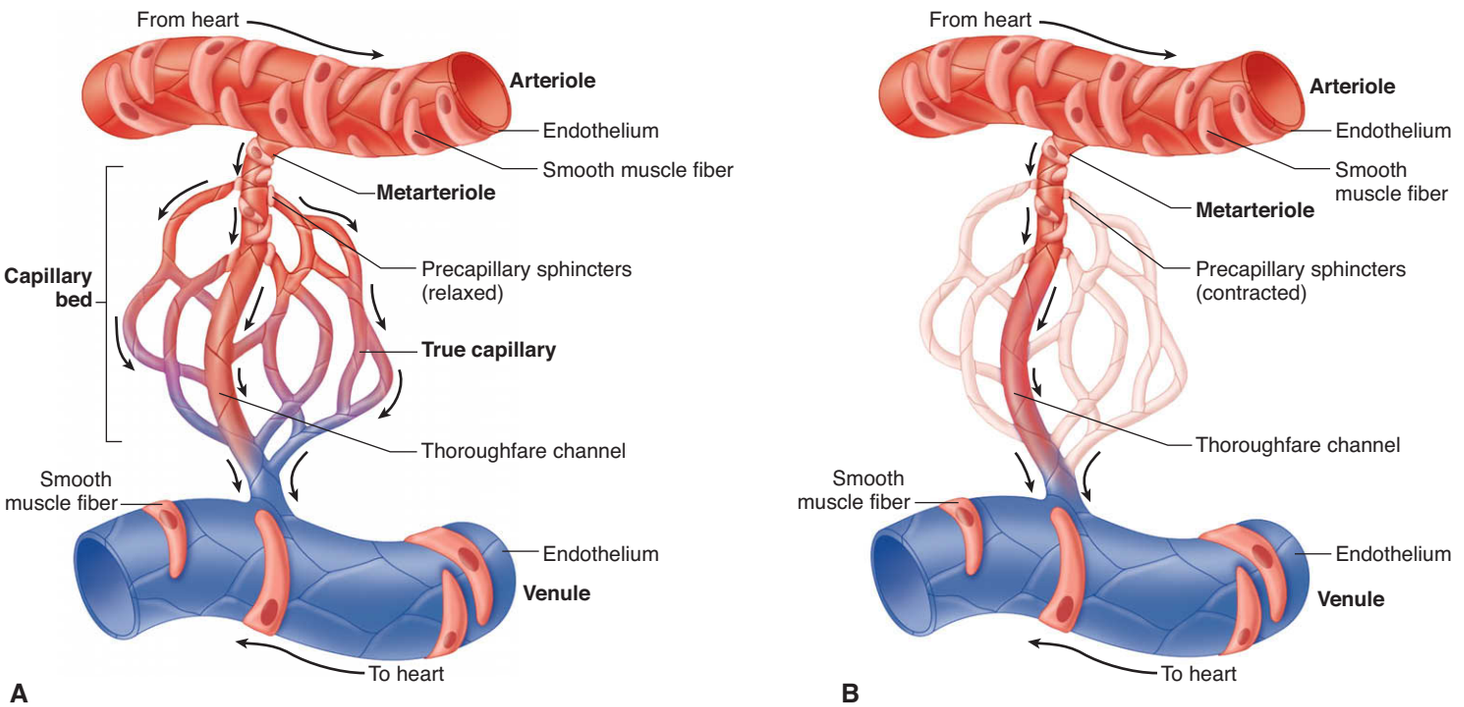


FIGURE 21-15

Microcirculation. Control of blood flow through a capillary network is regulated by the relative contraction of precapillary sphincters surrounding arterioles and metarterioles. **A,** Sphincters are relaxed, permitting blood flow to enter the capillary bed. **B,** With sphincters contracted blood flows from metarteriole directly into thoroughfare channel, bypassing the capillary bed.

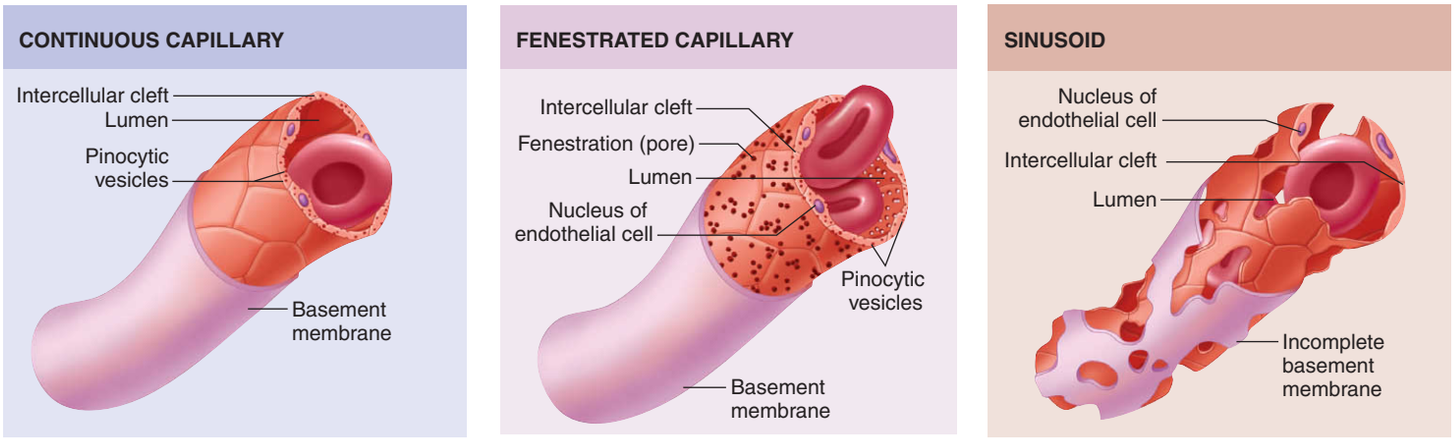


FIGURE 21-16

Types of capillaries. A, Continuous capillary. Note the presence of clefts only between adjacent endothelial cells. **B,** Fenestrated capillary. In addition to intercellular clefts, fenestrations (pores) exist in the plasma membranes of endothelial cells. **C,** Sinusoid. In addition to large intercellular clefts and cellular fenestrations, the basement membrane is incomplete or absent.

adaptation, sinusoids in the bone marrow and liver, for example, are able to permit migration of blood cells from the intravascular space into surrounding tissues.

Veins

A **vein** is a vessel that carries blood toward the heart. After passing through the complex capillary network of vessels, blood from several capillaries flows into the distal end of the metarteriole, the thoroughfare channel, or directly enters the first of a series of vessels that will eventually return it to the heart.

The first venous structures are small diameter vessels called **venules.** Initially, these tiny veins, especially those closest to the capillary bed, have very narrow lumens and porous, thin walls. As in capillaries, fluid can be exchanged between blood in the smallest venules and the tissue spaces. Their walls consist of little more than endothelial cells, a few smooth muscle cells and an occasional fibroblast. In addition to movement of fluid through the wall of the venule, phagocytic white blood cells (WBCs) also move out of the cardiovascular system and into areas of inflamed tissue by passing through the pores in walls of venules (see discussion of diapedesis on pp. 606 and 752).

As blood exits the smaller venules it enters progressively larger venous channels—the veins. Their names correspond to their arterial counterparts. However, whereas arteries become progressively smaller as blood flows away from the heart and into branches feeding other areas of the body, named veins become progressively larger as additional blood flows into them as they approach the heart. Structural changes occur in the walls of veins as they grow in size to accommodate and regulate additional blood volume and flow.

Veins can accommodate varying amounts of blood with almost no change in blood pressure. This results from their great ability to stretch. Ease of stretch is also called *capacitance*. Therefore, the veins are often referred to as the *capacitance vessels* of the cardiovascular system. High capacitance permits veins to serve as reservoirs for blood as well as conduits for its passage back to the heart.

Another structural adaptation in veins that has an important functional significance is the presence of one-way valves similar to the heart's semilunar valves. These valves develop from the thin membrane (endothelium) that lines the lumen of these vessels. The peripheral veins in the extremities have more valves than other veins of the body. Valves keep blood moving toward the heart and prevent its potential backflow.

The term **venous sinus** is used to describe large venous structures that have very thin endothelial walls. Since no smooth muscle cells or other support tissues found in the outer layers of typical large veins are located in the walls of venous sinuses, they cannot change their shape and thus depend on surrounding structures for support. Examples of venous sinuses include the dural venous sinuses of the brain (look ahead to Figure 21-28 on p. 660) and the coronary sinus of the heart (see Figure 21-12). After birth, all the veins except the pulmonary veins contain deoxygenated blood.

Structure of Blood Vessels

COMPONENTS OF THE BLOOD VESSEL WALL

Differences in the amounts of the tissue components present in blood vessel walls occur in different types of arteries and veins (see Figure 21-14). Regardless of how thick a vessel wall might be, four types of "fabrics" that make up a vessel wall are commonly present: (1) lining *endothelial tissue*, (2) *collagen fibers*, (3) *elastic fibers*, and (4) *smooth muscle tissue*.

Endothelial Tissue

Endothelial tissue or *endothelium* is a specific type of simple squamous epithelium. Recall from Chapter 6 (see Figure 6-2 on p. 136) that this tissue forms a thin, smooth membrane made up of flattened cells. The endothelial membrane that lines the entire vascular tree exhibits specific features and performs a number of different functions in different regions of the vascular system. By providing a smooth luminal surface, endothelium influences blood flow and inhibits intravascular coagulation.

Intercellular clefts between adjacent endothelial cells and the presence, size, and number of pores or fenestrations in their cytoplasmic membranes influence diffusion and movement of substances or cells out of and into the circulating blood (see Figure 21-16). Endothelial cells are also capable of transporting substances rapidly across their boundaries by using pinocytic vesicles (see Box 3-1, p. 71).

Cellular reproduction provides new cells to increase blood vessel size, replace damaged cells, and provide growing cords of cells that are forerunners of new blood vessels. Besides producing several important growth factors, endothelium releases a variety of signaling molecules that play important roles in maintaining cardiovascular health.

Collagen Fibers

Collagen fibers in the vascular wall are woven together much like the reinforcing strands found in the wall of a tire or hose. They form from fibrous protein molecules that aggregate into fibers several micrometers in diameter and are clearly visible with a light microscope (see Figure 6-13 on p. 143 and Figure 6-15 on p. 145).

Under physiological conditions collagen fibers are very flexible—but far less extensible than the elastic fibers described later. They do not stretch more than 2% to 3%. The collagen fibers function more to keep the lumen of the vessel open and strengthen the wall than to contribute to overall tension or recoil ability.

Elastic Fibers

Individual elastic fibers are composed largely of an insoluble protein polymer called *elastin* and are quite small (0.1 to 1 μm in diameter). Once secreted into the extracellular matrix, they form into a rubberlike network that is highly elastic and capable of stretching more than 100% under physiological conditions (see Figure 6-14 on p. 143).

In large elastic arteries, especially, wavy elastic fibers are organized or arranged in concentric, almost circular patterns. Elastic fibers allow for recoil after distention. This property of elastic fibers plays an important role in maintaining *passive tension* in the vessels of the cardiovascular system. This type of tension is required to maintain normal blood pressure levels throughout the cardiac cycle—a process that is discussed in Chapter 22.

Smooth Muscle Tissue

Smooth muscle cells are found in the wall of all segments of the vascular system except capillaries. Recall from Chapters 6 and 11 that smooth muscle is an involuntary muscle found in the wall of most hollow organs of the body.

Smooth muscle cells are most numerous in elastic and muscular arteries and exert *active tension* in these vessels when contracting.

LAYERS OF THE BLOOD VESSEL WALL

The walls of arteries and veins consist of three separate layers or "coats" called the *tunica externa*, *tunica media*, and *tunica intima*. These layers are arranged in sequence from the outside, to the middle, and then to the interior, or luminal, surface of the vessel. As blood vessels decrease in diameter, the relative thickness of their walls also decreases.

When considering the general structure of the walls of vessels in the circulatory system, capillaries are the exception. They consist of only a single layer of endothelial cells (tunica intima) surrounded by a basement membrane (see Figure 21-16).

Outer Layer

The walls of the larger blood vessels, the arteries and veins, have three layers (see Figure 21-14 and Table 21-1). The outermost layer is called the **tunica externa.** This Latin name literally means "outside coat." The tunica externa, also called *tunica adventitia*, is made of strong, flexible fibrous connective tissue. This layer prevents tearing of the vessel walls during body movements. Collagen fibers extend outward from this layer to connect to nearby structures—anchoring the vessel and helping to hold it open. In veins, the tunica externa is the thickest of the three layers of the venous wall. In arteries, it is usually a little thinner than the middle layer of the arterial wall.

Middle Layer

The middle layer, or **tunica media** (Latin for "middle coat"), is made of a layer of smooth muscle tissue sandwiched together with

TABLE 21-1 Structure of Blood Vessels

	TYPICAL DIAMETER	TYPICAL WALL THICKNESS	TUNICA INTIMA	TUNICA MEDIA	TUNICA EXTERNA
Typical histology			Endothelium	Smooth muscle; elastic fibers	Collagen fibers
Arteries	Aorta: 25 mm Small artery: 4 mm Arteriole: 30 μm	Aorta: 2 mm Small artery: 1 mm Arteriole: 8 μm	Smooth lining	Allows constriction and dilation of vessels; thicker than in veins; muscle innervated by autonomic fibers	Provides flexible support that resists collapse or injury; thicker than in veins; thinner than tunica media
Veins	Vena cava: 30 mm Vein: 5 mm Venule: 20 μm	Vena cava: 1.5 mm Vein: 0.5 mm Venule: 1μm	Smooth lining with valves to ensure one-way flow	Allows constriction and dilation of vessels; thinner than in arteries; muscle innervated by autonomic fibers	Provides flexible support that resists collapse or injury; thinner than in arteries; thicker than tunica media
Capillaries	5 μm	0.5 μm	Makes up entire wall of capillary; thinness permits ease of transport across vessel wall	(Absent)	(Absent)

a layer of elastic connective tissue. Some anatomists consider the elastic portion of the tunica media to be distinct enough to call it a separate *external elastic membrane* of the wall. The encircling smooth muscles of the tunica media permit changes in blood vessel diameter. The smooth muscle tissue of the tunica media is innervated by autonomic nerves called *nervi vasorum* ("nerves of the vessel") and supplied with blood by tiny *vasa vasorum* ("vessels of the vessel") that extend inward from the tunica externa. As a rule, arteries have a thicker layer of smooth muscle than do veins.

Inner Layer

The innermost layer of a blood vessel is called the **tunica intima**—Latin for "inside coat." The tunica intima is made up of endothelium that is continuous with the endothelium that lines the heart. The endothelium has a basement membrane to support it. Elastic arteries also have an *internal elastic membrane*.

In arteries, the endothelium provides a completely smooth lining. In veins, however, the endothelium also forms valves that help maintain the one-way flow of blood. The smallest of the vessels, the capillaries, have only one thin coat: the endothelium. This structural feature is important because the thinness of the capillary wall allows for efficient exchange of materials between the blood plasma and the interstitial fluid of the surrounding tissues.

| QUICK CHECK |

13. Name the three major types of blood vessels.
14. How does the structure of each major type of vessel differ from the other types?
15. How does the function of capillaries relate to the structure of their walls?

MAJOR BLOOD VESSELS

Circulatory Routes

The term *circulation of blood* suggests its meaning, namely, blood flow through vessels arranged to form a circuit or circular pattern.

The **systemic circulation** route conducts blood flow from the heart (left ventricle) through blood vessels to all parts of the body (except the gas-exchange tissues in the lungs) and back to the heart (to the right atrium) (Figure 21-17). The left ventricle pumps blood into the ascending aorta. From here it flows into arteries that carry it into the various tissues and organs of the body. Within each structure, blood moves, as indicated in Figure 21-17, from arteries to arterioles to capillaries. Here the vital two-way exchange of substances occurs between the blood and cells. Blood flows next out of each organ by way of its venules and then its veins to drain eventually into the inferior or superior vena cava. These two great veins of the body return venous blood to the right atrium of the heart to complete the systemic circulation. But the blood does not quite come full circle back to its starting point, the left ventricle.

To start on its way again, blood must first flow through another circuit, the **pulmonary circulation** route. Observe in Figure 21-17 that deoxygenated blood moves from the right atrium to the right ventricle to the pulmonary artery to lung arterioles and capillaries. Here, exchange of gases between blood and air takes place, converting

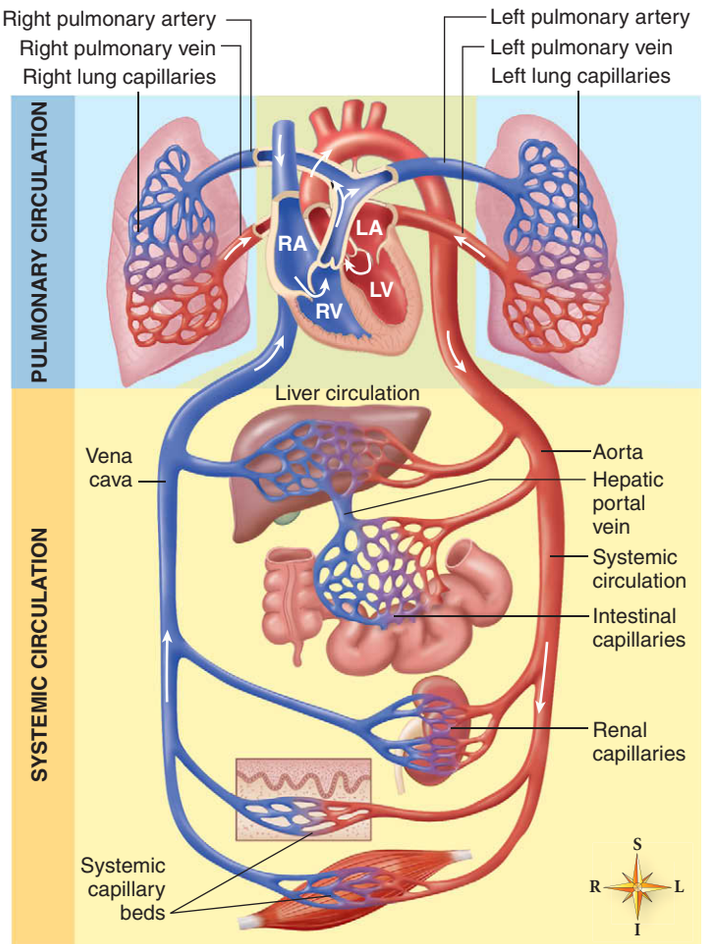


FIGURE 21-17

Circulatory routes. The pulmonary circulation routes blood flow to and from the gas-exchange tissues of the lungs. The systemic circulation, on the other hand, routes blood flow to and from the oxygen-consuming tissues of the body.

deoxygenated blood to oxygenated blood. This oxygenated blood then flows on through lung venules into four pulmonary veins and returns to the left atrium of the heart. From the left atrium it enters the left ventricle to be pumped again through the systemic circulation.

Movement of blood as shown in Figure 21-17 follows a general rule of thumb often used when studying the circulatory system, namely, that blood passes through only one capillary network in the systemic circulation from the time it leaves the heart until it returns. Although this is certainly true in most instances, two important exceptions to the rule do occur. In a **portal system,** blood flowing through the systemic circulation passes through two consecutive capillary beds rather than one. For example, notice in Figure 21-17 that blood coming from the digestive organs passes through a second capillary network in the liver before returning to the heart. The liver's portal circulation is discussed later in this chapter.

The term **vascular anastomosis** is used to describe a second type of exception. It involves the direct connection or merger of blood vessels to one another. In vascular anastomoses, blood moves from veins to other veins or arteries to other arteries without passing through an intervening capillary network.

Arterial anastomoses involve the merger of one artery directly into another artery and may develop in response to disease. Such an anastomosis may permit "bypass" of a partially blocked artery, thus allowing blood to flow into a capillary network and an area of tissue that would otherwise be deprived of an adequate supply of oxygen and nutrients. As stated earlier, arterial anastomoses between the smaller coronary arteries may permit development of "collateral circulation" and movement of blood into areas of ischemic cardiac muscle tissue. However, since very few natural arterial anastomoses exist between the larger coronary arteries, surgical arterial bypass procedures are often required to correct inadequate blood flow to heart muscle (see discussion of myocardial infarction in Mechanisms of Disease, p. 669).

Venous anastomoses, which are much more common, involve direct linkage between different veins. Multiple venous drainage routes from an organ or body area provide a safety mechanism if occlusion of one venous return route should occur. This is especially true of the deep veins. Catastrophic consequences from a so-called *deep venous thrombosis (DVT)* may be prevented or lessened because of these anastomoses.

Arteriovenous anastomoses, or **shunts,** occur when blood flows from an artery directly into a vein without passing through a capillary bed. Heat loss occurs when blood passes through capillary beds in the skin. In cases of hypothermia, heat loss can be avoided by shunting of blood directly from skin arteries to veins without permitting it to pass through capillary beds near the skin surface (see Figure 7-15 on p. 183).

Systemic Circulation

The systemic circulatory route includes most of the vessels of the body. The following paragraphs, tables, and illustrations outline some of the major vessels of the systemic circulation and give tips for understanding this circulatory route.

SYSTEMIC ARTERIES

Locate the arteries listed in Table 21-2 (see also Figures 21-18 to 21-26). You may find it easier to learn the names of blood vessels and the relation of the vessels to each other from diagrams and tables than from narrative descriptions.

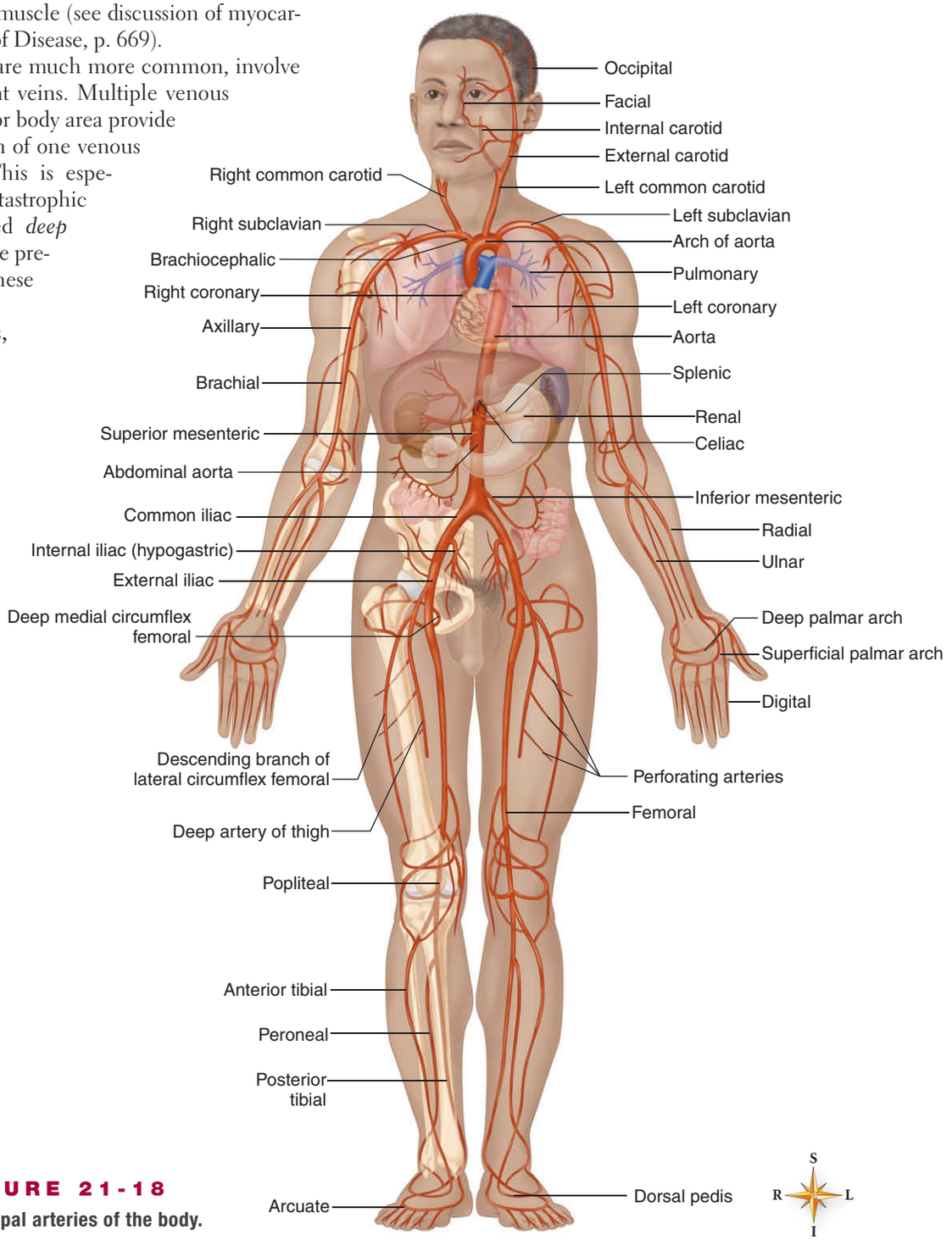


FIGURE 21-18
Principal arteries of the body.

TABLE 21-2 Major Systemic Arteries

ARTERY*	REGION SUPPLIED
Ascending Aorta	
Coronary arteries	Myocardium
Arch of Aorta	
Brachiocephalic (Innominate)	Head, upper extremity
Right common carotid	Head, neck
Right internal carotid†	Brain, eye, forehead, nose
Right external carotid†	Thyroid, tongue, tonsils, ear, etc.
Right subclavian	Head, upper extremity
Right vertebral†	Spinal cord, brain
Right axillary (continuation of subclavian)	Shoulder, chest, axillary region
Right brachial (continuation of axillary)	Arm, hand
Right radial	Forearm, hand (lateral)
Right ulnar	Forearm, hand (medial)
Superficial and deep palmar arches (formed by anastomosis of branches of radial and ulnar)	Hand, fingers
Digital	Fingers
Left Common Carotid	Head, neck
Left internal carotid†	Brain, eye, forehead, nose
Left external carotid†	Thyroid, tongue, tonsils, ear, etc.
Left Subclavian	Head, upper extremity
Left vertebral†	Spinal cord, brain
Left axillary (continuation of subclavian)	Shoulder, chest, axillary region
Left brachial (continuation of axillary)	Arm, hand
Left radial	Forearm, hand (lateral)
Left ulnar	Forearm, hand (medial)
Superficial and deep palmar arches (formed by anastomosis of branches of radial and ulnar)	Hand, fingers
Digital	Fingers
Descending Thoracic Aorta	
Visceral Branches	Thoracic viscera
Bronchial	Lungs, bronchi
Esophageal	Esophagus
Parietal Branches	Thoracic walls
Intercostal	Lateral thoracic walls (rib cage)
Superior phrenic	Superior surface of diaphragm
Descending Abdominal Aorta	
Visceral Branches	Abdominal viscera
Celiac artery (trunk)	Abdominal viscera
Left gastric	Stomach, esophagus
Visceral Branches (continued)	
Common hepatic	Liver
Splenic	Spleen, pancreas, stomach
Superior mesenteric	Pancreas, small intestine, colon
Inferior mesenteric	Descending colon, rectum
Suprarenal	Adrenal (suprarenal) gland
Renal	Kidney
Ovarian	Ovary, uterine tube, ureter
Testicular	Testis, ureter
Parietal Branches	Walls of abdomen
Inferior phrenic	Inferior surface of diaphragm, adrenal gland
Lumbar	Lumbar vertebrae, muscles of back
Median sacral	Lower vertebrae
Common Iliac (formed by terminal branches of aorta)	Pelvis, lower extremity
External Iliac	Thigh, leg, foot
Femoral (continuation of external iliac)	Thigh, leg, foot
Popliteal (continuation of femoral)	Leg, foot
Anterior tibial	Leg, foot
Posterior tibial	Leg, foot
Plantar arch (formed by anastomosis of branches of anterior and posterior tibial arteries)	Foot, toes
Digital	Toes
Internal Iliac	Pelvis
Visceral branches	Pelvic viscera
Middle rectal	Rectum
Vaginal	Vagina, uterus
Uterine	Uterus, vagina, uterine tube, ovary
Parietal branches	Pelvic wall, external regions
Lateral sacral	Sacrum
Superior gluteal	Gluteal muscles
Obturator	Pubic region, hip joint, groin
Internal pudendal	Rectum, external genitals, floor of pelvis
Inferior gluteal	Lower gluteal region, coccyx, upper thigh

*Branches of each artery are indented below its name.
†See text and/or figures for branches of the artery.

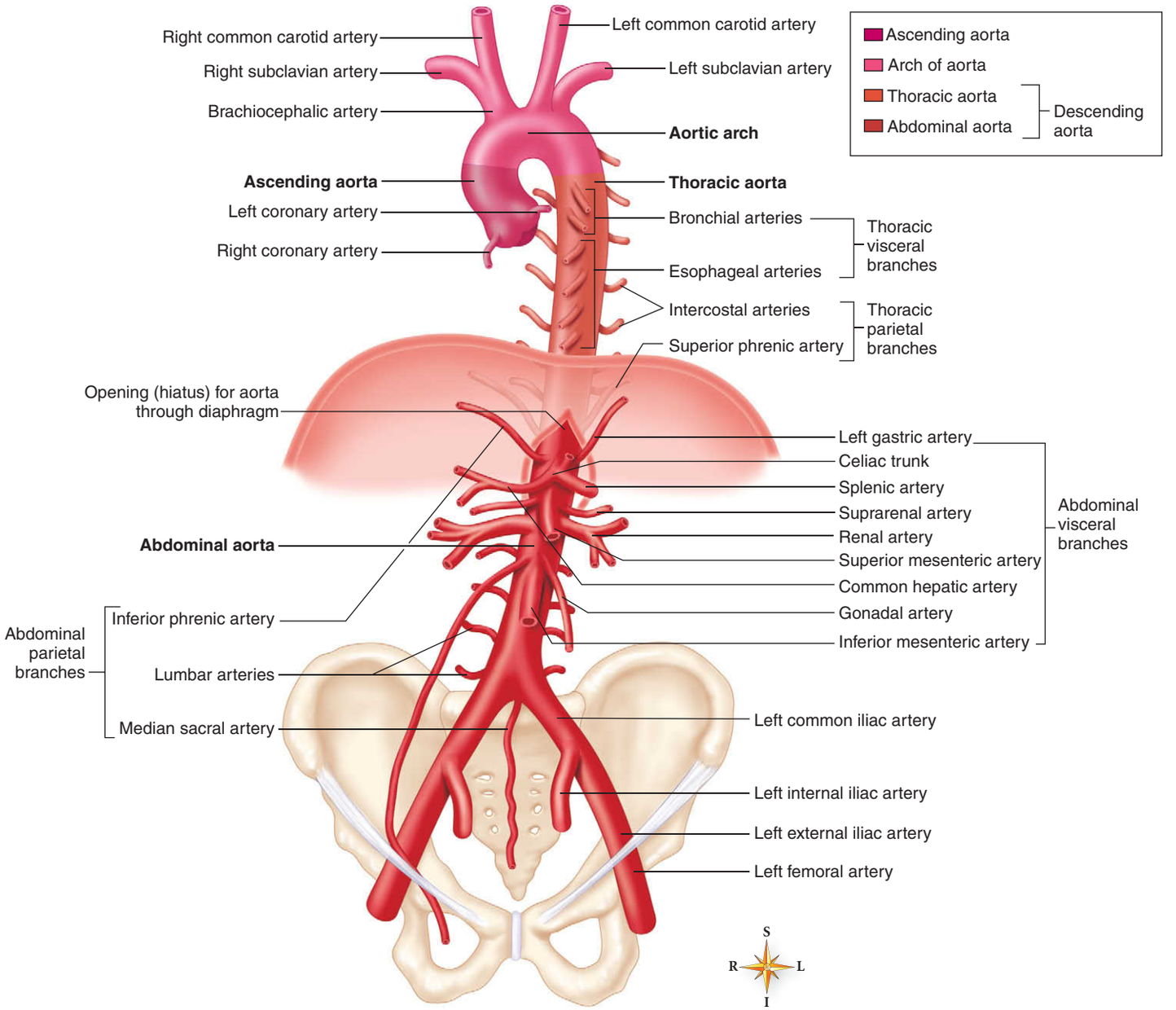


FIGURE 21-19

Divisions and primary branches of the aorta (anterior view). The aorta is the main systemic artery, serving as a trunk from which other arteries branch. Blood is conducted from the heart first through the ascending aorta, then through the arch of the aorta, and then through the thoracic and abdominal segments of the descending aorta. Note the designation of visceral and parietal branches in the thoracic and abdominal aortic divisions. Table 21-2 and the flow charts showing branches of the aortic divisions in Figures 21-22, 21-24, and 21-26 are intended to assist you in interpreting the artist's depiction of arterial vessels.

General Principles Concerning Arteries

As you learn the names of the main arteries, keep in mind that these are only the major pipelines distributing blood from the heart to the various organs and that, in each organ, the main artery resembles a tree trunk in that it gives off numerous branches that continue to branch and rebranch, forming ever-smaller vessels (arterioles), which also branch, forming microscopic vessels, the capillaries. In other words, most arteries eventually diverge into capillaries. Arteries of this type are called **end-arteries.** Important organs or areas of the body supplied by end-arteries are subject to serious damage or death in occlusive arterial disease. As an example, permanent blindness results when the central artery of the

retina, an end-artery, is occluded. Therefore arterial disease that occludes (blocks) blood flow, such as atherosclerosis, is of clinical concern when it affects important organs having an end-arterial blood supply.

A few arteries open into other branches of the same or other arteries. Such a communication was described earlier as an **arterial anastomosis.** Anastomoses, we have already noted, fulfill an important protective function in that they provide detour routes for blood to travel through in the event of obstruction of a main artery. The incidence of arterial anastomoses increases as distance from the heart increases, and smaller arterial branches tend to anastomose more often than larger vessels. Examples of arterial anastomoses are the palmar and plantar arches and the cerebral arterial circle (of Willis) at the base of the brain (look ahead to Figure 21-22 on p. 653). Other examples are found around several joints, as well as in other locations.

Another general principle to remember as you study the systemic arteries is that the **aorta** is the major artery that serves as the main trunk of the entire systemic arterial system. Notice in Figures 21-18 and 21-19 that different segments of the aorta are known by different names. Because the first few centimeters of the aorta conduct blood upward out of the left ventricle, this region is known as the **ascending aorta.** The coronary arteries are branches of the ascending aorta (look back to Figures 21-10 and 21-11). The aorta then turns 180 degrees, forming a curved segment called the *arch of the aorta* or simply **aortic arch.** Arterial blood is conducted downward from the arch of the aorta through the **descending aorta.** The descending aorta passes through the thoracic cavity, where it is known as the **thoracic aorta,** to the abdominal cavity, where it is known as the **abdominal aorta.**

If you check Table 21-2 or Figure 21-18, you will notice that all systemic arteries branch from the aorta or one of its branches.

Look again at Figures 21-18 and 21-19. Notice how the main branches from the arch of the aorta are different on the right compared with the left. The right side of the head and neck are supplied by the **brachiocephalic artery,** which branches to become the right **subclavian artery** and right **common carotid artery.** On the left, however, the left subclavian artery and the left common carotid artery branch directly from the arch of the aorta—without an intervening brachiocephalic artery.

Arteries of the Head and Neck

Figure 21-20 shows the major arteries of the head, neck, and face. Trace the branching of arteries in the figure with your finger as you read through Table 21-2. Notice in this figure how the right and left vertebral arteries extend from their origin as branches of the subclavian arteries up the neck, through foramina in the transverse processes of the cervical vertebrae, through the foramen magnum, and into the cranial cavity.

Next, take a look at Figure 21-21, which shows the arteries at the base of the brain. Note how the vertebral arteries unite on the undersurface of the brainstem to form the *basilar artery*, which

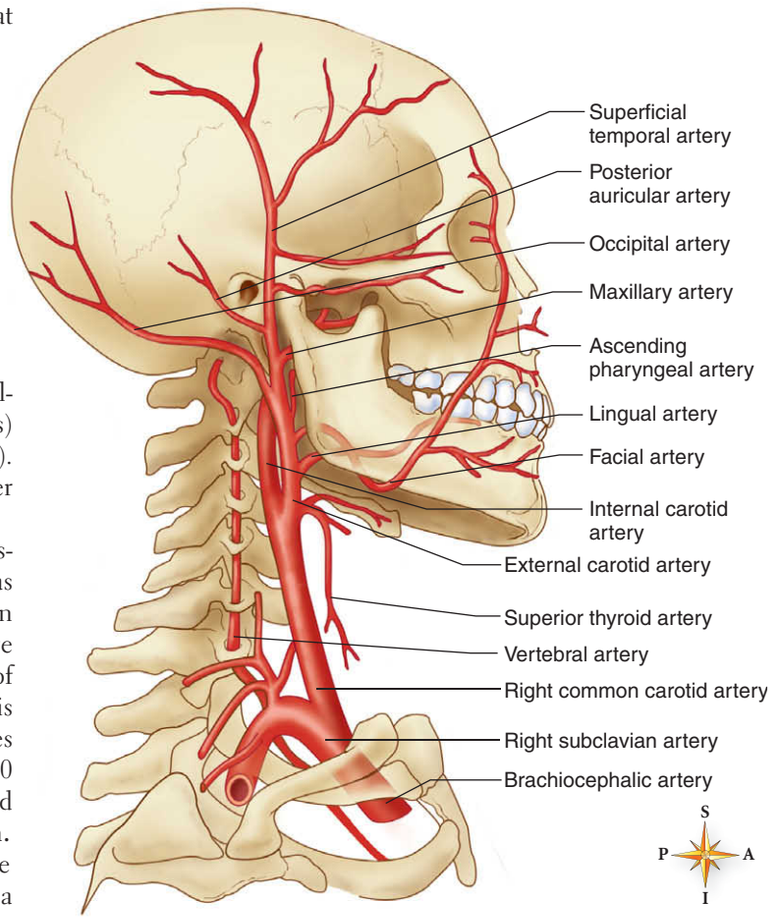


FIGURE 21-20

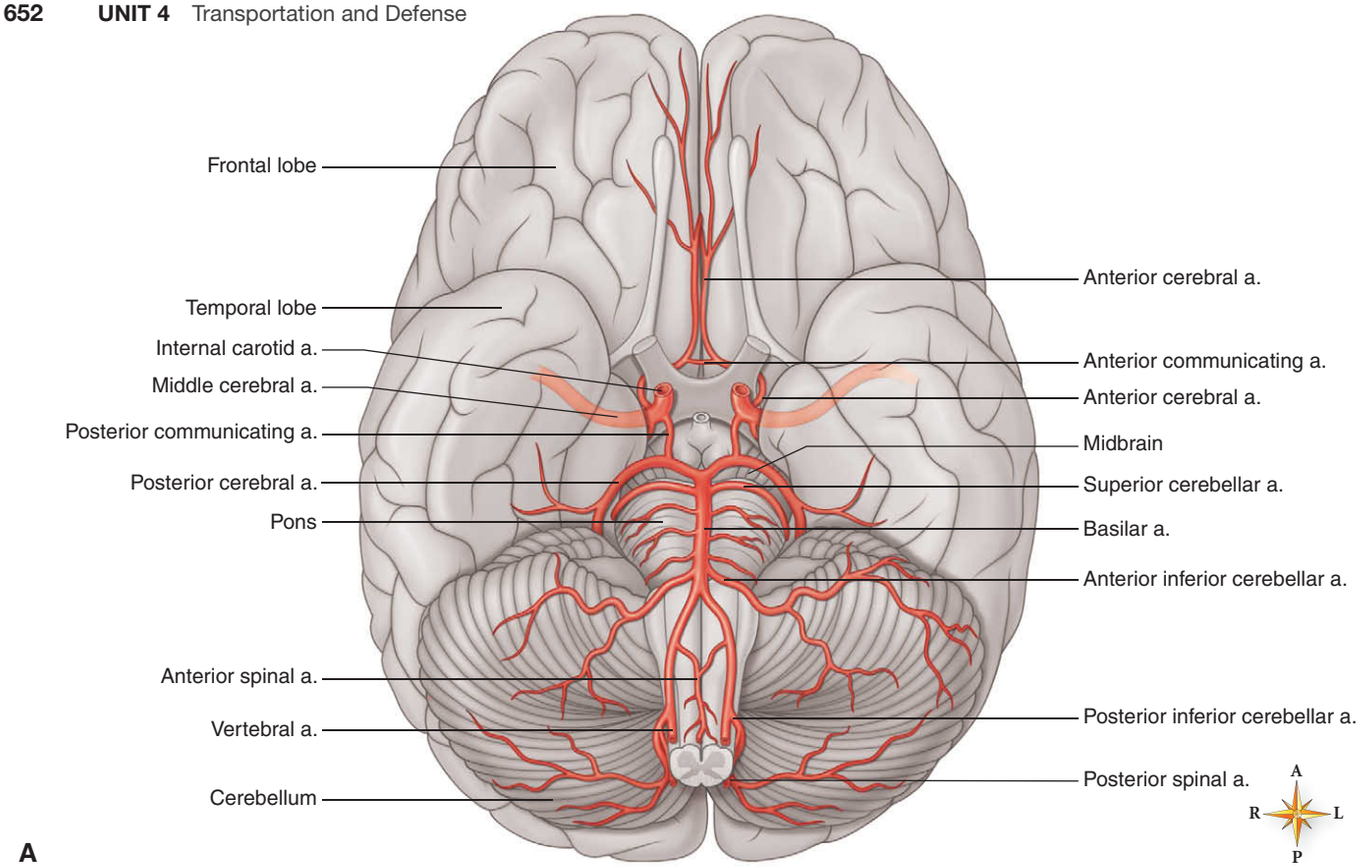
Major arteries of the head and neck. See Figure 21-21 for arteries at the base of the brain.

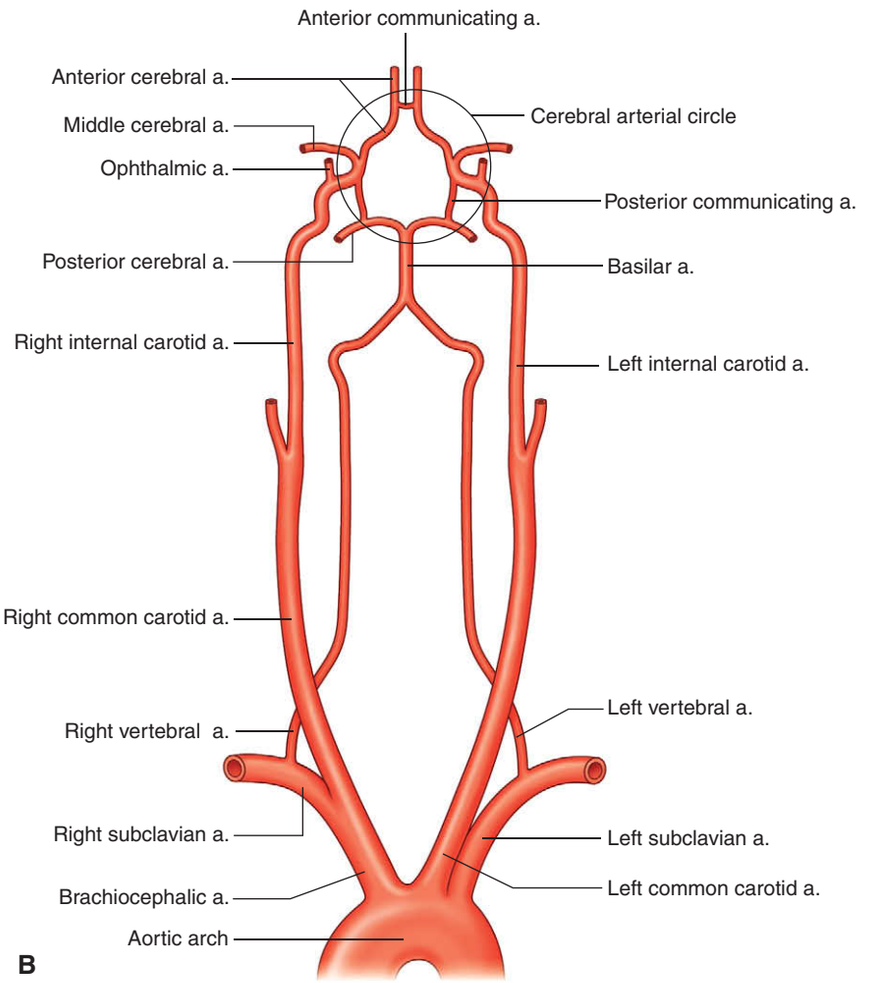
shortly branches into the right and left *posterior cerebral arteries* (see Figure 21-21). The basilar artery also braches to the pons and cerebellum (see Table 21-2). The internal carotid arteries enter the cranial cavity in the mid part of the cranial floor, where they become known as the *anterior cerebral arteries.* Small vessels, the *communicating arteries,* join the anterior and posterior cerebral arteries in such a way as to form the *cerebral arterial circle (of Willis)* at the base of the brain, a good example of arterial anastomosis (see Figure 21-21).

Arteries of the Trunk

The arch of the aorta continues downward as the **thoracic aorta.** It begins at the level of the fifth thoracic vertebra and ends at the diaphragm. *Parietal* branches of the thoracic aorta (posterior intercostal, superior phrenic, and subcostal arteries) supply blood to the body wall. Four *visceral* branches (mediastinal, bronchial, esophageal, and pericardial) provide arterial blood to internal thoracic structures.

Just as the thoracic aorta is a downward continuation of the aortic arch so, too, is the **abdominal aorta** a downward continuation





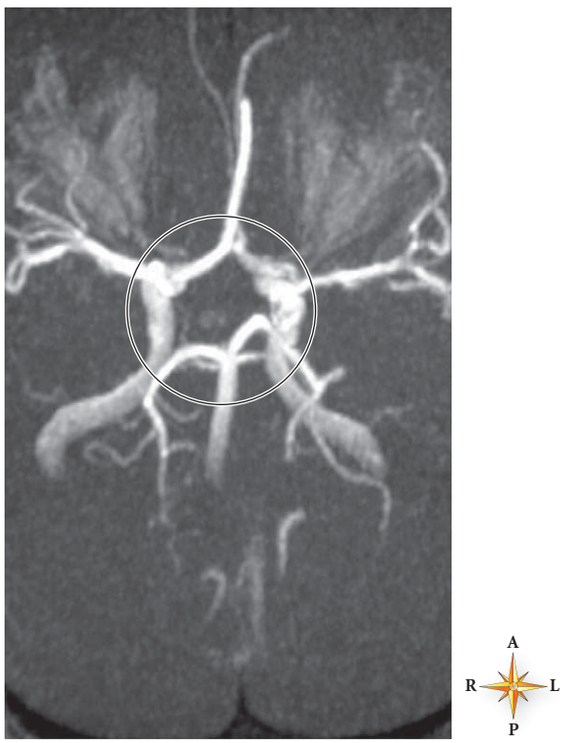


FIGURE 21-21

Arteries at the base of the brain. A, Diagram shows the cerebral arterial circle (of Willis) and related structures on the base of the brain. Note the arterial anastomoses. **B,** Origins of blood vessels that form the cerebral arterial circle. **C,** Magnetic resonance image of the cerebral arterial circle.

of the thoracic portion above it. It extends from the diaphragm above to the point where it divides into the right and left common iliac arteries at the level of the fourth lumbar vertebra. Note in Figure 21-20 that this segment of the aorta lies just anterior to the vertebral bodies. As a result, a physician can feel the aortic pulse during deep palpation of the abdomen when the vessel is compressed against the underlying vertebrae. The presence of a pulsating swelling along the aorta—an aortic aneurysm—is often diagnosed in this way.

Major abdominal and pelvic branches of the abdominal aorta may also be described as parietal or visceral depending on the location of the end organ or structures they supply with blood. Branches of this segment of the aorta are illustrated in Figures 21-18 and 21-20 and shown in schematic form in Figure 21-22.

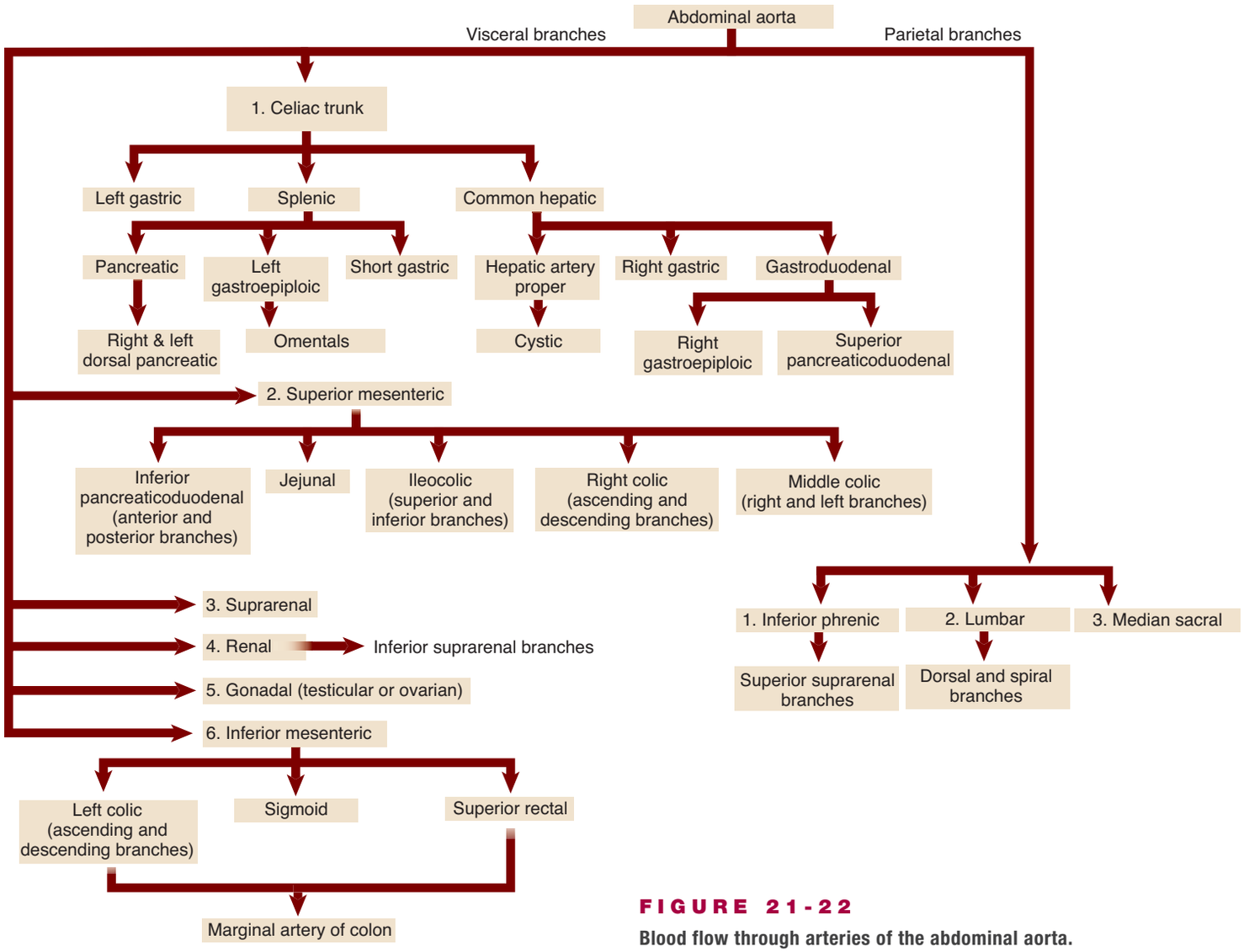


FIGURE 21-22

Blood flow through arteries of the abdominal aorta.

Arteries of the Extremities

Next, take a look at Figures 21-23 and 21-24, which outline the arteries of the upper extremity. Then take a look at Figures 21-25 and 21-26, which outline the arteries of the lower extremity. Trace these arteries with your finger as you compare each figure to Table 21-2. Because of differences in orientation, not every artery listed in the table appears in every illustration.

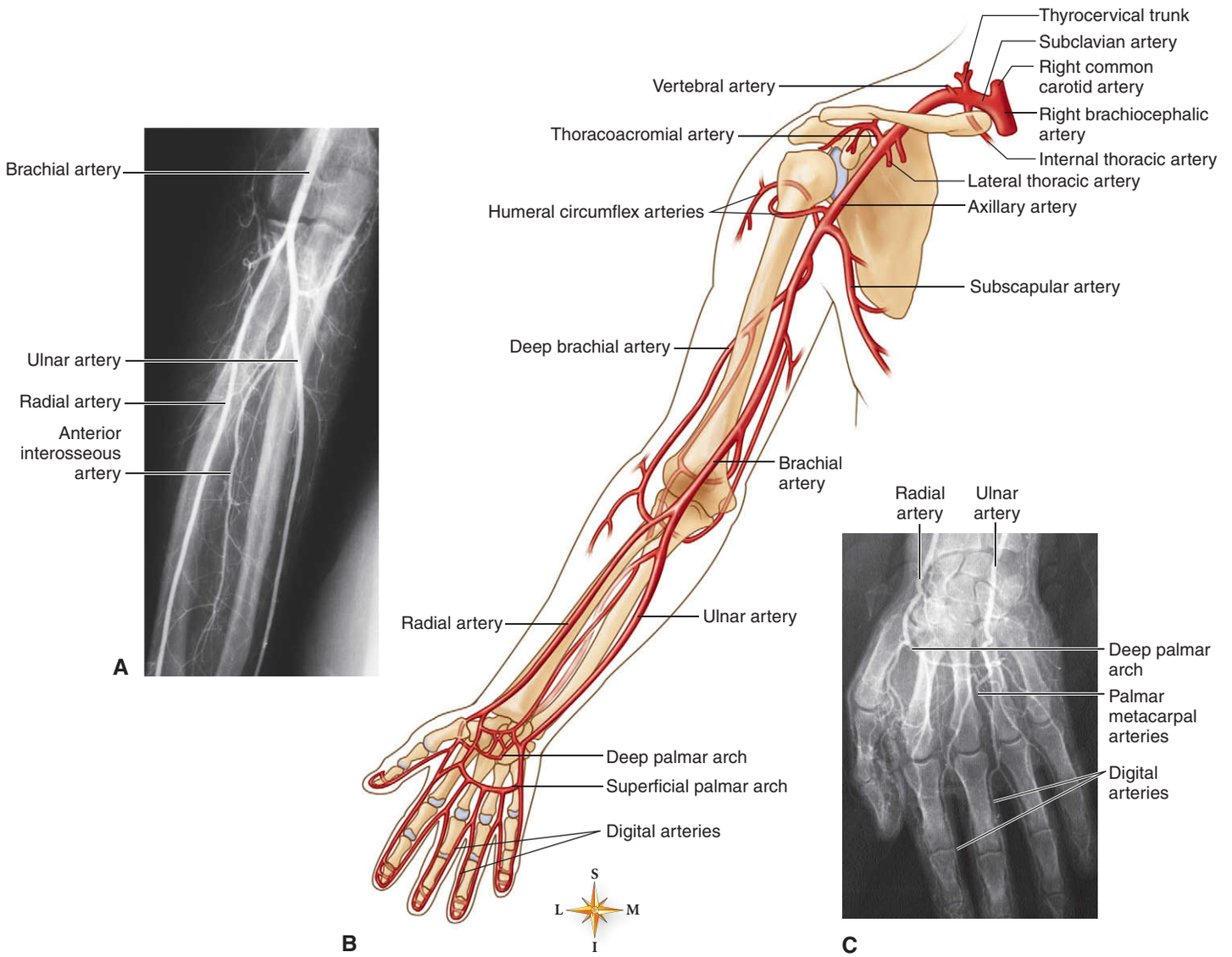


FIGURE 21-23

Major arteries of the upper extremity. A, Arteriogram of brachial and upper forearm arteries. **B,** Diagram of major arteries of upper extremity (anterior view). **C,** Arteriogram of hand arteries.

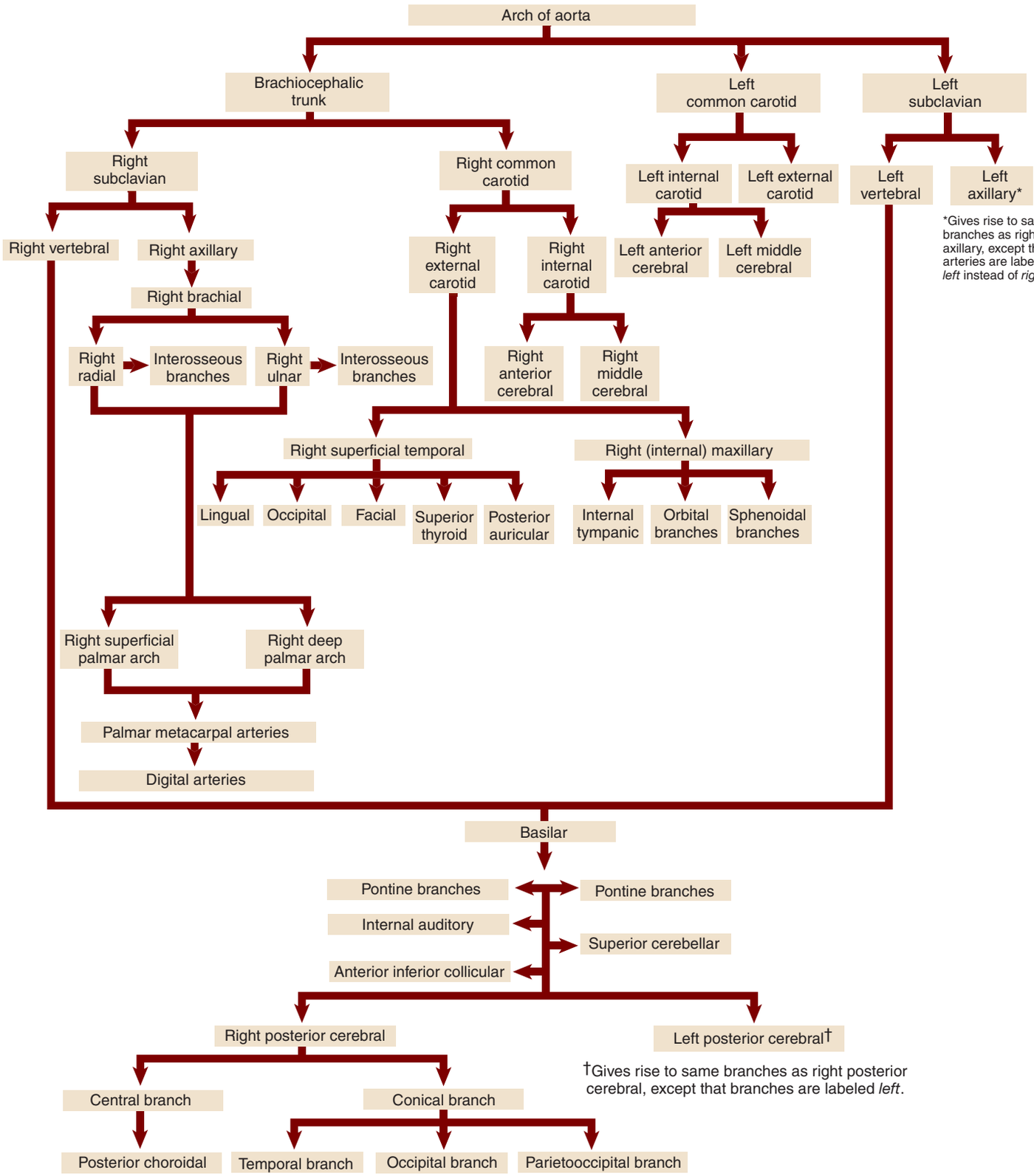


FIGURE 21-24

Blood flow through arteries of the aortic arch.

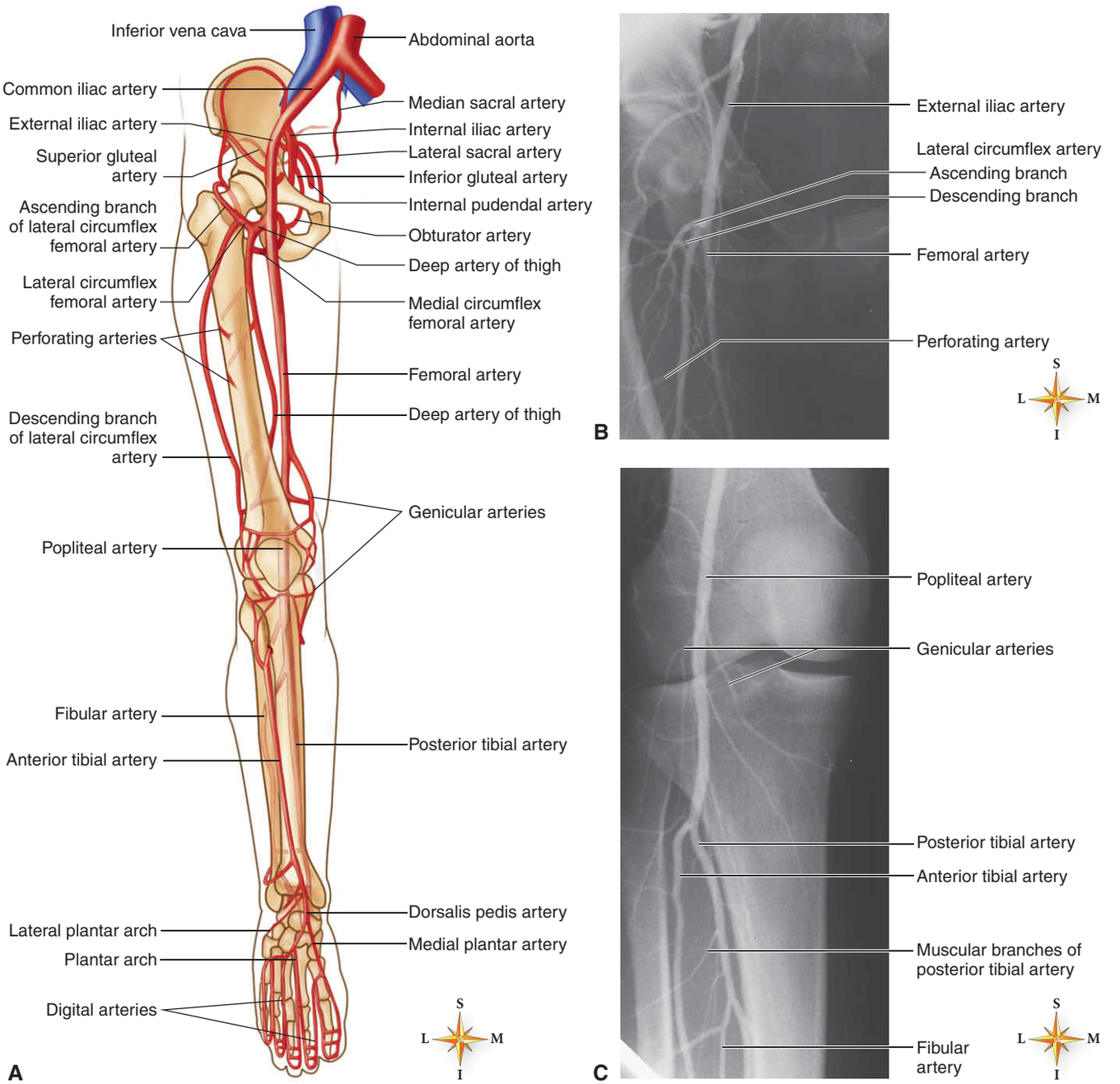


FIGURE 21-25

Major arteries of the lower extremity. A, Diagram of major arteries of lower extremity. Anterior view of the right hip and leg. **B,** Femoral arteriogram. Contrast material passing though the external iliac artery in the abdomen has entered the femoral artery and its branches in the thigh. **C,** Popliteal arteriogram.

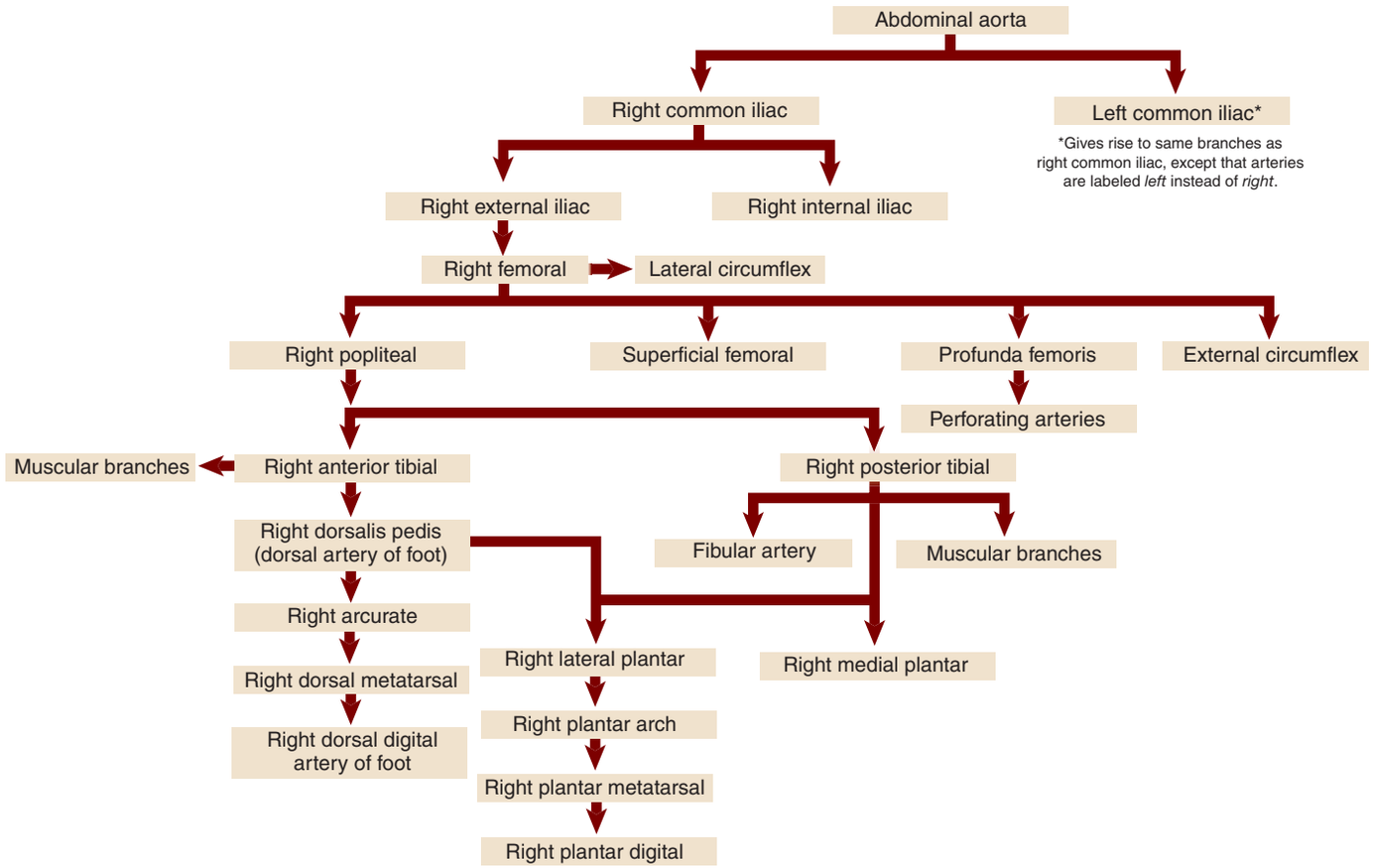


FIGURE 21-26

Blood flow through arteries of the lower extremity.

SYSTEMIC VEINS

Locate the veins listed in Table 21-3 (see also Figures 21-27 to 21-34). As with the arteries, you may find it easier to learn the names of veins and their anatomical relation to each other from diagrams and tables than from narrative descriptions.

General Principles Concerning Veins

The following facts should be borne in mind while learning the names and locations of veins:

- Veins are the ultimate extensions of capillaries, just as capillaries are the eventual extensions of arteries. Whereas arteries

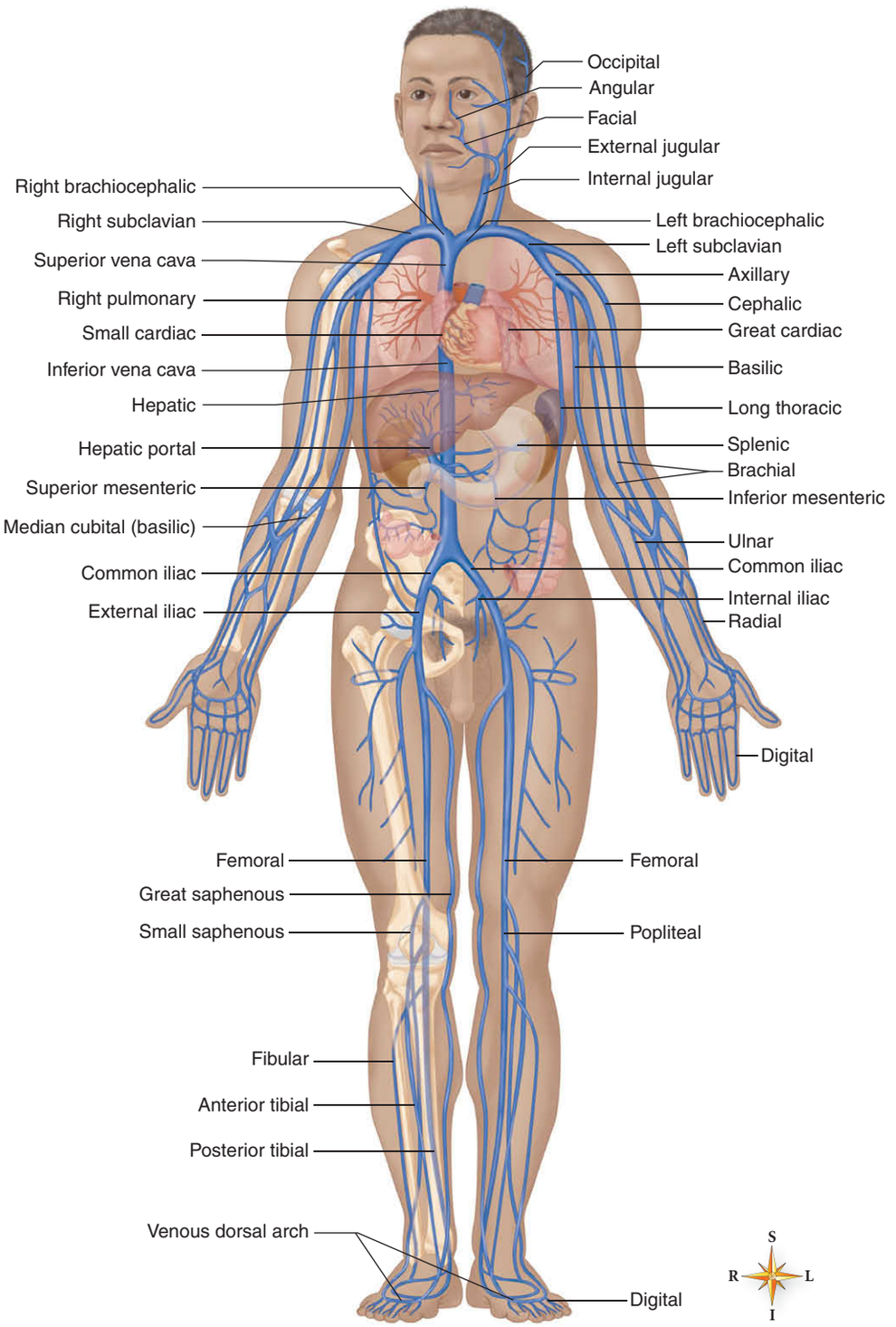


FIGURE 21-27

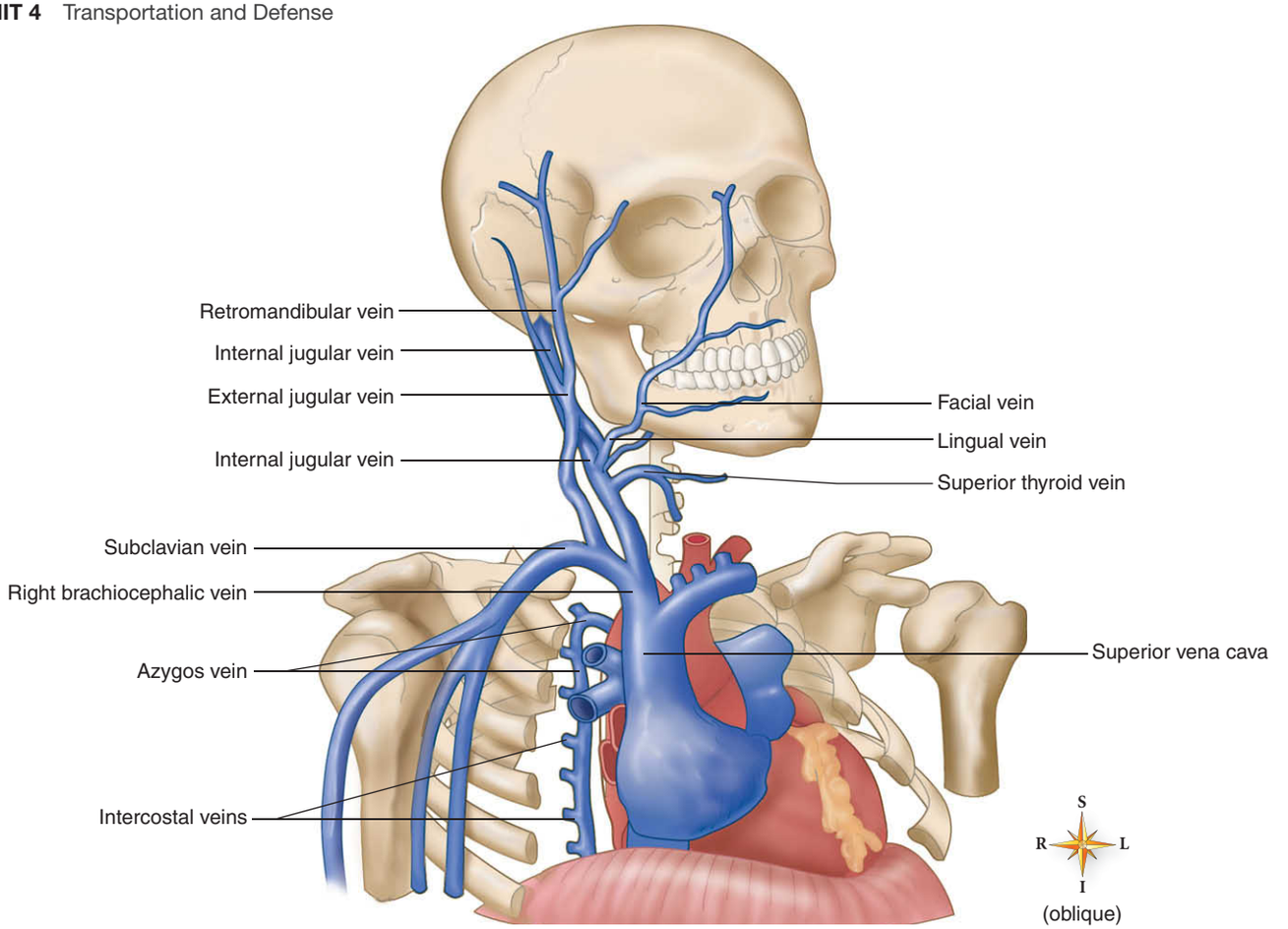
Principal veins of the body.

TABLE 21-3 Major Systemic Veins

VEIN*	REGION DRAINED
SUPERIOR VENA CAVA	Head, neck, thorax, upper extremity
Brachiocephalic (Innominate)	Head, neck, upper extremity
Internal jugular (continuation of sigmoid sinus)	Brain
Lingual	Tongue, mouth
Superior thyroid	Thyroid, deep face
Facial	Superficial face
Sigmoid sinus (continuation of transverse sinus; direct tributary of internal jugular)	Brain, meninges, skull
Superior and inferior petrosal sinuses	Anterior brain, skull
Cavernous sinus	Anterior brain, skull
Ophthalmic veins	Eye, orbit
Transverse sinus (direct tributary of sigmoid sinus)	Brain, meninges, skull
Occipital sinus	Inferior, central region of cranial cavity
Straight sinus	Central region of brain, meninges
Inferior sagittal sinus	Central region of brain, meninges
Superior sagittal (longitudinal) sinus	Superior region of cranial cavity
External jugular	Superficial, posterior head, neck
Subclavian (continuation of axillary; direct tributary of brachiocephalic)	Axilla, lower extremity
Cephalic	Lateral arm and forearm, hand
Axillary (continuation of basilic; direct tributary of subclavian)	Axilla, lower extremity
Brachial	Deep arm
Radial	Deep lateral forearm
Ulnar	Deep medial forearm
Basilic (direct tributary of axillary)	Medial arm and forearm, hand
Median cubital (formed by anastomosis of cephalic and basilic)	Forearm, hand
Deep and superficial palmar venous arches (formed by anastomosis of cephalic and basilic)	Hand
Digital	Fingers
Azygos (anastomoses with right ascending lumbar)	Right posterior wall of thorax and abdomen, esophagus, bronchi, pericardium, mediastinum
Hemiazygos (anastomoses with left renal)	Left inferior posterior wall of thorax and abdomen, esophagus, mediastinum
Accessory hemiazygos	Left superior posterior wall of thorax

VEIN*	REGION DRAINED
INFERIOR VENA CAVA	Lower trunk and extremity
Phrenic	Diaphragm
Hepatic portal system	Upper abdominal viscera
Hepatic veins (continuations of liver venules and sinusoids and ultimately the hepatic portal vein)	Liver
Hepatic portal vein	Gastrointestinal organs, pancreas, spleen, gallbladder
Cystic	Gallbladder
Gastric	Stomach
Splenic	Spleen
Inferior mesenteric	Descending colon, rectum
Pancreatic	Pancreas
Superior mesenteric	Small intestine, most of colon
Gastroepiploic	Stomach
Renal	Kidneys
Suprarenal	Adrenal (suprarenal) gland
Left ovarian	Left ovary
Left testicular	Left testis
Left ascending lumbar (anastomoses with hemiazygos)	Left lumbar region
Right ovarian (gonadal)	Right ovary
Right testicular (gonadal)	Right testis
Right ascending lumbar (anastomoses with azygos)	Right lumbar region
Common iliac (continuation of external iliac; common iliacs unite to form inferior vena cava)	Lower extremity
External iliac (continuation of femoral direct tributary of common iliac)	Thigh, leg, foot
Femoral (continuation of popliteal direct tributary of external iliac)	Thigh, leg, foot
Popliteal	Leg, foot
Small (external, short) saphenous	Superficial posterior leg, lateral foot
Dorsal veins of foot (also drain into great saphenous)	Anterior (dorsal) foot, toes
Medial and lateral plantar	Sole of foot
Anterior tibial	Anterior leg, foot
Fibular (peroneal)	Lateral and anterior leg, foot
Posterior tibial	Deep posterior leg
Great (internal, long) saphenous	Superficial medial and anterior thigh, leg, foot
Dorsal veins of foot	Anterior (dorsal) foot, toes
Dorsal venous arch	Anterior (dorsal) foot, toes
Digital	Toes
Internal iliac (unites with external iliac to form common iliac)	Pelvic region

*Tributaries of each vein are identified below its name; deep veins are printed in dark blue, and superficial veins are printed in light blue.



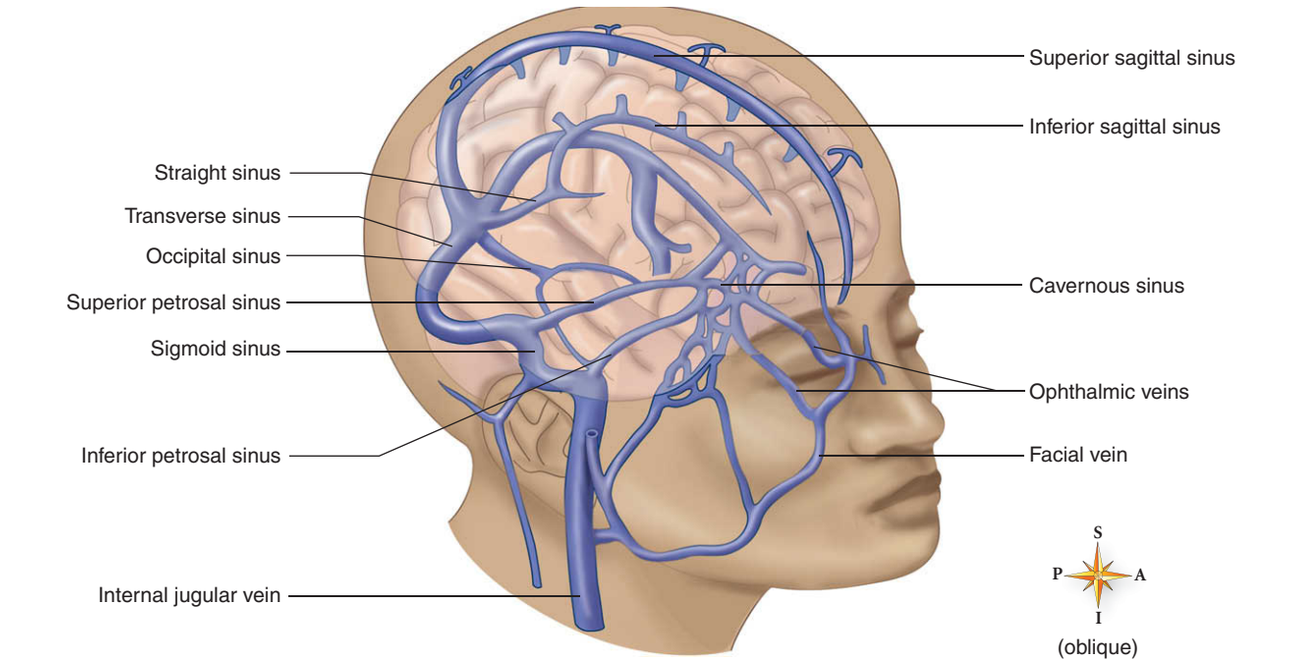


FIGURE 21-28

Major veins of the head and neck. A, Anterior view showing veins on the right side of the head and neck. **B,** Lateral, superior view showing the position of major veins relative to the brain. The venous sinuses shown here are within the dura mater and are thus called *dural sinuses*.

branch into vessels of decreasing size to form arterioles and eventually capillaries, capillaries unite into vessels of increasing size to form venules and, eventually, veins.

- Although all vessels vary considerably in location and branches—and whether or not they are even present—the veins are especially variable. For example, the **median cubital vein** in the forearm is absent in many individuals.
- Many of the main arteries have corresponding veins bearing the same name and are located alongside or near the arteries. These veins, like the arteries, lie in deep, well-protected areas, for the most part, close along the bones. Examples include the femoral artery and femoral vein, both located along the femur bone.
- Veins found in the deep parts of the body are called **deep veins** in contrast to **superficial veins,** which lie near the surface. The latter are the veins that can be seen through the skin.
- The large veins of the cranial cavity, formed by the dura mater, are not usually called veins but are instead called *dural sinuses,* or, simply, **sinuses.** They should not be confused with the bony, air-filled sinuses of the skull.
- Veins communicate (anastomose) with each other in the same way as arteries. In fact, the venous portion of the systemic circulation has even more anastomoses than the arterial portion. Such venous anastomoses provide for collateral return blood flow in cases of venous obstruction.
- Venous blood from the head, neck, upper extremities, and thoracic cavity, with the exception of the lungs, drains into the superior vena cava. Blood from the lower extremities and abdomen enters the inferior vena cava.

Table 21-3 identifies the major systemic veins. Locate each one as you read the table and trace them with your finger on Figures 21-27 to 21-34.

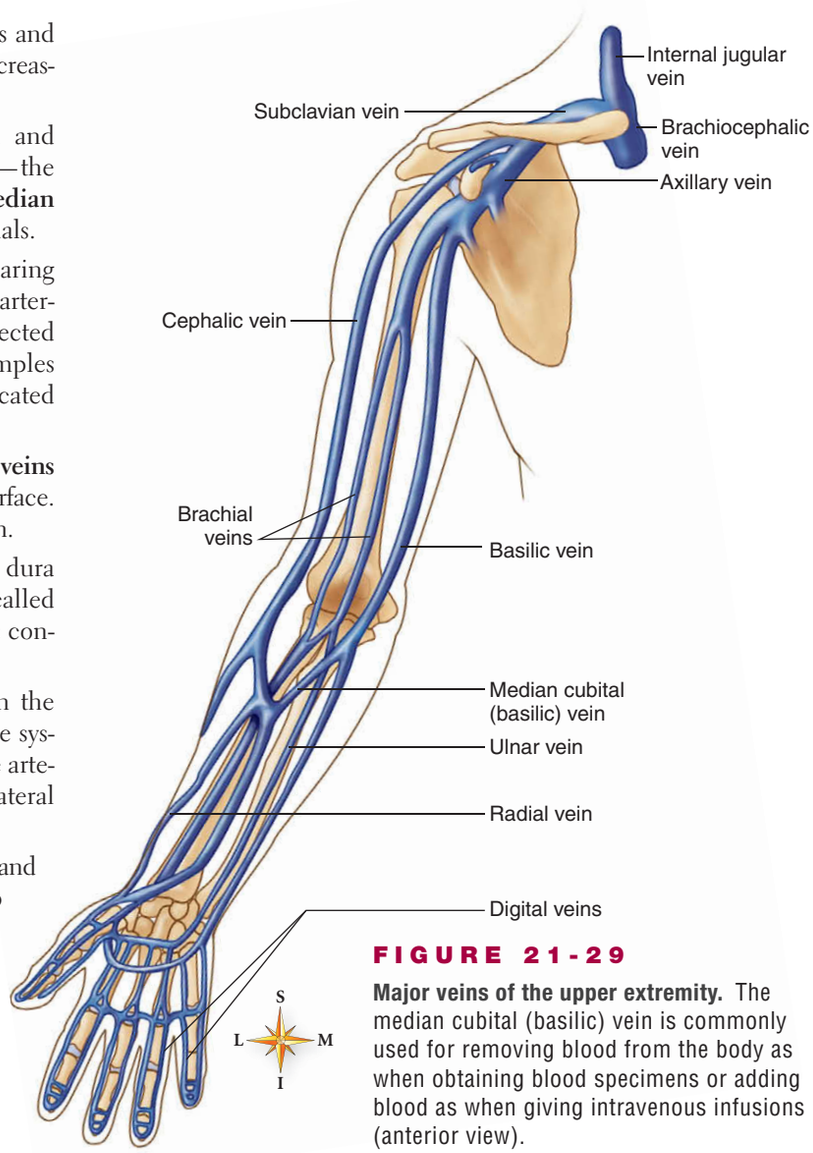


FIGURE 21-29

Major veins of the upper extremity. The median cubital (basilic) vein is commonly used for removing blood from the body as when obtaining blood specimens or adding blood as when giving intravenous infusions (anterior view).

Veins of the Head and Neck

The deep veins of the head and neck lie mostly within the cranial cavity (see Figure 21-28). These are mainly dural sinuses and other veins that drain into the **internal jugular vein.** The internal jugular vein also receives blood from superficial veins of the face and neck.

The superficial veins that lie over the cranium drain into the right and left **external jugular veins** in the neck. The external jugular veins also receive blood from deep veins of the face. Each external jugular vein terminates in a *subclavian vein.* Small emissary veins connect veins of the scalp and face with blood sinuses of the cranial cavity, a fact of clinical interest as a possible avenue for infections to enter the cranial cavity.

Veins of the Upper Extremity

Deep veins of the upper extremity drain into the **brachial vein,** which in turn drain into the **axillary vein** and then the **subclavian vein** before joining the **brachiocephalic vein,** a major tributary of the **superior vena cava.** The major veins of the upper extremity are shown in Figures 21-29 and 21-30. At this point, it is interesting to note that the tributaries of the superior vena cava are more symmetric from left to right than the nearby branches of the aorta. Compare Figures 21-18 and 21-27 to verify this point.

Superficial veins of the hand form the **palmar venous arches,** which, together with a complicated network of superficial veins of the forearm, finally pour their blood into two large veins: the **cephalic vein** (thumb side) and **basilic vein** (little finger side). These two veins empty into the deep **axillary vein.**

Veins of the Thorax

Several small veins—such as the **bronchial vein, esophageal vein,** and **pericardial vein**—return blood from thoracic organs (except gas exchange tissues in the lungs) directly into

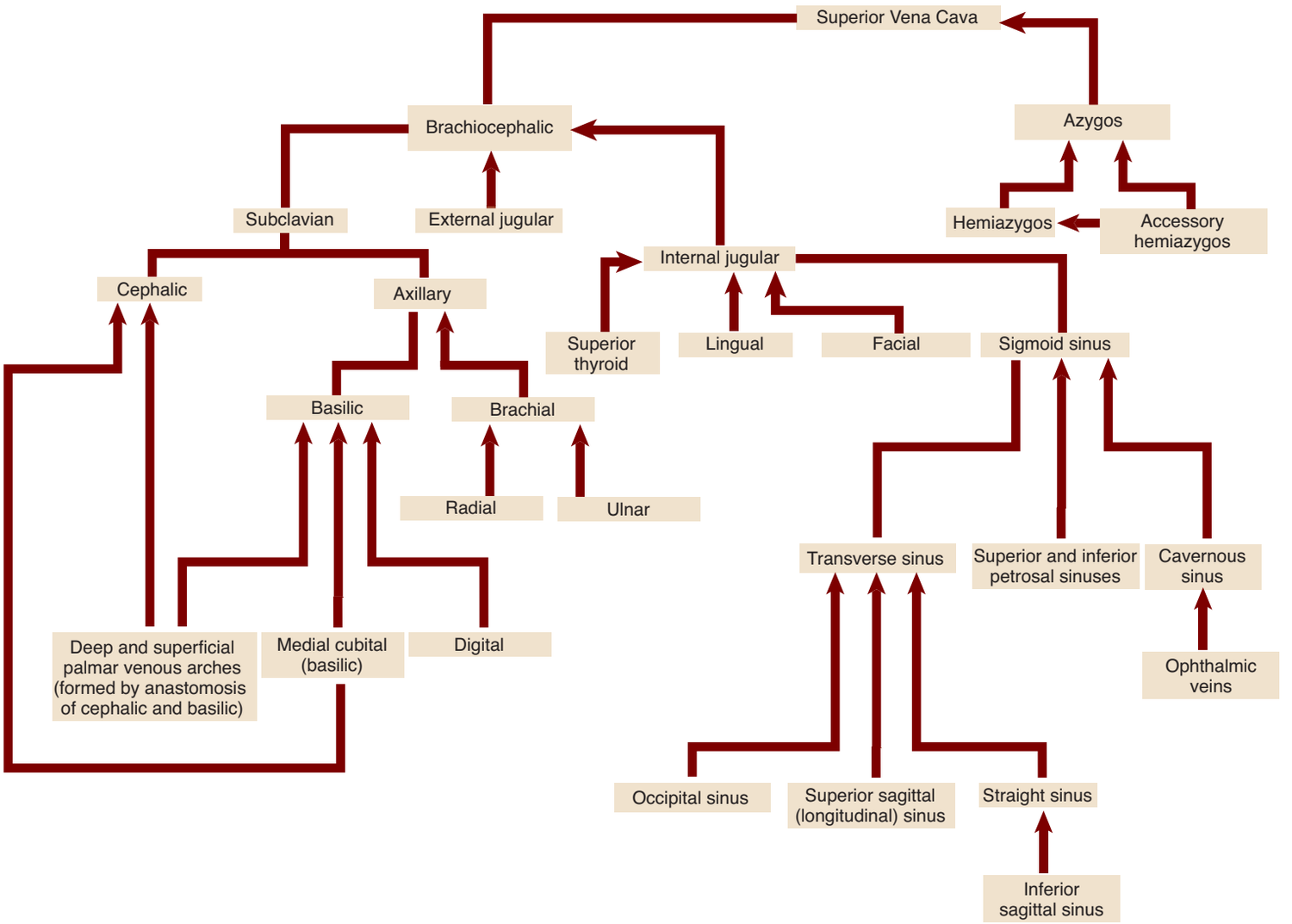


FIGURE 21-30

Blood flow into the superior vena cava from its major tributaries. Keep in mind that venous pathways show great variability among individuals.

the **superior vena cava** or **azygos vein.** Refer to Figure 21-31 to see how these veins are arranged. The azygos vein lies to the right of the spinal column and extends from the inferior vena cava (at the level of the first or second lumbar vertebra) through the diaphragm to the terminal part of the superior vena cava. The **hemiazygos vein** lies to the left of the spinal column, extending from the lumbar level of the inferior vena cava through the diaphragm to terminate in the azygos vein. The **accessory hemiazygos vein** connects some of the **superior intercostal veins** with the azygos or hemiazygos vein.

Veins of the Abdomen

The abdominal tributaries offer another opportunity to see a slight difference between the left and right portions of the systemic venous circulation. For example, Figure 21-31 shows that the gonadal veins—*ovarian vein* or *testicular (spermatic) vein*—and left **suprarenal vein** usually drain into the left **renal vein** instead of into the **inferior vena cava.** This is the opposite of the arrangement of these veins on the right. For a description of the return of blood from the abdominal digestive organs, see the subsequent discussion of the **hepatic portal circulation.**

Hepatic Portal Circulation

Veins from the spleen, stomach, pancreas, gallbladder, and intestines do not pour their blood directly into the inferior vena cava, as do the veins from other abdominal organs. They send their blood to the liver by means of the hepatic portal vein. Here the blood mingles with the arterial blood in the capillaries and is eventually drained from the liver by the hepatic veins that join the inferior vena cava. Any arrangement in which venous blood flows through

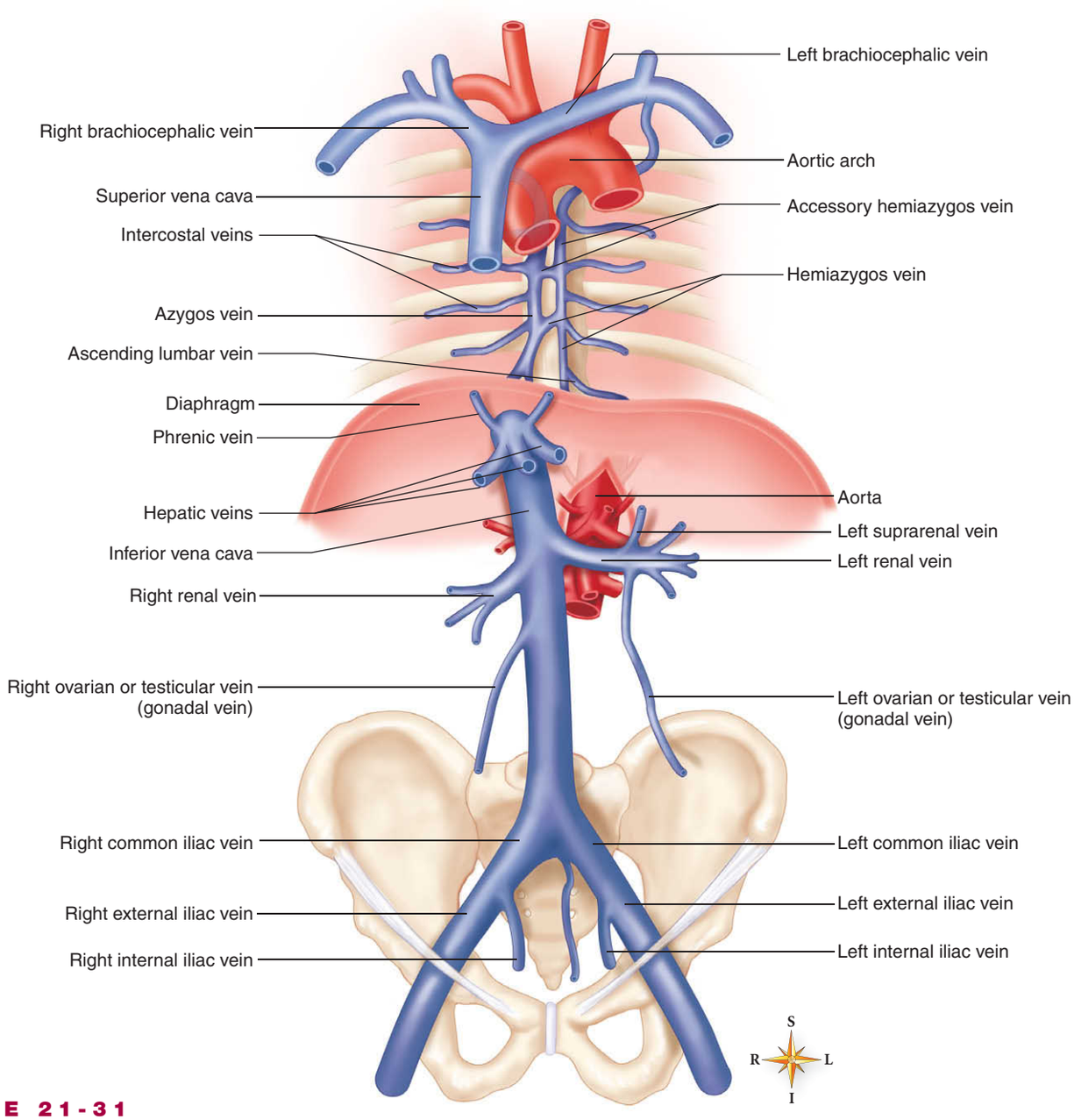


FIGURE 21-31

Inferior vena cava and its abdominopelvic tributaries. Anterior view of ventral body cavity with many of the viscera removed. Note the close anatomical relationship between the inferior vena cava and the descending aorta. Smaller veins of the thorax drain blood into the inferior vena cava or into the azygos vein—both are shown here. The hemiazygos vein and accessory hemiazygos vein on the left drain into the azygos vein on the right.

a second capillary network before returning to the heart is called a *portal* circulatory route. Portal comes from the Latin *porta*, meaning "gateway," and is used here because the liver is a gateway through which blood returning from the digestive tract must pass before it returns to the heart.

There are several advantages to detouring blood from the digestive tract through the liver before it returns to the heart. Shortly after a meal, blood flowing through digestive organs begins absorbing glucose and other simple nutrients. The result is a tremendous increase in the blood glucose level. As the blood travels through the liver, however, excess glucose is removed from the blood and stored in liver cells as glycogen. Thus blood returned to the heart carries only a moderate level of glucose. Many hours after food has yielded its nutrients,

low-glucose blood coming from the digestive organs can pick up glucose released from the glycogen stores held in the liver cells before returning to the heart.

Another advantage of the hepatic portal scheme is that toxic molecules such as alcohol can be partially removed or detoxified before the blood is distributed to the rest of the body. Additional information regarding the role of the liver, and the advantages of the portal circulation through the liver, is discussed in Chapters 28 and 29.

Figure 21-17 (p. 647) shows the plan of the hepatic portal system in relation to the overall scheme of circulation. Figure 21-32 shows the details of the veins involved in the hepatic portal circulation. In most individuals the hepatic portal vein is formed by the union of the splenic and superior mesenteric veins, but blood from the gastric, pancreatic, and inferior mesenteric veins drains into the splenic vein before it merges with the superior mesenteric vein.

If either hepatic portal circulation or venous return from the liver is interfered with (as often occurs in certain types of liver disease or heart disease), venous drainage from most of the other abdominal organs is necessarily obstructed also. The accompanying increased capillary pressure accounts, at least in part, for the occurrence of abdominal bloating, or *ascites* (ah-SITE-eez), under these conditions.

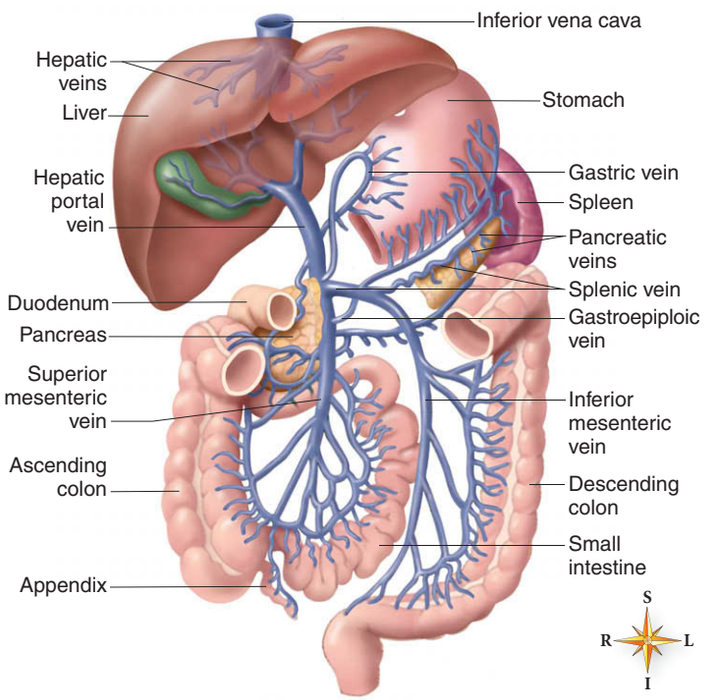


FIGURE 21-32

Hepatic portal circulation. In this unusual circulatory route, a vein is located between two capillary beds (see Figure 21-17). The hepatic portal vein collects blood from capillaries in visceral structures located in the abdomen and empties it into the liver. Hepatic veins return blood to the inferior vena cava.

Veins of the Lower Extremity

As Figure 21-33 shows, deep veins of the leg drain from the **anterior tibial vein,** the **fibular (peroneal) vein,** and the **posterior tibial vein.** These veins join the **popliteal vein,** which runs behind the knee joint and continues up along the femur as the deep femoral vein. The **femoral vein** continues as the **external iliac**

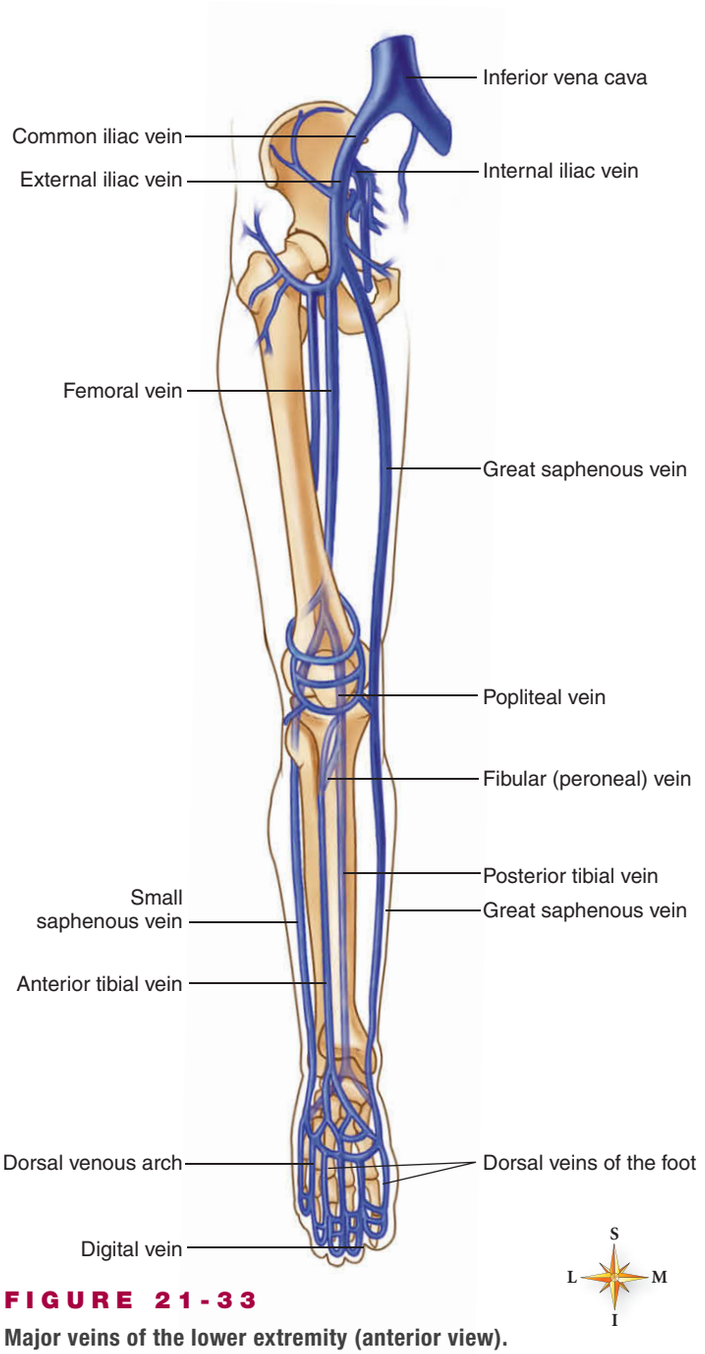


FIGURE 21-33

Major veins of the lower extremity (anterior view).

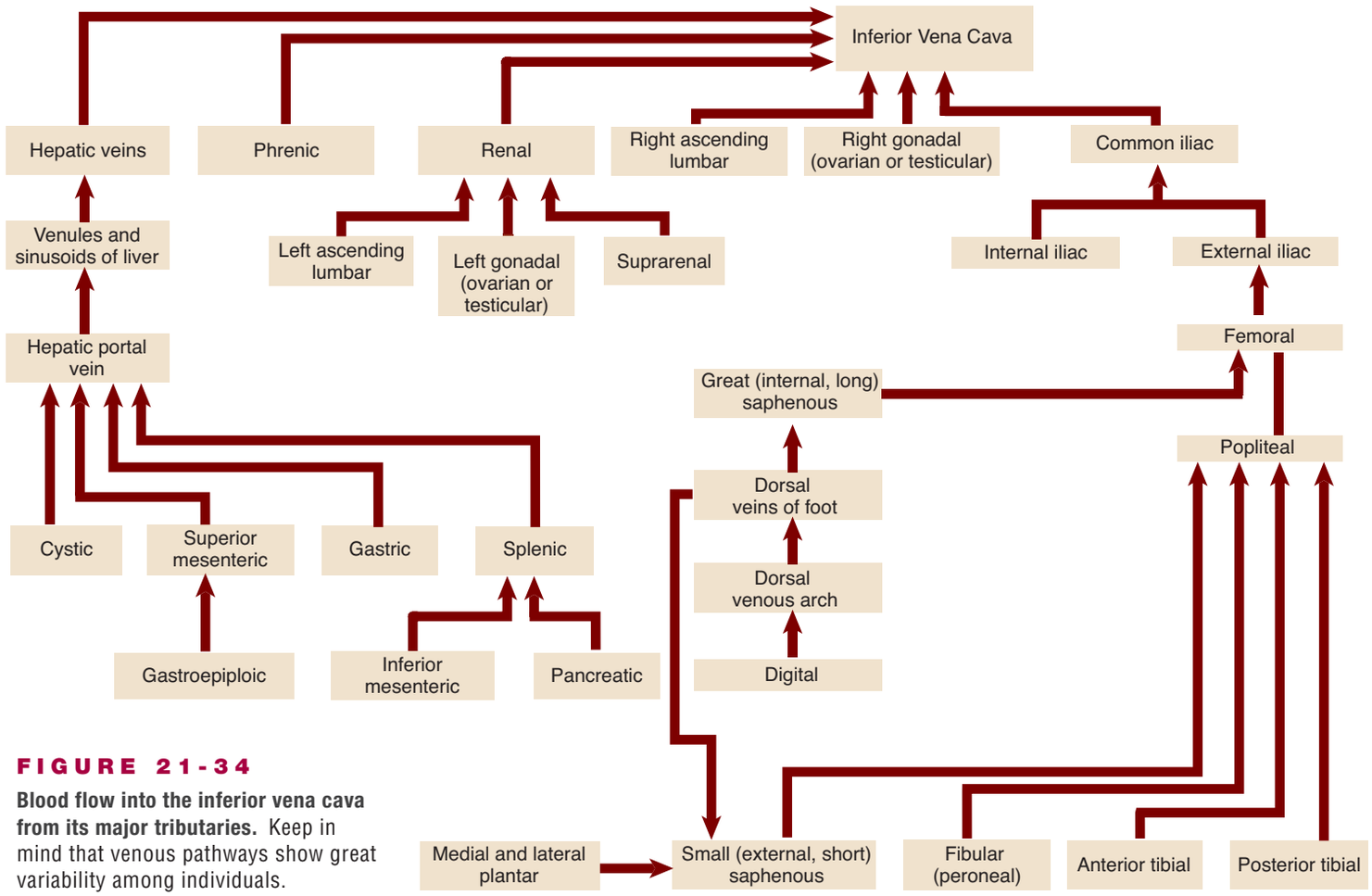


FIGURE 21-34

Blood flow into the inferior vena cava from its major tributaries. Keep in mind that venous pathways show great variability among individuals.

vein, draining into the common iliac vein and from there into the **inferior vena cava.**

Superficial veins of the lower extremity include the **small saphenous vein,** a tributary of the popliteal vein, and the **great saphenous vein,** which drains much of the superficial leg and foot. The name *saphenous* is from the Greek *saphenes,* a word that means "apparent"—an appropriate name for these visible, superficial veins.

Figure 21-34 summarizes blood flow from the abdomen and lower extremities into the inferior vena cava.

| QUICK CHECK |

16. What is the difference between the pulmonary circulation and the systemic circulation?
17. What is the function of arterial anastomoses? What is the function of venous anastomoses?
18. How are systemic arteries and veins usually named?
19. What are the advantages of a portal circulation through the liver?

| A&P CONNECT |

A valuable skill is the ability to trace the flow of blood completely through the normal adult circulatory route. Check out ***How to Trace the Flow of Blood*** online at ***A&P Connect*** for some tips and a handy diagram of the route of blood flow through the body.

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FETAL CIRCULATION

The Basic Plan of Fetal Circulation

Circulation in the body before birth necessarily differs from circulation after birth for one main reason—fetal blood secures oxygen and food from maternal blood instead of from fetal lungs and digestive organs. Obviously, then, there must be additional blood vessels in the fetus to carry the fetal blood into close approximation with the maternal blood and to return it to the fetal body. These structures are the two **umbilical arteries,** the **umbilical vein,** and the **ductus venosus.**

Also, some structure must function as the lungs and digestive organs do after birth, that is, provide a place where an exchange of gases, foods, and wastes between the fetal and maternal blood can occur. This structure is the *placenta* (Figure 21-35). The exchange of substances occurs without any actual mixing of maternal and fetal blood, because each flows in its own separate space.

In addition to the placenta and umbilical vessels, three structures located within the fetus's own body play an important part in fetal circulation. One of them (the ductus venosus) serves as a detour by which most of the blood returning from the placenta bypasses the fetal liver. The other two (the foramen ovale and ductus arteriosus) provide detours by which blood bypasses the lungs. A brief description of each of the six structures necessary for fetal circulation follows (Figure 21-36):

1. The two **umbilical arteries** are branches of the internal iliac (hypogastric) arteries and carry fetal blood to the placenta.
2. The **placenta** is a structure attached to the uterine wall. Exchange of oxygen and other substances between maternal and fetal blood takes place in the placenta, although no mixing of maternal and fetal blood occurs. Box 21-3 discusses how alcohol from the maternal blood can damage developing fetal tissues.
3. The **umbilical vein** returns oxygenated blood from the placenta, enters the fetal body through the umbilicus, extends up to the undersurface of the liver where it gives off two or three branches to the liver, and then continues on as the ductus venosus. Two umbilical arteries and the umbilical vein together constitute the umbilical cord; these are shed at birth along with the placenta.
4. The **ductus venosus** is a continuation of the umbilical vein along the undersurface of the liver and drains into the inferior vena cava. Most of the blood returning from the placenta bypasses the liver. Only a relatively small amount of blood enters the liver by way of the branches from the umbilical vein into the liver.
5. The **foramen ovale** is an opening in the septum between the right and left atria. A valve at the opening of the inferior vena cava into the right atrium directs most of the blood through

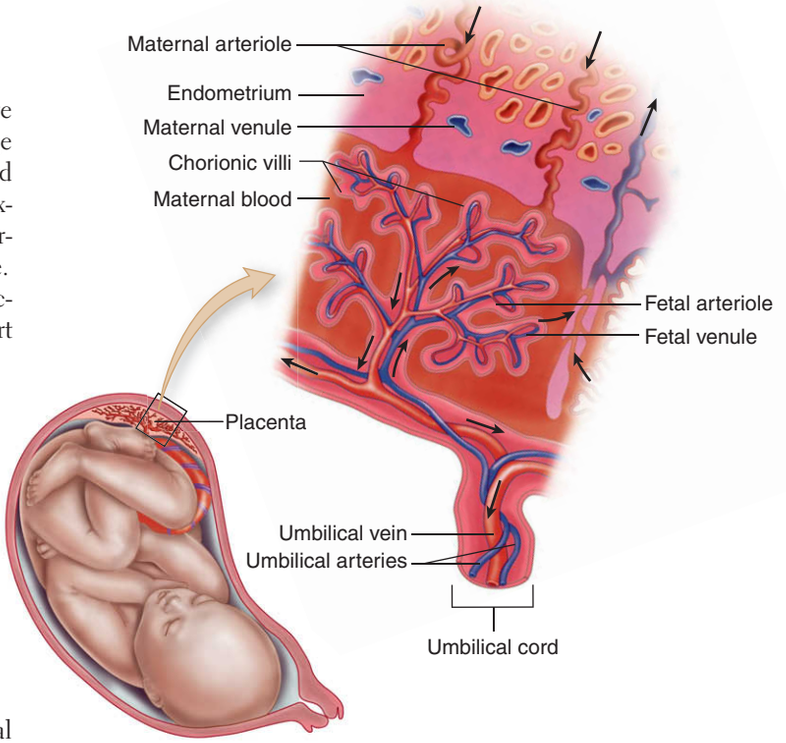


FIGURE 21-35

Placental circulation. The placenta is an organ that permits exchange of blood gases (O^2 and CO^2), nutrients, and wastes between fetal blood and maternal blood. Fetal capillaries found within branched villi are bathed in maternal blood. Note that fetal and maternal blood is separated by a membranous barrier. Other special features of fetal circulation are shown in Figures 21-36 and 21-37.

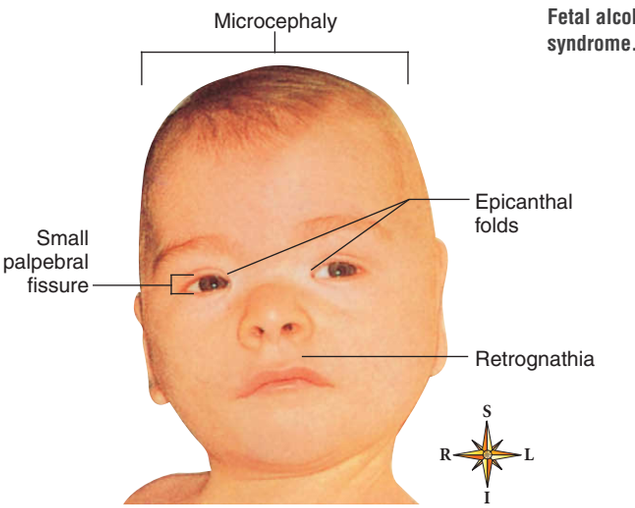
Box 21-3 | HEALTH matters

Fetal Alcohol Syndrome

Consumption of alcohol by a woman during her pregnancy can have tragic effects on the developing fetus. Educational efforts to inform pregnant women about the dangers of alcohol are now receiving national attention. Even very limited consumption of alcohol during pregnancy poses significant hazards to the developing fetus because alcohol can easily cross the placental barrier and enter the fetal bloodstream.

When alcohol enters the fetal blood, the potential result, called **fetal alcohol syndrome (FAS),** can cause tragic congenital abnormalities such as "small head," or *microcephaly* (my-kro-SEF-ah-lee); low birth weight; cardiovascular defects; developmental disabilities such as physical and mental retardation; and even fetal death.

The photograph shows the small head, thinned upper lip, horizontally narrow eye openings (palpebral fissures), epicanthal folds, and receded upper jaw (retrognathia) typical of infants born with fetal alcohol syndrome.



Fetal alcohol syndrome.

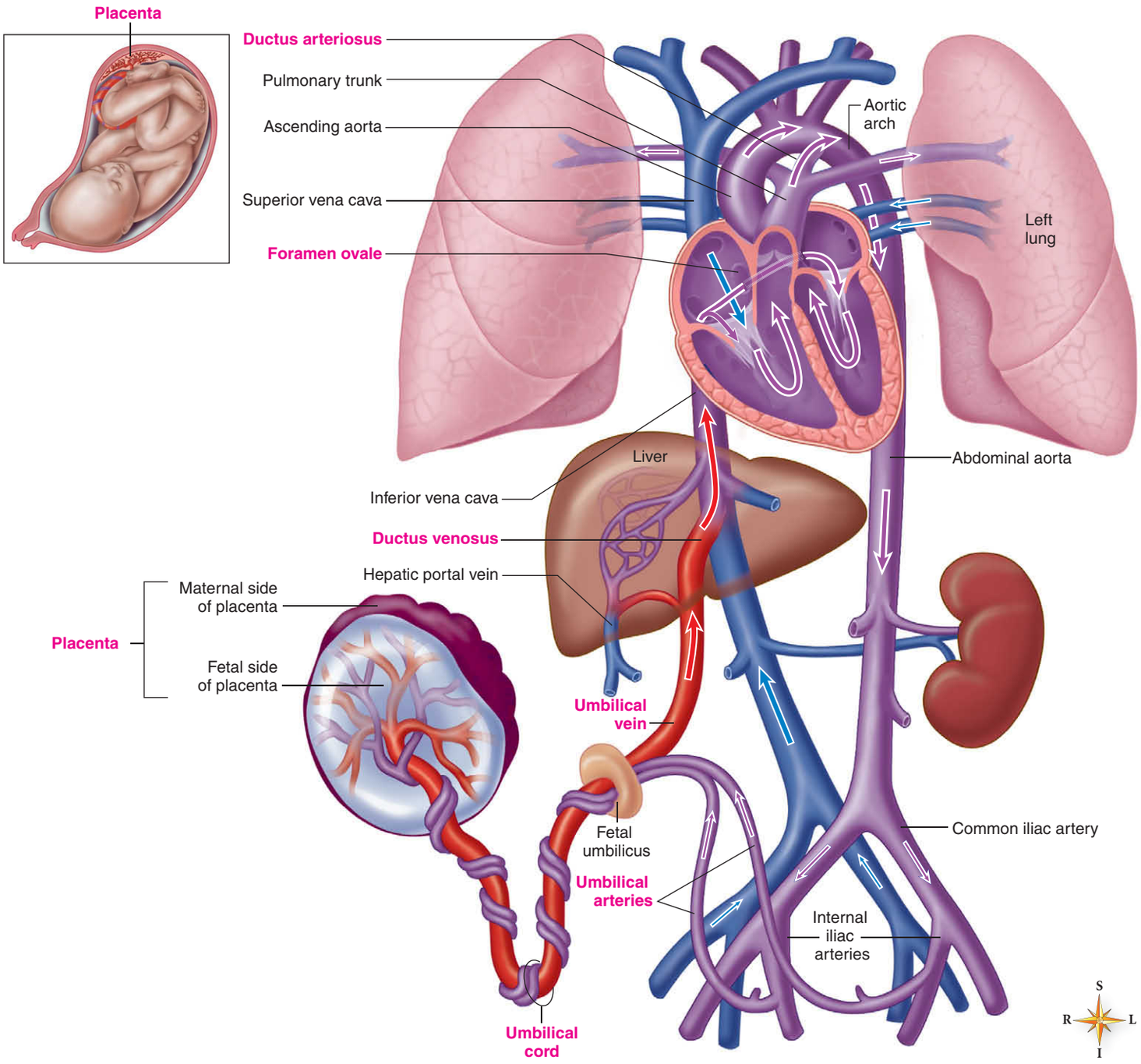


FIGURE 21-36

Plan of fetal circulation. Before birth, the human circulatory system has several special features that adapt the body to life in the womb. These features *(labeled in red type)* include two umbilical arteries, one umbilical vein, ductus venosus, foramen ovale, ductus arteriosus, and umbilical cord. The placenta, another essential feature of the fetal circulatory plan, is shown in Figure 21-35.

the foramen ovale into the left atrium so that it bypasses the fetal lungs. A small percentage of the blood leaves the right atrium for the right ventricle and pulmonary trunk. But most of this blood does not flow on into the lungs. Still another detour, the ductus arteriosus, diverts it.

6. The **ductus arteriosus** is a small vessel connecting the pulmonary trunk with the aortic arch. It therefore enables another portion of the blood to detour into the systemic circulation without going through the lungs.

Almost all fetal blood is a mixture of oxygenated and deoxygenated blood. Examine Figure 21-36 carefully to determine why this is so. What happens to the oxygenated blood returned from the placenta by way of the umbilical vein? Note that it flows into the inferior vena cava.

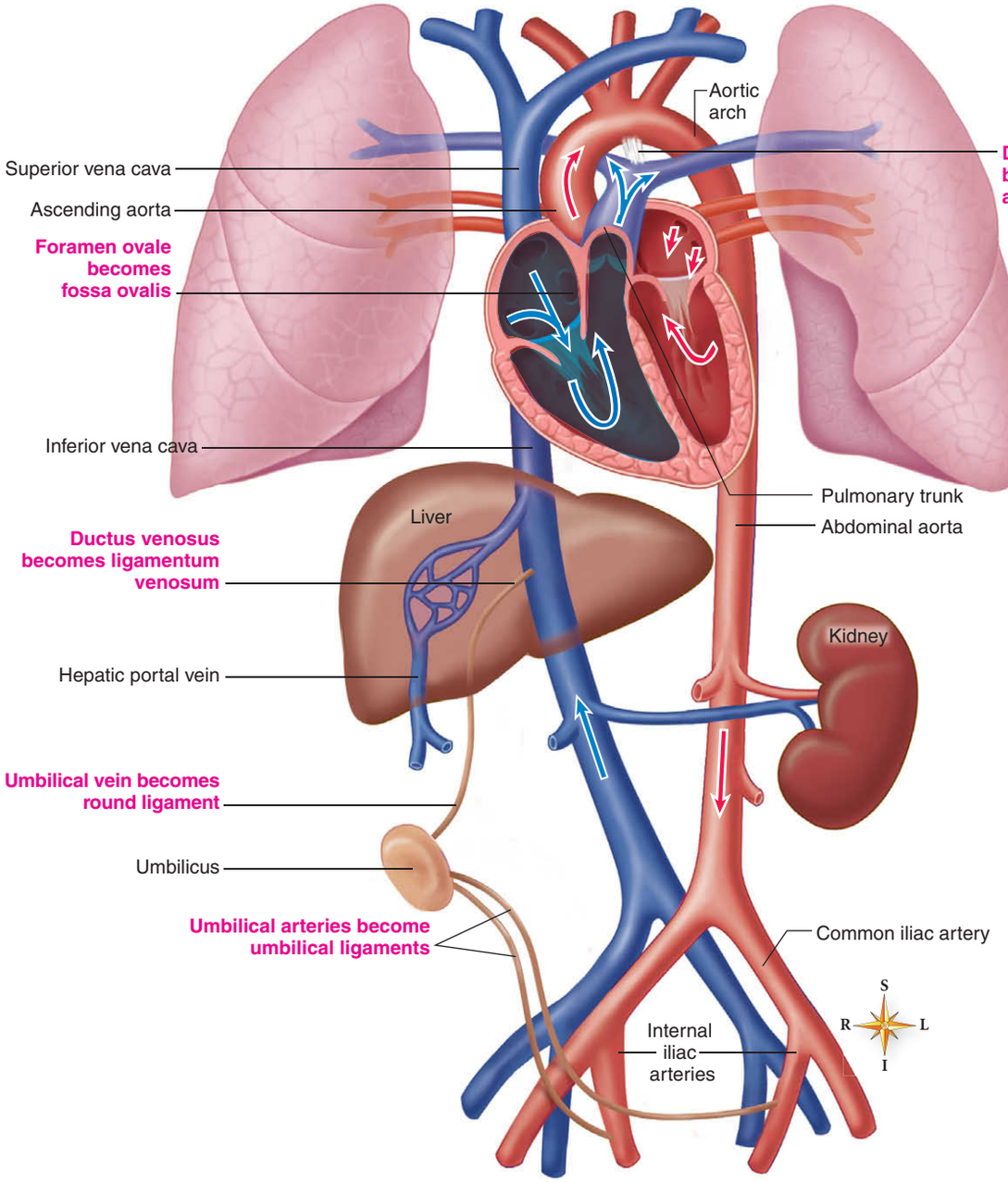


FIGURE 21-37

Changes in circulation after birth. Within the first year after the time of birth, certain changes in the circulatory plan occur to adapt the body to life outside the womb. The placenta and portions of the umbilical vessels outside the infant's body are removed or fall off at, or shortly after, the time of birth. The internal portion of the umbilical vein constricts and becomes fibrous, eventually forming the round ligament of the liver. Likewise, the internal umbilical arteries become umbilical ligaments, the ductus venosus becomes the ligamentum venosum, and the ductus arteriosus becomes the ligamentum arteriosum. The foramen ovale closes, forming a thin region of the atrial wall called the *fossa ovalis*.

Changes in Circulation at Birth

Because the six structures that serve fetal circulation are no longer needed after birth, several changes take place (Figure 21-37). As soon as the umbilical cord is cut, the two umbilical arteries, the placenta, and the umbilical vein obviously no longer function. The placenta is shed from the mother's body as the *afterbirth* with part of the umbilical vessels attached. The sections of these vessels remaining in the infant's body eventually become fibrous cords, which remain throughout life (the umbilical vein becomes the round ligament of the liver).

The ductus venosus, no longer needed to bypass blood around the liver, eventually becomes the ligamentum venosum of the liver.

The foramen ovale normally becomes functionally closed soon after a newborn takes the first breath and full circulation through the lungs becomes established. Complete structural closure, however, usually requires 9 months or more. Eventually, the foramen ovale becomes a mere depression (fossa ovalis) in the wall of the right atrial septum.

The ductus arteriosus contracts as soon as respiration is established. Eventually, it also turns into a fibrous cord, the ligamentum arteriosum. Compare the blood flow in Figures 21-36 and 21-37. Notice how separation of oxygenated and deoxygenated blood occurs *after* birth.

| QUICK CHECK |

20. Name some structures of the fetal circulation that are not part of the adult circulation.
21 What is the function of the placenta and umbilical vessels?
22. What changes in the circulatory system occur at the time of birth?

Cycle of LIFE

Cardiovascular Anatomy

As with all body structures, the heart and blood vessels undergo profound anatomical changes during early development in the womb. At birth, the switch from a placenta-dependent system causes another set of profound anatomical changes. Throughout childhood, adolescence, and adulthood, the heart and blood vessels normally maintain their basic structure and function—permitting continued survival of the individual. Perhaps the only apparent normal changes in these structures occur as a result of regular exercise. The myocardium thickens and the supply of blood vessels in skeletal muscle tissues increases in response to increased oxygen and glucose use during prolonged exercise.

As we pass through adulthood, especially later adulthood, various degenerative changes can occur in the heart and blood vessels. For example, a type of "hardening of the arteries," called **atherosclerosis,** can result in blockage or weakening of critical arteries—perhaps causing a myocardial infarction or stroke. The heart valves and myocardial tissues often degenerate with age, becoming hardened or fibrotic and less able to perform their functions properly. This reduces the heart's pumping efficiency and therefore threatens homeostasis of the entire internal environment.

the BIG picture

Cardiovascular Anatomy and the Whole Body

In this chapter, we have briefly outlined the functional anatomy of many different structures: the heart, major arteries and veins, and even the tiny arterioles, venules, and capillaries.

In essence, we have described a complex, interconnected network of transport pipes for blood. Part of what you learned from this description is how each component of this blood-transporting network is constructed and just a little bit about how each works as an individual unit. Step back from this collection of facts for a moment, and think about how each component of the heart works with the other components to keep blood flowing continuously through the heart. Broaden the picture now in your mind's eye to include each of the other components of the network: the arteries, the veins, and the capillaries. As you continue to study this chapter, keep this "big picture" in mind and add to it your deepening understanding of where each vessel and chamber gets its blood and where it delivers the blood. Before long, you will have a useful understanding of how the entire network functions as a system.

In the next chapter, we build on your understanding of the functional anatomy of the cardiovascular system by discussing mechanisms of blood flow. In other words, all of the next chapter deals with issues relating to the "big picture" of cardiovascular function and its importance to survival.

MECHANISMS of DISEASE

DISORDERS OF THE CARDIOVASCULAR SYSTEM

Disorders of Heart Structure

Disorders Involving the Pericardium

If the pericardium becomes inflamed, a condition called **pericarditis** results. Pericarditis may be caused by various factors: trauma, viral or bacterial infection, tumors, and other factors. The pericardial edema that characterizes this condition often causes the visceral and parietal layers of the serous pericardium to rub together—causing severe chest pain. Pericardial fluid, pus, or blood (in the case of an injury) may accumulate in the space between the two pericardial layers and impair the pumping action of the heart. This is termed **pericardial effusion** and may develop into a serious compression of the heart called **cardiac tamponade.**

Pericarditis may be acute or chronic, depending on the rate, severity, and duration of symptoms. Clinical manifestations include pericardial pain that increases with respirations or coughing, a "friction rub" (a grating, scratching sound heard over the left sternal border and upper ribs) resulting from the swollen pericardial layers rubbing against each other, difficulty breathing, restlessness, and an accumulation of pericardial fluid. Cardiac tamponade requires immediate pericardial drainage **(pericardiocentesis).** Antibiotics are usually prescribed to treat the causative organism, and nonsteroidal antiinflammatory agents such as aspirin are prescribed to reduce the inflammation and thus control the symptoms.

Disorders Involving Heart Valves

Disorders of the cardiac valves can have several effects. For example, a congenital defect in valve structure can result in mild to severe pumping inefficiency. Incompetent valves leak, allowing some blood to flow back into the chamber from which it came. **Stenosed valves** are valves that are narrower than normal, slowing blood flow from a heart chamber (Figure 21-38).

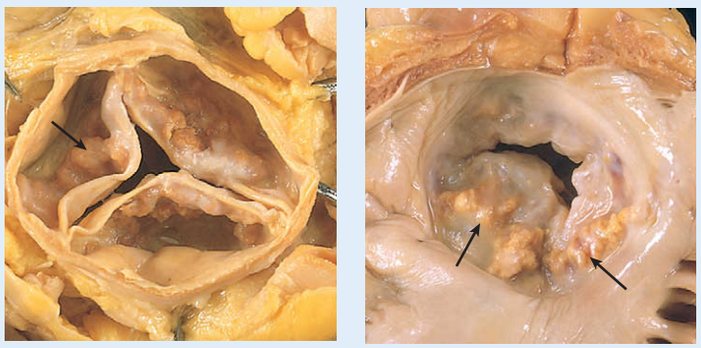


FIGURE 21-38

Stenosed mitral valve. Note the calcific nodules *(arrows)* attached to the cusps, thus narrowing the opening and slowing blood flow.

UNIT 4

Rheumatic heart disease results from a delayed inflammatory response to streptococcal infection that occurs most often in children. A few weeks after an improperly treated streptococcal infection, the cardiac valves and other tissues in the body may become inflamed—a condition called **rheumatic fever.** If severe, the inflammation can result in stenosis or other deformities of the valves, chordae tendineae, or myocardium.

Mitral valve prolapse (MVP), a condition affecting the bicuspid or mitral valve, has a genetic basis in some cases but can result from rheumatic fever or other factors. A prolapsed mitral valve is one whose flaps extend back into the left atrium, causing incompetence (leaking) of the valve (Figure 21-39). Although this condition is common, occurring in up to 1 in every 20 people, most cases are asymptomatic. In severe cases, patients suffer chest pain and fatigue.

Aortic regurgitation is a condition in which blood not only ejects forward into the aorta but also regurgitates back into the left ventricle because of a leaky aortic semilunar valve. This causes a volume overload on the left ventricle, with subsequent hypertrophy and dilation of the left ventricle. The left ventricle attempts to compensate for the increased load by increasing its strength of contraction—which may eventually stress the heart to the point of causing myocardial ischemia.

Damaged or defective cardiac valves can often be replaced surgically—a procedure called **valvuloplasty.** Artificial valves made from synthetic materials, as well as valves taken from other mammals such as swine, are frequently used in these valve replacement procedures.

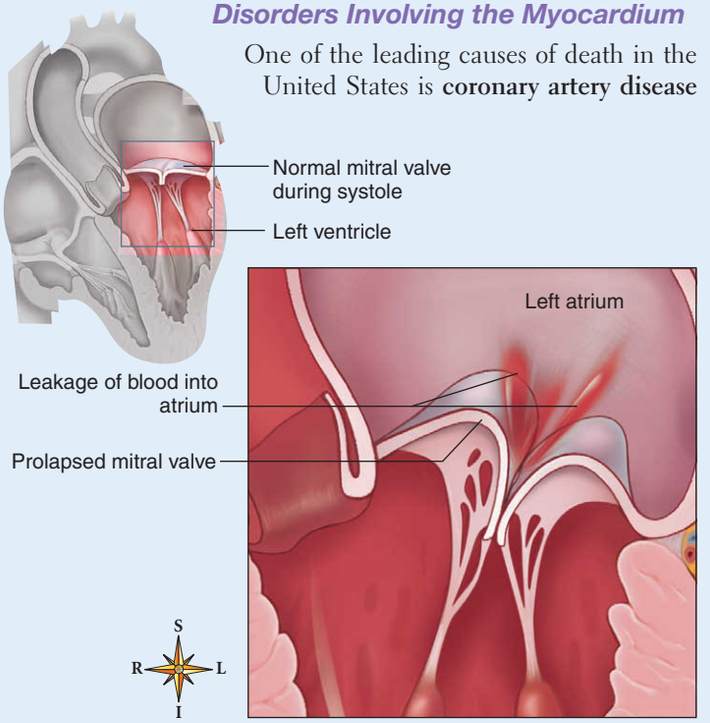


FIGURE 21-39

Mitral valve prolapse. The normal mitral valve *(left)* prevents backflow of blood from the left ventricle into the left atrium during ventricular systole (contraction). The prolapsed mitral valve *(inset)* permits leakage because the valve flaps billow backward, parting slightly.

Disorders Involving the Myocardium

One of the leading causes of death in the United States is **coronary artery disease (CAD).** This condition can result from many causes, all of which somehow reduce the flow of blood to the vital myocardial tissue. For example, in both coronary thrombosis and coronary embolism, a blood clot occludes, or plugs, some part of a coronary artery. Blood cannot pass through the occluded vessel and so cannot reach the heart muscle cells it normally supplies. Deprived of oxygen, these cells soon die or are damaged. In medical terms, a **myocardial infarction (MI),** or tissue death, occurs.

A myocardial infarction (heart attack) is a common cause of death during middle and late adulthood. Recovery from a myocardial infarction is possible if the amount of heart tissue damaged is small enough that the remaining undamaged heart muscle can pump blood effectively enough to supply the needs of the rest of the heart, as well as the body.

| A&P CONNECT |

How does a heart attack develop? Take a tour through an illustrated description of the process of an MI in ***Heart Attack!*** online at ***A&P Connect.***

evolve

Coronary arteries may also become blocked as a result of **atherosclerosis,** a type of "hardening of the arteries" in which lipids and other substances build up within the wall of blood vessels and eventually calcify, making the vessel wall hard and brittle. Mechanisms of atherosclerosis are discussed elsewhere in this chapter. Coronary atherosclerosis has increased dramatically over the last half century to become the leading cause of death in western countries. Many pathophysiologists believe this increase results from a change in lifestyle. They cite several important risk factors associated with coronary atherosclerosis: cigarette smoking, high-fat and high-cholesterol diets, diabetes, and hypertension (high blood pressure).

The term **angina pectoris** is used to describe the severe chest pain that occurs when the myocardium is deprived of adequate oxygen. It is often a warning that the coronary arteries are no longer able to supply enough blood and oxygen to the heart muscle. **Coronary bypass surgery** is a frequent treatment for those who suffer from severely restricted coronary artery blood flow. In this procedure, veins and sometimes arteries are "harvested" from other areas of the body and used to bypass partial blockages in coronary arteries (Figure 21-40).

Congestive heart failure (CHF), or simply, *left-side heart failure,* is the inability of the left ventricle to pump blood effectively. Most often, such failure results from chronic systemic hypertension (high blood pressure) or from myocardial infarction caused by coronary artery disease (Figure 21-41, A). It is called *congestive heart failure* because it decreases pumping pressure in the systemic circulation, which in turn causes the body to retain fluids. Portions of the systemic circulation thus become congested with extra fluid. Left-side heart failure also causes congestion of blood in the pulmonary circulation, termed **pulmonary edema**—possibly leading to right-side heart failure and pulmonary hypertension (Figure 21-41, *B*).

The term **cardiomyopathy** is used to describe a number of different types of heart diseases that result in abnormal enlargement.

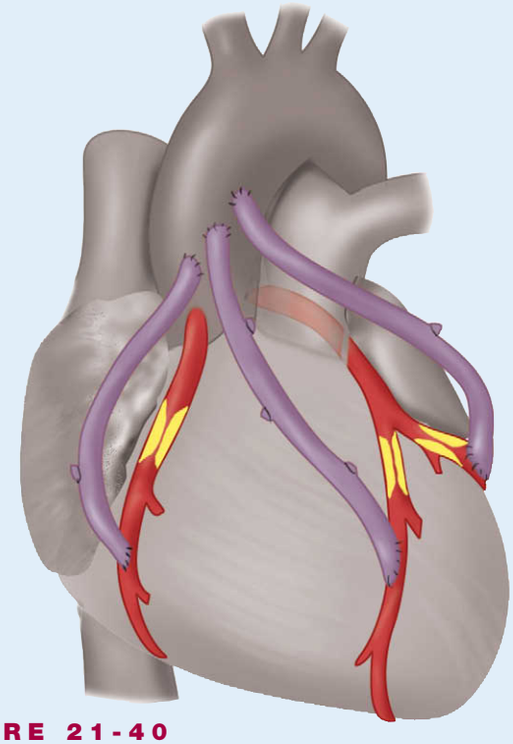
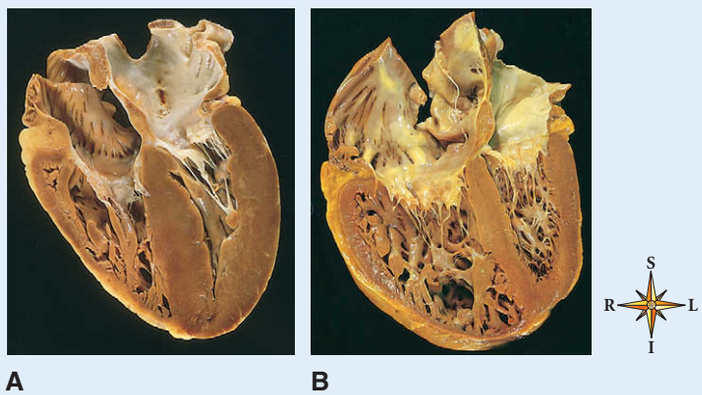


FIGURE 21-40

Coronary bypass. In coronary bypass surgery, blood vessels are "harvested" or "rerouted" from other parts of the body and used to construct detours around blocked coronary arteries. Artificial vessels can also be used.

In addition to left and right ventricular hypertrophy, another form of enlargement is called **hypertrophic cardiomyopathy** and is caused by a genetic defect. Figure 21-42 shows the appearance of the heart in this condition. It is one of the most common causes of sudden unexplained death in young athletes.

Patients in danger of death because of heart failure may be candidates for heart *transplants* or heart *implants*. Heart transplants are surgical procedures in which healthy hearts from recently deceased donors replace the hearts of patients with heart disease. Unfortunately, a continuing problem with this procedure is the tendency of the body's immune system to reject the new heart—perceiving it as a foreign tissue. More details about the rejection of transplanted tissues are found in Chapter 24.



A B

FIGURE 21-41

Congestive heart failure. A, Left ventricle hypertrophy (left-sided heart failure). Note the hypertrophy of the left ventricle often caused by chronic systemic hypertension. **B,** Right ventricular hypertrophy (right-sided heart failure or *cor pulmonale*). Note the right ventricular hypertrophy and dilation caused by pulmonary hypertension.

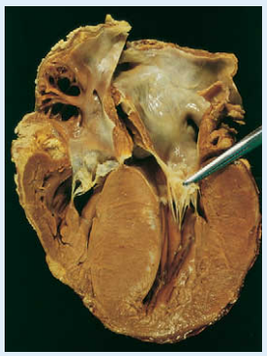


FIGURE 21-42

Hypertrophic cardiomyopathy. Note the dramatic increase of myocardial tissue. This genetic condition may cause sudden heart failure in the apparent absence of warning symptoms.

Heart implants are artificial hearts that are made of biologically inert synthetic materials. On July 3, 2001, the first artificial heart was successfully implanted into Robert Tools by University of Louisville researchers. The 1-kg (2-pound) *AbioCor Implantable Replacement Heart* ("artificial heart") allowed the patient to move about freely without any external pumps. Portable external battery packs are used to recharge the small internal battery that powers the internal pumping unit. The success of the AbioCor unit and other artificial heart models gives hope that artificial hearts will one day be a commonplace and effective treatment for patients with severe heart disease.

Disorders of Blood Vessels

Disorders of Arteries

As mentioned earlier in this chapter, arteries contain blood that is maintained at a relatively high pressure. This means the arterial walls must be able to withstand a great deal of force or they will burst. The arteries must also stay free of obstruction; otherwise they cannot deliver their blood to the capillary beds (and thus the tissues they serve).

A common type of vascular disease that occludes (blocks) arteries and weakens arterial walls is called **arteriosclerosis,** or *hardening of the arteries*. Arteriosclerosis is characterized by thickening of arterial walls that eventually progresses to hardening as calcium deposits form. The thickening and calcification reduce the flow of blood to the tissues. If blood slows in peripheral tissues such as the hands, legs, or feet, the condition is often referred to as **peripheral vascular disease (PVD)** or **peripheral arterial disease (PAD)** and the result is ischemia.

Ischemia, or decreased blood supply to a tissue, involves the gradual death of cells and may lead to complete tissue death—a condition called **necrosis.** If a large section of tissue becomes necrotic, it may begin to decay because of bacterial action. Necrosis that has progressed this far is called **gangrene.** Gangrene is a very serious consequence of ischemia or blocked blood flow in

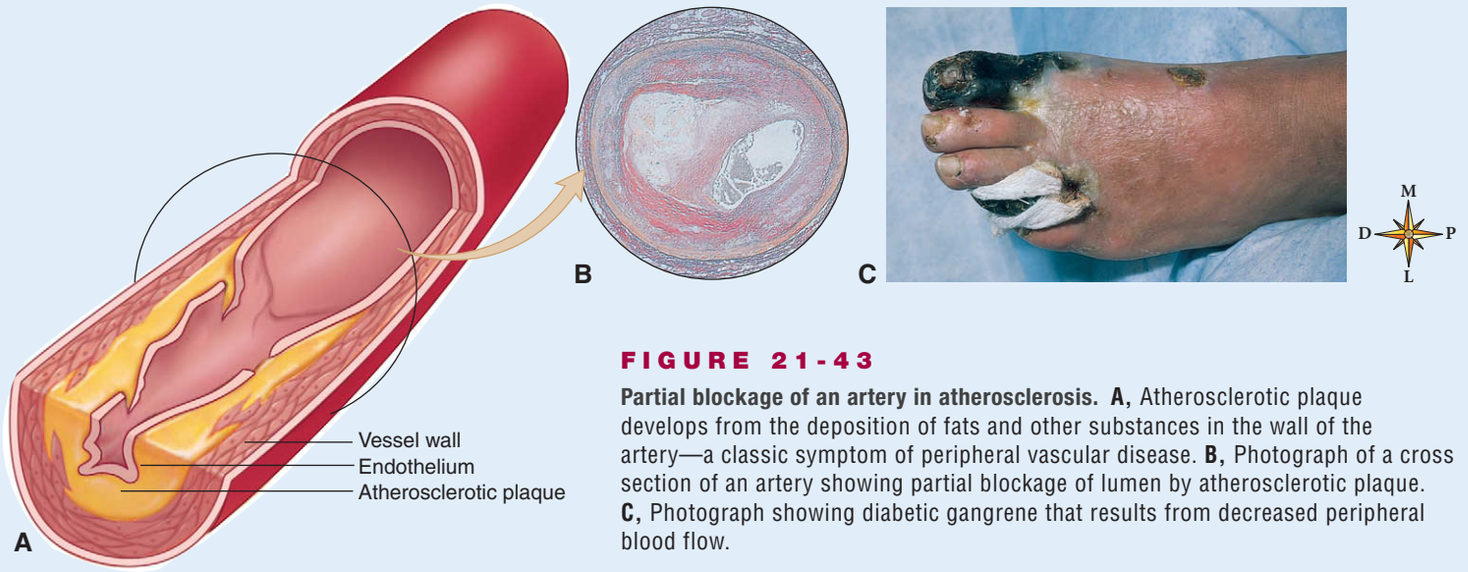


FIGURE 21-43

Partial blockage of an artery in atherosclerosis. A, Atherosclerotic plaque develops from the deposition of fats and other substances in the wall of the artery—a classic symptom of peripheral vascular disease. **B,** Photograph of a cross section of an artery showing partial blockage of lumen by atherosclerotic plaque. **C,** Photograph showing diabetic gangrene that results from decreased peripheral blood flow.

PVD and is, unfortunately, a common problem in uncontrolled diabetes (Figure 21-43). PVD may also cause occasional pain, cramping, or weakness in the extremities—a condition called *intermittent claudication* (see Box 20-5 on p. 617).

Because of the tissue damage involved, arteriosclerosis is not only painful—it is life threatening. As we have previously stated, ischemia of heart muscle can lead to *myocardial infarction* and death.

There are several types of arteriosclerosis, but perhaps the most well known is *atherosclerosis*—described earlier as the blockage of arteries by lipids and other matter (see Figure 21-43). Eventually, the fatty deposits in the arterial walls become fibrous and perhaps calcified—resulting in sclerosis (hardening). High blood levels of triglycerides and cholesterol, which may be caused by a high-fat and high-cholesterol diet, smoking, and a genetic predisposition, are associated with atherosclerosis.

In general, arteriosclerosis develops with advanced age, diabetes, high-fat and high-cholesterol diets, hypertension (high blood pressure), and smoking. Arteriosclerosis can be treated by drugs, called **vasodilators,** that trigger the smooth muscles of the arterial walls to relax, thus causing the arteries to dilate (widen).

Some cases of atherosclerosis are treated by mechanically opening the affected area of an artery in a type of procedure called **percutaneous coronary intervention (PCI).** In one PCI procedure called **angioplasty,** a deflated balloon attached to a long, thin tube called a **catheter** is inserted into a partially blocked artery and then inflated (Figure 21-44). As the balloon inflates, the *atherosclerotic plaque* (fatty deposits and tissue) is pushed outward, and the artery widens to allow near-normal blood flow. In a similar procedure, metal springs or mesh tubes, called **stents**, are inserted in affected arteries to hold them open.

Similar types of PCIs called **atherectomies** use lasers, drills, or spinning loops of wire to clear the way for normal blood flow. Severely affected arteries can also be surgically bypassed or replaced.

Damage to arterial walls caused by arteriosclerosis or other factors may lead to the formation of an **aneurysm.** An aneurysm is a section of an artery that has become abnormally widened because of a weakening of the arterial wall. Aneurysms sometimes form a saclike extension of the arterial wall. One reason aneurysms are dangerous is because they, like atherosclerotic plaques, promote the formation of thrombi (abnormal clots). A thrombus may cause an embolism (blockage) in the heart or some other vital tissue. Another reason aneurysms are dangerous is their tendency to burst, causing severe hemorrhaging that may result in death.

A brain aneurysm may lead to a **stroke,** or **cerebrovascular accident (CVA).** A stroke results from ischemia of brain tissue caused by an embolism or ruptured aneurysm. Depending on the amount of tissue affected and the place in the brain the CVA occurs, effects of a stroke may range from hardly noticeable to crippling to fatal.

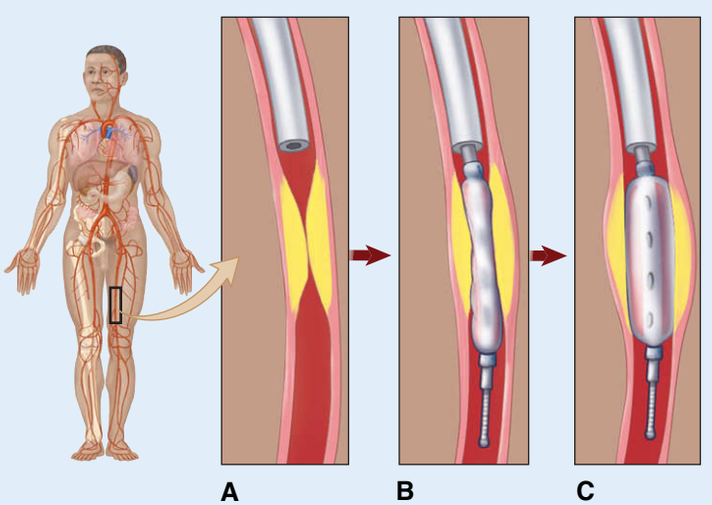


FIGURE 21-44

Balloon angioplasty. A, A catheter is inserted into the vessel until it reaches the affected region. **B,** A probe with a metal tip is pushed out the end of the catheter into the blocked region of the vessel. **C,** The balloon is inflated, pushing the walls of the vessel outward. Sometimes metal coils or tubes, called "stents," are inserted to keep the vessel open. Drug-coated stents may further reduce delayed scarring and reclogging of arteries following angioplasty in many patients.

Disorders of Veins

Varicose veins are enlarged veins in which blood tends to pool rather than continue on toward the heart. Varicose veins, also called *varices* (*singular*, **varix**), commonly occur in *superficial veins* near the surface of the body. The *great saphenous vein*, the largest superficial vein of the leg (see Figure 21-33), often becomes varicose in people who stand for long periods. The force of gravity slows the return of venous blood to the heart in such cases, causing blood-engorged veins to dilate. As the veins dilate, the distance between the flaps of venous valves widens—eventually making them incompetent (leaky) (Figure 21-45). Incompetence of valves causes even more pooling in affected veins—a positive feedback phenomenon.

Hemorrhoids, or *piles*, are varicose veins in the anal canal (look ahead to Figure 28-30 on p. 889). Excessive straining during defecation can create pressures that cause hemorrhoids. The unusual pressures of carrying a child during pregnancy predispose expectant mothers to hemorrhoids and other varicosities.

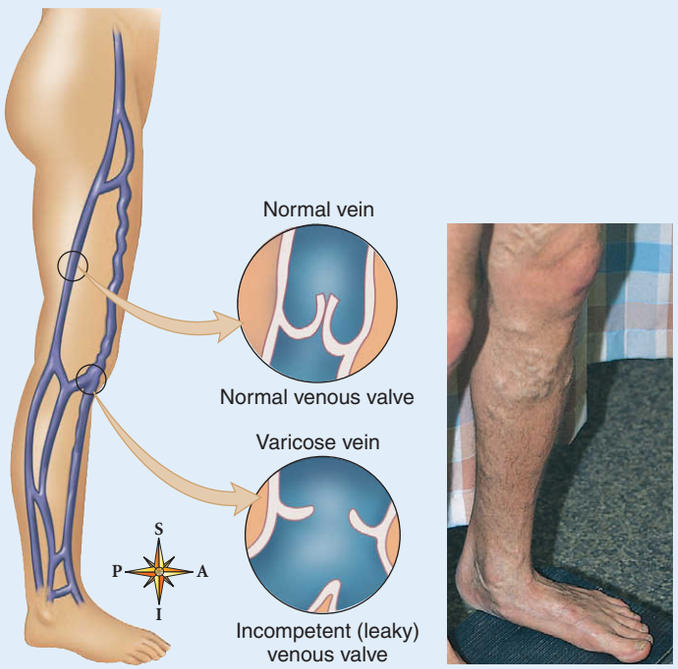
Varicose veins in some parts of the body can be treated by supporting the dilated veins from the outside. For instance, support stockings can reduce blood pooling in the great saphenous vein. Surgical removal of varicose veins can be performed in severe cases. Advanced cases of hemorrhoids are often treated by this type of surgery. Symptoms of milder cases of varicose veins can be relieved by removing the pressure that caused the condition.

Several factors can cause **phlebitis,** or vein inflammation. Irritation by an intravenous catheter, for example, is a common cause of vein inflammation. **Thrombophlebitis** is acute phlebitis caused by clot (thrombus) formation. Veins are more likely sites of thrombus formation than arteries because venous blood moves more slowly and is under less pressure.

A *deep vein thrombosis (DVT)* is a clot that has formed in a deep vein, especially in the legs, and is particularly dangerous. If a piece of a clot breaks free from a DVT, it may cause an embolism when it blocks a blood vessel. **Pulmonary embolism,** for example, could result when an embolus lodges in the circulation of the lung (Figure 21-46). Pulmonary embolism can lead to death quickly if too much blood flow is blocked.

Heart Medication

Although numerous drugs are used in the treatment of heart disease, the following have proven to be basic tools of the cardiologist: **anticoagulants** prevent clot formation; **beta-adrenergic blockers** block norepinephrine receptors and thus reduce the strength and rate of heart beats; **calcium channel blockers** reduce heart contractions by preventing the flow of Ca^{++} into cardiac muscle cells; **digitalis** slows and increases the strength of cardiac contractions; **nitroglycerin** dilates coronary blood vessels and thus improves O^2 supply to myocardium; and **tissue plasminogen activator (t-PA)** helps dissolve clots.



A B

FIGURE 21-45

Varicose veins. A, Veins near the surface of the body—especially in the legs—may bulge and cause venous valves to leak. **B,** Photograph showing varicose veins on the surface of the leg.



A B

FIGURE 21-46

Deep vein thrombosis (DVT). A, Note the swelling in the left leg of this patient caused by a deep femoral vein thrombosis secondary to cancer. **B,** Large embolus derived from a lower extremity DVT and now located in a pulmonary artery branch. This type of blood clot is sometimes called a "saddle" or "straddling embolism" because it straddles a dividing blood vessel.

LANGUAGE OF SCIENCE *(continued from p. 629)*

arteriovenous anastomosis
(ar-teer-ee-oh-VEE-nus ah-nas-teh-MOH-sis)
[*arteri-* **vessel**, *-ven-* **vein**, *-ous* **relating to**, *ana-* **anew**, *-stomo-* **mouth**, *-osis* **condition**]
pl., anastomoses

artery
(AR-ter-ee)
[*arteri-* **vessel**]

ascending aorta
(ah-SEND-ing ay-OR-tah)
[*ascend-* **climb**, *aort-* **lifted**, *-a* **thing**] *pl.,* aortae or aortas

atrioventricular (AV) valve
(ay-tree-oh-ven-TRIK-yoo-lar)
[*atrio-* **entrance courtyard**, *-ventr-* **belly**, *-icul-* **little**, *-ar* **relating to**]

atrium
(AY-tree-um)
[*atrium* **entrance courtyard**] *pl.,* atria

axillary vein
(AK-si-lair-ee)
[*axilla* **wing**, *-ary* **relating to**]

azygos vein
(AZ-i-gohs)
[*a-* **without**, *-zygo-* **union or yoke**]

basilic vein
(bah-SIL-ik)
[*bas-* **foundation**, *-ic* **relating to**]

bicuspid valve
(bye-KUS-pid)
[*bi-* **double**, *-cusp-* **point**, *-id* **characterized by**]

brachial vein
(BRAY-kee-al)
[*brachi-* **arm**, *-al* **relating to**]

brachiocephalic artery
(brayk-ee-oh-seh-FAL-ik AR-ter-ee)
[*brachi-* **arm**, *-cephal-* **head**, *-ic* **relating to**, *arteri-* **vessel**]

brachiocephalic vein
(brayk-ee-oh-seh-FAL-ik)
[*brachi-* **arm**, *-cephal-* **head**, *-ic* **relating to**]

bronchial vein
(BRONK-kee-al)
[*bronch-* **windpipe**, *-al* **relating to**]

capillary
(KAP-i-lair-ee)
[*capill-* **hair**, *-ary* **relating to**]

cephalic vein
(seh-FAL-ik)
[*cephal-* **head**, *-ic* **relating to**]

chordae tendineae
(KOR-dee ten-DIN-ee)
[*chorda* **string or cord**, *tendinea* **pulled tight**] *sing.,* chorda tendinea

common carotid artery
(kah-ROT-id AR-ter-ee)
[*caro-* **heavy sleep**, *-id* **relating to**, *arteri-* **vessel**]

continuous capillary
(KAP-i-lair-ee)
[*capill-* **hair**, *-ary* **relating to**]

coronary artery
(KOHR-oh-nair-ee AR-ter-ee)
[*corona-* **crown**, *-ary* **relating to**, *arteri-* **vessel**]

cuspid valve
(KUS-pid)
[*cusp-* **point**, *-id* **characterized by**]

deep vein

descending aorta
(ay-OR-tah)
[*aort-* **lifted**, *-a* **thing**] *pl.,* aortae or aortas

ductus arteriosus
(DUK-tus ar-teer-ee-OH-sus)
[*ductus* **duct**, *arteri-* **vessel**, *-osus* **relating to**]

ductus venosus
(DUK-tus veh-NO-sus)
[*ductus* **duct**, *ven-* **vein**, *-osus* **relating to**]

elastic artery
[*elast-* **to drive or beat out**, *-ic* **relating to**, *arteri-* **vessel**]

end-artery
[*-arteri-* **vessel**]

endocardium
(en-doh-KAR-dee-um)
[*endo-* **within**, *-cardi-* **heart**, *-um* **thing**]

endothelium
(en-doh-THEE-lee-um)
[*endo-* **within**, *-theli-* **nipple**, *-um* **thing**]

epicardium
(ep-i-KAR-dee-um)
[*epi-* **on or upon**, *-cardi-* **heart**, *-um* **thing**]

esophageal vein
(eh-sof-ah-JEE-al)
[*es-* **will carry**, *-phag-* **food (eat)**, *-al* **relating to**]

external iliac vein
(eks-TER-nal IL-ee-ak)
[*extern-* **outside**, *-al* **relating to**, *ilium* **flank**]

external jugular vein
(eks-TER-nal JUG-yoo-lar)
[*extern-* **outside**, *-al* **relating to**, *jugul-* **neck**, *-ar* **relating to**]

femoral vein
(FEM-or-al)
[*femor-* **thigh**, *-al* **relating to**]

fenestrated capillary
(fen-es-TRAY-tid KAP-i-lair-ee)
[*fenestra-* **window**, *-ate* **characterized by**, *capill-* **hair**, *-ary* **relating to**]

fibrous pericardium
(FYE-brus pair-i-KAR-dee-um)
[*fibr-* **fiber**, *-ous* **relating to**, *peri-* **around**, *-cardi-* **heart**, *-um* **thing**]

fibular (peroneal) vein
(FIB-yoo-lar [per-oh-NEE-al])
[*fibula-* **clasp**, **-ar relating to**, *perone-* **brooch**, *-al* **relating to**]

foramen ovale
(foh-RAY-men oh-VAL-ee)
[*foramen* **opening**, *ovale* **egg shaped**] *pl.,* foramina ovales

great saphenous vein
(sah-FEE-nus)
[*saphen-* **manifest**, *-ous* **relating to**]

hemiazygos vein
(hem-ee-AZ-i-gohs)
[*hemi-* **half**, *-a-* **without**, *-zygo-* **union or yoke**]

hepatic portal circulation
(heh-PAT-ik POR-tal)
[*hepa-* **liver**, *-ic* **relating to**, *port-* **doorway**, *-al* **relating to**, *circulat-* **go around**, *-tion* **process**]

inferior vena cava
(in-FEER-ee-or VEE-nah KAY-vah)
[*infer-* **lower**, *-or* **quality**, *vena* **vein**, *cava* **hollow**] *pl.,* venae cavae

internal jugular vein
(JUG-yoo-lar)
[*intern-* **inside**, *-al* **relating to**, *jugul-* **neck**, *-ar* **relating to**]

median cubital vein
(KYOO-bi-tall)
[*medi-* **middle**, *-an* **relating to**, *cubit-* **elbow**, *-al* **relating to**]

metarteriole
(met-ar-TEER-ee-ohl)
[*meta-* **change or exchange**, *arteri-* **vessel**, *-ole* **little**]

mitral valve
(MY-tral)
[*mitr-* **bishop's hat**, *-al* **relating to**]

muscular artery
(MUSS-kyoo-lar AR-ter-ee)
[*mus-* **mouse**, *-cul-* **little**, *-ar* **relating to**, *arteri-* **vessel**]

myocardium
(my-oh-KAR-dee-um)
[*myo-* **muscle**, *-cardi-* **heart**, *-um* **thing**] *pl.,* myocardia

palmar venous arch
(PAHL-mar VEE-nus)
[*palm-* **palm of hand**, *-ar* **relating to**, *ven-* **vein**, *-ous* **relating to**]

pericardial fluid
(pair-i-KAR-dee-al)
[*peri-* **around**, *-cardi-* **heart**, *-al* **relating to**]

pericardial space
(pair-i-KAR-dee-al)
[*peri-* **around**, *-cardi-* **heart**, *-al* **relating to**]

pericardial vein
(pair-i-KAR-dee-al)
[*peri-* **around**, *-cardi-* **heart**, *-al* **relating to**]

pericardium
(pair-i-KAR-dee-um)
[*peri-* **around**, *-cardi-* **heart**, *-um* **thing**] *pl.,* pericardia

placenta
(plah-SEN-tah)
[*placenta* **flat cake**] *pl.,* placentae or placentas

popliteal vein
(pop-lih-TEE-al)
[*poplit-* **back of knee**, *-al* **relating to**]

portal system
(POR-tal)
[*port-* **doorway**, *-al* **relating to**]

posterior tibial vein
(pohs-TEER-ee-or TIB-ee-al)
[*poster-* **behind**, *-or* **quality**, *tibia* **shin bone**, *-al* **relating to**]

pulmonary circulation
(PUL-moh-nair-ee)
[*pulmon-* **lung**, *-ary* **relating to**, *circulat-* **go around**, *-tion* **process**]

renal vein
(REE-nal)
[*ren-* **kidney**, *-al* **relating to**]

semilunar (SL) valve
(sem-i-LOO-nar)
[*semi-* **half**, *-luna* **moon**]

serous pericardium
(SEER-us pair-i-KAR-dee-um)
[*sero-* **watery fluid**, *-ous* **relating to**, *peri-* **around**, *-cardi-* **heart**, *-um* **thing**] *pl.,* pericardia

sinus
(SYE-nus)
[*sinus* **hollow**]

sinusoid
(SYE-nah-soyd)
[*sinus-* **hollow**, *-oid* **like**]

small saphenous vein
(sah-FEE-nus)
[*saphen-* **manifest**, *-ous* **relating to**]

subclavian artery
(sub-KLAY-vee-an)
[*sub-* **below**, *-clavi-* **key**, *-ula* **little**]

subclavian vein
(sub-KLAY-vee-an)
[*sub-* **below**, *-clavi-* **key** (**clavicle bone**), *-an* **relating to**]

superficial vein
(soo-per-FISH-al)
[*super-* **over or above**, *-fici-* **face**, *-al* **relating to**]

superior intercostal vein
(soo-PEER-ee-or inter-KOS-tal)
[*super-* **over or above**, *-or* **quality**, *inter-* **between**, *-costa-* **rib**, *-al* **relating to**]

superior vena cava
(soo-PER-ee-or VEE-nah KAY-vah)
[*super-* **over or above**, *-or* **quality**, *vena* **vein**, *cava* **hollow**] *pl.,* venae cavae

suprarenal vein
(soo-prah-REE-nal)
[*supra-* **above or over**, *-ren-* **kidney**, *-al* **relating to**]

systemic circulation
(sis-TEM-ik ser-kyoo-LAY-shun)
[*system-* **organized whole**, *-ic* **relating to**, *circulat-* **go around**, *-tion* **process**]

thoracic aorta
(tho-RASS-ik ay-OR-tah)
[*thorac-* **chest**, *-ic* **relating to**, *aort-* **lifted**, *-a* **thing**] *pl.,* aortae or aortas

tricuspid valve
(try-KUS-pid)
[*tri-* **three**, *-cusp-* **point**, *-id* **characterized by**]

true capillary
(KAP-i-lair-ee)
[*capill-* **hair**, *-ary* **relating to**]

tunica externa
(TOO-nih-kah ex-TER-nah)
[*tunica* **tunic or coat**, *extern-* **outside**] *pl.,* tunicae externae

tunica intima
(TOO-nih-kah IN-ti-mah)
[*tunica* **tunic or coat**, *intima* **innermost**] *pl.* tunicae intimae

tunica media
(TOO-nih-kah MEE-dee-ah)
[*tunica* **tunic or coat**, *media* **middle**] *pl.,* tunicae mediae

umbilical artery
(um-BIL-i-kul)
[*umbilic-* **navel**, *-al* **relating to**, *arteri-* **vessel**]

umbilical vein
(um-BIL-i-kul)
[*umbilic-* **navel**, *-al* **relating to**]

vascular anastomosis
(VAS-kyoo-lar ah-nastoh-MOH-sis)
[*vas-* **vessel**, *-ular* **relating to**, *ana-* **anew**, *-stomo-* **mouth**, *-osis* **condition**] *pl.,* anatomoses

vein

venous sinus
(VEE-nus SYE-nus)
[*ven-* **vein**, *-ous* **relating to**, *sinus* **hollow**]

ventricle
(VEN-tri-kul)
[*ventr-* **belly**, *-icle* **little**]

venule
(VEN-yool)
[*ven-* **vein**, *-ule* **little**]

LANGUAGE OF MEDICINE

aneurysm
(AN-yoo-riz-em)
[*aneurysm* **widening**]

angina pectoris
(an-JYE-nah PEK-tor-is)
[*angina* **strangling**, *pector-* **breast**, *-is* **relating to**]

angioplasty
(AN-jee-oh-plass-tee)
[*angio-* **vessel**, *-plasty* **surgical repair**]

anticoagulant
(an-tee-koh-AG-yoo-lant)
[*anti-* **against**, *-coagul-* **curdle**, *-ant* **agent**]

aortic regurgitation
(ay-OR-tik ree-gur-jih-TAY-shun)
[*aort-* **lifted**, *-ic* **relating to**, *re-* **again**, *-gurgit-* **flow**, *-ation* **process**]

arteriosclerosis
(ar-teer-ee-oh-skleh-ROH-sis)
[*arteri-* **vessel**, *-scler-* **hardening**, *-osis* **condition**]

atherectomy
(ath-er-EK-to-mee)
[*ather-* **gruel**, *-ec-* **out**, *-tom-* **cut**, *-y* **action**]

atherosclerosis
(ath-er-oh-skleh-ROH-sis)
[*athero-* **gruel**, *-scler-* **hardening**, *-osis* **condition**

beta-adrenergic blocker
(BAY-tah-ad-ren-ER-jik)
[*beta (β)* **second letter of Greek alphabet**, *ad-* **toward**, *-ren-* **kidney**, *-erg-* **work**, *-ic* **relating to**]

calcium channel blocker
(KAL-see-um CHAN-al)

cardiac tamponade
(KAR-dee-ak tam-pon-odd)
[*cardi-* **heart**, *-ac* **relating to**, *tampon-* **plug**, *-ade* **process**]

cardiomyopathy
(KAR-dee-oh-my-OP-ah-thee)
[*cardio-* **heart**, *-myo-* **muscle**, *-path-* **disease**, *-y* **state**]

catheter
(KATH-eh-ter)
[*cathe-* **send down**, *-er* **agent**]

cerebrovascular accident (CVA)
(SAIR-eh-broh-VAS-kyoo-lar)
[*cerebr-* **brain**, *-vas-* **vessel**, *-ular* **relating to**]

congestive heart failure (CHF)
(kon-JES-tive)
[*congest-* **crowd together**, *-ive* **relating to**]

coronary artery disease (CAD)
(KOR-oh-nair-ee AR-ter-ee)
[*corona-* **crown**, *-ary* **relating to**, *arteri-* **vessel**]

coronary bypass surgery
(KOR-oh-nair-ee)
[*corona-* **crown**, *-ary* **relating to**]

C-reactive protein

digitalis
(dij-i-TAL-is)
[*digit-* **finger**, *-alis* **relating to**]

echocardiography
(ek-oh-kar-dee-OG-rah-fee)
[*echo-* **reflect sound**, *-cardi-* **heart**, *-graph-* **draw**, *-y* **activity**]

fetal alcohol syndrome (FAS)
(FEE-tal AL-kohhol SIN-drohm)
[*fet-* **offspring**, *-al* **relating to**, *syn-* **together**, *-drome* **running or** (**race**) **course**]

gangrene
(GANG-green)
[*gangren-* **gnawing sore**]

hemorrhoid
(HEM-eh-royd)
[*hema-* **blood**, *-rhoi-* **flow**]

hypertrophic cardiomyopathy
(hye-PER-troh-fik KAR-dee-oh-my-OP-ah-thee)
[*hyper-* **excessive**, *-troph-* **nourishment**, *-ic* **relating to**, *cardi-* **heart**, *-myo-* **muscle**, *-path-* **disease**, *-y* **state**

ischemia
(is-KEE-mee-ah)
[*ische-* **hold back**, *-emia* **blood condition**]

mitral valve prolapse (MVP)
(MY-tral valv PROH-laps)
[*mitr-* **bishop's hat**, *-al* **relating to**, *pro-* **forward**, *-laps-* **fall**]

myocardial infarction (MI)
(my-oh-KAR-dee-al in-FARK-shun)
[*myo-* **muscle**, *-cardi-* **heart**, *-al* **relating to**, *in-* **in**, *-farc-* **stuff**]

necrosis
(neh-KROH-sis)
[*necr-* **death**, *-osis* **condition**]

LANGUAGE OF MEDICINE *(continued from p. 689)*

nitroglycerin
(nye-troh-GLIS-eh-rin)
[*nitro-* **nitrogen**, *-glyc-* **sweet** (**sugar**), *-in* **substance**]

percutaneous coronary intervention (PCI)
(perkyoo-TAYN-ee-us KOR-oh-nair-ee in-ter-VEN-shun)
[*per-* **through**, *cut-* **skin**, *-aneous* **relating to**, *corona-* **crown**, *-ary* **relating to**, *inter-* **between**, *-ven-* **go**, *-tion* **process**]

pericardial effusion
(pair-i-KAR-dee-all ef-FYOO-shen)
[*peri-* **around**, *-cardi-* **heart**, *-al* **relating to**, *e(x)-* **outside**, *-fus-* **pour**, *-sion* **process**]

pericardiocentesis
(pair-ee-KAR-dee-oh-sen-TEE-sis)
[*peri-* **around**, *-cardi-* **heart**, *-centesis* **pricking**]

pericarditis
(pair-i-kar-DYE-tis)
[*peri-* **around**, *-cardi-* **heart**, *-itis* **inflammation**]

peripheral arterial disease (PAD)
(peh-RIF-er-al ar-TEER-ee-al)
[*peri-* **around**, *-pher-* **boundary**, *-al* **relating to**, *-arteri-* **vessel**, *-al* **relating to**, *dis-* **opposite of**, *-ease* **comfort**]

peripheral vascular disease (PVD)
(peh-RIF-er-al VAS-kyoo-lar)
[*peri-* **around**, *-pher-* **boundary**, *-al* **relating to**, *-vas-* **vessel**, *-ular* **relating to**, *dis-* **opposite of**, *-ease* **comfort**]

phlebitis
(fleh-BYE-tis)
[*phleb-* **vein**, *-itis* **inflammation**]

pulmonary edema
(PUL-moh-nair-ee eh-DEE-mah)
[*pulmon-* **lung**, *-ary* **relating to**, *edema* **swelling**]

pulmonary embolism
(PUL-moh-nair-ee EM-boh-liz-em)
[*pulmon-* **lung**, *-ary* **relating to**, *embol-* **plug**, *-ism* **condition**]

rheumatic fever
(roo-MAT-ik FEE-ver)
[*rheuma-* **flow**, *-ic* **relating to**]

rheumatic heart disease
(roo-MAT-ik)
[*rheuma-* **flow**, *-ic* **relating to**, *dis-* **opposite of**, *-ease* **comfort**]

shunt

stenosed valve
(steh-NOSD)
[*stenos-* **narrow**, *-osis* **condition**]

stent

stroke

thrombophlebitis
(throm-boh-fleh-BYE-tis)
[*thrombo-* **clot**, *-phleb-* **vein**, *-itis* **inflammation**]

tissue plasminogen activator (t-PA)
(TISH-yoo plaz-MIN-oh-jen AK-ti-vay-tor)
[*tissue-* **fabric**, *plasm-* **substance** (**plasma**), *-in-* **substance**, *-gen* **produce**]

troponins test
(TROH-poh-ninz)
[*tropo-* **turn**, *-in* **substance**]

valvuloplasty
(VAL-vyoo-loh-plas-tee)
[*valv-* **folding door** (**valve**), *-plasty* **surgical repair**]

varicose vein
(VAIR-i-kohse)
[*varic-* **swollen vein**, *-ose* **characterized by**]

varix
(VAIR-iks)
[*varix* **swollen vein**] *pl.,* varices

vasodilator
(vay-so-DYE-lay-tor)
[*vas-* **vessel or duct**, *-dilat-* **widen**, *-or* **agent**]

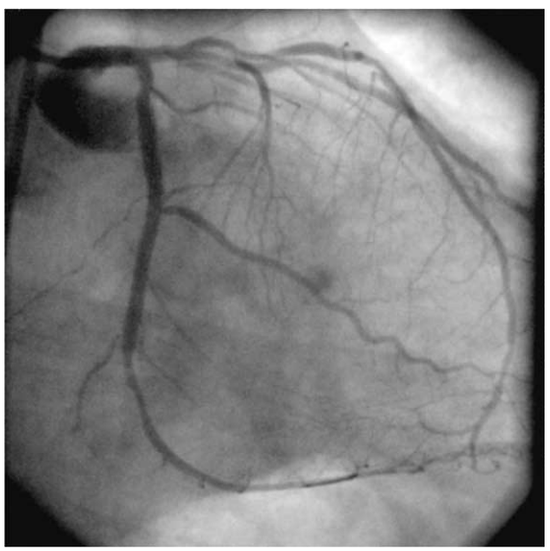
CASE study

Kyle (45 years old) finally gave in to his wife's insistence and stopped by his doctor's office. After all, it was in the same building where he was working on a construction job. He had been having some minor chest pain for a couple of days. But, he'd been telling himself the pain was just sore muscles caused by his recent weight-lifting. Kyle was expecting the receptionist to make an appointment for him. However, as he described his symptoms (chest pain, some sweating, slight nausea), she interrupted him and called over her shoulder to the triage nurse. As soon as the nurse was made aware of his symptoms, Kyle was rushed into an exam room, where his heart rate and blood pressure were checked and then the electrical activity of his heart was measured (by performing an ECG).

"What's going on?" he asked the doctor a few minutes later. The doctor replied, "Based on your symptoms, we think you may have some blockage in your coronary arteries. We'd like to do an angiogram to see what's going on."

1. The doctor suspects the potential blockage is in what part of Kyle's body?
   a. His brain
   b. His liver
   c. His neck
   d. His heart

"Let's take him over to the Cath Lab," ordered the doctor. Kyle said, "I've heard of a cath lab, but I'm not sure what that means." "Cardiac



catheterization lab," clarified the nurse. "We're going to insert a small tube…" She kept talking, but Kyle couldn't concentrate on her words. He was suddenly feeling a little anxious. He signed the consent form without really reading it.

In the lab, Kyle changed into a hospital gown as instructed; next he was asked to lie on the table. A nurse began cleaning a spot on his thigh

CASE study *(continued)*

in preparation for inserting a catheter. Kyle was confused—why were they cleaning his leg when it seemed like his heart was the problem?

2. Into which artery will the catheter be inserted?
   a. Brachial
   b. Popliteal
   c. Femoral
   d. Tibial

3. From this artery, the catheter will be moved toward the heart through which path?
   a. External iliac artery, abdominal aorta, descending aorta, aortic arch, ascending aorta
   b. Internal iliac artery, abdominal aorta, ascending aorta, aortic arch, descending aorta
   c. Abdominal aorta, descending aorta, aortic arch, ascending aorta
   d. Popliteal artery, external iliac artery, abdominal aorta, thoracic aorta, aortic arch

After some dye was injected, the screen monitor showed that Kyle's right coronary artery was partially blocked. The surgeon inserted a balloon through the catheter, which was then inflated to press against the sides of the artery and enlarge its diameter. Next she inserted a metal stent to keep the artery open.

4. The coronary arteries supply oxygen and nutrients for cardiac muscle contraction. The myocardium of which heart chamber receives the most abundant blood supply from the coronary arteries?
   a. Left atrium
   b. Left ventricle
   c. Right atrium
   d. Right ventricle

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

HEART

A. Location of the heart (Figure 21-2)
   1. Lies in the mediastinum, behind the body of the sternum between the points of attachment of ribs two through six; approximately two thirds of its mass is to the left of the midline of the body, and one third is to the right
   2. Posteriorly the heart rests on the bodies of thoracic vertebrae five through eight
   3. Apex lies on the diaphragm, pointing to the left
   4. Base lies just below the second rib
   5. Boundaries of the heart are clinically important as an aid in diagnosing heart disorders

B. Size and shape of the heart (Figures 21-1 and 21-2)
   1. At birth, the heart is transverse and appears large in proportion to the diameter of the chest cavity
   2. Between puberty and 25 years of age, the heart attains its adult shape and weight
   3. In adults, the shape of the heart tends to resemble that of the chest

C. Coverings of the heart
   1. Structure of the heart coverings
      a. Pericardium (Figure 21-4)
         (1) Fibrous pericardium—tough, loose-fitting inextensible sac
         (2) Serous pericardium—parietal layer lies inside the fibrous pericardium, and visceral layer (epicardium) adheres to the outside of the heart
         (3) Pericardial space—lies between visceral and parietal layers and contains 10 to 15 ml of pericardial fluid
   2. Function of the heart coverings—provides protection against friction

D. Structure of the heart
   1. Wall of the heart—made up of three distinct layers (Figure 21-5)
      a. Epicardium—outer layer of heart wall
      b. Myocardium—thick, contractile middle layer of heart wall; compresses the heart cavities, and the blood within them, with great force
      c. Endocardium—delicate inner layer of endothelial tissue
   2. Chambers of the heart—divided into four cavities with the right and left chambers separated by the septum (Figures 21-6 and 21-7)
      a. Atria
         (1) Two superior chambers known as "receiving chambers" because they receive blood from veins
         (2) Atria alternately relax to receive blood and then contract to push blood into ventricles
         (3) Myocardial wall of each atrium is not very thick, because little pressure is needed to move blood such a small distance
         (4) Auricle—earlike flap protruding from each atrium
      b. Ventricles
         (1) Two lower chambers known as "pumping chambers" because they push blood into the large network of vessels

UNIT 4

(2) Ventricular myocardium is thicker than the myocardium of the atria because great force must be generated to pump the blood a large distance; myocardium of left ventricle is thicker than the right, because it must push blood much farther

3. Valves of the heart—mechanical devices that permit the flow of blood in one direction only (Figure 21-8)
   a. Atrioventricular (AV) valves—prevent blood from flowing back into the atria from the ventricles when the ventricles contract
      (1) Tricuspid valve (right AV valve)—guards the right atrioventricular orifice; free edges of three flaps of endocardium are attached to papillary muscles by chordae tendineae
      (2) Bicuspid, or mitral, valve (left AV valve)—similar in structure to tricuspid valve except has only two flaps
   b. Semilunar (SL) valves—half-moon–shaped flaps growing out from the lining of the pulmonary trunk and aorta; prevent blood from flowing back into the ventricles from the aorta and pulmonary trunk
      (1) Pulmonary valve—valve at entrance of the pulmonary trunk
      (2) Aortic valve—valve at entrance of the aorta
   c. Skeleton of the heart
      (1) Set of connected rings that serve as a semirigid support for the heart valves and for the attachment of cardiac muscle of the myocardium
      (2) Serves as an electrical barrier between the myocardium of the atria and that of the ventricles
   d. Surface projection (review Figure 21-9)
   e. Flow of blood through heart (review Figure 21-7)
4. Coronary circulation—blood supply of heart tissue (Figures 21-10, 21-11, and 21-12)
   a. Coronary arteries—myocardial cells receive blood from the right and left coronary arteries
      (1) First branches to come off the aorta
      (2) Ventricles receive blood from branches of both right and left coronary arteries
      (3) Each ventricle receives blood only from a small branch of the corresponding coronary artery
      (4) Most abundant blood supply goes to the myocardium of the left ventricle
      (5) Right coronary artery is dominant in approximately 50% of all hearts and the left in about 20%; in approximately 30%, neither coronary artery is dominant
      (6) Few anastomoses exist between the larger branches of the coronary arteries
   b. Cardiac veins
      (1) As a rule, veins follow a course that closely parallels that of coronary arteries
      (2) After going through cardiac veins, blood enters the coronary sinus to drain into the right atrium
      (3) Several veins drain directly into the right atrium
5. Nerve supply of the heart
   a. Conduction system of the heart—made up of modified cardiac muscle, it generates and distributes the heart's own rhythmic contractions; can be regulated by afferent nerves
   b. Cardiac plexuses—located near the arch of the aorta, made up of the combination of sympathetic and parasympathetic fibers
   c. Fibers from the cardiac plexus accompany the right and left coronary arteries to enter the heart
   d. Most fibers end in the SA node, but some end in the AV node and in the atrial myocardium; the SA node acts as the heart's pacemaker (Chapter 22)
   e. Sympathetic nerves—accelerator nerves
   f. Vagus fibers—inhibitory, or depressor, nerves

BLOOD VESSEL TYPES

A. Types of blood vessels (Figures 21-13 and 21-14)
   1. Angiogenesis—formation of new blood vessels
   2. Arteries
      a. Carry blood away from heart—all arteries except pulmonary artery carry oxygenated blood
      b. Elastic (conducting) arteries—largest in body
         (1) Examples: aorta and its major branches
         (2) Able to stretch without injury
         (3) Accommodate surge of blood when heart contracts and able to recoil when ventricles relax
      c. Muscular (distributing) arteries
         (1) Smaller in diameter than elastic arteries
         (2) Muscular layer is thick
         (3) Examples: brachial, gastric, superior mesenteric
      d. Arterioles (resistance vessels)
         (1) Smallest arteries
         (2) Important in regulating blood flow to end organs
      e. Metarterioles
         (1) Short connecting vessel between true arteriole and 20 to 100 capillaries
         (2) Encircled by precapillary sphincters
         (3) Distal end called *thoroughfare channel*, which is free of precapillary sphincters
   3. Capillaries—primary exchange vessels
      a. Microscopic vessels
      b. Carry blood from arterioles to venules—together, arterioles, capillaries, and venules constitute the microcirculation (Figure 21-15)
      c. Not evenly distributed—highest numbers in tissues with high metabolic rate; may be absent in some "avascular" tissues, such as cartilage
      d. Types of capillaries (Figure 21-16)
         (1) True capillaries—receive blood flowing from metarteriole with input regulated by precapillary sphincters
         (2) Continuous capillaries
            (a) Continuous lining of endothelial cells
            (b) Openings called *intercellular clefts* exist between adjacent endothelial cells
         (3) Fenestrated capillaries
            (a) Have both intercellular clefts and "holes" or fenestrations through plasma membrane to facilitate exchange functions

(4) Sinusoids
(a) Large lumen and tortuous course
(b) Absent or incomplete basement membrane
(c) Very porous—permit migration of cells into or out of vessel lumen

4. Veins
a. Carry blood toward the heart
b. Act as collectors and as reservoir vessels; called *capacitance vessels*

B. Structure of blood vessels (Figure 21-13 and 21-14)
1. Components or "building blocks" commonly present
a. Lining endothelial tissue—one layer of squamous endothelial cells
(1) Only lining found in capillary
(2) Lines entire vascular tree
(3) Provides a smooth luminal surface—protects against intravascular coagulation
(4) Intercellular clefts, cytoplasmic pores, and fenestrations in cells allow exchange to occur between blood and tissue fluid
(5) Capable of secreting a number of substances
(6) Capable of reproduction
b. Collagen fibers
(1) Exhibit woven appearance
(2) Formed from protein molecules that aggregate into fibers
(3) Visible with light microscope
(4) Have only a limited ability to stretch (2% to 3%) under physiological conditions
(5) Function to strengthen and keep lumen of vessel open
c. Elastic fibers
(1) Composed of insoluble protein called *elastin*
(2) Form highly elastic networks
(3) Wavy fibers can stretch more than 100% under physiological conditions
(4) Play important role in creating passive tension to help regulate blood pressure throughout the cardiac cycle
d. Smooth muscle tissue
(1) Present in all segments of vascular system except capillaries
(2) Most abundant in elastic and muscular arteries
(3) Exerts active tension in vessels when contracting

2. Layers
a. Tunica externa—found in arteries and veins (tunica adventitia)
b. Tunica media—found in arteries and veins
c. Tunica intima—found in all blood vessels; only layer present in capillaries

MAJOR BLOOD VESSELS

A. Circulatory routes (Figure 21-17)
1. Systemic circulation—blood flows from the left ventricle of the heart through blood vessels to all parts of the body (except gas exchange tissues of lungs) and back to the right atrium
2. Pulmonary circulation—deoxygenated blood moves from right atrium to right ventricle to pulmonary artery to lung arterioles and capillaries, where gases are exchanged; oxygenated blood returns to left atrium by way of pulmonary veins; from left atrium, blood enters the left ventricle

B. Systemic circulation
1. Systemic arteries (review Table 21-2 and Figures 21-18 to 21-26)
a. Main arteries give off branches, which continue to rebranch, forming arterioles and then capillaries
b. End-arteries—arteries that eventually diverge into capillaries
c. Arterial anastomosis—arteries that open into other branches of the same or other arteries; incidence of arterial anastomoses increases as distance from the heart increases
d. Arteriovenous anastomoses or shunts occur when blood flows from an artery directly into a vein

2. Systemic veins (review Table 21-3 and Figures 21-27 to 21-34)
a. Veins are the ultimate extensions of capillaries; unite into vessels of increasing size to form venules and then veins
b. Large veins of the cranial cavity are called *dural sinuses*
c. Veins anastomose the same as arteries
d. Venous blood from the head, neck, upper extremities, and thoracic cavity (except lungs) drains into superior vena cava
e. Venous blood from thoracic organs drains directly into superior vena cava or azygos vein
f. Hepatic portal circulation (Table 21-34 and Figures 21-17 and 21-32)
(1) Veins from the spleen, stomach, pancreas, gallbladder, and intestines send their blood to the liver by way of the hepatic portal vein
(2) In the liver the venous blood mingles with arterial blood in the sinusoids and is eventually drained from the liver by hepatic veins that join the inferior vena cava
g. Venous blood from the lower extremities and abdomen drains into the inferior vena cava

C. Fetal circulation
1. Basic plan of fetal circulation—additional vessels needed to allow fetal blood to secure oxygen and nutrients from maternal blood at the placenta (Figure 21-36)
a. Two umbilical arteries—extensions of the internal iliac arteries; carry fetal blood to the placenta
b. Placenta—attached to uterine wall; where exchange of oxygen and other substances between the separated maternal and fetal blood occurs (Figure 21-35)
c. Umbilical vein—returns oxygenated blood from the placenta to the fetus; enters body through the umbilicus and goes to the undersurface of the liver where it gives off two or three branches and then continues as the ductus venosus
d. Ductus venosus—continuation of the umbilical vein and drains into inferior vena cava

e. Foramen ovale—opening in septum between the right and left atria
f. Ductus arteriosus—small vessel connecting the pulmonary trunk with the aortic arch

2. Changes in circulation at birth (compare Figures 21-36 and 21-37)
   a. When umbilical cord is cut, the two umbilical arteries, the placenta and umbilical vein, no longer function
   b. Umbilical vein within the baby's body becomes the round ligament of the liver
   c. Ductus venosus becomes the ligamentum venosum of the liver
   d. Foramen ovale—functionally closed shortly after a newborn's first breath and pulmonary circulation is established; structural closure takes approximately 9 months
   e. Ductus arteriosus—contracts with establishment of respiration, becomes ligamentum arteriosum

CYCLE OF LIFE: CARDIOVASCULAR ANATOMY

A. Birth—change from placenta-dependent system
B. Heart and blood vessels maintain basic structure and function from childhood through adulthood
C. Only apparent normal changes occur as a result of exercise
   1. Exercise thickens myocardium
   2. Exercise increases the supply of blood vessels in skeletal muscle tissue
D. Adulthood through later adulthood—degenerative changes
   1. Atherosclerosis—blockage or weakening of critical arteries (Figure 21-43)
   2. Heart valves and myocardial tissue degenerate—reduces pumping efficiency

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Discuss the size, position, and location of the heart in the thoracic cavity.
2. Describe the pericardium, differentiating between the fibrous and serous portions.
3. Exactly where is pericardial fluid found? Explain its function.
4. Define the following terms: *intercalated disks, syncytium, autorhythmic.*
5. Name and locate the chambers and valves of the heart.
6. Trace the flow of blood through the heart.
7. Identify, locate, and describe the functions of each of the following structures: SA node, AV node, AV bundle.
8. Identify the vessels that join to form the hepatic portal vein.
9. Describe the six unique structures necessary for fetal circulation.
10. Explain how the separation of oxygenated and deoxygenated blood occurs after birth.
11. Explain the purpose of echocardiography.
12. Identify the clinical significance of cardiac markers.
13. How might a jugular vein spread infection?
14. Briefly define the following terms: *aneurysm, atherosclerosis, phlebitis.*
15. Identify possible causes of coronary artery disease.
16. Define congestive heart failure.
17. Explain how hemorrhoids develop.

CRITICAL THINKING QUESTIONS

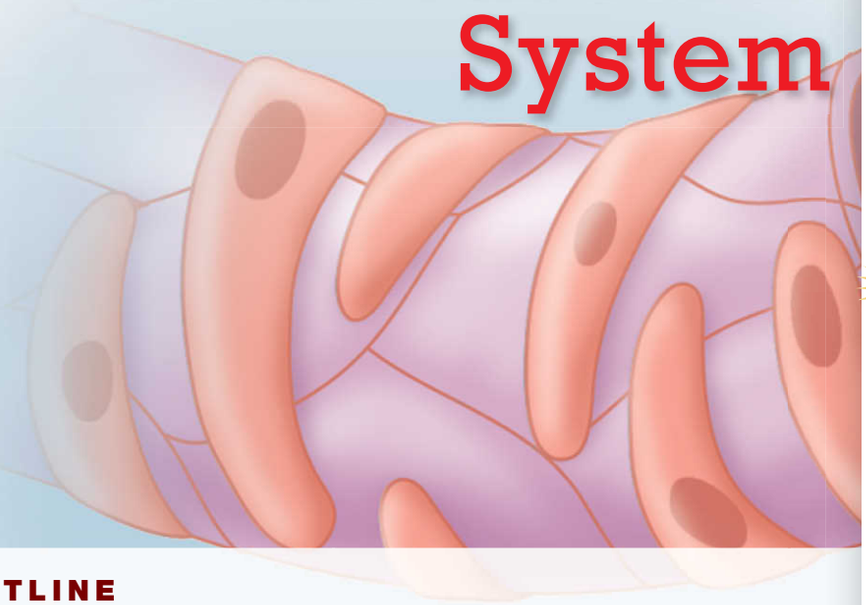


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. How is CPR accomplished? What is the significance of the placement of the heart in the thoracic cavity and successful CPR?
2. What would result if there were a lack of anastomosis in the arteries of the heart?
3. The general public thinks the most important structure in the cardiovascular system is the heart. Anatomists know it is the capillary. What information would you use to support this view?
4. Compare and contrast arterial blood in systemic circulation and arterial blood in pulmonary circulation.
5. Explain the distinction between an occlusion of an end-artery and an occlusion of other small arteries?
6. Determine which of the following veins drain into the superior vena cava and which drain into the inferior vena cava: longitudinal sinus, great saphenous, basilic, internal jugular, azygos, popliteal, and hepatic portal.
7. Describe the functional advantage of a portal system.
8. Naming the vessels and organs involved, trace the path taken by a single RBC. Begin at the right atrium, proceed to the left great toe, and return to the right atrium.
9. Explain the changes that occur in the cardiovascular system during the normal cycle of one's life.

Physiology of the Cardiovascular System

22



CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

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The Big Picture: Blood Flow and the Whole Body, 712

Mechanisms of Disease, 712

Case Study, 717

LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

aortic reflex
(ay-OR-tik REE-fleks)
[*aort-* **lifted,** *-ic* **relating to,** *re-* **back or again,** *-flex* **bend**]

atrioventricular (AV) bundle
(ay-tree-oh-ven-TRIK-yoo-lar BUN-del)
[*atrio-* **entrance courtyard,** *-ventr-* **belly,** *-icul-* **little,** *-ar* **relating to**]

atrioventricular (AV) node
(ay-tree-oh-ven-TRIK-yoo-lar)
[*atrio-* **entrance courtyard,** *-ventr-* **belly,** *-icul-* **little,** *-ar* **relating to,** *-ar* **relating to,** *nod-* **knot**]

baroreceptor
(bar-oh-ree-SEP-tor)
[*baro-* **pressure,** *-recept-* **receive,** *-or* **agent**]

capillary exchange
(KAP-i-lair-ee)
[*capill-* **hair,** *-ary* **relating to**]

cardiac cycle
(KAR-dee-ak)
[*cardi-* **heart,** *-ac* **relating to,** *cycle* **circle**]

cardiac output (CO)
(KAR-dee-ak)
[*cardi-* **heart,** *-ac* **relating to**]

carotid sinus reflex
(kah-ROT-id SYE-nus REE-fleks)
[*caro-* **heavy sleep,** *-id* **relating to,** *sinus* **hollow,** *re-* **back or again,** *-flex* **bend**]

chemoreceptor reflex
(kee-moh-ree-SEP-tor REE-fleks)
[*chemo-* **chemical,** *-recept-* **receive,** *-or* **agent,** *re-* **back or again,** *-flex* **bend**]

continued on p. 715

UNIT 4

The vital role of the cardiovascular system in maintaining homeostasis depends on the continuous and controlled movement of blood through the thousands of miles of capillaries that permeate every tissue and reach every cell in the body. It is in the microscopic capillaries that blood performs its ultimate transport function. Nutrients and other essential materials pass from capillary blood into fluids surrounding the cells as waste products are removed. Blood must not only be kept moving through its closed circuit of vessels by the pumping activity of the heart, but also must be directed and delivered to those capillary beds surrounding cells that need it most. Blood flow to cells at rest is minimal. In contrast, blood is shunted to the digestive tract after a meal or to skeletal muscles during exercise. The thousands of miles of capillaries could hold far more than the body's total blood volume if it were evenly distributed. Because variations in cellular activity require uneven distribution of blood, regulation of blood pressure and flow must change in response to cellular activity.

Numerous control mechanisms help regulate and integrate the diverse functions and component parts of the cardiovascular system to supply blood to specific body areas according to need. These mechanisms ensure a constant ***milieu intérieur,*** *that is, a constant internal environment surrounding each body cell regardless of differing demands for nutrients or production of waste products. This chapter explores the control mechanisms that regulate the pumping activity of the heart and the smooth and directed flow of blood through the complex channels of the circulation.*

HEMODYNAMICS

Hemodynamics is a term used to describe a collection of mechanisms that influence the active and changing—or dynamic—circulation of blood (Figure 22-1). Circulation is, of course, a vital function. It constitutes the only means by which cells can receive materials needed for their survival and can have their wastes removed. Circulation is necessary, and circulation of different volumes of blood per minute at different times is also essential for healthy survival. For example, more active cells need more blood per minute than less active cells. The reason underlying this principle is obvious. The more work cells do, the more energy they use, and the more oxygen and nutrients they remove from the blood. Because blood circulates, it can continually bring in more oxygen and nutrients to replace what is consumed. The greater the activity of any part of the body, the greater the volume of blood circulating through it. This requires that circulation control mechanisms accomplish two functions: maintain circulation (keep blood flowing) and vary the volume and distribution of the blood circulated. Therefore as any structure increases its activity, an increased volume of blood must be distributed to it; that is, blood must be shifted from the less active tissues to the more active tissues.

To achieve these two ends, a great many factors must operate together as one smooth-running, although complex, machine. Incidentally, this is an important physiological principle that you have no doubt observed by now—that every body function depends on many other functions. A constellation of separate processes or mechanisms acts as a single integrated mechanism.

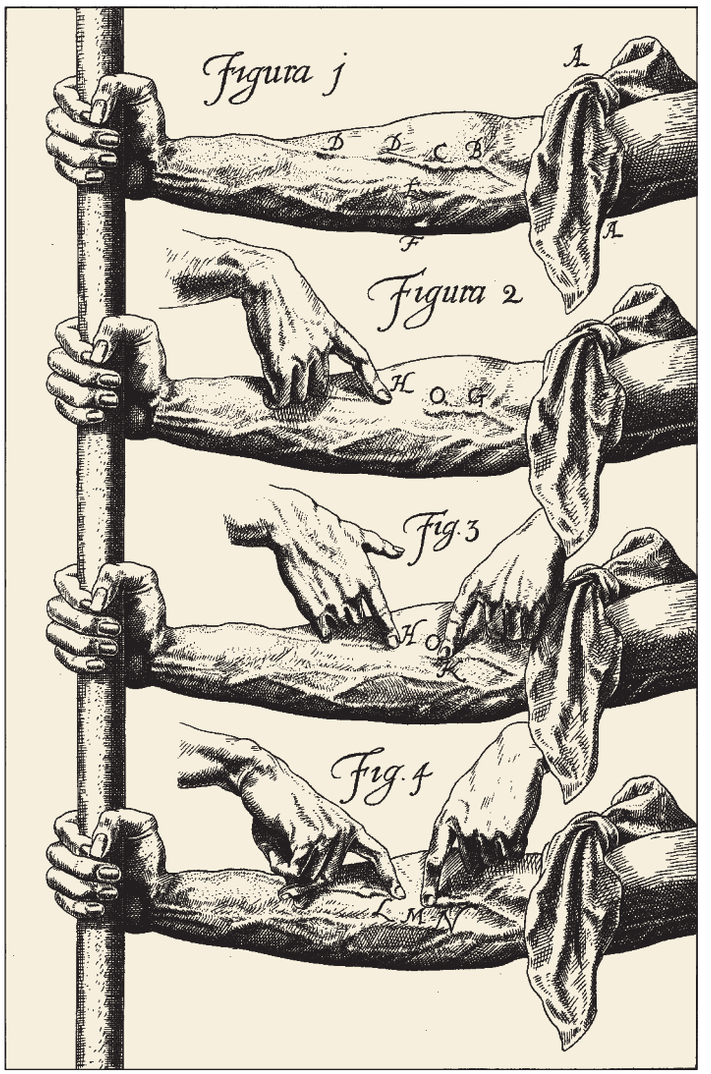


FIGURE 22-1

Hemodynamics. An illustration of a famous experiment in hemodynamics conducted by English scientist William Harvey in the early seventeenth century. Through a series of such experiments, Harvey finally proved that blood flows in a circuit out through the arteries and back through the veins—a concept on which most other hemodynamic concepts are based.

Together, these separate mechanisms perform one large function. For example, many mechanisms together accomplish the large function we call *circulation*.

This chapter is about hemodynamics—the mechanisms that keep blood flowing properly. We begin with a discussion of the heart as a pump and then move on to the even bigger picture of blood flow through the entire cardiovascular system.

THE HEART AS A PUMP

In Chapter 21 we discussed the functional anatomy of the heart. Its four chambers and their valves make up two pumps: a left pump and a right pump. The left pump (left side of the heart) helps move blood through the systemic circulation, and the right pump (right side of the heart) helps move blood through the pulmonary circulation. We will now step back from our previous discussion of the valves and chambers of the heart to look at the bigger picture and see how these two linked pumps function together as a single unit. First, we will discuss the role of the electrical conduction system of the heart in coordinating heart contractions. Then we will discuss how these coordinated contractions produce the pumping cycle of the heart.

Conduction System of the Heart

For the heart to pump effectively, the impulses (action potentials) that trigger myocardial contraction must be coordinated carefully. This requires a system for generating rhythmic impulses and distributing them quickly to the different regions of the myocardium along impulse-conducting pathways. Without such a system, different regions of the myocardium would be contracting too slowly and at slightly different rates.

Four structures make up the core of the electrical conduction system of the heart:

1. **Sinoatrial (SA) node**
2. **Atrioventricular (AV) node**
3. **AV bundle** (bundle of His)
4. **Subendocardial branches** (Purkinje fibers)

These structures are represented in Figure 22-2 and described in the following paragraphs.

Each of the structures of the heart's conduction system consists of cardiac muscle modified enough in structure to differ in function from ordinary cardiac muscle. The specialty of ordinary cardiac muscle is contraction. In this, it is like all muscle, and like all muscle, ordinary cardiac muscle can also conduct impulses. However, the myocardial fibers of the conduction system are more highly specialized, both structurally and functionally, than ordinary cardiac muscle tissue. They are not contractile. Instead, they permit only generation or rapid conduction of an action potential through the heart.

The normal cardiac impulse that initiates mechanical contraction of the heart arises in the SA node (or **pacemaker**), located just beneath the right atrial epicardium at its junction with the superior vena cava (Figure 22-2, A). Pacemaker cells in the node possess an *intrinsic rhythm*. This means that without any stimulation by nerve impulses from the brain and cord, they themselves initiate impulses at regular intervals. Even if pacemaker cells are removed from the

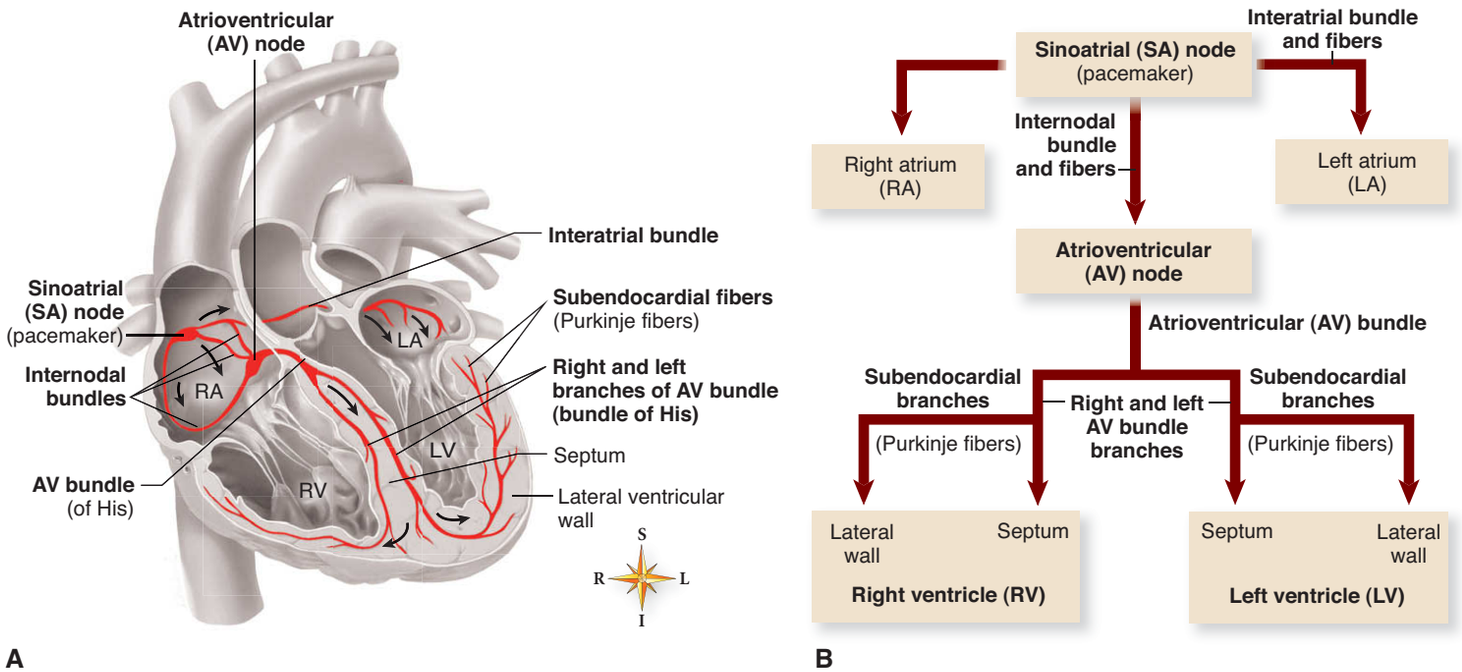


FIGURE 22-2

Conduction system of the heart. Specialized cardiac muscle cells *(boldface type)* in the wall of the heart rapidly initiate or conduct an electrical impulse throughout the myocardium. Both the sketch of the conduction system **(A)** and the flowchart **(B)** show the origin and path of conduction. The signal is initiated by the SA node (pacemaker) and spreads to the rest of the right atrial myocardium directly, to the left atrial myocardium by way of a bundle of interatrial conducting fibers, and to the AV node by way of three internodal bundles. The AV node then initiates a signal that is conducted through the ventricular myocardium by way of the AV bundle (of His) and subendocardial branches (Purkinje fibers).

body and placed in a nutrient solution, completely separated from all nervous and hormonal control, they will continue to beat! In an intact living heart, of course, nervous and hormonal regulation does occur and the SA node generates a pace accordingly.

Each impulse generated at the SA node travels swiftly throughout the muscle fibers of both atria. An **interatrial bundle** of conducting fibers facilitates rapid conduction to the left atrium. Thus stimulated, the atria begin to contract. As the action potential enters the AV node by way of three **internodal bundles** of conducting fibers, its conduction slows markedly, thus allowing for complete contraction of both atrial chambers before the impulse reaches the ventricles.

After passing slowly through the AV node, conduction velocity increases as the impulse is relayed through the AV bundle (bundle of His) into the ventricles. Here, right and left *bundle branches* and the subendocardial branches (Purkinje fibers) in which they terminate conduct the impulses throughout the muscle of both ventricles, stimulating them to contract almost simultaneously.

Thus the SA node initiates each heartbeat and sets its pace—it is the heart's own natural *pacemaker.* Under the influence of autonomic and endocrine control, the SA node will normally "discharge," or "fire," at an intrinsic rhythmical rate of 70 to 75 beats/min under resting conditions. However, if for any reason the SA node loses its ability to generate an impulse, pacemaker activity will shift to another excitable component of the conduction system, such as the AV node or the subendocardial branches (Purkinje fibers). Pacemakers other than the SA node are abnormal and are usually **ectopic pacemakers.** Ectopic is a word that means "out of place." Although ectopic pacemakers fire rhythmically, their rate of discharge is generally much slower than that of the SA node. For example, a pulse of 40 to 60 beats/min would result if the AV node were forced to assume pacemaker activity.

| A&P CONNECT |

If the heart's own pacemaker fails to maintain a healthy heart rhythm, an artificial pacemaker can be implanted to restore normal function. Check out ***Artificial Cardiac Pacemakers*** online at ***A&P Connect*** to see how this is done.

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Electrocardiogram (ECG)

ELECTROCARDIOGRAPHY

Impulse conduction generates tiny electrical currents in the heart that spread through surrounding tissues to the surface of the body.

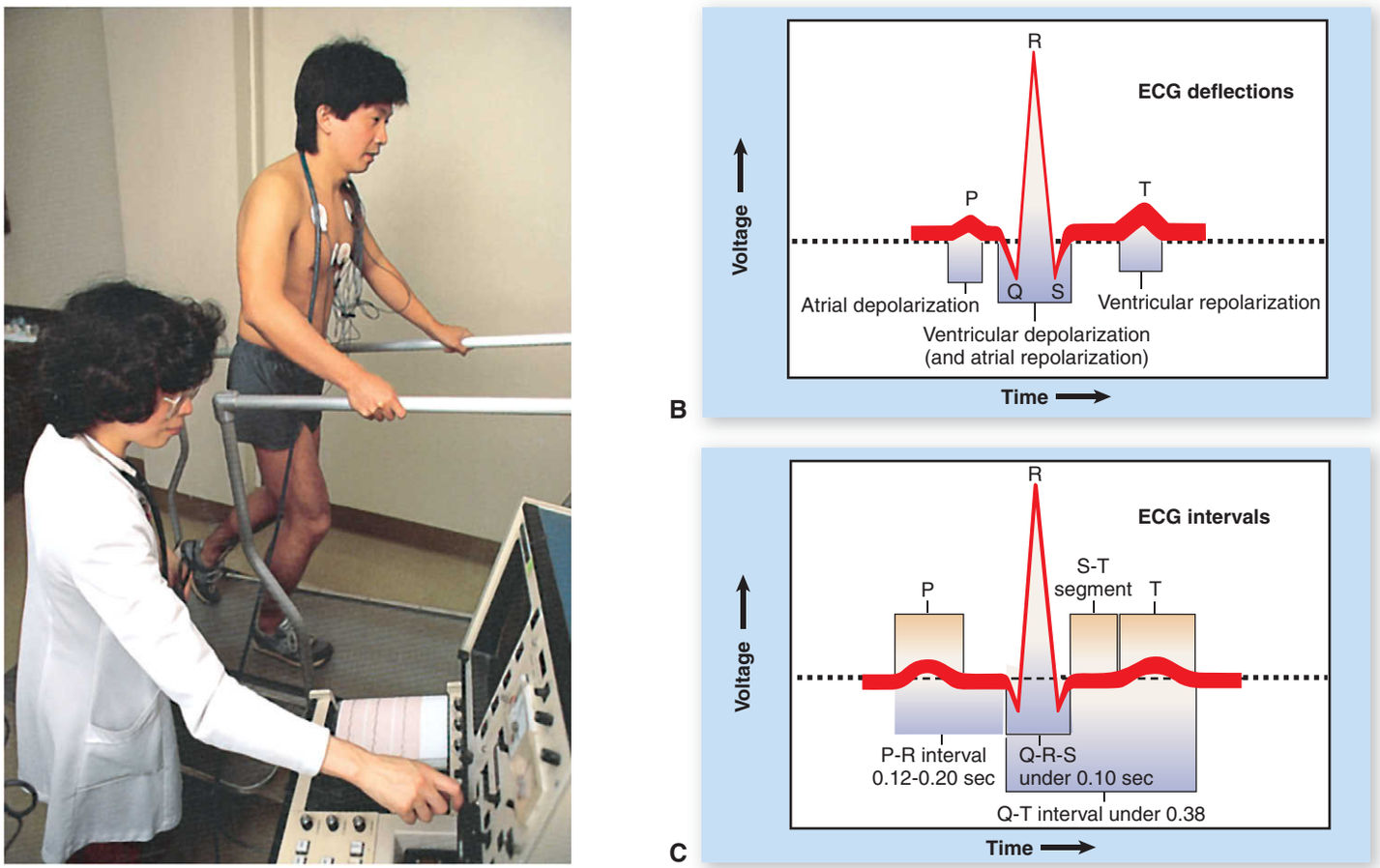


FIGURE 22-3

Electrocardiogram. A, A nurse monitors a patient's ECG as he exercises on a treadmill. **B,** Idealized ECG deflections represent depolarization and repolarization of cardiac muscle tissue. **C,** Principal ECG intervals between P, QRS, and T waves. Note that the P-R interval is measured from the start of the P wave to the start of the Q wave.

This fact has great clinical importance. Why? Because from the skin, visible records of the heart's electrical activity can be made with an instrument called an *electrocardiograph*. Skilled interpretation of these records may sometimes make the difference between life and death.

The **electrocardiogram** (**ECG** when written or **EKG** when spoken) is a graphic record of the heart's electrical activity, its conduction of impulses. It is not a record of the heart's contractions but of the *electrical events* that precede them. To produce an electrocardiogram, electrodes of a recording voltmeter (electrocardiograph) are attached to the limbs and/or chest of the subject (Figure 22-3, A). Changes in voltage, which represent changes in the heart's electrical activity, are observed as deflections of a line drawn on paper or traced on a video monitor.

Figure 22-4 explains the basic theory behind **electrocardiography.** To keep things simple, a single cardiac muscle fiber is shown with the two electrodes of a recording voltmeter nearby. Before the action potential reaches either electrode, there is no difference in charge between the electrodes, and thus no change in voltage is recorded on the voltmeter graph (Figure 22-4, step *1*). As an action potential reaches the first electrode, the external surface of the sarcolemma becomes relatively negative and so the voltmeter records a difference in charge between the two electrodes as an upward deflection of the pen on the recording chart (Figure 22-4, step 2). When the action potential also reaches the second electrode, the pen returns to the zero baseline because there is no difference in charge between the two electrodes (Figure 22-4, step 3). As the end of the action potential passes the first electrode, the sarcolemma

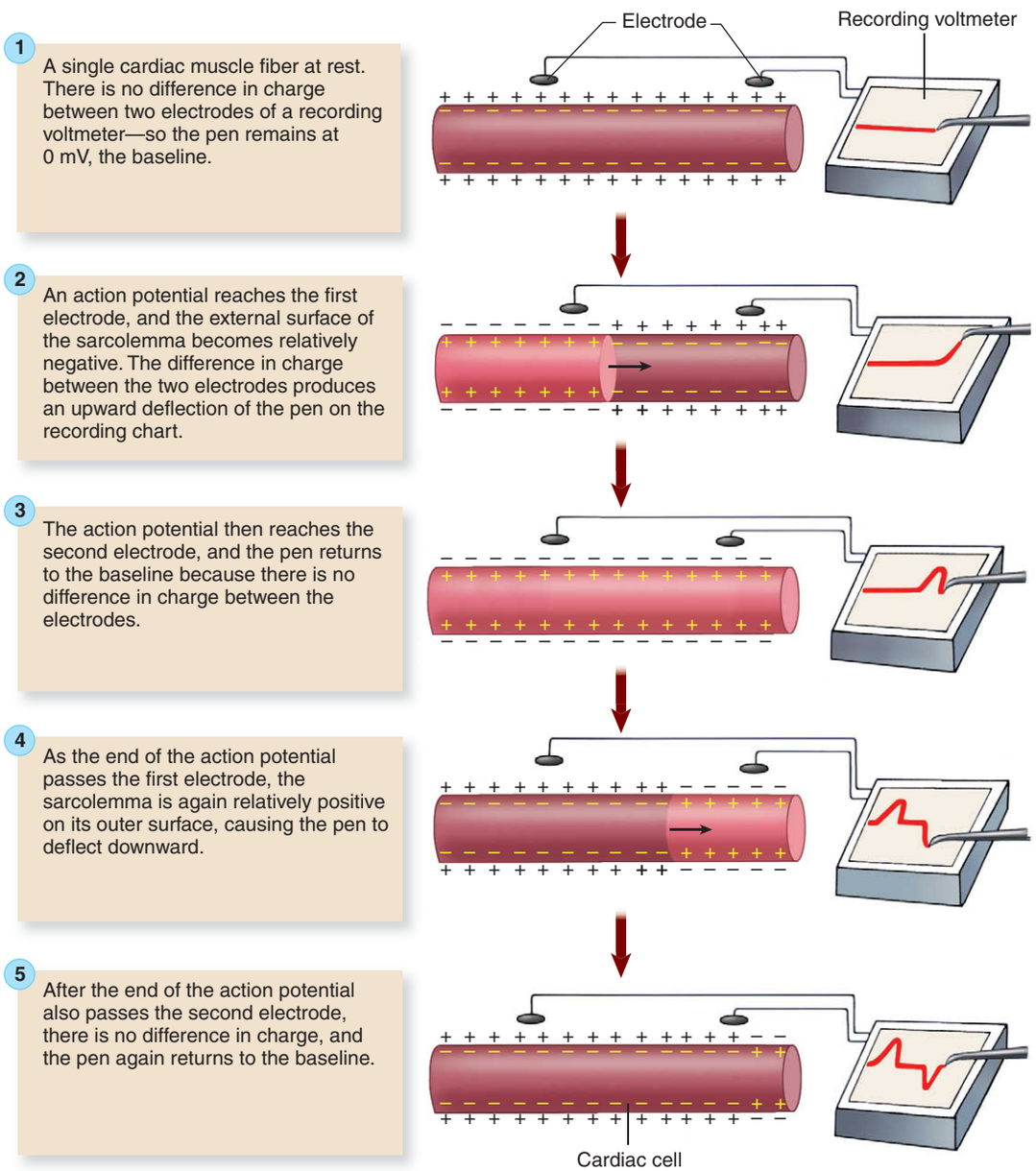


FIGURE 22-4

The basic theory of electrocardiography.

is again relatively positive on its outer surface, causing the pen to again deflect away from the baseline. This time, because the direction of the negative and positive electrodes is reversed, the pen deflects downward rather than upward (Figure 22-4, step 4). After the end of the action potential also passes the second electrode, the pen again returns to the zero baseline (Figure 22-4, step 5). In short, depolarization of cardiac muscle causes a deflection of the graphed line; repolarization causes a deflection in the opposite direction.

Electrocardiography electrodes are normally quite some distance from myocardial tissue, but, given the massive size of the myocardial syncytium, it should not be surprising that even cutaneous electrodes can detect changes in the heart's polarity.

| A&P CONNECT |

There are a number of locations and patterns of attaching ECG leads. Different ECG setups produce different results—thus allowing physicians to "see" the electrical activity of the heart from different angles. See how this is done in ***Electrocardiography*** online at ***A&P Connect.***

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ECG WAVES

Because electrocardiography is far too complex a subject to explain fully here, normal ECG *deflection waves* and the *ECG intervals* between them shall be discussed only briefly. As shown in Figures 22-3, *B*, and 22-5, the normal ECG is composed of deflection waves called the *P wave*, *QRS complex*, and *T wave*. (The letters do not represent any words; they are simply an arbitrarily chosen sequence of letters of the alphabet.)

P Wave

The **P wave** represents depolarization of the atria. That is, the P wave is the deflection caused by the passage of an electrical impulse from the SA node through the musculature of both atria. P wave abnormalities often reflect atrial enlargement.

QRS Complex

The **QRS complex** represents depolarization of the ventricles. Depolarization of the ventricles is a complex process, involving depolarization of the interventricular septum and the subsequent spread of depolarization by the subendocardial branches (Purkinje fibers) through the lateral ventricular walls. Rather than getting mired in a detailed explanation, let us simplify matters by stating that the combined duration of all three deflections of the QRS complex (Q, R, and S) represent the time required (0.07–0.11 seconds) for ventricular depolarization. (See Figure 22-2, C.)

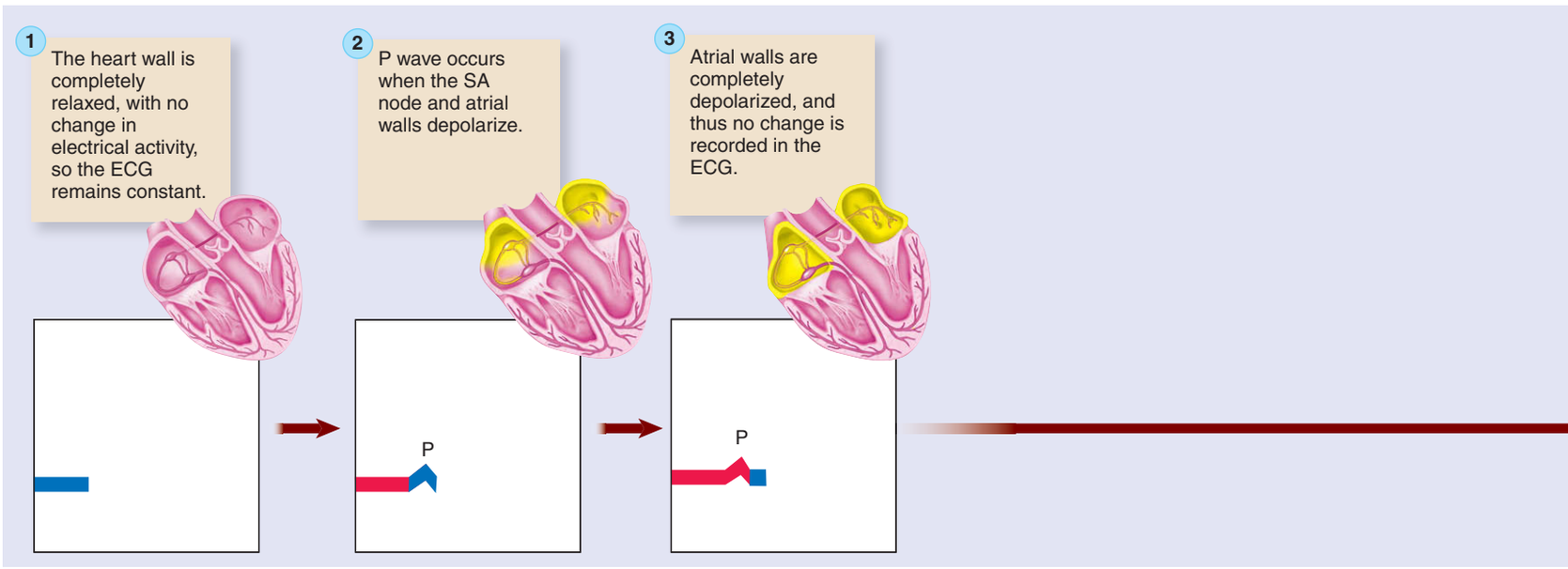
At the same time that the ventricles are depolarizing, the atria are repolarizing. As we explained earlier, we should expect to see a deflection that is opposite in direction to the P wave that represented depolarization. However, the massive ventricular depolarization that is occurring at the same time overshadows the voltage fluctuation produced by atrial repolarization. Thus we can say that the QRS complex represents both ventricular depolarization and atrial repolarization. If the QRS duration is prolonged, ventricular conduction delay is probably occurring.

T Wave

The **T wave** reflects repolarization of the ventricles. In atria, the first part of the myocardium to depolarize is the first to

FIGURE 22-5

Events represented by the electrocardiogram (ECG). It is impossible to illustrate the invisible, dynamic events of heart conduction in a few cartoon panels or "snapshots," but the sketches here give you an idea of what is happening in the heart as an ECG is recorded. Note that depolarization triggers contraction in the affected muscle tissue. Thus cardiac muscle contraction occurs *after* depolarization begins.



repolarize. In ventricles, on the other hand, the first part of the myocardium to depolarize is the last to repolarize. Thus ECG deflections for both depolarization and repolarization are in the same direction. An inverted T wave is often seen following myocardial muscle damage.

Sometimes, an additional **U wave** may be seen in the electrocardiogram (Figure 22-6). The U wave, when visible, appears as a tiny "hump" at the end of the T wave. The U wave is thought to represent late repolarization of subendocardial branches (Purkinje fibers) in the papillary muscle of the ventricular myocardium. However, some cardiologists believe it is simply a two-part T wave resulting from longer duration of the action potential in some ventricular myocardial cells. If not too big, U waves are usually considered to be normal. Sometimes, however, U waves can be a sign of **hypokalemia** (low blood potassium) or too much **digoxin** (a heart medication).

ECG INTERVALS

The principal ECG intervals between P, QRS, and T waves are shown in Figure 22-3, *C*. Measurement of these intervals can provide valuable information concerning the rate of conduction of an action potential through the heart, as we shall see later in this chapter. Figure 22-5 summarizes the relationship between the electrical events of the myocardium and the ECG recordings.

| QUICK CHECK |

1. List the principal structures of the heart's conduction system.
2. What are the three deflection waves seen in a typical ECG?
3. What event does each ECG wave represent?

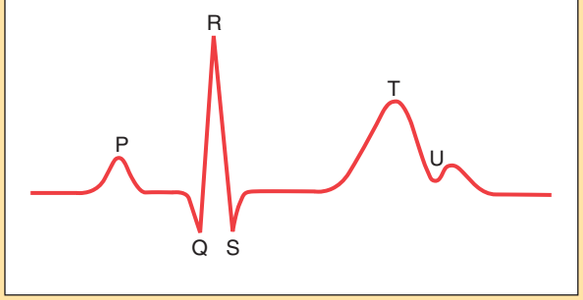
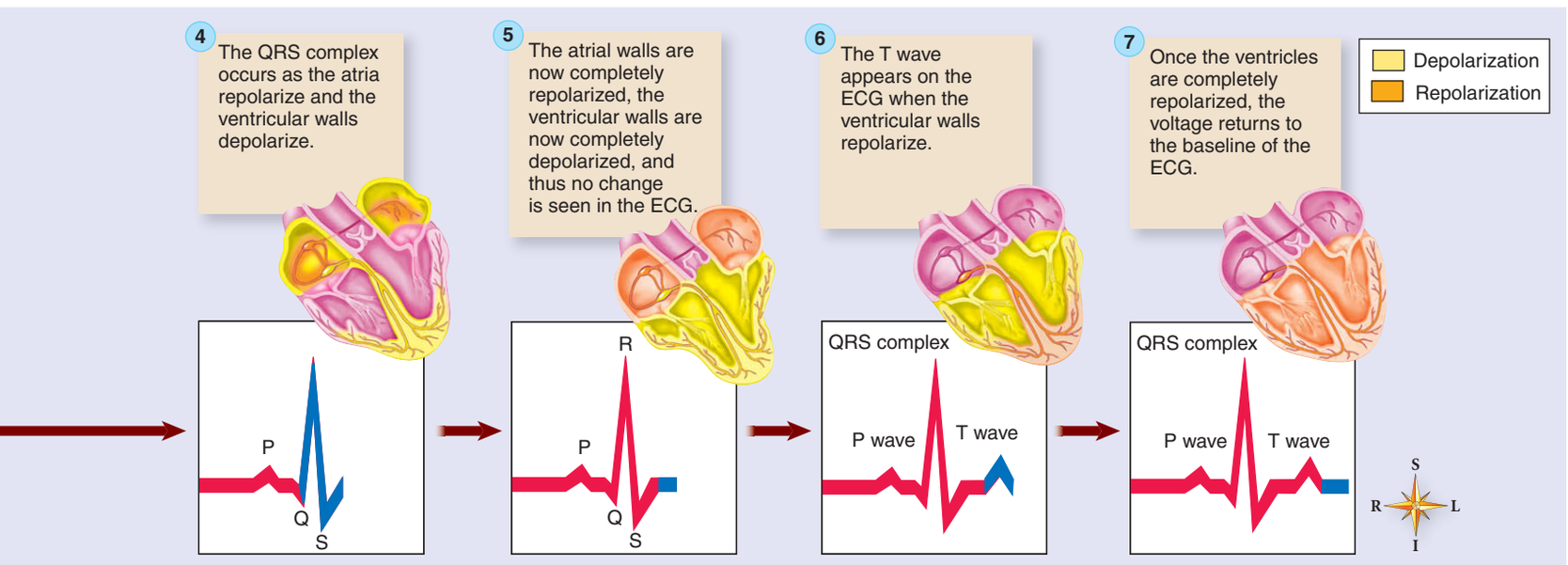


FIGURE 22-6

The U wave. This ECG recording shows the presence of a U wave, which follows the T wave—or appears as a "hump" on the back of the T wave. The U wave represents a sudden, late repolarization of subendocardial branches (Purkinje fibers) in the papillary muscle.

Cardiac Cycle

The term **cardiac cycle** means a complete heartbeat, or pumping cycle, consisting of contraction (**systole**) and relaxation (**diastole**) of both atria and both ventricles. The two atria contract simultaneously. Then, as the atria relax, the two ventricles contract and relax, instead of the entire heart contracting as a unit. This gives a kind of pumping action to the movements of the heart. The atria remain relaxed during part of the ventricular relaxation and then start the cycle over again. The cycle as a whole is often divided into time intervals for discussion and study. The following sections describe several of the important events of the cardiac cycle. As you read through these sections, refer frequently



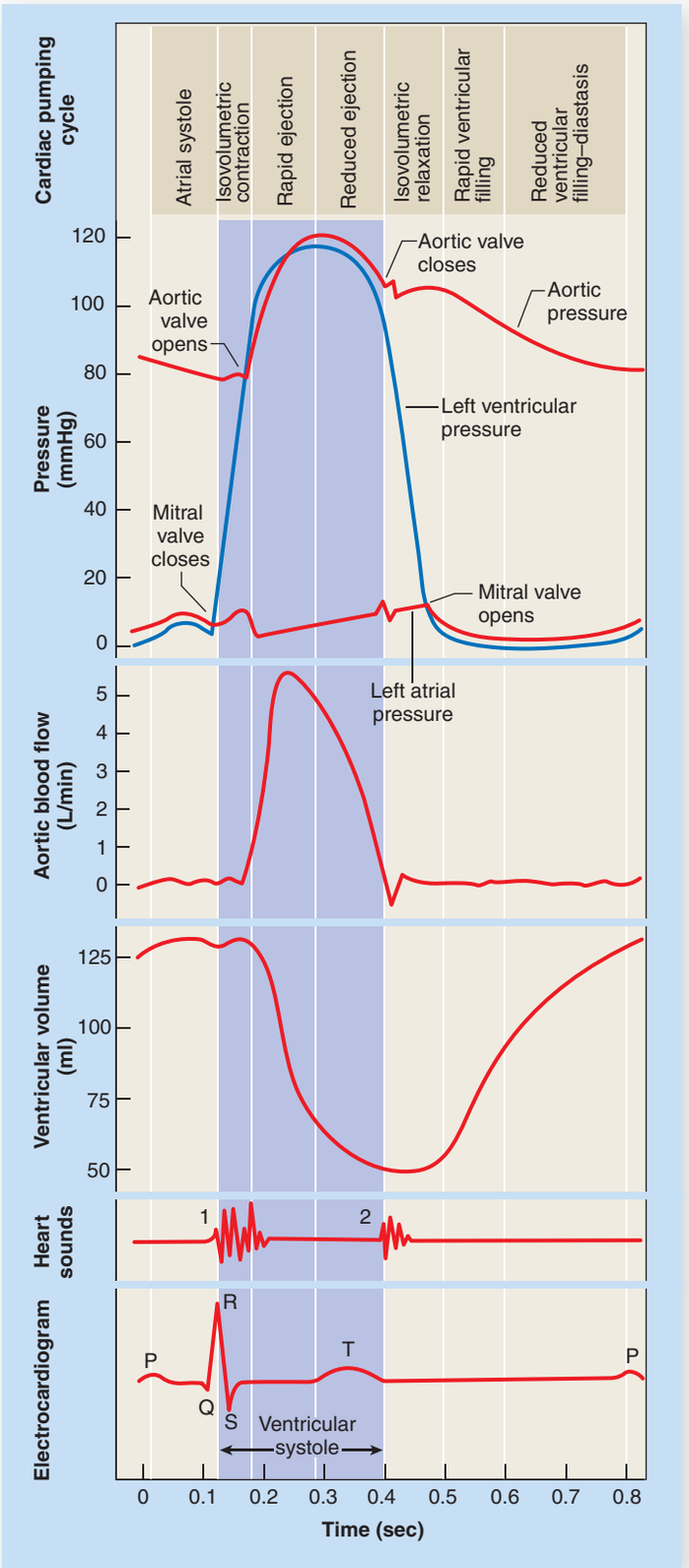


FIGURE 22-7

Composite chart of heart function. This chart is a composite of several diagrams of heart function (cardiac pumping cycle, blood pressure, blood flow, volume, heart sounds, and ECG), all adjusted to the same time scale. Although it appears daunting at first glance, you will find it a valuable reference tool as you proceed through this chapter.

to Figure 22-7, which is a composite chart that graphically illustrates and integrates changes in pressure gradients in the left atrium, left ventricle, and aorta with ECG and heart sound recordings. Aortic blood flow and changes in ventricular volume are also shown. Refer also to Figure 22-8, which shows the major phases of the cardiac cycle.

| A&P CONNECT |

Recall that damage to the myocardium that sometimes affects the heart's ECG and pumping cycle may result from a heart attack. Review the illustrated walk-through of a ***Heart Attack!*** online at ***A&P Connect.***

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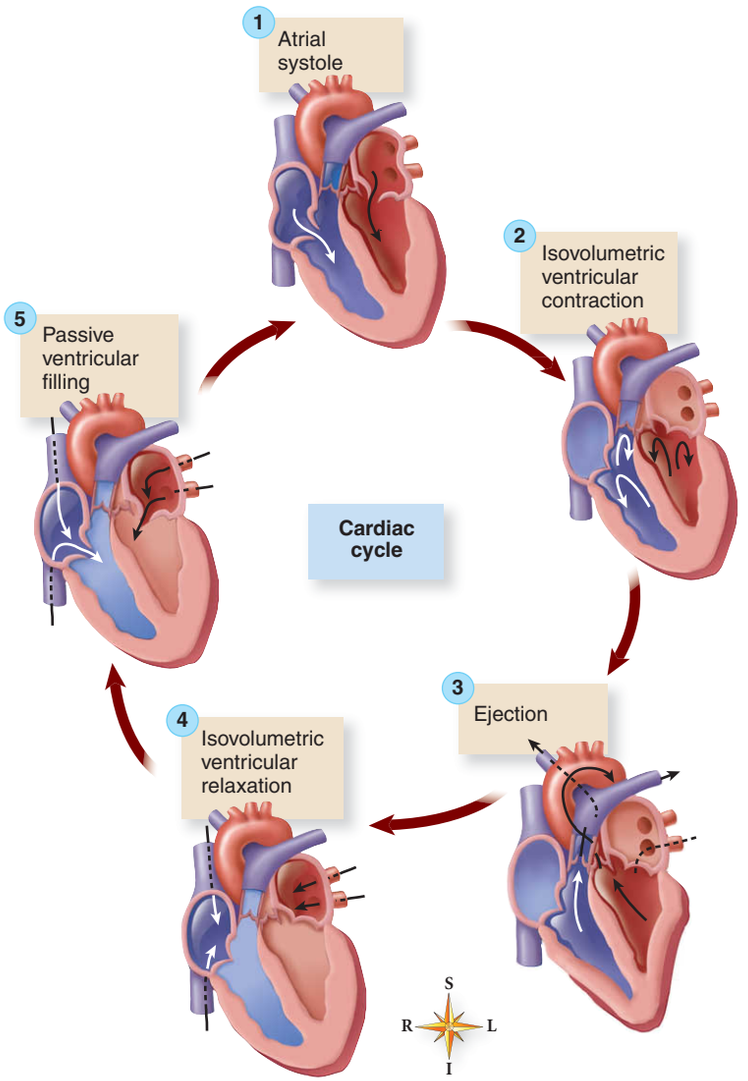


FIGURE 22-8

The cardiac cycle. The five steps of the heart's pumping cycle described in the text are shown as a series of changes in the heart wall and valves.

ATRIAL SYSTOLE

This phase of the cardiac cycle begins with the P wave of the ECG. Passage of the electrical wave of depolarization is then followed almost immediately by actual contraction (systole) of the atrial musculature.

The contracting force of the atria creates a pressure gradient that pushes blood out of the atria into the relaxed ventricles. Keep in mind that fluid moves from an area of high pressure toward an area of lower pressure—an important principle of hemodynamics that helps explain how the heart functions as a pump. Because of the high pressure of atrial blood during atrial systole, blood moves into the relaxed ventricles, where the pressure is lower.

The pressure gradient not only drives the movement of blood from the atria into the ventricles, it also keeps the atrioventricular (or cuspid) valves open during this phase. The ventricles are relaxed and rapidly filling with blood. The semilunar valves are closed because during this phase the arterial pressure is higher than pressure in the relaxed ventricles. This pressure gradient pushes blood against the semilunar valves and thereby prevents reentry of blood from the pulmonary artery or aorta.

ISOVOLUMETRIC VENTRICULAR CONTRACTION

The onset of ventricular systole coincides with the R wave of the ECG and the appearance of the first heart sound.

Iso- is a combining form denoting equality or uniformity, and *volumetric* denotes measurement of volume. Thus *isovolumetric* is a term that means "having the same measured volume." During the brief period of isovolumetric ventricular contraction the intraventricular pressure begins to increase. This is enough of a pressure increase in the ventricles to overcome atrial pressure and close the atrioventricular valves—producing the first heart sound—but not enough to overcome arterial pressure and open the semilunar valves. This phase occurs between the start of ventricular systole and the opening of the semilunar valves, during which ventricular volume remains constant as the pressure increases rapidly.

EJECTION

The semilunar valves open and blood is ejected from the heart when the pressure in the ventricles exceeds the pressure in the pulmonary artery and aorta. An initial, shorter phase, called *rapid ejection*, is characterized by a marked increase in ventricular and aortic pressure and in aortic blood flow. The T wave of the ECG appears during the later, longer phase of *reduced ejection* (characterized by a less abrupt decrease in ventricular volume). A considerable quantity of blood, called the **residual volume,** normally remains in the ventricles at the end of the ejection period. In heart failure the residual volume remaining in the ventricles may greatly exceed that ejected during systole.

ISOVOLUMETRIC VENTRICULAR RELAXATION

Ventricular diastole, or relaxation, begins with the isovolumetric ventricular relaxation period of the cardiac cycle. It is the period between closure of the semilunar valves and opening of the atrioventricular valves. At the end of ventricular ejection, the semilunar valves close when the ventricular pressure drops below arterial pressure and pushes the valve flaps closed. As the valves snap shut, they produce the second heart sound. Closure of the semilunar valves prevents blood from reentering the ventricular chambers from the pulmonary trunk and aorta. Both sets of valves are closed, and the ventricles are relaxing.

Ventricular relaxation causes a dramatic fall in intraventricular pressure but not enough to open the atrioventricular valves. Because the valves are closed, there is no change in volume. The atrioventricular valves do not open until the pressure in the atrial chambers increases above that in the relaxing ventricles.

PASSIVE VENTRICULAR FILLING

As the ventricles continue to relax, the intraventricular pressure continues to drop. That, along with rising intraatrial pressure produced by return of venous blood, produces a pressure gradient sufficient to force open the atrioventricular valves. Blood then rushes into the relaxing ventricles.

The rapid influx of blood into the ventricles lasts about 0.1 second and results in a dramatic increase in ventricular volume. The term *diastasis* is often used to describe a later, longer period of slow ventricular filling as ventricular diastole ends. The abrupt inflow of blood that occurred immediately after opening of the atrioventricular valves is followed by a slow but continuous flow of venous blood into the atria and then through the open atrioventricular valves into the ventricles. Diastasis lasts about 0.2 second and is characterized by a gradual increase in ventricular pressure and volume.

At the end of this phase of the cardiac cycle, a new P wave triggers the contraction of atria that marks the beginning of another *atrial systole* phase—and new cardiac cycle.

| A&P CONNECT |

Review ***Echocardiography*** online at ***A&P Connect*** to learn how sound waves are used to visualize the events of the cardiac cycle.

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Heart Sounds

The heart makes certain typical sounds during each cardiac cycle that are described as sounding like "lubb-dupp" when heard through a stethoscope.

The first, or systolic, sound is caused primarily by the contraction (systole) of the ventricles and also by vibrations of the closing atrioventricular, or cuspid, valves. It is longer and lower than the second, or diastolic, sound, which is short and sharp and is caused by vibrations of the closing semilunar valves as the ventricles relax (diastole) (see Figure 22-7).

Heart sounds have clinical significance because they provide information about the valves of the heart. Any variation from normal in the sounds indicates imperfect functioning of the valves. **Heart murmur** is one type of abnormal heart sound heard frequently. It is sometimes described as a "swishing" sound that may signify incomplete closing of the valves (valvular insufficiency) or stenosis (constriction, or narrowing) of them.

| QUICK CHECK |

4. Using Figure 22-8 as a guide, describe the major events of the cardiac cycle.
5. As the ventricles contract, their volume remains constant for a period of time. Explain why the volume does not begin to decrease immediately.

PRIMARY PRINCIPLE OF CIRCULATION

Blood circulates for the same reason that any fluid flows—whether it is water in a river, water in a garden hose, fluid in hospital tubing, or blood in vessels. A fluid flows because a pressure gradient exists between different parts of its volume (Figure 22-9).

This primary fluid flow principle derives from Newton's first and second laws of motion. In essence, these laws state the following principles:

1. A fluid does not flow when the pressure is the same throughout.
2. A fluid flows only when its pressure is higher in one area than in another, and it flows always from its higher pressure area toward its lower pressure area.

Thus the primary principle about circulation is this: blood flows because of a pressure gradient. We have already seen this principle operate to drive the flow of blood through the heart during the cardiac cycle (see pp. 687–689). It also applies to a whole circulatory loop—blood circulates from the left ventricle and returns to the right atrium of the heart because a blood pressure gradient exists between these two structures. Likewise, blood circulates from the right ventricle and returns to the left atrium because of a pressure gradient. By blood pressure gradient, we mean the difference between the blood pressure in one structure and the blood pressure in another.

An example of a normal blood pressure measurement in the aorta, as the left ventricle contracts and thereby pumps blood into it, is 120 mmHg; as the left ventricle relaxes, blood pressure decreases to 80 mmHg. The midpoint of aortic pressure in this instance is 100 mmHg. Figure 22-9 shows the systolic and diastolic pressures in the arterial system and illustrates the progressive fall in pressure from a midpoint of 100 mmHg in the aorta down to 0 mmHg by the time blood reaches the venae cavae and right atrium. The progressive fall in pressure as blood passes through the circulatory system is directly related to flow resistance. Resistance to blood flow in the aorta is almost zero. Although the pumping action of the heart causes fluctuations in aortic blood pressure (systolic 120 mmHg; diastolic 80 mmHg), the midpoint of pressure remains almost constant, dropping perhaps only 1 or 2 mmHg. The greatest drop in pressure (about 50 mmHg) occurs as blood goes through the arterioles because they present the greatest resistance to blood flow. The importance of flow resistance to maintaining a healthy pressure gradient is explored further in the next part of the chapter.

P_1–P_2 is often used to represent a pressure gradient, with P_1 the symbol for the higher pressure and P_2 the symbol for the lower pressure. For example, blood enters the arterioles at 85 mmHg and leaves at 35 mmHg. Which measurement is P_1? P_2? What is the blood pressure gradient? It would cause blood to flow through the arterioles toward the capillaries.

Of course, this principle applies to local blood flow as well as an entire circulatory loop. For example, pressure in the arteries and arterioles of the kidney must be higher than the blood pressure in the capillaries and veins of the kidney in order for blood to flow through the tissues of the kidney. This local pressure gradient needed to maintain blood flow in a tissue is called **perfusion pressure** (*perfusion* means "flow through").

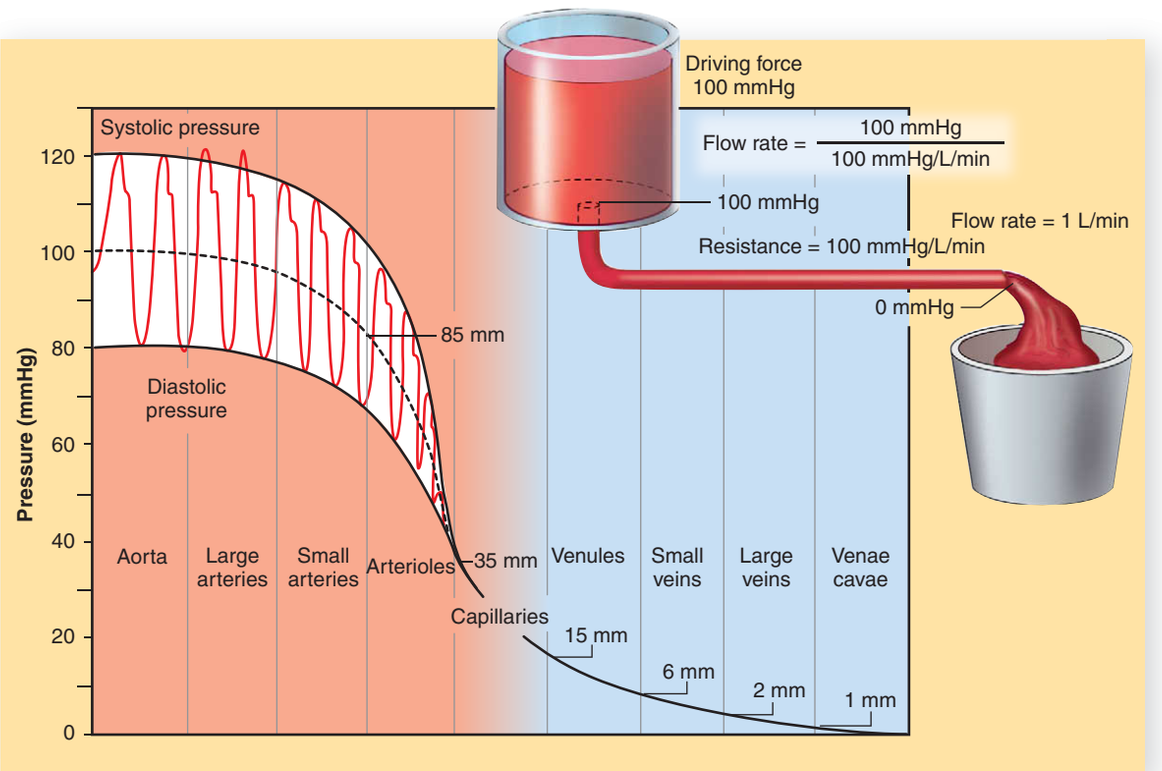


FIGURE 22-9

The primary principle of circulation. Fluid always travels from an area of high pressure to an area of low pressure. Water flows from an area of high pressure in the tank (100 mmHg) toward the area of low pressure above the bucket (0 mmHg). Blood tends to move from an area of high pressure at the beginning of the aorta (100 mmHg) toward the area of lowest pressure at the end of the venae cavae (0 mmHg). Blood flow between any two points in the circulatory system can always be predicted by the pressure gradient.

ARTERIAL BLOOD PRESSURE

According to the primary principle of circulation, high pressure in the arteries must be maintained to keep blood flowing through the cardiovascular system. The chief determinant of arterial blood pressure is the volume of blood in the arteries. Arterial blood pressure is directly proportional to arterial blood volume. This means that an increase in arterial blood volume tends to increase arterial pressure, and conversely, a decrease in arterial volume tends to decrease arterial pressure.

Many factors determine arterial pressure through their influence on arterial volume. Two of the most important—**cardiac output** and **peripheral resistance**—are directly proportional to blood volume (Figure 22-10).

Cardiac Output

Cardiac output (CO) is the amount of blood that flows out of a ventricle of the heart per unit of time. The resting cardiac output from the left ventricle into the systemic arteries is roughly 5000 ml/min, for example. As Figure 22-11 shows, the cardiac output influences the flow rate to the various organs of the body. For the sake of discussion, we focus mainly on cardiac output from the left ventricle into the systemic loop—but the same principles apply to cardiac output from either the left or the right ventricle.

Cardiac output is determined by the volume of blood pumped out of a ventricle by each beat (**stroke volume,** or **SV**) and by heart rate (HR). Because contraction of the heart is called *systole*, the volume of blood pumped by one contraction is known as *systolic discharge*. Stroke volume means the same thing, the amount of blood pumped by one stroke (contraction) of the ventricle.

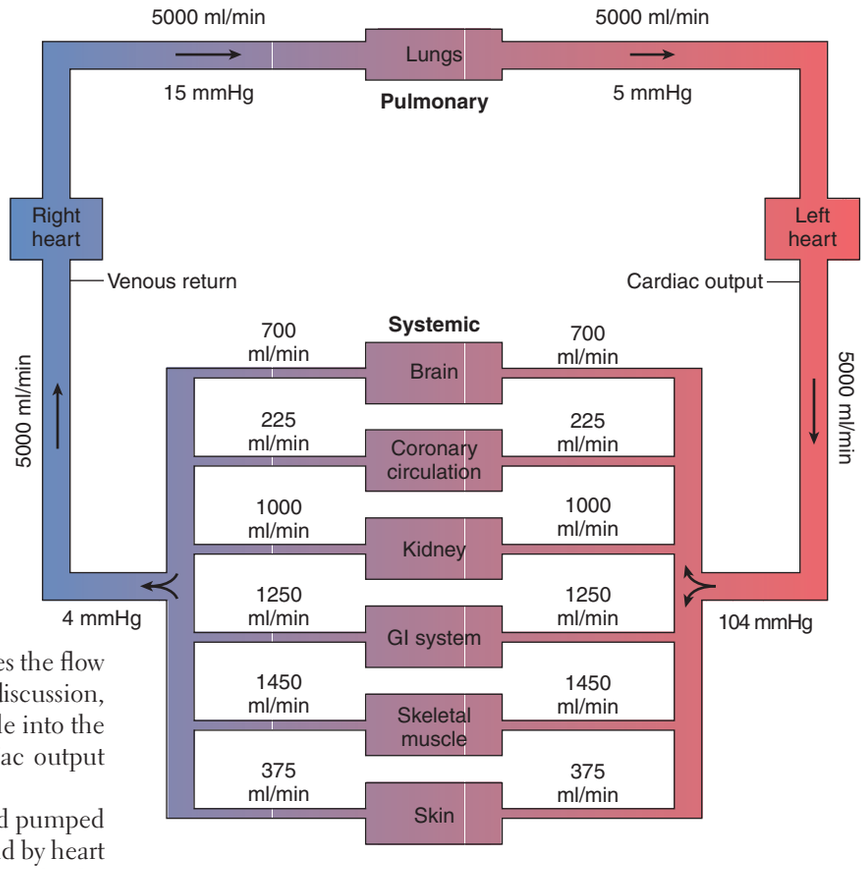


FIGURE 22-11

Cardiac output. This diagram shows that a typical resting cardiac output (CO) of 5000 ml/min (or 5 L/min) is distributed among the various systems and organs of the body. *GI,* Gastrointestinal.

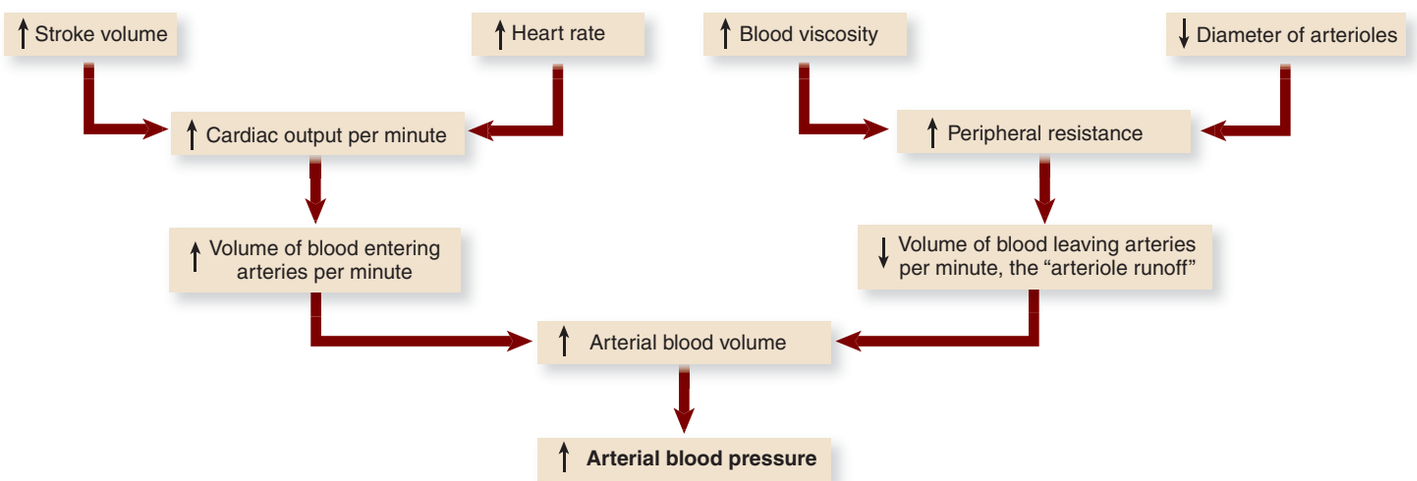


FIGURE 22-10

Relationship between arterial blood volume and blood pressure. Arterial blood pressure is directly proportional to arterial blood volume. Cardiac output (CO) and peripheral resistance (PR) are directly proportional to arterial blood volume, but for opposite reasons: CO affects blood *entering* the arteries, and PR affects blood *leaving* the arteries. If cardiac output increases, the amount of blood entering the arteries increases and tends to increase the volume of blood in the arteries. If peripheral resistance increases, it decreases the amount of blood leaving the arteries, which tends to increase the amount of blood left in them. Thus an increase in either CO or PR results in an increase in arterial blood volume, which increases arterial blood pressure.

Stroke volume, or volume pumped per heartbeat, is one of two major factors that determine CO. CO can be computed by the following simple equation:

SV (volume/beat) × HR (beat/min) = CO (volume/min)

Thus the greater the stroke volume, the greater the CO (but only if the heart rate remains constant). In practice, computing the CO is far from simple. It requires introducing a catheter into the right side of the heart (cardiac catheterization) and solving a computation known as *Fick's formula.*

Because the heart's rate and stroke volume determine its output, anything that changes the rate of the heartbeat or its stroke volume tends to change CO, arterial blood volume, and blood pressure in the same direction. In other words, anything that makes the heart beat faster or anything that makes it beat stronger (increases its stroke volume) *tends* to increase CO and therefore arterial blood volume and pressure. Conversely, anything that causes the heart to beat more slowly or more weakly tends to decrease CO, arterial volume, and blood pressure.

Do not overlook the word *tends* in the preceding sentences. A change in heart rate or stroke volume does not *always* change the heart's output, or the amount of blood in the arteries, or the blood pressure. To see whether this is true, do the following arithmetic calculation, using the simple formula for computing CO. Assume a normal rate of 72 beats/min and a normal stroke volume of 70 ml. Next, suppose the rate drops to 60 and the stroke volume increases to 100. Does the decrease in heart rate actually cause a decrease in CO in this case? Clearly not—the CO increases. Do you think it is valid, however, to say that a slower rate tends to decrease the heart's output? By itself, without any change in any other factor, would not a slowing of the heartbeat cause CO volume, arterial volume, and blood pressure to fall?

FACTORS THAT AFFECT STROKE VOLUME

Mechanical, neural, and chemical factors regulate the strength of the heartbeat and therefore its stroke volume. One mechanical factor that helps determine stroke volume is the length of myocardial fibers at the beginning of ventricular contraction.

Many years ago, an English physiologist named Ernest Starling described a principle that later became known as **Starling's law of the heart.** Because the principle was partly based on the earlier work of Otto Frank, it is sometimes called the *Frank-Starling mechanism.* In this principle, Starling stated the factor he had observed as the main regulator of heartbeat strength in experiments performed on denervated animal hearts. Starling's law of the heart is this: within limits, the longer, or more stretched, the heart fibers at the beginning of contraction, the stronger is their contraction. Compare this concept with the length-tension relationship in skeletal muscle described in Chapter 12 (p. 365).

The factor determining how stretched the animal hearts were at the beginning of contractions was, as you might deduce, the amount of blood in the hearts at the end of diastole—the **end-diastolic volume (EDV).** The more blood returned to the heart per minute, the more stretched were their fibers, the stronger were their contractions, and the larger was the volume of blood they ejected with each contraction. If, however, too much blood stretched the hearts beyond a certain critical point, they seemed to lose their elasticity. They then contracted less vigorously, similar to how a band of elastic, stretched too much, rebounds with less force (Figure 22-12).

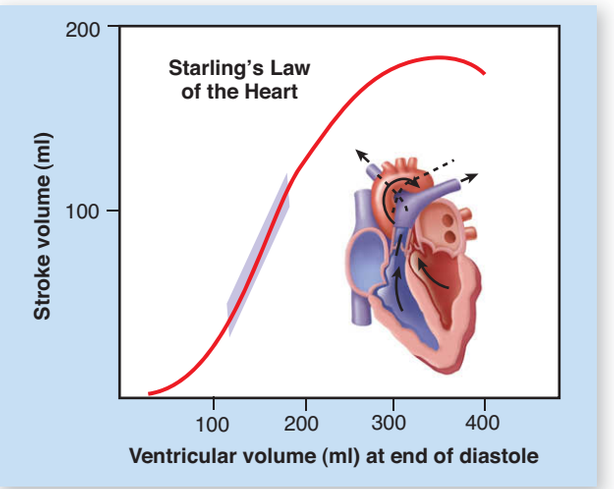


FIGURE 22-12

Starling's law of the heart. This curve represents the relationship between the stroke volume and the ventricular volume at the end of diastole. The range of values observed in a typical heart is shaded. Note that if the ventricle has an abnormally large volume at the end of diastole *(far right portion of the curve),* the stroke volume cannot compensate.

Thus, according to Starling's law of the heart, the heart pumps out what it receives. That is, within certain limits, the strength of myocardial contraction matches the pumping load—unlike mechanical pumps that do not adjust themselves to their input with every stroke.

Although Starling's law of the heart was first described in animal experiments, most physiologists agree that it operates in humans as a major regulator of stroke volume under ordinary conditions. Operation of Starling's law of the heart ensures that increased amounts of blood returned to the heart will be pumped out of it. It automatically adjusts CO to venous return under usual conditions. Factors that influence the amount of blood returned to the heart—venous return—are discussed in a later section.

Other factors that influence stroke volume are neural and endocrine chemical factors. You already know from our discussions in earlier chapters that norepinephrine (NE) released by sympathetic fibers in the cardiac nerve and epinephrine released into the blood by the adrenal medulla can both increase the strength of contraction, or *contractility*, of the myocardium. This increased contractility of heart muscle pushes more blood out of the heart per cardiac stroke—thus increasing the stroke volume. As Figure 22-13 shows, both the increased contractility from these chemical factors and the effects of Starling's law of the heart can change the stroke volume—and therefore also cardiac output. Factors such as the stress of exercise can trigger these neural and endocrine responses.

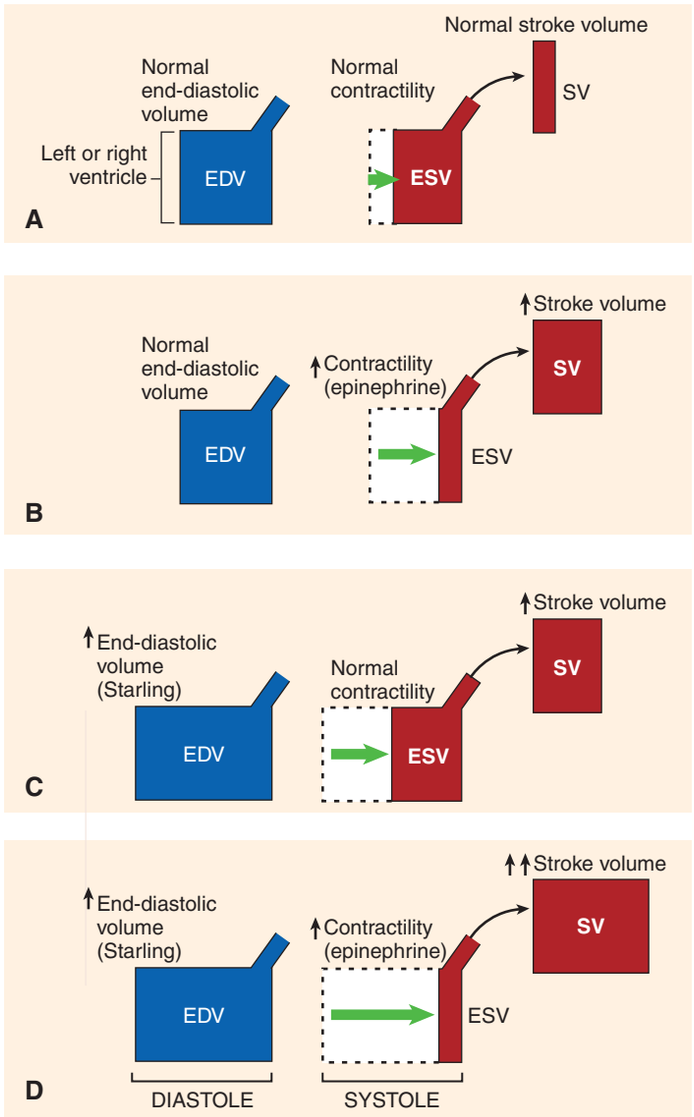


FIGURE 22-13

Stroke volume. Changes in stroke volume caused by increasing the end-diastolic volume (EDV) and/or contractility. **A,** Normal stroke volume (no external influences). **B,** When EDV remains constant and contractility increases (from epinephrine), then the stroke volume increases. **C,** When contractility remains constant and EDV increases, then the stroke volume increases (Starling's law of the heart). **D,** When both EDV and contractility increase, a combined effect increases the stroke volume even more. *EDV,* End-diastolic volume; *ESV,* end-systolic volume; *SV,* stroke volume.

The **ejection fraction (EF)** is related to the stroke volume. The ejection fraction is the ratio of the stroke volume (SV) to the end-diastolic volume (EDV), often expressed as a percentage. Expressed as a formula, EF = (SV/EDV) × 100. Thus as SV goes up, EF goes up—and as SV goes down, EF also goes down. An EF of 55% or higher is typical in healthy adults. The EF declines when the myocardium fails to function properly and cannot contract strongly enough to eject a normal amount of blood—as sometimes happens after a myocardial infarction (MI). The EF is usually measured by echocardiography, a procedure described in *Echocardiography* online at *A&P Connect.*

FACTORS THAT AFFECT HEART RATE

Although the sinoatrial node normally initiates each heartbeat, the rate it sets is not an unalterable one. Various factors can and do change the rate of the heartbeat. One major modifier of sinoatrial node activity—and therefore of the heart rate—is the ratio of sympathetic and parasympathetic impulses conducted to the node per minute. Autonomic control of heart rate is the result of opposing influences between parasympathetic (chiefly vagus) and sympathetic (cardiac nerve) stimulation. The results of parasympathetic stimulation on the heart are inhibitory and are mediated by vagal release of acetylcholine, whereas sympathetic (stimulatory) effects result from the release of norepinephrine at the distal end of the cardiac nerve.

Cardiac Pressoreflexes

Receptors sensitive to changes in pressure (**baroreceptors**) are located in two places near the heart (Figure 22-14). Called

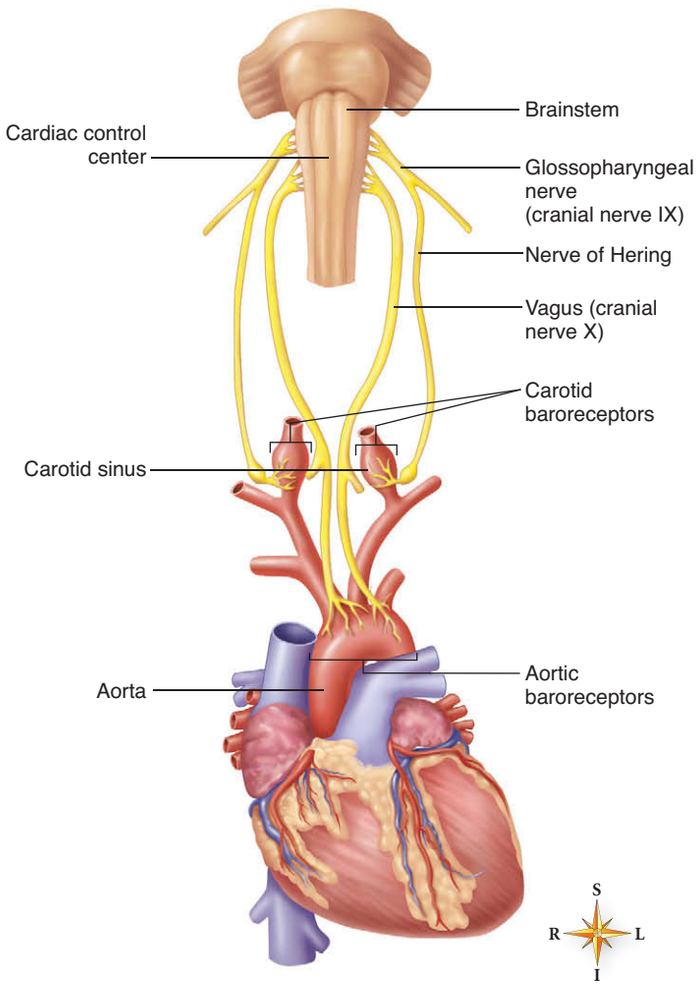


FIGURE 22-14

Cardiac baroreceptors. Location of aortic and carotid baroreceptors and the sensory nerves that carry feedback information about blood pressure back to the central nervous system.

the *aortic baroreceptors* and *carotid baroreceptors*, they send afferent nerve fibers to cardiac control centers in the medulla oblongata. These stretch receptors, located in the aorta and carotid sinus, constitute a very important heart rate control mechanism because of their effect on the autonomic cardiac control centers—and therefore on parasympathetic and sympathetic outflow. Baroreceptors operate with integrators in the cardiac control centers in negative feedback loops called **pressoreflexes** or *baroreflexes* that oppose changes in pressure by adjusting heart rate.

Carotid Sinus Reflex

The carotid sinus is a small dilation at the beginning of the internal carotid artery just above the branching of the common carotid artery to form the internal and external carotid arteries (see Figure 22-14).

The sinus lies just under the sternocleidomastoid muscle at the level of the upper margin of the thyroid cartilage. Sensory (afferent) fibers from carotid sinus baroreceptors (pressure sensors) run through the carotid sinus nerve (of Hering) and on through the glossopharyngeal (or ninth cranial) nerve. These nerves relay feedback information to an integrator area of the medulla called the *cardiac control center*. If the integrators in the cardiac control center detect an increase in blood pressure above the set point, then a correction signal is sent to the SA node by way of efferent parasympathetic fibers in the vagus (tenth cranial) nerve. Acetylcholine released by vagal fibers decreases the rate of SA node firing, thus decreasing the heart rate back toward the set point. The vagus is said to act as a "brake" on the heart—a situation called *vagal inhibition*. Figure 22-15 summarizes this negative feedback loop, which is often called the **carotid sinus reflex.**

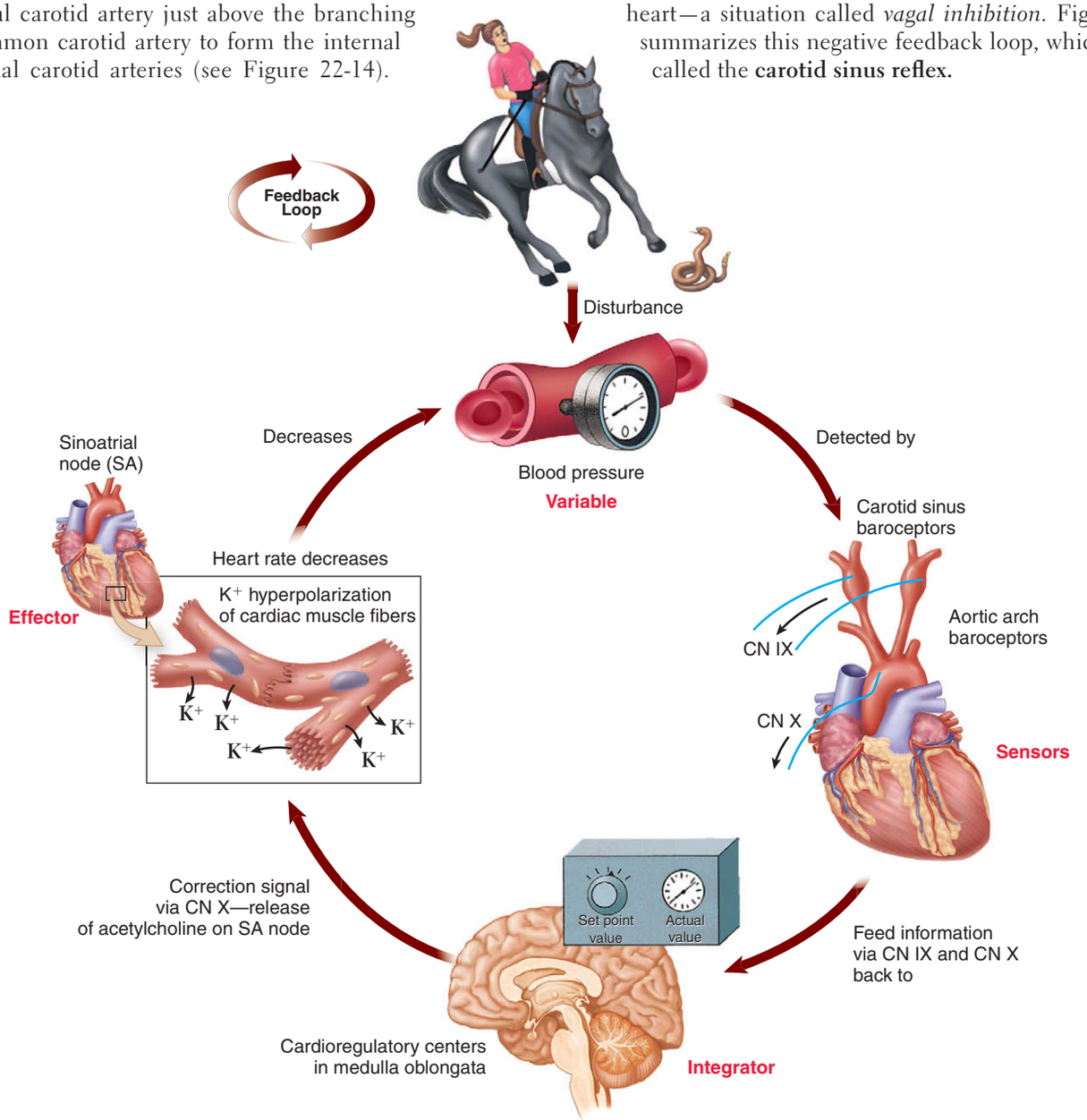


FIGURE 22-15

Aortic and carotid sinus pressoreflexes. These pressoreflexes operate in a feedback loop that maintains the homeostasis of blood pressure by decreasing the heart rate when the blood pressure surpasses the set point—as when recovering from a stress event after being startled.

Aortic Reflex

Sensory (afferent) nerve fibers also extend from baroreceptors located in the wall of the arch of the aorta through the aortic nerve and then through the vagus (tenth cranial) nerve to terminate in the cardiac control center of the medulla (see Figure 22-14).

If blood pressure within the aorta or carotid sinus suddenly increases beyond the set point, it stimulates the aortic or carotid baroreceptors, as shown in Figure 22-15. Stimulation of these stretch receptors causes the cardiac control center to increase vagal inhibition, thus slowing the heart and returning blood pressure back toward the normal set point. A decrease in aortic or carotid blood pressure usually allows some acceleration of the heart by way of correction signals through the cardiac nerve. Because it involves receptors located in the wall of the aorta, this feedback loop is called the **aortic reflex.**

More details of pressoreflex activity are included later in the chapter as part of a mechanism that tends to maintain or restore homeostasis of arterial blood pressure.

Other Reflexes That Influence Heart Rate

Reflexes involving important factors such as emotions, exercise, hormones, blood temperature, pain, and stimulation of various exteroceptors also influence heart rate. Anxiety, fear, and anger often make the heart beat faster. Grief, in contrast, tends to slow it. Emotions produce changes in the heart rate through the influence of impulses from the "higher centers" in the cerebrum by way of the hypothalamus. Such impulses can influence activity of the cardiac control centers.

During exercise the heart normally accelerates. The mechanism for this acceleration is not definitely known, but it is thought to include impulses from the cerebrum through the hypothalamus to the cardiac center. Epinephrine is the hormone most noted as a cardiac accelerator.

Increased blood temperature or stimulation of skin heat receptors tends to increase the heart rate, and decreased blood temperature or stimulation of skin cold receptors tends to slow it. Sudden, intense stimulation of pain receptors in visceral structures such as the gallbladder, ureters, or intestines can result in such slowing of the heart that fainting may result.

Reflexive increases in heart rate often result from an increase in sympathetic stimulation of the heart. Sympathetic impulses originate in the cardiac control center of the medulla and reach the heart by way of sympathetic fibers (contained in the middle, superior, and inferior cardiac nerves). Norepinephrine released as a result of sympathetic stimulation increases heart rate and strength of cardiac muscle contraction.

| QUICK CHECK |

6. State the primary principle of circulation.
7. Relate stroke volume and heart rate to cardiac output.
8. If the amount of blood returned to the heart increases, what happens to the stroke volume? What principle explains this?
9. How does the body use a pressoreflex to counteract an abnormal increase in heart rate? An abnormal decrease in heart rate?

Peripheral Resistance

HOW RESISTANCE INFLUENCES BLOOD PRESSURE

Peripheral resistance means the resistance to blood flow imposed by the force of friction between blood and the walls of its vessels. Friction develops partly because of a characteristic of blood—its **viscosity,** or stickiness—and partly from the small diameter of arterioles and capillaries. The resistance offered by arterioles, in particular, accounts for almost one half of the total resistance in systemic circulation.

Peripheral resistance in arterioles helps determine arterial blood pressure because the more resistance there is in the arterioles, the more blood "backs up" in the arteries to increase fluid pressure. This mechanism can help maintain the pressure gradient needed to keep blood flowing (review again Figure 22-9 on p. 690). Think of what happens when you pinch off the end of a garden hose. The water backs up in the hose and the increased pressure gradient gives more force to the water flowing out of the hose.

Blood viscosity stems mainly from the proportion of red blood cells (hematocrit) but also partly from the protein molecules present in blood. An increase in either blood protein concentration or hematocrit tends to increase viscosity, and a decrease in either tends to decrease it (Figure 22-16). Under normal circumstances, blood viscosity changes very little. But under certain abnormal conditions, such as marked anemia or hemorrhage, a decrease in blood viscosity may be the crucial factor lowering peripheral resistance and arterial pressure, even to the point of circulatory failure.

The muscular coat of the arterioles allows them to constrict or dilate and thus change the amount of resistance to blood flow. This muscular mechanism in the vessels is called the **vasomotor mechanism.** Reduction in vessel diameter caused by increased contraction of the muscular coat, or **vasoconstriction,** increases

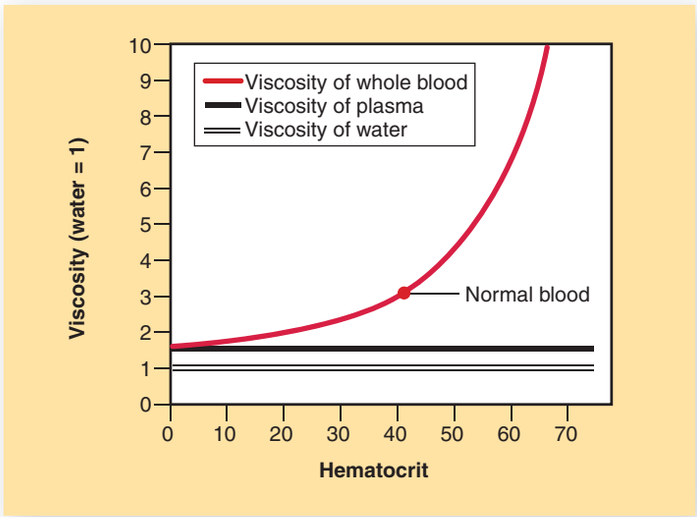


FIGURE 22-16

Blood viscosity. The effect of a changing hematocrit (% RBCs in blood) on blood viscosity is shown here. As hematocrit increases (horizontal axis of graph), the viscosity increases. Water is the reference value at viscosity = 1. Plasma is slightly more viscous than water—at approximately 1.5. As the total viscosity of blood increases, the resistance to blood flow increases.

resistance to blood flow, and thus blood flow into the tissue decreases. **Vasodilation,** the increase in vessel diameter caused by relaxation of vascular muscles, decreases resistance to blood flow, and thus blood flow into the tissue increases. As Figure 22-17 shows, small changes in diameter can cause proportionally large changes in resistance—and therefore large changes in local blood flow. This makes the vasomotor mechanism well suited for quickly and dramatically changing blood flow under varying conditions in the body, as we shall see.

Peripheral resistance helps determine arterial pressure by controlling the rate of "arteriole runoff," the amount of blood that runs out of the arteries into the arterioles (Figure 22-18). The greater the resistance, the less the arteriole runoff, or outflow, tends to be—and therefore the more blood left in the arteries, the higher the arterial pressure tends to be. This can occur locally, within a particular tissue or organ, or it can occur throughout the systemic loop when enough arterioles constrict and increase the **total peripheral resistance (TPR).**

VASOMOTOR CONTROL MECHANISM

Blood distribution patterns, as well as blood pressure, can be influenced by factors that control changes in the diameter of arterioles. Such factors might be said to constitute the vasomotor control mechanism. Like most physiological control mechanisms, it consists of many parts. An area in the medulla called the *vasomotor center*, or *vasoconstrictor center*, will, when stimulated, initiate an impulse outflow by way of sympathetic fibers that ends in the smooth muscle surrounding resistance vessels, arterioles, venules, and veins of the "blood reservoirs," causing their constriction. Thus the vasomotor control mechanism plays a role both in the maintenance of the general blood pressure and in the distribution of blood to areas of special need.

The main blood reservoirs are the venous plexuses and sinuses in the skin and abdominal organs (especially in the liver and spleen). In other words, blood reservoirs are the venous networks in most parts of the body—all but those in the skeletal muscles, heart, and brain. Figure 22-19 shows that the volume of blood in the systemic

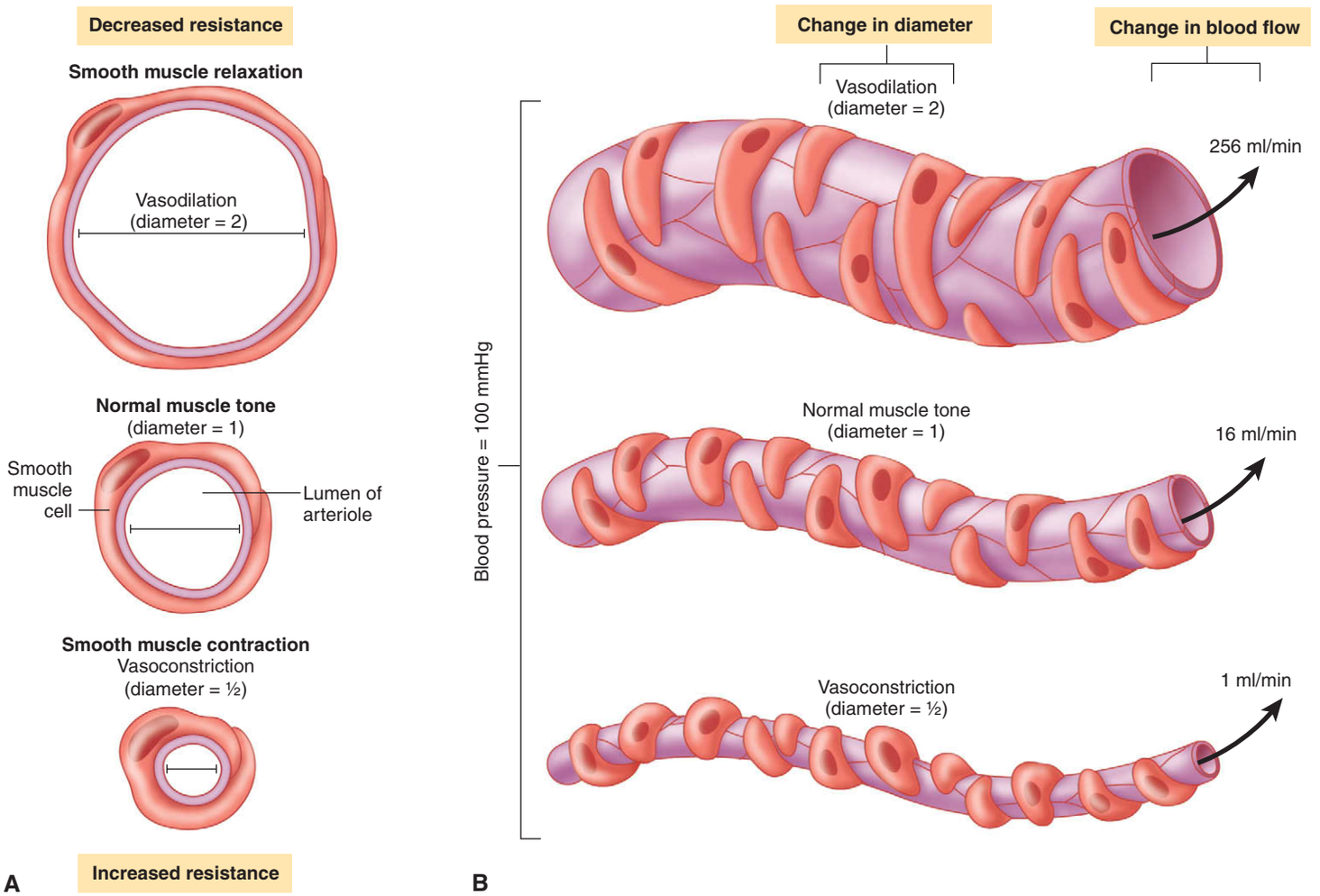


FIGURE 22-17

Vessel diameter. The effect of changing diameter of arterioles on peripheral resistance and blood flow. **A,** Cross sections of an arteriole showing vasodilation *(top),* normal diameter *(center),* and vasoconstriction *(bottom)* as tension in smooth muscle fibers changes. **B,** Diagram showing that relatively small changes from the normal diameter of an arteriole (normal = 1) cause very large changes in peripheral resistance to blood flow. For example, reducing diameter to one half of normal reduces blood flow to $^{1}/_{16}$ of normal. Likewise, doubling the vessel diameter does not double the blood flow—it increases blood flow 16 times the normal flow!

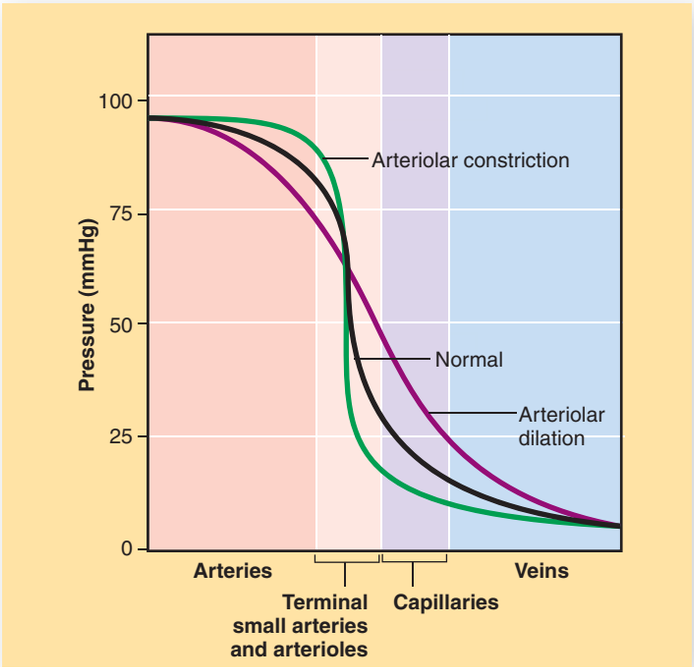


FIGURE 22-18

Vasomotor effects on blood pressure. The normal blood pressures in various vessels are shown by the black line. The green line shows a shift in blood pressures during vasoconstriction of the arterioles. Note that because there is more resistance in the arterioles, blood flow in the arteries backs up and thus increases arterial blood pressure. The purple line shows that vasodilation of the arterioles increases blood flow from the arteries and therefore reduces arterial blood pressure.

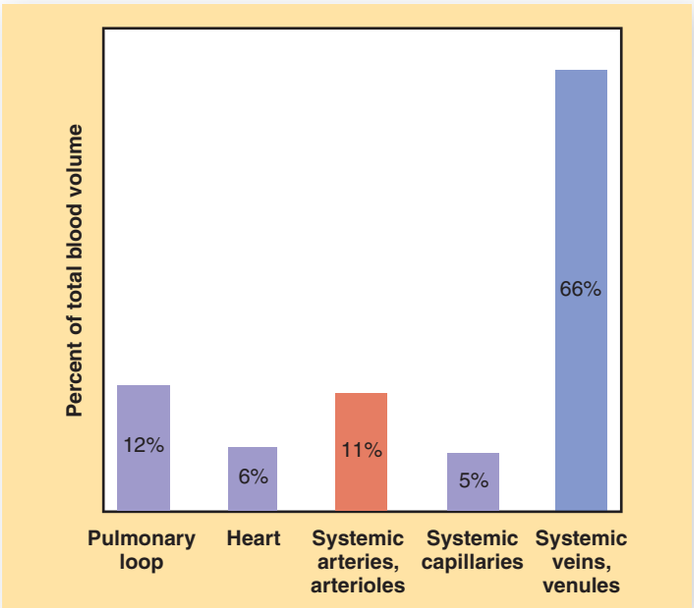


FIGURE 22-19

Relative blood volumes. The relative volumes of blood at rest in different parts of the adult cardiovascular system expressed as percentages of total blood volume. Note that at rest most of the body's blood supply is in the systemic veins and venules.

veins and venules in a resting adult is extremely large compared with the volume in other vessels of the body. The term *reservoir* is apt, because the systemic veins and venules serve as a kind of slowly moving stockpile or reserve of blood. Blood can quickly be moved out of blood reservoirs and "shifted" to arteries that supply heart and skeletal muscles when increased activity demands (Figure 22-20). A change in either arterial blood's oxygen or carbon dioxide content sets a chemical vasomotor control mechanism in operation. A change in arterial blood pressure initiates a **vasomotor pressoreflex.**

Vasomotor Pressoreflexes

A sudden increase in arterial blood pressure stimulates aortic and carotid baroreceptors—the same ones that initiate cardiac reflexes. Not only does this stimulate the cardiac control center to reduce heart rate (see Figure 22-15), but also it inhibits the vasoconstrictor center. More impulses per second go out over parasympathetic fibers to the heart. As a result, the heartbeat slows. Because sympathetic vasoconstrictor impulses predominate at normal arterial pressures, inhibition of these is considered the major mechanism

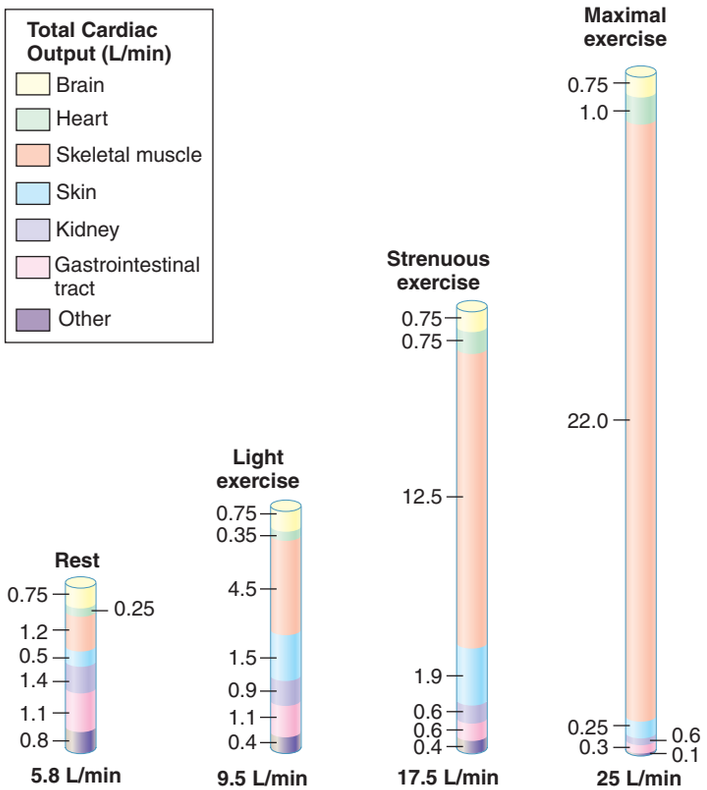


FIGURE 22-20

Changes in local blood flow during exercise. Graphic representation of blood flow (L/min) in an individual in various circumstances: at rest and during light, strenuous, and maximal exercise. During exercise, the vasomotor center of the medulla sends sympathetic signals to certain blood vessels to change diameter and thus shunt blood away from "maintenance" organs, such as the digestive organs in the abdomen, and toward the skeletal muscles. Local regulators of blood flow add to this effect. Note that blood flow in the brain is held constant. Note also that the total blood flow (cardiac output) in this individual increases from 5.8 L/min (rest) to 25 L/min—a fivefold increase in cardiac output—as the intensity of exercise increases.

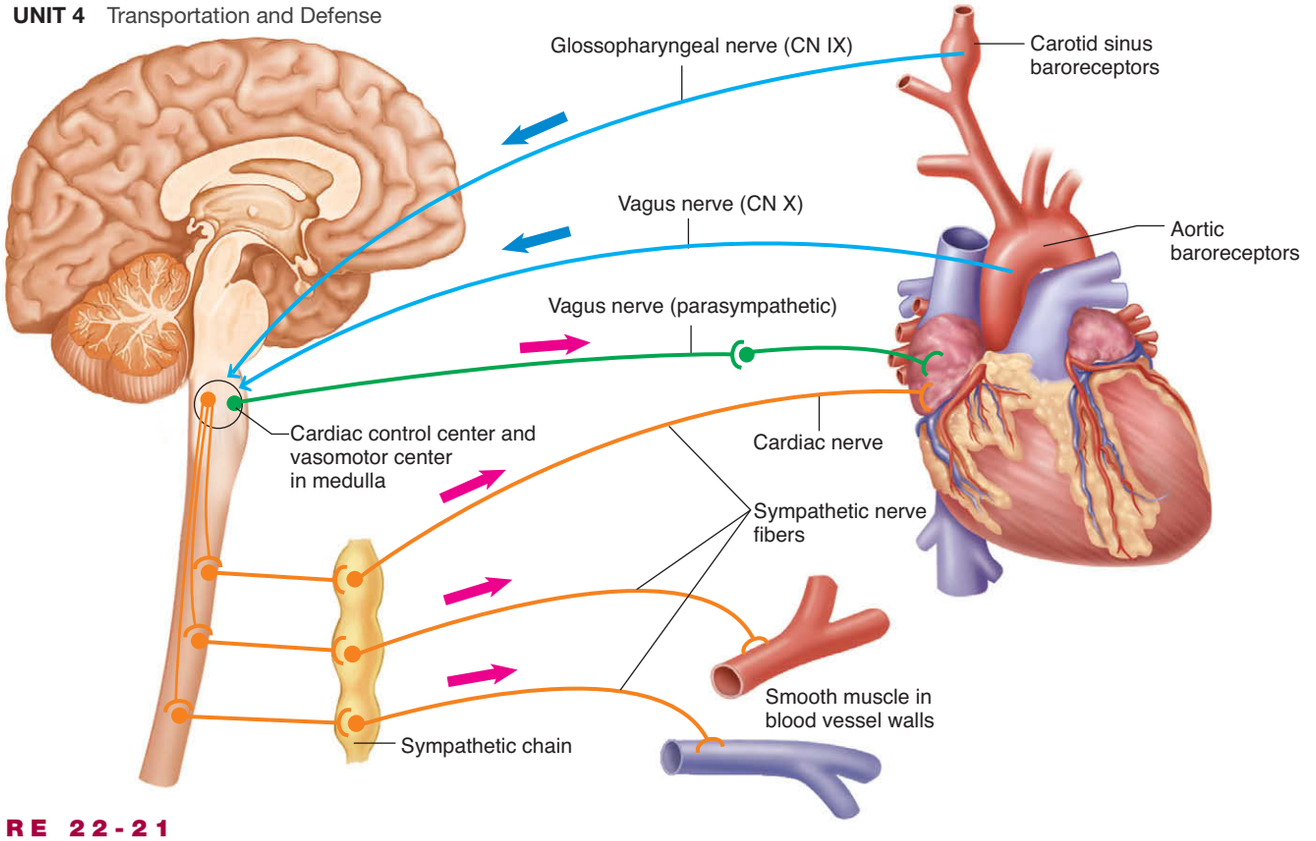


FIGURE 22-21

Vasomotor pressoreflexes. Carotid sinus and aortic baroreceptors detect changes in blood pressure and feed the information back to the cardiac control center and the vasomotor center in the medulla. In response, these control centers alter the ratio between sympathetic and parasympathetic output. If the pressure is too high, increased parasympathetic impulses and reduced sympathetic impulses will reduce it by slowing heart rate, reducing stroke volume, and dilating blood "reservoir" vessels. If the pressure is too low, an increase in sympathetic impulses will increase it by increasing heart rate and stroke volume and constricting arterioles and reservoir vessels.

of vasodilation. The nervous pathways involved in this mechanism are illustrated in Figure 22-21.

A decrease in arterial pressure causes the aortic and carotid baroreceptors to send more impulses to the medulla's vasoconstrictor centers, thereby stimulating them. These centers then send more impulses by way of the sympathetic fibers to stimulate vascular smooth muscle and cause vasoconstriction. When arterioles constrict, it "backs up" arterial blood and increases aterial blood pressure. Vasoconstriction also squeezes more blood out of the blood reservoirs, increasing the amount of venous blood return to the heart.

During exercise, blood from reservoirs is redistributed to more active structures such as skeletal muscles and heart because their arterioles become dilated largely from the operation of a local mechanism (discussed later). Thus the vasoconstrictor pressoreflex and the local vasodilating mechanism together serve as an important device for shifting blood from reservoirs to tissues that need it during exercise (see Figure 22-20 and Box 22-1).

Box 22-1 | SPORTS and FITNESS

The Cardiovascular System and Exercise

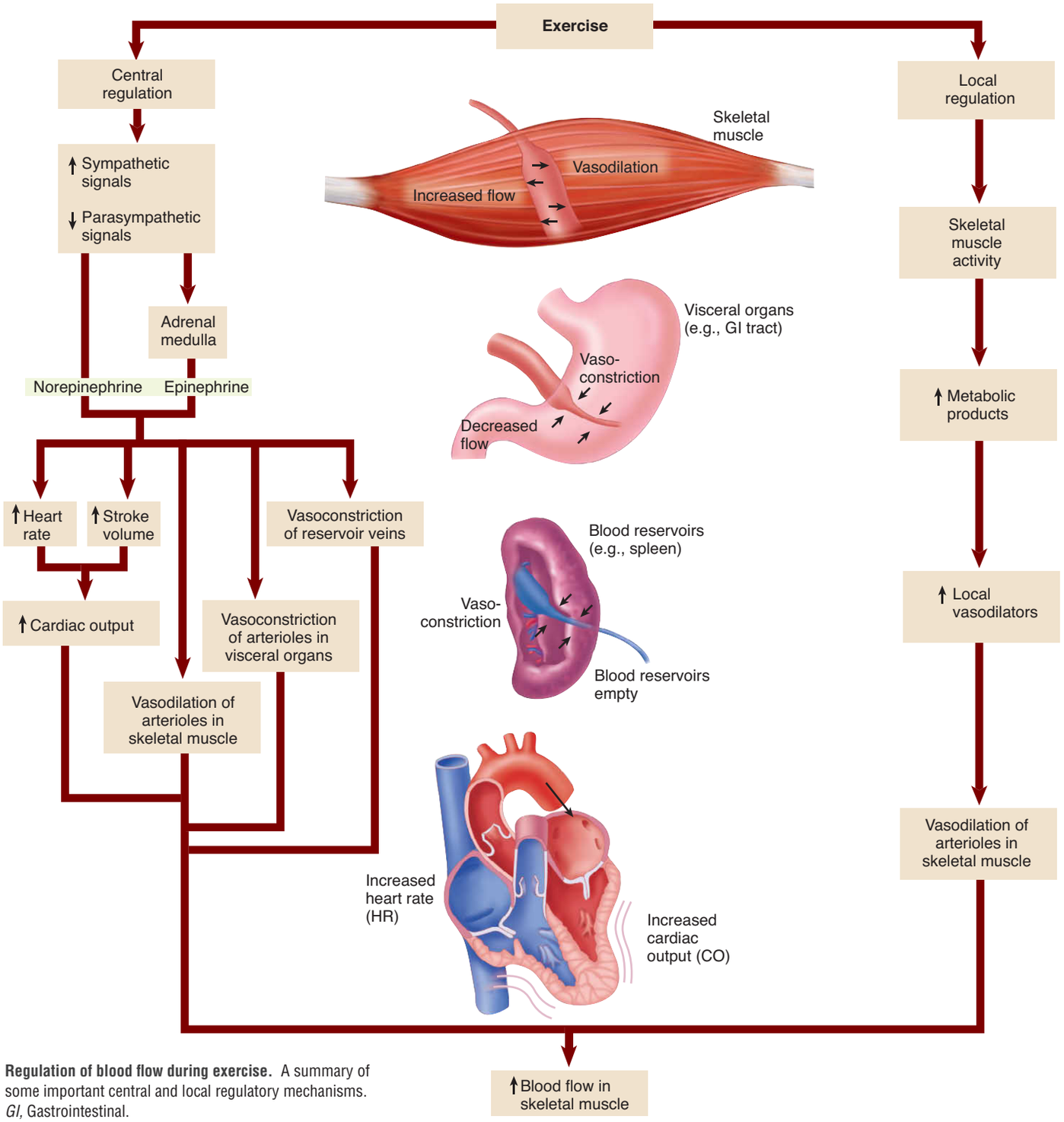
Exercise produces short-term and long-term changes in the cardiovascular system.

Short-term changes involve negative feedback mechanisms that maintain set point levels of blood oxygen and glucose, as well as other physiological variables. Because moderate to strenuous use of skeletal muscles greatly increases the body's overall rate of metabolism, oxygen and glucose are used up at a faster rate. This requires an increase in transport of oxygen and glucose by the cardiovascular system to maintain normal set point levels of these substances. One response by the cardiovascular system is to increase the cardiac output (CO) from 5 to 6 L/min at rest to up to 30 to 40 L/min during strenuous exercise. This represents a fivefold to eightfold increase in the blood output of the heart! Such an increase is accomplished by a reflexive increase in heart rate (see Figure 22-15) coupled with an increase in stroke volume (see Figures 22-12 and 22-13). Exercise can also trigger a reflexive change in local distribution of blood flow to various tissues, shown in Figure 22-20, that results in a larger share of blood flow going to the skeletal muscles than to some other tissues. A number of central and local regulatory effects that operate during exercise are summarized in the figure.

Long-term changes in the cardiovascular system come only when moderate to strenuous exercise occurs regularly over a long period.

Box 22-1 | SPORTS and FITNESS

Evidence indicates that 20 to 30 minutes of moderate aerobic exercise such as cycling or running three times per week produces profound, health-promoting changes in the cardiovascular system. Among these long-term cardiovascular changes are an increase in the mass and contractility of the myocardial tissue, an increase in the number of capillaries in the myocardium, a lower resting heart rate, and decreased peripheral resistance during rest. The lower resting heart rate coupled with the increase in stroke volume possible with increased myocardial mass and contractility produce a greater range of CO, and coupled with the other listed effects, a greater maximum CO. Exercise is also known to decrease the risk of various cardiovascular disorders, including arteriosclerosis, hypertension, and heart failure.



Regulation of blood flow during exercise. A summary of some important central and local regulatory mechanisms. *GI,* Gastrointestinal.

Vasomotor Chemoreflexes

Chemoreceptors located in the aortic and carotid bodies are particularly sensitive to excess blood carbon dioxide (**hypercapnia**) and somewhat less sensitive to a deficiency of blood oxygen (**hypoxia**) and to decreased arterial blood pH. When one or more of these conditions stimulates the chemoreceptors, their fibers transmit more impulses to the medulla's vasoconstrictor centers, and vasoconstriction of arterioles and venous reservoirs soon follows (Figure 22-22). This **chemoreceptor reflex** functions as an emergency mechanism when hypoxia or hypercapnia endangers the stability of the internal environment.

Medullary Ischemic Reflex

The **medullary ischemic reflex** mechanism is said to exert powerful control of blood vessels during emergency situations when blood flow to the brain drops below normal. When the blood supply to the medulla becomes inadequate (**ischemic**), its neurons suffer from both oxygen deficiency and carbon dioxide excess. But, presumably, it is hypercapnia that intensely and directly stimulates the vasoconstrictor centers to bring about marked arteriole and venous constriction (see Figure 22-22). If the oxygen supply to the medulla decreases below a certain level, its neurons, of course, cannot function, and the medullary ischemic reflex cannot operate.

Vasomotor Control by Higher Brain Centers

Impulses from centers in the cerebral cortex and in the hypothalamus are believed to be transmitted to the vasomotor centers in the medulla and to thereby help control vasoconstriction and dilation. Evidence supporting this view is that vasoconstriction and a rise in arterial blood pressure characteristically accompany emotions of intense fear or anger. Also, laboratory experiments on animals in which stimulation of the posterior or lateral parts of the hypothalamus leads to vasoconstriction support the belief that higher brain centers influence the vasomotor centers in the medulla.

LOCAL CONTROL OF ARTERIOLES

Several kinds of local mechanisms operate to produce vasodilation in localized areas. Although not all these mechanisms are clearly understood, they are known to function in times of increased tissue activity. For example, they probably account for the increased blood flow into skeletal muscles during exercise. They also operate in ischemic tissues, serving as a homeostatic mechanism that tends to restore normal blood flow. Some locally produced substances, such as nitric oxide, activate the local vasodilator mechanism, whereas others, such as *endothelin*, constrict the arterioles. Local vasodilation is also referred to as *active hyperemia*.

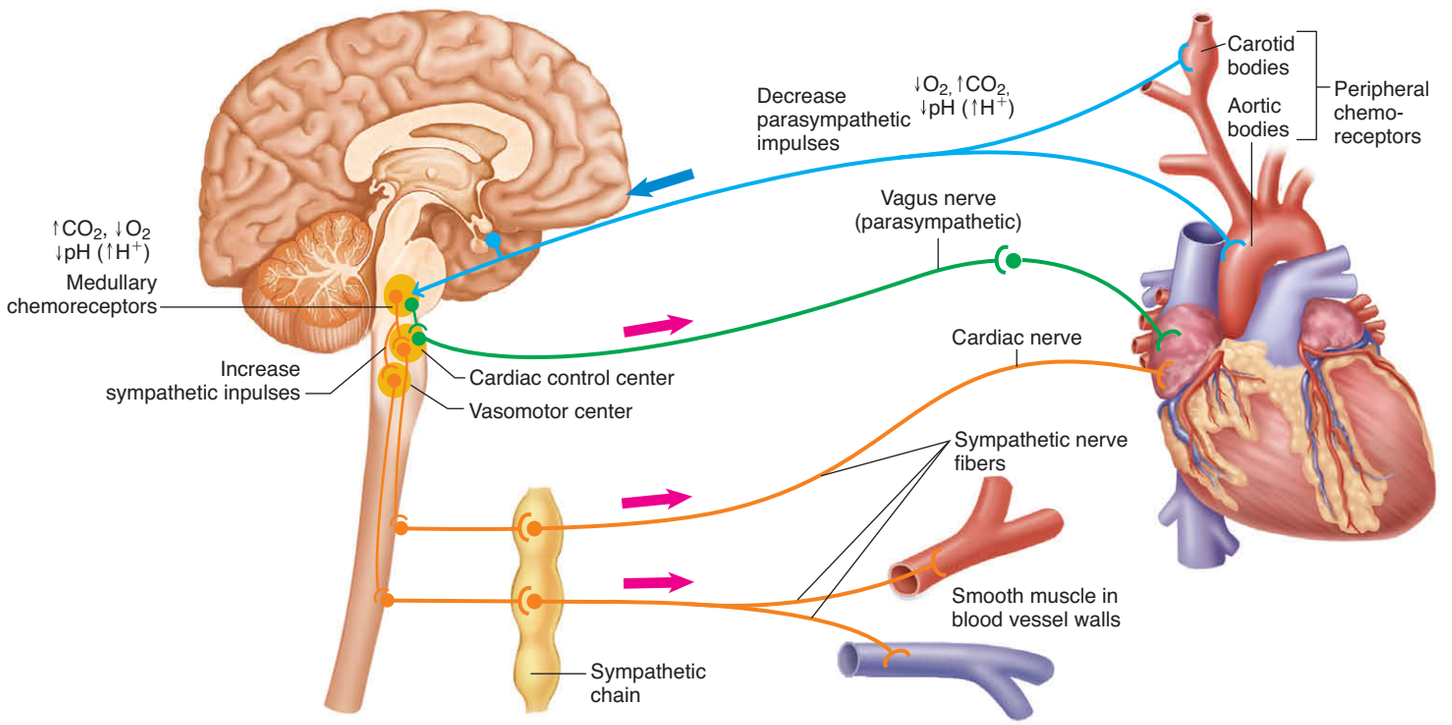


FIGURE 22-22

Vasomotor chemoreflexes. Chemoreceptors in the carotid and aortic bodies, as well as chemoreceptive neurons in the vasomotor center of the medulla itself, detect increases in carbon dioxide (CO_2), decreases in blood oxygen (O_2), and/or decreases in pH (which is really an increase in H^+). This information feeds back to the cardiac control center and the vasomotor control center of the medulla, which in turn alter the ratio of parasympathetic and sympathetic output. When O_2 drops, CO_2 increases, and/or pH drops, a dominance of sympathetic impulses increases heart rate and stroke volume and constricts reservoir vessels in response.

| QUICK CHECK |

10. Peripheral resistance is affected by two major factors: blood viscosity and what else?
11. If the diameter of the arteries decreases, what effect does it have on peripheral resistance?
12. In general, how do vasomotor pressoreflexes affect the flow of blood?
13. What is a chemoreflex? How do chemoreflexes affect the flow of blood?

VENOUS RETURN TO THE HEART

Venous return refers to the amount of blood that is returned to the heart by way of the veins. Various factors influence venous return, including the reservoir function of veins, which occurs whenever blood pressure drops and the elasticity of the venous walls adapts the diameter of veins to the lower pressure, thus maintaining blood flow and venous return to the heart. Likewise, when overall blood pressure rises, the elastic nature of blood vessels allows them to expand and adapt to the higher pressure to maintain normal blood flow. This effect, which occurs in all blood vessels to some degree (with certain limitations to its adaptability), is often called the **stress-relaxation effect.**

Another factor that influences venous return is gravity. Figure 22-23 shows that when a person is reclining, the force of gravity is not pulling blood downward toward the legs. However, when a person is sitting or standing, the blood *is* pulled by gravity toward the legs. Because the venous blood is already at a low blood pressure and because the venous walls are compliant (easily stretched), it is easy for the force of gravity to work against venous return back to the heart and cause some blood to remain in the veins of the limbs. The shift of the blood reservoir to the veins in the legs when standing is often called the **orthostatic effect** because *orthostasis* means "standing upright."

A factor that can help to overcome the influence of gravity is the operation of **venous pumps** that maintain the pressure gradients necessary to keep blood moving into the central veins (e.g., venae cavae) and from there into the atria of the heart. Changes in the total volume of blood in the vessels can also alter venous return. Venous return and total blood volume are discussed in the paragraphs that follow.

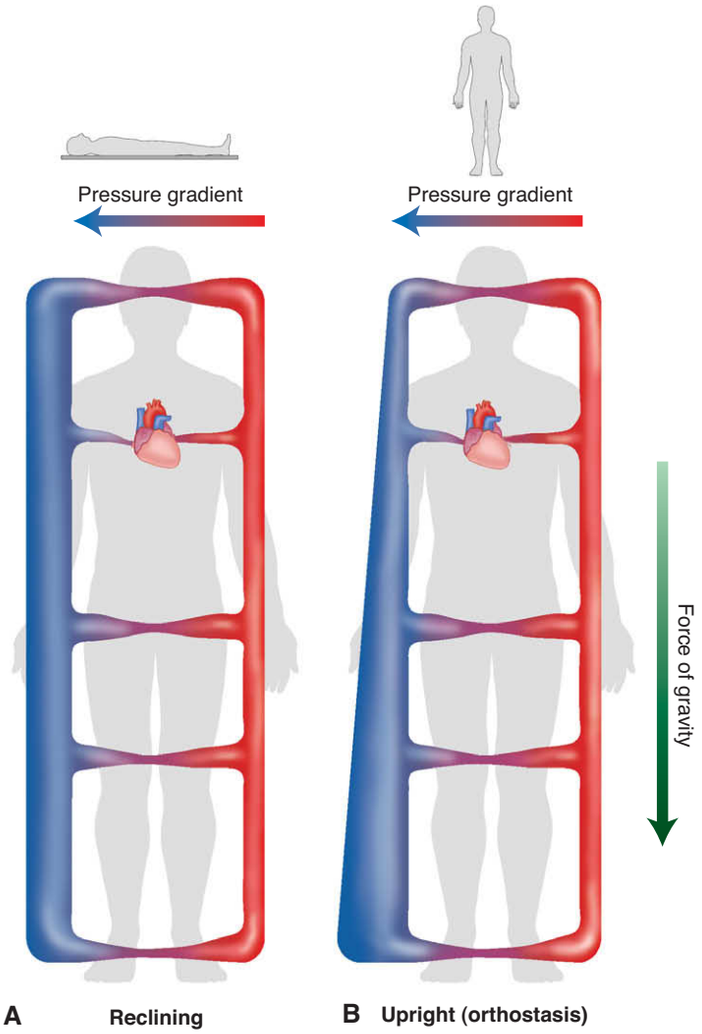


FIGURE 22-23

Influence of gravity on blood distribution in veins. A, When a person is lying flat, the pull of gravity is equal above and below the heart. **B,** When a person stands upright (orthostasis), the pull of gravity combined with the compliance (ease of stretch) of the veins causes a redistribution of venous blood to the lower limbs. This *orthostatic effect* can reduce venous return to the heart if not counteracted by other forces.

Venous Pumps

One important factor that promotes the return of venous blood to the heart is the blood-pumping action of respirations and skeletal muscle contractions. Both actions produce their facilitating effect on venous return by increasing the pressure gradient between the peripheral veins and the venae cavae (central veins).

The process of inspiration increases the pressure gradient between peripheral and central veins by decreasing central venous pressure and also by increasing peripheral venous pressure. Each time the diaphragm contracts, the thoracic cavity necessarily becomes larger and the abdominal cavity smaller. Therefore the pressures in the thoracic cavity, in the thoracic portion of the vena cava, and in the atria decrease, and those in the abdominal cavity and the abdominal veins increase. As Figure 22-24, A, shows, this change in pressure between expiration and inspiration acts as a "respiratory pump" that moves blood along the venous route.

Deeper respirations intensify these effects and therefore tend to increase venous return to the heart more than normal respirations. This is part of the reason the principle is true—increased respirations and increased circulation tend to go hand in hand.

Skeletal muscle contractions serve as "booster pumps" for the heart. The skeletal muscle pump promotes venous return in

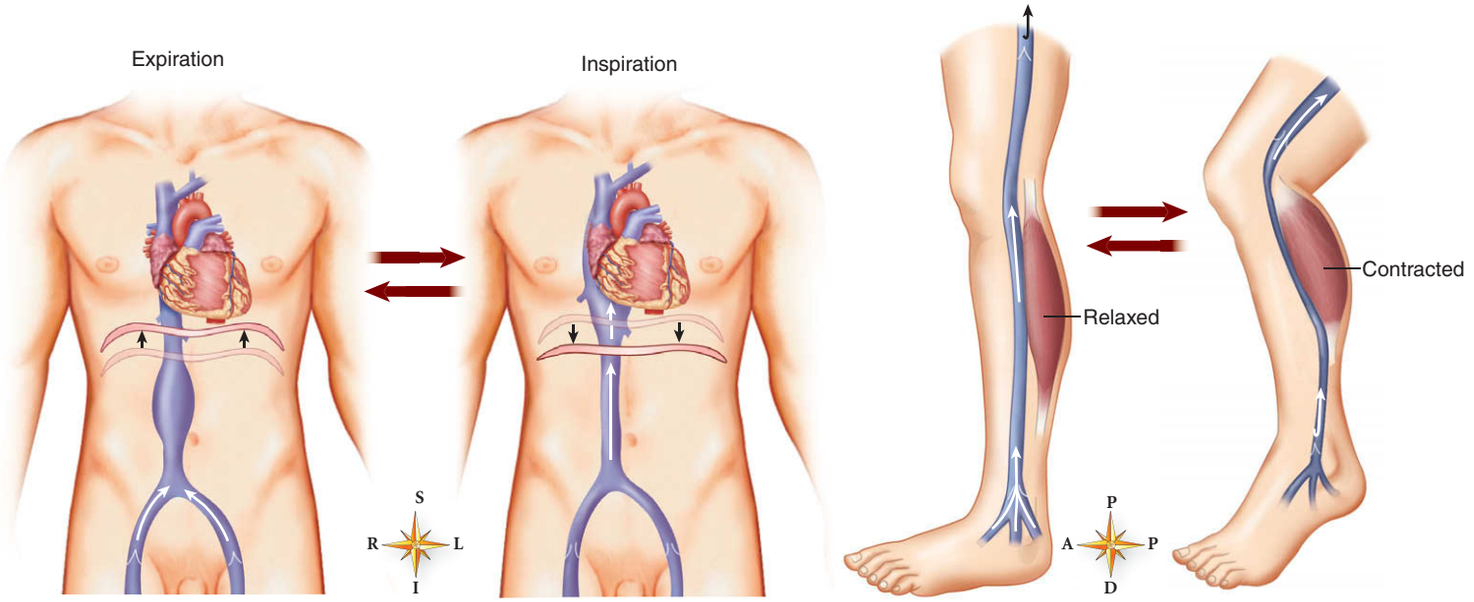


FIGURE 22-24

Venous pumping mechanisms. A, The respiratory pump operates by alternately increasing pressure in the thorax during expiration (thus pushing central venous blood into the heart) and decreasing thoracic pressure during inspiration (thus pulling venous blood into the central veins). **B,** The skeletal muscle pump operates by the alternate increase and decrease in peripheral venous pressure that normally occurs when the skeletal muscles are used for the activities of daily living. Both pumping mechanisms rely on the presence of one-way valves in the veins to prevent backflow during the low-pressure points in the pumping cycle (see Figure 22-25).

the following way. As each skeletal muscle contracts, it squeezes the soft veins scattered through its interior, thereby "milking" the blood in them upward, or toward the heart (Figure 22-24, *B*). The closing of the one-way valves present in veins prevents blood from falling back as the muscle relaxes. Their flaps catch the blood as gravity pulls backward on it (Figure 22-25). The net effect of skeletal muscle contraction plus venous valvular action therefore is to move venous blood toward the heart, to increase the venous return.

The value of skeletal muscle contractions in moving blood through veins is illustrated by a common experience. Who has not noticed how much more uncomfortable and tiring standing still is than walking? After several minutes of standing quietly, the feet and legs feel "full" and swollen. Blood has accumulated in the veins because the skeletal muscles are not contracting and squeezing it upward. The repeated contractions of the muscles when walking naturally in comfortable shoes, on the other hand, keep the blood moving in the veins and prevent the discomfort of distended veins.

Total Blood Volume

The return of venous blood to the heart can be influenced by factors that change the total volume of blood in the closed circulatory pathway. Stated simply, the more the total volume of blood, the greater the volume of blood returned to the heart. What mechanisms can increase or decrease the total volume of

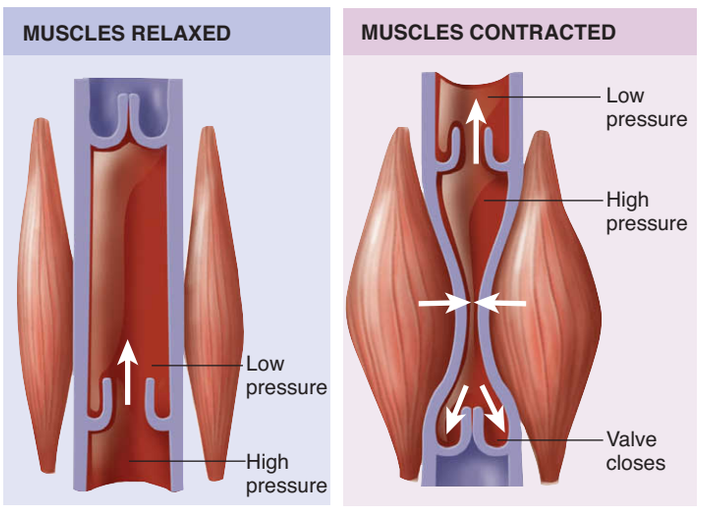


FIGURE 22-25

Venous valves. In veins, one-way valves aid circulation by preventing backflow of venous blood when pressure in a local area is low. **A,** Local high blood pressure pushes the flaps of the valve to the side of the vessel, allowing easy flow. **B,** When pressure below the valve drops, blood begins to flow backward but fills the "pockets" formed by the valve flaps, pushing the flaps together and thus blocking further backward flow.

blood? The mechanisms that change total blood volume most quickly, making them most useful in maintaining constancy of blood flow, are those that cause water to quickly move into the plasma (increasing total blood volume) or out of the plasma (decreasing total blood volume). Most mechanisms that accomplish such changes in plasma volume operate by altering the body's retention of water.

CAPILLARY EXCHANGE AND TOTAL BLOOD VOLUME

We begin our discussion of fluid movement into and out of the blood plasma with a brief overview of **capillary exchange**—the exchange of materials between plasma in the capillaries and the surrounding interstitial fluid of the systemic tissues.

According to a principle first proposed by Ernest Starling, several factors govern the movement of fluid (and solutes contained in the fluid) back and forth across a capillary wall—a principle now known as **Starling's law of the capillaries.** These factors, illustrated in Figure 22-26, include inwardly directed forces and outwardly directed forces. It is the balance between these forces that determines whether fluids will move into or out of the plasma at any particular point.

One type of force, osmotic pressure, tends to promote diffusion of fluid into the plasma. Osmotic pressure generated by blood colloids (large solute particles such as plasma proteins) in the plasma that cannot cross the vessel wall tends to draw water osmotically into the plasma. At the arterial end of a capillary (and in some thin-walled arterioles) the potential osmotic pressure is small and thus generates only a small, inwardly directed force. However, a much larger, outwardly directed force is operating at the arterial end of a capillary, namely, a hydrostatic pressure gradient. Recall from Chapter 4 that hydrostatic pressure gradients promote filtration across a barrier with filtration pores, such as the capillary wall. At the arterial end of a capillary, the blood pressure in the vessel is much greater than the hydrostatic pressure of the interstitial fluid (IF), thus generating a very large, outwardly directed force. In short, the stronger, outwardly directed forces at the arterial end of a capillary drive fluids out of the blood vessel and into the surrounding IF—producing a net loss of blood volume.

At the venous end of the capillary, however, the loss of water has increased the blood colloid osmotic pressure—promoting osmosis of water back into the plasma. This inwardly directed force is much larger than the hydrostatic pressure gradient, which has dissipated somewhat with the loss of water at the arterial end of the vessel. In short, the capillary recovers much of the fluid it lost—recovering some of the previously lost blood volume.

If you look carefully at Figure 22-26, A, you will notice that about 10% of the fluid lost at the arterial end of a capillary is not recovered by the forces operating in Starling's law of the capillaries. Does that mean that there is a constant loss of blood volume? No. Notice that the 10% fluid loss is recovered by the lymphatic system and returned to the venous blood before it reaches the heart. Details of how the lymphatic system accomplishes this fluid recovery are discussed in the next chapter. For now, we will simply state that if the lymphatic system operates normally and the

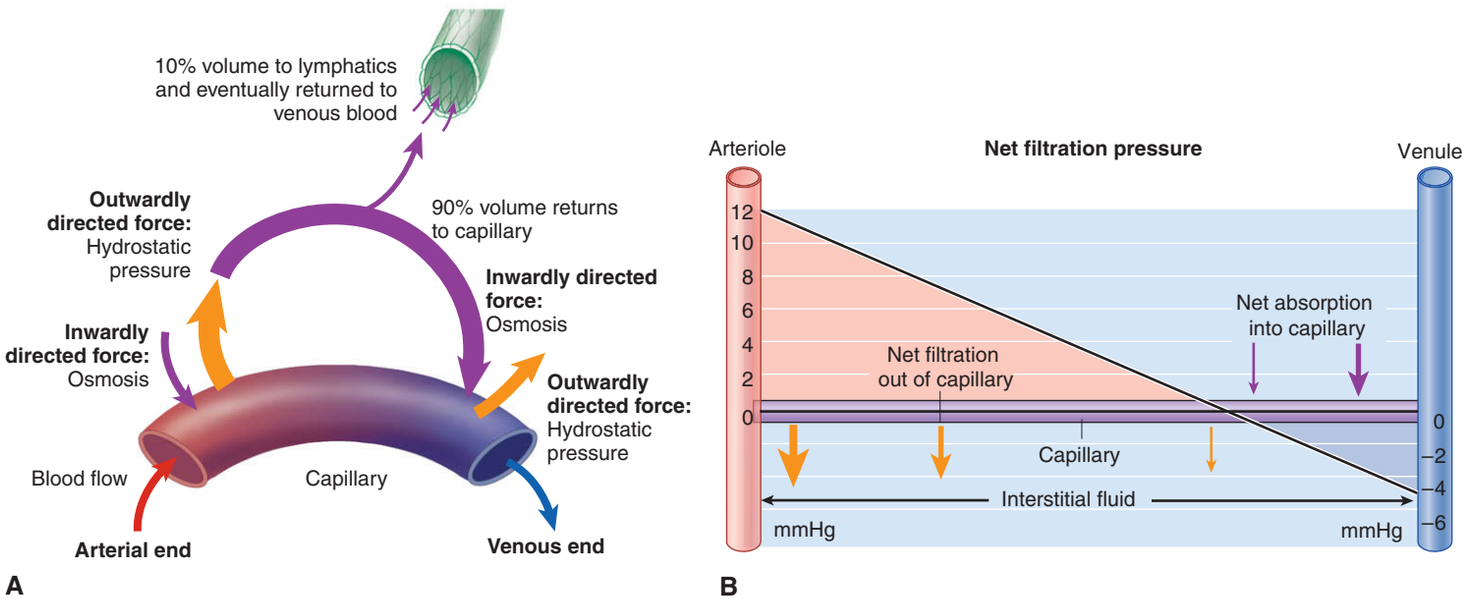


FIGURE 22-26

Starling's law of the capillaries. A, At the arterial end of a capillary the outward driving force of blood pressure (hydrostatic pressure of blood) is larger than the inwardly directed force of osmosis—thus fluid moves out of the vessel. At the venous end of a capillary the inward driving force of osmosis is greater than the outwardly directed force of hydrostatic pressure—thus fluid enters the vessel. About 90% of the fluid leaving the capillary at the arterial end is recovered by the blood before it leaves the venous end. The remaining 10% is recovered by the venous blood eventually, by way of the lymphatic vessels (see Chapter 23). **B,** Graph showing the shift in net filtration force along the length of a capillary, according to Starling's law of the capillaries. At the arterial end, net movement of fluid is *out of* the capillary; at the venous end, net movement of fluid shifts *into* the capillary.

osmotic and hydrostatic pressure gradients remain relatively constant, there is no net loss of blood volume resulting from capillary exchange. If any of these factors change, however, fluid retention by the blood will be affected.

CHANGES IN TOTAL BLOOD VOLUME

You have already studied the primary mechanisms for altering water retention in the body—they are the endocrine reflexes previewed in Chapter 19.

ADH Mechanism

One endocrine reflex that regulates total blood volume is the *ADH mechanism.* Recall that ADH (antidiuretic hormone) is released by the neurohypophysis (posterior pituitary) and acts on the kidneys in a way that reduces the amount of water lost by the body. ADH does this by increasing the amount of water that the kidneys reabsorb from urine before the urine is excreted from the body. The more ADH is secreted, the more water will be reabsorbed into the blood from the urine, and the greater the blood plasma volume will become. The ADH mechanism can be triggered by various factors, such as input from baroreceptors and input from osmoreceptors (which detect the balance between water and solutes in the internal environment).

Renin-angiotensin-aldosterone System (RAAS)

Another mechanism that changes blood plasma volume is the *renin-angiotensin mechanism* of aldosterone secretion—the **renin-angiotensin-aldosterone system, RAAS.** You may want to turn back to Figure 19-19 (p. 579) to see that the enzyme renin is released when blood pressure in the kidney is low. Renin triggers a series of events that leads to the secretion of aldosterone, a hormone of the adrenal cortex. Aldosterone promotes sodium retention by the kidney, which in turn stimulates the osmotic flow of water from kidney tubules back into the blood plasma—but only when ADH is present to permit the movement of water. Thus low blood pressure increases the secretion of aldosterone, which in turn stimulates retention of water and thus an increase in blood volume.

Another effect of the renin-angiotensin mechanism is the vasoconstriction of blood vessels caused by an intermediate compound called *angiotensin II.* This complements the volume-increasing effects of the mechanism and thus also promotes an increase in overall blood flow. Because ACE (angiotensin-converting enzyme) regulates the amount of available angiotensin II, drugs that act as ACE inhibitors can reduce angiotensin II and thus block vasoconstriction—an effect that is useful in reducing abnormally high blood pressure (hypertension).

ANH Mechanism

Yet another mechanism that can change blood plasma volume and thus venous return of blood to the heart is the *ANH mechanism.* Recall that ANH (atrial natriuretic hormone) is secreted by specialized cells in the atrial wall in response to overstretching. Overstretching of the atrial wall, of course, occurs when venous return to the heart is abnormally high. ANH adjusts venous return back down to its set point value by promoting the loss of water from the plasma and the resulting decrease in blood volume. ANH accomplishes this feat by increasing urine sodium loss, which causes water to follow osmotically. Sodium loss also inhibits the secretion of ADH. ANH may also have other complementary effects, such as promoting vasodilation of blood reservoirs.

Balance of Regulation

Thus various mechanisms influence blood volume and therefore venous return. These primary mechanisms are summarized in Figure 22-27. The ANH mechanism opposes ADH, renin-angiotensin, and aldosterone mechanisms to produce a balanced, precise control of blood volume. Precision of blood volume control contributes to precision in controlling venous return, which in turn contributes to precision in the overall control of blood circulation.

In summary, many different factors help regulate blood pressure and therefore regulate blood flow. Figure 22-28 summarizes some of the rapidly acting, intermediate, and long-term responses that can return blood pressure and blood flow back to normal after a sudden change. Most of these responses have been discussed in this chapter and Chapter 21, but some will be explored further in later chapters.

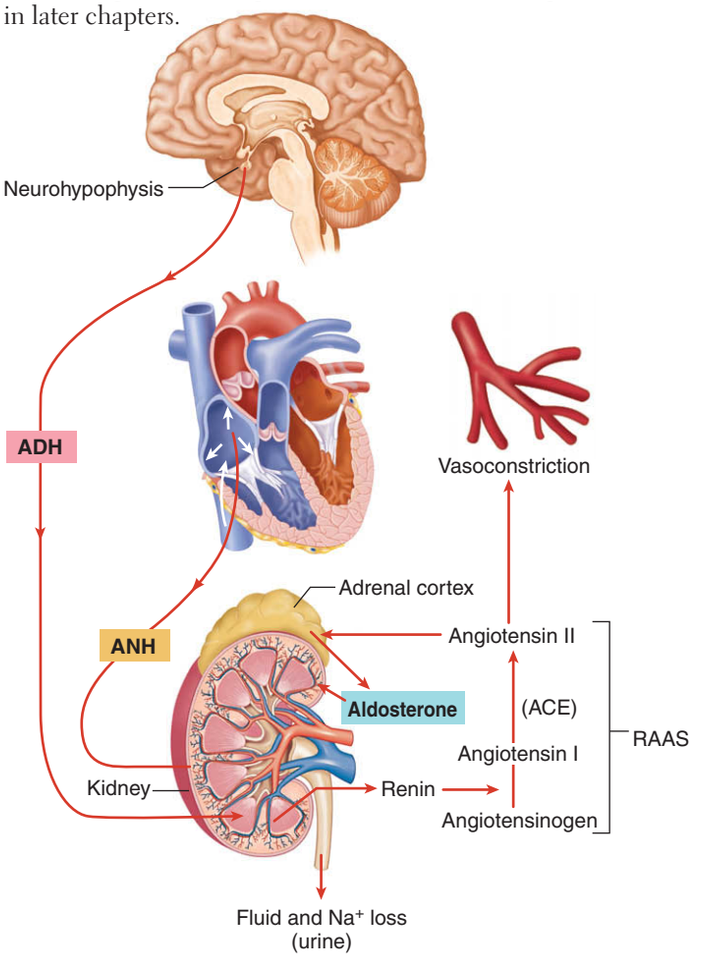


FIGURE 22-27

Three mechanisms that influence total plasma volume. The antidiuretic hormone (ADH) mechanism and renin-angiotensin-aldosterone system (RAAS) tend to increase water retention and thus increase total plasma volume. The atrial natriuretic hormone (ANH) mechanism antagonizes these mechanisms by promoting water loss and thus promoting a decrease in total plasma volume. *ACE,* Angiotensinogen-converting enzyme.

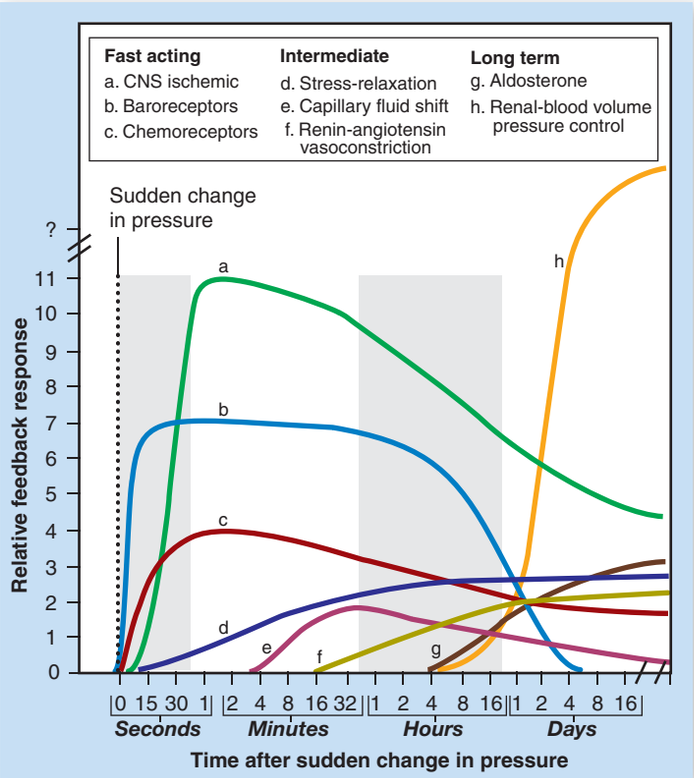


FIGURE 22-28

Feedback responses of various arterial pressure mechanisms. This composite graph shows the relative regulatory shifts that can be carried out by different regulatory mechanisms in response to a sudden shift in blood pressure—all with the outcome of moving arterial blood pressure back to its set point value. Note that some responses have their maximum effect within a few seconds or minutes. Other responses take longer to reach their maximum effect. *CNS,* Central nervous system.

| QUICK CHECK |

14. What is meant by the term *venous return?*
15. Briefly describe how the respiratory pump and skeletal muscle pump work.
16. How does Starling's law of the capillaries explain capillary exchange?
17. What three hormonal mechanisms work together to regulate blood volume?

MEASURING BLOOD PRESSURE

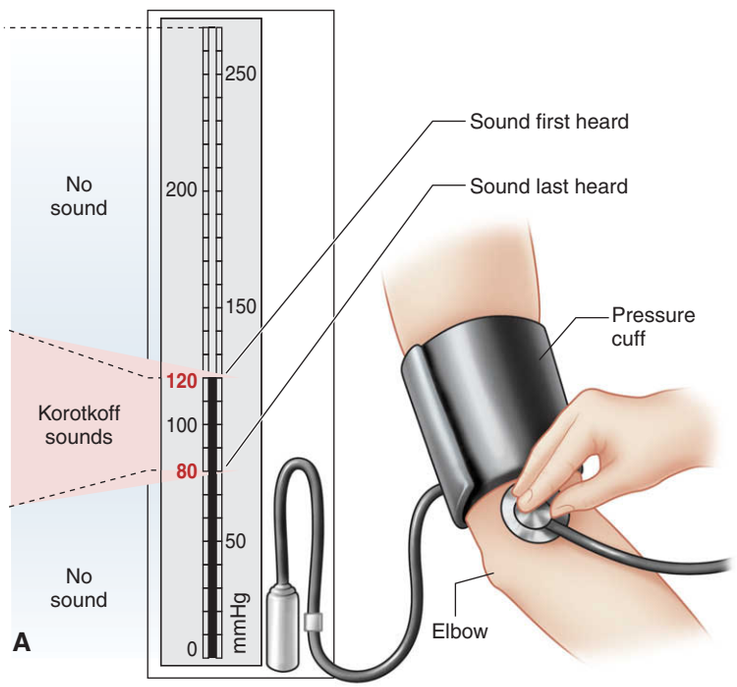
Arterial Blood Pressure

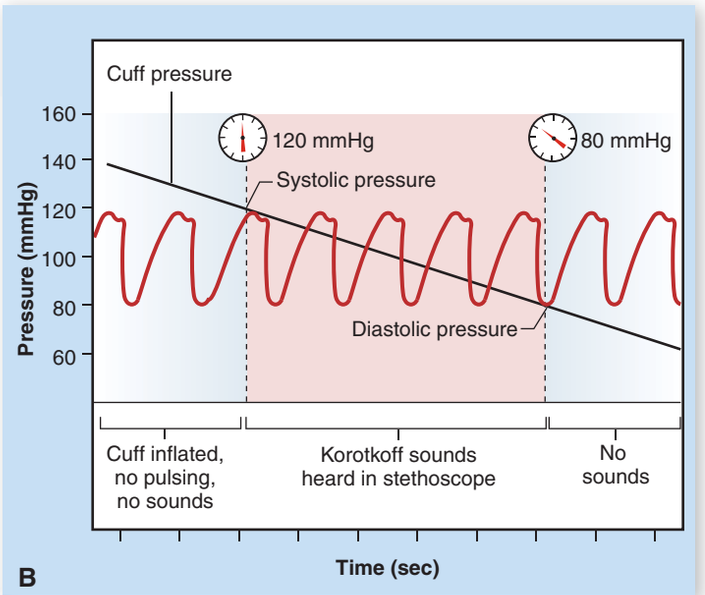
Blood pressure is measured with the aid of an apparatus known as a **sphygmomanometer,** which makes it possible to measure the amount of air pressure equal to the blood pressure in an artery. The measurement is made in terms of how many millimeters (mm) high the air pressure raises a column of mercury (Hg) in a glass tube.

Sphygmomanometers originally consisted of a rubber cuff attached by a rubber tube to a compressible bulb and by another tube to a column of mercury that was marked off in millimeters (Figure 22-29). Pressure in the cuff and rubber tube pushes the

FIGURE 22-29

Sphygmomanometer. This mercury-filled pressure sensor is used in clinical and research settings to quickly and accurately measure arterial blood pressure. **A,** The pressure cuff is pumped with air until the pressure inside the cuff exceeds the expected systolic pressure of the large arteries of the arm. No sound caused by pulsing of blood in the arteries can then be heard with a stethoscope. As the pressure inside the cuff is slowly released from a valve, the air pressure equals the maximum pressure of the pulse waves in the artery—thus the pulsing sounds can then be heard. **B,** The sounds of pulsing (Korotkoff sounds) continue as long as the cuff pressure is equal to pressures of the pulse wave. The sounds disappear at the point that cuff pressure drops below the minimum pulse pressure in the arteries.





column of mercury to a new height. Therefore, pressure can be expressed as *millimeters of mercury (mmHg)*. Because of the hazardous nature of mercury, many sphygmomanometers in use today have mercury-free mechanical or electronic pressure sensors that are calibrated to the mercury scale.

The cuff of the sphygmomanometer is wrapped around the arm over the brachial artery, and air is pumped into the cuff by means of the bulb. In this way, air pressure is exerted against the outside of the artery. Air is added until the air pressure exceeds the blood pressure within the artery or, in other words, until it compresses the artery. At this time, no pulse can be heard through a stethoscope placed over the brachial artery at the bend of the elbow along the inner margin of the biceps muscle.

By slowly releasing the air in the cuff, the air pressure is decreased until it approximately equals the blood pressure within the artery. At this point, the vessel opens slightly and a small spurt of blood comes through, producing sharp "tapping" sounds. This is followed by increasingly louder sounds that change suddenly. They become more muffled, then disappear altogether. These sounds are called *Korotkoff sounds* (Box 22-2). Health professionals train themselves to hear these different sounds and simultaneously read the column of mercury, because the first tapping sound appears when the column of mercury indicates the **systolic blood pressure.** Systolic pressure is the force with which the blood is pushing against the artery walls at its highest pressure—during the ejection phase of the cardiac cycle when the ventricles are contracting. The lowest point at which the sounds can be heard, just before they disappear, is approximately equal to the **diastolic blood pressure,** or the force of the blood against the arterial walls when the ventricles are relaxed. Diastolic pressure is observed at the end of ventricular relaxation,

Box 22-2 | DIAGNOSTIC study

Focus on Turbulent Blood Flow

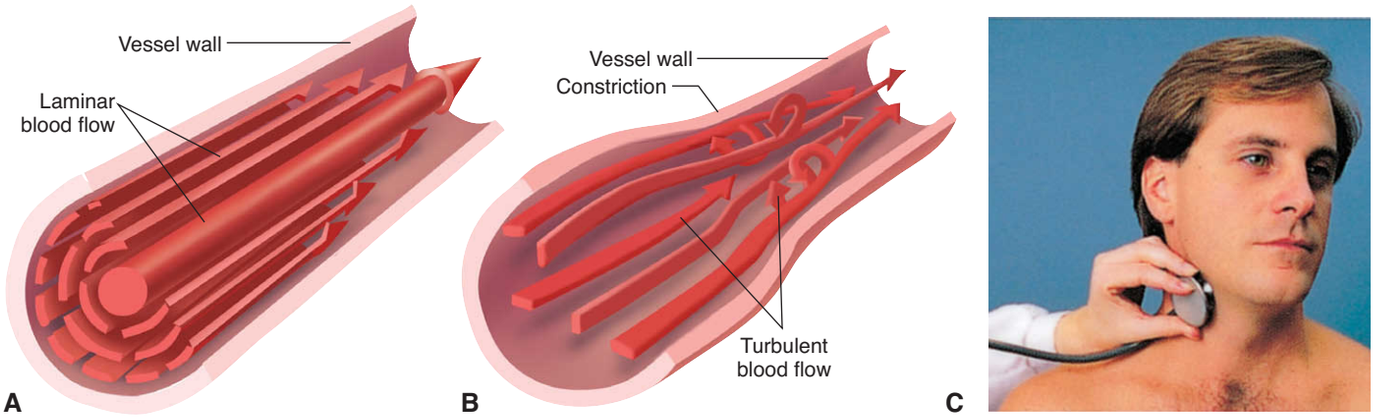
Understanding the mechanics of fluid flow through blood vessels facilitates comprehension of the bigger picture of hemodynamics.

Normally, blood flows through vessels with smooth walls that taper or enlarge only slightly, if at all. The manner in which a fluid, in this case blood, flows through a smooth vessel is termed **laminar flow.** The Latin word *lamina* means layer, an apt description of the way fluids flow through tubes in concentric, cylindrical layers—as you can see in part *A* of the figure. Because of friction against the inner face of the vessel wall, the outer layers of blood flow more slowly than the inner layers. Laminar flow is the normal pattern of blood flow in most healthy vessels.

When smooth, laminar flow is disrupted by branching or narrowing of a vessel, a sharp turn, or a sudden constriction or obstruction, the flow of blood becomes turbulent. **Turbulent flow,** shown in part *B* of the figure, occurs normally at heart valves and contributes to the first and second heart sounds described on p. 689.

However, significant turbulent flow in most vessels is not normal. If the sounds of turbulence are detected in a peripheral vessel, an abnormal or unusual constriction may exist. Such constrictions could be temporary and intentional, as in the case of an inflated blood pressure cuff pressing on an artery and creating turbulence. The sounds of turbulence generated by such blood pressure measurements are called **Korotkoff sounds** (see Figure 22-29). These sounds are named for Nicolai Korotkoff, the Russian surgeon who in 1905 developed the method for using these sounds to indirectly measure arterial blood pressure.

Some sounds of turbulence are caused by constrictions that are a serious threat to one's health. For example, in Chapter 21 we discussed the fact that arteriosclerosis can cause such a narrowing of a vessel's channel and can ultimately lead to death by ischemia, thrombosis, or other mechanisms (see Figure 21-44). Part *C* of the figure shows a stethoscope being used to listen for low-pitched blowing sounds called **bruits** (BROO-eez) that can occur in the carotid arteries. Bruits may result from obstruction caused by arteriosclerosis or abnormally increased pulse pressure. A usually benign, but abnormal, condition known as venous hum produces a humming noise in the internal jugular vein. Venous hum is common in children and probably results from vigorous myocardial contraction.



Turbulent blood flow. A, Laminar blood flow (no turbulence). **B,** Turbulent blood flow. **C,** Listening for bruits.

and as isovolumetric contraction of the ventricle occurs, as you can see near the top of the diagram in Figure 22-7 (p. 688).

Systolic pressure gives valuable information about the force of the left ventricular contraction, and diastolic pressure gives valuable information about the resistance of the blood vessels.

Blood in the arteries of an adult with a blood pressure reading at the high end of the normal range exerts a pressure equal to that required to raise a column of mercury about 120 mm (or a column of water more than 5 feet) high in a glass tube during systole of the ventricles and 80 mm high during diastole. For the sake of brevity, this is expressed as a blood pressure of "120 over 80" or 120/80. The first, or upper, figure represents systolic pressure, and the second represents diastolic pressure.

From the figures just given, we observe that blood pressure fluctuates considerably during each heartbeat. During ventricular systole, the force is great enough to raise the mercury column 40 mm higher than during ventricular diastole. This difference between systolic and diastolic pressure is called **pulse pressure.** It characteristically increases in arteriosclerosis, mainly because systolic pressure increases more than diastolic pressure. Pulse pressure increases even more markedly in aortic valve insufficiency because of both a rise in systolic pressure and a fall in diastolic pressure.

Be aware that although the classic method of indirect arterial blood pressure assessment involves a column of mercury, and the units in which blood pressure is expressed are based on the height of a mercury column, very few modern sphygmomanometers actually use mercury. The reason is twofold. First, mercury is a very hazardous substance and should the mercury column break, an environmental health hazard would be created. Second, it is much more cost effective to use inexpensive and durable electronic pressure sensors that are calibrated to the mercury scale than to construct fragile columns of mercury in glass.

Blood pressure can also be measured directly in various ways. For example, a small tube called a *cannula* with a removable pointed insert can be pushed directly into a vessel, the insert withdrawn, and the cannula connected to a manometer or electronic pressure sensor. A long, flexible tube called a *catheter* can likewise be placed in a blood vessel or even into a chamber of the heart. These techniques can be used in critical care, but the more indirect methods described previously are more practical for routine screening and clinical evaluation.

Blood Pressure and Bleeding

Because blood exerts a comparatively high pressure in arteries and a very low pressure in veins, it gushes forth with considerable force from a cut artery but seeps in a slow, steady stream from a vein. As we have just seen, each ventricular contraction raises arterial blood pressure to the systolic level, and each ventricular relaxation lowers it to the diastolic level. As the ventricles contract, the blood spurts forth forcefully because of the increased pressure in the artery, but as the ventricles relax, the flow ebbs to almost nothing because of the fall in pressure. In other words, blood escapes from an artery in spurts because of the alternate raising and lowering of arterial blood pressure but flows slowly and steadily from a vein because of the low, practically constant pressure. A uniform, instead of a pulsating, pressure exists in the capillaries and veins. Why? Because the arterial walls, being elastic, continue to squeeze the blood forward while the ventricles are in diastole. Therefore blood enters capillaries and veins under a relatively steady pressure (see Figure 22-9).

MINUTE VOLUME OF BLOOD

The volume of blood circulating through the body per minute **(minute volume)** is determined by the magnitude of the blood pressure gradient and the peripheral resistance (Figure 22-30).

A nineteenth century physiologist and physicist, Jean Poiseuille (pwah-SWEE), described the relation between these three factors—pressure gradient, resistance, and minute volume—with a mathematical equation known as **Poiseuille's law.** In general, but with certain modifications, it applies to blood circulation. We can state the law in a simplified form as follows: the volume of blood circulated per minute is directly related to mean arterial pressure minus central venous pressure and is inversely related to resistance:

$$\text{Volume of blood circulated per minute} = \frac{\text{Mean arterial pressure} - \text{Central venous pressure}}{\text{Resistance}}$$

$$\text{Minute volume} = \frac{\text{Pressure gradient}}{\text{Resistance}}$$

This mathematical relationship needs qualifying with regard to the influence of peripheral resistance on circulation. For instance, according to the equation, an increase in peripheral resistance tends to decrease blood flow. (Why? Increasing peripheral resistance increases the denominator of the fraction in the preceding equation. Increasing the denominator of any fraction necessarily does what to its value? It decreases the value of the fraction.)

Increased peripheral resistance, however, has a secondary action that opposes its primary tendency to decrease blood flow. An increase in peripheral resistance hinders or decreases arteriole runoff. This, of course, tends to increase the volume of blood left in the arteries and so tends to increase arterial pressure. Note also that increasing arterial pressure tends to increase the value of the fraction in Poiseuille's equation. Therefore it tends to increase circulation. In short, to say unequivocally what the effect of an increased peripheral resistance will be on circulation is impossible. It depends also on arterial blood pressure—whether it increases, decreases, or stays the same when peripheral resistance increases. The clinical condition *arteriosclerosis with hypertension* (high blood pressure) illustrates this point. Both peripheral resistance and arterial pressure are increased in this condition. If resistance were to increase more than arterial pressure, circulation (i.e., volume of blood flow per minute) would decrease. But if arterial pressure increases proportionately to resistance, circulation remains normal.

| QUICK CHECK |

18. What is meant by the term *minute volume?*
19. How is minute volume related to peripheral resistance?

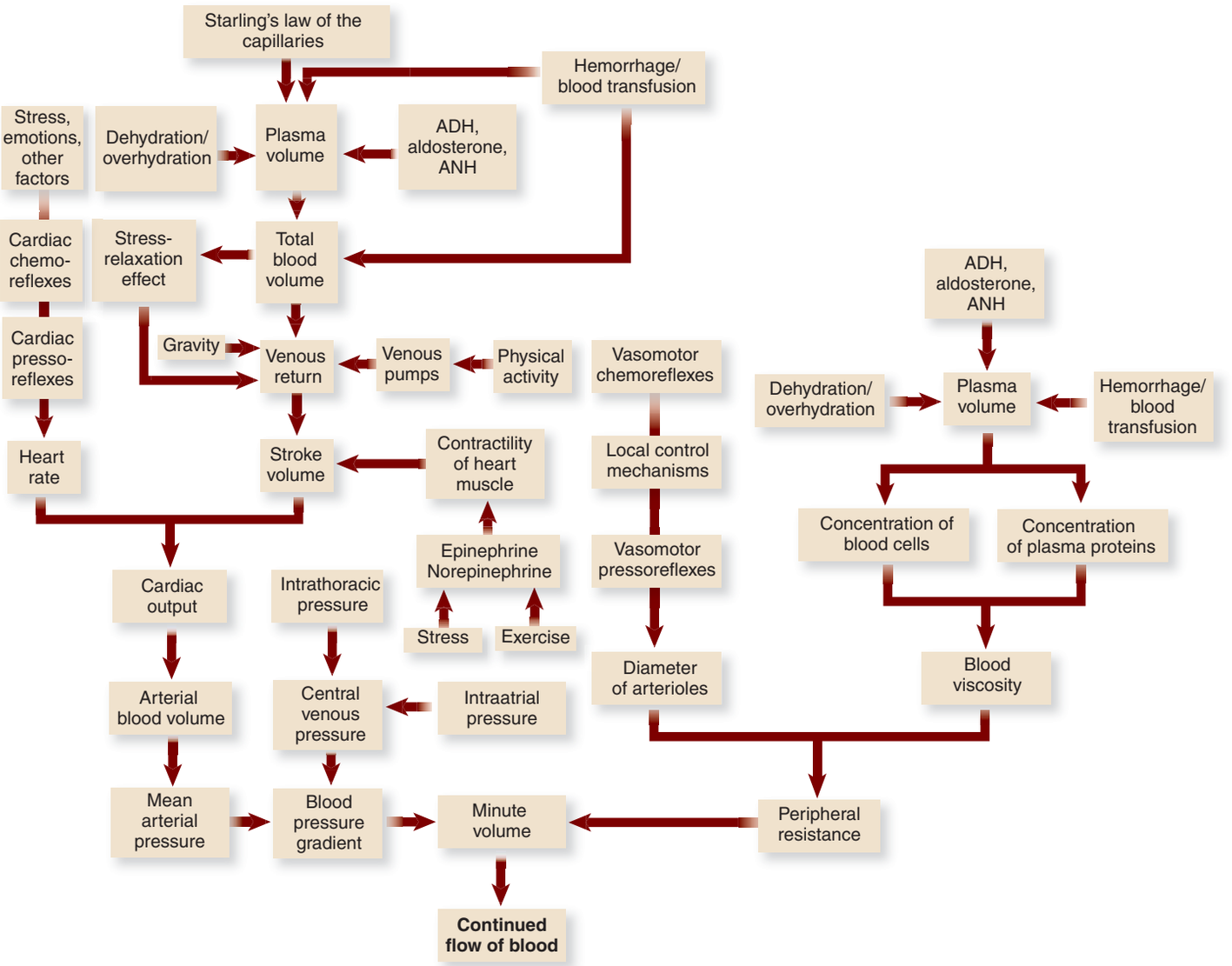


FIGURE 22-30

Factors that influence the flow of blood. The flow of blood, expressed as volume of blood flowing per minute (or *minute volume*), is determined by various factors. This chart shows only some of the major factors that influence blood flow. Note that some factors appear more than once in the chart, indicating that they can influence blood flow in several ways. *ADH,* Antidiuretic hormone; *ANH,* atrial natriuretic hormone.

VELOCITY OF BLOOD FLOW

The speed with which the blood flows, that is, distance per minute, through its vessels is governed in part by the physical principle that when a liquid flows from an area of one cross-sectional size to an area of larger size, its velocity slows in the area with the larger cross section (Figure 22-31). For example, a narrow river whose bed widens flows more slowly through the wide section than through the narrow section. In terms of the blood vascular system, the total cross-sectional area of all arterioles together is greater than that of the arteries. Therefore blood flows more slowly through arterioles than through arteries. Likewise, the total cross-sectional area of all capillaries together is greater than that of all arterioles, and therefore capillary flow is slower than arteriole flow. The venule cross-sectional area, on the other hand, is smaller than the capillary cross-sectional area. Therefore blood velocity increases in venules and again in veins, which have a still smaller cross-sectional area. In short, the most rapid blood flow takes place in arteries and the slowest in capillaries. Can you think of a valuable effect stemming from the fact that blood flows most slowly through the capillaries?

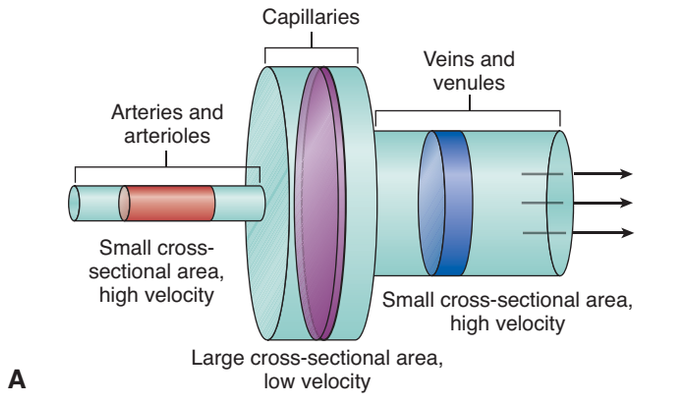


FIGURE 22-31

Relationship between cross-sectional area and velocity of blood flow. As you can see in the simple diagram **(A)** and the blood vessel chart **(B)**, blood flows with great speed in the large arteries. However, branching of arterial vessels increases the total cross-sectional area of the arterioles and capillaries, reducing the flow rate. When capillaries merge into venules and venules merge into veins, the total cross-sectional area decreases, causing the flow rate to increase.

PULSE

Mechanism

Pulse is defined as the alternate expansion and recoil of an artery. Two factors are responsible for the existence of a pulse that can be felt:

1. Intermittent injections of blood from the heart into the aorta, which alternately increase and decrease the pressure in that vessel. If blood poured steadily out of the heart into the aorta, the pressure there would remain constant, and there would be no pulse.
2. The elasticity of the arterial walls, which allows them to expand with each injection of blood and then recoil. If the vessels were fashioned from rigid material such as glass, there would still be an alternate raising and lowering of pressure within them with each systole and diastole of the ventricles, but the walls could not expand and recoil, and therefore no pulse could be felt.

Pulse Wave

Each ventricular systole starts a new pulse that proceeds as a wave of expansion throughout the arteries and is known as the pulse wave. It gradually dissipates as it travels, disappearing entirely in the capillaries. The pulse wave felt at the common carotid artery in the neck is large and powerful, rapidly following the first heart sound. Figure 22-32 shows that the carotid pulse wave begins during ventricular systole. Note that the closure of the aortic valve produces a detectable *dicrotic notch* in the pulse wave. However, the pulse felt in the radial artery at the wrist does not coincide with the contraction of the ventricles. It follows each contraction by an appreciable interval (the length of time required for the pulse wave to travel from the aorta to the radial artery). The farther from the heart the pulse is taken, therefore, the longer that interval is.

Almost everyone is aware of the diagnostic importance of the pulse. It reveals important information about the cardiovascular system, heart action, blood vessels, and circulation.

Not everyone is aware of the basic functional role of the pulse wave, however. The pulse wave actually conserves energy produced by the pumping action of the heart (Figure 22-33). The great force of pressure with which blood is ejected from the heart during ventricular systole expands the wall of the aorta. At that point, the stretched aortic wall has potential energy stored in it—just as a stretched rubber band has potential energy. During ventricular diastole, the elastic nature of the aortic wall allows it to recoil. This recoil exerts pressure on the blood and thus keeps it moving. If the wall of the aorta were inelastic, it would not alternately expand and recoil—and would thus not keep blood moving continuously. Instead, arterial blood would simply spurt, then stop, then spurt, then stop, and so on.

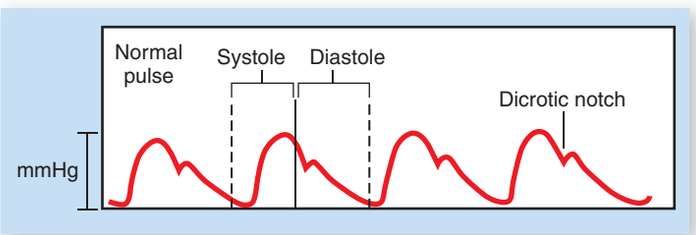


FIGURE 22-32

Normal carotid pulse wave. This series of pulse waves shows rhythmic increases and decreases in pressure as measured at the common carotid artery in the neck. The dicrotic notch represents the pressure fluctuation generated by closure of the aortic valve.

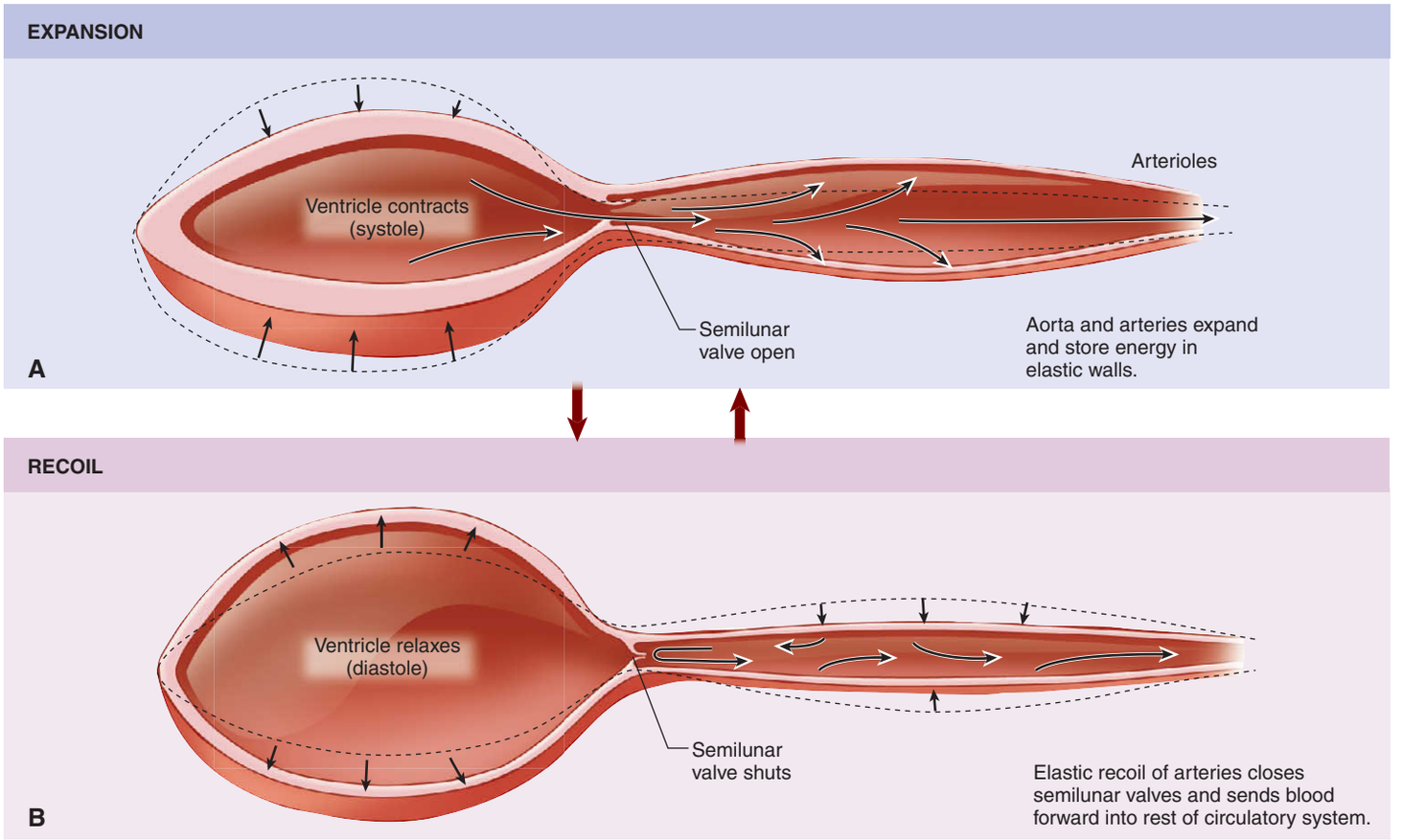


FIGURE 22-33

Functional role of the pulse wave. The arterial pulse conserves energy by absorbing and storing force from the ventricular contraction by causing elastic expansion of the arterial wall. The energy is used to maintain continued blood flow during ventricular relaxation by elastic recoil of the arterial wall—thus producing enough arterial pressure to keep blood flowing.

Where the Pulse Can Be Felt

The pulse can be felt wherever an artery lies near the surface and over a bone or other firm background. Some specific locations where the pulse point is most easily felt are listed here and shown in Figure 22-34:

Radial artery—at wrist
Temporal artery—in front of ear or above and to outer side of eye
Common carotid artery—along anterior edge of sternocleidomastoid muscle at level of lower margin of thyroid cartilage
Facial artery—at lower margin of lower jawbone on a line with corners of mouth and in groove in mandible about one third of the way forward from angle
Brachial artery—at bend of elbow along inner margin of biceps muscle
Femoral artery—in middle of groin, where artery passes over pelvic bone
Popliteal artery—behind the knee
Posterior tibial artery—behind the medial malleolus (inner "ankle bone")
Dorsalis pedis artery—on dorsum (upper surface) of foot

Six important pressure points can be used to stop arterial bleeding:

1. **Temporal artery**—in front of ear
2. **Facial artery**—same place at which pulse is taken
3. **Common carotid artery**—point where pulse is taken, with pressure back against spinal column
4. **Subclavian artery**—behind medial third of clavicle, pressing against first rib
5. **Brachial artery**—few inches above elbow on inside of arm, pressing against humerus
6. **Femoral artery**—in middle of groin, where artery passes over pelvic bone; pulse can also be felt here

In trying to stop arterial bleeding by pressure, one must always remember to apply the pressure at the pulse point, or *pressure point*, that lies between the bleeding part and the heart. Why? Blood flows from the heart through the arteries to the affected part. Pressure between the heart and bleeding point therefore cuts off the source of the blood flow to that point.

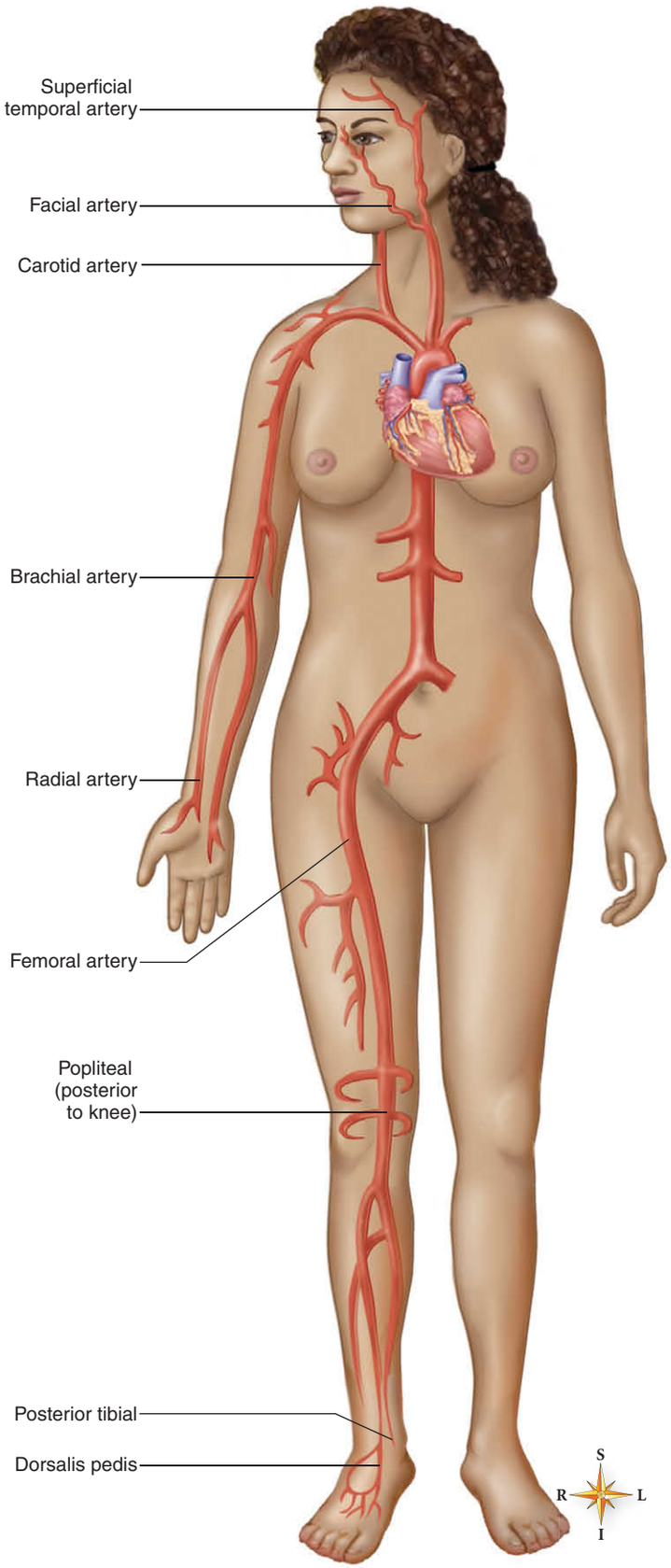


FIGURE 22-34

Pulse points. Each pulse point is named after the artery with which it is associated. (Some arteries in the figure have been enlarged to clarify the location of pulse points.)

Venous Pulse

A detectable pulse exists in the large veins only. It is most prominent in the veins near the heart because of changes in venous blood pressure brought about by alternate contraction and relaxation of the atria of the heart. The clinical significance of venous pulse is not as great as that of arterial pulse, and thus it is less often measured.

| QUICK CHECK |

20. What device is used in clinical settings to measure arterial blood pressure?
21. Which is more important for assessing health—the systolic pressure or the diastolic pressure?
22. In which type of vessel is blood most likely to be flowing at a very slow rate—an artery, a capillary, or a vein?
23. Without being specific, where are pulse points normally located in the body?

Cycle of LIFE

Cardiovascular Physiology

Changes in the function of the heart and blood vessels usually parallel the structural changes in these organs over the life span. For example, changes at the time of birth that adapt the circulatory system to life outside the womb cause changes in the blood pressure gradients that alter the flow of blood in many parts of the body. Likewise, the degenerative changes associated with aging reduce the heart's ability to maintain cardiac output and the ability of arteries to withstand high pressure.

Changes in arterial blood pressure are among the most apparent changes in the function of the cardiovascular system associated with the progression through the life cycle. In a newborn, normal arterial blood pressure is only about 90/55 mmHg—much lower than the arterial pressure of just under 120/80 mmHg in most healthy young adults. In older adults hypertension can develop—with arterial blood pressures commonly reaching 150/90 mmHg.

Another commonly observed change in cardiovascular function relates to heart rate. The heart rates of infants and children typically vary more than those in adults. Compared with adults, children often exhibit very large increases in heart rate in response to stressors such as illness, pain, tension, and exercise. Whereas a typical resting heart rate for adults is about 72 beats/min, the resting heart rate of a newborn can range from 120 to 170 beats/ min, and the resting heart rate of a preschooler can range from 80 to 160 beats/min. In older adults, resting heart rates range from lows of around 40 beats/min to 100 beats/min.

the BIG picture

Blood Flow and the Whole Body

As stated in this chapter and many times throughout this book, one of the essential concepts of homeostasis is the renewable fluid that makes up our internal environment. If we were not able to maintain the chemical nature and other physical characteristics of our internal fluid environment, we would not survive. To maintain the constancy of the internal fluid, we must be able to shift nutrients, gases, hormones, waste products, agents of immunity, and other materials around in the body. As certain materials are depleted in one tissue and new materials enter the internal environment in another tissue, redistribution must occur. What better way than through a system of circulating fluid? This fluid shifts materials from place to place and also redistributes heat and pressure. Recall from your study of the integumentary and muscular systems that shifting the flow of blood to or away from warm tissues at the proper time is essential to maintaining the homeostasis of body temperature. As we will learn in Chapter 31, the ability of our blood to increase or decrease blood pressure in the kidney has a great impact on that organ's vital function of filtering the internal environment. Understanding the basic mechanisms of almost any system in the body requires an understanding of the dynamics of blood flow.

What we have seen in this chapter is a wonderfully complex array of mechanisms that work together in concert with the actions of other systems to maintain the constancy of the *milieu intérieur*—the internal environment.

MECHANISMS of DISEASE

DISORDERS OF CARDIOVASCULAR PHYSIOLOGY

Cardiac Dysrhythmia

Various conditions such as inflammation of the endocardium (endocarditis) or myocardial infarction (heart attack) can damage the heart's conduction system and thereby disturb the normal rhythmical beating of the heart (Figure 22-35, *A*). The term **dysrhythmia** refers to an abnormality of heart rhythm. Dysrhythmia may also be called *arrhythmia*.

One kind of dysrhythmia is called a **heart block.** In AV node block, impulses are blocked from getting through to the ventricular myocardium, resulting in the ventricles contracting at a much slower rate than normal. On an ECG, there may be a large interval between the P wave and the R peak of the QRS complex (Figure 22-35, *B*). *Complete heart block* occurs when the P waves do not match up at all with the QRS complexes—as in an ECG that shows two or more P waves for every QRS complex. A physician may treat heart block by implanting in the heart an *artificial pacemaker.*

Bradycardia is a slow heart rhythm—below 60 beats/min (Figure 22-35, *C*). Slight bradycardia is normal during sleep and in conditioned athletes while they are awake (but at rest). Abnormal bradycardia can result from improper autonomic nervous control of the heart or from a damaged SA node. If the problem is severe, artificial pacemakers can be used to increase the heart rate by taking the place of the SA node.

Tachycardia is a very rapid heart rhythm—more than 100 beats/min (Figure 22-35, *D*). Tachycardia is normal during and just after exercise and during the stress response. Abnormal tachycardia can result from improper autonomic control of the heart, blood loss or shock, the action of drugs and toxins, fever, and other factors.

Sinus dysrhythmia is a variation in heart rate during the breathing cycle. Typically, the rate increases during inspiration and decreases during expiration. The causes of sinus dysrhythmia are not clear. This phenomenon is common in young people and usually does not require treatment.

Premature contractions, or *extrasystoles,* are contractions that occur before the next expected contraction in a series of cardiac cycles. For example, *premature atrial contractions (PACs)* may occur shortly after the ventricles contract—seen as early P waves on the ECG (Figure 22-35, *E*). Premature atrial contractions often occur with lack of sleep, too much caffeine or nicotine, alcoholism, or heart damage. Ventricular depolarizations that appear earlier than expected are called *premature ventricular contractions* (PVCs). PVCs appear on the ECG as early, wide QRS complexes without a preceding related P wave. PVCs are caused by a variety of circumstances that include stress, electrolyte imbalance, acidosis, hypoxemia, ventricular enlargement, or drug reactions. Occasional PVCs are not clinically significant in otherwise healthy individuals. However, in people with heart disease they may reduce cardiac output.

Frequent premature contractions can lead to fibrillation, a condition in which cardiac muscle fibers contract out of step with each other. This event can be seen in an ECG as the absence of regular P waves or abnormal QRS and T waves. In fibrillation, the affected heart chambers do not effectively pump blood.

Atrial fibrillation (A-fib or AF) occurs commonly in mitral stenosis, rheumatic heart disease, and infarction of the atrial myocardium (Figure 22-35, *F*). This condition can be treated with drugs such as digoxin (a **digitalis** preparation) or by *cardioversion*—the application of carefully timed electrical shocks to restore the normal myocardial rhythm.

Ventricular fibrillation (V-fib or VF) is an immediately life-threatening condition in which the lack of ventricular pumping suddenly stops the flow of blood to vital tissues (Figure 22-35, *G*). Ventricular fibrillation is often treated by *defibrillation*—application of electrical shock to force cardiac muscle fibers to contract in unison (Figure 22-36). Unless ventricular fibrillation is corrected immediately by defibrillation or some other method, death may occur within minutes.

Other types of defibrillators, besides those used by health professionals in emergency situations, also save lives. For example, *automatic internal cardiac defibrillators (AICDs)* are preprogrammed devices placed inside the body of a patient who is at a high risk for fibrillation. An AICD will automatically fire a

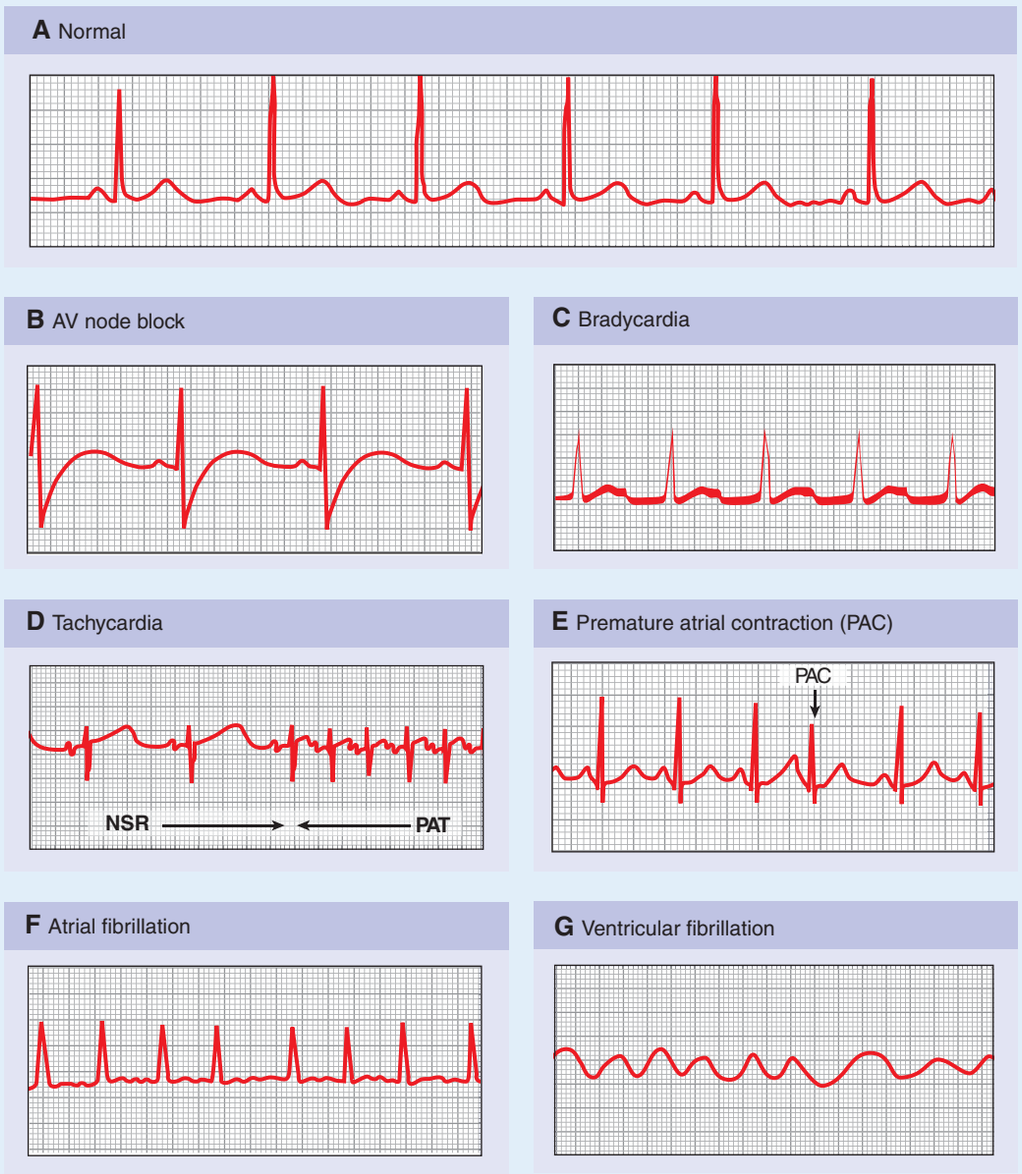


FIGURE 22-35

ECG strip chart recordings. A, Normal ECG. **B,** AV node block. Very slow ventricular contraction (25 to 45 beats/min at rest); P waves widely separated from peaks of QRS complexes. **C,** Bradycardia. Slow heart rhythm (less than 60 beats/min); no disruption of normal rhythm pattern. **D,** Tachycardia. Rapid heart rhythm (greater than 100 beats/min); no disruption of normal rhythm pattern. *NSR,* Normal sinus rhythm; *PAT,* paroxysmal (sudden) atrial tachycardia. **E,** Premature atrial contraction (PAC). Unexpected, early P wave that differs from normal P waves; PR interval may be shorter or longer than normal; normal QRS complex; more than 6 PACs per minute may precede atrial fibrillation. **F,** Atrial fibrillation. Irregular, rapid atrial depolarizations; P wave rapid (greater than 300/min) with irregular QRS complexes (150 to 170 beats/min). **G,** Ventricular fibrillation. Complete disruption of normal heart rhythm.

defibrillating shock as needed. Increasingly, *automatic external defibrillators (AEDs)* that can be used by nearly anyone have become available in public areas or for private use (see Figure 22-36).

Heart Failure

Heart failure is the inability of the heart to pump enough blood to sustain life. Heart failure is often measured as a decline in the *ejection fraction (EF)* below normal. The lower the EF, the more severe the heart failure.

Heart failure can result from many different heart diseases. Valve disorders can reduce the pumping efficiency of the heart enough to cause heart failure. **Cardiomyopathy** (kar-dee-oh-my-OP-ah-thee), or disease of the myocardial tissue, may reduce pumping effectiveness. A specific event such as myocardial infarction can result in myocardial damage that causes heart failure. Dysrhythmias such as complete heart block or ventricular fibrillation can also impair the pumping effectiveness of the heart and thus cause heart failure.

Congestive heart failure (CHF), or simply, *left-side heart failure,* is the inability of the left ventricle to pump blood



FIGURE 22-36

Defibrillation. Application of electrical shock to force cardiac muscle fibers to contract in unison, as with this *AED (automatic external defibrillator),* has saved many lives by correcting fibrillation of the atria and/or ventricles.

effectively. Most often, such failure results from myocardial infarction caused by coronary artery disease. It is called *congestive heart failure* because it decreases pumping pressure in the systemic circulation, which in turn causes the body to retain fluids. Portions of the systemic circulation thus become congested with extra fluid. As previously stated, left-side heart failure also causes congestion of blood in the pulmonary circulation (termed *pulmonary edema*)—possibly leading to right-side heart failure.

Failure of the right side of the heart, or *right-side heart failure*, accounts for about one fourth of all cases of heart failure. Right-side heart failure often results from the progression of disease that begins in the left side of the heart. Failure of the left side of the heart results in reduced pumping of blood returning from the lungs. Blood backs up into the pulmonary circulation and then into the right side of the heart—causing an increase in pressure that the right side of the heart simply cannot overcome. Right-side heart failure can also be caused by lung disorders that obstruct normal pulmonary blood flow and thus overload the right side of the heart—a condition called **cor pulmonale** (kohr pul-mah-NAL-ee). (See also Mechanisms of Disease section in Chapter 21.)

Circulatory Shock

The term **circulatory shock** refers to the failure of the circulatory system to adequately deliver oxygen to the tissues, resulting in the impairment of cell function throughout the body. If left untreated, circulatory shock may lead to death. Circulatory failure has many causes, all of which somehow reduce the flow of blood through the blood vessels of the body. Because of the variety of causes, circulatory shock is often classified into the following types:

Cardiogenic shock results from any type of heart failure, such as that after severe myocardial infarction (heart attack), heart infections, and other heart conditions. Because the heart can no longer pump blood effectively, blood flow to the tissues of the body decreases or stops.

Hypovolemic shock results from the loss of blood volume in the blood vessels (hypovolemia means "low blood volume"). Reduced blood volume results in low blood pressure and reduced flow of blood to tissues. Hemorrhage is a common cause of blood volume loss leading to hypovolemic shock. Hypovolemia can also be caused by loss of interstitial fluid, causing a drain of blood plasma out of the vessels and into the tissue spaces. Loss of interstitial fluid is common in chronic diarrhea or vomiting, dehydration, intestinal blockage, severe or extensive burns, and other conditions.

Neurogenic shock results from widespread dilation of blood vessels caused by an imbalance in autonomic stimulation of smooth muscle in vessel walls. It is also sometimes called **vasodilatory shock.** You may recall from Chapter 16 that autonomic effectors such as smooth muscle tissues are controlled by a balance of stimulation from the sympathetic and parasympathetic divisions of the autonomic nervous system. Normally, sympathetic stimulation maintains the muscle tone that keeps blood vessels at their usual diameter. If sympathetic stimulation is disrupted by an injury to the spinal cord or medulla, depressive drugs, emotional stress, or some other factor, blood vessels dilate significantly. Widespread vasodilation reduces blood pressure, thus reducing blood flow.

Anaphylactic shock results from an acute allergic reaction called *anaphylaxis*. Anaphylaxis causes the same kind of blood vessel dilation characteristic of neurogenic shock.

Septic shock results from complications of septicemia, a condition in which infectious agents release toxins into the blood. The toxins often dilate blood vessels, thereby causing shock. The situation is usually made worse by the damaging effects of the toxins on tissues combined with the increased cell activity caused by the accompanying fever. One type of septic shock is *toxic shock syndrome* (TSS), which usually results from staphylococcal infections that begin in the vagina of menstruating women and spread to the blood.

The body has numerous mechanisms that compensate for the changes that occur during shock. However, these mechanisms may fail to compensate for changes that occur in severe cases, and this failure often results in death.

Hypertension

The largest number of office visits to physicians is due to a condition called **hypertension (HTN),** or high blood pressure. More than 60 million cases of HTN have been diagnosed in the United States. This condition occurs when the force of blood exerted by the arterial blood vessel exceeds a blood pressure of 140/90 mmHg. Ninety percent of HTN cases are classified as *primary-essential*, or idiopathic, with no single known causative etiology. Another classification, *secondary HTN*, is caused by kidney disease or hormonal problems or induced by oral contraceptives, pregnancy, or other causes.

Another way of classifying hypertension is illustrated in the accompanying chart adapted from the National High Blood Pressure Education Program (Figure 22-37). This system uses systolic and diastolic blood pressure values to classify hypertension into stages according to severity. The guidelines that accompany this scheme emphasize the belief that there is no precise distinction between normal and abnormal values—thus even those in the high-normal range or the *prehypertension* range may be treated as having HTN.

Many risk factors have been identified in the development of HTN. Genetic factors play a large role. There is an increased susceptibility or predisposition with a family history of HTN. Men experience higher rates of HTN at an earlier age than women, and HTN in African Americans far exceeds that of Caucasians in the United States. There is also a direct relationship between age and high blood pressure. This is because as age advances, the blood vessels become less compliant and there is a higher incidence of atherosclerotic plaque buildup. HTN can also be fatal if undetected in women taking oral contraceptives. Risk factors include high stress levels, obesity, calcium deficiencies, high levels of alcohol and caffeine intake, smoking, and lack of exercise.

Untreated HTN has many potential complications. Ischemic heart disease and heart failure, kidney failure, and stroke are some examples. As many as 400,000 people per year experience a stroke. Because HTN manifests minimal or no overt signs, it is known as the "silent killer." Headaches, dizziness, and fainting have been

Blood Pressure (BP) Classification

Classification	Systolic BP		Diastolic BP
Normal	<120	and	<80
Prehypertension	120-139	or	80-89
	High BP		
Stage 1 hypertension	140-159	or	90-99
Stage 2 hypertension	≥160	or	≥100

FIGURE 22-37

Classification of hypertension. This chart is adapted from the National High Blood Pressure Education Program.

reported but are not always symptomatic of HTN. Regular screenings at the worksite and screening booths in malls and in hospitals often help to identify asymptomatic HTN.

Hypotension

Blood pressure that is lower than normal is called **hypotension,** or low blood pressure. Hypotension may be temporary, as in *orthostatic hypotension* when a person stands up suddenly (see Figure 22-23 on p. 701) or when blood pressure drops because of a sudden loss of blood. Unexplained or *essential* hypotension is generally chronic and may result from heart disease or genetic influences. Whether acute or chronic, hypotension may cause rapid heart rate and pulse as the body attempts to maintain constant blood pressure for good circulation. Rapid heart rate may, in turn, lead to heart rhythm or other cardiac problems. If normal circulation cannot be maintained, reduced blood flow in local areas may cause damage or dysfunction in the affected areas. For example, hypotension in the elderly may cause cognitive impairment when proper blood flow to the brain cannot be maintained.

LANGUAGE OF SCIENCE *(continued from p. 681)*

diastole
(dye-ASS-toh-lee)
[*dia-* **through,** *-stole* **contraction**]

ejection fraction (EF)
(ee-JEK-shun FRAK-shun)

end-diastolic volume (EDV)
(end-dye-ASS-toh-lik)
[*dia-* **through,** *-stol-* **contraction,** *-ic* **relating to**]

hemodynamics
(hee-moh-dye-NAM-iks)
[*hemo-* **blood,** *-dynami-* **force,** *-ic* **relating to**]

interatrial bundle
(in-ter-AT-tree-al)
[*inter-* **between,** *-atri-* **entrance courtyard,** *-al* **relating to**]

internodal bundle
(in-ter-NOH-dal)
[*inter-* **between,** *-nod-* **knot,** *-al* **relating to**]

ischemic
(is-KEE-mik)
[*ischem-* **hold back,** *-ic* **relating to**]

medullary ischemic reflex
(MED-uh-lair-ee is-KEE-mik REE-fleks)
[*medulla-* **middle,** *-ary* **relating to,** *ischem-* **hold back,** *-ic* **relating to,** *re-* **back or again,** *-flex* **bend**]

minute volume

orthostatic effect
(or-thoh-STAT-ik)
[*ortho-* **upright,** *-stat-* **standing,** *-ic* **relating to**]

P wave
[**named for letter of Roman alphabet**]

pacemaker
(PAYS-may-ker)

perfusion pressure
(per-FYOO-shun)
[*per-* **through,** *-fus-* **pour,** *-sion* **process**]

peripheral resistance
(peh-RIF-er-al)
[*peri-* **around,** *-phera-* **boundary,** *-al* **relating to**]

Poiseuille's law
(pwah-SWEEZ)
[*Jean L.M. Poiseuille* **French physiologist**]

pressoreflex
(pres-oh-REE-fleks)
[*press-* **pressure,** *-re-* **back or again,** *-flex* **bend**]

QRS complex
(Q R S KOM-pleks)
[**named for letters of Roman alphabet**]

renin-angiotensin-aldosterone system (RAAS)
(REE-nin-an-jee-oh-TEN-sin-al-DAH-stair-ohn)
[*ren-* **kidney,** *-in* **substance,** *angio-* **vessel,** *-tens-* **pressure or stretch,** *-in* **substance,** *aldo-* **aldehyde,** *-stero-* **solid or steroid derivative,** *-one* **chemical**]

residual volume
(ree-ZID-yoo-al)
[*residu-* **remainder,** *-al* **relating to**]

sinoatrial (SA) node
(sye-no-AY-tree-al)
[*sin-* **hollow (sinus),** *atri-* **entrance courtyard,** *-al* **relating to,** *nod-* **knot**]

Starling's law of the capillaries
(STAR-lingz)
[*Ernest H. Starling* **English physiologist,** *capill-* **hair,** *-ary* **relating to**]

Starling's law of the heart
(STAR-lingz)
[*Ernest H. Starling* **English physiologist**]

stress-relaxation effect

stroke volume (SV)

subendocardial branch
(sub-en-doh-KAR-dee-al)
[*sub-* **under,** *-endo-* **within,** *-cardi-* **heart,** *-al* **relating to**]

systole
(SIS-toh-lee)
[*systole* **contraction**]

T wave
[**named for letter of Roman alphabet**]

total peripheral resistance (TPR)
(peh-RIF-er-al)
[*peri-* **around,** *-phera-* **boundary,** *-al* **relating to,** *-al* **relating to,** *resist-* **withstand,** *-ance* **act of**]

U wave
[**named for letter of Roman alphabet**]

vasoconstriction
(vay-soh-kon-STRIK-shun)
[*vas-* **vessel,** *-constrict-* **draw tight,** *-tion* **state**]

vasodilation
(vay-soh-DYE-lay-shun)
[*vaso-* **vessel,** *-dilat-* **widen,** *-tion* **state**]

vasomotor mechanism
(vay-so-MOH-tor)
[*vas-* **vessel,** *-motor* **move,** *mechan-* **machine,** *-ism* **state**]

vasomotor pressoreflex
(vay-so-MOH-tor press-oh-REE-fleks)
[*vas-* **vessel,** *-motor* **move,** *press-* **pressure,** *-re-* **back or again,** *-flex* **bend**]

venous pump
(VEE-nus)
[*ven-* **vein,** *-ous* **relating to**]

venous return
(VEE-nus)
[*ven-* **vein,** *-ous* **relating to**]

viscosity
(vis-KOS-i-tee)
[*viscos-* **sticky,** *-ity* **state**]

LANGUAGE OF MEDICINE (continued from p. 715)

anaphylactic shock
(an-ah-fih-LAK-tik)
[*ana-* **without**, *-phylact-* **protection**, *-ic* **relating to**]

atrial fibrillation (A-fib or AF)
(AY-tree-al fi-bril-LAY-shun)
[*atri-* **entrance courtyard**, *-al* **relating to**, *fibr-* **fiber**, *-illa-* **little**, *-ation* **process**]

bradycardia
(bray-dee-KAR-dee-ah)
[*brady-* **slow**, *-cardi-* **heart**, *-ia* **condition**]

bruits
(BROO-eez)
[*bruits* **noise**]

cardiogenic shock
(kar-dee-oh-JEN-ik)
[*cardi-* **heart**, *-gen-* **produce**, *-ic* **relating to**]

cardiomyopathy
(kar-dee-oh-my-OP-ah-thee)
[*cardi-* **heart**, *-myo-* **muscle**, *-path-* **disease**, *-y* **state**]

circulatory shock
(SER-kyoo-lah-tor-ee)
[*circulat-* **go around**, *-ory* **relating to**]

congestive heart failure (CHF)
(kon-JES-tiv)
[*congest-* **crowd together**, *-ive* **relating to**]

cor pulmonale
(kohr pul-mah-NAL-ee)
[*cor* **heart**, *pulmon-* **lung**, *-ale* **relating to**]

diastolic blood pressure
(dye-ah-STOL-ik)
[*dia-* **apart or through**, *-stol-* **contraction**, *-ic* **relating to**]

digitalis
(dij-i-TAL-is)
[*digit-* **finger**, *-alis* **relating to (from finger-shaped flowers of foxglove plant)**]

digoxin
(di-JOK-sin)
[*dig-* **finger (from digitalis or foxglove)**, *-oxin* **poison or toxin**]

dysrhythmia
(dis-RITH-mee-ah)
[*dys-* **disordered**, *-rhythm-* **rhythm**, *-ia* **condition**]

ectopic pacemaker
(ek-TOP-ik PAYS-may-ker)
[*ec-* **out of**, *-top-* **place**, *-ic* **relating to**]

electrocardiogram (ECG or EKG)
(eh-lek-troh-KAR-dee-oh-gram)
[*electro-* **electricity**, *-cardio-* **heart**, *-gram* **drawing**]

electrocardiography
(eh-lek-troh-kar-dee-OG-rah-fee)
[*electro-* **electricity**, *-cardio-* **heart**, *-graph-* **draw**, *-y* **process**]

heart block
heart failure
heart murmur
[*murmur* **hum**]

hypercapnia
(hye-per-KAP-nee-ah)
[*hyper-* **excessive**, *-capn-* **vapor (CO_2)**, *-ia* **condition**]

hypertension (HTN)
(hye-per-TEN-shun)
[*hyper-* **excessive**, *-tens-* **stretch or pull tight**, *-sion* **state**]

hypokalemia
(hye-poh-kal-EE-mee-ah)
[*hypo-* **under or below**, *-kal-* **potassium**, *-emia* **blood condition**]

hypotension
(hye-poh-TEN-shun)
[*hypo-* **under or below**, *-tens-* **stretch or pull tight**, *-sion* **state**]

hypovolemic shock
(hye-poh-voh-LEE-mik)
[*hypo-* **under or below**, *-vol-* **whirl**, *-emi(a)-* **blood condition**, *-ic* **relating to**]

hypoxia
(hye-POK-see-ah)
[*hypo-* **under or below**, *-ox-* **oxygen**, *-ia* **condition**]

Korotkoff sound
(kor-ROT-koff)
[*Nicolai Korotkoff* **Russian physician**]

laminar flow
(LAM-i-nar)
[*lamina-* **plate**, *-ar* **relating to**]

neurogenic shock
(noo-roh-JEN-ik)
[*neuro-* **nerve**, *-gen-* **produce**, *-ic* **relating to**]

premature contraction
pulse pressure
[*pulse* **beat**]

septic shock
(SEP-tik shok)
[*septi-* **putrid**, *-ic* **relating to**]

sinus dysrhythmia
(SYE-nus dis-RITH-mee-ah)
[*sinus* **hollow**, *dys-* **disordered**, *-rhythm-* **rhythm**, *-ia* **condition**]

sphygmomanometer
(sfig-moh-mah-NOM-eh-ter)
[*sphygmo-* **pulse**, *-mano-* **thin**, *-meter* **measure**]

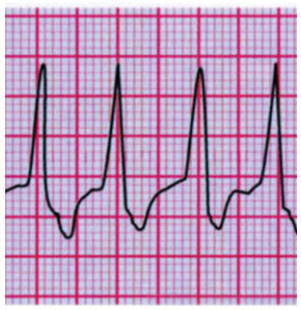
systolic blood pressure
(sis-TOL-ik)
[*systole-* **contraction**, *-ic* **relating to**]

tachycardia
(tak-i-KAR-dee-ah)
[*tachy-* **rapid**, *-cardi-* **heart**, *-ia* **condition**]

turbulent flow (TER-byoo-lent)
vasodilatory shock
(vay-soh-DYE-lah-tor-ee)
[*vas-* **vessel**, *-dilat-* **widen**, *-ory* **relating to**]

ventricular fibrillation (V-fib or VF)
(ven-TRIK-yoo-lar fib-ril-LAY-shun)
[*ventr-* **belly**, *-icul-* **little**, *-ar* **relating to**, *fibr-* **fiber**, *-illa-* **little**, *-ation* **process**]

CASE study



Bobby was in a hurry to finish the last job of the day. Being an electrician, he had been called in to help complete and inspect the wiring in a museum that was due to open the next week. Bobby called to his coworker, Jerry, to confirm the current was off to the electrical box on which he was working. When he heard a positive response, he climbed the ladder and reached up to tighten a few loose screws. As he was tightening the screws with his right hand, he lost his balance and reached up with his left hand to catch hold of the ladder . . . but instead caught a live wire that sent a jolt of electricity through his body. Jerry came running and knocked the ladder out from under Bobby so he would fall to the floor, breaking the electric arc. "Are you okay?" he asked Bobby, who appeared dazed, but was conscious. "I don't feel so great," he replied, smiling weakly. Then he collapsed. Jerry yelled at the other workers in the room to call 911, checked Bobby's pulse, and started CPR. The foreman rushed in with an AED (automated external defibrillator) and attached the electrodes to Bobby's chest. The AED's mechanical voice said, "V-fib. Recommend shock. Press button when clear."

1. What is this V-fib that the AED registered?
   a. Ventricular fibrosis
   b. Venous fibrillation
   c. Ventricular fibrillation
   d. Vasomotor fibrosis

CASE study

When activated, the AED shocks the heart—the intended purpose being electrical stimulation of the cardiac muscle cells to elicit a response from the heart's pacemaker that will cause the cells to contract in unison to effectively pump blood.

2. What bundle of cells in Bobby's heart (and yours) is known as the pacemaker?
   a. SV node
   b. SA node
   c. AV node
   d. AV bundle

When the paramedics arrive, they rush Bobby to the hospital. "Let's get an EKG!" the attending physician calls out.

3. What is an EKG?
   a. Electrocardiogram
   b. Electrocirculogram
   c. Encephalocardiogram
   d. Enhancercardiogram

4. Ventricular depolarization is shown as which part of the EKG?
   a. V wave
   b. P wave
   c. T wave
   d. QRS complex

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

INTRODUCTION

A. Vital role of the cardiovascular system in maintaining homeostasis depends on the continuous and controlled movement of blood through the capillaries
B. Numerous control mechanisms help regulate and integrate the diverse functions and component parts of the cardiovascular system to supply blood in response to specific body area needs

HEMODYNAMICS

A. Hemodynamics—collection of mechanisms that influence the dynamic (active and changing) circulation of blood (Figure 22-1)
B. Circulation of different volumes of blood per minute is essential for healthy survival
C. Circulation control mechanisms must accomplish two functions
   1. Maintain circulation
   2. Vary volume and distribution of the blood circulated

THE HEART AS A PUMP

A. Conduction system of the heart (Figure 22-2)
   1. Composed of four major structures
      a. Sinoatrial node (SA node)
      b. Atrioventricular (AV) node
      c. AV bundle (bundle of His)
      d. Subendocardial branches (Purkinje fibers)
   2. Conduction system structures are more highly specialized than ordinary cardiac muscle tissue and permit rapid conduction of an action potential through the heart
   3. SA node (pacemaker)
      a. Initiates each heartbeat and sets its pace
      b. Specialized pacemaker cells in the node possess an intrinsic rhythm
   4. Sequence of cardiac stimulation
      a. After being generated by the SA node, each impulse travels throughout the muscle fibers of both atria and the atria begin to contract
      b. As the action potential enters the AV node from the right atrium, its conduction slows to allow complete contraction of both atrial chambers before the impulse reaches the ventricles
      c. After the AV node, conduction velocity increases as the impulse is relayed through the AV bundle into the ventricles
      d. Right and left branches of the bundle fibers and subendocardial branches (Purkinje fibers) conduct the impulses throughout the muscles of both ventricles, stimulating them to contract almost simultaneously
B. Electrocardiogram (ECG or EKG)
   1. Graphic record of the heart's electrical activity, its conduction of impulses; a record of the electrical events that precede the contractions of the heart
   2. Production of an ECG (Figure 22-3)
      a. Electrodes are attached to the subject
      b. Voltage changes that represent the heart's electrical activity are sensed by electrodes and recorded on paper (Figure 22-4)
   3. Composition (ECG waves) of normal ECG recording (Figures 22-3 and 22-5) is composed of:
      a. P wave—represents depolarization of the atria
      b. QRS complex—represents depolarization of the ventricles and repolarization of the atria

c. T wave—represents repolarization of the ventricles
d. U wave—tiny "hump" at end of T wave—represents repolarization of the papillary muscle (or a two-part T wave) and may appear on ECG as well (Figure 22-6)
(1) Absent or small U waves usually considered normal
(2) U waves may be a sign of hypokalemia or too much digoxin
e. ECG intervals between P, QRS, and T waves can provide information about rate of conduction of an action potential through the heart

C. Cardiac cycle—a complete heartbeat
1. Consists of contraction (systole) and relaxation (diastole) of both atria and both ventricles
2. Cycle is often divided into time intervals (Figures 22-7 and 22-8)
3. Atrial systole
a. This cycle begins with the P wave of the ECG, which triggers atrial contraction
b. Contraction of atria creates a pressure gradient that pushes blood out of the atria into the relaxed ventricles
c. Due to pressure gradients, AV valves are open; SL valves are closed
d. Ventricles are relaxed and filling with blood from atria
4. Isovolumetric ventricular contraction
a. Onset of ventricular systole coincides with the R wave of the ECG and the appearance of the first heart sound
b. Occurs between the start of ventricular systole and the opening of the SL valves
c. Ventricular volume remains constant as the pressure increases rapidly
(1) Intraventricular pressure rises enough to close AV valves, producing the first heart sound
(2) Intraventricular pressure is not yet high enough to open the SL valves
5. Ejection
a. SL valves open and blood is ejected from the ventricles when the intraventricular pressure exceeds the pressure in the pulmonary artery and aorta
b. Rapid ejection—initial short phase characterized by a marked increase in ventricular and aortic pressure and in aortic blood flow
c. Reduced ejection—characterized by a less abrupt decrease in ventricular volume; coincides with the T wave of the ECG
6. Isovolumetric ventricular relaxation
a. Ventricular diastole begins with this phase
b. Occurs between closure of the SL valves and opening of the AV valves
c. A dramatic fall in intraventricular pressure but not enough to open the AV valves, thus no change in volume
d. Second heart sound is heard during this period
7. Passive ventricular filling
a. Continued ventricular relaxation reduces intraventricular pressure and returning venous blood increases intraatrial pressure, producing enough of a pressure gradient to push open the AV valves
b. Blood rushes into the relaxing ventricles; influx lasts approximately 0.1 second and results in a dramatic increase in ventricular volume
c. Diastasis—later longer period of slow ventricular filling near end of ventricular diastole lasting approximately 0.2 second; characterized by a gradual increase in ventricular pressure and volume
d. The cardiac cycle then begins again with a new atrial systole

D. Heart sounds
1. Systolic sound—first sound, believed to be caused primarily by contraction of the ventricles and by vibrations of the closing AV valves
2. Diastolic sound—short, sharp sound; thought to be caused by vibrations of the closing of SL valves
3. Heart sounds have clinical significance because they provide information about the functioning of the valves of the heart

PRIMARY PRINCIPLE OF CIRCULATION

A. Blood flows because a pressure gradient exists between different parts of its volume; this is based on Newton's first and second laws of motion (Figure 22-9)
B. For example, blood circulates from the left ventricle to the right atrium of the heart because a blood pressure gradient exists between these two structures; likewise, a blood pressure gradient drives blood flow from the right ventricle to the left atrium
C. P_1–P_2 is the symbol used to represent a pressure gradient, with P_1 representing the higher pressure and P_2 the lower pressure
D. Perfusion pressure—the pressure gradient needed to maintain blood flow through a local tissue

ARTERIAL BLOOD PRESSURE

A. Primary determinant of arterial blood pressure is the volume of blood in the arteries; a direct relationship exists between arterial blood pressure and arterial blood volume (Figure 22-10)
B. Cardiac output (CO)—volume of blood pumped out of the heart per unit of time (ml/min or L/min) (Figure 22-11)
1. General principles and definitions
a. Cardiac output (CO)—determined by stroke volume and heart rate
b. Stroke volume (SV)—volume pumped per heartbeat
c. CO (volume/min) = SV (volume/beat) × HR (beats/min)
d. In practice, CO is computed by Fick's formula
e. Heart rate and stroke volume determine CO, so anything that changes either also tends to change CO, arterial blood volume, and blood pressure in the same direction
2. Stroke volume
a. Starling's law of the heart (Frank-Starling mechanism) (Figure 22-12)

(1) Within limits, the longer, or more stretched, the heart fibers at the beginning of contraction, the stronger the contraction
(2) The amount of blood in the heart at the end of diastole determines the amount of stretch placed on the heart fibers
(3) The myocardium contracts with enough strength to match its pumping load (within certain limits) with each stroke—unlike mechanical pumps

b. Contractility (strength of contraction) can also be influenced by chemical factors (Figure 22-13)
(1) Neural—norepinephrine; endocrine—epinephrine
(2) Triggered by stress, exercise

c. Ejection fraction (EF)—the ratio of stroke volume (SV) to end-diastolic volume (EDV)
(1) Usually expressed as a percentage: EF = (SV/EDV) × 100
(2) Healthy adults have EFs of at least 55%
(3) EF goes down as the myocardium fails

3. Factors that affect heart rate—SA node normally initiates each heartbeat; however, various factors can and do change the rate of the heartbeat
a. Cardiac pressoreflexes
(1) Aortic baroreceptors and carotid baroreceptors, located in the aorta and carotid sinus
(2) Extremely important because they affect the autonomic cardiac control center, and therefore parasympathetic and sympathetic outflow, to aid in control of blood pressure (Figures 22-14 and 22-15)

b. Carotid sinus reflex
(1) Located at the beginning of the internal carotid artery
(2) Sensory fibers from carotid sinus baroreceptors run through the carotid sinus nerve and the glossopharyngeal nerve to the cardiac control center
(3) Parasympathetic impulses leave the cardiac control center, travel through the vagus nerve to reach the SA node

c. Aortic reflex
(1) Sensory fibers extend from baroreceptors located in the wall of the arch of the aorta through the aortic nerve and through the vagus nerve to terminate in the cardiac control center
(2) Stimulation causes cardiac control center to increase vagal inhibition, thus slowing the heart

d. Other reflexes that influence heart rate
(1) Anxiety, fear, and anger often increase heart rate
(2) Grief tends to decrease heart rate
(3) Emotions produce changes in heart rate through the influence of impulses from the cerebrum by way of the hypothalamus
(4) Exercise normally increases heart rate
(5) Increased blood temperature or stimulation of skin heat receptors increases heart rate
(6) Decreased blood temperature or stimulation of skin cold receptors decreases heart rate

C. Peripheral resistance—resistance to blood flow imposed by the force of friction between blood and the walls of its vessels
1. Factors that influence peripheral resistance
a. Blood viscosity—the thickness of blood as a fluid (Figure 22-16)
(1) High plasma protein concentration can slightly increase blood viscosity
(2) High hematocrit (% RBC) can increase blood viscosity
(3) Anemia, hemorrhage, or other abnormal conditions may also affect blood viscosity

b. Diameter of arterioles (Figure 22-17)
(1) Vasomotor mechanism—muscles in walls of arteriole may constrict vessel (vasoconstriction) or dilate vessel (vasodilation), thus changing diameter of arteriole
(2) Small changes in blood vessel diameter cause large changes in resistance, making the vasomotor mechanism ideal for regulating blood pressure and blood flow

2. How resistance influences blood pressure
a. Arterial blood pressure tends to vary directly with peripheral resistance
b. Friction caused by viscosity and small diameter of arterioles and capillaries
c. Muscular coat of arterioles allows them to constrict or dilate and change the amount of resistance to blood flow
d. Peripheral resistance helps determine arterial pressure by controlling the amount of blood that runs from the arteries to the arterioles (Figure 22-18)
(1) Increased resistance and decreased arteriole runoff lead to higher arterial pressure
(2) Can occur locally (in one organ), or the total peripheral resistance (TPR) may increase, thus generally raising systemic arterial pressure

3. Vasomotor control mechanism—controls changes in the diameter of arterioles; plays role in maintenance of the general blood pressure and in distribution of blood to areas of special need (Figures 22-19 and 22-20)
a. Vasomotor pressoreflexes (Figure 22-21)
(1) Sudden increase in arterial blood pressure stimulates aortic and carotid baroreceptors; results in arterioles and venules of the blood reservoirs dilating
(2) Decrease in arterial blood pressure results in stimulation of vasoconstrictor centers, causing vascular smooth muscle to constrict

b. Vasomotor chemoreflexes (Figure 22-22)—chemoreceptors located in aortic and carotid bodies are sensitive to hypercapnia, hypoxia, and decreased arterial blood pH

c. Medullary ischemic reflex—acts during emergency situation when there is decreased blood flow to the medulla; causes marked arteriole and venous constriction

d. Vasomotor control by higher brain centers—impulses from centers in cerebral cortex and hypothalamus are transmitted to vasomotor centers in medulla to help control vasoconstriction and dilation

4. Local control of arterioles—several local mechanisms produce vasodilation in localized areas; referred to as *active hyperemia*

VENOUS RETURN TO THE HEART

A. Venous return—amount of blood returned to the heart by the veins

B. Stress-relaxation effect—occurs when a change in blood pressure causes a change in vessel diameter (because of elasticity) that accommodates the new pressure and thereby keeps blood flowing (works only within certain limits)

C. Gravity—the pull of gravity on venous blood while sitting or standing tends to cause a decrease in venous return (orthostatic effect) (Figure 22-23)

D. Venous pumps—blood-pumping action of respirations and skeletal muscle contractions facilitate venous return by increasing pressure gradient between peripheral veins and venae cavae (Figure 22-24)

1. Respirations—inspiration increases the pressure gradient between peripheral and central veins by decreasing central venous pressure and also by increasing peripheral venous pressure
2. Skeletal muscle contractions—promote venous return by squeezing veins through a contracting muscle and milking the blood toward the heart
3. One-way valves in veins prevent backflow (Figure 22-25)

E. Total blood volume—changes in total blood volume change the amount of blood returned to the heart

1. Capillary exchange—governed by Starling's law of the capillaries (Figure 22-26)
   a. At arterial end of capillary, outward hydrostatic pressure is strongest force; moves fluid out of plasma and into IF
   b. At venous end of capillary, inward osmotic pressure is strongest force; moves fluid into plasma from IF; 90% of fluid lost by plasma at arterial end is recovered
   c. Lymphatic system recovers fluid not recovered by capillary and returns it to the venous blood before it is returned to the heart
2. Changes in total blood volume—mechanisms that change total blood volume most quickly are those that cause water to quickly move into or out of the plasma (Figure 22-27)
   a. ADH mechanism—decreases the amount of water lost by the body by increasing the amount of water that kidneys resorb from urine before the urine is excreted from the body; triggered by input from baroreceptors and osmoreceptors
   b. Renin-angiotensin-aldosterone system (RAAS)—decreases water loss
      (1) Renin—released when blood pressure in kidney is low; leads to increased secretion of aldosterone, which stimulates retention of sodium, causing increased retention of water and an increase in blood volume
      (2) Angiotensin II—intermediate compound that causes vasoconstriction, which complements the volume-increasing effects of renin and promotes an increase in overall blood flow
   c. ANH mechanism—adjusts venous return from an abnormally high level by promoting the loss of water from plasma, causing a decrease in blood volume; increases urine sodium loss, which causes water to follow osmotically

F. A variety of feedback responses restore normal blood pressure after a sudden change in pressure (Figure 22-28)

MEASURING BLOOD PRESSURE

A. Arterial blood pressure

1. Measured with the aid of a sphygmomanometer and stethoscope; listen for Korotkoff sounds as the pressure in the cuff is gradually decreased (Figure 22-29)
2. Systolic blood pressure—force of the blood pushing against the artery walls while ventricles are contracting
3. Diastolic blood pressure—force of the blood pushing against the artery walls when ventricles are relaxed and during isovolumetric ventricular contraction
4. Pulse pressure—difference between systolic and diastolic blood pressure

B. Relation to arterial and venous bleeding

1. Arterial bleeding—blood escapes from artery in spurts because of alternating increase and decrease of arterial blood pressure
2. Venous bleeding—blood flows slowly and steadily because of low, practically constant pressure

MINUTE VOLUME OF BLOOD (FIGURE 22-30)

A. Minute volume—determined by the magnitude of the blood pressure gradient and peripheral resistance

B. Poiseuille's law—Minute volume = Pressure gradient ÷ Resistance

VELOCITY OF BLOOD FLOW

A. Governed by the physical principle that when a liquid flows from an area of one cross-sectional size to an area of larger size, its velocity decreases in the area with the larger cross section (Figure 22-31)

B. Blood flows more slowly through arterioles than arteries because total cross-sectional area of arterioles is greater than that of arteries, and capillary blood flow is slower than arteriole blood flow

C. Venule cross-sectional area is smaller than capillary cross-sectional area, causing blood velocity to increase in venules and then veins with a still smaller cross-sectional area

PULSE

A. Mechanism

1. Pulse—alternate expansion and recoil of an artery (Figure 22-32)

   a. Clinical significance: reveals important information regarding the cardiovascular system, blood vessels, and circulation
   b. Physiological significance: expansion stores energy released during recoil, conserving energy generated by the heart and maintaining relatively constant blood flow (Figure 22-33)
2. Existence of pulse is due to two factors
   a. Alternating increase and decrease of pressure in the vessel
   b. Elasticity of arterial walls allows walls to expand with increased pressure and recoil with decreased pressure

B. Pulse wave
1. Each pulse starts with ventricular contraction and proceeds as a wave of expansion throughout the arteries
2. Gradually dissipates as it travels, disappearing in the capillaries

C. Where the pulse can be felt—wherever an artery lies near the surface and over a bone or other firm background (Figure 22-34)

D. Venous pulse—detectable pulse exists only in large veins; most prominent near the heart; not of clinical importance

THE BIG PICTURE: BLOOD FLOW AND THE WHOLE BODY

A. Blood flow shifts materials from place to place and redistributes heat and pressure

B. Vital to maintaining homeostasis of internal environment

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Identify, locate, and describe the function of each of the following structures: SA node, AV node, AV bundle, and subendocardial branches (Purkinje fibers).
2. What does an electrocardiogram measure and record? List the normal ECG deflection waves and intervals. What do the various ECG waves represent?
3. What is meant by the term *cardiac cycle*?
4. List the "phases" of the cardiac cycle and briefly describe the events that occur in each.
5. What is meant by the term *residual volume* as it applies to the heart?
6. Describe and explain the origin of the heart sounds.
7. Which blood vessels present the greatest resistance to blood flow?
8. What is the primary determinant of arterial blood pressure?
9. List the two most important factors that indirectly determine arterial pressure by their influence on arterial volume.
10. How is cardiac output determined?
11. List and give the effect of several factors, such as grief or pain, on heart rate.
12. What mechanisms control peripheral resistance? Cite an example of the operation of one or more parts of this mechanism to increase resistance and to decrease it.
13. What are the components of the vasomotor control mechanism?
14. Explain how antidiuretic hormone can change the total blood volume.
15. What is the effect of low blood pressure in relation to aldosterone and antidiuretic hormone secretion?
16. Describe the measurement of arterial blood pressure.
17. Identify the eight locations where the pulse point is most easily felt. List the six pressure points at which pressure can be applied to stop arterial bleeding distal to that point.
18. Describe the various types of cardiac dysrhythmias.

CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. What is an ectopic pacemaker? What would be the effect on the heart rate if an ectopic pacemaker took over for the SA node?
2. State in your own words the primary principle of circulation. How does it govern the various mechanisms involved in blood flow?
3. What is Starling's law of the heart? What role does *venous return* play in Starling's law?
4. Explain how the heart rate is a good example of dual innervation in the autonomic nervous system. Include the nerves and neurotransmitters involved.
5. Explain how blood pressure in the brain is prevented from getting too high.
6. What is arterial runoff? What is the relationship of arteriole runoff and peripheral resistance?
7. Explain what occurs when the carbon dioxide level in the medulla rises above set point.
8. By the time blood gets to the veins, almost all the pressure from the contracting ventricles has been lost. What mechanisms does the body use to assist in returning blood to the heart?
9. Explain the forces that act on capillary exchange on both the arterial and venous ends of the capillary. Is the recovery of fluid at the venous end 100% effective?
10. State in your own words Poiseuille's law. What equation expresses this law? According to the equation, an increase in resistance would lower the minute volume. Give an example of where this would not be the case.
11. What two factors determine blood viscosity? What does viscosity mean? Give an example of a condition in which blood viscosity decreases. Explain its effects on resistance, arterial pressure, and circulation.

23 Lymphatic System



LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

aggregated lymphoid nodules
(ag-rah-GAYT-ed LIM-foyd NOD-yoolz)
[*a[d]-* **to,** *-grega-* **collect,** *lymph-* **water,** *-oid* **like,** *nod-* **knot,** *-ule* **small**]

anastomosis
(ah-nas-toh-MOH-sis)
[*ana-* **anew,** *-stomo-* **mouth,** *-osis* **conditions of**] *pl.,* anastomoses

axillary lymph node
(AK-sil-lair-ee limf)
[*axilla-* **wing,** *-ary* **relating to,** *lymph* **water,** *nod-* **knot**]

chyle
(kile)
[*chyl-* **juice**]

cisterna chyli
(sis-TER-nah KYE-lye)
[*cisterna* **vessel,** *chyli* **of juice**]

cortical nodule
(KOHR-ti-kal NOD-yool)
[*cortic-* **bark (cortex),** *-al* **relating to,** *nod-* **knot,** *-ule* **small**]

iliac lymph node
(ILL-ee-ak limf)
[*ilia-* **loin or gut** [**ileum**], *-ac* **relating to,** *lymph* **water,** *nod-* **knot**]

inguinal lymph node
(ING-gwi-nal limf)
[*inguin-* **groin,** *-al* **relating to,** *lymph* **water,** *-atic* **relating to,** *nod-* **knot**]

interstitial fluid (IF)
(in-ter-STISH-al)
[*inter-* **between,** *-stit-* **stand,** *-al* **relating to**]

involution
(in-voh-LOO-shun)
[*in-* **in,** *-volu-* **roll,** *-tion* **state**]

continued on p. 740

CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

Overview of the Lymphatic System, 723

Lymph and Interstitial Fluid, 724

Lymphatic Vessels, 724
- Distribution of Lymphatic Vessels, 724
- Structure of Lymphatic Vessels, 725
- Functions of Lymphatic Vessels, 725

Circulation of Lymph, 726
- The Lymphatic Pump, 727

Lymph Nodes, 728
- Structure of Lymph Nodes, 728
- Locations of Lymph Nodes, 729
- Functions of Lymph Nodes, 730
  - Defense Functions: Filtration and Phagocytosis, 730
  - Hematopoiesis, 732

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- Distribution of Lymphatics in the Breast, 732
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Thymus, 734
- Location and Appearance of the Thymus, 734
- Structure of the Thymus, 734
- Function of the Thymus, 734

Spleen, 735
- Location of the Spleen, 735
- Structure of the Spleen, 735
- Functions of the Spleen, 735

Cycle of Life: Lymphatic System, 737

The Big Picture: Lymphatic System and the Whole Body, 737

Mechanisms of Disease, 738

Case Study, 741

The lymphatic system serves various functions in the body. The two most important functions of this system are maintenance of fluid balance in the internal environment and immunity. Although both of these important functions are discussed in this chapter, details of immunity are discussed more fully in Chapter 24. A third, somewhat less important, function of the lymphatic system is the absorption of lipids from digested food in the small intestine and its transport to the large systemic veins. This fat-transport function of the lymphatic system is discussed in Chapter 29.

OVERVIEW OF THE LYMPHATIC SYSTEM

The importance of the lymphatic system in maintaining a balance of fluid in the internal environment is best explained by the diagram in Figure 23-1. As this figure shows, plasma filters into interstitial spaces from blood flowing through capillaries. Most of this interstitial fluid (IF) is absorbed by tissue cells or reabsorbed by the blood before it flows out of the tissue. However, a small percentage of the interstitial fluid remains behind (review Figure 22-26, *A*, on p. 703). If this continued for even a brief period, the increased interstitial fluid would cause massive edema (swelling) of the tissue. The high fluid pressure from this edema could cause tissue destruction or perhaps even death as normal functions became disrupted. Such a problem is avoided by the presence of lymphatic vessels that act as "drains" to collect the excess tissue fluid and return it to the venous blood just before it reaches the heart.

The lymphatic system is a component of the circulatory system because it consists of a moving fluid (lymph) derived from the blood and tissue fluid and a group of vessels (lymphatics) that return the lymph to the blood. In general, the lymphatic vessels that drain the peripheral areas of the body parallel the venous return.

In addition to lymph and the lymphatic vessels, the system includes various structures that contain **lymphoid tissue**—a type of reticular tissue (see Chapter 6) that contains lymphocytes and other defensive cells. For example, lymph nodes are located along the paths of the collecting lymphatic vessels. Isolated nodules of lymphatic tissue, such as the **aggregated lymphoid nodules** called *Peyer patches* in the intestinal wall or the nodules of the vermiform appendix of the large intestine, are other examples. Additional lymphoid structures include the tonsils, thymus, spleen, and bone marrow (Figure 23-2).

Although it serves a unique transport function by returning tissue fluid, proteins, fats, and other substances to the general circulation, lymph flow differs from the true "circulation" of blood seen in the cardiovascular system. Unlike vessels in the blood vascular system, lymphatic vessels do not form a closed ring, or circuit, but instead begin blindly in the intercellular spaces of the soft tissues of the body (see Figure 23-1).

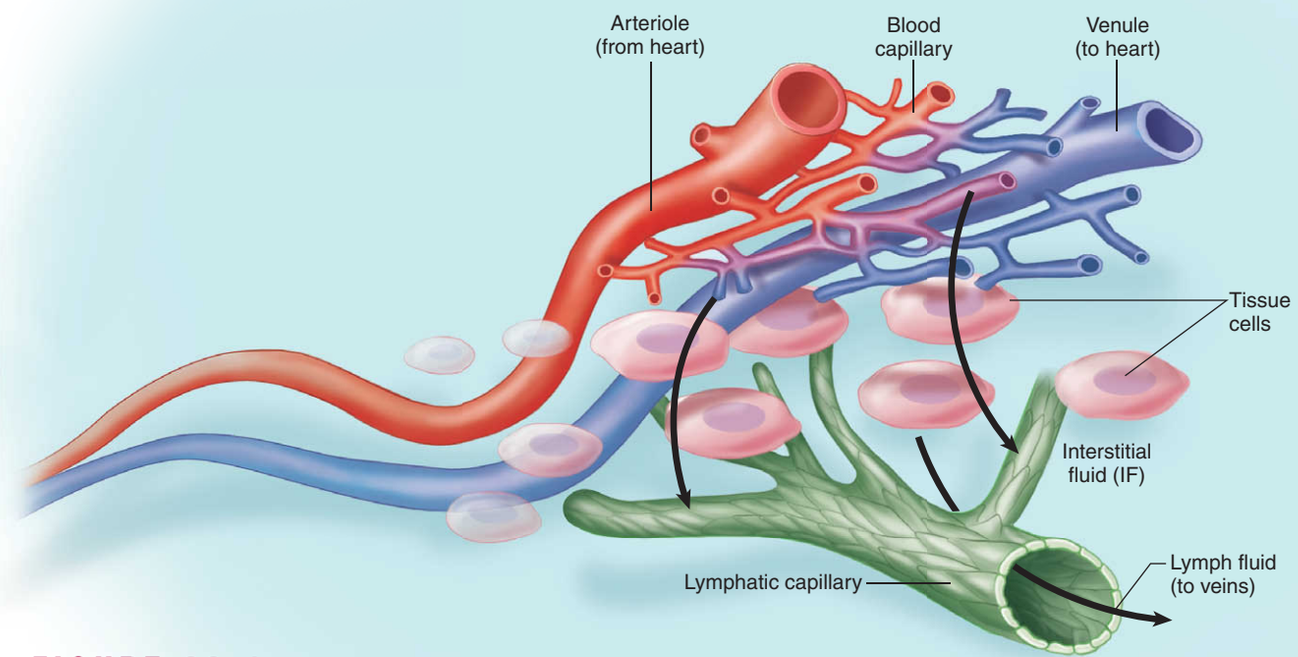


FIGURE 23-1

Role of the lymphatic system in fluid balance. Fluid from plasma flowing through the capillaries moves into interstitial spaces. Although *most* of this interstitial fluid is either absorbed by tissue cells or resorbed by blood capillaries, *some* of the fluid tends to accumulate in the interstitial spaces. As this fluid builds up, it tends to drain into lymphatic vessels (green) that eventually return the fluid to the venous blood. Lymphatic structures are not actually green. Green is used in diagrams to contrast lymphatic structures with nearby blood vessels (red, blue) or nerves (yellow).

LYMPH AND INTERSTITIAL FLUID

Lymph (or *lymphatic fluid*) is the clear, watery-appearing fluid found in the lymphatic vessels. **Interstitial fluid (IF),** which fills the spaces between the cells, is not the simple fluid it seems to be. Studies show that it is an important and complex part of the *ECM (extracellular matrix)*. Interstitial fluid and blood plasma together constitute the extracellular fluid compartment of the body, or in the words of Claude Bernard, the "internal environment of the body"—the fluid environment of cells in contrast to the atmosphere, or external environment, of the body.

Both lymph and interstitial fluid closely resemble blood plasma in composition. The main difference is that they contain a lower percentage of proteins than does plasma. Lymph is isotonic and almost identical in chemical composition to interstitial fluid when comparisons are made between the two fluids taken from the same area of the body. However, the average concentration of protein (4 grams/100 ml) in lymph taken from the thoracic duct (see Figure 23-2) is about twice that found in most interstitial fluid samples.

The elevated protein level of thoracic duct lymph (a mixture of lymph from all areas of the body) results from protein-rich lymph flowing into the duct from the liver and small intestine. A little more than one half of the 2800 to 3000 ml total daily lymph flowing through the thoracic duct is derived from these two organs.

Box 23-1 discusses the effects of abnormal loss of lymphatic fluid.

Box 23-1 | HEALTH matters

Loss of Lymphatic Fluid

Lymph does not clot. Therefore, if damage to the main lymphatic trunks in the thorax occurs as a result of penetrating injury, the flow of lymph must be stopped surgically or death ensues. It is impossible to maintain adequate plasma protein concentration by dietary means if significant loss of lymph continues over time. As lymph is lost, rapid emaciation occurs, with a progressive and eventually fatal decrease in total blood fat and protein concentration.

LYMPHATIC VESSELS

Distribution of Lymphatic Vessels

Lymphatic vessels—often simply called *lymphatics*—originate as microscopic blind-end vessels called *lymphatic capillaries.* (Those originating in the villi of the small intestine are called *lacteals*; see Chapter 29.) The wall of each **lymphatic capillary** consists of a single layer of flattened endothelial cells. Each blindly ending capillary is attached, or fixed, to surrounding cells by tiny connective tissue filaments. Networks of lymphatic capillaries branch and anastomose extensively. Lymphatic networks are located in the intercellular (interstitial) spaces and are widely distributed throughout the body. As a rule, lymphatic and blood capillary networks lie side by side but are always independent of each other.

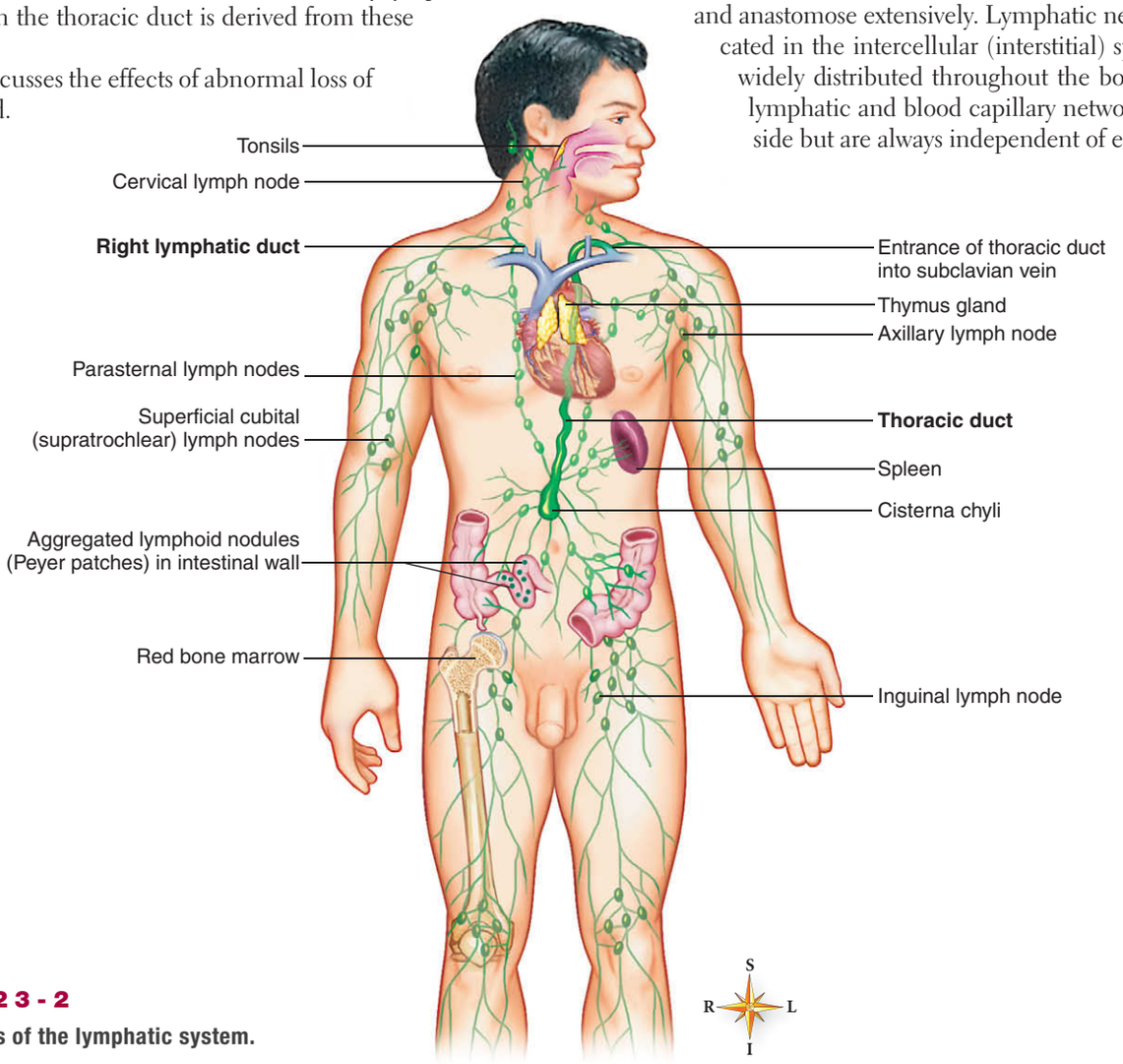


FIGURE 23-2
Principal organs of the lymphatic system.

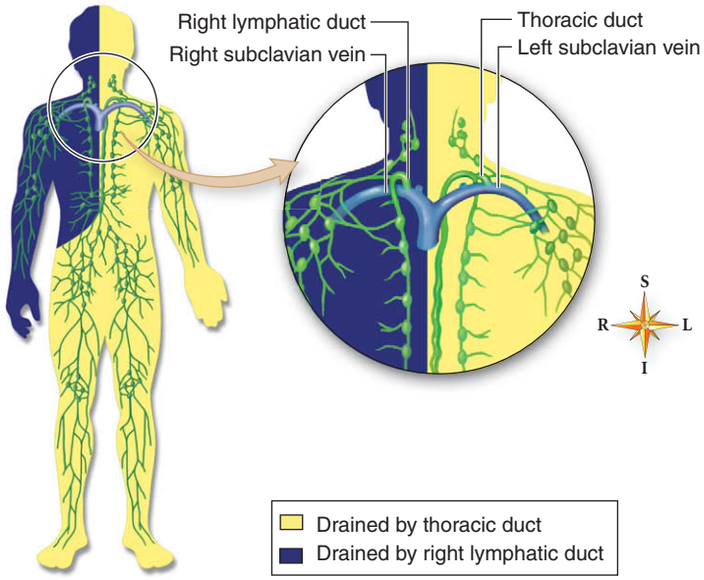


FIGURE 23-3

Lymphatic drainage. The right lymphatic duct drains lymph from the upper right quadrant *(dark blue)* of the body into the right subclavian vein. The thoracic duct drains lymph from the rest of the body *(green)* into the left subclavian vein. The lymphatic fluid is thus returned to the systemic blood just before entering the heart.

As twigs of a tree join to form branches, branches join to form larger branches, and larger branches join to form the tree trunk, so do lymphatic capillaries merge, forming slightly larger lymphatics that join other lymphatics to form still larger vessels, which merge to form the main lymphatic trunks: the **right lymphatic duct** and the **thoracic duct** (see Figure 23-2).

Lymph from the entire body, except for the upper right quadrant, drains eventually into the thoracic duct, which drains into the left subclavian vein at the point where it joins the left internal jugular vein (Figure 23-3). Lymph from the upper right quadrant of the body empties into the right lymphatic duct and then into the right subclavian vein. However, this structure can be vary among individuals. For example, in most people there are three separate lymphatic ducts that drain into the right subclavian vein rather than a single right lymphatic duct.

Because most of the lymph of the body returns to the bloodstream by way of the thoracic duct, this vessel is considerably larger than the other main lymph channels, the right lymphatic ducts, but is much smaller than the large veins, which it resembles in structure. It has an average diameter of about 5 mm (1.5 inches) and a length of about 40 cm (16 inches). It originates as a dilated structure, the **cisterna chyli** or *chyle cistern*, in the lumbar region of the abdominal cavity—where fatty lymph called *chyle* from the intestinal tract collects. The thoracic duct then ascends a curving pathway to the root of the neck, where it joins the subclavian vein as just described (see Figures 23-2 and 23-3).

Structure of Lymphatic Vessels

Lymphatics resemble veins in structure with these exceptions:

- Lymphatics have thinner walls.
- Lymphatics contain more valves.
- Lymphatics contain lymph nodes located at certain intervals along their course.

The lymphatic capillary wall is formed by a single layer of large but very thin and flat endothelial cells (Figure 23-4). Although the openings (clefts) between endothelial cells of lymphatic capillary walls are small, they are larger than those found in blood capillaries—a fact that explains the remarkable permeability of this system.

As lymph flows from the thin-walled capillaries into vessels with a larger diameter (0.2 to 0.3 mm), the walls become thicker and exhibit the three coats, or layers, typical of arteries and veins (see Table 21-1, p. 646). Interlacing elastic fibers and several strata of circular smooth muscle bundles are found in both the tunica media and the tunica externa of the large lymphatic vessel wall. Boundaries between layers are less distinct in the thinner lymphatic vessel walls than in arteries or veins.

One-way valves are extremely numerous in lymphatics of all sizes and give the vessels a somewhat varicose and beaded appearance. Valves are present every few millimeters in large lymphatics and are even more numerous in the smaller vessels. Formed from folds of the tunica intima, each valve projects into the vessel lumen in a slightly expanded area circled by bundles of smooth muscle fibers.

Experimental evidence suggests that most lymph vessels have the capacity for repair or regeneration when damaged. Formation of new lymphatic vessels occurs by extension of solid cellular cores, or sprouts, formed by mitotic division of endothelial cells in existing vessels, which later become "canalized."

Functions of Lymphatic Vessels

The lymphatics play a critical role in numerous interrelated homeostatic mechanisms. The high degree of permeability of the lymphatic capillary wall permits very large molecules and even

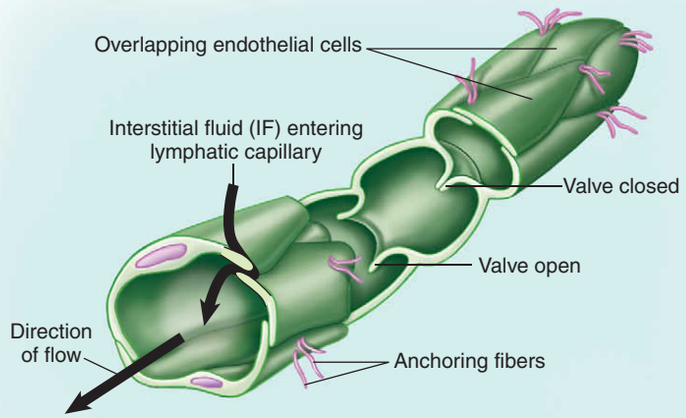


FIGURE 23-4

Structure of a typical lymphatic capillary. Notice that interstitial fluid enters through clefts between overlapping endothelial cells that form the wall of the vessel. Valves ensure one-way flow of lymph out of the tissue. Small fibers anchor the wall of the lymphatic capillary to the surrounding ECM (extracellular matrix) and cells, thus holding it open to allow entry of fluids and small particles.

particulate matter, which cannot be absorbed into a blood capillary, to be removed from the interstitial spaces. Proteins that accumulate in the tissue spaces can return to blood only by way of lymphatics. This fact has great clinical importance. For instance, if anything blocks lymphatic return, blood protein concentration and blood osmotic pressure soon fall below normal, and fluid imbalance and death will result (discussed in Chapter 32).

Lacteals (lymphatics in the villi of the small intestine) serve an important function in the absorption of fats and other nutrients. The milky lymph found in lacteals after digestion contains 1% to 2% fat and is called **chyle.** Interstitial fluid has a much lower lipid content than chyle (see Chapter 29).

CIRCULATION OF LYMPH

Water and solutes continually filter out of capillary blood into the interstitial fluid (see Figure 23-1). To balance this outflow, fluid continually reenters blood from the interstitial fluid. Newer evidence has disproved the old idea that healthy capillaries do not "leak" proteins. In truth, each day about 50% of the total blood proteins leak out of the capillaries into the tissue fluid and return to the blood by way of the lymphatic vessels. For more details about fluid exchange between blood and interstitial fluid, see Chapter 32. From lymphatic capillaries, lymph flows through progressively larger lymphatic vessels to eventually reenter blood at the junction of the internal jugular and subclavian veins (Figure 23-5).

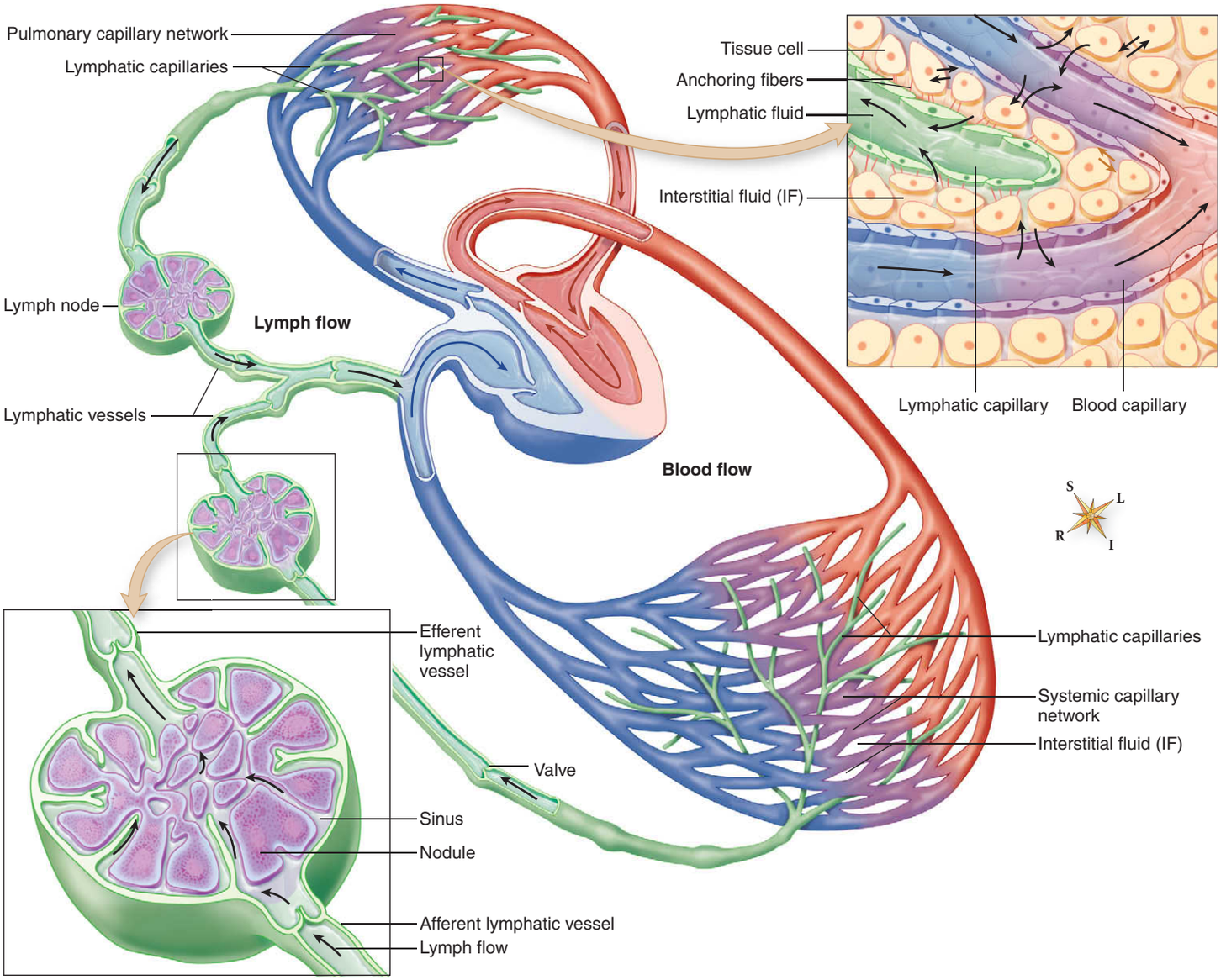


FIGURE 23-5

Circulation plan of lymphatic fluid. This diagram outlines the general scheme for lymphatic circulation. Fluids from the systemic and pulmonary capillaries leave the bloodstream and enter the interstitial space, thus becoming part of the IF (interstitial fluid). The IF also exchanges materials with the surrounding tissues. Often, because less fluid is returned to the blood capillary than had left it, IF pressure increases—causing IF to flow into the lymphatic capillary. The fluid is then called *lymph* (lymphatic fluid) and is carried through one or more lymph nodes and finally to large lymphatic ducts. The lymph enters a subclavian vein, where it is returned to the systemic blood plasma. Thus fluid circulates through blood vessels, tissues, and lymphatic vessels in a sort of "open circulation."

The Lymphatic Pump

Although there is no muscular pumping organ connected with the lymphatic vessels to force lymph onward as the heart forces blood, lymph still moves slowly and steadily along in its vessels. Lymph flows through the thoracic duct and reenters the general circulation at the rate of about 3 liters per day. This occurs despite the fact that most of the flow is against gravity, or "uphill." It moves through the system in the right direction because of the large number of valves that permit fluid flow only in the central direction.

What mechanisms establish the pressure gradient required by the basic law of fluid flow? Two of the same mechanisms that contribute to the blood pressure gradient in veins also establish a lymph pressure gradient. These are breathing movements and skeletal muscle contractions (see Figure 22-24, p. 702). Box 23-2 explains one of many reasons a working knowledge of lymphatic flow is important.

Activities that result in central movement, or flow, of lymph are called *lymphokinetic* actions (from the Greek *kinetos*, "movable"). Thus the flow of lymph may be called **lymphokinesis.** X-ray films taken after radiopaque material is injected into the lymphatics show that lymph pours into the central veins most rapidly at the peak of inspiration. This method of visualizing lymphatic vessels is called **lymphangiography** (Figure 23-6).

The mechanism of inspiration, resulting from the descent of the diaphragm, causes intraabdominal pressure to increase as intrathoracic pressure decreases. This simultaneously causes pressure to increase in the abdominal portion of the thoracic duct and to decrease in the thoracic portion. In other words, the process of inspiring establishes a pressure gradient in the thoracic duct that causes lymph to flow upward through it.

Research studies have shown that thoracic duct lymph is literally "pumped" into the venous system during the inspiration phase of pulmonary ventilation. The rate of flow, or ejection, of lymph into the venous circulation is proportional to the depth of inspiration. The total volume of lymph that enters the central veins during a given period depends on the depth of the inspiration phase and the overall breathing rate.

Most lymph flow in the body is the result of contracting skeletal muscles. As muscles contract, they "milk" the lymphatic vessels and push the lymph forward (Figure 23-7). The actual pressure

Box 23-2 | HEALTH matters

Lymphatic Drainage and Artificial Limbs

An understanding of the anatomy of lymphatic drainage of the skin is critically important in surgical amputation of an extremity. A majority of the lymphatics draining the skin are located in plexus-like networks lying on the deep fascia. To prevent stasis of lymph in the stump following amputation, the surgeon retains the deep fascia and its lymphatic vessels with the skin flaps that are used to cover the cut end of the extremity. This procedure results in minimal edema and swelling—a matter of obvious importance to the patient and artificial-limbfitter.

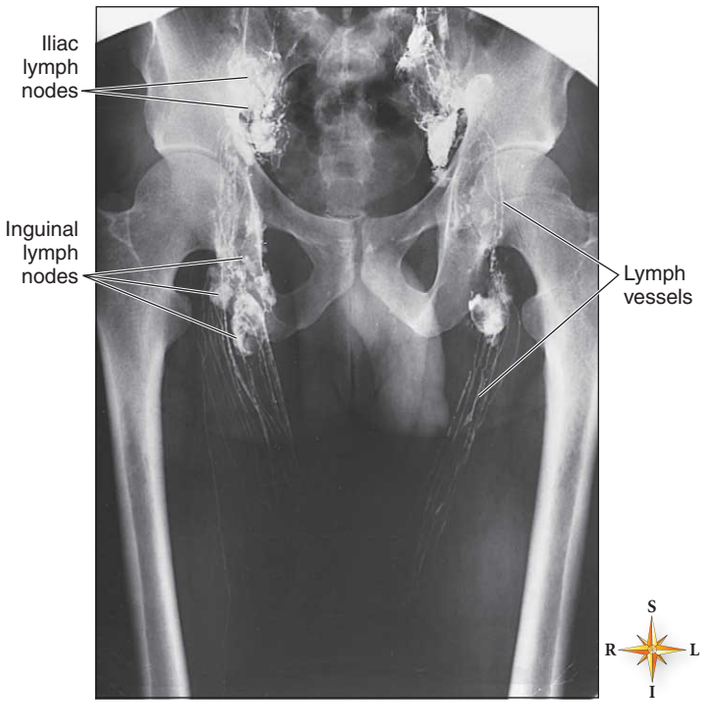


FIGURE 23-6

Lymphangiogram. A dye that is radiopaque (blocks x rays) is injected into the interstitial fluid that eventually drains into nearby lymphatic pathways. There the dye is seen as bright areas outlining the location of pelvic (iliac) and inguinal lymphatic vessels and lymph nodes.

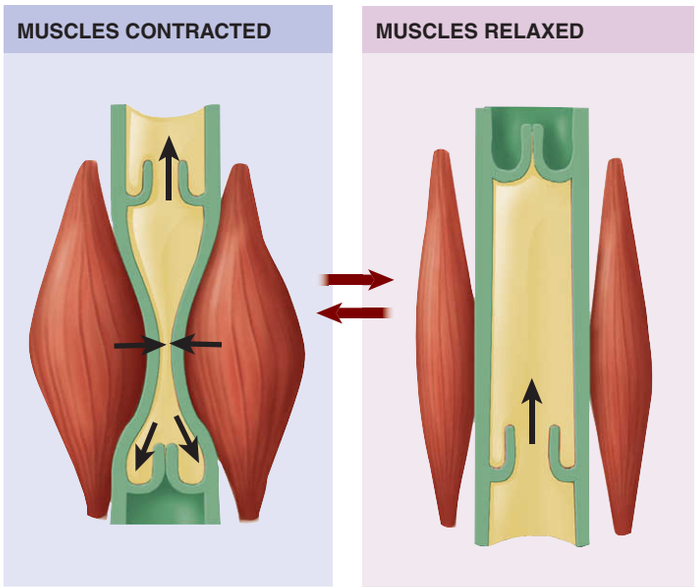


FIGURE 23-7

Lymphatic pump. The diagram shows a "muscle pump" in a lymphatic vessel similar to that which moves blood through the veins. Increased external pressure from muscle contraction also increases lymphatic pressure, pushing it past one-way lymphatic valves. Because the valves prevent backflow, the system becomes a pump that keeps lymph moving in one direction (toward a subclavian vein).

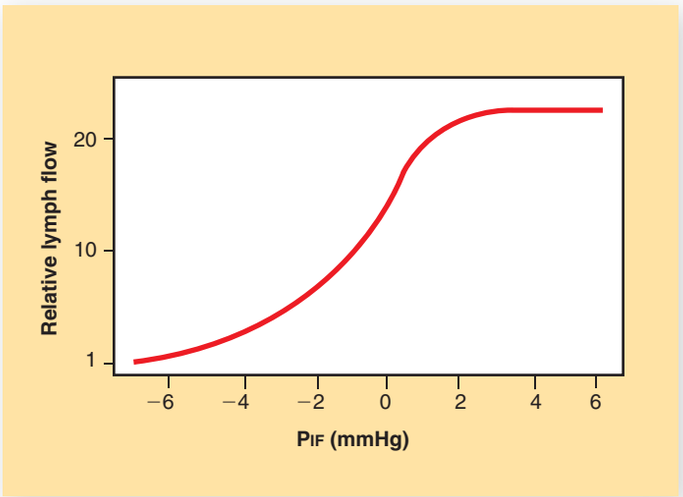


FIGURE 23-8

Lymph flow and interstitial fluid (IF) pressure. As the pressure of IF increases, the flow of lymph increases. Muscle pumps can increase IF pressure, as can other factors, such as accumulation of additional interstitial fluid volume within a tissue.

generated in the system remains very low, and movement of lymph proceeds quite slowly when compared with the circulation of blood. During exercise, lymph flow may increase as much as 10 to 15 times. In addition to lymph flow caused by skeletal muscle contractions, a very limited amount of smooth muscle exists in the walls of the large lymphatic trunks. Contraction of the smooth muscle in the thoracic vessel walls permits lymphatic vessels to pulse rhythmically and thus help move lymph from one valved segment to the next.

Other pressure-generating factors that can compress the lymphatics also contribute to the effectiveness of the "lymphatic pump." Examples of such lymphokinetic factors include interstitial fluid pressure (Figure 23-8), arterial pulsations, postural changes, and passive compression (massage) of the body soft tissues.

Although the overall volume of lymph that enters the bloodstream during each 24-hour period averages about 3 L, it may enter the system at different rates during the day. The rate of return varies, depending on the level of generalized physical activity and other factors, including changes in the interstitial fluid pressure and the rate and depth of respiration. As physical activity increases, so does the outflow of fluid from blood capillaries into the tissue spaces of the body. The increased flow of lymph that occurs with increased physical activity helps return this fluid to the cardiovascular system and thus serves as an important balancing or homeostatic mechanism.

| QUICK CHECK |

1. What is the overall function of the lymphatic system?
2. What is the origin of lymph?
3. Compare lymphatic vessels with blood vessels.

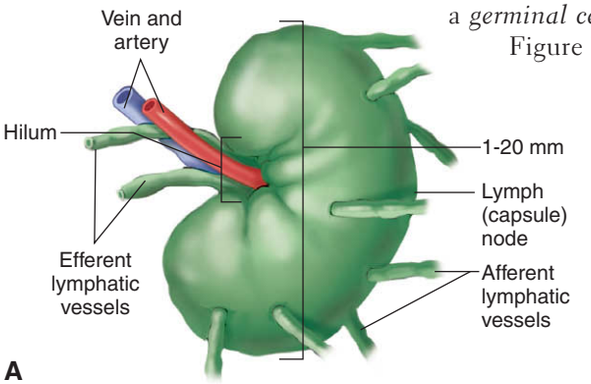
LYMPH NODES

Structure of Lymph Nodes

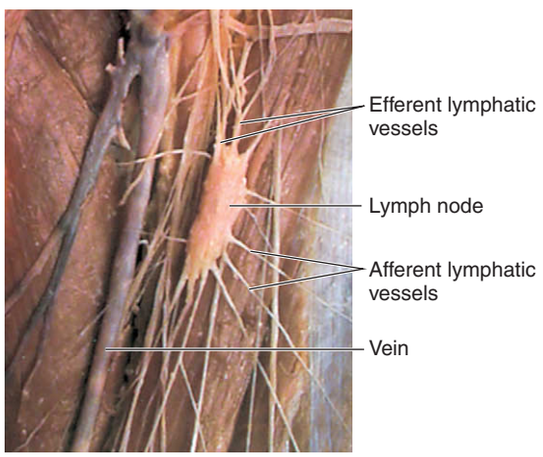
Lymph nodes, or *lymph glands,* as some people call them, are oval-shaped or bean-shaped structures (Figure 23-9). Some are as small as a pinhead, and others are as large as a lima bean. Each lymph node (from 1 mm to more than 20 mm in diameter) is enclosed by a fibrous capsule. Note in Figure 23-10 that lymph moves into a node by way of *afferent* lymphatic vessels and emerges by one or more *efferent* vessels.

Think of a lymph node as a biological filter placed in the channel of several afferent lymph vessels (as you saw in Figure 23-5). Once lymph enters the node, it "percolates" slowly through the spaces known as sinuses before draining into the single efferent exit vessel. One-way valves in both the afferent and efferent vessels keep lymph flowing in one direction.

Fibrous septa, or *trabeculae,* extend from the covering capsule toward the center of the node. **Cortical nodules** within sinuses along the periphery, or cortex, of the node are separated from each other by these connective tissue trabeculae. Each cortical nodule is composed of packed lymphocytes that surround a less dense area called a *germinal center* (see Figure 23-10).



A



B

FIGURE 23-9

External structure of a lymph node. A, A lymph node is typically a small structure into which afferent lymphatic ducts empty their lymph and out of which efferent lymphatic ducts drain the lymph. An outer fibrous capsule maintains the structural integrity of the node. **B,** Photograph of a dissected cadaver shows a lymph node and its associated lymphatic vessels, along with nearby muscles, nerves, and blood vessels.

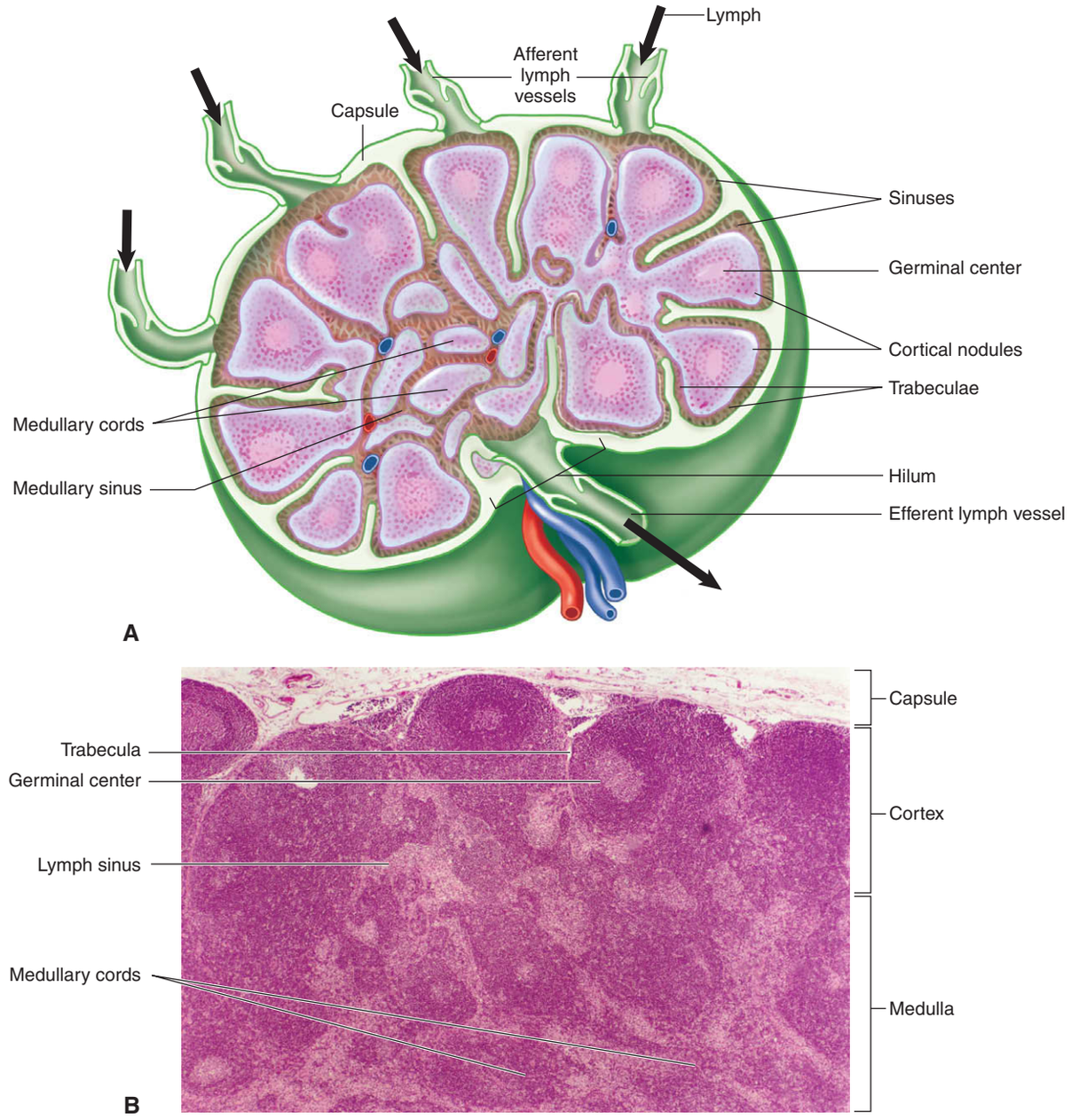


FIGURE 23-10

Internal structure of a lymph node. A, Several afferent valved lymphatics bring lymph to the node. In this example, a single efferent lymphatic leaves the node at a concave area called the *hilum.* Note that the artery and vein also enter and leave at the hilum. Arrows show direction of lymph flow. **B,** Photomicrograph and drawing showing a portion of the cortex and medulla of a lymph node.

Figure 23-10, *B*, is a low-power (×35) light micrograph of a portion of a typical lymph node. When an infection is present, germinal centers form and the node begins to release lymphocytes. B lymphocytes (B cells) begin their final stages of maturation within the less dense germinal center of the nodule and then are pushed to the more densely packed outer layers as they mature to become antibody-producing plasma cells. The center, or medulla, of a lymph node is composed of sinuses and medullary cords (see Figure 23-10). Both the cortical and medullary sinuses are lined with reticuloendothelial cells (macrophages) capable of phagocytosis.

Locations of Lymph Nodes

With the exception of comparatively few single nodes, most lymph nodes occur in groups, or clusters, in certain areas. The group locations of greatest clinical importance are as follows:

Preauricular lymph nodes—located just in front of the ear; these nodes drain the superficial tissues and skin on the lateral side of the head and face (Figure 23-11).

Submental group and **submandibular group** *(submaxillary)*—in the floor of the mouth; lymph from the nose, lips, and teeth drains through these nodes (see Figure 23-11).

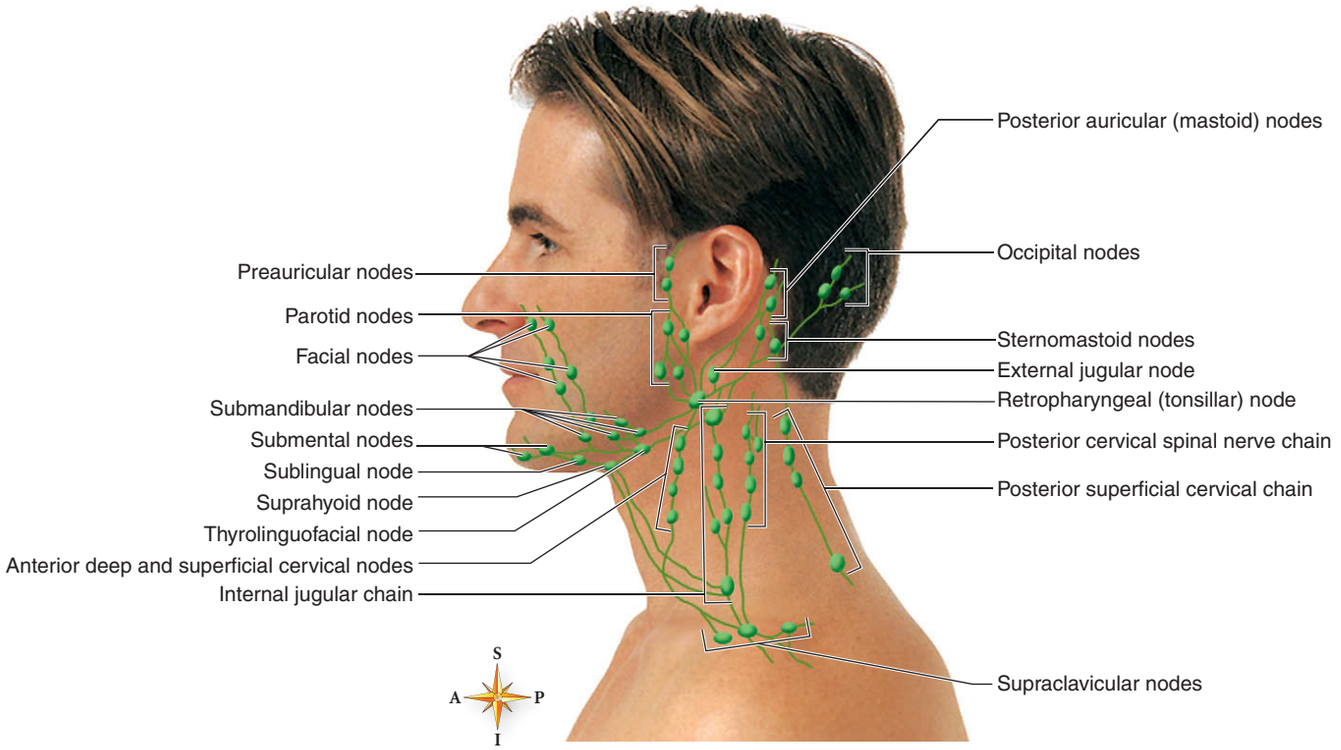


FIGURE 23-11

Lymphatic drainage of the head and neck. The head and neck contain many lymph nodes (and associated lymphatic vessels) that are often of clinical significance in certain infections and cancers.

Superficial cervical lymph nodes—in the neck along the sternocleidomastoid muscle, these nodes drain lymph (which has already passed through other nodes) from the head and neck (see Figures 23-11 and 23-12).

Superficial cubital lymph nodes (supratrochlear lymph nodes)—located just above the bend of the elbow; lymph from the forearm passes through these nodes (see Figure 23-2).

Axillary lymph nodes—(20 to 30 large nodes clustered deep within the underarm and upper chest regions); lymph from the arm and upper part of the thoracic wall, including the breast, drains through these nodes (see Figure 23-2).

Iliac lymph nodes and **inguinal lymph nodes**—in the pelvis and groin; lymph from the pelvic organs, legs, and external genitals drains through these nodes (Figures 23-6 and 23-13).

Functions of Lymph Nodes

Lymph nodes perform at least two distinct functions: defense and hematopoiesis.

DEFENSE FUNCTIONS: FILTRATION AND PHAGOCYTOSIS

The structure of the sinus channels within lymph nodes slows the lymph flow through them. This gives the reticuloendothelial cells that line the channels time to remove the microorganisms and other injurious particles—soot, for example—from the lymph

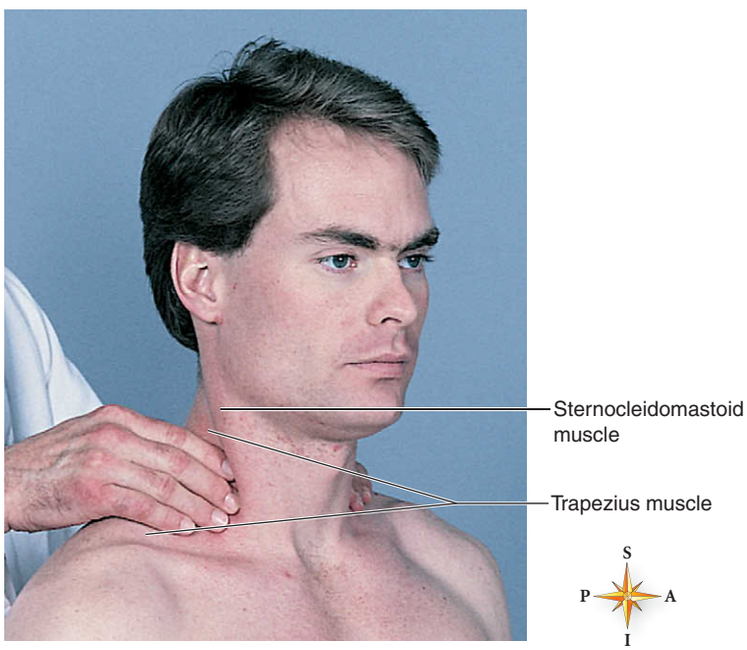


FIGURE 23-12

Palpation of the posterior cervical lymph nodes. The pads of the fingertips are used to palpate (feel) along the anterior surface of the trapezius muscle and then moved slowly in a circular motion to the posterior surface of the sternocleidomastoid muscle. Swollen lymph nodes may be a sign of infection, cancer, blocked lymphatic drainage, or some other abnormal condition.

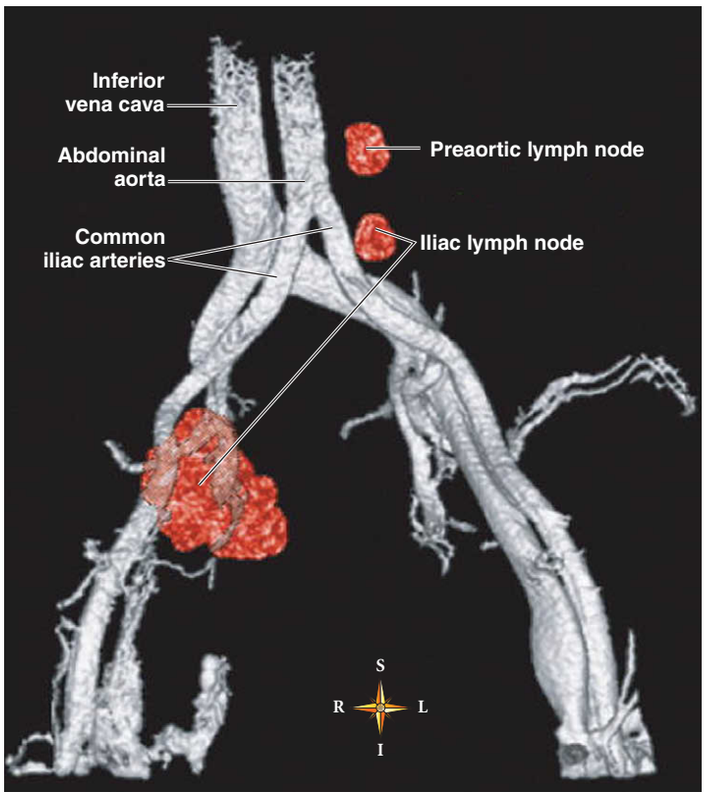


FIGURE 23-13

MRI of lymph nodes. This three-dimensional MRI (magnetic resonance image) has been enhanced by the use of specially engineered nanoparticles that are injected into the blood and then later ingested by macrophages in the lymphoid tissue of the lymph nodes. In lymphoid tissue containing metastasized cancer cells, there is a recognizable, abnormal pattern calculated in the MRI software (color-coded red in this image). Thus cancerous lymph nodes can be identified and accurately located for surgical removal or other therapy.

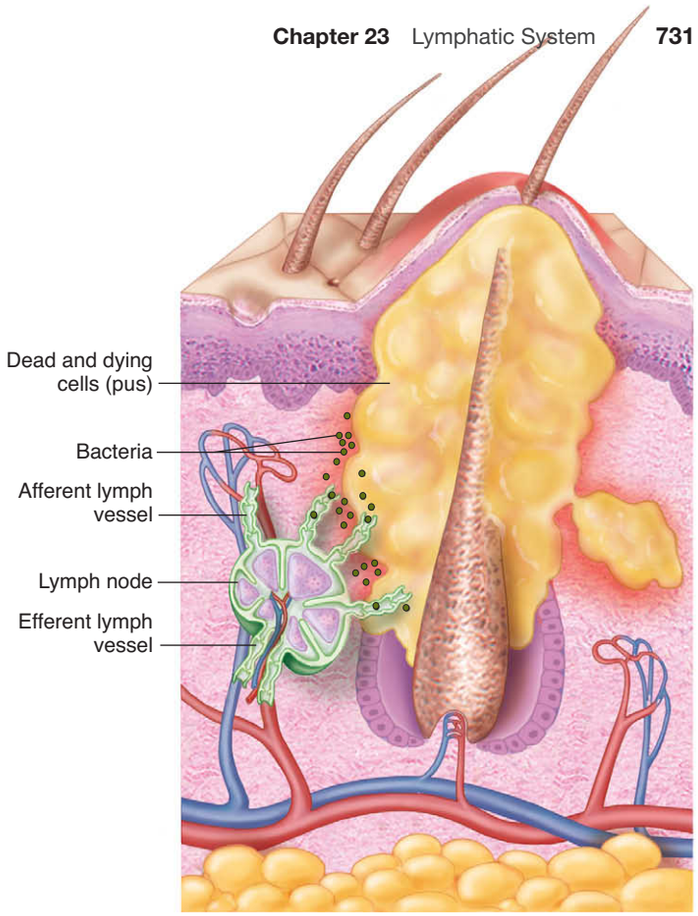


FIGURE 23-14

Role of a lymph node in a skin infection. Leukocytes phagocytose many bacteria in tissue spaces. Others may enter the lymph nodes by way of afferent lymphatics. The nodes filter out these bacteria; reticuloendothelial cells within the nodes usually destroy all the bacteria by phagocytosis. (Lymph node is shown smaller than actual size.)

and phagocytose them (Figure 23-14). Lymph nodes physically stop particles from progressing farther in the body—a process called *mechanical filtration*. Because lymph nodes also make use of biological processes such as phagocytosis to destroy particles, *biological filtration* also occurs here.

Sometimes, however, such hordes of microorganisms enter the nodes that the phagocytes cannot destroy enough of them to prevent injury to the node. An infection of the node, *adenitis*, then results. Also, because cancer cells often break away from a malignant tumor and enter lymphatics, they travel to the lymph nodes, where they may set up new growths and block flow of lymph. This may leave too few channels for lymph to return to the blood. For example, if tumors block axillary node channels, fluid accumulates in the interstitial spaces of the arm, causing the arm to become markedly swollen. Even viruses such as HIV (human immunodeficiency virus) and other types of pathogens can infect or infest lymph nodes, as seen in Figure 23-15.

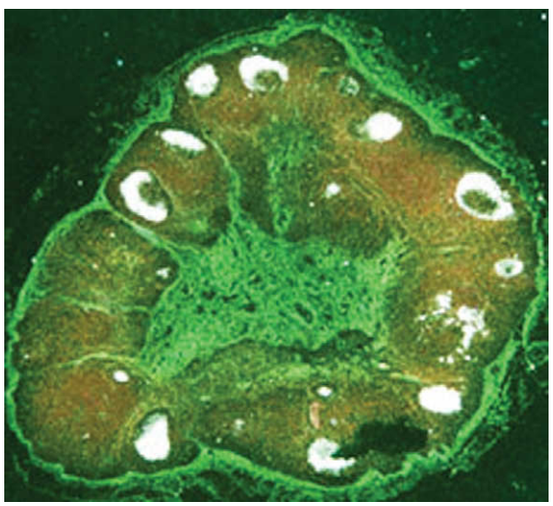


FIGURE 23-15

Infected lymph node. This lymph node is infected with HIV (human immunodeficiency virus), seen in this specially stained micrograph as white areas. Researchers at the National Institute of Allergy and Infectious Disease (NIAID) found that lymphoid tissue is a major reservoir for HIV, thus providing a sanctuary for viral replication while the virus is being cleared from the bloodstream by the immune system.

HEMATOPOIESIS

The lymphoid tissue of lymph nodes serves as the site of the final stages of maturation for some types of lymphocytes and monocytes that have migrated from the bone marrow. In addition to lymph nodes and the major lymphatic organs described later in the chapter, small aggregates of diffuse lymphoid tissue and other lymphatic cell types are found throughout the body—especially in connective tissues and under mucous membranes.

LYMPHATIC DRAINAGE OF THE BREAST

Cancer of the breast is one of the most common forms of malignancy in women. Unfortunately, cancerous cells from a single "primary" tumor in the breast often spread to other areas of the body through the lymphatic system. An understanding of the lymphatic drainage of the breast is therefore of particular importance in the diagnosis and treatment of this type of malignancy (Box 23-3).

Breast infections (**mastitis**) are also a serious health concern, especially among women who are nursing infants. Breast infections, like cancer, can also spread easily through lymphatic pathways associated with the breast. Refer to Figure 23-16 as you study the lymphatic drainage of the breast.

Box 23-3 | HEALTH matters

Lymphedema After Breast Surgery

Surgical procedures called *mastectomies,* in which some or all of the breast tissues are removed, are sometimes performed to treat breast cancer. Because cancer cells can spread so easily through the extensive network of lymphatic vessels associated with the breast (see Figure 23-16), the lymphatic vessels and their nodes are sometimes also removed. Occasionally, such procedures interfere with the normal flow of lymph fluid from the arm. When this happens, tissue fluid may accumulate in the arm—resulting in swelling, or **lymphedema.** Fortunately, adequate lymph drainage is almost always restored by the reestablishment of new lymphatic vessels, which grow back into the area.

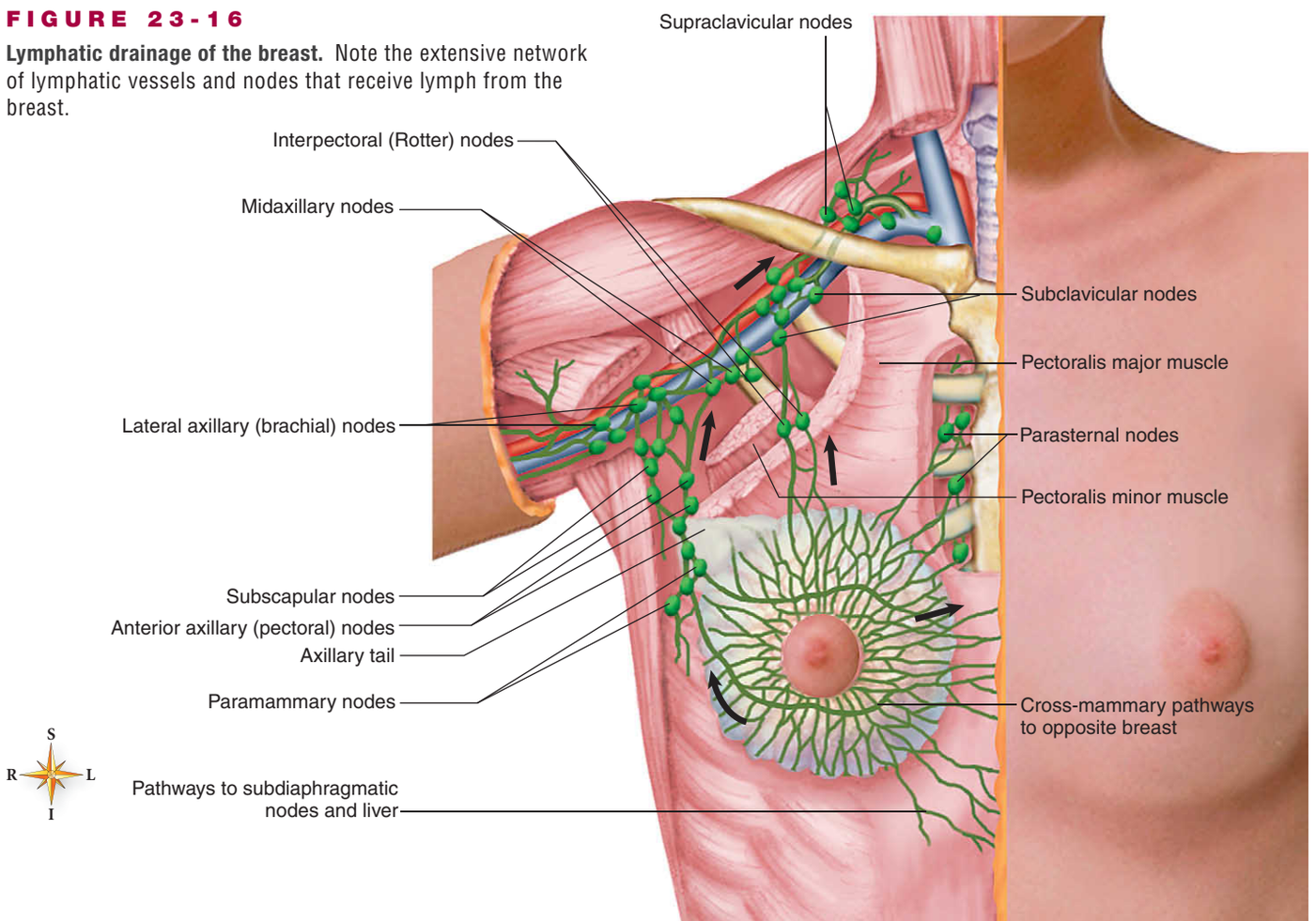
Distribution of Lymphatics in the Breast

The breast—mammary gland and surrounding tissues—is drained by the following two sets of lymphatic vessels:

1. Lymphatics that originate in and drain the skin over the breast with the exception of the areola and nipple
2. Lymphatics that originate in and drain the underlying substance of the breast itself, as well as the skin of the areola and nipple

FIGURE 23-16

Lymphatic drainage of the breast. Note the extensive network of lymphatic vessels and nodes that receive lymph from the breast.



Superficial vessels that drain lymph from the skin and surface areas of the breast converge to form a diffuse *cutaneous lymphatic plexus*. Communication between the cutaneous plexus and large lymphatics that drain the secretory tissue and ducts of the breast occurs in the *subareolar plexus (plexus of Sappey)* located under the areola surrounding the nipple.

Box 23-4 discusses the numerous connections of the breast lymphatic pathways.

Lymph Nodes Associated with the Breast

More than 85% of the lymph from the breast enters the lymph nodes of the axillary region (see Figure 23-16). Most of the remainder enters lymph nodes along the lateral edges of the sternum.

Several very large nodes in the axillary region are in actual physical contact with an extension of breast tissue called the *axillary tail (tail of Spence)*. Because of the physical contact between these nodes and breast tissue, cancerous and infectious cells may spread by both lymphatic extension and contiguity of tissue. Other nodes in the axilla or chest wall will enlarge and swell after being "seeded" with malignant cells or bacteria as lymph from a cancerous or infected breast flows through them. For example, interpectoral (Rotter) nodes found between the pectoralis major and minor muscles often contain metastases from mammary cancer.

A **sentinel lymph node (SLN)** is the first lymph node to which a cancerous tumor can spread. When a tumor is detected, the nearby SLN may be examined in a biopsy to determine whether cancer cells are present—showing that the cancer has metastasized.

| QUICK CHECK |

4. Describe the overall structure of a typical lymph node.
5. Where are lymph nodes usually found?
6. What functions are carried out by lymph nodes?
7. How do the lymphatic structures of the breast relate to breast cancer?

Box 23-4 | HEALTH matters

Lymphatic Anastomoses and Breast Cancer

Anastomoses (connections) occur between superficial lymphatics from both breasts across the middle line. Such communication can result in the spread of cancerous cells in one breast to previously healthy tissue in the other breast.

Both superficial and deep lymphatic vessels also communicate with lymphatics in the fascia of the pectoralis major muscle. Removal of a wide area of deep fascia is therefore required in surgical treatment of advanced or diffuse breast malignancy (radical mastectomy). In addition, cancer cells from a breast tumor sometimes reach the abdominal cavity because of lymphatic communication through the upper part of the linea alba.

A more thorough discussion of breast cancer is found in Chapter 35, beginning on p. 1090.

TONSILS

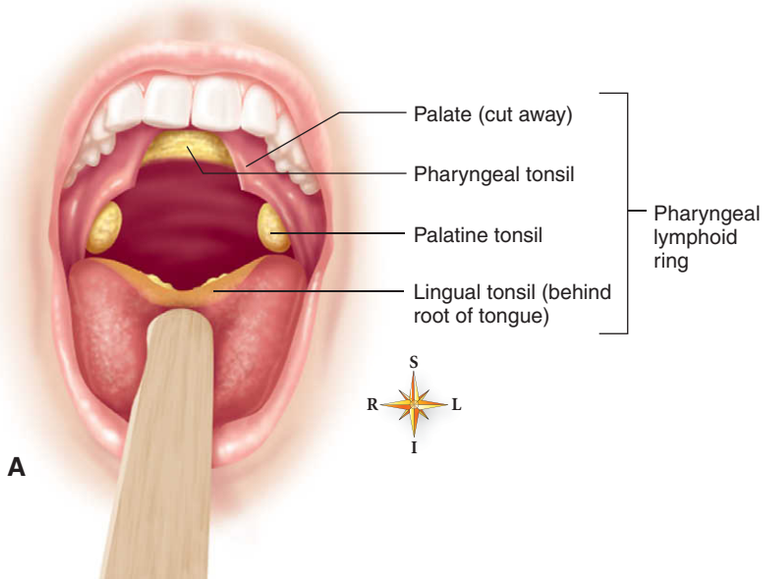
Masses of lymphoid tissue, called **tonsils,** are located in a protective ring under the mucous membranes in the mouth and back of the throat (Figure 23-17, A). This ring is called the *pharyngeal lymphoid ring*. The ring of tonsils helps protect against bacteria that may invade tissues in the area around the openings between the nasal and oral cavities.

The **palatine tonsils** are located on each side of the throat. The **pharyngeal tonsils,** known as *adenoids* when they become swollen, are near the posterior opening of the nasal cavity. A third type of tonsil, the **lingual tonsils,** is near the base of the tongue. A fourth type of tonsil, the *tubal tonsils*, are located near the opening of the auditory (eustachian) tube. Each of the tonsils has deep recesses called *tonsillar crypts* that trap bacteria and put them in close contact with cells of the immune system.

The tonsils serve as the first line of defense from the exterior and as such are subject to chronic infection, or tonsillitis

FIGURE 23-17

Location of the tonsils. A, Small segments of the roof and floor of the mouth have been removed to show the protective ring of tonsils (pharyngeal lymphoid ring) around the internal openings of the nose and throat. Tubal tonsils are not visible in this view. **B,** Tonsillitis. Note the swelling and presence of a white coating (exudate) indicating an infection.





UNIT 4

(Figure 23-17, *B*). They are sometimes removed surgically if antibiotic therapy is not successful or if swelling impairs breathing. This procedure, called **tonsillectomy,** has become controversial because of the critical immunological role played by the lymphoid tissue.

| A&P CONNECT |

Because it is exposed to the external environment, the respiratory tract could be extremely vulnerable. Look at the structure of a tonsil and learn about its defensive role in ***Protective Strategies of the Respiratory Tract*** online at ***A&P Connect.***

evolve

THYMUS

Location and Appearance of the Thymus

Intensive study and experimentation have identified the **thymus** as a primary organ of the lymphatic system. It is an unpaired organ consisting of two pyramidal lobes with delicate and finely lobulated surfaces. The thymus is located in the mediastinum, extending up into the neck as far as the lower edge of the thyroid gland and inferiorly as far as the fourth costal cartilage (Figure 23-18, A). Its size relative to the rest of the body is largest in a child about 2 years old. Its absolute size is largest at puberty, when its weight ranges between 35 and 40 grams. From then on, it gradually atrophies until, in advanced old age, it may be largely replaced by fat, weigh less than 10 grams, and be barely recognizable. The process of shrinkage of an organ in this manner is called **involution.** The thymus is pinkish gray in color early in childhood but, with advancing age, becomes yellowish as lymphoid tissue is replaced by fat.

Structure of the Thymus

The lobes of the thymus are subdivided into small (1- to 2-mm) lobules by connective tissue septa that extend inward from a fibrous covering capsule. Each lobule is composed of a dense cellular cortex and an inner, less dense medulla (Figure 23-18, *B*). Both cortex and medulla are composed of lymphocytes in an epithelial framework quite different from the supporting connective tissue seen in other lymphoid organs.

In stained histological sections of thymus, medullary tissue can be identified by the presence of rather large (30- to 150-mm) laminated spherical structures called **thymic corpuscles,** or *Hassall corpuscles.* Composed of concentric layers of keratinized epithelial cells, thymic corpuscles have a unique onionlike appearance. These corpuscles may serve as a place to break down dead, keratinized epithelial cells migrating inward from the outer parts of each lobule. They also secrete some of the regulatory molecules that affect white blood cell (WBC) development described in the next section.

Function of the Thymus

One of the body's best-kept secrets has been the function of the thymus. Before 1961 there were no significant clues as to its role. Then a young Briton, Dr. Jacques F.A.P. Miller, removed the thymus glands from newborn mice. His findings proved startling and crucial. Almost like a chain reaction, further investigations followed, leading to the gradual uncovering of the thymus's long-held secrets. It is now clear that this small structure plays a critical part in the body's defenses against infections—in its vital immunity mechanism (see Chapter 24).

The thymus performs at least two important functions. First, it serves as the final site of lymphocyte development before birth. (The fetal bone marrow forms immature lymphocytes, which then move to the thymus.) Many lymphocytes leave the thymus and circulate to the spleen, lymph nodes, and other lymphoid tissues. Second, soon after birth the thymus begins secreting a group of hormones (collectively called

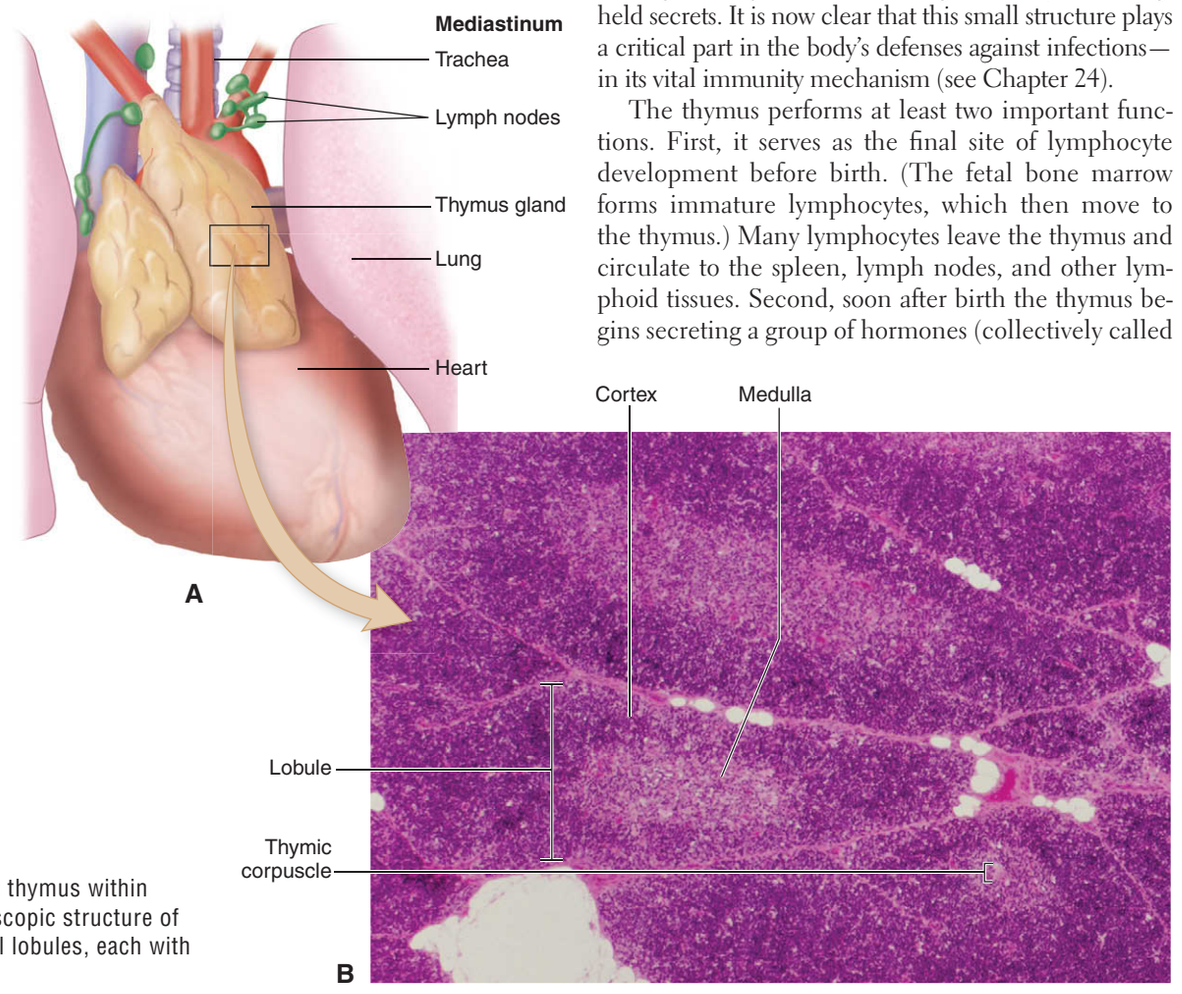


FIGURE 23-18

Thymus. A, Location of the thymus within the mediastinum. **B,** Microscopic structure of the thymus showing several lobules, each with a cortex and a medulla.

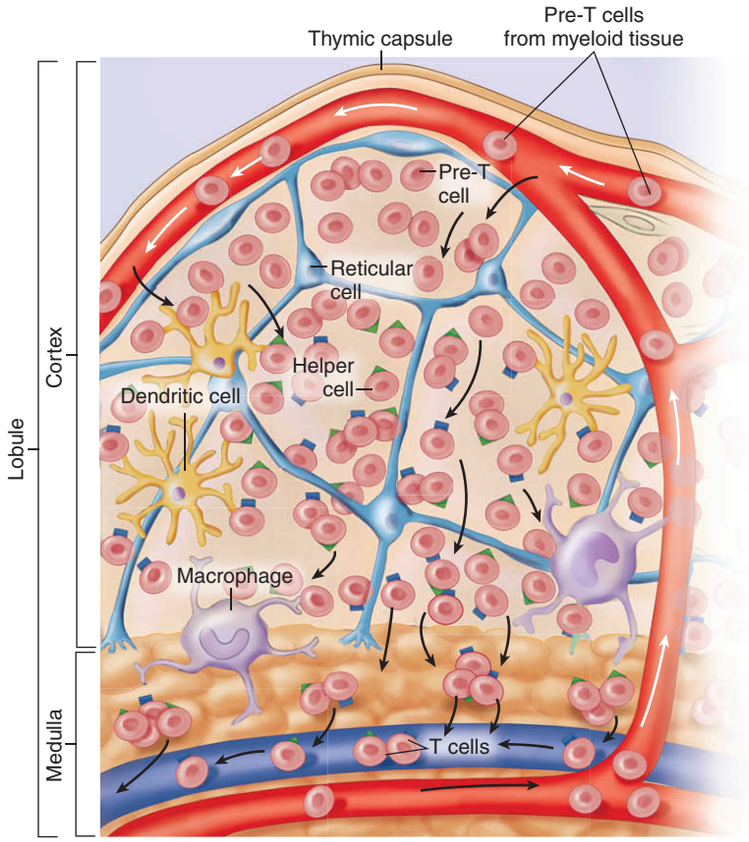


FIGURE 23-19

T-cell development in the thymus. This diagram shows part of a lobule, with the cortex at the top and the medulla at the bottom. Pre–T cells derived from hematopoietic stem cells in red bone marrow (myeloid tissue) travel through the bloodstream to the cortex of the thymus. Under the influence of thymosin and other regulators, the pre–T cells divide and mature as they migrate toward the medulla. Along the way, the developing T cells (T lymphocytes) are tested for immune capability against various lymphoid immune cells, such as dendritic cells and macrophages. Only about 5% of the cells pass these tests and are released into the bloodstream to defend the body.

thymosin) and other regulators that enable lymphocytes to develop into mature T cells. Only T cells (T lymphocytes) that pass immunological testing by lymphoid cells such as *macrophages* and *dendritic cells*—only about 5% of the cells that mature each day—are released into the bloodstream. Figure 23-19 outlines some essential steps in T cell development within the thymus.

Because T cells attack foreign or abnormal cells and also serve as regulators of immune function, the thymus functions as an important part of the immune mechanism. It is most active in childhood. Beginning at puberty, involution of the thymus reduces its function gradually through adulthood. By time a person is 50, only 10% of functional thymus tissue remains. Elderly people have virtually no functional thymus tissue left, a factor that contributes to reduced immune function associated with aging.

SPLEEN

Location of the Spleen

The **spleen** is located in the left hypochondrium of the abdominopelvic cavity, directly below the diaphragm. The spleen is just above most of the left kidney and the descending colon and behind the fundus of the stomach (Figures 23-2 and 23-20). In addition, it is common to find small *accessory spleens* embedded in the double fold of serous membrane that connects the spleen and stomach.

Structure of the Spleen

As Figures 23-20 and 23-21 show, the spleen is roughly ovoid in shape. Its size varies in different individuals and in the same individual at different times (Box 23-5). For example, it hypertrophies during infectious diseases and atrophies in old age.

Like other lymphoid organs, the spleen is surrounded by a fibrous capsule with inward extensions that roughly divide the organ into compartments. One such compartment is shown in Figure 23-21, *B*. Arteries leading into each compartment are surrounded by dense masses (nodules) of developing lymphocytes. Because of its whitish appearance, this tissue is called *white pulp*.

Near the outer regions of each compartment is tissue called *red pulp*, made up of a network of fine reticular fibers submerged in blood that comes from the nearby arterioles. The red pulp network supports cords of WBCs and related cells surrounded by blood-filled sinusoids. After passing through the reticular meshwork, blood collects in venous sinuses and then returns to the heart through veins.

Functions of the Spleen

The spleen has many and sundry functions, including defense, hematopoiesis, and red blood cell and platelet destruction; it also serves as a reservoir for blood.

Defense. As blood passes through the sinusoids of the spleen, reticuloendothelial cells (macrophages) lining these venous spaces remove microorganisms from the blood and destroy

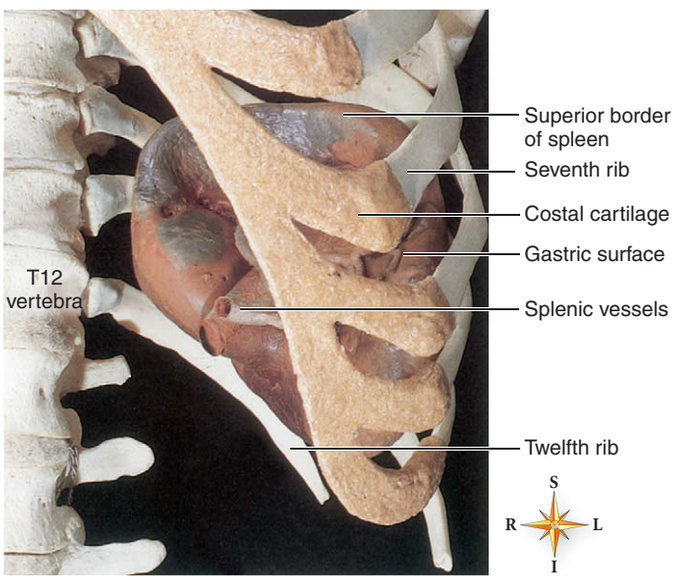


FIGURE 23-20

Location of the spleen. The spleen is located in the left hypochondrium of the abdominopelvic cavity, just inferior to the diaphragm and just deep to the lower portion of the rib cage.

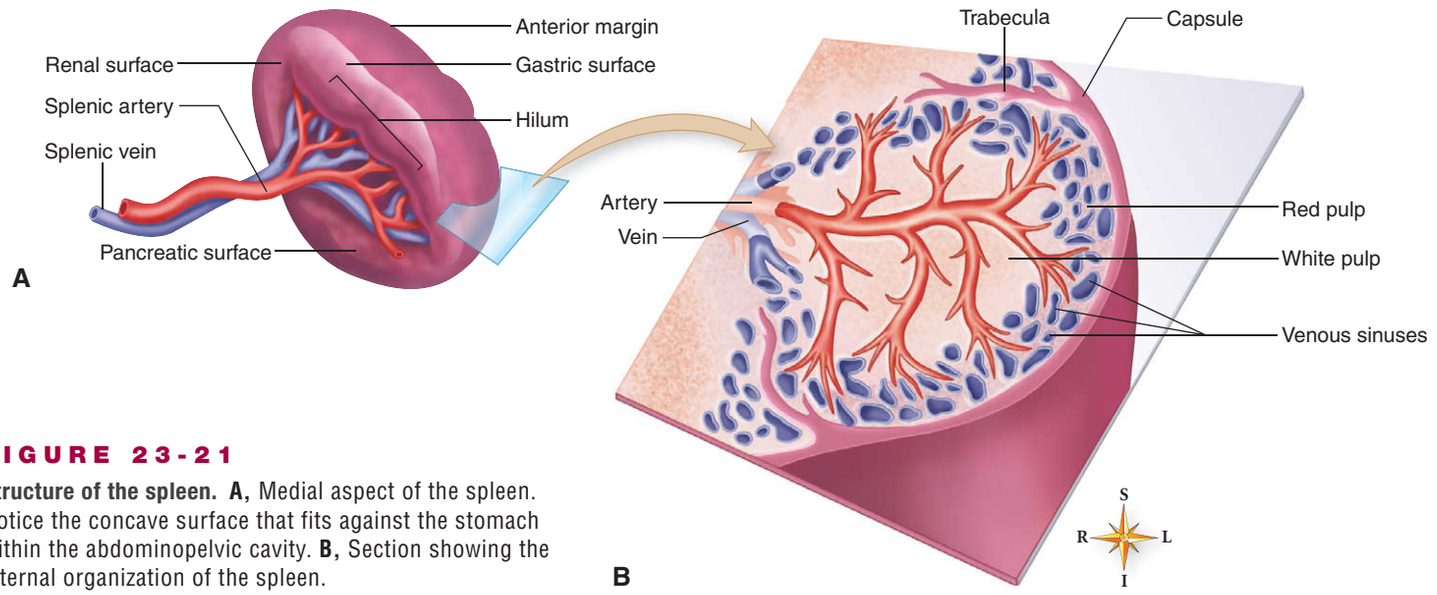


FIGURE 23-21

Structure of the spleen. A, Medial aspect of the spleen. Notice the concave surface that fits against the stomach within the abdominopelvic cavity. **B,** Section showing the internal organization of the spleen.

them by phagocytosis. Therefore the spleen plays a part in the body's defense against microorganisms.

Tissue repair. Monocytes found in the cords of WBCs in red pulp just under the spleen's outer capsule are mobilized when significant tissue damage occurs, such as in an MI (myocardial infarction or "heart attack"). A large number of monocytes migrate quickly to the injured tissue and assist in healing and repair.

Hematopoiesis. Nongranular leukocytes, that is, monocytes and lymphocytes, complete their development and become activated in the spleen. Before birth, red blood cells are also formed in the spleen, but after birth, the spleen forms red blood cells only in cases of extreme hemolytic anemia.

Red blood cell destruction *and* ***platelet destruction.*** Macrophages lining the spleen's sinusoids remove worn out red blood cells and imperfect platelets from the blood and destroy them by phagocytosis. They also break apart the hemoglobin molecules from the destroyed red blood cells and salvage their iron and globin content by returning them to the bloodstream for storage in bone marrow and liver.

Blood reservoir. At any given point in time the pulp of the spleen and its venous sinuses contain a considerable amount of blood. Although continually moving slowly through the spleen, blood can rapidly be added back into the circulatory system from this functional reservoir if needed. Its normal volume of about 350 ml is said to decrease by about 200 ml in less than 1 minute following sympathetic stimulation that produces marked constriction of its smooth-muscle capsule. This "self-transfusion" occurs, for example, as a response to the stress imposed by hemorrhage.

Although the spleen's functions make it a most useful organ, it is not a vital one. Dr. Charles Austin Doan in 1933 took the daring step of performing the first **splenectomy.** He removed the spleen from a 4-year-old girl who was dying of hemolytic anemia. Presumably, he justified his radical treatment on the basis of what was then merely conjecture, that is, that the spleen destroys red blood cells. The child recovered, and Dr. Doan's operation proved to be a landmark. It created a great upsurge of interest in the spleen and led to many investigations of this organ.

Because of its role as a blood reservoir, the spleen contains a high volume of blood at any one time—especially during rest. If the spleen is accidentally ruptured, as it might when the ribs are broken and pushed into the spleen, significant internal bleeding could occur. If the blood loss is rapid and is not stopped in time, death could result. Surgical repair or removal of the spleen can stop the blood loss and save a life.

Table 23-1 summarizes the essential characteristics of the major types of lymphatic organs.

Box 23-5 | HEALTH matters

Splenomegaly

Splenomegaly, or abnormal spleen enlargement, is observed in various disorders. For example, infectious conditions such as scarlet fever, syphilis, and typhoid fever may be characterized by splenomegaly. Spleen enlargement sometimes accompanies hypertension. Splenomegaly also accompanies some forms of hemolytic anemia in which red blood cells appear to be broken apart at an abnormally fast rate. Surgical removal of the spleen often prevents death in such cases.

| QUICK CHECK |

8. Where are the major tonsils located? What is their role?
9. What major role does the thymus play in immunity?
10. What are the major functions of the spleen?

TABLE 23-1 Major Lymphatic Organs

ORGAN	STRUCTURE	FUNCTION
Lymphatic vessels	Thin-walled vessels with numerous valves that ensure one-way flow of lymphatic fluid (lymph); larger vessels have three layers (similar to veins)	Collect fluids draining from tissues of the body (lymph) and return it to the blood circulation
Lymphatic capillaries	Microscopic, blind-end vessels, made up of single endothelial layer having many gaps	Collect tissue fluid (forming lymph) Transport lymph to larger lymphatic vessels
Lymphatic ducts	Large lymphatic vessels formed by many tributaries throughout the body; connect to the subclavian veins	Collect lymph from network of lymphatic vessels and drain it into the blood circulation
Lymphoid organs	Have a significant component of lymphoid tisse (developing white blood cells)	Hematopoiesis (WBCs) Immunity Filter body fluids
Lymph nodes	Fibrous capsule surrounding a maze of sinuses, each with lymphoid tissue nodule suspended by reticular fibers	Filtration of lymph before it enters bloodstream Mechanical filtration: removing particles Biological filtration: cells destroy and remove particles
Aggregated lymph nodules (tonsils, Peyer patches)	Groupings of nodules (lumps of lymphoid tissue) embedded in mucous membranes	Immunity at common points of entry for pathogenic microbes
Thymus	Two pyramid-shaped lobes subdivided into smaller lobules containing lymphoid tissue	Hematopoiesis—site of T-lymphocyte (T-cell) development Hormone production—thymosin regulates T-cell development
Spleen	Ovoid fibrous capsule with internal maze of sinuses containing dense lymphoid tissue (white pulp) surrounded by blood sinusoids having cords of lymphoid tissue (red pulp)	Hematopoiesis (WBCs) Immunity Filtration of blood Tissue repair Destruction of old RBCs, platelets Blood reservoir

RBC, red blood cell
WBC, white blood cell

Cycle of LIFE
Lymphatic System

Many of the structural features of the lymphatic system exhibit dramatic changes as a person progresses through a life span. Most of the organs containing masses of developing lymphocytes appear before birth and continue growing through most of childhood until just before puberty. After puberty, these lymphoid organs typically begin to slowly atrophy until they reach much smaller size by late adulthood. These organs—including the thymus, lymph nodes, tonsils, and other lymphoid structures—shrink in size and become fatty or fibrous. The notable exception to this principle is the spleen, which develops early in life and remains intact until very late adulthood.

Despite the fact that lymphocyte-producing lymphoid tissues decline after puberty, the overall function of the immune system is maintained until late adulthood. During the late adult years, deficiency of the immune system permits a greater risk of infections and cancer, and hypersensitivity of the immune system may make autoimmune conditions more likely to occur.

the BIG picture

Lymphatic System and the Whole Body

One way to imagine the role of the lymphatic system in the "society of cells" that makes up the human body is as a sort of waste-water system. Like waste-water systems used in the cities of human society, the lymphatic system drains away excess, or "runoff," water from large areas. After collecting the body's runoff, or lymph, the lymphatic system conducts it through a network of lymphatic vessels, or "drain pipes," to miniature "treatment facilities" called *lymph nodes.* Contaminants are there removed from lymph, just as contaminants are removed in a waste-water treatment plant. The "clean" fluid is then returned to the bloodstream much as clean waste water is returned to a nearby river or lake. Like municipal waste-water systems, the lymphatic system not only prevents dangerous fluid buildups, or "floods," but also prevents the spread of disease.

All systems of the body benefit from the fluid-balancing and immune functions of the lymphatic system. Some parts of the body such as the digestive and respiratory tracts make special use of the defensive capacities of lymphatic organs such as aggregated lymph nodules (Peyer patches) and tonsils. Likewise, body structures such as the breasts and limbs make more use of the fluid-draining capacities of the lymphatic system than do other regions of the body. Overall, however, the entire body benefits from the fluid balance and freedom from disease conferred by the proper functioning of this important body system.

MECHANISMS of DISEASE

DISORDERS OF THE LYMPHATIC SYSTEM

Disorders Associated with Lymphatic Vessels

Lymphedema is an abnormal condition in which swelling of tissues in the extremities occurs because of an obstruction of the lymphatics and accumulation of lymph (Figure 23-22). The most common type of lymphedema is *congenital lymphedema* (lymphedema praecox), more often seen in women between the ages of 15 and 25 years. The obstruction in lymphedema can be in both the lymphatic vessels and lymph nodes themselves. Initially, the swelling, or edema, in the extremity will be soft, but as the condition progresses, it becomes firm, painful, and unresponsive to treatment. Frequent infections, involving high fever and chills, may occur with chronic lymphedema. Diuretics (agents that cause water loss) to reduce the swelling have been shown to be effective, along with strict bed rest, massage, and elevation of the involved extremities. If the edema is severe and unresponsive to these measures, or infection has occurred, or the person's mobility is severely compromised, surgical removal of the involved subcutaneous tissue and fascia may be required. Other procedures involving surgically "shunting" of superficial lymphatic drainage into the deep lymphatic system have been tried.

Lymphedema may be caused by small parasitic worms (nematodes) called **filaria** that infest the lymph vessels. This condition is rare in most of North America and is more often seen in the tropics. The flow of lymph is blocked, causing edema in the affected extremities that, in severe cases, become so swollen that they resemble an elephant's limbs (Figure 23-23). For this reason, the condition is referred to as **elephantiasis**—literally "condition of being an elephant." Chronic swelling, thickening of the subcutaneous tissue, and frequent bouts of infections are common in this condition.

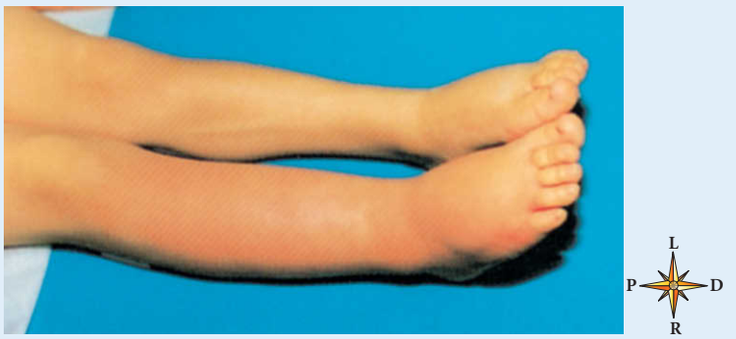


FIGURE 23-22

Lymphedema. Notice the significant swelling in the subject's right leg and foot.



FIGURE 23-23

Elephantiasis. Prolonged infestation of the lymphatic system by *Filaria* worms produces so much swelling (lymphedema) that the affected limbs begin to resemble those of an elephant!

Lymphangitis, an acute inflammation of the lymphatic vessels, stems from invasion of an infectious organism. This condition is characterized by thin, red streaks extending from an infected region up the arm or leg (Figure 23-24). The lymph nodes also become enlarged, tender, and reddened. Necrosis, or tissue death, along with development of an abscess (collection of fluid and pus) can occur, leading to a condition known as *suppurative lymphadenitis*. The lymph nodes commonly involved are in the groin, axilla, and cervical regions. The infectious agents that cause lymphangitis may eventually spread into the bloodstream, causing *septicemia* (blood poisoning) and possible death from septic shock, but this is rare if the proper antibiotic therapy is initiated.

Disorders Associated with Lymph Nodes and Other Lymphatic Organs

Tonsillitis

The tonsils, composed of lymphoid tissue, serve as the first line of defense from the exterior and also are subject to acute or chronic

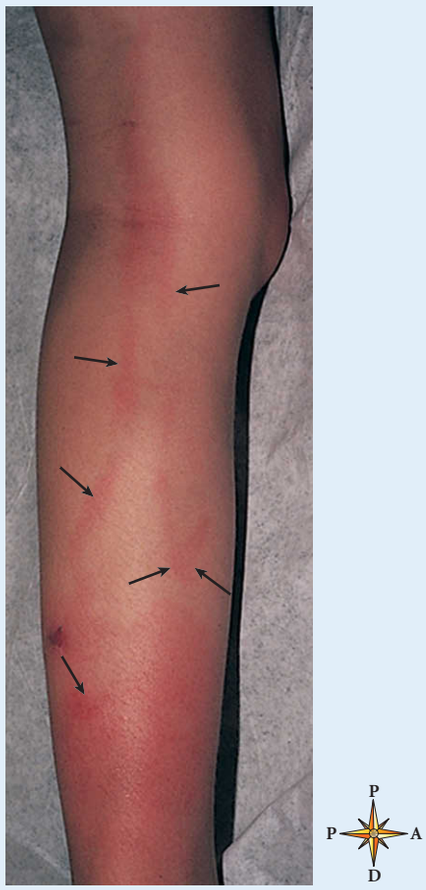


FIGURE 23-24

Lymphangitis. Red streaks mark the location of inflamed lymphatic vessels in this leg. Arrows highlight some of the red streaks.

infection, known as **tonsillitis.** Fever, sore throat, and difficulty swallowing are common signs and symptoms. Enlarged pharyngeal tonsils *(adenoids)* may cause nasal obstruction. The infection may extend to the middle ear by way of the auditory (eustachian) tubes, causing *acute otitis media* (middle ear infection) and possible deafness if left untreated. Antibiotics are usually initiated after diagnosis of tonsillitis. If these are unsuccessful, and swelling has endangered the airway and breathing, a *tonsillectomy*, or surgical removal of the tonsils, may be performed.

Lymphoma

Lymphoma is a term that refers to a tumor of the cells of lymphoid tissue. Lymphomas are often malignant but, in rare cases, can be benign. They usually originate in isolated lymph nodes but can involve lymphoid tissue in the liver, spleen, and gastrointestinal tract. Widespread involvement is common because the disease spreads from node to node through the many anastomoses of the lymphatic vessels throughout the body. The exact cause of these neoplasms is unknown.

Two principal categories of lymphomas are *Hodgkin lymphoma (HL)* and *non-Hodgkin lymphoma (NHL)*. Hodgkin lymphoma (or **Hodgkin disease**) is a malignancy with an uncertain etiology. Some pathophysiologists believe that it originates as a pathogen-induced tumor of T cells, although there is currently no evidence to support this conclusively. Other factors such as exposure to chemicals or other environmental hazards may also be involved. This condition usually begins as painless, nontender, enlarged lymph nodes in the neck or axilla (Figure 23-25). Soon, lymph nodes in other regions enlarge in the same manner. If they involve the trachea or esophagus, pressure results in difficulty breathing or swallowing. HL is considered to be one of the most curable forms of cancer if detected early.

Lymphedema caused by blockage of lymph nodes may cause enlargement of the extremities. Occasionally the disease may obstruct flow into or out of the liver, leading to liver enlargement and failure. Anemia, leukocytosis, fever, and weight loss occur as the condition progresses. Hodgkin lymphoma is potentially curable with radiation therapy, provided it has not spread beyond the lymphatic system. Chemotherapy is used in addition to radiation therapy in more advanced cases. Infection, from both the disease and the treatments, is a common complication.

Non-Hodgkin lymphoma is the name given to a malignancy of lymphoid tissue other than Hodgkin lymphoma. Again, the etiology is uncertain but has been hypothesized to be caused by a virus. Patients with immunodeficiencies such as AIDS often develop this condition. Manifestations are similar to Hodgkin lymphoma, but there is usually a more generalized involvement of lymph nodes. The central nervous system is also often involved. Radiation and chemotherapy are treatments of choice.



FIGURE 23-25

Hodgkin lymphoma. Enlarged lymph nodes in the neck or axilla characterize this condition.

LANGUAGE OF SCIENCE *(continued from p. 722)*

lacteal
(LAK-tee-al)
[*lact-* **milk**, *-al* **relating to**]

lingual tonsil
(LING-gwal TAHN-sil)
[*lingua-* **tongue**, *-al* **relating to**]

lymph
(limf)
[*lymph* **water**]

lymph node
(limf)
[*lymph* **water**, *nod-* **knot**]

lymphatic capillary
(lim-FAT-ik KAP-i-lair-ee)
[*lymph-* **water**, *-atic* **relating to**, *capill-* **hair**, *-ary* **relating to**]

lymphatic vessel
(lim-FAT-ik)
[*lymph-* **water**, *-atic* **relating to**]

lymphoid tissue
(LIM-foyd)
[*lymph-* **water**, *-oid* **like**, *tissu-* **fabric**]

lymphokinesis
(lim-foh-kih-NEE-sis)
[*lymph-* **water**, *-kinesis* **activation**]

palatine tonsil
(PAL-ah-tine TAHN-sil)
[*palat-* **palate**, *-ine* **relating to**]

pharyngeal tonsil
(fair-IN-jee-al TAHN-sil)
[*pharyng-* **throat**, *-al* **relating to**]

preauricular lymph node
(pree-ah-RIK-yoo-lar limf)
[*pre-* **before**, *-auric-* **ear**, *-ula-* **little**, *-ar* **relating to**, *lymph* **water**, *nod-* **knot**]

right lymphatic duct
(lim-FAT-ik)
[*lymph-* **water**, *-atic* **relating to**]

spleen

submandibular group
(sub-man-DIB-yoo-lar)
[*sub-* **beneath**, *-mandibul-* **chew (mandible or jawbone)**, *-ar* **relating to**]

submental group
(sub-MEN-tal)
[*sub-* **beneath**, *-ment-* **chin**, *-al* **relating to**]

superficial cervical lymph node
(soo-per-FISH-al SER-vi-kal limf)
[*super-* **over or above**, *-fici-* **face**, *-al* **relating to**, *cervic-* **neck**, *-al* **relating to**, *lymph* **water**, *nod-* **knot**]

superficial cubital lymph node
(soo-per-FISH-al KYOO-bi-tal limf)
[*super-* **over or above**, *-fici-* **face**, *-al* **relating to**, *cubit-* **elbow**, *-al* **relating to**, *lymph* **water**, *nod-* **knot**]

supratrochlear lymph node
(soo-prah-TROHK-lee-ar limf)
[*supra-* **above**, *-trochlea-* **pulley**, *-ar* **relating to**, *lymph* **water**, *nod-* **knot**]

thoracic duct
(thoh-RAS-ik)
[*thorac-* **chest (thorax)**, *-ic* **relating to**]

thymic corpuscle
(THYE-mik KOR-pus-ul)
[*thym-* **thyme flower (thymus gland)**, *-ic* **relating to**, *corpus-* **body**, *-cle* **little**]

thymus
(THY-mus)
[*thymus* **thyme flower**]
pl., thymuses

tonsil
(TAHN-sil)

LANGUAGE OF MEDICINE

elephantiasis
(el-eh-fan-TYE-ah-sis)
[*elephant-* **elephant**, *-iasis* **condition**]

filaria
(fi-LAR-ee-a)
[*fila-* **thread**, *-ar-* **like**, *-ia* **things**]
pl., filariae

Hodgkin disease
(HOJ-kin)
[*Thomas Hodgkin* **English physician**]

lymphangiography
(lim-fan-jee-OG-reh-fee)
[*lymph-* **water**, *-angi-* **vessel**, *-graph-* **draw**, *-y* **process**]

lymphangitis
(lim-fan-JYE-i-tis)
[*lymph-* **water**, *-angi-* **vessel**, *-itis* **inflammation**]

lymphedema
(lim-fah-DEE-mah)
[*lymph-* **water**, *-edema* **swelling**]

lymphoma
(lim-FOH-mah)
[*lymph-* **water**, *-oma* **tumor**]

mastitis
(mass-TYE-tis)
[*mast-* **breast**, *-itis* **inflammation**]

sentinel lymph node (SLN)
(SEN-tin-el limf nohd)
[*sentinel* **lookout**, *lymph* **water**, *nod-* **knot**]

splenectomy
(spleh-NEK-toh-mee)
[*splen-* **spleen**, *-ec-* **out**, *-tom-* **cut**, *-y* **action**]

tonsillectomy
(tahn-sih-LEK-toh-mee)
[*-ec-* **out**, *-tom-* **cut**, *-y* **action**]

tonsillitis
(tahn-sih-LYE-tis)
[*tonsil-* **tonsil**, *-itis* **inflammation**]

CASE study

Courtney, a dental hygiene student, was in Ghana with several of her classmates. Each summer, the students had an opportunity to combine study abroad with volunteering at a dental clinic in Accra. On their second day at the clinic, Courtney met Juba, a local farmer's daughter. Juba's right foot and leg below the knee were extremely swollen, seemingly blown up like a balloon. In contrast, Juba's left leg had no swelling at all and appeared quite normal. One of the local dentists told Courtney that Juba had elephantiasis, a type of lymphedema caused by a blockage.

1. With Juba's condition, what vessels are blocked?
   a. Arteries
   b. Veins
   c. Capillaries
   d. Lymphatic vessels

2. Which of the following is NOT a function of the lymphatic system?
   a. Removing excess fluid from the blood
   b. Absorbing lipids from the small intestines
   c. Returning fluid from the interstitial areas back to the bloodstream
   d. Filtering lymph to remove foreign organisms and particulates

3. What helps circulate the lymph (fluid) through the lymph vessels?
   a. Ventricular contraction
   b. Skeletal muscle contractions
   c. Exhalation
   d. Lymphatic vessel contraction

4. Before Juba's leg became affected by this disorder, the lymph would have passed first through which nodes?
   a. Cervical
   b. Axillary
   c. Inguinal
   d. Mediastinal



HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook, **A&P Connect,** and other resources.*

CHAPTER SUMMARY

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HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

OVERVIEW OF THE LYMPHATIC SYSTEM

A. Two most important functions—maintain fluid balance in the internal environment and immunity; a third function is to collect absorbed fat from the intestines and transport it to the systemic veins
B. Lymph vessels act as "drains" to collect excess tissue fluid and return it to the venous blood just before it returns to the heart (Figure 23-1)
C. Lymphatic system—component of the circulatory system; made up of lymph, lymphatic vessels, and isolated structures containing lymphoid tissue: lymph nodes, aggregated lymphoid nodules, tonsils, thymus, spleen, and bone marrow (Figure 23-2)
D. Transports tissue fluid, proteins, fats, and other substances to the general circulation
E. Lymphatic vessels begin blindly in the intercellular spaces of the soft tissues; do not form a closed circuit

LYMPH AND INTERSTITIAL FLUID

A. Lymph (lymphatic fluid)
   1. Clear, watery-appearing fluid found in the lymphatic vessels
   2. Closely resembles blood plasma in composition but has a lower percentage of protein; isotonic
   3. Elevated protein concentration in thoracic duct lymph because of protein-rich lymph from the liver and small intestine

B. Interstitial fluid (IF)
   1. Complex, organized fluid that fills the spaces between the cells and is part of the ECM (extracellular matrix)
   2. Resembles blood plasma in composition with a lower percentage of protein
   3. Along with blood plasma, constitutes the extracellular fluid

LYMPHATIC VESSELS

A. Distribution of lymphatic vessels (lymphatics) (Figures 23-2 and 23-3)
   1. Lymphatic capillaries—microscopic blind-end vessels where lymphatic vessels originate; wall consists of a single layer of flattened endothelial cells; networks branch and anastomose freely
   2. Lymphatic capillaries merge to form larger lymphatics and eventually form the main lymphatic trunks, the right lymphatic ducts, and the thoracic duct

3. Lymph from upper right quadrant empties into right lymphatic duct and then into right subclavian vein
4. Lymph from rest of the body empties into the thoracic duct, which then drains into the left subclavian vein; thoracic duct originates as the cisterna chyli (chyle cistern)

B. Structure of lymphatic vessels (Figure 23-4)
1. Similar to veins except lymphatic vessels have thinner walls, have more valves, and contain lymph nodes
2. Lymphatic capillary wall is formed by a single layer of thin, flat endothelial cells
3. As the diameter of lymphatic vessels increases from capillary size, the walls become thicker and have three layers
4. One-way valves are present every few millimeters in large lymphatics and even more frequently in smaller lymphatics

C. Functions of the lymphatic vessels
1. Remove high–molecular-weight substances and even particulate matter from interstitial spaces
2. Lacteals absorb fats and other nutrients from the small intestine

CIRCULATION OF LYMPH

A. From lymphatic capillaries, lymph flows through progressively larger lymphatic vessels to eventually reenter blood at the junction of the internal jugular and subclavian veins (Figure 23-5).

B. The lymphatic pump
1. Lymphokinesis—the movement (flow) of lymph; can be visualized in a lymphangiogram (Figure 23-6)
2. Lymph moves through the system in the right direction because of the large number of valves
3. Breathing movements and skeletal muscle contractions (Figure 23-7) establish a fluid pressure gradient, as they do with venous blood
4. Other factors, such as IF pressure, also drive lymphokinesis (Figure 23-8)
5. Lymphokinetic actions—activities that result in a central flow of lymph

LYMPH NODES

A. Structure of lymph nodes
1. Lymph nodes are oval-shaped structures enclosed by a fibrous capsule (Figure 23-9)
2. Nodes are a type of biological filter
3. Once lymph enters a node, it moves slowly through sinuses to drain into the efferent exit vessel (Figure 23-10)
4. Trabeculae extend from the covering capsule toward the center of the node
5. Cortical and medullary sinuses are lined with reticuloendothelial cells capable of phagocytosis

B. Locations of lymph nodes
1. Most lymph nodes occur in groups
2. Groups with greatest clinical importance are preauricular lymph nodes, submental and submaxillary groups, and superficial cervical, superficial cubital, axillary, iliac, and inguinal lymph nodes (Figures 23-11 through 23-13)

C. Functions of lymph nodes—perform two distinct functions
1. Defense functions
   a. Filtration
      (1) Mechanical filtration—physically stopping particles from progressing further in the body
      (2) Biological filtration—biological activity of cells destroys and removes particles
   b. Phagocytosis—reticuloendothelial cells remove microorganisms and other injurious particles from lymph and phagocytose them (biological filtration)
   c. If overwhelmed, lymph nodes can become infected or damaged (Figures 23-14 and 23-15)
2. Hematopoiesis—lymphoid tissue is the site for the final stages of maturation of some lymphocytes and monocytes

LYMPHATIC DRAINAGE OF THE BREAST

A. Clinically important because cancer cells and infections can spread along lymphatic pathways to lymph nodes and other organs of the body

B. Distribution of lymphatics in the breast (Figure 23-16)
1. Drained by two sets of lymphatic vessels
   a. Lymphatics that drain the skin over the breast with the exception of the areola and nipple
   b. Lymphatics that drain the underlying substance of the breast, as well as the skin of the areola and nipple
2. Superficial vessels converge to form a diffuse, cutaneous lymphatic plexus
3. Subareolar plexus—located under the areola surrounding the nipple; where communication between the cutaneous plexus and large lymphatics that drain the secretory tissue and ducts of the breast occurs

C. Lymph nodes associated with the breast
1. More than 85% of the lymph from the breast enters the lymph nodes of the axillary region
2. Remainder of lymph enters lymph nodes along the lateral edges of the sternum

TONSILS

A. Form a broken ring under the mucous membranes in the mouth and back of the throat—the pharyngeal lymphoid ring (Figure 23-17)
1. Palatine tonsils—located on each side of the throat
2. Pharyngeal tonsils—located near the posterior opening of the nasal cavity
3. Lingual tonsils—located near the base of the tongue
4. Tubal tonsils—located near the openings of the auditory (eustachian) tubes

B. Protect against bacteria that may invade tissues around the openings between the nasal and oral cavities; bacteria are trapped in tonsillar crypts and put in close contact with immune system cells

THYMUS

A. Location and appearance of the thymus (Figure 23-18)
   1. Primary organ of lymphatic system
   2. Single, unpaired organ located in the mediastinum, extending upward to the lower edge of the thyroid and inferiorly as far as the fourth costal cartilage
   3. Thymus is pinkish gray in childhood; with advancing age, becomes yellowish as lymphoid tissue is replaced by fat

B. Structure of the thymus
   1. Two pyramid-shaped lobes are subdivided into small lobules
   2. Each lobule is composed of a dense cellular cortex and an inner, less dense medulla
   3. Medullary tissue can be identified by presence of thymic corpuscles

C. Function of the thymus
   1. Plays vital role in immunity mechanism
   2. Source of lymphocytes before birth
   3. Shortly after birth, thymus secretes thymosin and other regulators, which enables lymphocytes to develop into T cells (Figure 23-19)

SPLEEN

A. Location of the spleen—in the left hypochondrium, directly below the diaphragm, above the left kidney and descending colon, and behind the fundus of the stomach (Figures 23-2 and 23-20)

B. Structure of the spleen (Figure 23-21)
   1. Ovoid in shape
   2. Surrounded by fibrous capsule with inward extensions that divide the organ into compartments
   3. White pulp—dense masses of developing lymphocytes
   4. Red pulp—near outer regions, made up of a network of fine reticular fibers submerged in blood that comes from nearby arterioles; made up of cords of WBCs and related cells surrounded by sinusoids

C. Functions of the spleen
   1. Defense—macrophages lining the sinusoids of the spleen remove microorganisms from the blood and phagocytose them
   2. Tissue repair—the spleen holds a reservoir of monocytes that migrate in a large mass to sites of injury to help with tissue healing and repair
   3. Hematopoiesis—monocytes and lymphocytes complete their development in the spleen
   4. Red blood cell and platelet destruction—macrophages remove worn-out RBCs and imperfect platelets and destroy them by phagocytosis; also salvage iron and globin from destroyed RBCs
   5. Blood reservoir—pulp of spleen and its sinuses store blood

CYCLE OF LIFE: LYMPHATIC SYSTEM

A. Dramatic changes throughout life

B. Organs with lymphocytes appear before birth and grow until puberty

C. Postpuberty
   1. Organs atrophy through late adulthood
      a. Shrink in size
      b. Become fatty or fibrous
   2. Spleen—develops early, remains intact

D. Overall function maintained until late adulthood
   1. Later adulthood
      a. Deficiency permits risk of infection and cancer
      b. Hypersensitivity—likelihood of autoimmune conditions

THE BIG PICTURE: THE LYMPHATIC SYSTEM AND THE WHOLE BODY

A. Lymphatic system drains away excess water from large areas

B. Lymph is conducted through lymphatic vessels to nodes, where contaminants are removed

C. Lymphatic system benefits the whole body by maintaining fluid balance and freedom from disease

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. List the anatomical components of the lymphatic system.
2. How do interstitial fluid and lymph differ from blood plasma?
3. How do lymphatic vessels originate?
4. Briefly describe the anatomy of the lymphatic capillary wall.
5. Lymph from what body areas enters the general circulation by way of the thoracic duct? By way of the right lymphatic ducts?
6. What is the cisterna chyli?
7. Where does lymph enter the blood vascular system?
8. In general, lymphatics resemble veins in structure. List three exceptions to this general rule.
9. What are the unique lymphatic vessels that originate in the villi of the small intestine called?
10. What is chyle? Where is it formed?
11. Give examples of lymphokinetic factors and explain how they contribute to the "lymphatic pump."
12. List several important groups, or clusters, of lymph nodes.
13. Explain how lymph nodes function in body defense and hematopoiesis.
14. If cancer cells from breast cancer enter the lymphatics of the breast, where are they likely to lodge and start new growths? Explain why, using your knowledge of the anatomy of the lymphatic and circulatory systems.
15. Locate the thymus, and describe its appearance and size at birth, at maturity, and in old age.
16. Explain the function of the thymus.
17. Describe the location and functions of the spleen.

18. What happens when there is a loss of lymphatic fluid?
19. Explain why lymphedema may occur after breast surgery.

CRITICAL THINKING QUESTIONS

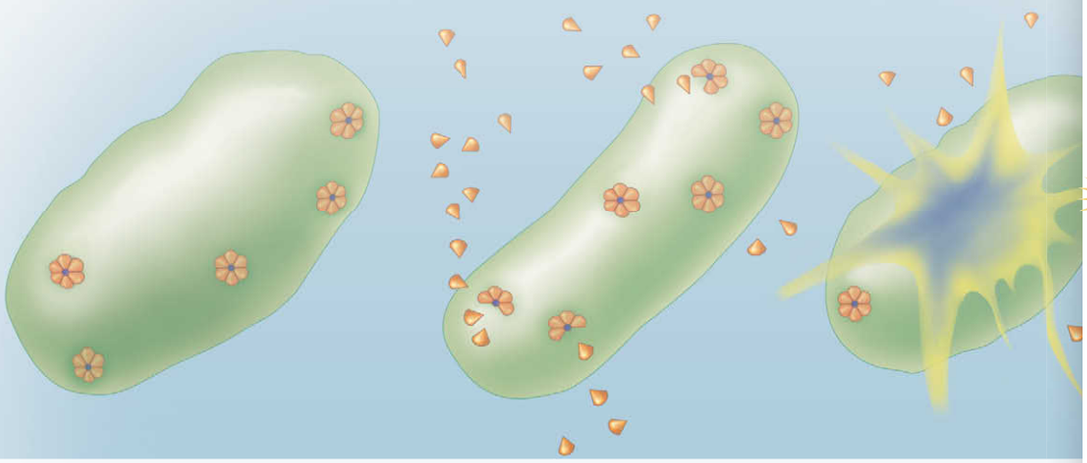


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Even though the lymphatic system is a component of the circulatory system, why is the term *circulation* not the most appropriate term to describe the flow of lymph?
2. Explain how lymph is formed. What would be the impact on lymph formation if the osmotic force at the venous end of the capillary was more successful at recovering fluid lost at the arterial end?
3. Discuss the importance of valves in the lymphatic system.
4. Explain the role of the lymphatic system in the spread of breast cancer and its surgical treatment.

Immune System

24



CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

Organization of the Immune System, 746

Innate Immunity, 748
- Species Resistance, 748
- Mechanical and Chemical Barriers, 748
- Inflammation and Fever, 749
  - The Inflammatory Response, 749
  - Fever, 750
- Phagocytosis, 752
- Natural Killer Cells, 753
- Interferon, 754
- Complement, 755
- Toll-like Receptors, 755

Overview of Adaptive Immunity, 756

B Cells and Antibody-Mediated Immunity, 758
- Development and Activation of B Cells, 758
- Antibodies (Immunoglobulins), 758
  - Structure of Antibody Molecules, 758
  - Diversity of Antibodies, 759
  - Classes of Antibodies, 759
  - Functions of Antibodies, 759
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T Cells and Cell-Mediated Immunity, 764
- Development of T Cells, 764
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Types of Adaptive Immunity, 768

Summary of Adaptive Immunity, 769

The Big Picture: Immune System and the Whole Body, 772

Mechanisms of Disease, 772

Case Study, 777

LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

adaptive immunity
(ah-DAP-tiv i-MYOO-ni-tee)
[*adapt-* **adjust**, *-ive* **relating to**, *immun-* **free**, *-ity* **state**]

antibody
(AN-ti-bod-ee)
[*anti-* **against**]

antibody-mediated immunity
(AN-ti-bo-dee-MEE-dee-ayt-ed i-MYOO-nih-tee)
[*anti-* **against**, *medi-* **middle**, *-ate* **process**, *immun-* **free**, *-ity* **state**]

antigen
(AN-ti-jen)
[*anti-* **against**, *-gen* **produce**]

antigen-antibody complex
(AN-ti-jen-AN-ti-bod-ee KOM-pleks)
[*anti-* **against**, *-gen* **produce**, *anti-* **against**, *body, complex* **embrace**]

antigenic determinant
(AN-ti-jen-ik dih-TUR-mah-nant)
[*anti-* **against**, *-gen* **produce**, *-ic* **relating to**, *determin-* **limit**, *-ant* **agent of**]

antigen-presenting cell (APC)
(AN-ti-jen)
[*anti-* **against**, *-gen* **produce**, **presenting**, *cell* **storeroom**]

autoimmunity
(aw-toh-i-MYOO-ni-tee)
[*auto-* **self**, *-immun-* **free**, *-ity* **state**]

B cell
[*B* **bursa-equivalent tissue**, *cell* **storeroom**]

cell-mediated immunity
(sell-MEE-dee-ayt-ed i-MYOO-nih-tee)
[*cell* **storeroom**, *medi-* **middle**, *-ate* **process**, *immun-* **free**, *-ity* **state**]

continued on p. 776

Enemies of many kinds and in great numbers assault the body during a lifetime. Among the most threatening are hordes of microorganisms. We live our lives in a virtual sea of protozoa, fungi, bacteria, viruses, and other pathogens. So ever-present and potentially lethal are these small but formidable foes that no newborn could live through infancy, much less survive to adulthood or old age, without effective defenses against them. We also are threatened by enemies from within. Inside the body, abnormal cells appear on an irregular but continual basis. If allowed to survive, these abnormal cells reproduce and form a tumor. At the very least, a tumor alone can damage surrounding tissues and can be life threatening as it continues to enlarge, and there is always the possibility that a tumor could become cancerous and spread (metastasize) to many other locations within the body. Without an internal "security force" to deal with such abnormal cells when they first appear, we would live very short lives. This chapter presents a brief overview of the system that provides defenses against both external and internal enemies—the immune system.

ORGANIZATION OF THE IMMUNE SYSTEM

Like any security force, the components and mechanisms of the immune system are organized in an efficient—almost military-like—manner. They are not just ready on a moment's notice; they are *continually* patrolling the body for foreign or internal enemies and shoring up the various lines of defense to fend off a possible attack. Before we begin studying the specifics of immunity, we will spend a moment mapping out the overall defensive strategy of the immune system.

First, it is important to recognize that cells, viruses, and other particles have unique molecules and groups of molecules on their surfaces that can be used to identify them. These molecular markers visible to the immune system are called **antigens.** This is similar to military operations in which enemy aircraft, vehicles, or soldiers can be identified by their distinctive insignia that are different from the insignia seen on "our side." Likewise, our own cells have unique cell markers embedded in our plasma membranes that identify each of our cells as **self**—that is, belonging to us as an individual. And foreign cells or particles have **nonself** molecules that serve as recognition markers for our immune system. The ability of our immune system to attack abnormal or foreign cells but spare our own normal cells is called **self-tolerance.**

In human society, any good security force employs numerous and varied strategies to guard its territory and take action if necessary. So, too, does the body's "society of cells" employ a system that uses many different kinds of mechanisms to ensure the integrity and survival of the internal environment. All of these defense mechanisms can be categorized into one of two major categories of immune mechanisms: **innate immunity** and **adaptive immunity.**

Innate immunity is called such because it is "in place" before a person is exposed to a particular harmful particle or condition. The word *innate* refers to something that is already present naturally at birth. Because it includes mechanisms that resist a wide variety of threatening agents or conditions, innate immunity is also called **nonspecific immunity.** The term *nonspecific* implies that these immune mechanisms do not act on only one or two specific invaders but rather provide a more general defense by simply acting against a wide variety of particles recognized as *nonself.*

Adaptive immunity, on the other hand, involves mechanisms that recognize *specific* threatening agents and then *adapt,* or respond, by targeting their activity against these agents—and these agents only. Because it targets only specific harmful particles, adaptive immunity is also called **specific immunity.** Adaptive immune mechanisms often take some time to recognize their targets and react with sufficient force to overcome the threat, at least on their first exposure to a specific kind of threatening agent. Innate mechanisms, because they are already in place, have the advantage of being able to meet an enemy as soon as it presents itself. As we discuss examples of each major type of immunity, you will come to understand how each type works and appreciate the distinction between them. You will also come to appreciate the value in having two complementary strategies for defending the body.

As in any body system, the work of the immune system is done by cells or substances made by cells. The primary types of cells involved in innate immunity are these: epithelial barrier cells, phagocytic cells (neutrophils, macrophages), and aptly named *natural killer (NK) cells.* The primary types of cells involved in adaptive immunity are two types of lymphocytes called *T cells* and *B cells.*

Cytokines, which are chemicals released from cells to trigger or regulate innate and adaptive immune responses, also participate in innate immunity. Examples of cytokines include *interleukins (ILs), leukotrienes,* and *interferons (IFNs)*—all of which are described later in this chapter. Other chemicals, in addition to cytokines, play a regulatory role in immunity—these include *complements,* other enzymes, and the amine *histamine.*

Awesome indeed is the army of cells and molecules that make up the immune system. Over one trillion lymphocytes, for example, and 100 million trillion (10^{20}) plasma protein molecules (antibodies) are a few of the many agents that help your body resist damage and disease. Figure 24-1 and Table 24-1 summarize some of the essential characteristics of innate and adaptive immunity that we discuss in this chapter.

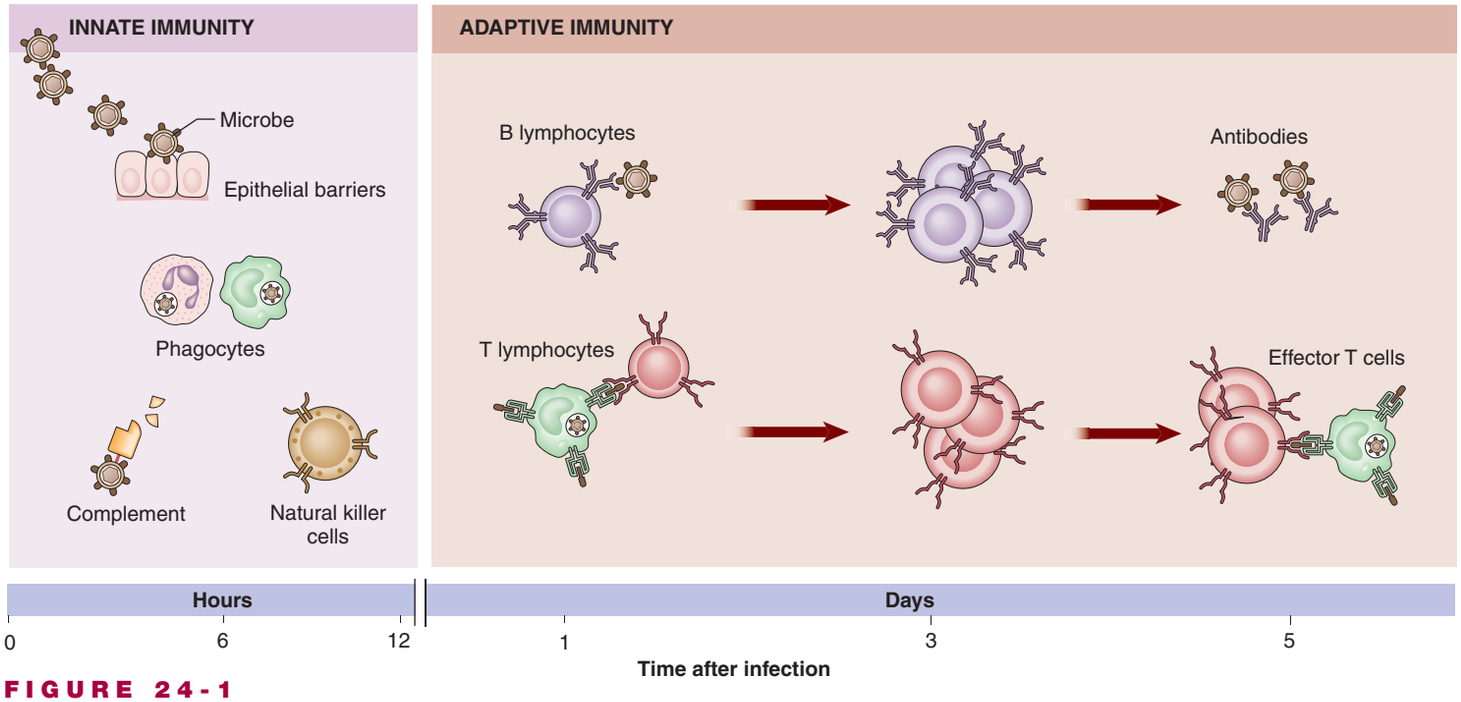


FIGURE 24-1

Innate and adaptive immunity. Innate (nonspecific) immune mechanisms are "built in" and ready for action—thus providing the initial defense against infections and other assaults on the body. Adaptive (specific) immune mechanisms develop later, as lymphocytes are activated to work against specific foreign or abnormal cells and particles. The timeframes are generalizations.

TABLE 24-1 Innate and Adaptive Immunity

		INNATE IMMUNITY	ADAPTIVE IMMUNITY
Synonyms	Frequently used alternate terminology	Nonspecific immunity, native immunity, genetic immunity	Specific immunity, acquired immunity
Characteristics			
Specificity	Unique antigens produce unique responses of the immune system	Not specific—recognizes variety of different groups of foreign cells or particles	Specific—recognizes specific antigens on specific cells or particles
Speed of reaction	Reaction time of the immune responses	Rapid: immediate up to several hours	Slower: several hours to several days
Memory	Enhanced responses to repeated exposures to the same antigen	None	Yes
Does not react to self	Prevents injury to the individual's own cells*	Yes	Yes
Components			
Barriers	Prevent entry of harmful particles	Skin, mucosa, antimicrobial chemicals	Lymphocytes in epithelia; antibodies released at epithelial surfaces
Blood proteins	Circulate throughout body, providing wide area of protection	Complement, interferon (IFN), others	Antibodies
Cells	Types of leukocytes involved in immunity	Phagocytes (macrophages, neutrophils), natural killer (NK) cells	Lymphocytes (B cells and T cells)

*Assumes healthy function. Anti-self immunity (autoimmunity) is a characteristic of many disorders.

| QUICK CHECK |

1. What is the difference between *self* and *nonself?*
2. What is the difference between *adaptive* and *innate* immunity?
3. What is a *cytokine?* What are some examples of cytokines?

INNATE IMMUNITY

The general, innate defensive mechanisms of the body are many and varied (Table 24-2). Only the major types of innate immune mechanisms are listed here; many other examples appear in other chapters throughout this book. You will probably recognize examples in this chapter that you have encountered already in previous chapters. Phagocytes are a good example. They are often referred to by different names when identified in specific body areas. For example, phagocytic cells in the skin were identified as *dendritic cells (DCs)* of the epidermis (Langerhans cells; Chapter 7, p. 173).

Species Resistance

Species resistance refers to a phenomenon in which the genetic characteristics common to a particular kind of organism, or *species*, provide defense against certain *pathogens* (disease-causing agents). The human species *(Homo sapiens)*, for example, is resistant to many life-threatening infections and infestations that often spread easily among plants and other animals. For example, humans do not have to worry about getting Dutch elm disease, a fungal infection that nearly eradicated the American elm tree, or becoming infected with canine viral distemper, a virus to which young dogs are susceptible. Usually, species resistance in humans results from the fact that our internal environment is not suitable for certain pathogens. We may also have resistance because a particular microbe may not be biochemically compatible with the various molecules on our cell membranes that the microbes would need to gain entry into a host cell.

Mechanical and Chemical Barriers

The internal environment of the human body is protected by a continuous mechanical barrier formed by the cutaneous membrane (skin) and mucous membranes (see Figure 6-39, p. 155).

TABLE 24-2 Mechanisms of Innate Defense

MECHANISM	DESCRIPTION
Species Resistance	Genetic characteristics of the human species protect the body from certain pathogens
Mechanical and Chemical Barriers	Physical impediments to the entry of foreign cells or substances
Skin and mucosa	Forms a continuous wall that separates the internal environment from the external environment, preventing the entry of pathogens
Secretions	Secretions such as sebum, mucus, acids, and enzymes chemically inhibit the activity of pathogens
Inflammation	The inflammatory response isolates the pathogens and stimulates the speedy arrival of large numbers of immune cells
Fever	Fever may enhance immune reactions and inhibit pathogens
Phagocytosis	Ingestion and destruction of pathogens by phagocytic cells
Neutrophils	Granular leukocytes that are usually the first phagocytic cell to arrive at the scene of an inflammatory response
Macrophages	Monocytes that have enlarged to become giant phagocytic cells capable of consuming many pathogens; often called by other, more specific names when found in specific tissues of the body
Natural Killer (NK) Cells	Group of lymphocytes that kill many different types of cancer cells and virus-infected cells
Interferon	Protein produced by cells after they become infected by a virus; inhibits the spread or further development of a viral infection
Complement	Group of plasma proteins (inactive enzymes) that produce a cascade of chemical reactions that ultimately causes lysis (rupture) of a foreign cell; the complement cascade can be triggered by adaptive or innate immune mechanisms
Toll-like Receptors (TLRs)	Membrane receptors that recognize nonspecific patterns in microbial molecules (not human molecules) and trigger a variety of innate immune responses (many of those listed in this table)

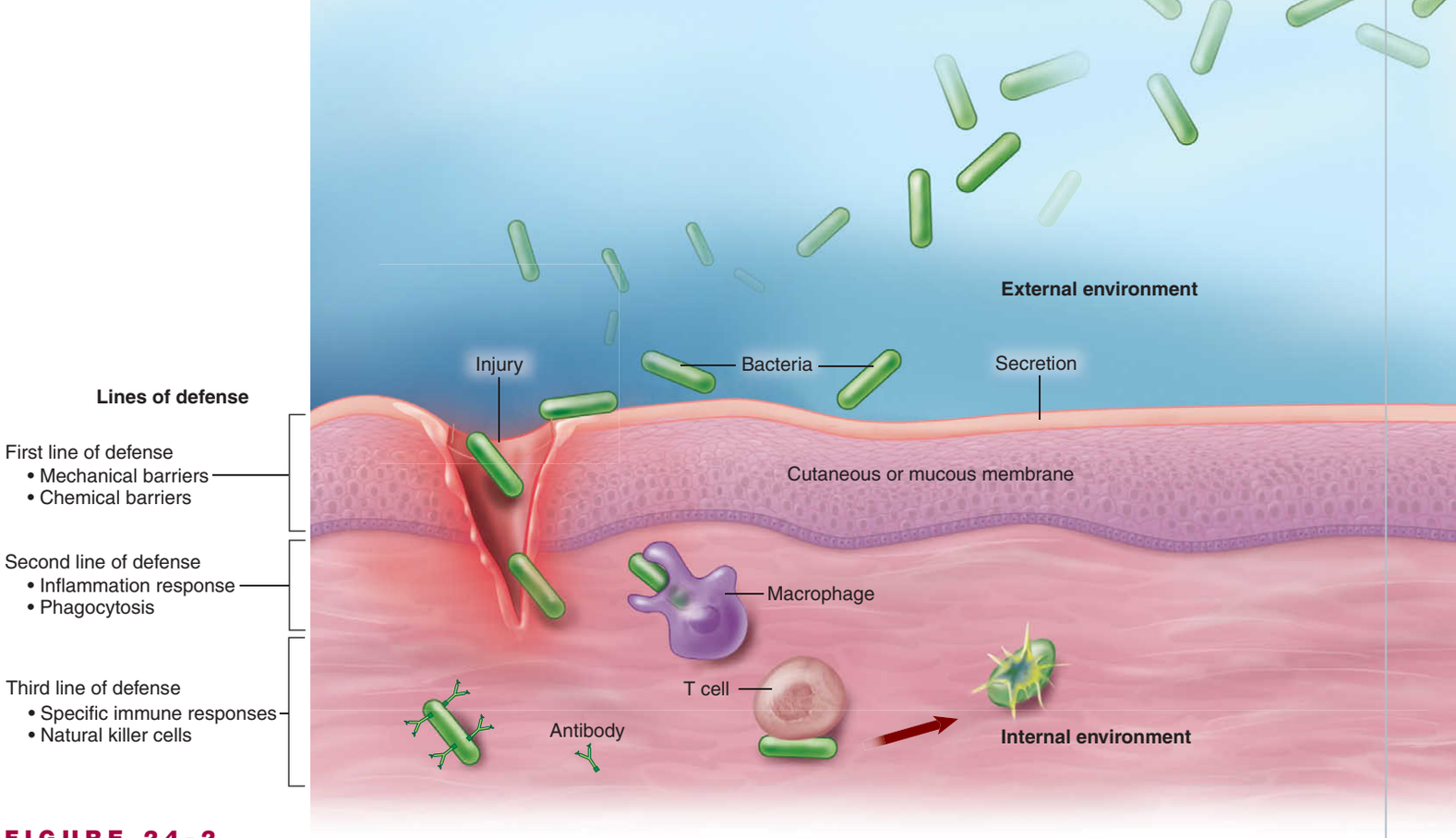


FIGURE 24-2

Lines of defense. Immune function, that is, defense of the internal environment against foreign cells, proteins, and viruses, includes three layers of protection. The first line of defense is a set of barriers between the internal and external environments, the second involves the innate inflammatory response (including phagocytosis), and the third includes the adaptive immune responses and the innate defense offered by natural killer cells. Of course, tumor cells that arise within the body are not affected by the first two lines of defense and must be attacked by the third line of defense. This diagram is a simplification of the complex function of the immune system; in reality, a great deal of crossover of mechanisms occurs between these "lines of defense."

Often called the *first line of defense*, these membranes provide several layers of densely packed cells and other materials—forming a sort of "castle wall"—that protects the internal environment from invasion by foreign cells (Figure 24-2).

Besides forming a protective wall, the skin and mucous membranes operate various additional immune mechanisms. For example, substances such as *sebum* (which contains pathogen-inhibiting agents), *mucus* (in which pathogens become stuck and are then swept away), enzymes (which may hydrolyze pathogens), and hydrochloric acid in gastric mucosa (which may destroy pathogens) also may be present to act as innate defense mechanisms. These chemical barriers act as a sort of moat around the castle wall formed by the membranes.

The epithelial barriers of the body are essentially innate, nonspecific defenses. However, the protective epithelial membranes also have adaptive (specific) defenses that reinforce them. The combined innate and adaptive immune functions of protective mucous membranes are discussed later in the chapter in a separate boxed essay (see Box 24-8 on p. 771).

Inflammation and Fever

THE INFLAMMATORY RESPONSE

If bacteria or other invaders break through the chemical and mechanical barriers formed by the membranes and their secretions, the body has a *second line of defense* at the ready: the inflammatory response (see Figure 24-2). The **inflammatory response** has already been discussed in some detail in Chapter 6 (see Box 6-3 on p. 146 and ***A&P Connect: Inflammation*** online). For the purpose of a quick review, recall that tissue damage elicits a host of responses that counteract the injury and promote a return to normal. An example of how local inflammation works is illustrated

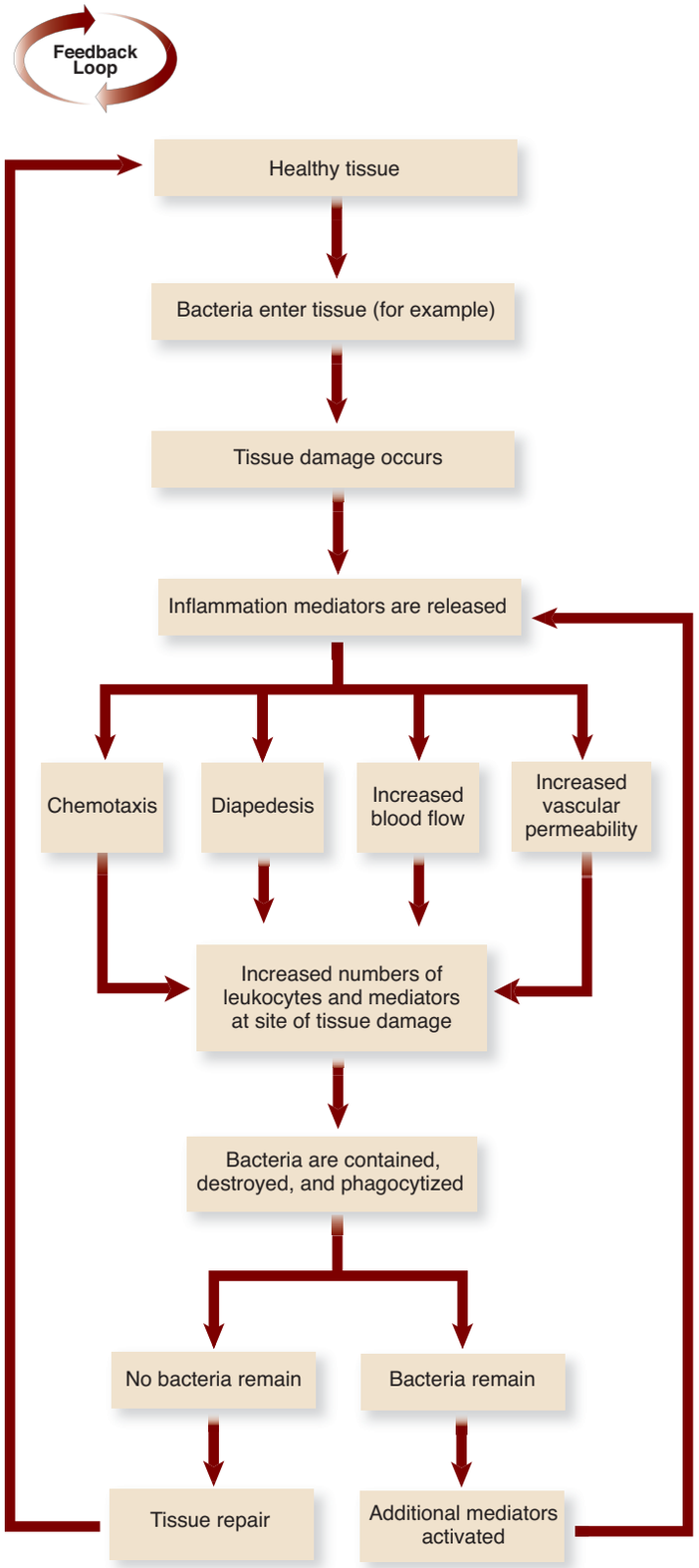


FIGURE 24-3

Example of the inflammatory response. Tissue damage caused by bacteria triggers a series of events that produces the inflammatory response and promotes phagocytosis at the site of injury. These responses tend to inhibit or destroy the bacteria, eventually bringing the tissue back to its healthy state. Similar reactions will occur in the presence of other abnormal or injurious particles or conditions.

in Figure 24-3. In the example, bacteria cause tissue damage that, in turn, triggers the release of various inflammation mediators from cells such as the *mast cells* found in connective tissues (Figure 24-4). These inflammation mediators include *histamine*, *kinins*, *prostaglandins*, *leukotrienes*, *interleukins (ILs)*, and related compounds. Many of these mediators are chemotactic factors, that is, substances that attract white blood cells to the area in a process called **chemotaxis.** As Figure 24-5 shows, chemotaxis is the process by which a cell navigates toward the source of the **chemotactic factor** *(chemotaxin)* by way of detecting and then moving toward higher concentrations of the factor.

Additionally, many of the factors released from tissue cells and phagocytes, such as the peptide fragment called *C5a* from complement, produce the mechanisms that cause characteristic signs of inflammation: heat, redness, pain, and swelling (Figure 24-6). These signs result from increased blood flow and vascular permeability in the affected region, which help phagocytic white blood cells reach the general area and then enter the affected tissue. Also, some inflammation mediators trigger fibroblasts to grow and produce more collagen fibers to promote repair and regeneration.

| A&P CONNECT |

Inflammation is an important defensive reaction in the body's tissues. Check out ***Inflammation*** online at ***A&P Connect*** for a brief review of the inflammatory response and its effects on the tissues of your body.

evolve

FEVER

Besides local inflammation, systemic inflammation may occur when the inflammation mediators trigger responses that occur on a body-wide basis. A body-wide inflammatory response may be manifested by a **fever**—a state of abnormally high body temperature. For example, bacterial infections that spread widely throughout the body may produce *systemic inflammatory response syndrome (SIRS)*. SIRS involves an abnormally high neutrophil (phagocytic white blood cell [WBC]) count and fever. Viral infections, tumors, allergies, and other abnormal conditions also can cause fevers.

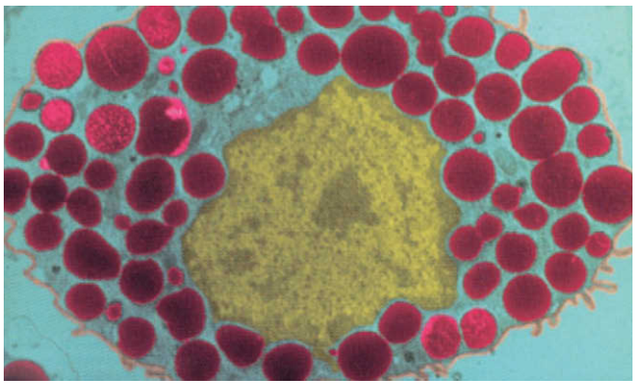


FIGURE 24-4

Mast cell. This colorized micrograph shows a mast cell filled with dense red granules of the inflammation mediator called *histamine.*

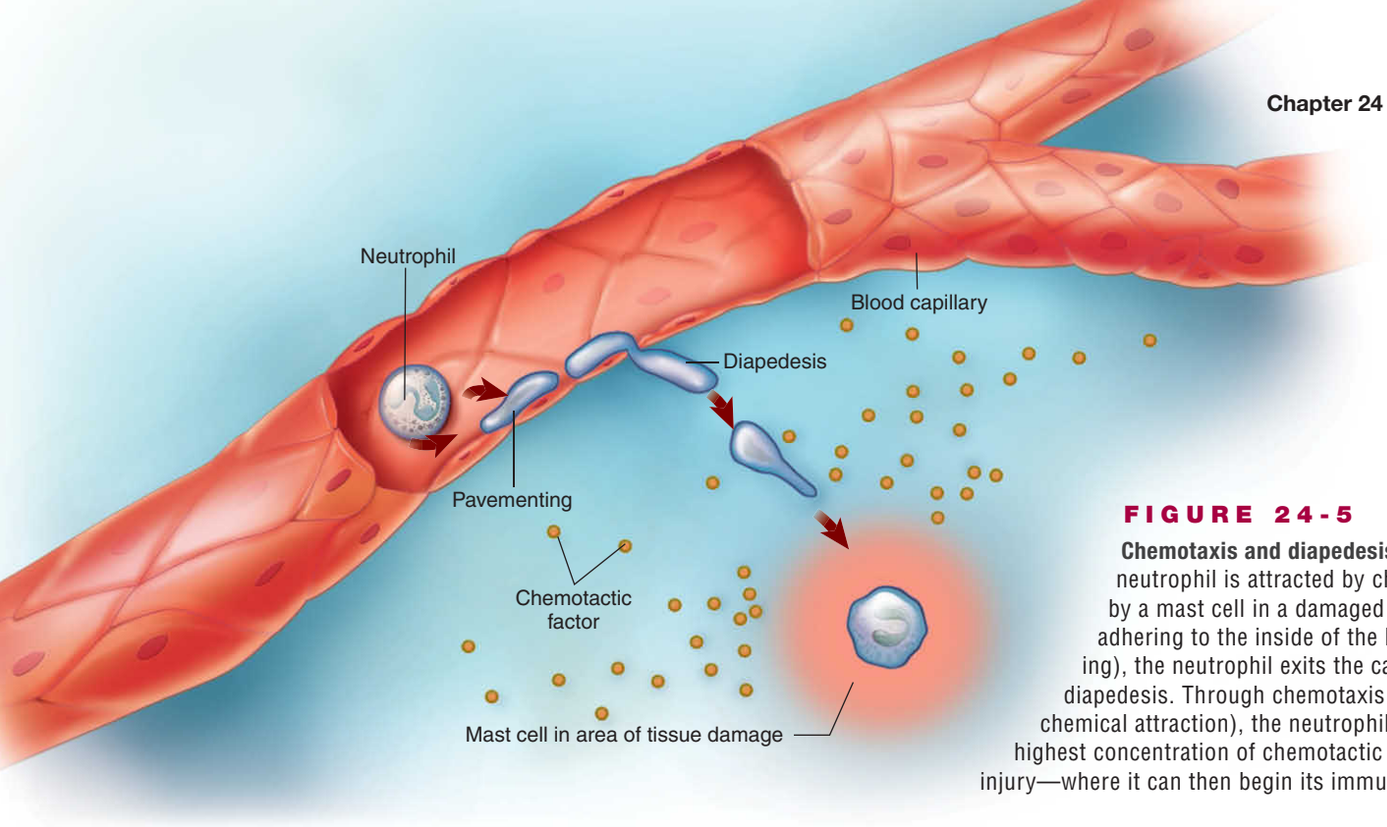


FIGURE 24-5

Chemotaxis and diapedesis. In this example, a neutrophil is attracted by chemotactic agents released by a mast cell in a damaged or infected tissue. After adhering to the inside of the blood capillary (pavementing), the neutrophil exits the capillary by the process of diapedesis. Through chemotaxis (movement directed by chemical attraction), the neutrophil migrates toward the highest concentration of chemotactic factor—the site of the injury—where it can then begin its immune functions.

Recall from Box 1-2 on p. 21 that fevers result from a "reset" of the body's thermostat in the hypothalamus, which temporarily increases the set point or target temperature to a higher-than-normal value. The body then shivers or we cover ourselves and otherwise seek heat until the new set point temperature—a fever—is reached.

As we have already learned in earlier chapters, *pyrogen* molecules trigger the fever response by promoting production of prostaglandins (PGs), which then reset the body's thermostat in the hypothalamus. Aspirin and other cyclooxygenase (COX) inhibitors reduce the activity of the COX enzymes (COX-1 and COX-2) that produces these prostaglandins—thus having a fever-reducing effect (see Figure 18-13 on p. 557). Pyrogens can be released from damaged cells (endogenous pyrogens) or could be introduced from outside the body (exogenous pyrogens).

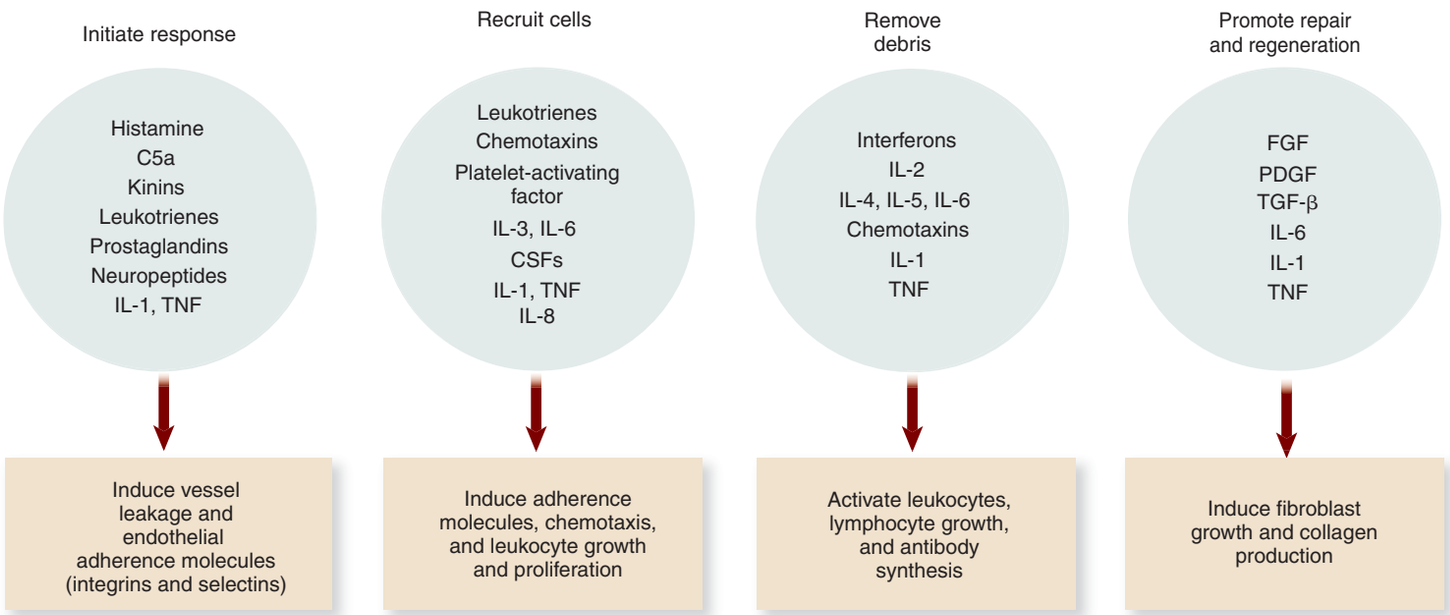


FIGURE 24-6

Inflammation mediators. A wide variety of chemical mediators help regulate the immune response, as this generalized chart shows. Some of the processes shown overlap in time and are thus sometimes concurrent.

The elevated temperature of a fever may facilitate some immune reactions and may also inhibit the reproduction of some microbial pathogens. However, immunologists still debate the role of fever in protecting the body.

Phagocytosis

A major component of the body's second line of defense is the mechanism of **phagocytosis**—the ingestion and destruction of microorganisms or other small particles. There are many types of *phagocytes*, that is, cells capable of phagocytosis, in the body. As Figure 24-7 shows, when phagocytes approach a microorganism, they extend footlike projections (pseudopods) toward it. Soon the pseudopods encircle the organism and form a complete sac, called a *phagosome*, around it. The phagosome then moves into the interior of the cell, where a lysosome fuses with it. The contents of the lysosome, chiefly digestive enzymes and hydrogen peroxide, drain into the phagosome and destroy the microorganisms within it.

Because phagocytosis defends us against various kinds of agents, it is classified as an *innate defense*. However, phagocytes also "cross over" to play an important role in adaptive immunity as well. After digesting the offending particle, a phagocyte will often process the proteins and display bits of the protein—peptides—on the surface of the phagocyte. These peptides are then recognized by cells of the adaptive immune system as antigens, thus possibly triggering an adaptive immune response. Cells that perform this function are called *antigen-presenting cells (APCs)*.

You learned in Chapter 20 that the most numerous type of phagocyte is the *neutrophil*, a granular, neutral-staining type of WBC. After being released at a site of inflammation or tissue damage, chemotactic factors diffuse into adjoining capillaries. Once in the bloodstream, they cause neutrophils and other phagocytes to adhere to the vessel's endothelial lining in a process called **pavementing** (see Figure 24-5). Numbers of these adherent phagocytes pass between the endothelial cells that form the capillary wall, dissolve the underlying basement membrane, and then exit through the vessel wall in the inflamed area. The movement of phagocytes from blood vessel to inflammation site is called **diapedesis.** Phagocytes have a very short life span, and thus dead cells tend to "pile up" at the inflammation site—forming most of the white substance called **pus.**

Another common type of phagocyte is the **macrophage** (meaning "large eater"). Macrophages are phagocytic monocytes (nongranular WBCs) that have grown to several times their original size after migrating out of the bloodstream. Macrophages are important APCs.

Yet another important type of phagocyte is the **dendritic cell (DC)** found in many tissues of the body that are in contact with the external environment, such as the skin and mucous membranes (Figure 24-8). This type of phagocytic APC is called *dendritic* because of its many branches (*dendr-* branch). Dendritic cells are also sometimes called *stellate* ("star shaped") *cells*.

Phagocytic APCs of various types are present in many areas of the body, even on the outside surface of some mucous membranes (e.g., in the respiratory tract). Phagocyte types are often known by

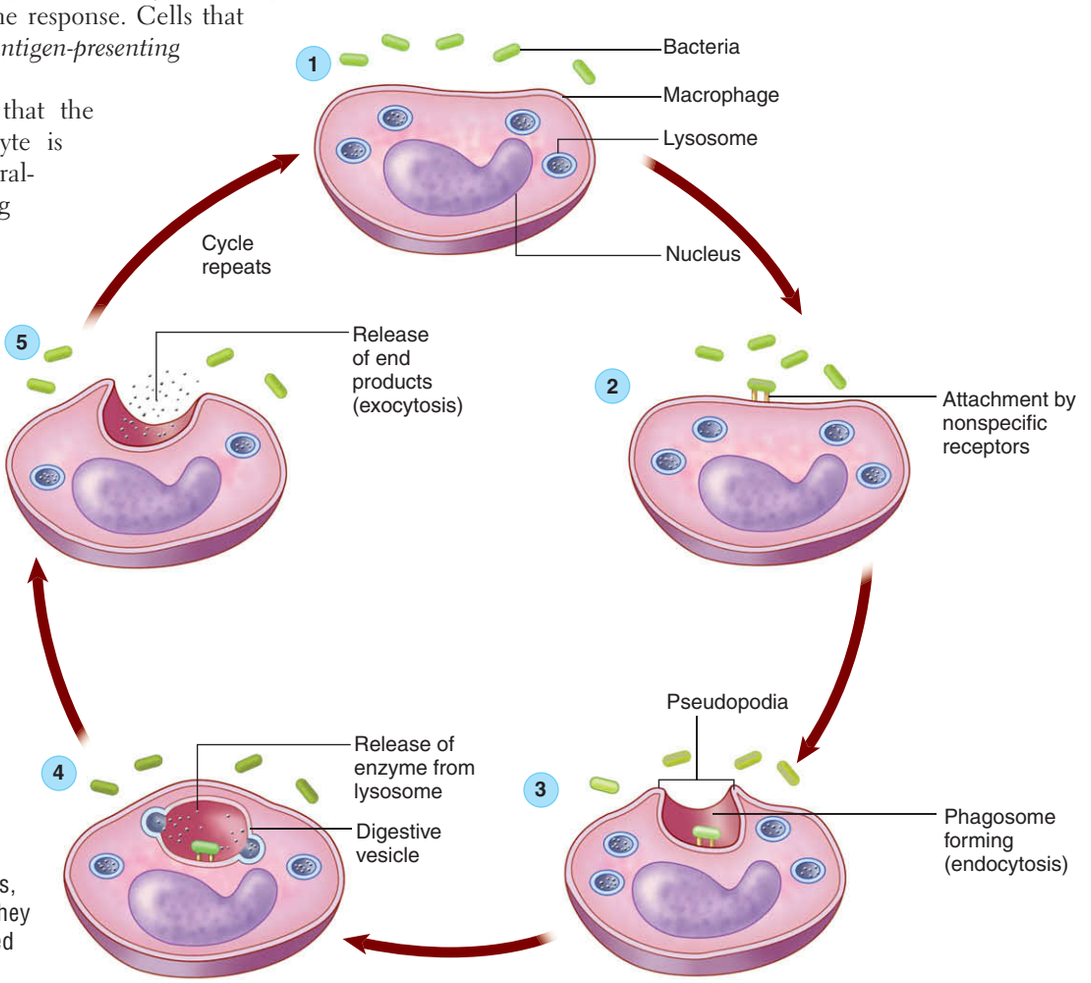


FIGURE 24-7

Phagocytosis of bacteria. Drawing shows sequence of steps in phagocytosis of bacteria. The plasma membrane extends (as a pseudopod) toward the bacterial cells, then envelops them. Once trapped, they are engulfed by the cell and destroyed by lysosomal enzymes.

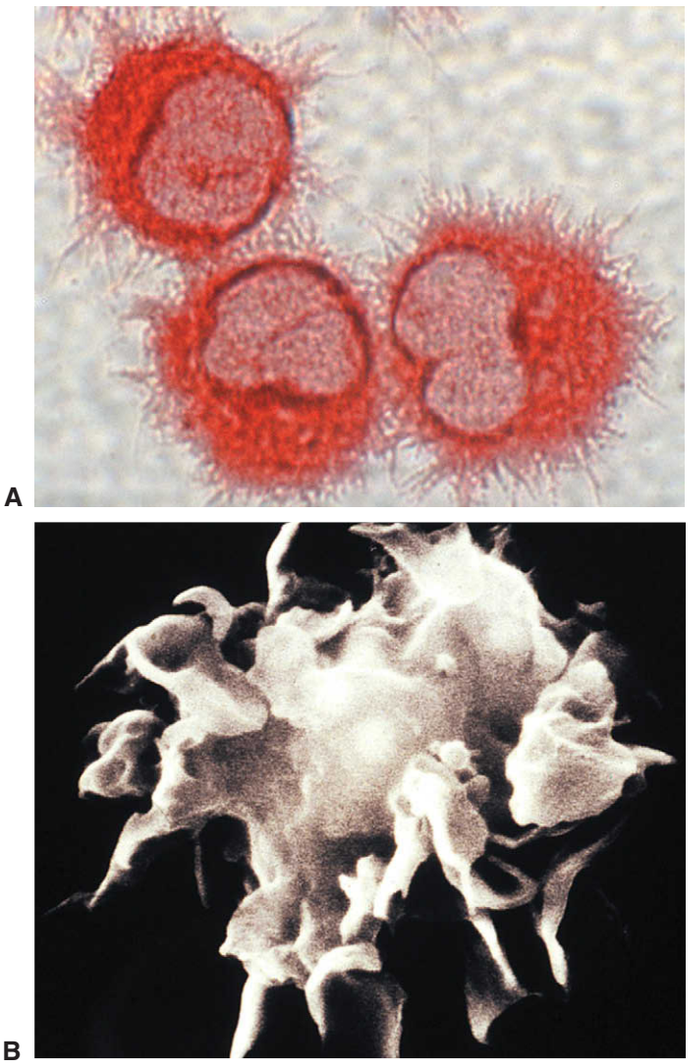


FIGURE 24-8

Dendritic cells (DCs). DCs, also called *stellate (star-shaped) cells,* are phagocytic antigen-presenting cells (APCs) that are found in many areas of the body. **A,** Light micrograph of DCs from the bone marrow. **B,** Scanning electron micrograph showing the detail of projections of the plasma membrane in DCs (see also Figure 24-15).

specific names that designate their location (Table 24-3). The importance of phagocytes to our overall defense of the body is made clear by the fact that 10% to 15% (by number) of all cells in any organ of the body are phagocytic cells!

Natural Killer Cells

Besides phagocytes, the body has another important set of cells that provides innate defense of the body. These are the **natural killer (NK) cells.** NK cells are a group of lymphocytes that kill many types of tumor cells and cells infected by different kinds of viruses. As a group they are produced in the red bone marrow and constitute about 15% of the total lymphocyte cell numbers. NK cells are neither T cells nor B cells, as described later under the topic of adaptive immunity. Because they have such a broad action and do not have to be activated by a specific foreign antigen to become active, they are usually included among the innate immune strategies.

TABLE 24-3 Examples of Phagocyte Locations

PHAGOCYTES	LOCATION
Circulating phagocytes	Bloodstream
Osteoclasts; bone marrow (fixed) phagocytes	Bone and bone marrow
Microglia	Central nervous system
Histiocytes	Connective tissues
Epidermal dendritic cells	Epidermis
Kupffer cells	Liver
Alveolar macrophages (dust cells); dendritic cells	Lung
Fixed and free lymphoid macrophages; dendritic cells	Lymph nodes
Pleural macrophages; peritoneal macrophages	Serous fluids
Splenic macrophages	Spleen

NK cells recognize abnormal cells by using two different recognition receptors: a killer-activating receptor and a killer-inhibiting receptor (Figure 24-9). The killer-activating receptor binds to any

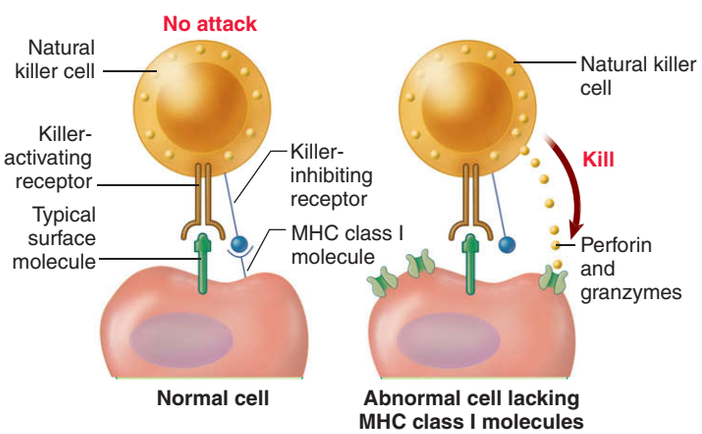


FIGURE 24-9

Natural killer (NK) cells. NK cells are a type of lymphocyte distinct from B cells and T cells. NK cells have killer-activating receptors that recognize any of several molecules commonly found in plasma membranes. NK cells also have killer-inhibiting receptors that recognize major histocompatibility complex (MHC) class I surface molecules, which act as "self" markers (see Box 24-1 on p. 754). If both the NK receptors bind, as they would in a normal cell with the proper MHC class I surface molecule, then the killing action of the cell is inhibited and the target cell remains alive. However, if the MHC class I marker is absent—as would happen with a foreign cell or a virus-infected cell—then the killer-inhibiting receptor has nothing to bind. Thus the killing action of the NK cell is not inhibited and the target cell is destroyed by chemicals released from the NK cell.

of several common surface molecules found in cells. Thus the NK cell can bind to any cell of the body as well as any foreign cells. However, if the killer-inhibiting receptor happens to bind to an MHC (major histocompatibility complex) protein also, then the killing action is stopped. Box 24-1 explains that MHCs are surface proteins on all normal cells and are unique to each individual person. Thus only abnormal and foreign cells fail to bind to the killer-inhibitor centers—and therefore are killed by the NK cell.

The NK cells use several different methods for killing cells, most of which involve chemically triggering apoptosis (programmed

Box 24-1 | FYI

Major Histocompatibility Complex

The **major histocompatibility complex (MHC)** is a set of genes in chromosome 6 that all code for antigen-presenting proteins and other immune system proteins (part *A* of figure). Antigens are proteins that potentially trigger a specific immune response. The MHC proteins produced by MHC genes in class I and class II also are called *human leukocyte antigens (HLAs).* Their function is to present different protein fragments (peptides) at the surface of the cell for possible recognition as either self or nonself antigens by immune system cells.

The MHC class I proteins, or HLAs, are present in every nucleated cell of the body. Their function is to present protein fragments from within the cell at the surface as antigens. An immune cell will then recognize the presented antigen as a *self-antigen* or as a *nonself-antigen* (part *B* of figure). Self-antigens are normally ignored by the immune cell. Nonself-antigens are instead recognized as abnormal and attacked by the mechanisms described later in this chapter. If a normal cell becomes infected with a virus or becomes cancerous, it may present some abnormal antigens on the surface and thus be identified by the immune system.

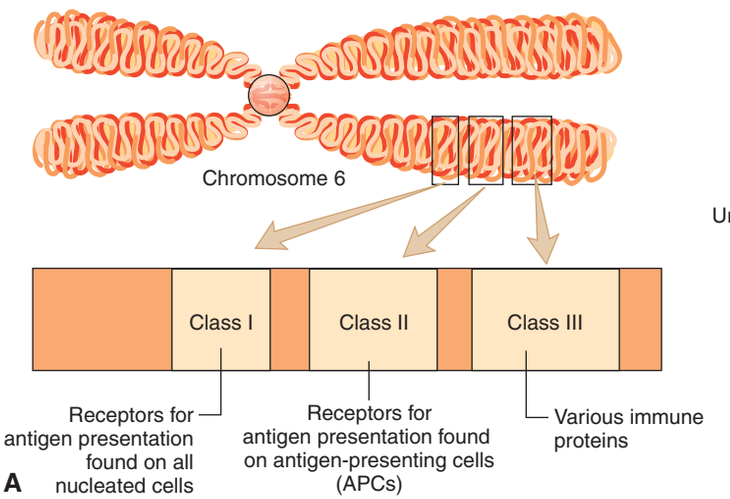
MHC class I proteins are also involved in the mechanism by which natural killer (NK) cells recognize abnormal cells. As Figure 24-9 shows, the absence of MHC class I proteins fails to inhibit the killing action of the NK cell. Cells from outside the body are likely to have no MHC class I proteins or have a different version of the MHC class I proteins. Infected or damaged cells are also likely to have missing or damaged MHC class I surface proteins.

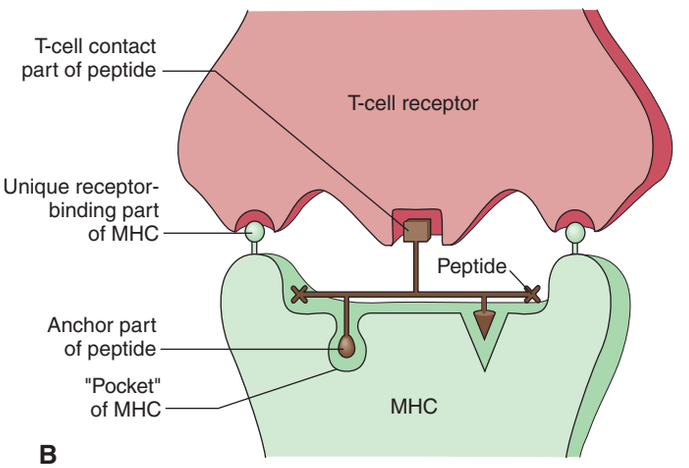
MHC class II proteins are expressed in immune cells that specialize in presenting antigens. These "professional" **antigen-presenting cells (APCs)** include macrophages, dendritic cells (DCs), and B cells, for example. The APCs use their MHC class II proteins to present fragments of proteins that they've brought in from outside the cell—perhaps from a bacterial cell. Thus they alert the immune system to the presence of these invaders and trigger certain adaptive (specific) immune responses.

MHC class III proteins include a wide variety of different immune-related proteins such as complement components, some cytokines, and a number of immune and nonimmune proteins.

The major histocompatibility complex (MHC) first came to the attention of researchers trying to find out why transplants and tissue grafts were often rejected by the recipient. They found that individuals with different MHC genes rejected tissues transplanted from one to the other. Thus they coined the term "histocompatibility" for this set of genes because the genes seemed to regulate the compatibility of transplants and grafts.

There are hundreds of different versions or alleles of the principal MHC genes—far more genetic variability than in any other group of genes in the human genome! Scientists are still trying to find a satisfactory explanation for this tremendous variation.





A, Major histocompatibility complex (MHC). The MHC is a region of chromosome 6 that codes for proteins important in immune system function. MHC class I proteins present antigens on the surfaces of all cells of the body that possess a nucleus—which is most cells. MHC class II proteins present antigens on the surfaces of cells that specialize in presenting antigens—the antigen-presenting cells (APCs). MHC class III proteins include complement, cytokines, and other proteins of the immune system. **B, MHC function.** This simplified diagram shows that the MHC protein displays an antigen (protein fragment or peptide) on the surface of the cell. A receptor on the surface of a T cell may then bind to the unique receptor-binding part of the MHC and to a complementary part of the T cell. Antigens (peptides) presented this way can then be recognized by immune cells as being "self" or "nonself."

cell death) that progresses to lysis (breaking apart). NK cells must engage their target cells by direct contact (binding of receptors) to cause cell destruction.

Interferon

Several types of cells, if invaded by viruses, respond rapidly by synthesizing the protein **interferon (IFN)** and releasing some of it into the circulation. As the name suggests, interferon proteins interfere with the ability of viruses to cause disease. One way that they do this is by preventing viruses from multiplying in cells. IFN production is triggered by viral infection in a cell, probably by the presence of viral dsRNA (double-strand RNA). The IFN is then released to nearby cells, where it triggers signal transduction that activates antiviral genes in the neighboring cells. These genes produce an "antiviral state" by producing several enzymes that block viral replication if the cell becomes infected. Thus IFN acts as a paracrine (local) hormone that allows virus-infected cells to send an "alarm" to nearby cells that protects the uninfected cells.

Some interferons also promote synthesis of more MHC proteins, thus allowing them to present viral antigens and promote immune destruction of infected cells (see Box 24-1). By promoting the destruction of cells that are already infected, the chance of the virus spreading to other cells is reduced.

Interferon comes in several varieties, each with somewhat different antiviral actions. Leukocyte interferon (β), fibroblast interferon (α), and immune interferon (γ) are the three major types of interferon proteins. All three have now been produced by using gene-splicing techniques. Studies exploring antiviral and anticancer activities of interferons are currently under way (Box 24-2).

Box 24-2 | HEALTH matters

Interferon Therapy

Although interferon (IFN) has not proven to be the "magic bullet" cure researchers may have once hoped, some useful therapies have emerged from ongoing research into clinical uses of this protein. Several types of leukocyte interferon, including *IFN alpha-2a* and *IFN alpha-2b,* are approved by the FDA for therapeutic use in viral hepatitis C. Interferons can be manufactured by splicing human genes that encode the amino acid sequence for this protein into the DNA of a common type of bacterium called *Escherichia coli.* These easily cultured bacteria, which normally would not make interferon, are thus converted into miniature "interferon factories." Interferon is often combined with polyethylene glycol to make it last longer in the body—and thus reduce the number of injections needed from three per week to just one per week.

Having both anticancer and antiviral properties, interferons are sometimes used with other therapies in the treatment of AIDS-related Kaposi sarcoma (see Fig. 7-28, p. 191), hairy-cell leukemia, other cancers, and genital warts. A type of interferon called *IFN beta* has also been used to treat multiple sclerosis (MS).

Complement

Complement is the name given to each of a group of about 20 inactive enzymes in the plasma and on cell surfaces. Individual complement proteins are often designated by C (for complement) followed by a number, such as C1, C2, C3, and so on. Subtypes of each complement are usually identified by a lower-case letter, such as C4b or C5a—or by Greek letters, as in C5bα or C8β.

Complement molecules are activated in a cascade of chemical reactions triggered by either adaptive or innate mechanisms. Ultimately, the complement cascade causes lysis (rupture) of the foreign cell that triggered the response. Complement also marks microbes for destruction by phagocytic cells—a process called *opsonization*—and it promotes the inflammatory response. Some of these functions of complement are discussed in more detail later in this chapter (Figure 24-10).

Toll-like Receptors

Triggering of many of the innate responses already mentioned requires action by **Toll-like receptors (TLRs)** in the membranes of host cells. They get their odd name from *Toll* (German for "weird"), the name of a gene for this receptor family that was first discovered to cause strange body shapes in fruit flies when damaged. Later, the proteins produced by the gene were also found to have a primitive immune function.

Each of the many types of TLRs present in membranes of human cells can recognize the general pattern of a whole group of molecules that originate in microbes (but not in human cells). That is, they are *pattern-recognition receptors (PRRs)* and thus do not identify specific antigens. Instead, they have a *nonspecific* ability to identify a large variety of different bacterial molecules such as toxins and flagella proteins, viral RNA and glycoproteins, and fungal molecules.

When triggered, TLRs facilitate many of the nonspecific immune mechanisms described earlier. For example, they help initiate the inflammatory response, antigen presentation to immune

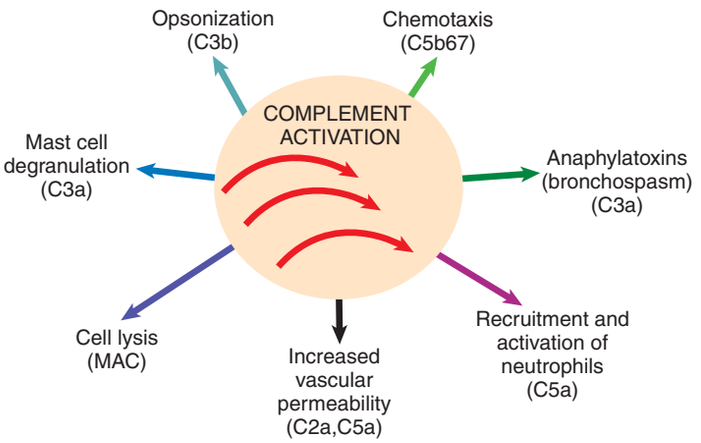


FIGURE 24-10

Summary of complement function. Complement (C), when activated in a cascade of reactions, may participate in a variety of immune functions. *MAC,* Membrane attack complex (see Figure 24-21, page 762).

cells, phagocytosis, release of cytokines and interferon—and even apoptosis of an infected host cell. TLRs are key facilitators of the overall innate immune response of the body.

| QUICK CHECK |

4. Why are the skin and mucous membranes together called the body's *first line of defense?*
5. Name some of the events of the inflammatory response. How does each help protect the body?
6. What is the role of macrophages in the defense of the body?
7. How do *interferons* and *complement* protect the body?

OVERVIEW OF ADAPTIVE IMMUNITY

Unlike the innate, nonspecific mechanisms of immunity, the various types of adaptive immune mechanisms attack *specific* agents that the body recognizes as abnormal or nonself. Adaptive immunity, part of the body's *third line of defense*, is orchestrated by two different classes of a type of white blood cell called the *lymphocyte* (Figure 24-11).

Originally, lymphocytes are formed in the red bone marrow of the fetus. They, like all blood cells, derive from primitive cells known as *hematopoietic stem cells* (see Chapter 20). The stem cells destined to become lymphocytes of the adaptive immune system follow two developmental paths and differentiate into two major classes of lymphocytes—*B lymphocytes* and *T lymphocytes*, or simply **B cells** and **T cells** (Figure 24-12).

B cells do not attack pathogens themselves but instead produce molecules called **antibodies** that attack the pathogens or direct other cells, such as phagocytes, to attack them. B cell mechanisms are therefore often classified as **antibody-mediated immunity.** Because antibodies disperse freely in the blood plasma, where they accomplish their immune functions, this type of immunity is sometimes also called **humoral immunity.** The word *humoral* refers to body fluids, especially blood plasma. Many of these terms are further explained in Box 24-3.

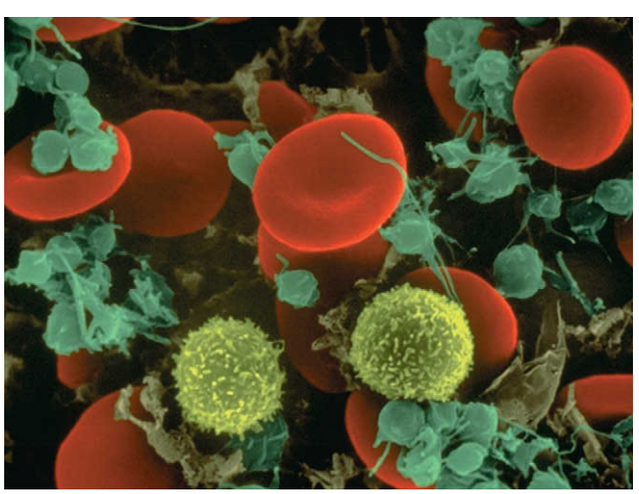


FIGURE 24-11

Lymphocytes. Color-enhanced scanning electron micrograph showing lymphocytes in yellow, red blood cells in red, and platelets in green.

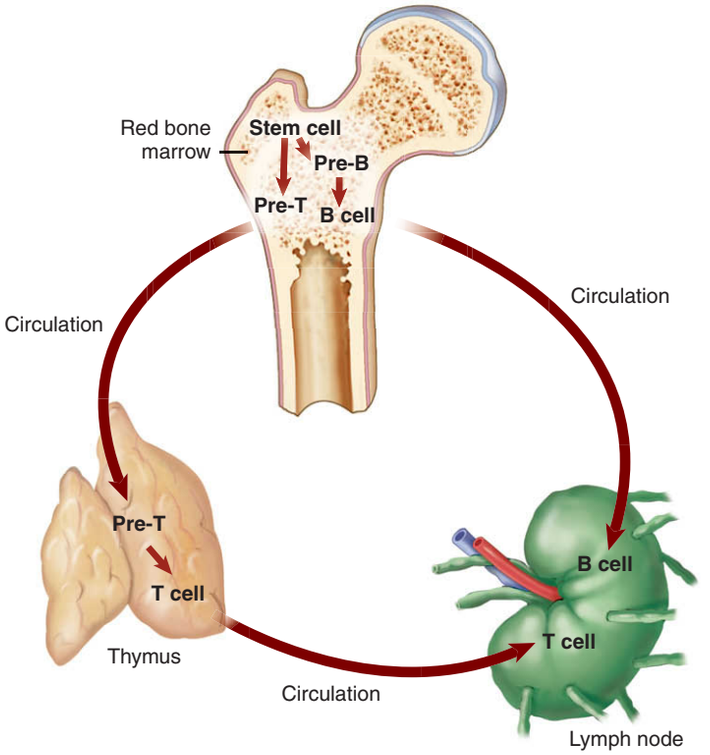


FIGURE 24-12

Development of B cells and T cells. Both types of lymphocytes originate from stem cells in the red bone marrow. Pre–B cells that are formed by dividing stem cells develop in the "bursa-equivalent" tissues in the yolk sac, fetal liver, and bone marrow. Likewise, pre–T cells migrate to the thymus, where they continue developing. Once they are formed, B cells and T cells circulate to the lymph nodes and spleen.

Because T cells attack pathogens more directly, T cell immune mechanisms are classified as **cell-mediated immunity** or, more simply, **cellular immunity** (Figure 24-13).

Lymphocytes express proteins on their surfaces known as *surface markers*. Some of these proteins are unique to lymphocytes; some are shared by other types of cells. B cells and T cells each have some unique surface markers that not only distinguish B cells from T cells but also subdivide these categories into *subsets*. Lymphocyte subsets are clinically meaningful. For example, the condition of a patient's T-cell subsets is very important in understanding AIDS. The international system for naming surface markers on blood cells is the **CD system** (CD stands for cluster of differentiation; the number after "CD" refers to a single, defined surface marker protein). For example, the T-cell subsets that are clinically important in diagnosing and assessing AIDS or other immune deficiencies are the CD4 and CD8 T-cell subsets.

Adaptive immunity requires activation of lymphocyte populations, which then begin their immune attack of specific antigens (or cells or viruses bearing those antigens). Such activation requires two activating signals: a specific antigen and a chemical signal (Figure 24-14). Each lymphocyte has receptors both for antigens and for signaling chemicals. Both receptors must be activated for the lymphocyte to begin its active immune function.

Box 24-3 | FYI

The Language of Adaptive Immunity

Learning the mechanisms of adaptive (specific) immunity will be easier if you first become familiar with the following terms:

Antigens—macromolecules (large molecules) that induce the immune system to make certain responses. Most antigens are foreign proteins. Some, however, are polysaccharides, and some are nucleic acids. *Haptens,* sometimes called "incomplete antigens," are very small molecules that must first bind to a protein before they can induce an immune response. Many antigens that enter the body are macromolecules located in the walls or outer membranes of microorganisms or the outer coats of viruses. Of course, antigens on the surfaces of some tumor cells (tumor markers) are not really from outside the body but are "foreign" in the sense that they are recognized as "not belonging." The membrane molecules that identify all the normal cells of the body are called *self-antigens* or *major histocompatibility complex (MHC) antigens* (see Box 24-1 on p. 754). Foreign and tumor cell antigens can be called *nonself-antigens.*

Antigenic determinants—variously shaped, small regions on the surface of an antigen molecule; a less cumbersome name is *epitopes.* In a protein molecule, for instance, an epitope consists of a sequence of only about 10 amino acids that are part of a much longer, folded chain of amino acids. The sequence of the amino acids in an epitope determines its shape. Because the sequence differs in different kinds of antigens, each kind of antigen usually has specific and uniquely shaped epitopes.

Antibodies—plasma proteins of the class called *immunoglobulins.* Unlike most antigens, all antibodies are native molecules, that is, they are normally present in the body.

Combining sites—two small concave regions on the surface of an antibody molecule. Like epitopes, combining sites have specific and unique shapes. An antibody's combining sites are shaped so that an antigen's epitope that has a complementary shape can fit into the combining site and thereby bind the antigen to the antibody to form an **antigen-antibody complex.** Because combining sites receive and bind antigens, they are also called *antigen receptors* and *antigen-binding sites.*

Clone—family of cells, all of which have descended from one cell.

Complement—a group of proteins that, when activated, work together to destroy foreign cells.

Effector cell—a B cell or T cell that is actively producing an immune response, such as secreting antibodies (effector B cells) or directly attacking other cells (effector T cells); effector cells usually die during or just after their immune response; effector B cells are also called *plasma cells.*

Memory cell—a B or T cell that has been activated (no longer naïve) but is not an effector cell producing an active response; rather, a memory cell survives for a long period in the lymph nodes and if later exposed to the same specific antigen, forms a clone of cells that rapidly produce a specific immune response.

Naïve—refers to a B or T cell that is inactive, has not yet been exposed to (or had an opportunity to react with) a specific antigen; synonymous with "inactive" or "virgin."

	Antibody-mediated (humoral) immunity	Cell-mediated immunity	
Microbe	Extracellular microbes	Phagocytosed microbes in macrophage	Intracellular microbes (e.g., viruses) replicating within infected cell
Responding lymphocytes	B lymphocyte	Helper T lymphocyte	Cytotoxic T lymphocyte
Effector mechanism	Secreted antibody		
Distributed by	Blood plasma (antibodies)	Cells (T lymphocytes)	Cells (T lymphocytes)
Main functions	**Block infections and eliminate extracellular microbes**	**Activate macrophages to kill phagocytosed microbes**	**Kill infected cells and eliminate reservoirs of infection**

FIGURE 24-13

Two strategies of adaptive immunity. Simplified summary of antibody-mediated (humoral) immunity and cell-mediated (cellular) immunity.

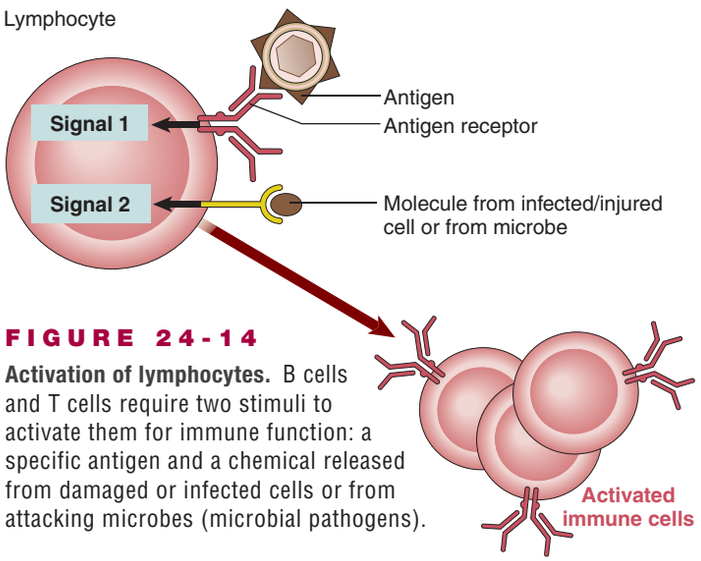


FIGURE 24-14

Activation of lymphocytes. B cells and T cells require two stimuli to activate them for immune function: a specific antigen and a chemical released from damaged or infected cells or from attacking microbes (microbial pathogens).

Chemicals required to stimulate immune function may come from injured/infected cells or from microbes themselves.

The densest populations of lymphocytes occur in the bone marrow, thymus gland, lymph nodes, and spleen (Figure 24-15). From these structures, lymphocytes pour into the blood and then distribute themselves throughout the tissues of the body. After wandering through the tissue spaces, they eventually find their way into lymphatic capillaries. Lymph flow transports the lymphocytes through a succession of lymph nodes and lymphatic vessels and empties them by way of the thoracic and right lymphatic ducts into the subclavian veins. Thus returned to the blood, the lymphocytes embark on still another long journey—through blood, tissue spaces, and lymph and then back to blood. The survival value of the continued recirculation of lymphocytes and of their widespread distribution throughout body tissues seems apparent. It provides these major cells of the immune system ample opportunity to perform their functions of searching out, recognizing, and destroying foreign invaders.

Before reading further, please review the basic terminology used to explain adaptive immunity, which is presented in Box 24-3.

| QUICK CHECK |

8. What is an antigen? What is the difference between a *self-antigen* and a *nonself-antigen?*
9. What is meant by the term *clone?*

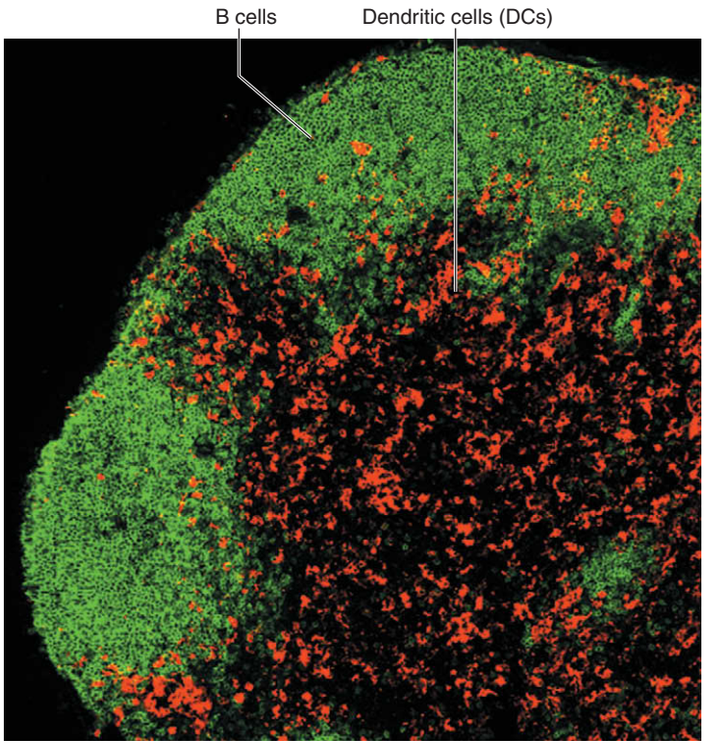


FIGURE 24-15

B cells in a lymph node. This micrograph of a lymph node shows fluorescent green stain in B cells, which are densely packed in the nodules of the lymph node. The cells marked by the red stain are a type of macrophage called *dendritic cells* (see Figure 24-8).

B CELLS AND ANTIBODY-MEDIATED IMMUNITY

Development and Activation of B Cells

The development of the lymphocytes called *B cells* occurs in two stages (Figure 24-16). In chickens the first stage of B-cell development occurs in the *bursa of Fabricius*—hence the name *B cells.* Because humans do not have a bursa of Fabricius, another organ must serve as the site for the first stage of B-cell development. The bursa-equivalent tissue in humans is the yolk sac and fetal liver during early development and then later the red marrow. After completing their first developmental stage, the B cells are then known as **naïve B cells,** or sometimes *inactive* or *virgin* B cells.

Naïve B cells synthesize antibody molecules but secrete few if any of them. Instead, they insert on the surface of their plasma membranes perhaps 100,000 antibody molecules. The combining sites of these surface antibody molecules serve as receptors for a specific antigen if encountered. After being released from the bone marrow, naïve B cells circulate to the lymph nodes, spleen, and other lymphoid structures.

The second major stage of B-cell development occurs when the naïve B cells become activated. Activation of a B cell must be initiated by an encounter between a naïve B cell and its specific antigen, that is, one whose epitopes fit the combining sites of the B cell's surface antibodies (see Figure 24-16).

The antigen binds to these antibodies on the B cell's surface. Antigen-antibody binding activates the B cell, triggering a rapid series of mitotic divisions. By dividing repeatedly, a single B cell produces a clone, or family, of identical B cells. Some of them differentiate to form **effector B cells** or **plasma cells.** Others do not differentiate completely but remain in the lymphatic tissue as the so-called **memory B cells.**

Plasma cells synthesize and secrete huge amounts of antibody. A single plasma cell, according to one estimate, secretes 2000 antibody molecules per second during the few days that it lives. All the cells in a clone of plasma cells secrete identical antibodies because they have all descended from the same B cell.

Memory B cells do not themselves secrete antibodies, but if they are later exposed to the antigen that triggered their formation, memory B cells then rapidly divide to produce more plasma cells and memory cells. The newly formed plasma cells then quickly secrete antibodies that can combine with the initiating antigen (see Figure 24-16)—thus quickly combating the antigen. Thus the ultimate function of B cells is to serve as ancestors of antibody-secreting plasma cells (effector B cells).

Antibodies (Immunoglobulins)

STRUCTURE OF ANTIBODY MOLECULES

Antibodies are proteins of the family called **immunoglobulin (Ig).** Like all proteins, antibodies are very large molecules and are composed of long chains of amino acids (polypeptides). Each immunoglobulin molecule consists of four polypeptide chains—two heavy chains and two light chains. Each polypeptide chain is intricately folded to form globular regions that are joined together in such a way that the immunoglobulin molecule as a whole is Y-shaped. Look now at Figure 24-17, A. The twisted strands of red

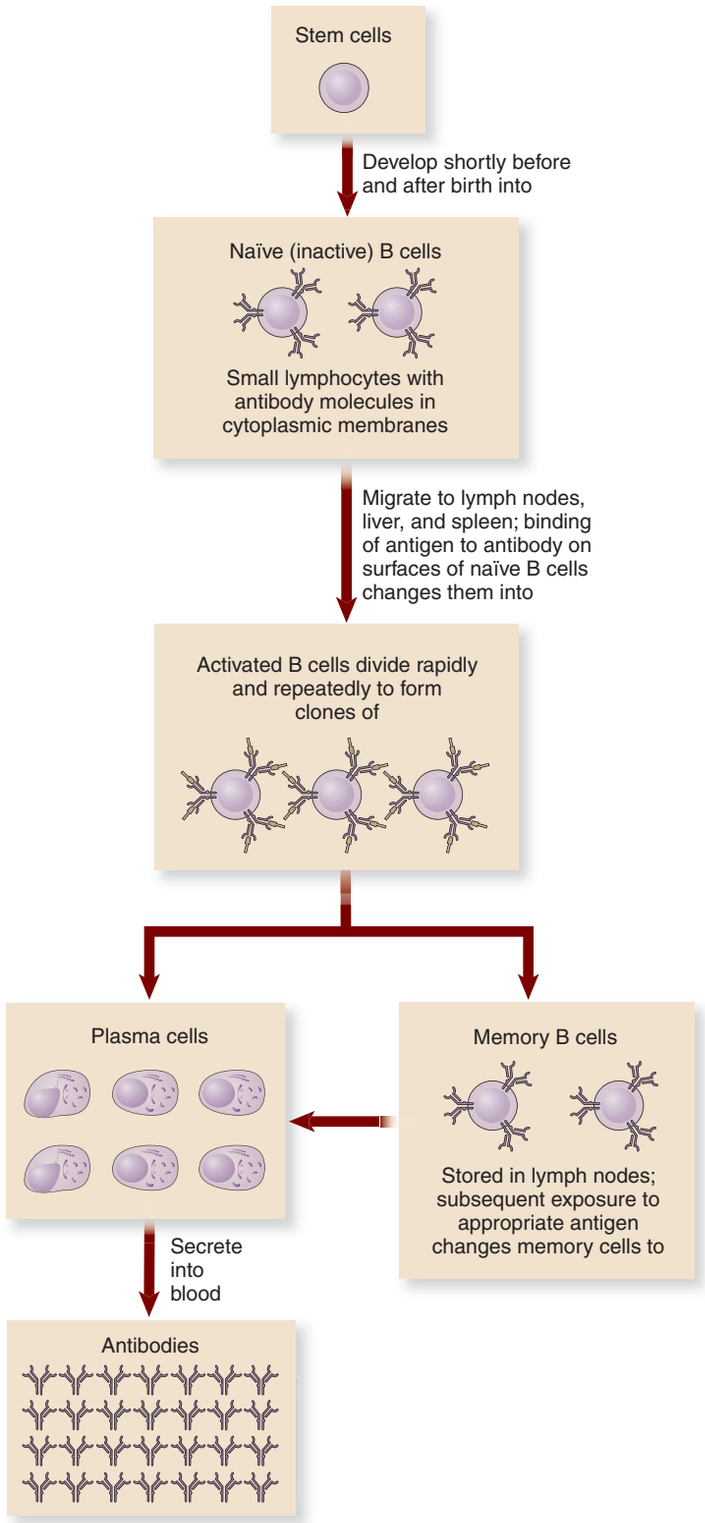


FIGURE 24-16

B cell development. B cell development takes place in two stages. *First stage:* shortly before and after birth, stem cells develop into naïve B cells. *Second stage* (occurs only if naïve B cell contacts its specific antigen): naïve B cell develops into activated B cell, which divides rapidly and repeatedly to form a clone of plasma cells and a clone of memory cells. Plasma cells secrete antibodies capable of combining with specific antigens that cause naïve B cell to develop into active B cell. Stem cells maintain a constant population of newly differentiating cells.

spheres (amino acids) in the diagram represent the light chains, and the two twisted strands of blue spheres represent the heavy chains. Each heavy chain consists of 446 amino acids. Heavy chains therefore are about twice as long and weigh about twice as much as light chains.

The regions with colored bars seen in Figure 24-17, *B*, represent *variable regions*, that is, regions in which the sequence of amino acids varies in different antibody molecules. Note the relative positions of the variable regions of the light and heavy chains; they lie directly opposite each other. Because the amino acid sequence determines conformation or shape, and because different sequences of amino acids occur in the variable regions of different antibodies, the shapes of the sites between the variable regions also differ. At the end of each "arm" of the Y-shaped antibody molecule, the unique shapes of the variable regions form a cleft that serves as the antibody's combining sites, or antigen-binding sites. It is this structural

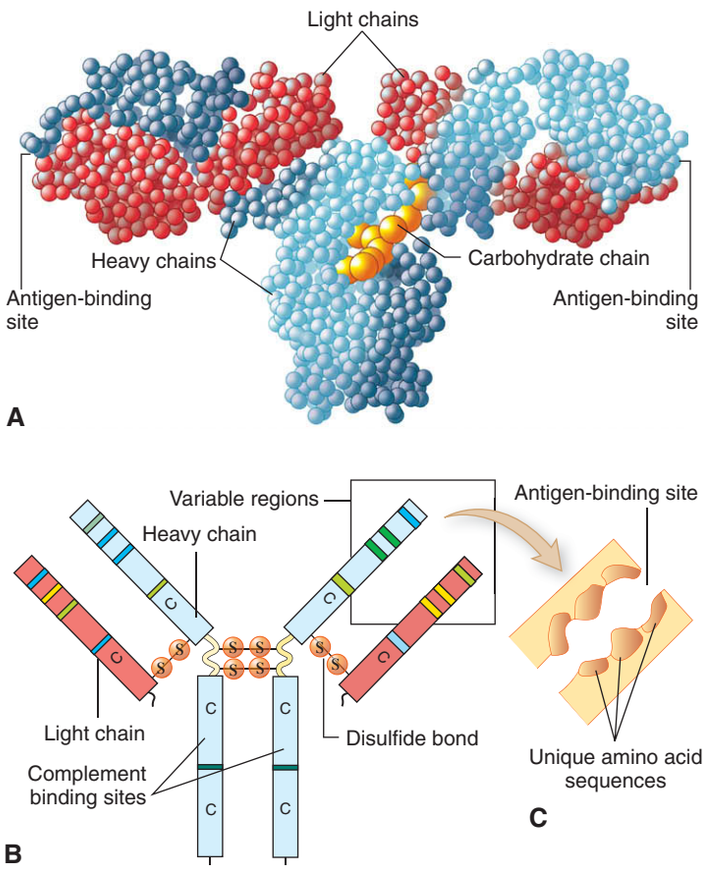


FIGURE 24-17

Structure of the antibody molecule. A, In this molecular model of a typical antibody molecule, the light chains are represented by strands of red spheres (each represents an individual amino acid). Heavy chains are represented by strands of blue spheres. Notice that the heavy chains can complex with a carbohydrate chain. **B,** This simplified diagram shows the variable regions, highlighted by colored bars, that represent amino acid sequences unique to that molecule. Constant regions of the heavy and light chains are marked. **C.** The inset shows that the variable regions at the end of each arm of the molecule form a cleft that serves as an antigen-binding site.

feature that enables antibodies to recognize and combine with specific antigens, both of which are crucial first steps in the body's defense against invading microorganisms and other foreign cells.

In addition to its variable region, each light chain in an antibody molecule also has a constant region. The constant region consists of 106 amino acids whose sequence is identical in all antibody molecules. Each heavy chain of an antibody molecule consists of three constant regions in addition to its one variable region. Identify the constant and variable regions of the light and heavy chains in Figure 24-17. Note the location of two *complement-binding sites* on the antibody molecule (one on each heavy chain).

In summary, an immunoglobulin, or antibody molecule, consists of two heavy and two light polypeptide chains. Each light chain consists of one variable region and one constant region. Each heavy chain consists of one variable region and three constant regions. Disulfide bonds join the two heavy chains to each other; they also bind each heavy chain to its adjacent light chain. An antibody has two antigen-binding sites—one at the top of each pair of variable regions—and two complement-binding sites located as shown in Figure 24-17.

DIVERSITY OF ANTIBODIES

Every normal baby is born with an enormous number of different clones of B cells populating his or her bone marrow, lymph nodes, and spleen. All the cells of each clone are committed to synthesizing a specific antibody with a sequence of amino acids in its variable regions that is different from the sequence synthesized by any other of the innumerable clones of B cells.

How does this astounding diversity originate? One suggested answer is called the *somatic recombination hypothesis*. According to this explanation, our chromosomes do not contain whole genes for producing the heavy and light polypeptide chains that make up each antibody molecule. Instead, the genetic code is a set of separate sequences that are assembled into whole genes as a B cell develops. Because the separate sequences can be assembled in an astounding number of different combinations to form each whole gene, and because several different polypeptides are needed to make one antibody, any particular B cell is not likely to synthesize *exactly* the same antibody as any other B cell. Thus somatic recombination is a sort of "genetic lottery" that produces millions of unique genes by combining different gene segments and millions of unique antibodies by combining different polypeptides.

Antibody diversity may also be influenced by occasional mutations in the gene segments used to form the genes needed to produce antibodies. Evidence from several different studies shows that random genetic mutations—slight changes in the master DNA code—result in slight differences in the variable regions of antibodies.

If these hypotheses about antibody diversity are correct, it is possible to produce B cells that make antibodies against self-antigens. It is thought that although most such B cells are eliminated early in their development, before they produce antibodies that would attack a person's own cells, all humans have some "anti-self" B cells in their bodies.

CLASSES OF ANTIBODIES

There are five classes of antibodies, identified by letter names as immunoglobulins M, G, A, E, and D (Figure 24-18). *IgM* (abbreviation for immunoglobulin M) is the antibody that immature B cells synthesize and insert into their plasma membranes. It is also the predominant class of antibody produced after initial contact with an antigen. The most abundant circulating antibody, the one that normally makes up about 75% of all the antibodies in the blood, is *IgG*. It is the predominant antibody of the secondary antibody response—that is, following subsequent contacts with a given antigen. The IgG antibodies are those that cross the placental barrier during pregnancy to impart natural passive immunity to the offspring (see Table 24-4 and Box 24-7). *IgA* is the major class of antibody present in the mucous membranes of the body, in saliva, and in tears (see Box 24-8). *IgE*, although minor in amount, can produce major harmful effects, such as those associated with allergies. *IgD* is present in the blood in very small amounts, and its precise function is as yet unknown. As Figure 24-18 shows, some immunoglobulin molecules are formed by the joining of several basic antibody units.

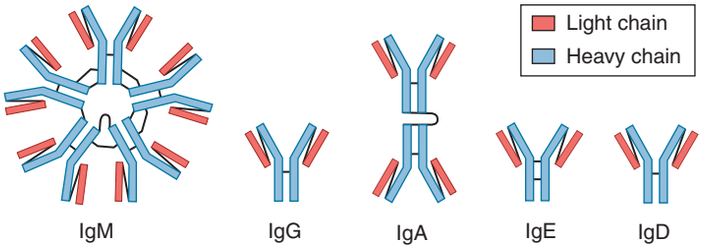


FIGURE 24-18

Classes of antibodies. Antibodies are classified into five major groups: immunoglobulin M (IgM), immunoglobulin G (IgG), immunoglobulin A (IgA), immunoglobulin E (IgE), and immunoglobulin D (IgD). Notice that each IgM molecule has five Y-shaped basic antibody units and most of the others have a single basic antibody unit. IgA is shown here with two antibody units, which is the form found in mucous secretions. But IgA also has a single-unit form found in the blood plasma.

FUNCTIONS OF ANTIBODIES

The function of antibody molecules—some 100 million trillion of them—is to produce **antibody-mediated immunity.** As we stated earlier, this type of immunity is also called *humoral immunity* because it occurs within plasma, which is one of the humors, or fluids, of the body.

TABLE 24-4 Types of Adaptive Immunity

TYPE	DESCRIPTION OR EXAMPLE
Natural Immunity	Exposure to the causative agent is not deliberate
Active (exposure)	A child develops measles and acquires an immunity to a subsequent infection
Passive (exposure)	A fetus receives protection from the mother through the placenta, or an infant receives protection through the mother's milk
Artificial Immunity	Exposure to the causative agent is deliberate
Active (exposure)	Injection of the causative agent, such as a vaccination against polio, confers immunity
Passive (exposure)	Injection of protective material (antibodies) that was developed by another individual's immune system

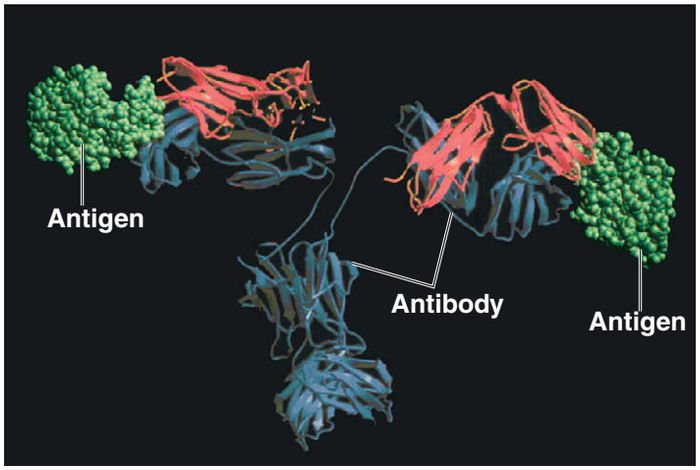


FIGURE 24-19

Binding of antigen by an antibody. This ribbon model of an antibody shows the heavy chains in blue and the light chains in red. Note the green antigen molecules bound to each antigen-binding site.

Antigen-Antibody Reactions

Antibodies fight disease first by recognizing substances that are foreign or abnormal. In other words, they distinguish nonself-antigens from self-antigens. Recognition occurs when an antigen's epitopes (small regions on its surface) fit into and bind to an antibody molecule's antigen-binding sites (Figure 24-19). The binding of the antigen to antibody forms an antigen-antibody complex that may produce one or more effects. For example, it transforms antigens that are toxins (chemicals poisonous to cells) into harmless substances. It agglutinates antigens that are molecules on the surface of microorganisms. In other words, it makes them stick together in clumps, and this in turn makes it possible for macrophages and other phagocytes to dispose of them more rapidly by ingesting and digesting large numbers of them at one time. The binding of antigens to antibodies frequently produces still another effect—it alters the shape of the antibody molecule, not very much, but enough to expose the molecule's previously hidden complement-binding sites. This seems a trivial enough change, but it is not so. It initiates an astonishing series of reactions that culminate in the destruction of microorganisms and other foreign cells (Figure 24-20).

Complement

Complement is a component of blood plasma that consists of about 20 protein compounds. They are inactive enzymes that become activated in a definite sequence to catalyze a series of intricately linked reactions. The binding of an antibody to an antigen located on the surface of a cell alters the shape of the antibody molecule in a way that exposes its complement-binding sites. By binding to these sites, complement protein 1 becomes activated and touches off the catalytic activity of the next complement protein in the series. A rapid sequence, or cascade, of activity by the next protein, then the next, and the next, follows until the entire series of enzymes has functioned. The end result of this rapid-fire

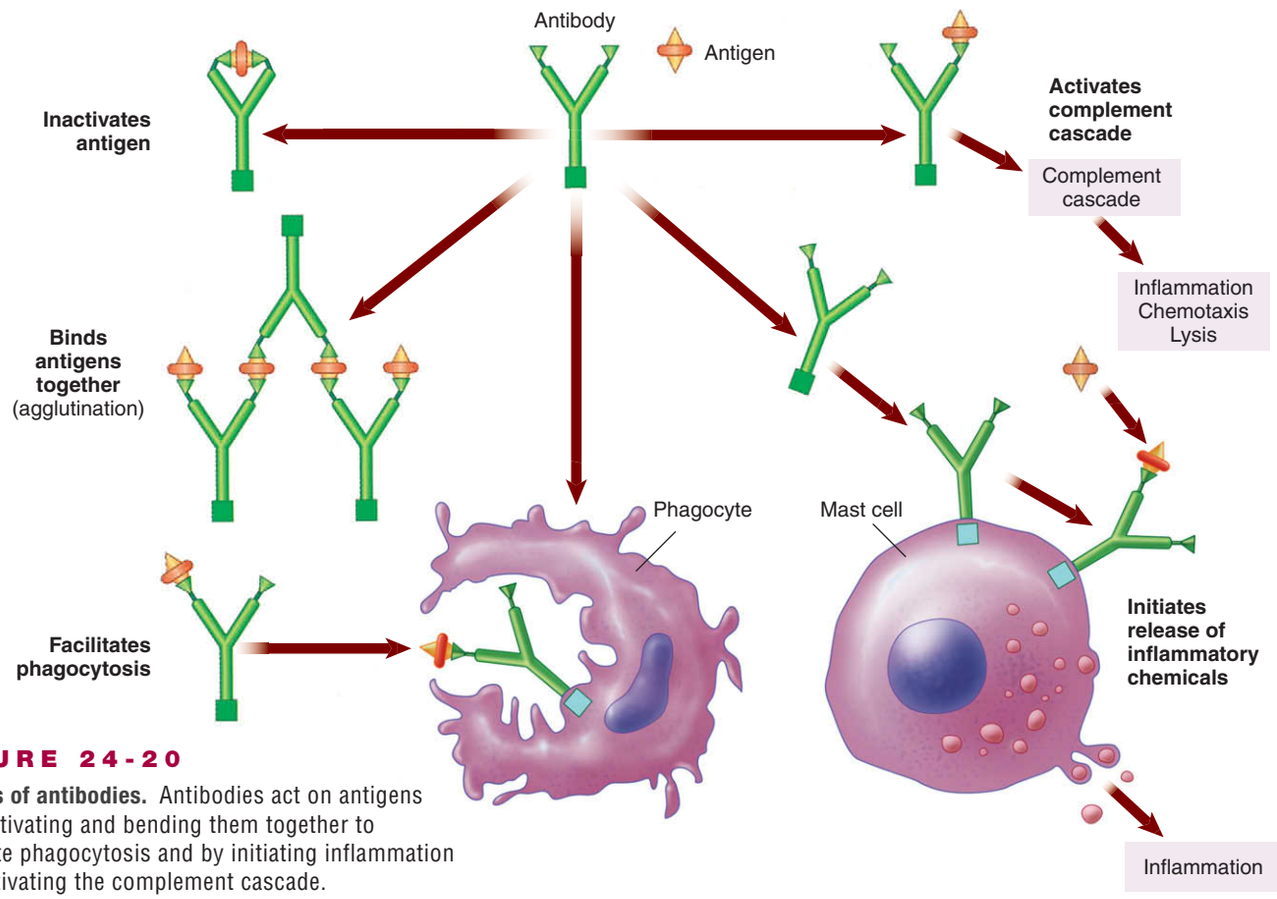


FIGURE 24-20

Actions of antibodies. Antibodies act on antigens by inactivating and bending them together to facilitate phagocytosis and by initiating inflammation and activating the complement cascade.

activity challenges the imagination. Some of the resulting reactions were summarized in Figure 24-10 (p. 755).

One of the more spectacular results of the complement cascade is the formation of **membrane attack complexes (MACs).** Molecules formed by the reactions of the complement cascade assemble themselves on the enemy cell's surface in such a way as to form a doughnut-shaped structure—complete with a hole in the middle (Figure 24-21). In effect, the complement has drilled a hole through the foreign cell's surface membrane. Ions and water rush into the cell through the MAC; consequently, it swells and bursts (Figure 24-22). **Cytolysis** is the technical name for this process. Nucleated cells usually resist cytolysis, but the influx of ions triggers apoptosis and thus kills the target cell another way.

Briefly, then, complement functions to kill foreign cells by cytolysis. In addition, various complement proteins serve other functions. Some, for example, cause vasodilation in the invaded area, and some attract neutrophils to the site and enhance phagocytosis.

The complement cascade can also be initiated by innate immune mechanisms. Complement protein 3 (C3) can become activated without any stimulation by an antigen. C3 is normally inactivated by enzymes, but it can produce the full complement effect if it binds to bacteria or viruses in the presence of a protein called *properdin*. Thus lysis of various foreign cells and viruses by complement can occur even when antibodies are not involved. This method of activating the complement cascade is often called the "alternate pathway" to distinguish it from the "classical pathway" involving antibodies.

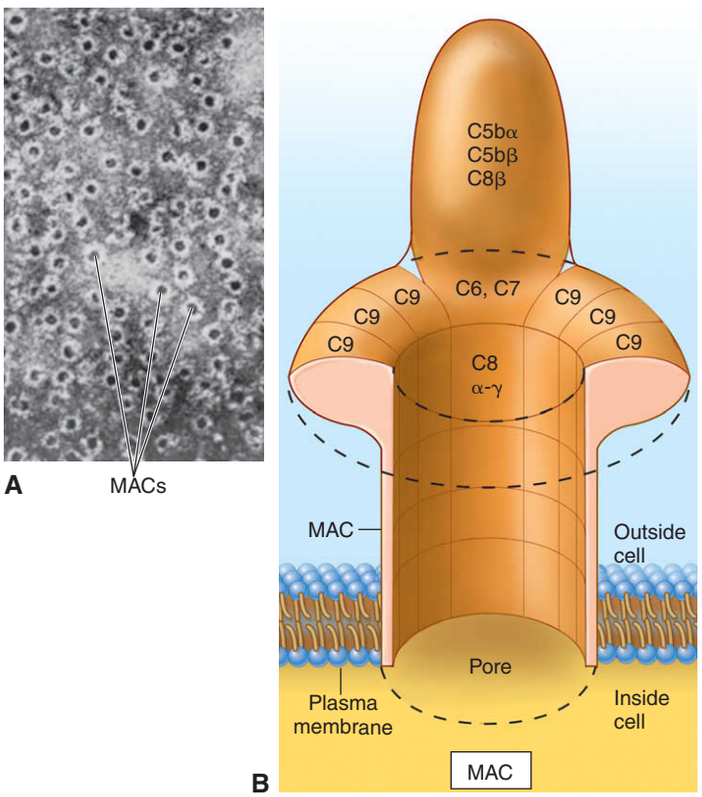


FIGURE 24-21

Membrane attack complex (MAC). Complement components assemble to form a ringlike complex that forms a pore in the membrane of a cell. **A,** Electron micrograph showing numerous MAC pores, each about 100 Å in diameter. **B,** Diagram of the structure of a MAC embedded in a plasma membrane.

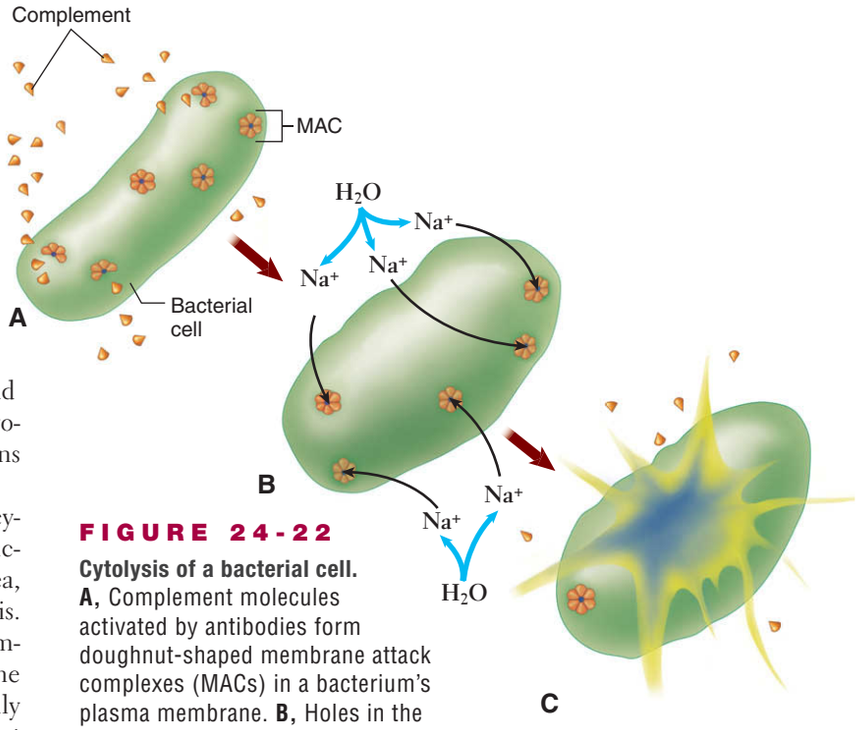


FIGURE 24-22

Cytolysis of a bacterial cell. **A,** Complement molecules activated by antibodies form doughnut-shaped membrane attack complexes (MACs) in a bacterium's plasma membrane. **B,** Holes in the complement complex allow sodium (Na^+) and then water (H_2O) to diffuse into the bacterium. **C,** After enough water has entered, the swollen bacterium bursts. In nucleated cells that resist cytolysis, the influx of calcium ions triggers apoptosis and thus kills the target cell another way.

Primary and Secondary Responses

As Figure 24-23 shows, an initial encounter with a specific antigen produces a *primary response* of increased antibody production in a few days. As the antigen is dealt with, the antibody levels decrease to their normal baseline levels. However, memory B cells that can respond to the triggering antigen have also been produced and wait for another encounter with the antigen. A later encounter with the same antigen triggers the waiting memory B cells and thus produces a secondary response in much less time. The memory B cells quickly divide to form more memory cells and a large number of plasma cells that produce antibodies against the known antigen. Thus the secondary response can be quicker and thus more effective. The strength of the secondary response can be used to boost the effectiveness of immunizations (Box 24-4).

| A&P CONNECT |

Techniques that permit biologists to produce and isolate large quantities of pure and very specific antibodies called monoclonal antibodies (MAbs) and tiny antibody fragments called nanobodies have resulted in dramatic advances in medicine. Learn how this works in ***Monoclonal Antibodies and Nanobodies*** online at ***A&P Connect.***

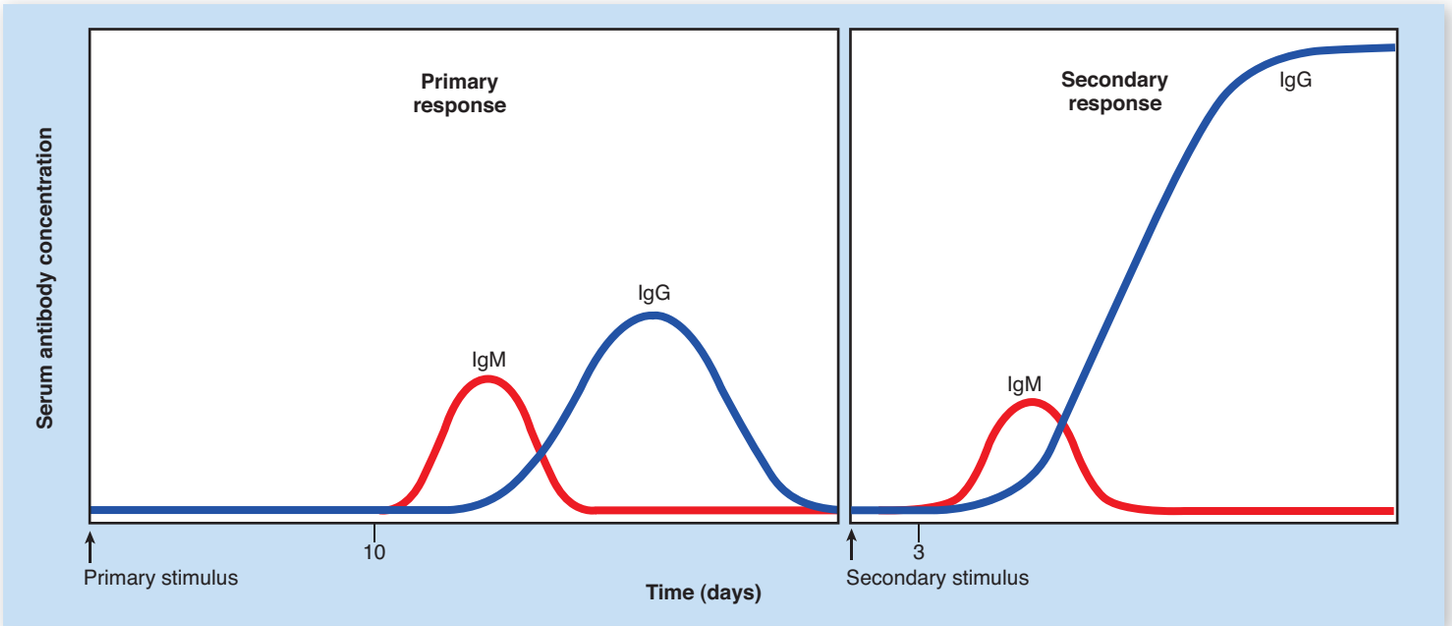


FIGURE 24-23

Antibody response times. The initial encounter with a specific antigen (primary stimulus) produces a primary response (increased production of IgM and IgG) in a few days. A later encounter (secondary stimulus) produces a secondary response in much less time. Note that both IgM production and IgG production occur more quickly in the secondary response—and IgG production also increases in the total amount of antibody produced.

Box 24-4 | HEALTH matters

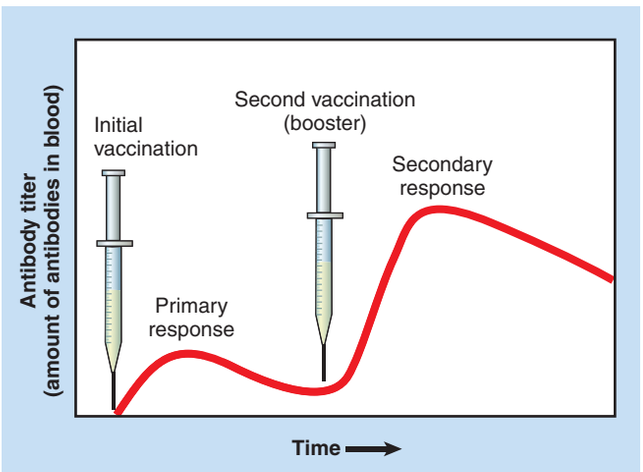
Immunization

Active immunity can be established artificially by using a technique called **vaccination.** The first vaccine was a live cowpox virus that was injected into healthy people to cause a mild cowpox infection. The term *vaccine* literally means "cow substance." Because the cowpox virus is similar to the deadly *smallpox virus,* vaccinated individuals developed antibodies that imparted immunity against both cowpox and smallpox viruses.

Modern vaccines work on a similar principle; substances that trigger the formation of antibodies against specific pathogens are introduced orally or by injection. Some of these vaccines are killed pathogens or live, *attenuated* (weakened) pathogens. Such pathogens still have their specific antigens intact, so they can trigger formation of the proper antibodies, but they are no longer *virulent* (able to cause disease). Although rare, these vaccines sometimes backfire and actually cause an infection. Many of the newer vaccines avoid this potential problem by using only the part of the pathogen that contains antigens. Because the disease-causing portion is missing, such vaccines cannot cause infection.

The amount of antibodies in a person's blood produced in response to vaccination or an actual infection is called the **antibody titer.** As you can see in the figure, the initial injection of vaccine triggers a rise in the antibody titer that gradually diminishes. Often, a **booster shot,** or second injection, is given to keep the antibody titer high or to raise it to a level that is more likely to prevent infection. The secondary response is more intense than the primary response because memory B cells are ready to produce a large number of antibodies at a moment's notice. A later accidental exposure to the pathogen will trigger an even more intense response—thus preventing infection.

Toxoids are similar to vaccines but use an altered form of a bacterial toxin to stimulate production of antibodies. Injection of toxoids imparts protection against toxins, whereas administration of vaccines imparts protection against pathogenic organisms and viruses.



Changes in blood antibody titers following primary and secondary (booster) vaccinations.

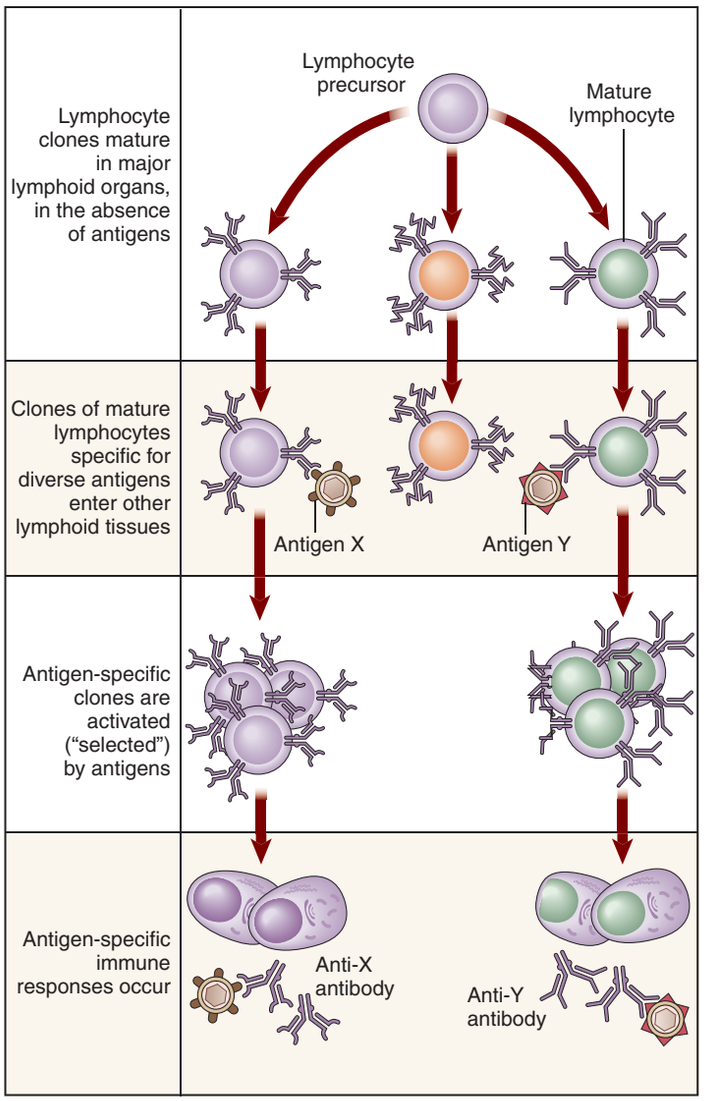


FIGURE 24-24

The clonal selection theory. This theory of immunity states that each specific antigen (here shown as X and Y) activates—selects—a previously produced clone of lymphocytes. The clone is "selected" because it is specifically targeted at the selecting antigen. The clone, when thus activated, produces effector cells that attack the antigen. B cells are shown here, but the same principle also applies to T cells.

Clonal Selection Theory

The *clonal selection theory*, which deals with antigen destruction, was first proposed in 1959 by Sir Macfarlane Burnet (Figure 24-24). It has two basic tenets. First, it holds that the body contains an enormous number of diverse clones of cells, each committed by certain of its genes to synthesize a different antibody. Second, the clonal selection theory postulates that when an antigen enters the body, it selects the clone whose cells are committed to synthesizing its specific antibody and stimulates these cells to proliferate and to thereby produce more antibodies. We now know that the clones selected by antigens consist of lymphocytes. We also know how antigens select lymphocytes—by the shape of antigen receptors on the lymphocyte's plasma membrane. An antigen recognizes receptors that fit its epitopes and combines with them. By thus selecting the precise clone committed to making its specific antibody, each antigen provokes its own destruction.

| QUICK CHECK |

10. From what structure was the term *B cell* originally derived?
11. How do B cells help defend the body against pathogens?
12. How does the structure of an antibody relate to its function?
13. Describe the mechanism by which complement destroys foreign cells.

T CELLS AND CELL-MEDIATED IMMUNITY

Development of T Cells

T cells, by definition, are lymphocytes that have made a detour through the thymus gland before migrating to the lymph nodes and spleen (see Figure 24-12). During their residence in the thymus, pre–T cells develop into **thymocytes,** cells that proliferate as rapidly as any in the body. Thymocytes divide up to three times each day, and, as a result, their numbers increase enormously in a relatively short time. They stream out of the thymus into the blood and find their way to a new home in areas of the lymph nodes and spleen called *T-dependent zones.* From this time on, they are known as T cells.

Activation and Functions of T Cells

Each T cell, like each B cell, displays antigen receptors on its surface membrane. They are not immunoglobulins as are B-cell receptor molecules but are proteins similar to them. When an antigen (preprocessed and presented by phagocytes) encounters a naïve T cell whose surface receptors fit the antigen's epitopes, the antigen binds to the T cell's receptors. Here is where we see one of several differences between antibody-mediated immunity and cell-mediated immunity: antibodies can react to soluble antigens dissolved in the plasma, but T cells can only react to protein fragments presented on the surfaces of APCs (antigen-presenting cells) or infected cells. Thus T cells react to cells that are already infected—or have otherwise engulfed the antigen. B cells, on the other hand, react mainly to antigens that are in the plasma.

The presentation of an antigen by an antigen-presenting cell activates or sensitizes the T cell. The T cell then divides repeatedly to form a clone of identical *sensitized T cells* that form **effector T cells** and **memory T cells.** Effector T cells include **cytotoxic T cells,** which cause contact killing of a target cell. Cytotoxic T cells are also called *cytolytic T lymphocytes (CDLs)* or *killer T cells.* Memory T cells remain in red bone marrow until they ultimately produce additional active T cells when

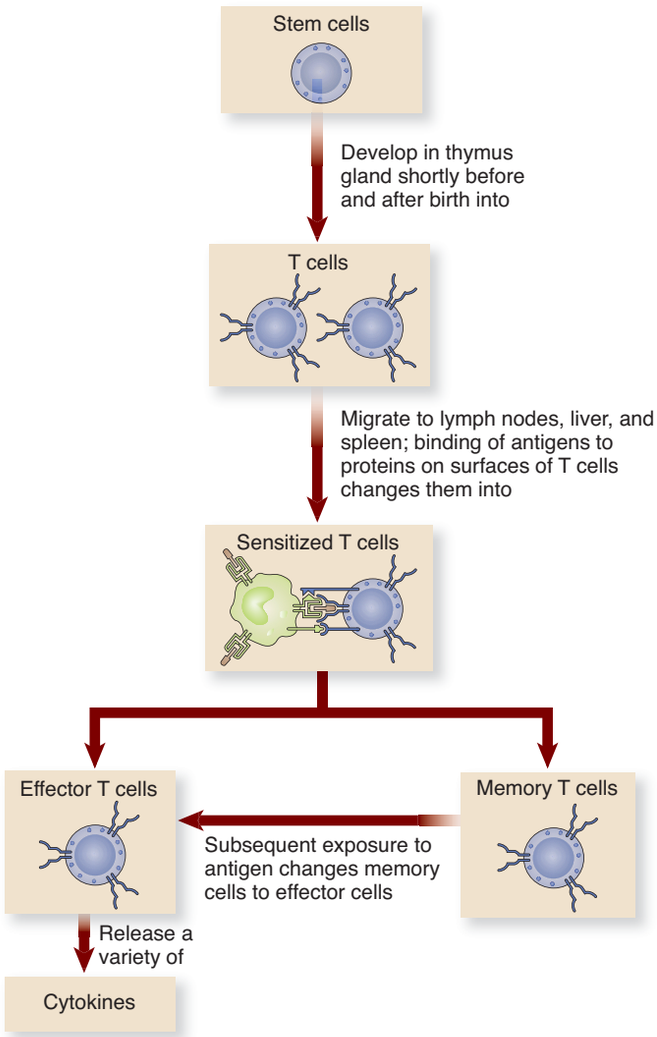


FIGURE 24-25

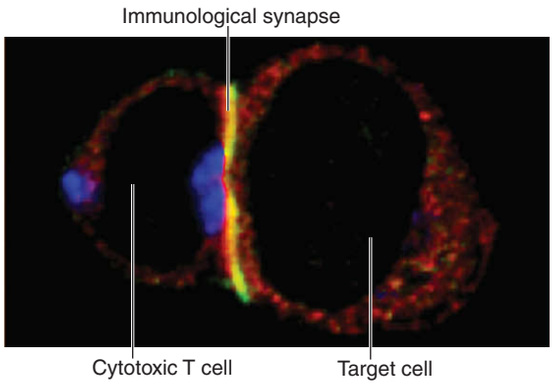
T cell development. The *first stage* occurs in the thymus gland shortly before and after birth. Stem cells maintain a constant population of newly differentiating cells as they are needed. The *second stage* occurs only if a T cell is presented an antigen, which combines with certain proteins on the T cell's surface.

Box 24-5 | FYI

Immunological Synapses

Immune cells often make contact with other immune cells or their target cells so that they can carry out their various functions. Their contact points are similar in many ways to the neurological synapse that you learned about in Chapter 13 (see Figure 13-25 on p. 401). Therefore, these contact points made by immune cells are called **immunological synapses (ISs).**

Some ISs are temporary junctions formed when an antigen-presenting cell (APC) connects to an effector cell, such as a cytotoxic T cell. For example, see the effector mechanisms for cell-mediated immunity in Figure 24-13. ISs also form when natural killer (NK) cells or cytotoxic T cells temporarily attach to a target cell to destroy it (see the figure). The junctions seen in Figures 24-9 and 24-26 are examples. ISs also form a temporary junction between immune cells to allow cytokines to pass efficiently from one cell to another. The junctions seen in the effector functions of helper T cells are shown in Figure 24-27.



Immunological synapses (IS). Fluorescence micrograph that highlights integral membrane proteins involved in the formation of a temporary junction—immunological synapse—between a cytotoxic T cell and the target cell it is about to destroy. Other types of ISs permit efficient communication between two or more immune cells.

needed. The process of T-cell development and activation is summarized in Figure 24-25.

The effector T cells then travel to the site where the antigens originally entered the body. There, in the inflamed tissue, the sensitized T cells bind to antigens of the same kind that led to their formation. However, T cells bind to their specific antigen only if the antigen is presented by an APC such as a macrophage or dendritic cell. The T cell and APC form a temporary junction called an **immunological synapse (IS),** as explained in Box 24-5. The antigen-bound sensitized T cells then release chemical messengers into the inflamed tissues.

The chemical messengers released by T cells, as we have stated earlier in this chapter, are called **cytokines.** Because some cytokines are secreted mainly by lymphocytes, such cytokines are sometimes called *lymphokines.* Names of a few individual cytokines are chemotactic factor, migration inhibition factor, macrophage activating factor, interleukin, and lymphotoxin.

Chemotactic factors attract macrophages, causing hundreds of them to migrate into the vicinity of the antigen-bound, sensitized T cell. *Migration inhibition factor* halts macrophage migration. *Macrophage activating factor* prods the assembled macrophages to destroy antigens by phagocytosing them at a rapid rate. **Interleukins (ILs)** are a class of about a dozen different cytokines that are involved in regulating a wide variety of immune functions in different cell types. **Lymphotoxin** is a powerful poison that acts more directly, quickly killing any cell it attacks.

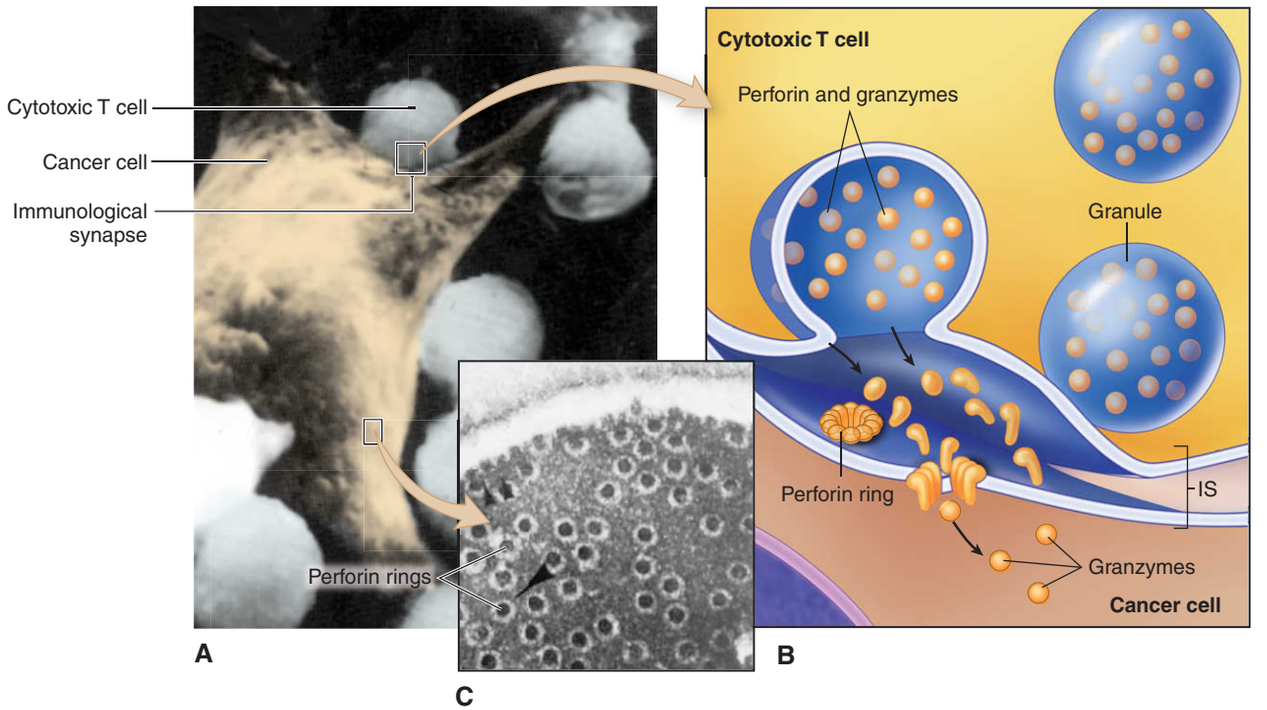


FIGURE 24-26

Killing by cytotoxic T cells. A, The blue spheres seen in this scanning electron microscope view are cytotoxic T cells attacking a much larger cancer cell. T cells are a significant part of our defense against cancer and other abnormal or foreign cells. **B,** After forming an immunological synapse (IS) with the tumor cell, the cytotoxic T cell releases perforin, which forms ringlike holes in the tumor cell's membrane, and granzymes, which pass through the perforin rings to trigger apoptosis (programmed cell death) in the tumor cell. **C,** Electron micrograph showing perforin rings with an average diameter of about 160 Å, which is much larger than the major histocompatibility complex (MHC) rings formed by complement (compare with Figure 24-21).

Effector T cells that release lymphotoxin are the *cytotoxic T cells*. Figure 24-26 shows how lymphotoxins work in killing a cell—a cancer cell in this case. After having been activated by the presentation of tumor cell antigens by an APC such as a dendritic cell, the cytotoxic T cell then becomes active and finds a tumor cell bearing that antigen. The cytotoxic T cell binds directly to the surface of the tumor cell and releases two kinds of molecules: perforin and granzymes. The lymphotoxins called *perforin* produce a ringlike hole in the plasma membrane of the target cell, similar to the one produced by the MAC formed by complement (see Figure 24-26). The *granzymes* enter the target cell through the perforin-ring hole and trigger apoptosis of the cell—thus killing it.

Besides cytotoxic T cells, at least two other populations of effector T cells are found in the body: **helper T cells (T_H cells)** and **suppressor T cells.** Both types of cells help regulate adaptive immune function by regulating B-cell and T-cell function. Helper T cells help other lymphocytes by secreting cytokines

Box 24-6 | HEALTH matters

Immunity and Cancer

One of the many functions of the immune system is to constantly guard against the development of cancer. Cell mutations occur frequently in the normal body, and many of the mutated cells formed are cancer cells. Cancer cells, you may recall, are cells capable of forming tumors in many different parts of the body—unless they are destroyed before this can happen. Abnormal antigens presented on cancer cells, called **tumor-specific antigens,** are present in the plasma membranes of some cancer cells in addition to self-antigens. Lymphocytes, in their continual wanderings through body tissues, are almost sure to come in contact with newly formed cancer cells. Hopefully, the lymphocytes recognize these cells by their abnormal antigens and quickly initiate reactions that kill the cancer cells. Abnormal antigens on cancer cells, called tumor-specific antigens or **tumor markers,** are present in the plasma membranes of some cancer cells in addition to self-antigens or major histocompatibility complex (MHC) antigens. Examples of cancer markers include (1) **carcinoembryonic antigen (CEA)**—found normally in the fetus and elevated in colorectal and other adult cancers; (2) **alpha-fetoprotein (AFP)**—normal fetal protein, whose presence in the adult strongly suggests liver or germ cell cancer; (3) **CA-125**—tumor antigen associated with ovarian cancer; and (4) **prostate-specific antigen (PSA),** which is elevated in both benign and malignant prostate disease. The relationship between cancer and the immune system continues to be an area of intense research by scientists looking for effective cancer treatments.

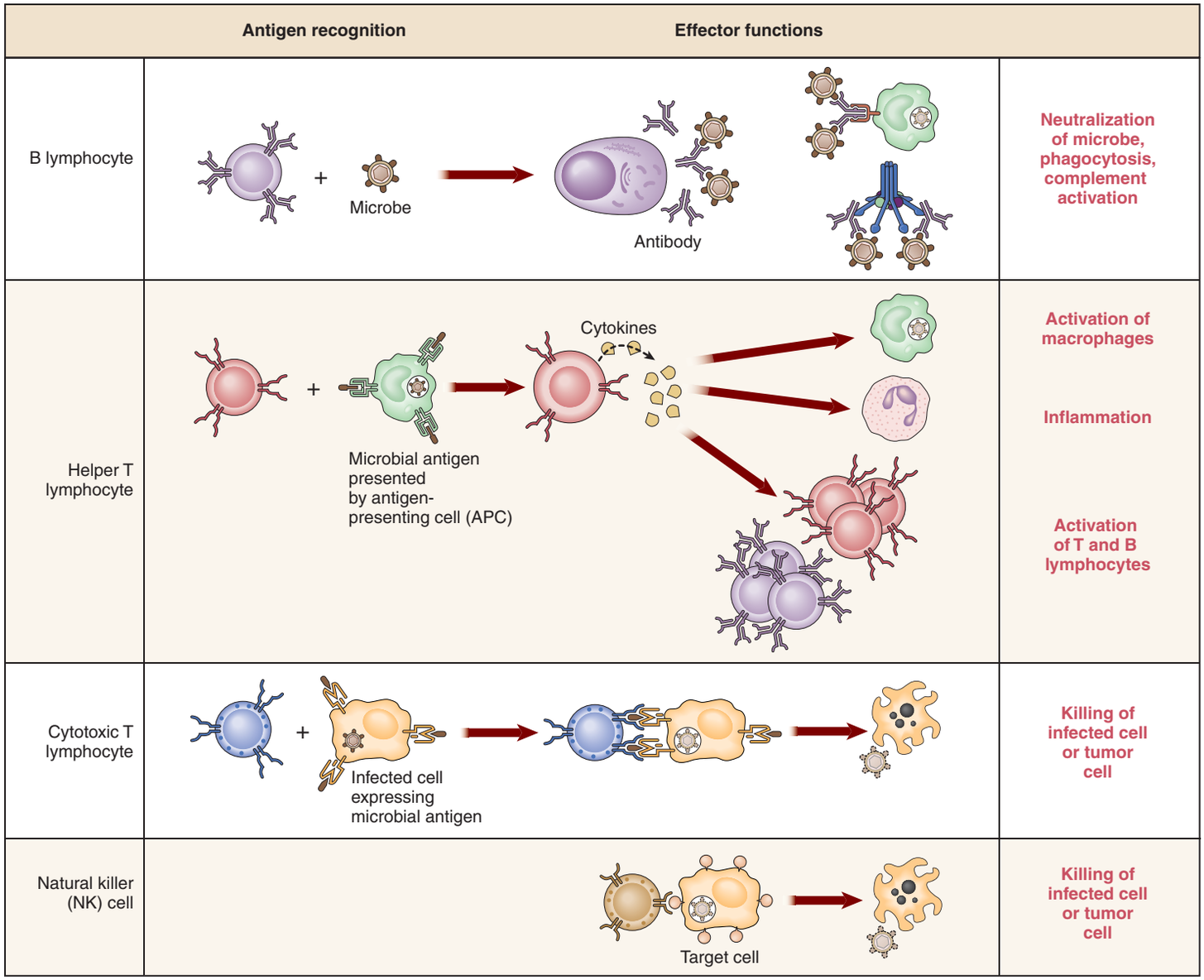


FIGURE 24-27

Lymphocyte functions. This diagram summarizes, in a simplified way, the main functions of the major classes of lymphocytes. B and T lymphocytes participate in adaptive immunity and NK cells participate in innate immunity.

that stimulate B cells and cytotoxic T cells. T_H cytokines also stimulate phagocytes and other leukocytes (Figure 24-27). These cytokines include *interleukin-2 (IL-2)* and *interleukin-4* (IL-4 or B-cell differentiating factor). Like other effector T cells, naïve T_H cells are activated by antigens presented on the surfaces of APCs and form a clone that differentiates into *effector T_H cells* and *memory T_H cells*.

Suppressor T cells, often called *regulator T cells (T-regs)*, act to suppress B-cell differentiation into plasma cells. The antagonistic action allows the immune system to finely tune its antibody-mediated response. Suppressor T cells also regulate other T cells, helping "turn off" an immune response to restore homeostasis, for example. Suppressor T cells help maintain self-tolerance by reducing T-cell reactions to self-antigens. For this reason, researchers are trying to find ways to enhance suppressor T-cell function to treat autoimmunity (see p. 772) or in organ transplants to prevent rejection of donor tissue.

Summarizing briefly, the function of T cells is to produce cell-mediated immunity. They search out, recognize, and bind to appropriate antigens located on the surfaces of cells. This kills the cells—the ultimate function of killer T cells. Usually these are not the body's own normal cells but are cells that have been invaded by viruses, that have become malignant (Box 24-6), or that have been transplanted into the body. Killer T cells therefore function to defend us from viral diseases and cancer, but they also bring about rejection of transplanted tissues or organs. T cells also serve as overall regulators of adaptive immune mechanisms.

| QUICK CHECK |

14. From what structure is the term *T cell* derived?
15. What causes a T cell to become sensitized or activated?
16. How do cytotoxic T cells destroy pathogens?

TYPES OF ADAPTIVE IMMUNITY

B-cell immunity and T-cell immunity, the two major types of adaptive immunity, can be further classified according to the manner in which they develop.

Recall that innate immunity, also called *inborn* or *inherited immunity*, occurs when nonspecific immune mechanisms are put in place by genetic mechanisms during the early stages of human development in the womb (see Table 24-2).

Adaptive immunity, our focus here, is instead a specific kind of resistance that develops after we are born. Acquired immunity may be further classified as either *natural immunity* or *artificial immunity*, depending on how the body is exposed to the antigen.

Natural exposure is not deliberate and occurs in the course of everyday living. We are naturally exposed to many disease-causing agents on a regular basis. Artificial, or deliberate, exposure to potentially harmful antigens is called *immunization*.

Natural and artificial immunity may be "active" or "passive." Active immunity occurs when an individual's own immune system responds to a harmful agent, regardless of whether that agent was naturally or artificially encountered. Passive immunity results when immunity to a disease that has developed in another individual or animal is transferred to an individual who was not previously immune. For example, antibodies in a mother's milk confer passive immunity to her nursing infant (see also Box 24-7). Active

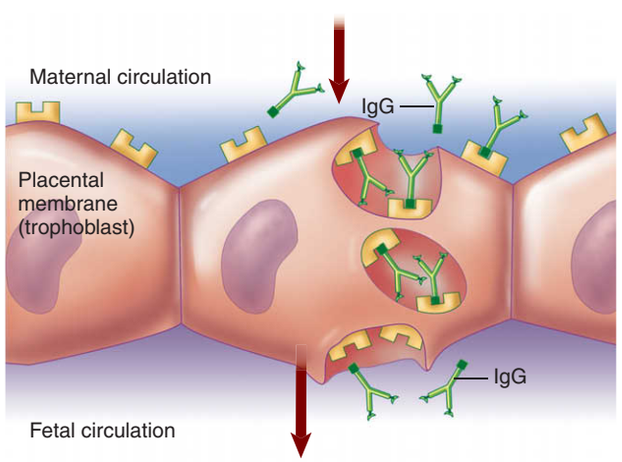
Box 24-7 | FYI

Prenatal Immunity

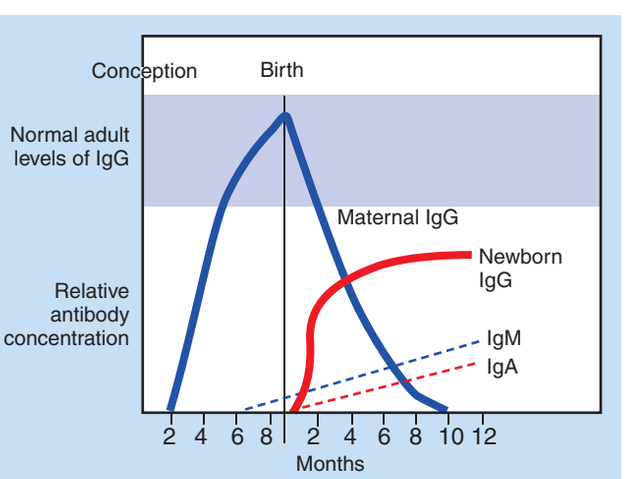
Without direct access to external antigens, it is no wonder that the immune system is not very capable (on its own) of a vigorous defense during its maturation process before birth (prenatal development). However, as part *A* of the figure shows, certain antibodies from the mother (maternal antibodies) can be actively transported across the maternal-fetal blood barrier (trophoblast). Only IgG antibodies in the mother's blood can bind to the receptors, which then trigger endocytosis and transport each IgG antibody across to the fetal bloodstream. This mechanism provides passive natural immunity before and shortly after birth.

Part *B* of the figure shows that at birth, the newborn has adult levels of IgG—but nearly all of it came from the mother (maternal IgG, *black line*). Shortly after birth, the maternal IgG is broken down *(black line)* and replaced with new IgG made by the newborn's own immune system *(purple line)*.

Note also in part *B* of the figure that the concentration of IgM *(broken black line)* is only about 20% of the adult level at birth but steadily increases after birth. IgM reaches adult levels in about 2 years. IgA, an important component of the mucosal immune system (see Box 24-8), also begins to rise at birth. IgA reaches adult levels in just a few months. All three types of antibody are also found in breast milk, providing another avenue of passive immunity after birth.



A



B

A, Transport of antibodies across the placenta. B, Antibody concentrations before and after birth.

immunity generally lasts longer than passive immunity. Passive immunity, although temporary, provides immediate protection. Table 24-4 lists the various forms of adaptive immunity.

SUMMARY OF ADAPTIVE IMMUNITY

Adaptive immunity is specific immunity—that is, it targets specific antigens. Two special types of lymphocytes play a major role in immunity: B cells and T cells. As Figure 24-27 shows, B cells recognize specific antigens and produce specific antibodies (immunoglobulins) to destroy the antigen—antibody-mediated or humoral immunity. T cells recognize antigens presented on cell surfaces to attack infected and abnormal cells in several ways—cell-mediated or cellular immunity.

Adaptive immunity progresses along a pathway of stages outlined in Figure 24-28. First, B cells and T cells recognize a specific antigen. Next, the B and T cells are activated—expanding their population (a clone) and thus producing effector cells and memory cells. Then, the effector cells get to work attacking the source or sources of the antigen. When there are no longer enough antigens to continue stimulating these immune responses, the effector B and effector T cells die off through the process of apoptosis. This represents a return to a homeostatic balance after the immune response. However, a number of memory cells

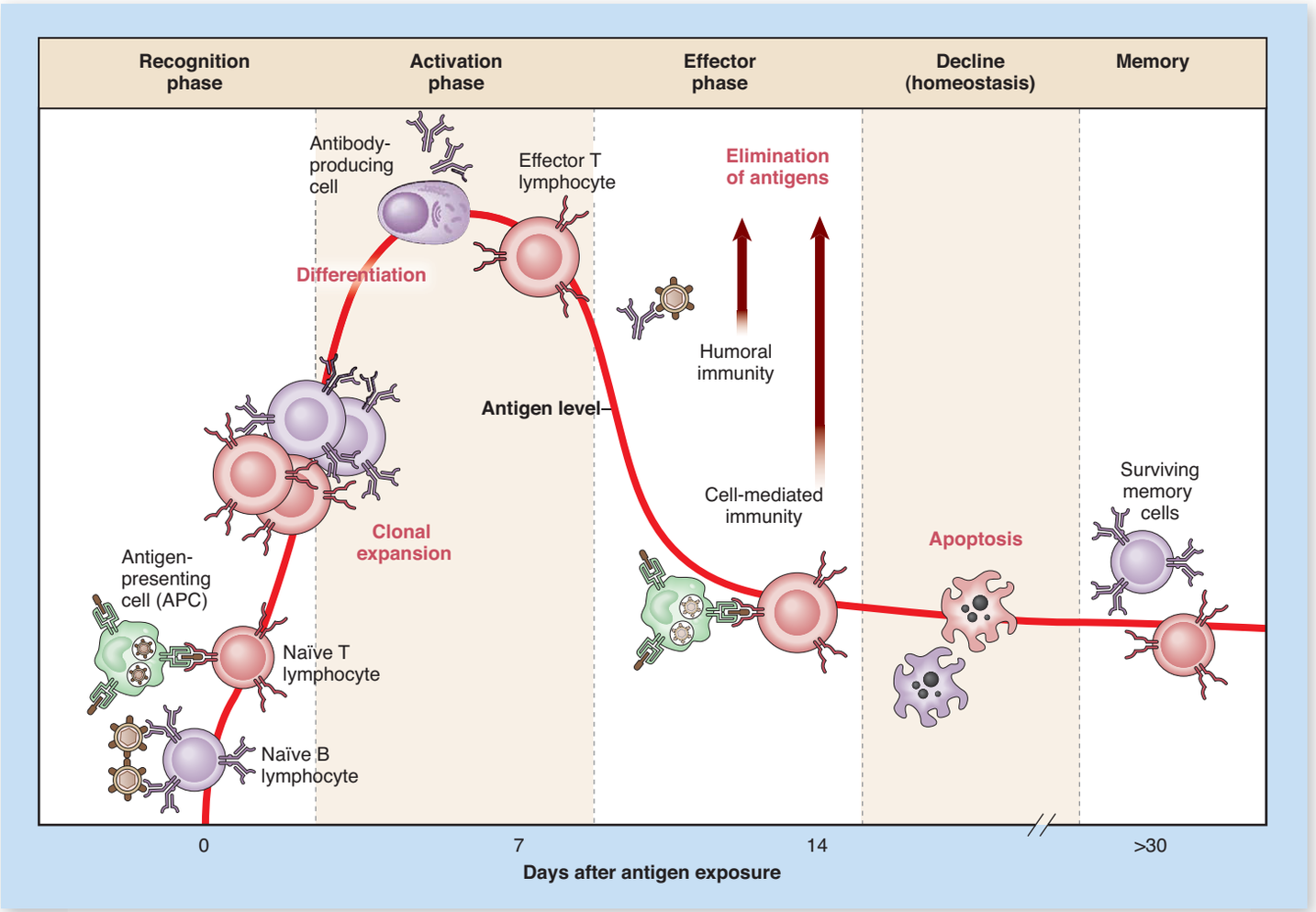
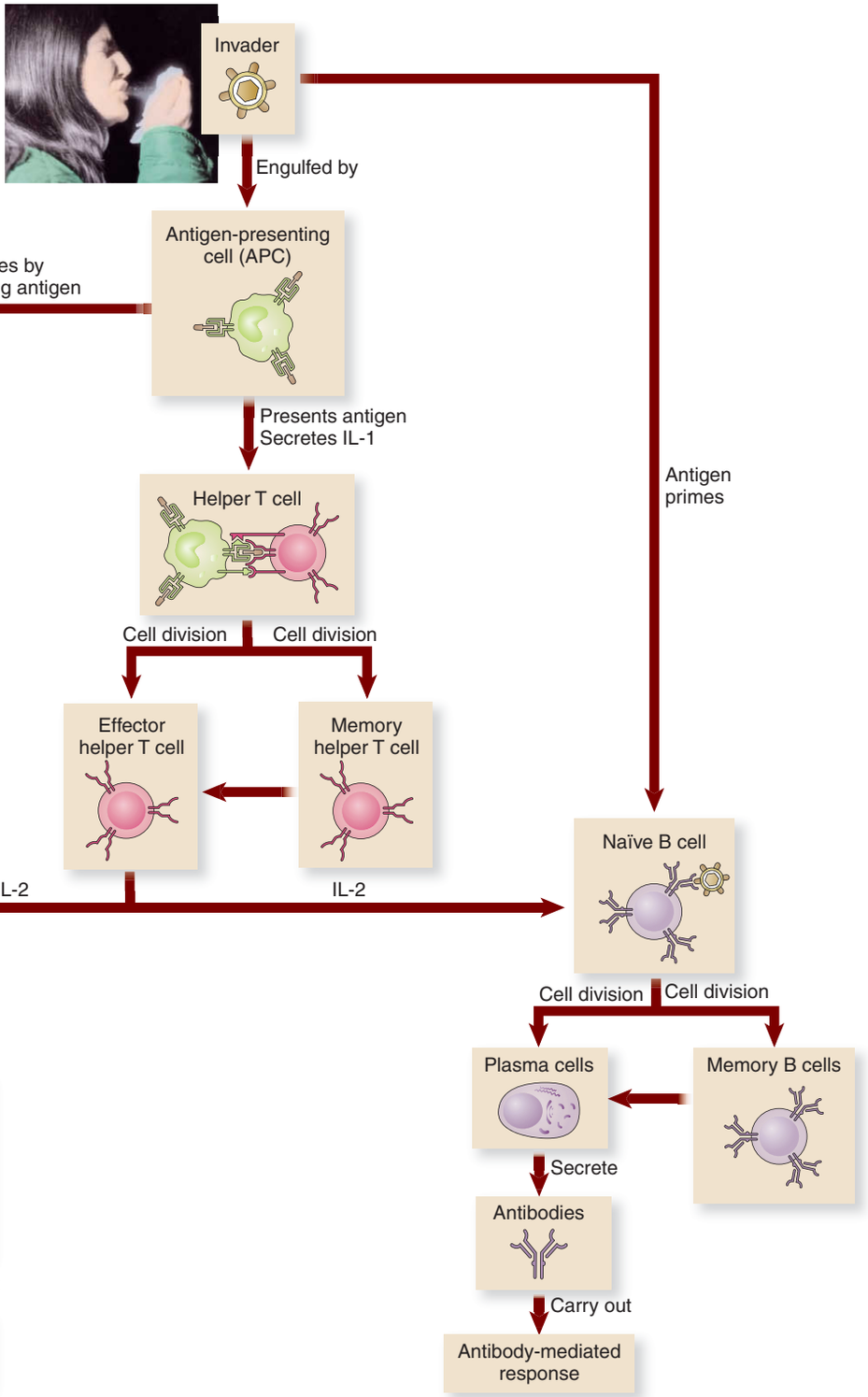


FIGURE 24-28

Stages of adaptive immune response. First, B cells and T cells recognize a specific antigen. Next, the B and T cells are activated—expanding their population (clonal expansion) while differentiating into effector cells and memory cells. Then the effector cells get to work attacking the source or sources of the antigen—humoral (antibody-mediated) immunity and cell-mediated immunity. As antigen levels decline, effector cells die off (apoptosis). Memory cells then remain—ready to quickly engage the antigen again later.

FIGURE 24-29

Summary of adaptive immunity. Flowchart summarizing an example of adaptive immune response when exposed to a microbial pathogen.



remain—ready to quickly engage the antigen again should it reappear later.

Figure 24-29 summarizes the activity of the adaptive immune system in a different way. This figure shows the interaction of different cells and cytokines (in this case, interleukins) in a simplified model of the cooperative nature of the adaptive immune responses.

Box 24-8 explores an additional immune system of the body found in the mucosa.

| QUICK CHECK |

17. What is the difference between inherited and acquired immunity?
18. What is the difference between natural and artificial immunity?
19. What is the difference between active and passive immunity?

Box 24-8 | FYI

Mucosal Immunity

The **mucosal immune system** is a complex system of defense distinct from the systemic (internal) immune system that we have been discussing in most of this chapter. It is an innate and adaptive system that is localized to the mucous barriers of the body: digestive tract, urinary/reproductive tracts, respiratory tract, exocrine ducts, conjunctiva, middle ear, and so on. The immune cells that make up the mucosal immune system are located mainly in or near **mucosal-associated lymphoid tissue (MALT).**

The main functions of the mucosal immune system involve preventing pathogens from colonizing the mucous surfaces of the body, preventing the accidental absorption of antigens from outside the body, and preventing inappropriate or intense responses of the systemic immune system to these external antigens.

As the figure shows, there are several components of the mucosal immune system. Large numbers of IgA antibodies are secreted by effector B cells (plasma cells) into the mucous layer lining the mucosal surfaces of the body. These secretory IgA molecules are dimers (double molecules) that resist being broken down by digestive and other enzymes (see Figure 24-18). Secretory IgA protects against a diverse group of pathogens such as viruses, bacteria, fungi, and animal parasites, thus forming an effective first line of defense.

Besides B cells, T cells also make up part of the mucosal immune system. T cells are located in both the epithelial layer and connective layer (lamina propria) of the mucous membrane, as well as in organized *regional lymphoid nodules* such as the aggregated lymphoid nodules (Peyer patches) of the intestines, the appendix, and the tonsils. Most of these T cells have distinctive structural and functional characteristics that distinguish them from the T cells of the systemic immune system. The mucosal T cells may be activated by antigens presented by APCs such as dendritic cells (DCs) present in the mucous membrane. Some antigens are processed by special *M (membrane) cells* in the surface of the epithelial layer and sent to lymphoid nodules, where APCs can present them to T cells. Interestingly, T cells activated in one mucosal membrane can migrate directly to mucous membranes in other parts of the body. They accomplish this through special "homing" receptors on the surface of each mucosal T cell.

Understanding the mucosal immune system and its cooperation with the systemic (internal) immune system promises to reveal new strategies of immunization. For example, researchers have found that immunizing through the bloodstream activates only the internal (systemic) B cells and T cells. Thus a pathogen would have to actually enter the internal environment before this type of specific immunity could protect us. Immunization of the mucosal lymphocytes, however, can activate both mucosal and systemic lymphocytes—providing a more thorough type of protection. Another advantage of mucosal immunization is that it is easier to administer to patients than immunizations injected under the skin or into the bloodstream. For example, immunization can be delivered by nasal sprays or drops instead of "shots."

Understanding how the mucosal immune system cooperates with microbes within the various microbiomes inhabiting our body's mucous membranes also promises to provide new strategies of preventing or managing infections. For example, scientists have already observed how *probiotic* (protective) bacteria found in yogurt can help stimulate mucosal immunity in ways that prevent infection by pathogenic bacteria.

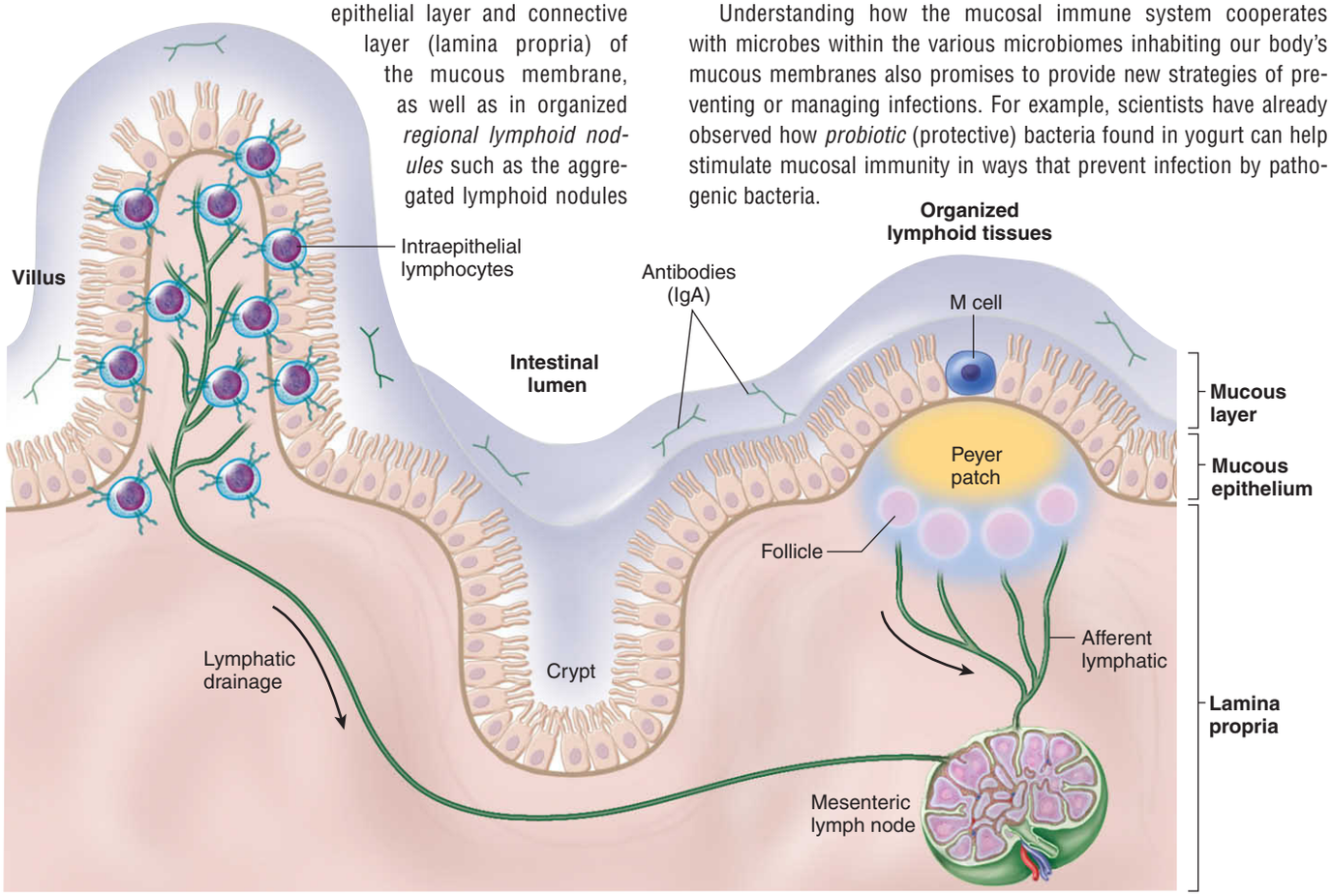


Diagram of the mucosal immune system. Lymphoid tissue associated with mucous membranes is called mucosal-associated lymphoid tissue (MALT).

the BIG picture

Immune System and the Whole Body

The "big picture" of the immune system's role in maintaining the relative constancy of the internal environment is probably easier to "see" than any other system. After all, its agents—antibodies, lymphocytes, and other substances and cells—are everywhere in the body. They even stand guard on the outside surface of the body. Without the defensive activity of the immune system, our internal constancy would be decimated by cancer, infections, and even minor injuries.

In describing the various mechanisms of the immune system, we have used the analogy of a militaristic-style security force. As useful as this analogy might be, it may mislead us into believing that the immune system is a completely independent group of defensive agents. Nothing could be further from the truth.

First of all, evidence shows that the immune system is regulated to some degree by the nervous and endocrine systems—triggering the development of the emerging field of *neuroimmunology.* These systems, as you already know, are in turn influenced by feedback from all parts of the body.

Second, the agents of the immune system are not a separate, distinct group of cells and substances. They include blood cells, skin cells, mucosal cells, brain cells, liver cells, and many other types of cells and their secretions. Thus the immune system is more like a self-defense force made up of ordinary citizens who work shoulder-to-shoulder with military specialists.

MECHANISMS of DISEASE

DISORDERS OF THE IMMUNE SYSTEM

There are two basic mechanisms for disorders of immunity. The immune defenses can either overreact to antigens or fail to react to an antigen and thus produce disease. A few examples of each of these mechanisms are briefly described in the paragraphs that follow.

Hypersensitivity of the Immune System

Hypersensitivity is a type of inappropriate or excessive response of the immune system. The three major types of immune hypersensitivity discussed in the following sections are allergy, autoimmunity, and isoimmunity.

Allergy

The term **allergy** is used to describe hypersensitivity of the immune system to relatively harmless environmental antigens. Antigens that trigger an allergic response are often called **allergens** (AL-er-jens). One in six Americans has a genetic predisposition to an allergy of some kind.

Immediate allergic responses involve antigen-antibody reactions, mainly IgE. Before such a reaction occurs, a susceptible person must be exposed repeatedly to an allergen—triggering the production of antibodies. After a person is thus *sensitized,* exposure to an allergen causes antigen-antibody reactions that trigger the release of histamine, kinins, and other inflammatory substances. These responses usually cause typical allergy symptoms such as runny nose, conjunctivitis, and *urticaria* (hives). In some cases, however, these substances may cause constriction of the airways, relaxation of blood vessels, and irregular heart rhythms that can progress to a life-threatening condition called **anaphylactic shock** (see Chapter 22, p. 714). Drugs called **antihistamines** are sometimes used to relieve the symptoms of this type of allergy.

Delayed allergic responses, on the other hand, involve cell-mediated immunity. In **contact dermatitis,** for example, T cells trigger events that lead to local skin inflammation a few hours or days after initial exposure to an antigen. Exposure to poison ivy, soaps, and certain cosmetics may cause contact dermatitis in this manner. Hypersensitive individuals may use **hypoallergenic** products (products without common allergens) to avoid such allergic reactions.

Autoimmunity

Autoimmunity is an inappropriate and excessive response to self-antigens. Disorders that result from autoimmune responses are called **autoimmune diseases.** Table 24-5 gives examples of autoimmune diseases. Self-antigens are molecules that are native to a person's body and that are used by the immune system to identify components of "self." In autoimmunity, the immune system inappropriately attacks these antigens.

A common autoimmune disease is **systemic lupus erythematosus (SLE),** or simply *lupus.* Lupus is a chronic inflammatory disease that affects many tissues in the body: joints, blood vessels, kidney, nervous system, and skin. The name *lupus erythematosus* refers to the red rash that often develops on the faces of those afflicted with SLE. The "systemic" part of the name comes from the fact that the disease affects many systems throughout the body. The systemic nature of SLE results from the production of IgG antibodies against a person's own DNA.

Isoimmunity

Isoimmunity is a normal but often undesirable reaction of the immune system to antigens from a different individual of the same

TABLE 24-5 Examples of Autoimmune Diseases

DISEASE	POSSIBLE SELF-ANTIGEN	DESCRIPTION
Addison disease	Surface antigens on adrenal cells	Hyposecretion of adrenal hormones, resulting in weakness, reduced blood sugar, nausea, loss of appetite, and weight loss
Cardiomyopathy	Cardiac muscle	Disease of cardiac muscle (i.e., the myocardium), resulting in loss of pumping efficiency (heart failure)
Diabetes mellitus (type 1)	Pancreatic islet cells, insulin, insulin receptors	Hyposecretion of insulin by the pancreas, resulting in extremely elevated blood glucose levels (in turn causing a host of metabolic problems, even death if untreated)
Glomerulonephritis	Blood antigens that form immune complexes that deposit in kidney	Disease of the filtration apparatus of the kidney (renal corpuscle), resulting in fluid and electrolyte imbalance and possibly total kidney failure and death
Graves disease (type of hyperthyroidism)	TSH receptors on thyroid cells	Hypersecretion of thyroid hormone and resulting increase in metabolic rate
Hemolytic anemia	Surface antigens on RBCs	Condition of low RBC count in the blood resulting from excessive destruction of mature RBCs (hemolysis)
Hypothyroidism	Antigens in thyroid cells	Hyposecretion of thyroid hormone in adulthood, causing decreased metabolic rate and characterized by reduced mental and physical vigor, weight gain, hair loss, and edema
Multiple sclerosis (MS)	Antigens in myelin sheaths of nervous tissue	Progressive degeneration of myelin sheaths, resulting in widespread impairment of nerve function (especially muscle control)
Myasthenia gravis	Antigens at neuromuscular junction	Muscle disorder characterized by progressive weakness and chronic fatigue
Pernicious anemia	Antigens on parietal cells, intrinsic factor	Abnormally low RBC count resulting from the inability to absorb vitamin B_{12}, a substance critical to RBC production
Reproductive infertility	Antigens on sperm or tissue surrounding ovum (egg)	Inability to produce offspring (in this case, resulting from destruction of gametes)
Rheumatic fever	Cardiac cell membranes (cross reaction with group A streptococcal antigen)	Rheumatic heart disease; inflammatory cardiac damage (especially to the endocardium/valves)
Rheumatoid arthritis (RA)	Collagen	Inflammatory joint disease characterized by synovial inflammation that spreads to other fibrous tissues
Systemic lupus erythematosus (SLE)	Numerous	Chronic inflammatory disease with widespread effects and characterized by arthritis, a red rash on the face, and other signs
Ulcerative colitis	Mucous cells of colon	Chronic inflammatory disease of the colon characterized by watery diarrhea containing blood, mucus, and pus

RBC, Red blood cell; *TSH,* thyroid-stimulating hormone.

species. Isoimmunity is important in two situations: pregnancy and tissue transplants.

During pregnancy, antigens from the fetus may enter the mother's blood supply and sensitize her immune system. Antibodies that are formed as a result of this sensitization may enter the fetal circulation and cause an inappropriate immune reaction. One example, erythroblastosis fetalis, was discussed in Chapter 20. Other pathological conditions may also be caused by damage to developing fetal tissues resulting from attack by the mother's immune system. Examples include congenital heart defects, Graves disease, and myasthenia gravis.

Tissue or organ **transplants** are medical procedures in which tissue from a donor is surgically *grafted* into the body. For example, skin grafts are often performed to repair damage caused by burns. Donated whole blood tissue is often transfused into a recipient after massive hemorrhaging. A kidney is sometimes removed from a living donor or cadaver and grafted into a person suffering from kidney failure. Unfortunately, the immune system sometimes reacts against foreign antigens in the grafted tissue, causing what is often called a **rejection syndrome.** The antigens commonly involved in transplant rejection are called MHC proteins—or **human leukocyte antigens (HLAs).**

Rejection of grafted tissues can occur in two ways: (1) **host-versus-graft rejection**—the recipient's immune system recognizes foreign HLAs and attacks them, destroying the donated tissue, and (2) **graft-versus-host rejection**—the donated tissue (e.g., bone marrow) attacks the recipient's HLAs, destroying tissue throughout the recipient's body. Graft-versus-host rejection may lead to death.

There are two ways to prevent rejection syndrome. One strategy is called *tissue typing* in which HLAs and other antigens of a potential donor and recipient are identified. If they match, tissue rejection is unlikely to occur. Another strategy is the use of **immunosuppressive drugs** in the recipient. Immunosuppressive drugs such as *cyclosporine* and *prednisone* suppress the immune system's ability to attack the foreign antigens in the donated tissue.

Deficiency of the Immune System

Immune deficiency, or *immunodeficiency*, is the failure of immune system mechanisms to defend against pathogens. Immune system failure usually results from disruption of lymphocyte (B cell or T cell) function. The chief characteristic of immune deficiency is the development of unusual or recurring severe infections or cancer. Although immune deficiency by itself does not cause death, the resulting infections or cancer can.

The two broad categories of immune deficiencies, based on the mechanism of lymphocyte dysfunction, are *congenital* and *acquired*. Each of these types is outlined in the following discussion.

Congenital Immune Deficiency

Congenital immune deficiency, which is rare, results from improper lymphocyte development before birth. Depending on which stage of the development of stem cells, B cells, or T cells the defect occurs, different diseases can result. For example, improper B-cell development can cause insufficiency or absence of antibodies in the blood. If stem cells are missing or are unable to grow properly, a condition called **severe combined immune deficiency (SCID)** occurs. In most forms of SCID, both humoral immunity and cell-mediated immunity are defective. Temporary immunity can be imparted to children with SCID by injecting them with a preparation of antibodies (gamma globulin). Bone marrow transplants, which replace the defective stem cells with healthy donor cells, have proven effective in treating some cases of SCID.

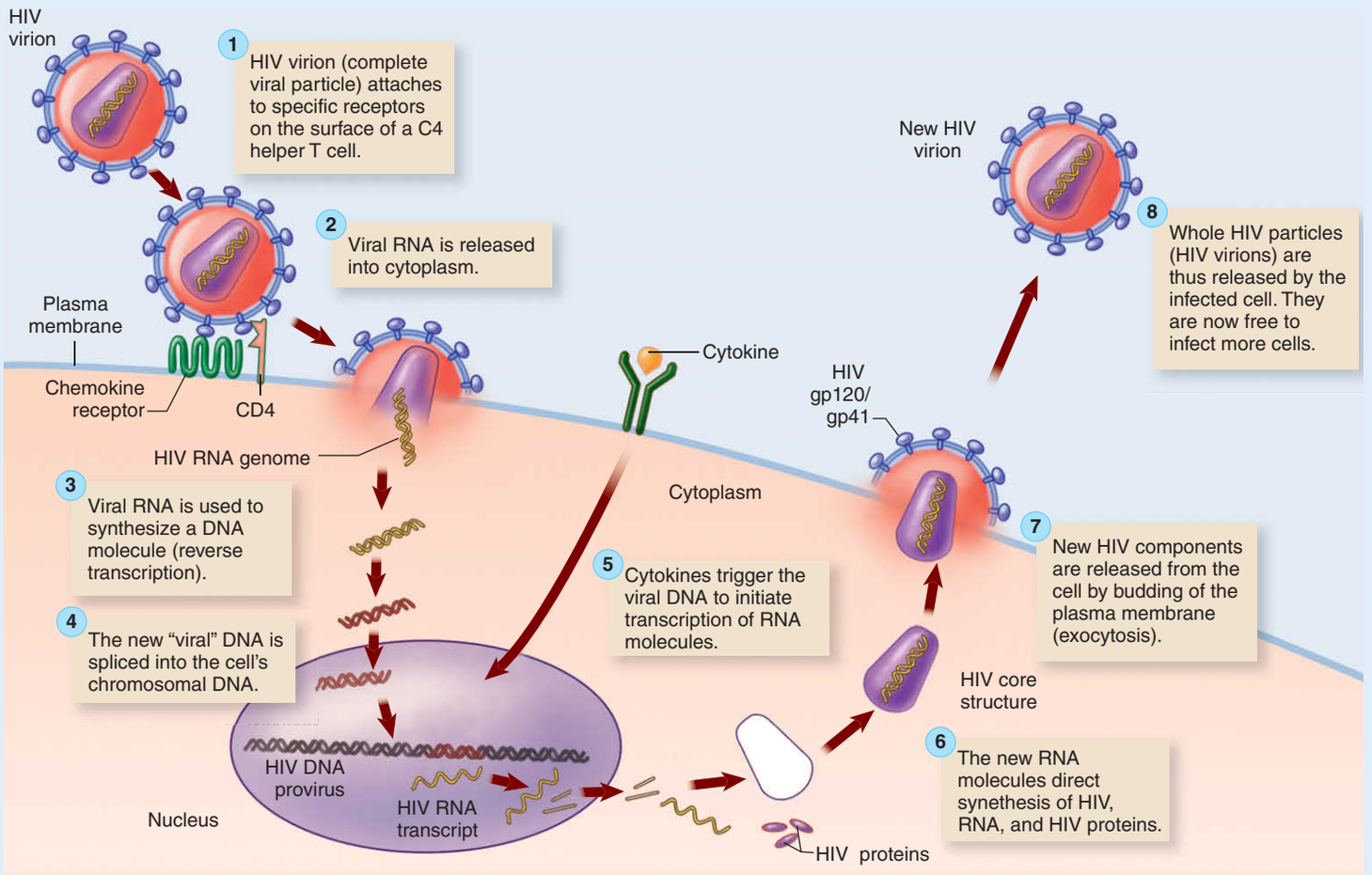
Acquired Immune Deficiency

Acquired immune deficiency develops after birth (and is not related to genetic defects). Many factors can contribute to acquired immune deficiency: nutritional deficiencies, immunosuppressive drugs or other medical treatments, trauma, stress, and viral infection.

One of the best known examples of acquired immune deficiency is **acquired immune deficiency syndrome (AIDS).** AIDS affects millions of people worldwide. This syndrome is caused by the **human immunodeficiency virus,** or **HIV.** HIV, a retrovirus, contains RNA that produces its own DNA inside infected cells. The viral DNA often becomes part of the cell's DNA (Figure 24-30). When the viral DNA is activated by cytokines, it directs the cell to synthesize viral RNA and viral proteins—producing new retroviruses. HIV thus "steals" raw materials from the cell. When this

FIGURE 24-30

Mechanisms of HIV infection. HIV is an RNA-containing virus *(retrovirus)* that appears to infect T cells by way of the mechanism described in the diagram and simplified into 8 steps.



occurs in the CD4 subset of T cells (helper T cells), the cell is destroyed and immunity is seriously impaired.

As the T cell dies, it releases new retroviruses that can spread the HIV infection. As the HIV infection progresses, more and more CD4 lymphocytes are lost. This change in CD4 lymphocyte number is one of the principal clinical methods for monitoring AIDS (Figure 24-31, *A*).

HIV can invade several types of human cells, including brain cells. However, when CD4 T-cell (helper T-cell) function is impaired, infectious organisms and cancer cells can grow and spread much more easily than normal. Infections and tumors that rarely occur in healthy people, such as *Pneumocystis jiroveci pneumonia* (a protozoal infection) and *Kaposi sarcoma* (a type of skin cancer), frequently are seen in AIDS patients. Because their immune system is deficient, AIDS patients usually die from one of these infections or cancers.

After they are infected with HIV, T cells may not show signs of AIDS for years. This is because the immune system can hold the infection at bay for a long time before finally succumbing to it. Figure 24-31, *B*, shows the progression of HIV infection to AIDS.

There are several strategies for controlling AIDS and related conditions. Many agencies are trying to slow the spread of AIDS by educating people about how to avoid contact with the HIV retrovirus. HIV is spread by direct contact with body fluids, so preventing such contact reduces HIV transmission. Sexual relations, blood transfusions, breastfeeding, and intravenous use of contaminated needles are the usual modes of HIV transmission.

Most patients with AIDS have an abundance of antibodies against the HIV in their blood. This is another important clinical test for diagnosing and monitoring AIDS patients (frequently referred to as a *Western blot*). Unfortunately, for the majority of patients, the antibody response to HIV is not sufficient to suppress the disease. However, a few patients who demonstrated a strong antibody response were able to shed the virus completely. Studies of these few cases are fueling an intensive, worldwide research effort to develop a vaccine for treating AIDS. The fast rate at which these viruses mutate (change their protein structure), however, is making vaccine development an extremely difficult challenge.

A drug called Fuzeon (enfuvirtide) can disrupt the HIV particle's ability to fuse with a host cell—the first drug in a class called *fusion inhibitors*. Inhibition of fusion can stop HIV from infecting cells that are not yet infected.

A way to inhibit symptoms of the disease is by means of chemicals such as zidovudine (Azidothymidine [AZT]) and ritonavir (Norvir) that block HIV's ability to reproduce within infected cells.

A breakthrough in the treatment of HIV occurred when it was discovered that a "cocktail" of several antiviral drugs working together greatly reduces the number of virus particles in a patient's blood. More than 100 such compounds in various combinations are being evaluated for use in halting the progress of HIV infections. Currently, the recommended treatment for HIV infection is a combination of at least three medications in an individually tailored regimen called *highly active antiretroviral therapy (HAART)*.

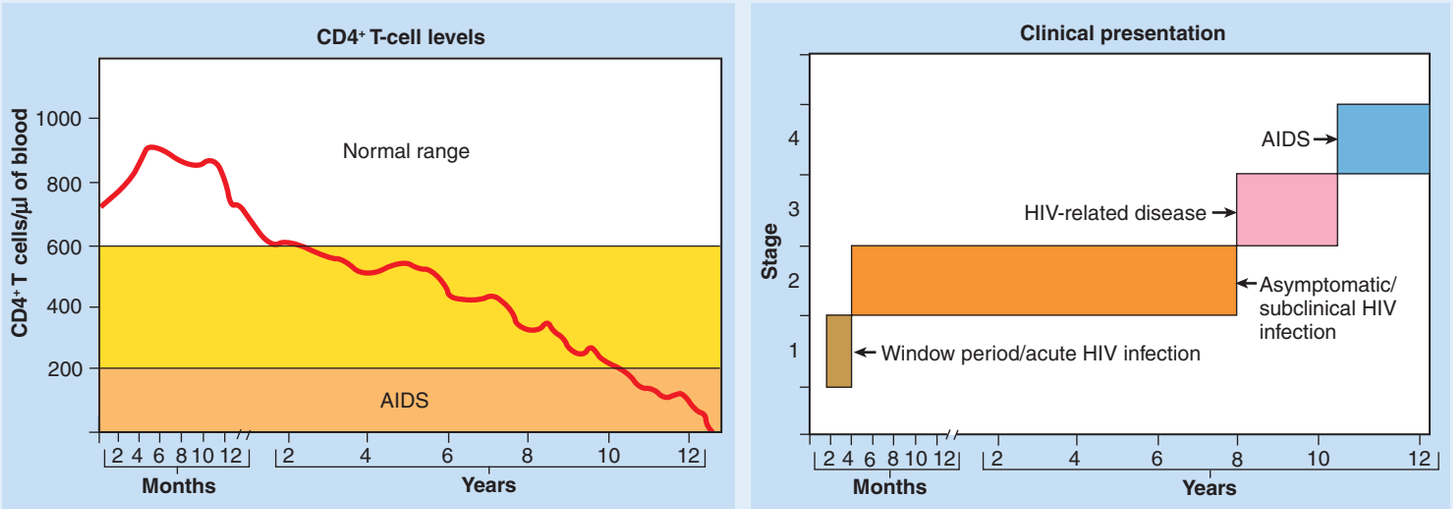


FIGURE 24-31

Clinical progression of HIV/AIDS. A, Changing numbers of CD4 T cells as an HIV infection progresses to AIDS. **B,** Progression from initial HIV infection to full-blown AIDS is usually described in four stages: (1) Acute viral infection with common viral symptoms; called "window period" because anti-HIV antibodies are not yet detectable by laboratory tests. (2) Subclinical stage in which there are often no (or minor) symptoms—but the virus is replicating. (3) HIV-related disease, with symptoms of acute viral infection and high levels of anti-HIV antibodies found in laboratory tests. (4) AIDS, including opportunistic infections and cancers.

LANGUAGE OF SCIENCE *(continued from p. 745)*

cellular immunity
(SELL-yoo-lar i-MYOO-ni-tee)
[*cell-* **storeroom**, *-ular* **relating to**, *immun-* **free**, *-ity* **state**]

chemotactic factor
(kee-moh-TAK-tik)
[*chemo-* **chemical**, *-tact-* **movement**, *-ic* **relating to**]

chemotaxis
(kee-moh-TAK-sis)
[*chemo-* **chemical**, *-taxis* **movement**]

clone
(klohn)
[*clon* **a plant cutting**]

combining site

complement
[*comple-* **complete**, *-ment* **result of action**]

cytokine
(SYE-toh-kyne)
[*cyto-* **cell**, *-kine* **movement**]

cytolysis
(sye-TOL-i-sis)
[*cyto-* **cell**, *-lysis* **loosening**]

cytotoxic T cell
(sye-toh-TOK-sik)
[*cyto-* **cell**, *-toxic* **poison**, *T* **thymus gland**, *cell* **storeroom**]

dendritic cell (DC)
(DEN-dri-tik)
[*dendrit-* **tree branch**, *-ic* **relating to**, *cell* **storeroom**]

diapedesis
(dye-ah-peh-DEE-sis)
[*dia-* **through**, *-pedesis* **an oozing**]

effector B cell
[*effect-* **accomplish**, *-or* **agent**, *B* **bursa-equivalent tissue**, *cell* **storeroom**]

effector cell

effector T cell
[*effect-* **accomplish**, *-or* **agent**, *T* **thymus gland**, *cell* **storeroom**]

fever
(FEE-ver)

helper T cell (TH cell)
[*T* **thymus gland**, *cell* **storeroom**]

human leukocyte antigen (HLA)
(LOO-koh-syte AN-ti-jen)
[*leuko-* **white**, *-cyte* **cell**, *anti-* **against**, *-gen* **produce**]

humoral immunity
(HYOO-mor-al i-MYOO-ni-tee)
[*humor-* **liquid**, *-al* **relating to**, *immun-* **free**, *-ity* **state**]

immunoglobulin (Ig)
(i-myoo-noh-GLOB-yoo-lin)
[*immuno-* **free (immunity)**, *-glob-* **ball**, *-ul-* **small**, *-in* **substance**]

immunological synapse (IS)
(i-myoo-no-LOJ-ikal SIN-aps)
[*immuno-* **free (immunity)**, *-log-* **words (study of)**, *-ical* **relating to**, *syn-* **together**, *-aps-* **join**]

inflammatory response
(in-FLAM-ah-toh-ree)
[*inflamm-* **set afire**, *-ory* **relating to**]

innate immunity
(IN-ayt i-MYOO-ni-tee)
[*innat-* **inborn**, *immun-* **free**, *-ity* **state**]

interferon (IFN)
(in-ter-FEER-on)
[*inter-* **between**, *-fer-* **strike**, *-on* **substance**]

interleukin (IL)
(in-ter-LOO-kin)
[*inter-* **between**, *-leuk-* **white (blood cell)**, *-in* **substance**]

lymphotoxin
(lim-foh-TAWK-sin)
[*lympho-* **water (lymphocyte)**, *-tox-* **poison**, *-in* **substance**]

macrophage
(MAK-roh-fayj)
[*macro-* **large**, *-phage* **eat**]

major histocompatibility complex (MHC)
[*histo-* **tissue**, *-compatibil-* **agreeable**, *-ity* **state**, *complex* **embrace**]

membrane attack complex (MAC)
[*complex* **embrace**]

memory B cell
[*B* **bursa-equivalent tissue**, *cell* **storeroom**]

memory cell

memory T cell
[*T* **thymus gland**, *cell* **storeroom**]

mucosal-associated lymphoid tissue (MALT)
(myoo-KOH-sal-ah-soh-she-AYT-ed LIM-foyd)
[*mucos-* **slime or mucus**, *-al* **relating to**, *associa-* **unite**, *-ate* **process**, *lymph-* **water**, *-oid* **like**, *tissue-* **fabric**]

mucosal immune system
(myoo-KOH-sal i-MYOON)
[*mucos-* **slime or mucus**, *-al* **relating to**, *immun-* **free**]

naïve
(nye-EVE)
[*naïve* **natural**]

naïve B cell
(nye-EVE)
[*naïve* **natural**, *B* **bursa-equivalent tissue**, *cell* **storeroom**]

natural killer (NK) cell

nonself

nonspecific immunity
(non-speh-SIF-ik i-MYOO-ni-tee)
[*non-* **not**, *-specif-* **form or kind**, *-ic* **relating to**, *immun-* **free**, *-ity* **state**]

pavementing

phagocytosis
(fag-oh-sye-TOH-sis)
[*phago-* **eating**, *-cyt-* **cell**, *-osis* **condition**]

plasma cell
(PLAZ-mah)
[*plasma* **something molded (blood plasma)**, *cell* **storeroom**]

pus

self

self-tolerance

species resistance
(SPEE-sheez ree-SIS-tens)
[*species* **form or kind**]

specific immunity
(i-MYOO-ni-tee)
[*specif-* **form or kind**, *-ic* **relating to**, *immun-* **free**, *-ity* **state**]

suppressor T cell
[*suppress-* **press down**, *-or* **agent**, *T* **thymus gland**, *cell* **storeroom**]

T cell
[*T* **thymus gland**, *cell* **storeroom**]

thymocyte
(THY-moh-syte)
[*thymo-* **thyme flower (thymus gland)**, *-cyte* **cell**]

LANGUAGE OF MEDICINE

acquired immune deficiency syndrome (AIDS)
(ah-KWYRD i-MYOON deh-FISH-en-see)
[*acquire* **obtain**, *immun-* **free**, *syn-* **together**, *-drome* **running or (race)course**]

allergen
(AL-er-jen)
[*all-* **other**, *-erg-* **work**, *-gen* **produce**]

allergy
(AL-er-jee)
[*all-* **other**, *-erg-* **work**, *-y* **state**]

alpha-fetoprotein (AFP)
(AL-fah-fee-toh-PRO-teen)
[*alpha-* **first letter of Greek alphabet (α)**, *feto-* **offspring (fetus)**]

anaphylactic shock
(an-ah-fih-LAK-tik)
[*ana-* **without**, *-phylact-* **protection**, *-ic* **relating to**]

antibody titer
(AN-ti-bod-ee TYE-ter)
[*anti-* **against**, *titer* **proportion (in a solution)**]

antihistamine
(an-ti-HIS-tah-meen)
[*anti-* **against**, *-histo-* **tissue**, *-amine* **ammonia compound**]

autoimmune diseases
(aw-toh-i-MYOON)
[*auto-* **self**, *-immun-* **free (immunity)**]

booster shot

CA-125
[*C* **cancer**, *A* **antigen**]

carcinoembryonic antigen (CEA)
(kar-sin-oh-em-bree-AHN-ik AN-ti-jen)
[*carcino-* **cancer**, *-em-* **in**, *-bryo-* **fill to bursting**, *-ic* **relating to**, *anti-* **against**, *-gen* **produce**]

CD system
[*C* **cluster**, *D* **differentiation**]

contact dermatitis
(KON-takt der-mah-TYE-tis)
[*derma-* **skin**, *-itis* **inflammation**]

graft-versus-host rejection
host-versus-graft rejection

human immunodeficiency virus (HIV)
(i-myoono-deh-FISH-en-see VYE-rus)
[*immuno-* **free (immunity)**, *virus* **poison**]

hypersensitivity
(hye-per-SEN-sih-tiv-i-tee)
[*hyper-* **excessive**, *sensitiv-* **able to feel**, *-ity* **state**]

hypoallergenic
(hye-poh-AL-er-jen-ik)
[*hypo-* **under or below**, *-aller-* **other**, *-gen-* **produce**, *-ic* **relating to**]

immune deficiency
(i-MYOON deh-FISH-en-see)
[*tox-* **poison**, *-oid* **like**]

immunosuppressive drugs
(i-myoo-no-soo-PRES-iv)
[*immuno-* **free (immunity)**, *-suppress-* **press down**, *-ive* **relating to**]

isoimmunity
(eye-soh-i-MYOO-ni-tee)
[*iso-* **equal**, *-immun-* **free**, *-ity* **state**]

monoclonal antibody (MAb)
(mon-oh-KLONE-al AN-ti-bod-ee)
[*mono-* **single**, *-clon-* **plant cutting**, *-al* **relating to**, *anti-* **against**]

nanobody
(NAN-oh-bod-ee)
[*nano* **small**]

prostate-specific antigen (PSA)
(PROSS-tayt speh-SIF-ik AN-ti-jen)
[*pro-* **before**, *-stat-* **set or place (prostate gland)**, *specif-* **form**, *-ic* **relating to**, *anti-* **against**, *-gen* **produce**]

rejection syndrome
(reh-JEK-shun SIN-drohm)
[*syn-* **together**, *-drome* **running or (race)course**]

severe combined immune deficiency (SCID)
(i-MYOON deh-FISH-en-see)
[*immun-* **free**]

systemic lupus erythematosus (SLE)
(sis-TEM-ik LOO-pus er-i-them-ah-TOH-sus)
[*lupus* **wolf**, *erythema-* **redness**, *-osus* **condition**]

Toll-like receptor (TLR)
[*Toll-* **weird or amazing**, *-like*, *recept-* **receive**, *-or* **agent**]

toxoid
(TOK-soyd)
[*immun-* **free (immunity)**]

transplant

tumor marker
(TOO-mer)
[*tumor* **swelling**]

tumor-specific antigen
(TOO-mer-speh-SIF-ik AN-ti-jen)
[*tumor* **swelling**, *specif-* **form**, *-ic* **relating to**, *anti-* **against**, *-gen* **produce**]

vaccination
(vak-si-NAY-shun)
[*vaccin-* **cow (cowpox)**, *-ation* **process**]

CASE study



Kostas remembered getting the flu (influenza) last winter: coughing, fever, achiness all over his body, watery eyes, and fatigue. He felt awful! But he argued, "What's the point of a flu shot, when all it does is give you the flu?" Kostas did not understand that the flu vaccine is a combination of several *inactivated* (killed) viruses injected into muscles in your body (usually in your arm). No live viruses are injected. So, as for the injected form of the vaccine "causing" the flu—people who claim that could already have been exposed to a flu virus before the vaccination or could have been exposed to one of the strains not included in that year's vaccine. Some people produce a mild immune reaction that can be mistaken for the flu. In the end, Kostas relented and got his flu shot!

1. Which of Kostas' cells will respond to the flu antigens introduced by the vaccine?
   a. Erythrocytes
   b. Thrombocytes
   c. Lymphocytes
   d. Platelets

2. Which specific cell types will begin producing antibodies to the antigens?
   a. Z cells
   b. T cells
   c. A cells
   d. B cells

3. Which antibody is primarily involved in this response to vaccine?
   a. IgM
   b. IgE
   c. IgG
   d. IgD

4. Kostas' fever during the previous winter's flu was caused by the release of _____, molecules that help increase his body's "set point" to higher than normal.
   a. Vulcanogens
   b. Histamine
   c. Pyrogens
   d. Nanobodies

5. What would you call the specific type of immunity Kostas developed as a result of the vaccination?
   a. Natural active immunity
   b. Artificial active immunity
   c. Natural passive immunity
   d. Artificial passive immunity

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

INTRODUCTION

A. The immune system protects against assaults on the body
   1. External assaults include microorganisms—protozoans, bacteria, and viruses
   2. Internal assaults—abnormal cells reproduce and form tumors that may become cancerous and spread

ORGANIZATION OF THE IMMUNE SYSTEM

A. Immune system continually patrols and protects the body
B. Identification of cells and other particles
   1. Markers, or antigens, are unique molecules recognized by the immune system
   2. Self markers—molecules on the surface of our cells that are unique to an individual, thus identifying the cell as "self" to the immune system
   3. Nonself markers—molecules on the surface of foreign or abnormal cells or particles that identify the particle as "nonself" to the immune system
   4. Self-tolerance—the ability of our immune system to attack abnormal or foreign cells but spare our own normal cells
C. Two major categories of immune mechanisms—innate immunity and adaptive immunity (Figure 24-1; Table 24-1)
   1. Innate immunity provides a general, nonspecific defense against anything that is not "self"
   2. Adaptive immunity acts as a specific defense against specific threatening agents
   3. Primary cells of innate immunity—epithelial barrier cells, phagocytes (neutrophils, macrophages, DCs), and natural killer cells; chemicals used in innate immunity—complement and interferon
   4. Primary cells of adaptive immunity—lymphocytes called T cells and B cells
   5. Cytokines—chemicals released from cells to promote or trigger innate and adaptive immune responses (e.g., interleukin, interferon, leukotriene)
   6. Other chemicals (e.g., complement, other enzymes, histamine) also play regulatory roles in immunity

INNATE IMMUNITY (TABLE 24-2)

A. Species resistance—genetic characteristics of an organism or species defend against pathogens
B. Mechanical and chemical barriers—first line of defense (Figure 24-2)
   1. Internal environment of the body is protected by a barrier formed by the skin and the mucous membranes
   2. Skin and mucous membranes provide additional immune mechanisms—sebum, mucus, enzymes, and hydrochloric acid in the stomach
C. Inflammation and fever—second line of defense (Figure 24-3)
   1. Inflammatory response—tissue damage elicits responses to counteract injury and promote normalcy
      a. Inflammation mediators include histamine, kinins, prostaglandins, and related compounds (Figure 24-4)
      b. Chemotactic factors—substances that attract white blood cells to area of injury in a process called *chemotaxis* (Figure 24-6)
      c. Characteristic signs of inflammation—heat, redness, pain, and swelling
      d. Systemic inflammation—occurs from a body-wide inflammatory response
   2. Fever—abnormally high body temperature triggered by inflammation mediators
      a. Triggered in SIRS (systemic inflammatory response syndrome) and other events such as viral infections, tumors, allergies
      b. Pyrogens released from damaged tissues (endogenous) or introduced into the body (exogenous)
         (1) Promote prostaglandin (PG) production
         (2) PGs reset the hypothalamic "thermostat" to a higher temperature
         (3) Aspirin and other COX inhibitors interfere with PG production
      c. Fever is thought to increase immune function and inhibit pathogens
D. Phagocytosis—ingestion and destruction of microorganisms or other small particles by phagocytes (Figure 24-7)
   1. Phagocytes—many types capable of phagocytosis (Table 24-3)
   2. Antigen-presenting cells (APCs)—phagocytes that ingest foreign particles, isolate protein segments (peptides), and display them as antigens on their surface to trigger an immune response when recognized by a specific (adaptive) immune cell
      a. Neutrophil—most numerous phagocyte; usually first to arrive at site of injury; migrates out of bloodstream during diapedesis; forms pus
      b. Diapedesis—process by which immune cells squeeze through the wall of a blood vessel to get to the site of injury or infection (Figure 24-5)
      c. Macrophage—large phagocytic monocyte cells that grow to several times original size after migrating out of bloodstream; important APCs
      d. Dendritic cell (DC)—type of APC with long branches or extensions (Figure 24-8)
      e. Phagocytes often identified by location—histiocytes in connective tissue, microglia in nervous system, and Kupffer cells in liver
E. Natural killer (NK) cells—lymphocytes that kill tumor cells and cells infected by viruses (Figure 24-9)
   1. Method of recognizing abnormal or nonself cells—target cell is killed if killer-inhibiting receptor on NK cell does not bind to a proper MHC surface protein

2. Method of killing cells—lysing cells by damaging plasma membranes

F. Interferon (IFN)—protein synthesized and released into circulation by certain cells if invaded by viruses to signal other nearby cells to enter a protective antiviral state

G. Complement—group of enzymes that produce a cascade of reactions resulting in a variety of immune responses (Figure 24-10)
1. Lyse cells when activated by either adaptive or innate mechanisms
2. Opsonization—process that marks cells for destruction by phagocytes
3. Variety of other immune responses (Figure 24-10)

H. Toll-like receptors (TLRs)—pattern-recognition receptors in the membranes of host cells; when triggered, TLRs stimulate many different kinds of innate immune responses

OVERVIEW OF ADAPTIVE IMMUNITY

A. Adaptive immunity
1. Part of the third line of defense consisting of lymphocytes
2. Two different classes of a white blood cell (lymphocyte) involved (Figure 24-11)

B. Classes of lymphocytes (Figure 24-12)—B lymphocytes (B cells) and T lymphocytes (T cells)
1. B-cell mechanisms—antibody-mediated immunity (humoral immunity); produce antibodies that attack pathogens (Figure 24-13)
2. T cell mechanisms—attack pathogens more directly—classified as cell-mediated immunity (cellular immunity)
3. Lymphocytes have protein markers on their surfaces
   a. Surface markers named using the CD (cluster of differentiation) system
   b. Examples include CD4 and CD8 cells, clinically important in diagnosing AIDS
4. Activation of lymphocytes require two stimuli: a specific antigen and activating chemicals (Figure 24-14)
5. Lymphocytes are densest where they develop—in bone marrow, thymus gland, lymph nodes, and spleen (Figure 24-15)
6. Lymphocytes flow through the bloodstream, become distributed in tissues, and return to the bloodstream in a continuous recirculation

B CELLS AND ANTIBODY-MEDIATED IMMUNITY

A. Development and activation of B cells
1. Development occurs in two stages (Figure 24-16)
a. Pre–B cells develop in red bone marrow (prenatal, in the yolk sac and fetal liver)
b. Second stage occurs in lymph nodes and spleen—activation of a naïve B cell after it binds to a specific antigen
c. B cells divide repeatedly—serve as ancestors to antibody-secreting plasma cells
   (1) Some of the clone cells differentiate to form B cells or plasma cells
   (2) Others remain in lymphatic tissue and become memory B cells

B. Antibodies—proteins (immunoglobulins) secreted by activated B cell (Figure 24-16)
1. Structure of antibody molecules
   a. An antibody molecule consists of two heavy and two light polypeptide chains
   b. Each molecule has two antigen-binding sites and two complement-binding sites (Figure 24-17)
2. Diversity of antibodies
   a. Babies are born with different clones of B cells in bone marrow, lymph nodes, and spleen
   b. Cells of the clone synthesize a specific antibody with a sequence of amino acids in its variable region that differs from the sequence synthesized by other clones
3. Classes of antibodies (Figure 24-18)—immunoglobulins M, G, A, E, and D
   a. IgM—antibody that naïve B cells synthesize and insert into their own plasma membranes; the predominant class produced after initial contact with an antigen
   b. IgG—makes up 75% of antibodies in the blood; predominant antibody of the secondary antibody response
   c. IgA—major class of antibody in the mucous membranes, in saliva and tears (also found in plasma)
   d. IgE—small amount; produces harmful effects such as allergies
   e. IgD—small amount in blood; precise function unknown
4. Functions of antibodies (Figure 24-19)
   a. Antigen-antibody reactions
      (1) Transforms toxic antigens into harmless substances
      (2) Agglutinates antigens to make disposal by phagocytes more rapid
      (3) Alters the shape of antigen molecule to expose complement-binding sites (Figure 24-20)
   b. Complement—a component of blood plasma consisting of several protein compounds (inactive enzymes)
      (1) Antibodies can activate complement after binding to an antigen by exposing complement-binding sites that trigger a cascade of linked chemical reactions to produce a variety of immune effects
         i. Membrane attack complex (MAC)—complement cascade can form doughnut-shaped structures that produce a hole in a foreign cell's membrane, causing cytolysis (cell rupture) (Figures 24-21 and 24-22)
         ii. Complement can also cause vasodilation, enhances phagocytosis, and other effects
      (2) Complement activity can also be initiated by innate immune mechanisms
         i. Complement protein 3 (C3)—activated without antigen stimulation—produces full complement effect by binding to bacteria or viruses in presence of properdin
         ii. Complement activation by innate immunity is called the alternate pathway
   c. Primary and secondary responses (Figure 24-23)
      (1) Primary response—initial encounter with a specific antigen triggers the formation and release

of specific antibodies that reaches its peak in a few days
(2) Secondary response—a later encounter with the same antigen triggers a much quicker response; B memory cells rapidly divide, producing more plasma cells and thus more antibodies

C. Clonal selection theory (Figure 24-24)
1. Two basic tenets
a. Body contains many diverse clones of cells, each committed by its genes to synthesize a different antibody
b. When an antigen enters the body, it selects the clone whose cells are synthesizing its antibody and stimulates them to proliferate and create more antibody
2. The clones selected by antigens consist of lymphocytes and are selected by the shape of antigen receptors on the lymphocyte's plasma membrane

T CELLS AND CELL-MEDIATED IMMUNITY

A. Development of T cells
1. T cells are lymphocytes that go through the thymus gland before migrating to the lymph nodes and spleen
2. Pre–T cells develop into thymocytes while in the thymus
3. Thymocytes stream into the blood and are carried to the T-dependent zones in the spleen and the lymph nodes

B. Activation of T cells
1. T cells display antigen receptors on their surface membranes that are similar to antibodies
2. A T cell is activated when an antigen (in an infected cell or presented by an APC) binds to its receptors (at an IS), causing the T cell to divide repeatedly to form a clone of identical T cells (Figure 24-25)
a. Cells of the clone differentiate into effector T cells and memory T cells
b. Effector T cells go to the site where the antigen entered, bind to antigens, and begin their attack
c. Memory T cells remain in bone marrow until needed later to produce more effector T cells and memory T cells

C. Functions of T cells
1. Cytotoxic T cells—T cells release lymphotoxin to kill cells (Figure 24-26)
2. Helper T cells (T_H cells)—regulate the function of B cells, T cells, phagocytes, and other leukocytes (Figure 24-27)
3. Suppressor T cells—regulatory T cells that suppress lymphocyte function, thus regulating immunity and promoting self tolerance
4. T cells function to produce cell-mediated immunity and help to regulate adaptive immunity in general

TYPES OF ADAPTIVE IMMUNITY (TABLE 24-4)

A. Innate immunity (inborn or inherited immunity)—genetic mechanisms put innate immune mechanisms in place during development in the womb

B. Adaptive or acquired immunity; resistance developed after birth; two types:
1. Natural immunity results from nondeliberate exposure to antigens
2. Artificial immunity results from deliberate exposure to antigens, called *immunization*

C. Natural and artificial immunity may be active or passive
1. Active immunity—when the immune system responds to a harmful agent regardless of whether it was natural or artificial; lasts longer than passive
2. Passive immunity—immunity developed in another individual is transferred to an individual who was not previously immune; it is temporary but provides immediate protection

SUMMARY OF ADAPTIVE IMMUNITY

A. Adaptive immunity is specific immunity—targeting specific antigens

B. Adaptive immunity involves two classes of lymphocyte: B cells and T cells (Figure 24-27)
1. B cells—antibody-mediated (humoral) immunity
2. T cells—cell-mediated (cellular) immunity

C. Adaptive immunity occurs in a series of stages (Figure 24-28)
1. Recognition of antigen
2. Activation of lymphocytes
3. Effector phase (immune attack)
4. Decline of antigen causes lymphocyte death (homeostatic balance)
5. Memory cells remain for later response if needed

D. B cells and T cells work together in a coordinated system of adaptive immunity (Figure 24-29)

THE BIG PICTURE: IMMUNE SYSTEM AND THE WHOLE BODY

A. Immune system regulated to some degree by nervous and endocrine systems

B. Agents of the immune system include blood cells, skin cells, mucosal cells, brain cells, liver cells, and other types of cells and their secretions

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Define the term *innate immunity*.
2. List several mechanisms of innate defense, and give a brief description of each one.
3. Identify the body's first line of defense.
4. Describe chemotactic factors released from the mast cell.
5. What is the function of interferon?
6. Define the following terms: antigens, antibodies, antigenic determinants, combining sites, clone.
7. What two terms are synonyms for combining sites?

8. When an antigen-antibody complex is formed, what region on the antigen molecule fits into what region on the antibody molecule?
9. Activated B cells develop into clones of what two kinds of cells?
10. What cells synthesize and secrete copious amounts of antibodies?
11. Explain the function of memory cells.
12. Antibodies belong to what class of compounds? Diagram and describe the structure of an antibody.
13. Explain the two basic tenets of Burnet's clonal selection theory.
14. What are cytokines? Lymphotoxins?
15. Differentiate between the classifications of natural and artificial immunity.
16. Describe the process behind the functioning of modern vaccines.
17. What are monoclonal antibodies, and how do they function?

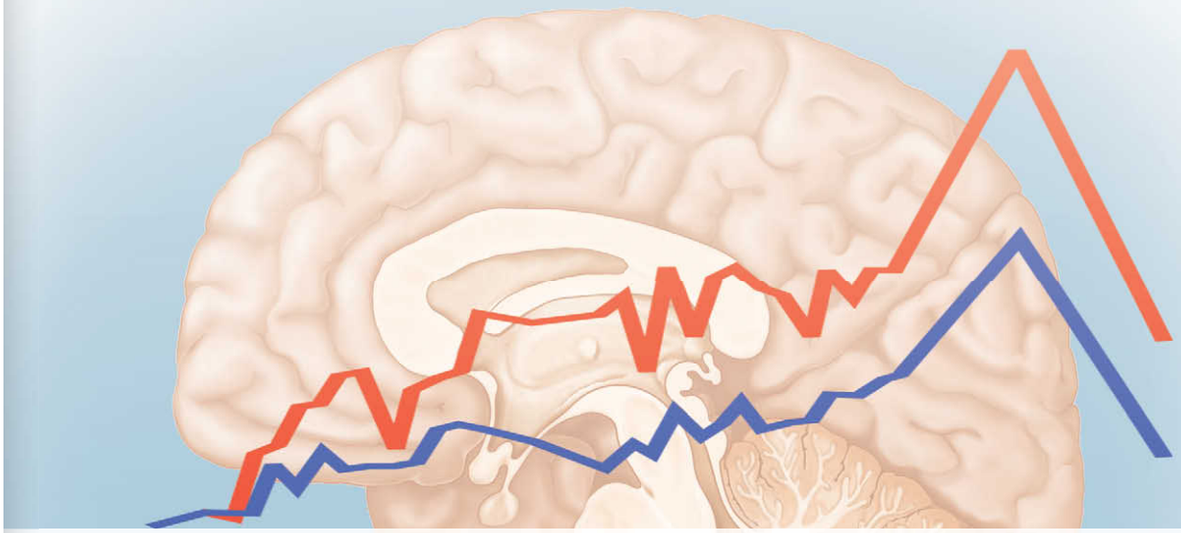
CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. The causative organism of tuberculosis has a coat around it that makes it much more resistant than other bacteria to digestive enzymes and hydrogen peroxide. What can you say about this characteristic, and why is it more difficult for the body to fight off these bacteria?
2. If a person had a mutation that prevented the formation of the complement proteins, what capabilities would be lessened in the immune system?
3. How would you explain how the various types of T cells can fine-tune the immune system?
4. Why do you think the development of cancer can be seen as a failure of the immune system?
5. Explain the distinction between inherited immunity and acquired immunity?
6. One of the best-known examples of acquired immune deficiency is acquired immune deficiency syndrome (AIDS). The human immunodeficiency virus (HIV) causes this syndrome. How would you summarize the mechanism of HIV infection?
7. If the genes that produce Toll-like receptors (TLRs) were abnormal, what effect might that have on a person's immunity?

25 Stress



LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

adaptation
(ad-ap-TAY-shun)
[*adapt-* **adjust,** *-ation* **process**]

alarm reaction

allostasis
(al-lo-STAY-sis)
[*allo-* **different,** *-stasis* **standing still**]

corticoid
(KOHR-tih-koyd)
[*cortic-* **cortex or bark,** *-oid* **like**]

fetal programming
(FEE-tal)
[*fet-* **offspring,** *-al* **relating to**]

fight-or-flight reaction

hypothalamic-pituitary-adrenal axis (HPA)
(hye-poh-THAL-ah-mik pi-TOO-itair-ee ah-DREE-nal)
[*axis* **axle**]

neuropeptide Y
(NOOR-oh-pep-tyde)
[*neuro-* **nerve,** *-pept-* **digest,** *-ide* **chemical**]

psychological stressor
(sye-koh-LOJ-ikal STRESS-or)
[*psycho-* **the mind,** *-logos-* **words (study),** *-al* **relating to,** *stress-* **tighten,** *-or* **agent**]

stage of exhaustion

stage of resistance

stress
[*stress-* **tighten**]

stress response
[*stress-* **tighten**]

stress triad
(TRYE-ad)
[*stress-* **tighten,** *triad* **group of three**]

stressor
(STRESS-or)
[*stress-* **tighten,** *-or* **agent**]

continued on p. 794

CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

Selye's Concept of Stress, 783
- Development of the Stress Concept, 783
- Definitions, 784
- Stressors, 784
- General Adaptation Syndrome, 784
  - Manifestations, 784
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Some Current Concepts About Stress, 788
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Case Study, 794

Stress affects people of all ages and in all walks of life. Children at play, students preparing for an examination, workers on the job, and even a baby before birth are all subject to stress. Although some stress can result in beneficial outcomes, excessive and long-term stress often has disastrous consequences for the health and quality of life of many people.

People experiencing severe stress are often overwhelmed by tension, anger, fear, and frustration. As a result, adrenaline levels rise, blood pressure and heart rate increase, and breathing patterns change. Blood levels of nutrients such as glucose and fatty acids deviate from their normal set points and the immune system becomes less effective. People who have difficulty in dealing with stress over time suffer from a number of stress-related illnesses. Every individual responds somewhat differently to stress, making diagnosis and treatment difficult. There is often a decrease in efficiency of study habits or job-related problem-solving skills; susceptibility to infections increases; and complaints of stomach pains, heart palpitations, fatigue, and muscle aches are common. Sleep disorders and depression frequently accompany stress, and affected individuals often have difficulty in staying with tasks.

Contemporary medicine now recognizes excessive and long-term stress as a critically important and widespread cause of disease. It causes disruption in the homeostasis of numerous physiological control systems in the body and must be controlled to ensure good health.

Our current concept of stress extends beyond the nonspecific physiological responses suggested by researchers nearly 70 years ago. However, the pioneering and classic research on stress by Hans Selye (described in the next section) continues to provide a scientific basis for ongoing work in this complex and important area.

A growing understanding of stress has resulted from insights and research data from diverse disciplines such as molecular genetics, neurobiology, psychology, endocrinology, immunology, and sociology. The result is a holistic model of stress—one that affirms the importance of mind-body interactions in both health and disease.

SELYE'S CONCEPT OF STRESS

In 1935, Hans Selye of McGill University in Montreal made an accidental discovery that launched him on a lifelong career and led him to conceive the idea of stress. This chapter tells briefly the story of how Selye developed his stress concept and also describes the mechanism of stress that he postulated. It then presents some current ideas about stress.

Development of the Stress Concept

Selye made his accidental discovery when he was trying to determine whether there was another sex hormone besides those already known. He injected rats with various extracts derived from ovaries and placenta, expecting to find different changes had occurred in animals injected with different hormonal preparations. But to his surprise and puzzlement, he found the same three changes in all the animals. The cortices of their adrenal glands were enlarged, but their lymphatic organs—thymus glands, spleens, and lymph nodes—were atrophied, and bleeding ulcers of the stomach and duodenum had developed in every animal. Next he injected many other substances, for example, extracts from pituitary glands, kidneys, and spleens and even a poison, formaldehyde. Every time he found the same three changes in the animal subjects: enlarged adrenals, shrunken lymphatic organs, and bleeding gastrointestinal ulcers. Selye believed that these symptoms were a specific syndrome.

A syndrome, according to the classical definition, is a set of signs and symptoms that occur together and that characterize one particular disease. The three changes, or "stress triad," Selye had observed occurred together, but they seemed to characterize not any one particular kind of injury but instead all kinds of harmful stimuli. More experiments using various chemicals and injurious agents confirmed for him that the three changes truly were a syndrome of injury. His first publication on the subject was a short paper entitled "A Syndrome Produced by Diverse Nocuous Agents"; it appeared in the July 1936 issue of the British journal *Nature*. Years later, in 1956, he published his monumental technical treatise, *The Stress of Life*.

Although a majority of the current literature credits Hans Selye with the first published reports on stress, Walter B. Cannon used the term "emotional stress" much earlier (1914) when discussing his theory of homeostasis. It seems Cannon was also convinced stress had both a psychological (emotional) and a physiological origin. It was Selye, however, who brought our knowledge of stress and its importance in health and disease into the forefront of modern medicine.

Definitions

Stress, according to Selye's use of the word, is a state, or condition, of the body produced by "diverse nocuous agents" and manifested by a syndrome of changes. We know as well that stress and its negative effects can also be caused by a wide variety of mental, emotional, and other psychological events that an individual may perceive as threatening or undesirable. Selye named the agents that produce stress *stressors* and coined a name—*general adaptation syndrome (GAS)*—for the syndrome or group of changes that make the presence of stress in the body known.

Stressors

A **stressor** is any agent or stimulus that produces stress. However, just how an individual interacts with or relates to a particular type of physiological or cognitive situation may well determine whether that particular event is stressful or not. Even the same intensity of a particular physiological stressor, such as temperature change, may be perceived as a threat and activate a stress response in one individual and not another.

In addition to variances in ability to handle physiological stress, some people have the ability to cope better than others when faced with difficult events in life, such as divorce or bereavement. As a result, they suffer less from negative stress-related symptoms or illness.

Clearly, a precise classification of stimuli as stressors or nonstressors is not possible. We can, however, make these five generalizations about the character of stressors.

1. Stressors are extreme stimuli—too much or too little of almost anything. The *perception* of the individual is critical. A particular event or circumstance that is viewed as undesirable or goes beyond what the individual is capable of coping with may be viewed as "extreme" and cause one or more of the psychological or physiological responses associated with stress. In contrast, almost anything in moderation or that engenders only mild stimuli are nonstressors. Thus coolness, warmth, and soft sounds are nonstressors, whereas extreme cold, extreme heat, and extremely loud sounds almost always act as stressors. Not only extreme excesses but also extreme deficiencies may be perceived as stressors. One example of this kind of stressor is an extreme lack of social contact stimuli. Solitary confinement in a prison, space travel, social isolation because of blindness or deafness, and in some cases, old age have all been identified as stressors. But the opposite extreme, an excess of social contact stimuli (e.g., caused by overcrowding), also acts as a stressor (Figure 25-1). We now know that various types of stress in young children and even prenatal infants may occur as a result of negative stimuli that are experienced by a parent. For example, severe psychological or physical trauma, environmental hazards, and nutritional deficiencies or abuses, when encountered by a pregnant or nursing woman, can all have a stress-related impact on her child that may result in immediate or delayed behavioral, physiological, or anatomical anomalies. Intrauterine stress is discussed in detail later in the chapter. Poverty and illness, typically associated with stress, are often coupled with alcoholism, drug abuse, and malnutrition. These conditions often result either directly or indirectly in premature births, developmental anomalies, increased susceptibility to many types of mental and physical diseases, and a myriad of other physical defects that may occur immediately in the children involved or these conditions may develop later in life.
2. Stressors very often are injurious, unpleasant, or painful stimuli—but not always. "A painful blow and a passionate kiss," Selye wrote, "can be equally stressful."
3. Anything that an individual perceives as a threat, whether real or imagined, arouses fear or anxiety. These emotions act as stressors. So, too, does the emotion of grief.
4. The reaction to stressors differs in different individuals and in one individual at different times. A stimulus that is a stressor for you may not be a stressor for me. A stimulus that is a stressor for you today may not be a stressor for you tomorrow and might not have been a stressor for you yesterday. Many factors—including one's physical and mental health, heredity, past experiences, coping habits, and even diet—determine which stimuli are stressors for each individual.
5. Stress can occur even in a developing fetus—a circumstance called *prenatal stress*. In many instances prenatal stress will result from a physical or nutritional stressor experienced by the mother. For example, in the United States alone, fetal alcohol syndrome (FAS) affects more than 40,000 infants each year (see Box 18-3 on p. 556). FAS involves signs ranging from poor prenatal and infant growth to mental retardation. In this context, alcohol consumed during pregnancy is a dangerous stressor. Even in small amounts it can produce prenatal brain damage that may permanently affect the ability of the child to concentrate, think abstractly, use appropriate judgment, or learn effectively. When a woman consumes alcohol during pregnancy, real or perceived stress is often the impetus for such behavior. Education that promotes healthy habits and teaches coping strategies must be a part of any social programs intended to eliminate alcohol consumption during pregnancy and the incidence of FAS.

| QUICK CHECK |

1. Define the terms *stress syndrome* and *stress.*
2. Identify the three changes Hans Selye called the "stress triad."
3. List four characteristics of stressors.

General Adaptation Syndrome

MANIFESTATIONS

Stress, like health or any other state or condition, is an intangible phenomenon. It cannot be seen, heard, tasted, smelled, felt, or measured directly. How, then, can we know that stress exists? It can be inferred to exist when certain visible, tangible, and

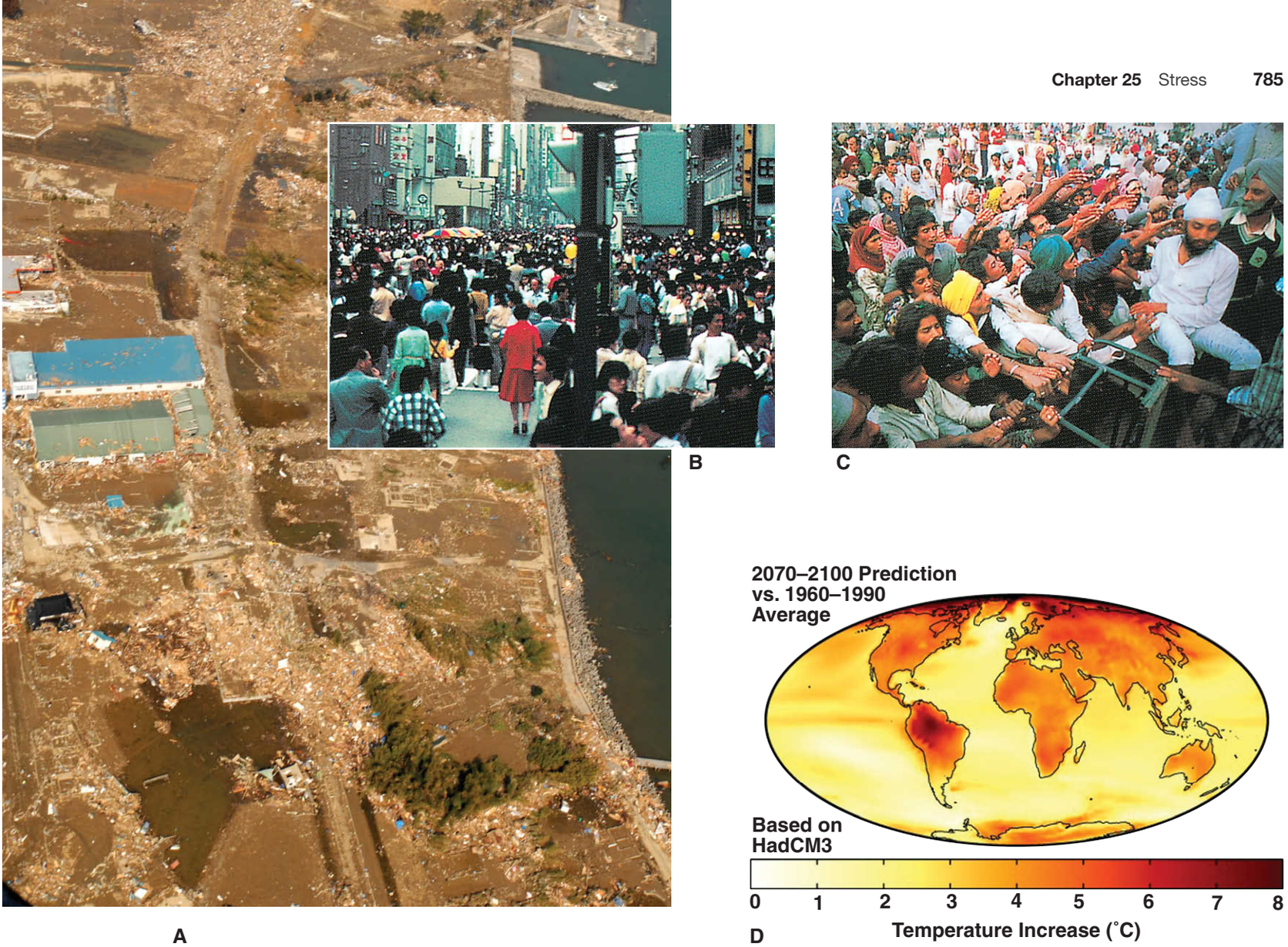


FIGURE 25-1

Causes of stress. A, Natural disaster (Japan tsunami). **B,** Overcrowding (Asia). **C,** Food shortages (refugee camp, New Delhi, India). **D,** Environmental dangers (climate change).

measurable responses occur. Selye, for example, inferred that the animals on which he experimented were in a state of stress when he found the syndrome of the three changes previously noted—hypertrophied adrenals, atrophied lymphatic organs, and bleeding gastrointestinal ulcers. Because this syndrome indicated the presence of stress and consisted of three changes, he called them the "**stress triad.**"

Eventually he found that many other changes also took place as a result of stress. He named the entire group of changes or responses the **general adaptation syndrome (GAS).** In coining this term, he reasoned that the word *general* suggested that the syndrome was "produced only by agents that have a general effect on large portions of the body." The word **adaptation** was meant to imply that the syndrome of changes made it possible for the body to adapt, to cope successfully with stress. Selye thought that these responses seemed to protect the animals from serious damage by extreme stimuli and to promote their healthy survival. He looked on the general adaptation syndrome as a crucial part of the body's complex defense mechanism.

STAGES

Changes that make up the general adaptation syndrome do not all take place simultaneously but over time in three stages. Selye named these stages: (1) the alarm reaction, (2) the stage of resistance or adaptation, and (3) the stage of exhaustion. A different syndrome of changes, he noted, characterized each stage.

Among the responses characteristic of the **alarm reaction,** for example, were the stress triad already described—hypertrophied adrenal cortex, atrophied lymphatic organs (thymus, spleen, lymph nodes), and bleeding gastric and duodenal ulcers. In

addition, the adrenal cortex increased its secretion of glucocorticoids, the number of lymphocytes decreased markedly, and so, too, did the number of eosinophils. Also, the sympathetic nervous system and the adrenal medulla greatly increased their activity (Figure 25-2). Each of these changes, in turn, produced other widespread changes. Figure 25-3 indicates some of the changes stemming from adrenal cortical hypertrophy. Figure 25-4 shows responses produced by increased sympathetic activity and increased secretion by the adrenal medulla of its hormone, epinephrine (adrenaline).

Quite different responses characterize the **stage of resistance.** For instance, the adrenal cortex and medulla return to their normal rates of hormone secretion. The changes that take place during the alarm stage as a result of increased corticoid secretion disappear during the stage of resistance. All of us go through the first and second stages of the stress syndrome many times in our lifetimes. Stressors of one kind or another act on most of us every day. They may upset or alarm us, but we soon resist them successfully. In short, we adapt; we cope.

The **stage of exhaustion** develops only when stress is extremely severe or when it continues over long periods. Otherwise, when stress is mild and of short duration, it ends with a successful stage of resistance and adaptation to the stressor. If stress continues until the body reaches the stage of exhaustion, corticoid secretion and adaptation eventually decrease markedly. The body can no longer cope successfully with the stressor and death may ensue as a result. For a brief summary of the changes characteristic of the three stages of the general adaptation syndrome, see Table 25-1.

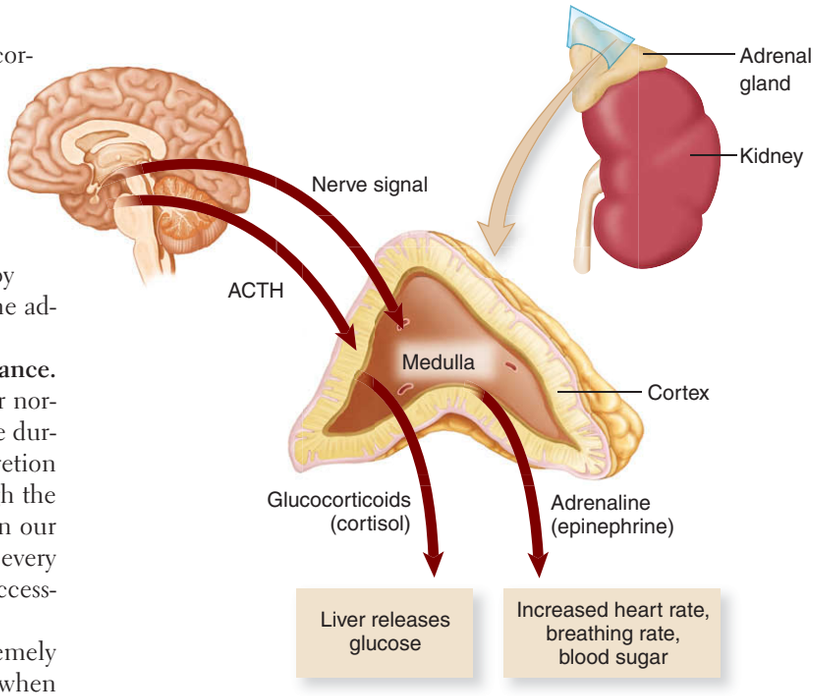


FIGURE 25-2

The alarm reaction. Note the interaction of nervous and hormonal responses. *ACTH,* Adrenocorticotropic hormone.

Mechanism of Stress

Stressors produce a state of stress. A state of stress in turn inaugurates a series of responses that Selye called the *general adaptation syndrome.* More simply, a state of stress turns on the stress response mechanism. It activates the organs that produce the responses that make up the general adaptation syndrome; but just how stress—a state of the body—does this is not clear. Selye could only guess about it, and his terms were vague. For instance, he postulated that, by some unknown "alarm signals," stress "acted through the floor of the brain" (presumably the hypothalamus) to stimulate the sympathetic nervous system and the pituitary gland.

TABLE 25-1 The Three Stages of the General Adaptation Syndrome

ALARM	RESISTANCE	EXHAUSTION
Increased secretion of glucocorticoids and resultant changes (see Figure 25-2)	Glucocorticoid secretion returns to normal	Initially increased glucocorticoid secretion but eventually markedly decreased secretion
Increased activity of sympathetic nervous system	Sympathetic activity returns to normal	Stress triad (hypertrophied adrenals, atrophied thymus and lymph nodes, bleeding ulcers in stomach and duodenum)
Increased norepinephrine secretion by adrenal medulla	Norepinephrine secretion returns to normal	
Fight-or-flight reaction (see Figure 25-4)	Fight-or-flight reaction disappears	
Low resistance to stressors	High resistance (adaptation) to stressor	Loss of resistance to stressor; may lead to death

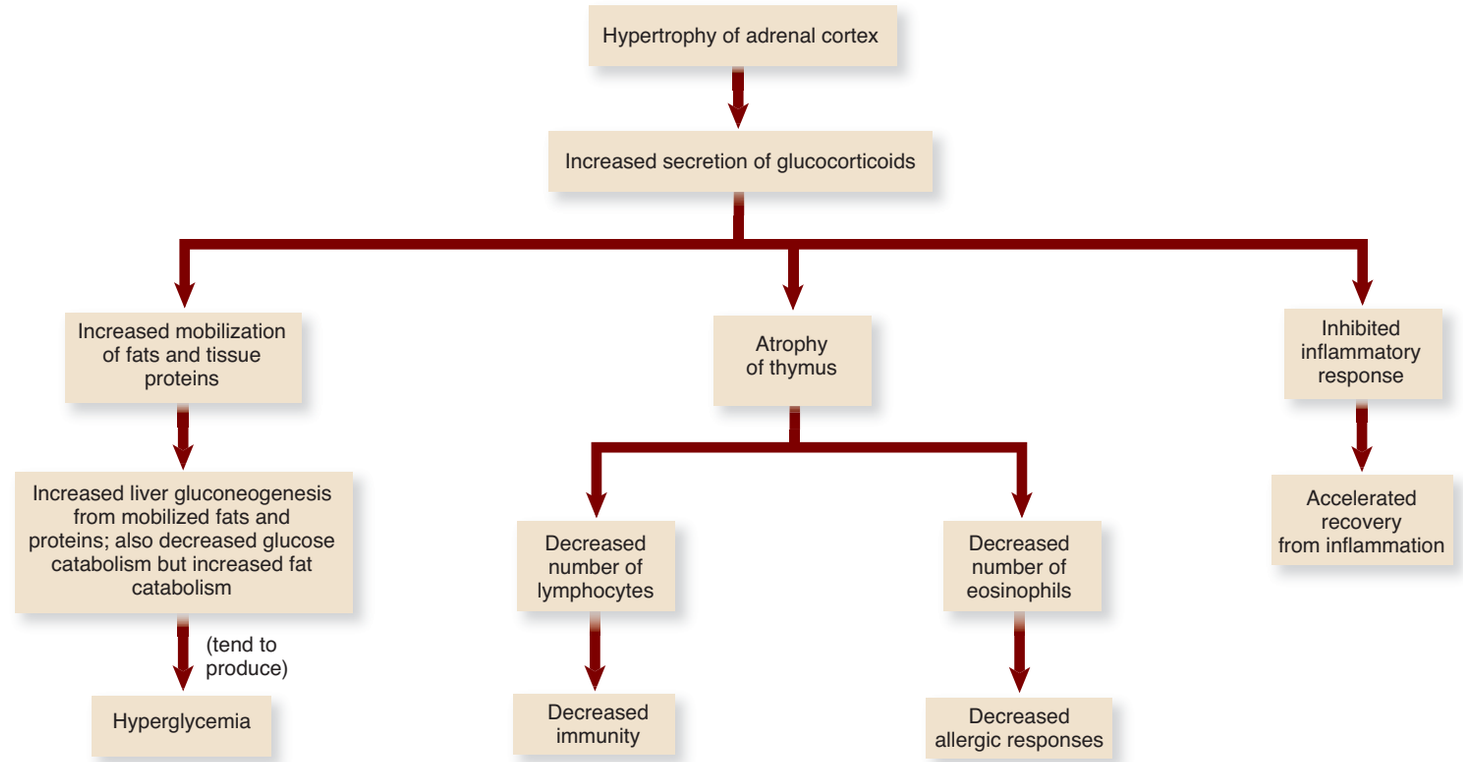


FIGURE 25-3

Alarm reaction responses resulting from hypertrophy of adrenal cortex.

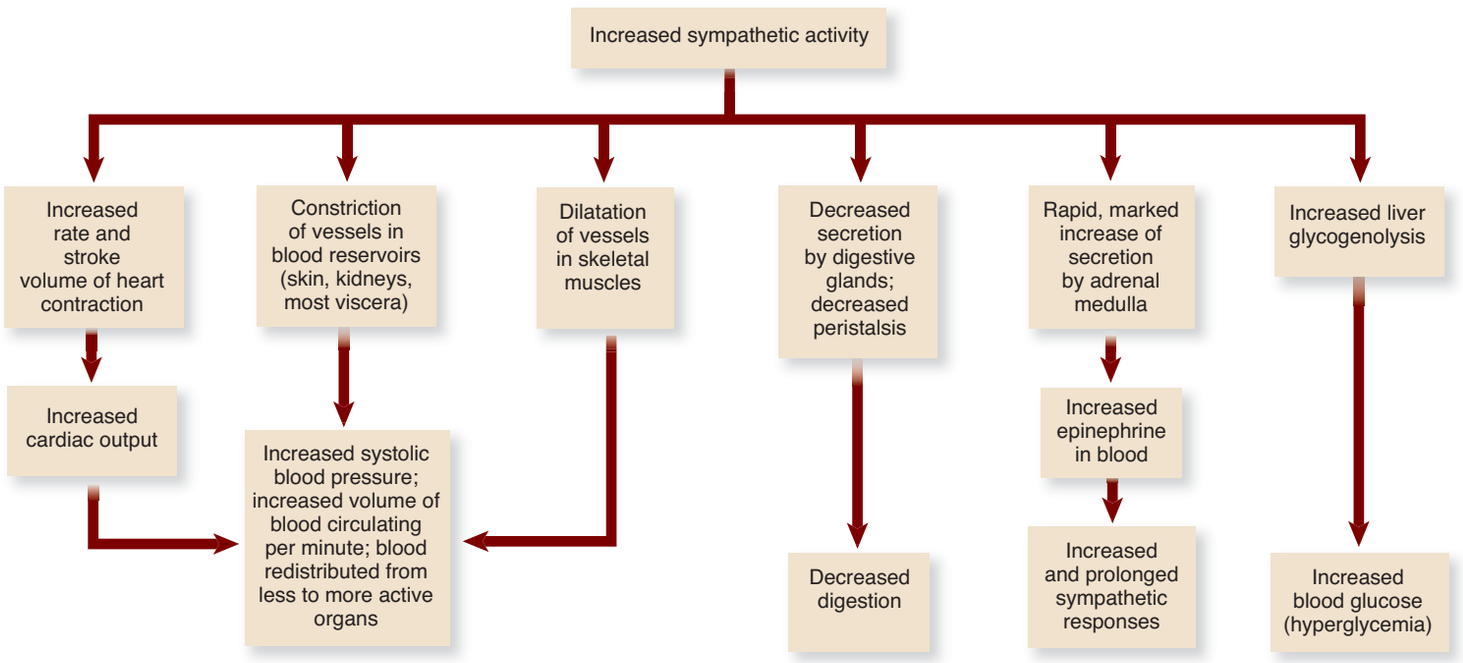


FIGURE 25-4

Alarm reaction responses resulting from increased sympathetic activity. Note that these are the responses commonly referred to as the "fight-or-flight" reaction.

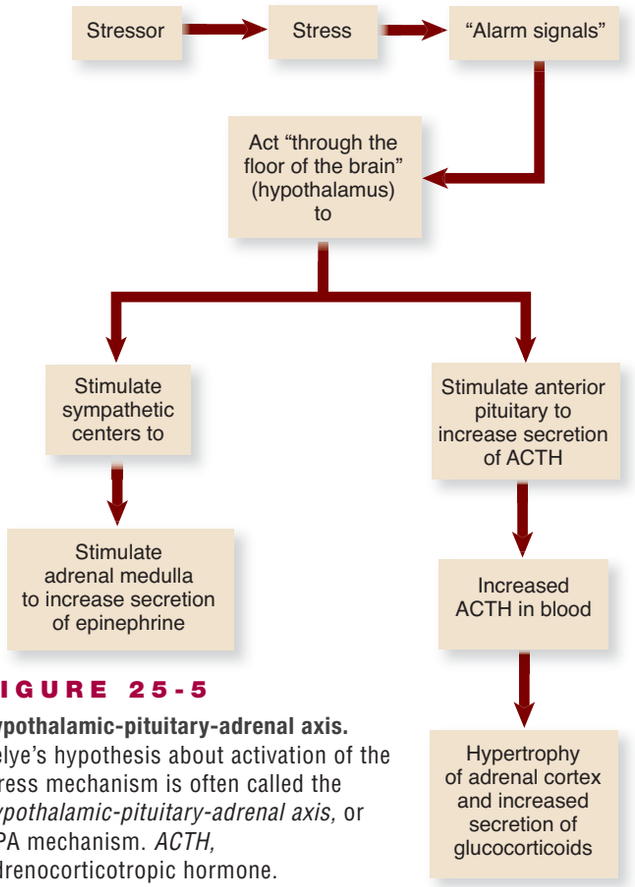


FIGURE 25-5

Hypothalamic-pituitary-adrenal axis. Selye's hypothesis about activation of the stress mechanism is often called the *hypothalamic-pituitary-adrenal axis,* or HPA mechanism. *ACTH,* Adrenocorticotropic hormone.

In Figure 25-5 you can see Selye's hypothesis in diagram form. Many scientists refer to this process as the **hypothalamic-pituitary-adrenal "axis,"** or **HPA** mechanism.

| QUICK CHECK |

4. What is the general adaptation syndrome?
5. Identify the three stages of the general adaptation syndrome. How do they differ?
6. Discuss the types of responses produced in the body by increased sympathetic activity.

SOME CURRENT CONCEPTS ABOUT STRESS

Definitions

Some of today's physiologists use the terms *stressors* and *stress* as Selye did—that is, they define stressors as stimuli that produce stress, a state (or condition) of the body. In contrast, many physiologists now use the word *stress* to mean something much more specific than a state of the body. **Stress,** according to their operational definition, is any stimulus that directly or indirectly stimulates neurons of the hypothalamus to release corticotropin-releasing hormone (CRH). CRH acts as a trigger that initiates many diverse changes in the body. Together, these changes constitute a syndrome now commonly called the **stress syndrome,** or simply, the **stress response.**

The term **allostasis** is sometimes used to refer to the stress syndrome, or the body's attempts to reestablish homeostatic balance while under stress. The word part *allo-* means "different." One can think of allostasis as the body's coping mechanisms when things are different. *Allostatic load* refers to the broad effects of allostasis on the body, such as increased energy expenditure, alterations of neural and endocrine mechanisms, and changes in behavior. One can think of allostatic load as the physiological load placed on the body by stress.

Stress Syndrome

Look now at Figure 25-6. It summarizes some current major ideas about the syndrome of stress responses. Beginning at the top of the diagram, note that the initiator of the stress syndrome is stress—any factor that stimulates the hypothalamus to release CRH. Most often, stress consists of injurious or extreme stimuli. These may act directly on the hypothalamus to stimulate it. Instead, or in addition, they may act indirectly on the hypothalamus.

An example of stress that stimulates the hypothalamus directly is hypoglycemia. A lower than normal concentration of glucose in the blood circulating to the hypothalamus stimulates it to release CRH.

Indirect stimulation of the hypothalamus occurs in this way: stress stimulates the cerebral part of the brain's limbic system—the so-called *emotional brain*—and other parts of the cerebral cortex, and these regions then send stimulating impulses to the hypothalamus (also part of the limbic system). The hypothalamus releases CRH in response.

In addition to releasing CRH, note in Figure 25-6 that the stress-stimulated hypothalamus sends stimulating impulses to sympathetic centers and to the posterior pituitary gland.

CRH stimulates the anterior pituitary gland to secrete increased amounts of adrenocorticotropic hormone (ACTH). ACTH stimulates the adrenal cortex to secrete greatly increased amounts of cortisol and more moderately increased amounts of aldosterone. These two hormones induce various stress responses. Some important ones worth remembering are listed in Figure 25-6 under cortisol effects and aldosterone effects.

Recall from Chapter 16 that stimulation of sympathetic centers by impulses from the stress-stimulated hypothalamus leads to many stress responses, known collectively as the **fight-or-flight reaction.** These *adrenergic responses* include important changes such as an increase in the rate and strength of the heartbeat, a rise in blood pressure, and hyperglycemia. Other sympathetic stress responses are pallor and coolness of the skin, sweaty palms, and dry mouth. Review Table 16-4 on p. 500 for a listing of the adrenergic effects observed in the fight-or-flight reaction.

Water retention and an increase in blood volume are common stress responses. They stem, as you can see in Figure 25-6, from increased ADH and increased aldosterone secretion.

Evidence also suggests that prolonged stress produces yet another hormone, called **neuropeptide Y,** that is secreted from the sympathetic nerves and adrenal medulla. This stress-related hormone causes vasoconstriction, platelet aggregation, and over time, hypertrophy of vascular smooth muscle.

Stress and Disease

Stress, as we have observed several times, produces different results in different individuals and different results in the same individual at different times. In one person, a certain amount of stress

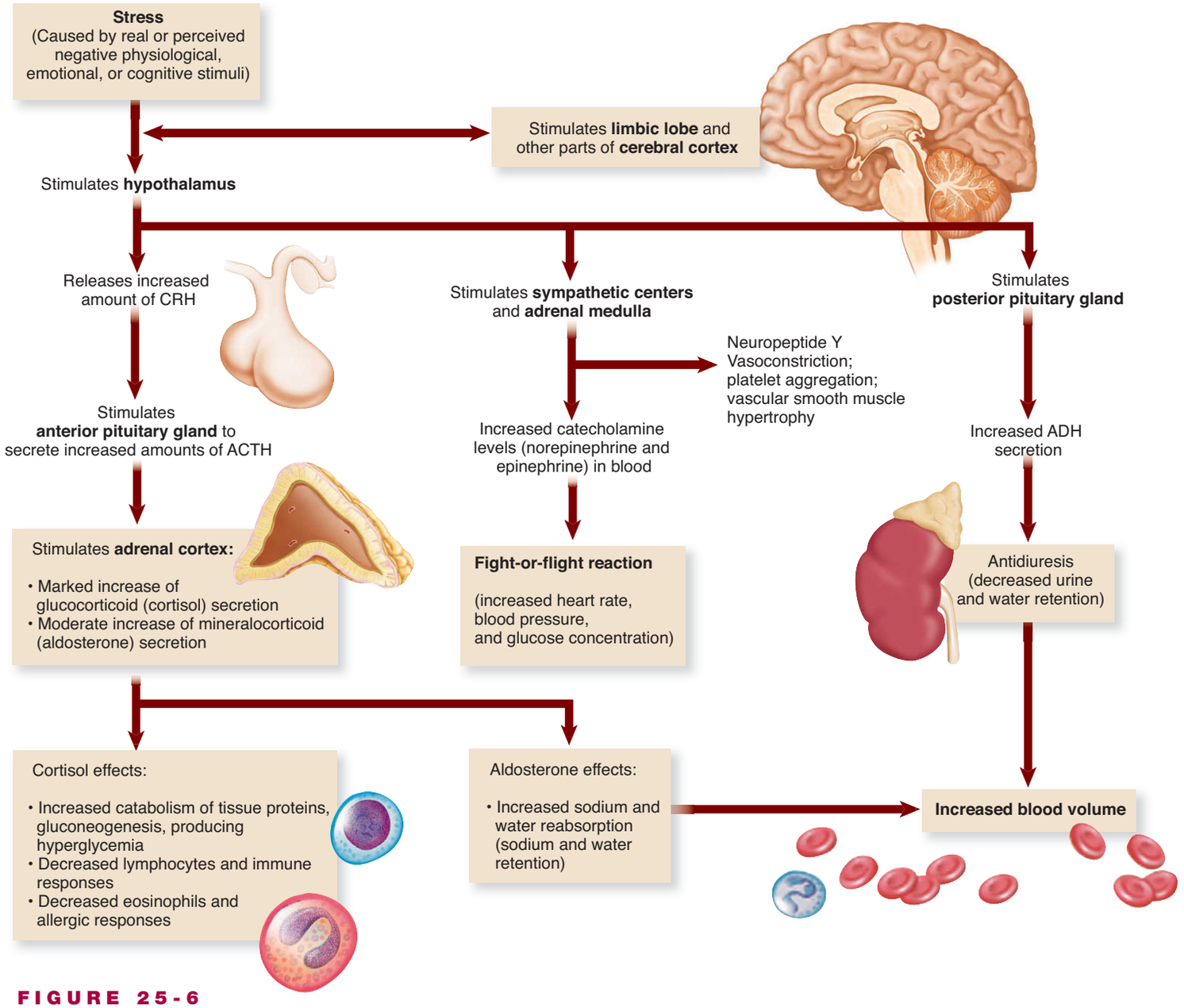


FIGURE 25-6

Current concepts of the stress syndrome. Some effects are immediate, such as the sympathetic fight-or-flight reaction, and some effects are longer term, such as the hormonal effects. CRH, Corticotropin-releasing hormone; ACTH, adrenocorticotropic hormone; ADH, antidiuretic hormone.

may induce responses that maintain or even enhance health. But in another person the same amount of stress appears to cause sickness. Whether stress is "good" or "bad" for you seems to depend more on your own body's responses to it than on the severity of the stressors inducing it.

You may recall that Selye emphasized the adaptive nature of stress responses. He coined the term *general adaptation syndrome* because he believed that stress responses usually enable the body to adapt successfully to the many stressors that assail it. He held that the state of stress activates physiological mechanisms to meet the challenge imposed by stressors. But a challenge issued does not necessarily mean a challenge successfully met. Selye proposed that sometimes the body's adaptive mechanisms fail to meet the challenge issued by stressors and that when they fail, disease results—diseases of adaptation, he called them. In today's terms, we might say that when the allostatic load becomes high, fatigue or disease may result.

Around the middle of the last century, one of the problems studied was the relationship of blood glucocorticoid concentration to disease. If stress is adaptive, the investigators reasoned, and helps the body combat the effects of many kinds of stressors (e.g., infection, injury, and burns), then possibly various diseases might be treated by adding to the body's natural output of glucocorticoids (cortisone).

Indicators of Stress

Whether an individual's body is responding to stress stimuli can be determined by certain measurements and observations (Figure 25-7). Some examples follow: an increase in the rate and force of heartbeat, a rise in systolic blood pressure, an increase in blood and urine concentration of epinephrine and norepinephrine, sweating of the palms of the hands, and dilation of pupils. The heart rate has been shown to increase in response to varied stress stimuli, such as anesthesia and annoying sounds. Even anticipation by patients in a coronary care unit of their upcoming transfer to a less closely supervised convalescent unit has been identified as a stress stimulus that causes the heart rate to speed up.

A decrease in the number of eosinophils and lymphocytes in the blood indicates that the individual is responding to stress stimuli. Soldiers stressed by prolonged marching, for example, have been found to have fewer circulating eosinophils than normal. This same stress indicator has been observed in college athletes when they were anticipating performing in an important event. It has also been observed in heart patients when they were anticipating the various types of procedures required to treat their illness.

The amount of urinary adrenocorticoids is often used as a measure of stress. It has been found to increase in depressed persons feeling hopeless and doomed, in test pilots anticipating a scheduled flight, and in college students taking examinations or watching exciting movies. In contrast, urinary corticoids were found to drop markedly in persons watching boring films.

The level of adrenocorticoids in the blood plasma of disturbed patients having acute psychotic episodes has been found to be 70% higher than that in normal individuals or in calm patients. Another study showed that the plasma corticoid levels of chronically depressed patients were significantly lower than those of acutely anxious patients. Smoking and exposure to nicotine have also been shown to be stressors that caused a marked rise in plasma adrenocorticoids—by as much as 77% in humans and in experimental animals.

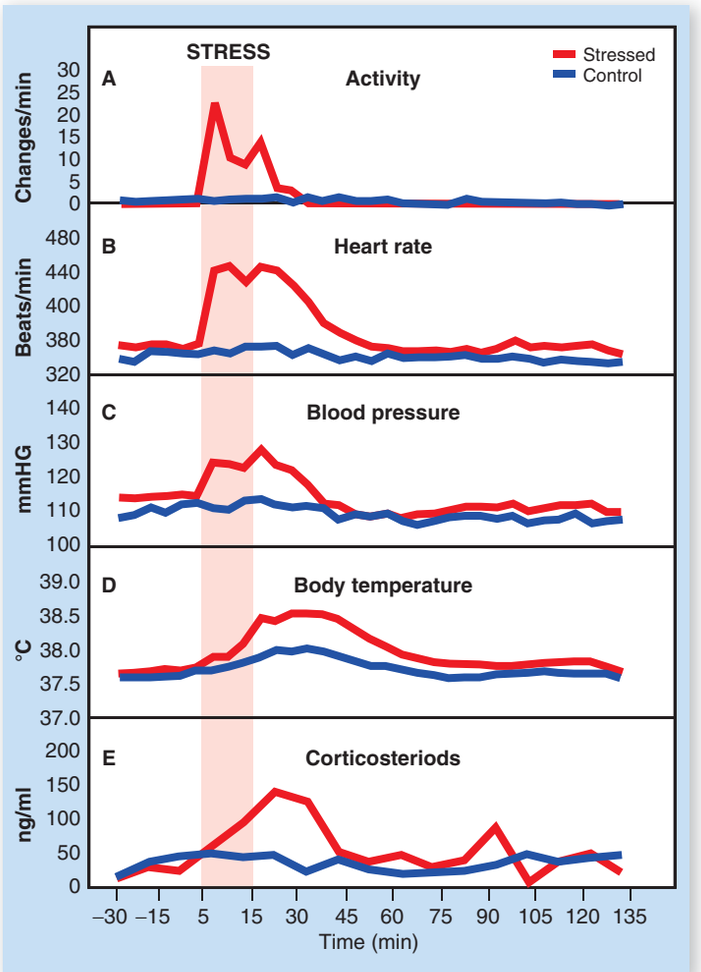


FIGURE 25-7

Stress indicators. Graphs showing a variety of physiological changes in mice when presented with a stressor: increased movements **(A)**, elevated heart rate **(B)**, elevated blood pressure **(C)**, elevated body temperature **(D)**, and increased plasma corticosteroids **(E)**. Similar stress responses occur in all mammals.

Corticoids and Resistance to Stress

Selye thought that the increase in **corticoids** that occurred in his stressed animals enabled them to adapt to and resist stress. Today many physiologists doubt this. No one questions that adrenal cortical hormones increase during stress. That fact has been clearly established. But what many question is how essential this increase is for *resisting stress.*

No one has proved by an unequivocal experiment that a higher than normal blood level of corticoids increases an animal's ability to adapt to stress, and increasing corticoid levels may in themselves be problematic—especially in the developing fetus. Some clinical evidence, however, seems to indicate that it does increase a human's coping ability. For instance, patients who have been taking cortisol for some time are known to require increased doses of this hormone to successfully resist stresses such as surgery or severe injury.

Psychological Stress

Stress as defined by Selye is physiological stress, that is, a state of the body. Psychological stress, in contrast, might be defined as a state of the mind. It is caused by psychological stressors and manifested by a syndrome.

A **psychological stressor** is anything that an individual perceives as a threat—a threat to survival or to self-image. Moreover, the threat does not need to be real—it needs only to be real to the individual, who must see it as a threat, although in truth, it may not be so. The ability to recognize threats is vital to the survival of any animal, including humans (Figure 25-8). But perceiving nonharmful stimuli as stressors will also produce stress effects in the body.

Psychological stressors produce a syndrome of subjective and objective responses. Dominant among the subjective reactions is a feeling of anxiety. Other emotional reactions, such as anger, hate, depression, fear, and guilt, are also common subjective responses to psychological stressors.

Some characteristic objective responses are restlessness, fidgeting, criticizing, quarreling, lying, and crying. Another objective indicator of psychological stress is that the concentration of lactate in the blood increases. Lactate, a molecule related to glucose, is released by glia to nourish nearby neurons. Increased blood lactate is an indicator of tissue hypoxia. Hypoxia may result from changes in breathing patterns.

Does psychological stress relate to physiological stress? The answer is clearly "yes." Physiological stress usually is accompanied by



FIGURE 25-8

Psychological stress. For any animal, a stressor is a perceived threat to survival. The threat may be real (pictured) or imagined. Regardless, it will produce protective stress responses in the body.

some degree of psychological stress. And conversely, in most people, psychological stress produces some physiological stress responses. Ancient peoples intuitively recognized this fact. For example, it is said that in ancient times when the Chinese suspected a person of lying, they made that person chew rice powder and then spit it out. If the powder came out dry, not moistened by saliva, they judged the suspect guilty. They seemed to know that lying makes a person nervous—and that nervousness makes a person's mouth dry. We "moderns" also know these facts, but we describe them with more technical language. Lying, we might say, induces psychological stress, and psychological stress acts in some way to cause the physiological stress response of decreased salivation.

Within recent decades, a scientific discipline called *psychophysiology* has come into being. Psychophysiologists, using accepted research methods, blood analyses, and sophisticated instruments—including polygraphs designed especially for this type of research—have investigated various physiological responses made by individuals subjected to psychological stressors. Their findings amply confirm the principle that psychological stressors often produce physiological stress responses in all age-groups.

Especially apparent are the links between the immune, nervous, and endocrine systems. Table 25-2 lists a number of stress-related diseases and conditions. Psychophysiologists have found, however, that identical psychological stressors do not necessarily induce identical physiological responses in different individuals. For example, stress may result in heart rate and blood pressure changes in one individual and changes in breathing patterns in another. Another of their interesting discoveries is that some organ systems become less responsive after they have been stimulated a number of times. We now know that infancy and early childhood, once overlooked

TABLE 25-2 Stress-Related Diseases and Conditions

TARGET ORGAN OR SYSTEM	DISEASE OR CONDITION
Cardiovascular system	Coronary artery disease
	Hypertension
	Stroke
	Disturbances of heart rhythm
Muscles	Tension headaches
	Muscle contraction backache
Connective tissues	Rheumatoid arthritis (autoimmune disease)
	Related inflammatory diseases of connective tissue
Pulmonary system	Asthma (hypersensitivity reaction)
	Hay fever (hypersensitivity reaction)
	Changes in breathing patterns
Immune system	Immunosuppression or immune deficiency
	Autoimmune diseases
Gastrointestinal system	Ulcer
	Irritable bowel syndrome
	Diarrhea
	Nausea and vomiting
	Ulcerative colitis
Genitourinary system	Diuresis
	Impotence (erectile dysfunction)
	Loss of libido (sexual desire)
Skin	Eczema
	Neurodermatitis
	Acne
Endocrine system	Diabetes mellitus
	Amenorrhea
Central nervous system	Fatigue and lethargy
	Type A behavior
	Overeating
	Depression
	Insomnia

as potentially stressful periods in life, do indeed present youngsters with challenges that result in stress. The result is often manifested by physical or behavioral adaptations intended to assist in coping. As young children mature, they continue to face multiple periods of often stressful transition to new roles in social relationships, self-concept, personal identity, and later, sexual identity and behavior. These challenges are highly individualistic and often temporary—existing for only short periods during childhood and adolescence.

In the adult years, the types of stressors characteristic of earlier periods of development, such as the transition from childhood to sexual maturity, will often change and maladaptive responses will vary. Adults often face higher levels of ongoing stress than do children because of the many complex social interactions they must deal with day in and day out, including the need to make ethical judgments and decisions related to standards of conduct.

Maladaptive responses to chronic stress in adults often affect not only their physical health but also the emotional, social, and

intellectual aspects of their lives. Living with chronic stress as an adult often leads to a decreased quality of life. Ulcers, hypertension, chemical dependency, impaired relationships, and even loss of contact with reality may occur. Adults struggling with unhealthy levels of stress over time often develop multiple problems that limit their ability to function in society as their general level of both physical and psychological health deteriorates.

Teaching these individuals how to manage stress is an important component of holistic treatment programs designed to improve both their physical and psychological health. In addition to specific drugs and counseling, such programs may include use of relaxation techniques, such as massage, meditation, and positive imagery, and educational components that focus on development of coping strategies.

Elderly people are at high risk for stress-related illness (Box 25-1). It is estimated that the U.S. population of very elderly individuals (80 years or older) will increase from a current number of about 31 million to more than 65 million by 2030. These individuals must deal with unique and very significant stressors during their later years. Unfortunately, loss of health and general well-being, fear of death or dying, a sense of abandonment and social isolation, poverty, and often the death of a spouse result in frequent maladaptive responses to stress in this age-group. Family support and societal support are particularly important for elderly individuals struggling with stress.

In summary, here are some principles to remember about psychological stress:

- Physiological stress almost always is accompanied by some degree of psychological stress.
- In most people, psychological stress leads to some physiological stress responses. Many of these are measurable autonomic responses, for example, accelerated heart rate and increased systolic blood pressure (Box 25-2).
- Identical psychological stressors do not always induce identical physiological responses in different individuals.
- In any one individual, certain autonomic responses are better indicators of psychological stress than others.

Box 25-1 | FYI

The Stress-Age Syndrome

The **stress-age syndrome** refers to a group of anatomical, neurohormonal, and immune system changes related to aging that influence both physiological and psychological stress responses. The syndrome includes a wide array of changes, including:

- Decrease in coping skills
  - Alteration of limbic system and hypothalamus excitability
  - Increases in catecholamines, adrenocorticotropic hormone (ACTH), and cortisol
  - Decreases in testosterone, estrogen, thyroxine, and other hormones
  - Immunodepression
  - Decreases in neuromuscular transmitter chemicals resulting in chronic fatigue and reduced physical strength
  - Changes in blood lipid profile
  - Increased potential for hypercoagulation of the blood
- Disturbances of the sleep/wake cycle

Although not all age-related changes connected with stress are damaging, a majority result in a lower potential for positive adaptation to change.

Effects of Intrauterine Stress

We now know that a fetus develops both short-term and long-term responses to stress experienced during intrauterine development.

Maternal malnutrition is one of the most common "stressors" experienced by a pregnant woman and her unborn child. In malnourished women who smoke, oxygen delivery to the fetus will also decrease. The result is hypoxic as well as nutritional stress. Physicians have known for years that when a fetus is stressed by toxins such as alcohol (see generalization #5 on p. 784) or by a lack of necessary nutrients or oxygen during development, the immediate outcome for the fetus is often preterm delivery and low birth weight. Both of these outcomes are associated with potential problems, including developmental delays, anatomical (congenital) anomalies, functional deficits, and overt disease.

The fetus is not simply a passive recipient of the negative results of maternal stress during pregnancy. And early delivery, low birth weight, or both are not the only outcomes related to fetal stress. Stress-related changes in the intrauterine environment may also trigger numerous development problems that may become apparent during gestation or at the time of delivery. Many are related to oversecretion of endocrine secretions, especially cortisol, by both mother and developing baby (Figure 25-9). Intrauterine levels of cortisol are influenced by the maternal-fetoplacental unit and by the shared maternal-fetal hypothalamic-pituitary-adrenal axis, or HPA mechanism (review Figure 25-5).

Not only do abnormal increases in the intrauterine level of cortisol have an immediate impact on the fetus or newborn infant, they also produce intermediate and long-term effects on the individual over a lifetime. The process is now called **fetal programming.** It refers to the relationship between events occurring during the course of fetal development and the appearance of specific anatomical, physiological, or disease states that develop later in life. Early research in the area of fetal programming focused on trying to explain the relationship known to exist between the stress of inadequate fetal nutrition, low birth weight, and adult rates of cardiovascular disease and its precursors—including elevated cholesterol levels, high blood pressure, and diabetes.

Fetal programming is strongly influenced by elevated intrauterine levels of cortisol and other stress hormones, and it affects not only the cardiovascular system but also many other body systems and physiological variables over a lifetime. Cortisol-induced fetal programming

Box 25-2 | FYI

Type A Behavior and Stress

Hard-driving, competitive type A individuals who put themselves in high-stress situations have been found to be at a somewhat greater risk of elevated systolic blood pressure and coronary disease than individuals with the more relaxed and less impatient type B personality. Studies show that type A behavior patterns can be reduced by psychological guidance. Counseling of type A individuals helps them reduce stress and may cut in half their chances of suffering a heart attack (myocardial infarction, or MI) because of stress.

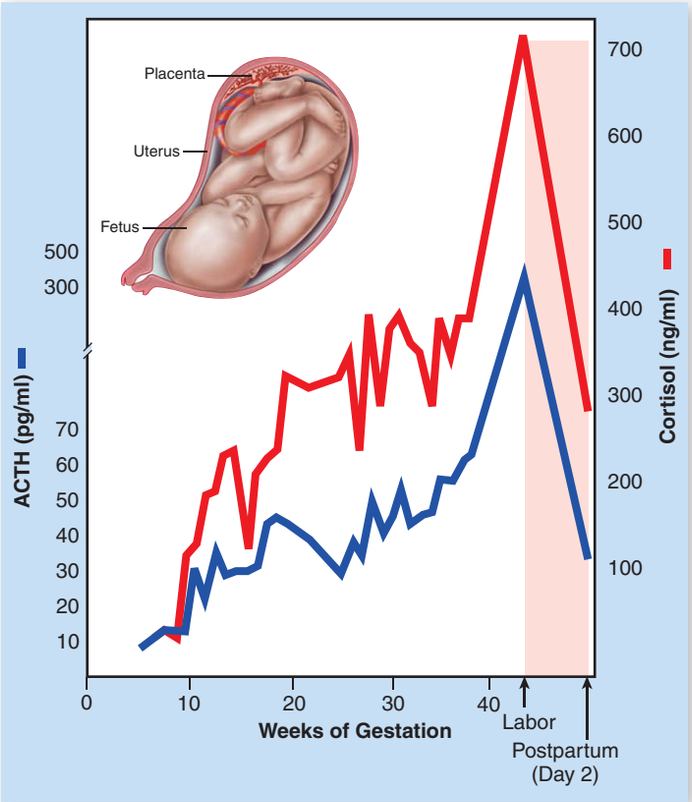


FIGURE 25-9

Stress hormones during pregnancy. The graph shows increasing levels of maternal stress hormones cortisol and ACTH during pregnancy. Notice that they decrease dramatically after birth (shaded area).

changes are known to influence body composition; growth rates; age at maturity; the functioning of the adult immune, endocrine, renal, and reproductive systems; the aging process; and even life expectancy.

Although sophisticated experimental work has shown that fetal programming does indeed occur and that it is often influenced by stress before birth, the mechanism that would explain exactly how it works has yet to be discovered. Fully understanding the role of cortisol in regulating the "partitioning" or allocation of energy (nutrients) available for use by different organ systems during intrauterine development will most certainly be important in solving the puzzle.

Many scientists believe the answer will be related to what are described as *biological tradeoffs*. For example, for a developing fetus, the "tradeoff" of simply surviving a dangerous pregnancy caused by the stress of maternal malnutrition might be to "accept" the dangers associated with preterm delivery and low birth weight. Or, diverting very limited nutrients to support central nervous system development required to sustain life at birth rather than using the same amount of energy resource to protect future reproductive system function might be another "acceptable" biological tradeoff. In a biological sense, in the cycle of life, the "big picture" focuses on survival. It is therefore appropriate to state that stress plays an important role in the health of an individual in every stage of the cycle of life from conception to death.

New research data related to fetal programming and its relationship to stress experienced by the fetus during development have dramatically increased interest in this area in both the scientific and medical communities. For example, knowing that a particular disease or condition is caused by prenatal stress related to a nutritional deficiency in the maternal diet, and not by genetic susceptibility, will drastically change public health and disease prevention strategies intended to reduce the incidence of that disease or condition in the population. A good example is prevention of certain congenital defects in the central nervous system by addition of an important micronutrient, folic acid, to the diet of pregnant women.

Expanding our knowledge about prenatal stress has resulted in new commitments being made to improve nutrition for women during pregnancy and to increase access to educational programs intended to decrease smoking and alcohol consumption.

| QUICK CHECK |

7. What is meant by the phrase "diseases of adaptation"?
8. What is the fight-or-flight reaction?
9. List four indicators of stress.
10. What is the difference between physiological and psychological stress?

the BIG picture

Stress and the Whole Body

Although our understanding of physiological and psychological stress is still evolving, we are certain of this: stress affects the entire body. Stress responses involve numerous physiological mechanisms, many of which are suspected to occur but are as yet unproven.

So far, we understand that stress responses involve nearly every system of the body. The nervous system detects and integrates the factors, or stressors, that trigger the stress responses. Physiological stress responses result from signals sent from the nervous system directly—or by way of the endocrine system. Many of these "stress signals" have been discovered in recent decades. Many different kinds of neurotransmitters, hormones, and perhaps other regulatory chemicals influence the function of the skeletal muscles, the digestive system, the urinary system, the reproductive system, the respiratory system, the cardiovascular system, the integumentary system—perhaps every system, organ, and tissue in the body.

Because the regulatory agents associated with stress influence the function of blood cells, stress can have a profound effect on the function of the immune system. Although the fact that stress inhibits immune function has been known for some time, many of the exact mechanisms that accomplish this have been discovered only in the past few decades. Biologists now better appreciate the link between the mind and the immune system and thus are better able to explain how stress causes disease—and even death. In fact, an emerging field within human biology is devoted to studying the mind-immunity link—the field of neuroimmunology. Some researchers in this emerging field have found their studies tend to incorporate diverse fields such as endocrinology, psychology, and hematology.

Considering the effect that stress can have on the entire internal environment—the whole body—and the high levels of stress that characterize the modern cultures in which many of us live and work, advancements in stress research hold the promise of improving the length and quality of our lives.

LANGUAGE OF MEDICINE *(continued from p. 782)*

general adaptation syndrome (GAS)
[*adapt-* **adjust,** *-tion* **process,** *syn-* **together,** *-drome* **running or (race) course**]

stress syndrome
(SIN-drohm)
[*stress-* **tighten,** *syn-* **together,** *-drome* **running or (race) course**]

stress-age syndrome
[*stress-* **tighten,** *syn-* **together,** *-drome* **running or (race) course**]

CASE study

"What's going on with me?" Jiang-Mei thought. Her palms were sweaty; her heart was racing; her mouth felt dry. She was finding it difficult to concentrate on the physiology test sitting on her desk. No matter how many times she told herself to calm down, the symptoms continued. She glanced over at her friend, who was taking the same test. Her friend seemed perfectly calm!

1. Which stage of the general adaptation syndrome is Jiang-Mei experiencing?
   a. Alert reaction
   b. Stage of resistance
   c. Stage of exhaustion
   d. Alarm reaction
2. If we were to do a blood test on Jiang-Mei at this moment, the levels of which hormone would be elevated?
   a. TRH
   b. CRH
   c. TSH
   d. Melatonin
3. Which of the following is not included in the "stress triad"?
   a. Enlarged lymphatic organs
   b. Increased size of adrenal glands
   c. Gastrointestinal ulcers
   d. Decreased size of lymphatic organs
4. All of the following statements are FALSE, except which one?
   a. Stressors are perceived in an infant before and after birth
   b. All stressors have the same effect on all people
   c. Stressors are always intensely negative experiences
   d. Stressors cannot be an imagined threat; they must be a real, physical threat

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CAREER choices



Dominic Steward, NREMT-P

Paramedic

As a paramedic my primary function is to maintain life in critically ill or injured people, often during transport to a care facility.

My involvement with the profession came about while serving as a safety and security specialist at a mental health facility. I found that, in order to do my job effectively, I needed to know more about medical matters. I enrolled in an Emergency Medical Technician (EMT) course, and became a full-time EMT. I've had a lifelong interest in science and technology, so the next natural step was to further my education and become an EMT-Paramedic (EMT-P), eventually obtaining National Registry status (NREMT-P).

Paramedics are trained as generalists, and our scope of practice is expanding yearly. I have medic friends who have chosen to leave "the street" to work in hospital emergency departments, in hyperbaric chambers, and in flight medicine. Continuing education is mandatory to maintain state and national certification, and many paramedics choose to further their careers in other medical fields. I know of one paramedic who is currently completing her residency to become a physician's assistant, and many of us are taking courses to become registered nurses. Credentialing, with the goal of national certification, is becoming key. This will allow lateral (i.e., from state to state) mobility for paramedics. Pay and benefits are increasing, in part because of shortages. There is also a trend for colleges to offer associates' or bachelors' degrees in conjunction with paramedic training. This will allow the profession to grow and mature.

My profession is rewarding in several tangible ways. It's important to me to have the opportunity to help people in need. And, especially since recent national events, paramedics have received public appreciation and recognition. It is an honorable way to make a living, although you won't get rich!

A paramedic's effectiveness hinges on knowledge of the anatomy and physiology of the human body. One of my responsibilities is to precept new paramedics, and those who do not have a broad foundation in A&P do not go on the street. The laboratory component of the course was key to my comprehension of the text content. If you have

CAREER choices

the chance, try to attend a dissection. I was once in a laboratory where we learned about the components of the heart by dissecting a cow's heart in a carcass obtained from a local meat market. The organ was four times the size of a human heart, so it was easy to see the various features. Pharmacology was integrated into the class, and I had the opportunity to inject multiple doses of epinephrine into the tissue. This caused the long-dead organ to begin to beat. To this day I remember all of my heart A&P!

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

SELYE'S CONCEPT OF STRESS

A. Development of the stress concept
   1. Selye found that animals exposed to noxious agents all responded with the same syndrome of changes, or "stress triad"
   2. Changes included enlarged adrenal glands, atrophied lymphatic organs, and bleeding ulcers of the stomatch and duodeum

B. Definitions
   1. Stress—a state, or condition, of the body produced by "diverse nocuous agents" and manifested by a syndrome of changes
   2. Stressors—agents that produce stress
   3. General adaptation syndrome—group of changes that manifest the presence of stress

C. Stressors
   1. Stressors are extreme stimuli—too much or too little of almost anything
   2. Stressors are very often injurious or painful stimuli
   3. Anything an individual perceives as a threat is a stressor for that individual
   4. Reaction to stressors differ for different individuals and for one individual at different times
   5. Physical or nutritional stressors experienced by a pregnant woman can cause her fetus to develop prenatal stress

D. General adaptation syndrome
   1. Manifestations
      a. Stress is intangible but can be inferred by physiological changes
      b. Three changes initially noted by Selye named *stress triad;* subsequently, many other changes were noted
      c. Entire group of changes or responses were named *general adaptation syndrome (GAS)*
   2. Stages
      a. Changes occur in stages over time, not simultaneously
      b. Three successive stages: alarm reaction, stage of resistance, stage of exhaustion
      c. Each stage characterized by different syndrome of changes (Table 25-1)

E. Mechanism of stress
   1. State of stress turns on stress response mechanism—general adaptation syndrome
   2. Stimulus that produces stress and thereby activates stress mechanism is nonspecific or variable
   3. Stress mechanism often referred to as hypothalamic-pituitary axis (HPA mechanism) (Figure 25-5)

SOME CURRENT CONCEPTS ABOUT STRESS

A. Definitions
   1. Stress—any stimulus that directly or indirectly stimulates the hypothalamus to release CRH
   2. Stress syndrome—also called the *stress response;* many diverse changes initiated by stress
   3. Allostasis—term sometimes used instead of stress syndrome to describe the body's attempts to restore homeostasis during stress
   4. Allostatic load—the effect of allostasis on the body (stress effects)

B. Stress syndrome—see Figure 25-6
   1. Direct or indirect stress stimulation of hypothalamus triggers release of CRH and stimulation of sympathetic centers and posterior pituitary gland
      a. CRH triggers release of adrenocortitropic hormone (ACTH), which in turn triggers release of cortisol and aldosterone from adrenal cortex
      b. Sympathetic activation produces collection of adrenergic effects called the fight-or-flight reaction (e.g., increased heart rate and blood pressure); review Table 16-4 on p. 500
   2. Additional hormones such as neuropeptide Y may produce additional stress responses

C. Stress and disease—Selye held that stress could result in disease instead of adaptation; in today's terms: high allostatic load can produce fatigue or disease

D. Indicators of stress (Figure 25-7)
   1. Stress response determined by physiological measurements and observations—faster, stronger heartbeat; higher blood pressure; sweaty palms; dilated pupils

2. Laboratory tests reveal decreased eosinophils and lymphocytes; increased level of adrenocorticoids

E. Corticoids and resistance to stress
   1. Increase in corticoids when experiencing stress is proved reaction to stress
   2. Role of higher levels of corticoids in helping body resist stress not yet proven

F. Psychological stress
   1. Psychological stressors—anything that an individual perceives as a threat to survival or self-image (Figure 25-8)
   2. A syndrome of subjective and objective responses characterizes the mental state of psychological stress including anxiety (dominant subjective response) restlessness, irritability, lying, crying
   3. Psychological stressors produce physiological stress (see summary of principles on p. 792)

G. Effects of intrauterine stress
   1. Fetus develops short- and long-term responses to stress experienced during intrauterine development (Figure 25-9)
      a. Frequent stressors include maternal malnutrition, hypoxia, and exposure to toxins such as alcohol
      b. Low birth weight and preterm delivery are common immediate responses to intrauterine stress
   2. Maternal-fetal blood levels of cortisol, important mediators of stress, are influenced by endocrine secretory activity of maternal-fetoplacental unit and the shared maternal-fetal hypothalamic-pituitary-adrenal (HPA) mechanism
   3. Fetal programming responses to stress often result in negative outcomes later in life and affect many organ systems and even life expectancy
   4. Concept of *biological tradeoffs* may be involved in fetal programming outcomes; for example, low birth weight and preterm delivery may be tradeoffs for stress of maternal malnutrition by the fetus to ensure survival

THE BIG PICTURE: STRESS AND THE WHOLE BODY

A. Stress affects the entire body
B. Nervous system detects and integrates stressors that trigger stress responses
C. Stress can have profound affect on immune system
D. Emerging field of neuroimmunology studies mind-immunity link

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Define the terms *stress*, *stressor*, and *general adaptation syndrome*.
2. Describe a few generalizations about the kinds of stimuli that constitute stressors.
3. What three stages make up the general adaptation syndrome? What changes characterize each stage?
4. What changes constitute the "stress triad"?
5. An increase in what three hormones brought about the changes that Selye named the general adaptation syndrome?
6. What function, according to Selye, does the general adaptation syndrome serve?
7. Stress, according to Selye, is a state, or condition, of the body. According to a current operational definition, what is stress?
8. What part of the brain, according to current ideas, plays the key role in initiating stress syndrome responses?
9. What parts of the nervous system other than that named in question 8 are involved in inducing the stress syndrome?
10. Briefly, what role, if any, does each of the following hormones play when the body is subjected to stress: ACTH, ADH, aldosterone, cortisol, CRH, epinephrine, and norepinephrine?
11. What has been proven about corticoids in relation to stress?
12. What issue is considered controversial regarding corticoids as they relate to stress?
13. Cite several examples of psychological stressors.
14. Are psychological stressors the same for all individuals? Give an example.
15. Give some examples of subjective indicators of psychological stress.
16. Give some examples of objective responses that are part of psychological stress.

CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

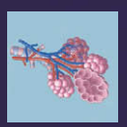
1. Based on what you know regarding Selye's experimental results, how would you explain why stress could be described as a nonspecific response?
2. What is the relationship between stress and disease? If stress levels were high in a person, how might age and personality type affect the risk for specific diseases?
3. What observations and clinical test results would indicate an individual was under stress?
4. How would you use psychophysiology to explain the Chinese rice powder test?
5. Compare and contrast psychological stress and physiological stress. What is the relationship between physiological stress and psychological stress?

Unit Five

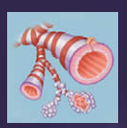
Respiration, Nutrition, and Excretion

The chapters in Unit Five provide a discussion of respiration, digestion, processing of nutrients, and excretion of wastes by the urinary system. The concluding chapters of this unit discuss fluid and electrolyte balance and acid-base balance. Ultimately, all homeostatic mechanisms function to maintain what can best be described as a "dynamic constancy" at the cellular level. For example, although under normal conditions the oxygen (O_2) and carbon dioxide (CO_2) content of blood does not change much over time, the quantity of O_2 and CO_2 that enters and exits the blood can vary widely with exercise. Delivery of oxygen and elimination of carbon dioxide and other wastes resulting from the metabolism of nutrients must be regulated within narrow limits so that cellular function remains normal. Maintaining the dynamic constancy of fluid and electrolyte balance and acid-base balance at the cellular level is also required for survival. The anatomical structures and functional control mechanisms discussed in this unit all relate, in the last analysis, to cellular homeostasis.

SEEING THE BIG PICTURE



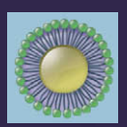
26 Anatomy of the Respiratory System, 798



27 Physiology of the Respiratory System, 823



28 Anatomy of the Digestive System, 861



29 Physiology of the Digestive System, 901



30 Nutrition and Metabolism, 931



31 Urinary System, 970



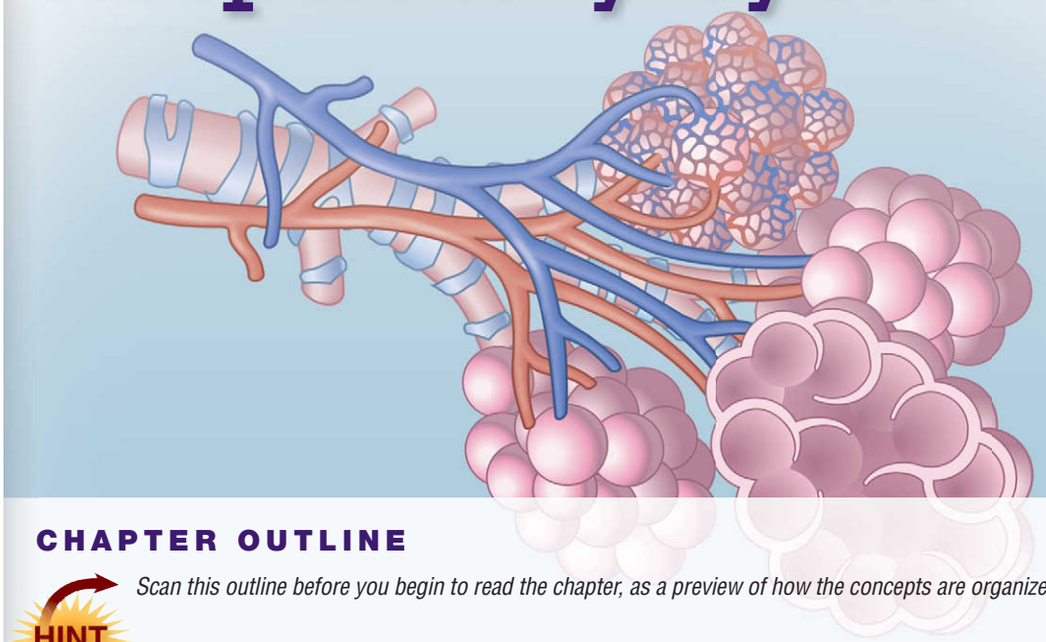
32 Fluid and Electrolyte Balance, 1003



33 Acid-Base Balance, 1025

26

Anatomy of the Respiratory System



LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

alveolar duct
(al-VEE-oh-lar)
[*alve-* **hollow,** *-ol-* **little,** *-ar* **relating to**]

alveolus
(al-VEE-oh-lus)
[*alve-* **hollow,** *-olus* **little**] *pl.,* alveoli

apex
(AY-peks)
[*apex* **tip**] *pl.,* apices

arytenoid
(ar-eh-TEH-noyd)
[*aryten-* **ladle,** *-oid* **like**]

base
[*bas-* **foundation**]

bronchial tree
(BRONG-kee-al)
[*bronch-* **windpipe,** *-al* **relating to**]

bronchiole
(BRONG-kee-ohl)
[*bronch-* **windpipe,** *-ol-* **little**]

bronchopulmonary segment
(brong-koh-PUL-moh-nair-ee)
[*bronch-* **windpipe,** *-pulmon-* **lung,** *-ary* **relating to**]

concha
(KONG-kah)
[*concha* **sea shell**] *pl.,* conchae

costal surface
(KOS-tal)
[*costa-* **rib,** *-al* **relating to**]

cribriform plate
(KRIB-ri-form)
[*cribr-* **sieve,** *-form* **shape**]

epiglottis
(ep-i-GLOT-is)
[*epi-* **upon,** *-glottis* **tongue**]
pl., epiglottides or epiglottises

glottis
(GLOT-is)
[*glottis* **tongue**] *pl.,* glottides or glottises

continued on p. 819

CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

Structural Plan of the Respiratory System, 799

Upper Respiratory Tract, 799
- Nose, 799
  - Structure of the Nose, 799
  - Functions of the Nose, 802
- Pharynx, 802
  - Structure of the Pharynx, 802
  - Functions of the Pharynx, 803
- Larynx, 803
  - Location of the Larynx, 803
  - Structure of the Larynx, 803
  - Cartilages of the Larynx, 805
  - Muscles of the Larynx, 805
  - Functions of the Larynx, 805

Lower Respiratory Tract, 807
- Trachea, 807
  - Structure of the Trachea, 807
  - Function of the Trachea, 808
- Bronchi and Alveoli, 808
  - Structure of the Bronchi, 808
  - Structure of the Alveoli, 809
  - Functions of the Bronchi and Alveoli, 809
- Lungs, 812
  - Structure of the Lungs, 812
  - Functions of the Lungs, 814
- Thorax, 814
  - Structure of the Thoracic Cavity, 814
  - Functions of the Thoracic Cavity, 814

Cycle of Life: Respiratory System, 816

The Big Picture: Anatomy of the Respiratory System, 816

Mechanisms of Disease, 816

Case Study, 820

The respiratory system functions as an air distributor and a gas exchanger so that oxygen can be supplied to and carbon dioxide removed from the body's cells. Because most of our trillions of cells lie too far from air to exchange gases directly with it, air must first exchange gases with blood, blood must circulate, and finally, blood and cells must exchange gases. These events require the functioning of two systems, namely, the respiratory system and the circulatory system. All parts of the respiratory system—except its microscopic-sized sacs called alveoli*—function as air distributors. Only the alveoli and the tiny alveolar ducts that open into them serve as gas exchangers.*

In addition to air distribution and gas exchange, the respiratory system effectively filters, warms, and humidifies the air we breathe. Respiratory organs also help produce sounds, including speech used in communicating oral language. Special sensory epithelium in the respiratory tract makes the sense of smell (olfaction) possible. The respiratory system also plays an important role in the regulation, or homeostasis, of pH in the body.

In this chapter, we explore the structural aspects of the respiratory system and in Chapter 27 we explore the functional aspects.

STRUCTURAL PLAN OF THE RESPIRATORY SYSTEM

For purposes of study, the respiratory system may be divided into upper and lower tracts, or structural divisions. The organs of the upper respiratory tract are located outside the thorax, or chest cavity, whereas those in the lower tract, or division, are located almost entirely within it (Figure 26-1).

The **upper respiratory tract** is composed of the nose, nasopharynx, oropharynx, laryngopharynx, and larynx. The **lower respiratory tract,** or division, consists of the trachea, all segments of the bronchial tree, and the lungs. Functionally, the respiratory system also includes several accessory structures, such as the oral cavity, rib cage, and respiratory muscles including the diaphragm. Together, these structures constitute the lifeline, the air supply line of the body. This chapter describes the functional anatomy of these organs. The physiology of the respiratory system as a whole is discussed in Chapter 27. Cells require a constant supply of oxygen for the vital energy conversion process carried out within each cell's mitochondria—a process called *cellular respiration* (Chapter 30). Cellular respiration produces carbon dioxide (CO_2) as a waste product, which must be removed before it accumulates to dangerously high levels.

Box 26-1 | FYI

Danger Area of the Face

The fact that the skin of the external nose contains many sebaceous glands has great clinical significance. If these glands become infected, it is possible for infectious material to enter and pass from facial veins near the nose to one of the intracranial venous sinuses (see Chapter 21). For this reason, the triangle-shaped zone surrounding the external nose is often known as the "danger area of the face."

UPPER RESPIRATORY TRACT

Nose

STRUCTURE OF THE NOSE

The nose has external and internal structures. The external portion, that is, the part that protrudes from the face, consists of a bony and cartilaginous framework overlaid by skin containing many sebaceous glands (Box 26-1). The two nasal bones meet in the center of the face just below the forehead, where they are surrounded by the frontal bone to form the root of the nose. The nose is surrounded by the maxilla laterally and inferiorly at its base. The flaring cartilaginous expansion forming and supporting the outer side of each oval nostril opening is called the *ala*.

The internal portion of the nose, or nasal cavity, lies over the roof of the mouth where the palatine bones, which form the floor of the nose and the roof of the mouth, separate the nasal cavities from the mouth cavity. Sometimes the palatine bones fail to unite completely and produce a condition known as **cleft palate.** When this abnormality exists, the mouth is only partially separated from the nasal cavity, and consequently, difficulties arise in swallowing and speaking.

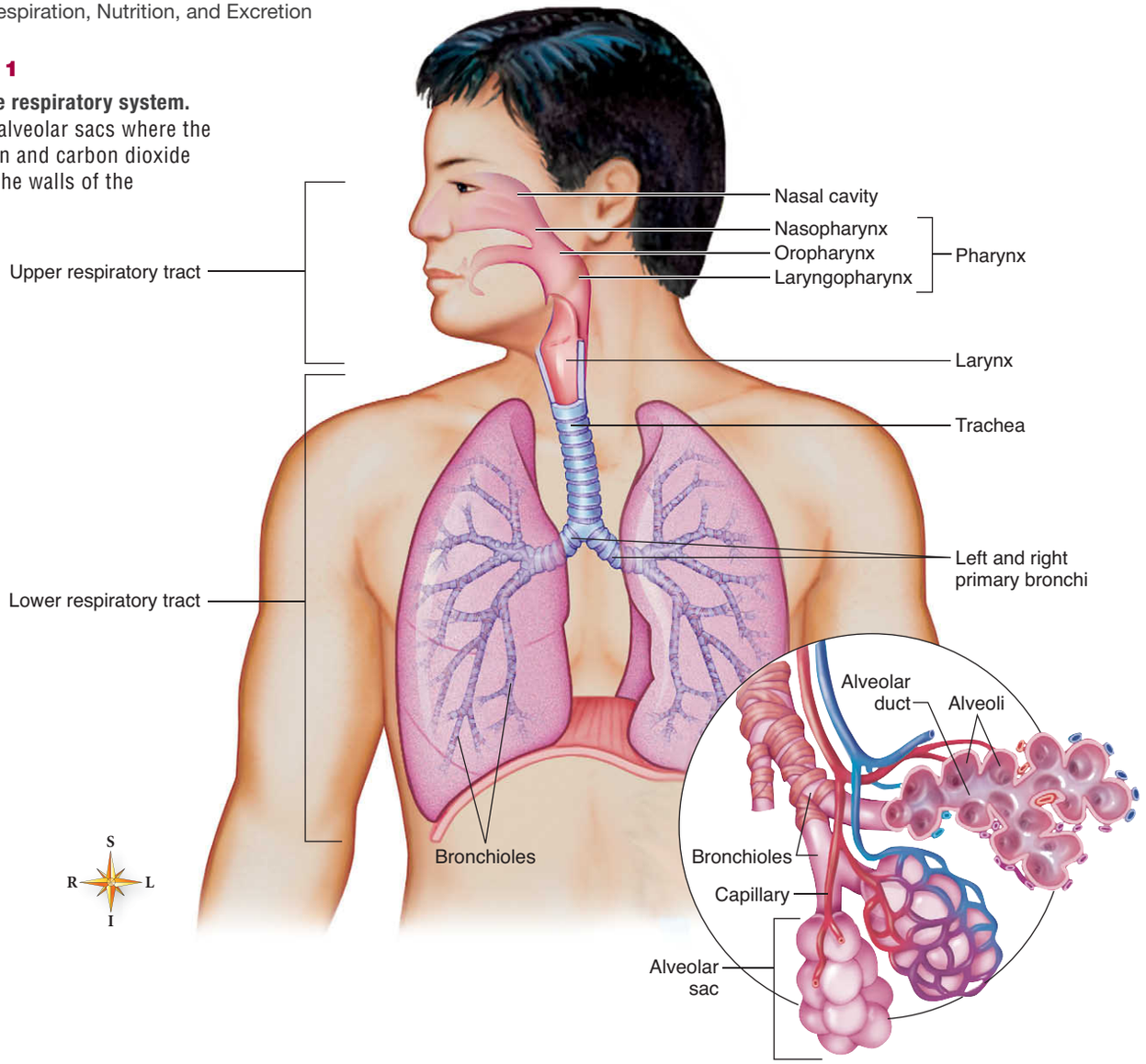
The roof of the nose is separated from the cranial cavity by a portion of the ethmoid bone called the **cribriform plate** (Figures 26-2 and 26-3). The cribriform plate is perforated by many small openings that permit branches of the olfactory nerve responsible for the special sense of smell to enter the cranial cavity and reach the brain.

Separation of the nasal and cranial cavities by a thin, perforated plate of bone presents real hazards. If the cribriform plate is damaged as a result of trauma to the nose, it is possible for potentially infectious material to pass directly from the nasal cavity into the cranial fossa and infect the brain and its covering membranes.

The hollow nasal cavity is separated by a midline partition, the **septum** (see Figure 26-2), into right and left cavities. Note in Figure 26-2 that the nasal septum is made up of four main structures: the perpendicular plate of the ethmoid bone above, the vomer bone, and the septal nasal and vomeronasal cartilages below. In the adult the nasal septum is frequently deviated to one

FIGURE 26-1

Structural plan of the respiratory system. The inset shows the alveolar sacs where the interchange of oxygen and carbon dioxide takes place through the walls of the grapelike alveoli.



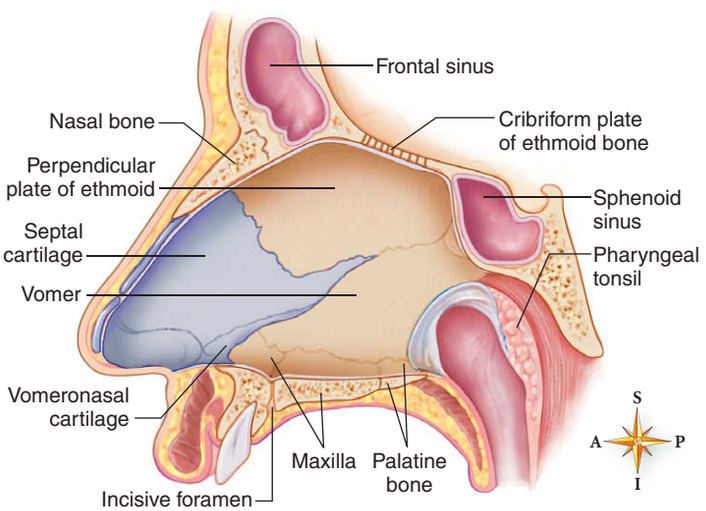


FIGURE 26-2

Nasal septum. The nasal septum consists of the perpendicular plate of the ethmoid bone, the vomer, and the septal and vomeronasal cartilages.

side or the other, interfering with respiration and with drainage of the nose and sinuses. The nasal septum has a rich blood supply. Nosebleeds, or *epistaxis*, often occur as a result of septal contusions caused by a direct blow to the nose. Epistaxis may also result from weak blood vessels combined with high blood pressure. Though seemingly dramatic, nosebleeds are seldom a serious health problem.

Each nasal cavity is divided into three passageways named the *superior*, *middle*, and *inferior meatuses*. These incomplete tubes are formed by the projection of the **conchae,** or **turbinates,** curving from the lateral walls of the internal portion of the nose (see Figure 26-3). The superior and middle conchae are processes of the ethmoid bone, whereas the inferior conchae are separate bones.

The external openings into the nasal cavities, commonly referred to as nostrils, have the technical name of *anterior nares*

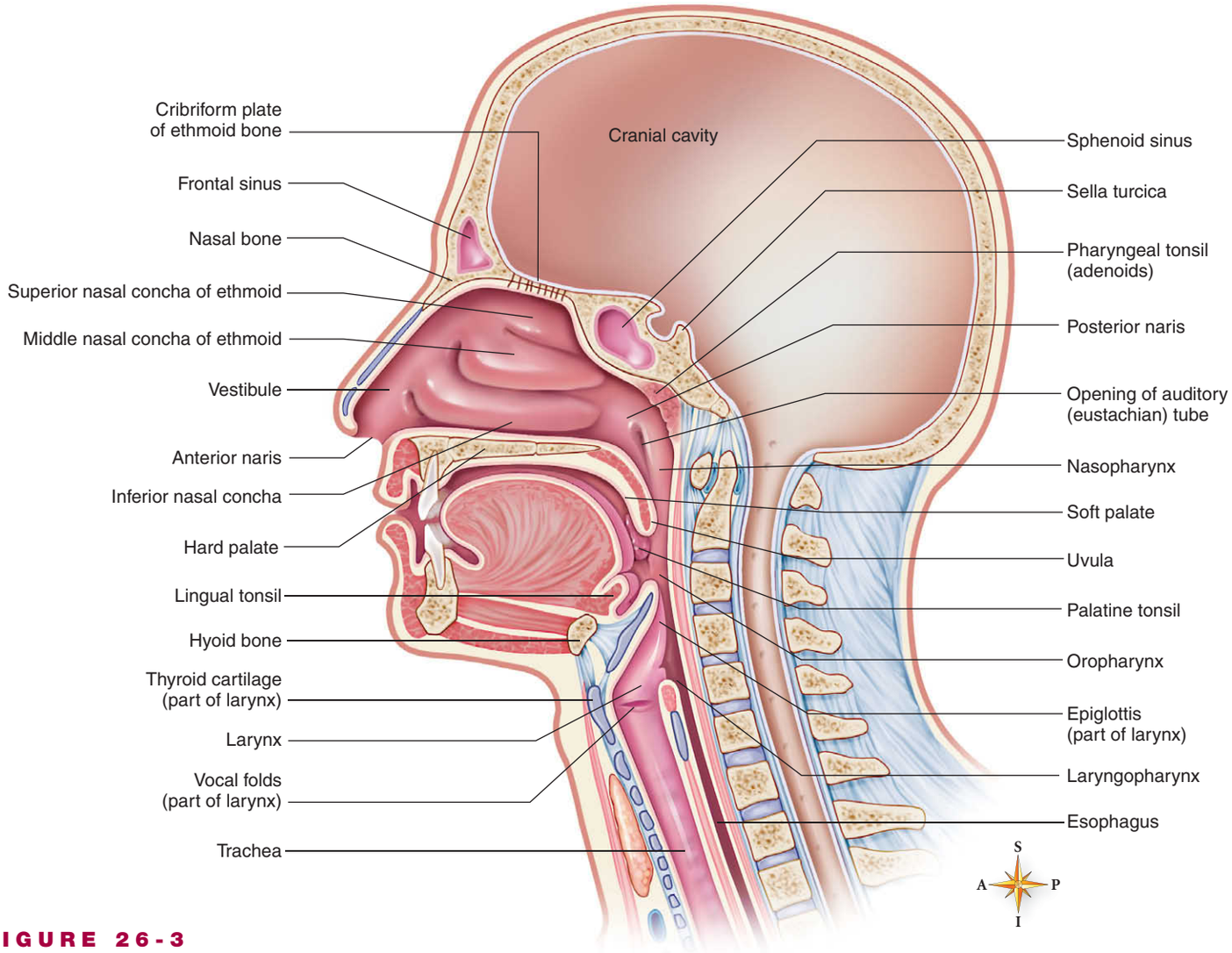


FIGURE 26-3

Upper respiratory tract. In this midsagittal section through the upper respiratory tract, the nasal septum has been removed to reveal the turbinates (nasal conchae) of the lateral wall of the nasal cavity. The three divisions of the pharynx (nasopharynx, oropharynx, and laryngopharynx) are also visible.

(singular, *naris*). They are sometimes called *external nares*. The anterior nares open into an area covered by skin that is reflected from the wings (ala) of the nose. This area, called the **vestibule,** is located just inside the nasal cavity below the inferior meatus. The vestibule is lined with skin. Coarse hairs called **vibrissae,** sebaceous glands, and numerous sweat glands are found in the skin of the vestibule. Once air has passed over the skin of the vestibule, it enters the **respiratory portion** of each nasal passage. This area extends from the inferior meatus to the small funnel-shaped orifices of the *posterior (internal) nares*. The posterior nares are openings that allow air to pass from the nasal cavity into the next major segment of the upper respiratory tract—the pharynx.

If one were to "trace" the movement of air through the nose into the pharynx, it would be found that air passes through several structures on the way. The sequence is as follows:

1. Anterior (external) nares
2. Vestibule
3. Inferior, middle, and superior meatuses, simultaneously
4. Posterior (internal) nares

Nasal Mucosa

Once air has passed over the skin of the vestibule and enters the respiratory portion of the nasal passage, it passes over the **respiratory mucosa.** This mucous membrane has a pseudostratified ciliated columnar epithelium rich in goblet cells (Figure 26-4). The respiratory mucosa possesses a rich blood supply, especially over the inferior turbinate, and is bright pink or red. Near the roof of the nasal cavity and over the superior turbinate and opposing portion of the septum, the mucosa turns pale and has a yellowish tint. In this area it is referred to as the **olfactory epithelium.** This membrane contains many olfactory nerve cells and has a rich lymphatic plexus. Ciliated mucous membrane lines the rest of the respiratory tract down as far as the smaller bronchioles.

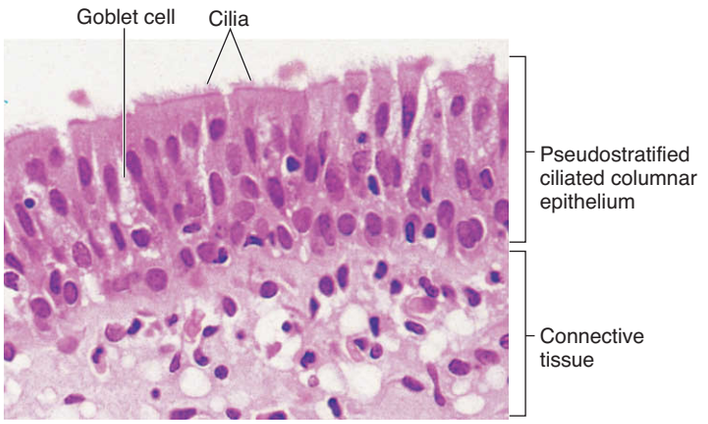


FIGURE 26-4

Respiratory mucosa. This epithelium is typically ciliated and exhibits numerous goblet cells that produce and release mucus.

| A&P CONNECT |

Besides the olfactory sensory neurons imbedded in the nasal mucosa, a structure called the *vomeronasal organ (VNO)* is located in the mucosa of the inferior nasal septum. The VNO is thought to be involved in sensing pheromones, which are sex signaling chemicals. Want to know more? Check out ***Pheromones and the Vomeronasal Organ*** and ***Nerve Zero*** online at ***A&P Connect.***

evolve

Paranasal Sinuses

The four pairs of **paranasal sinuses** are air-containing spaces that lighten the weight of the skull and open, or drain, into the nasal cavity. They take their names from the skull bones in which they are located (see Chapter 9). These paranasal sinuses are the frontal, maxillary, ethmoid, and sphenoid sinuses (Figure 26-5). Like the nasal cavity, each paranasal sinus is lined by respiratory mucosa. The mucous secretions produced in the sinuses are continually being swept into the nose by the ciliated surface of the respiratory membrane.

The right and left frontal sinuses are located just above the corresponding orbit, whereas the maxillary, the largest of the sinuses, extends into the maxilla on either side of the nose. The sphenoid sinuses lie in the body of the sphenoid bone on either side of the midline in close proximity to the optic nerves and pituitary gland.

Note in Figure 26-5 that the ethmoid sinuses are not single large cavities but a collection of small air cells divided into anterior, middle, and posterior groups that open independently into the upper part of the nasal cavity (Box 26-2). The paranasal sinuses drain as follows:

- Into the middle meatus (passageway below the middle concha)—frontal, maxillary, anterior, and middle ethmoidal sinuses
- Into the superior meatus—posterior ethmoidal sinuses
- Into the space above the superior conchae (sphenoethmoidal recess)—sphenoid sinuses

Box 26-2 | FYI

Development of the Paranasal Sinuses

The paired and often asymmetrical sinuses are small or rudimentary at birth but increase in size with growth of the skull. Although fairly well developed by 7 years of age, they do not reach maximal size until after puberty. In adults, the sinuses are subject to considerable variation in size and shape.

FUNCTIONS OF THE NOSE

The nose serves as a passageway for air going to and from the lungs. However, if the nasal passages are obstructed, it is possible for air to bypass the nose and enter the respiratory tract directly through the mouth.

Air that enters the system through the nasal cavity is filtered of impurities, warmed, moistened, and chemically examined (by olfaction) to detect substances that might prove irritating to the delicate lining of the respiratory tract. The vibrissae, or *nasal hairs*, in the vestibule serve as an initial "filter" that screens particulate matter from air that is entering the system. The conchae, or turbinates, then serve as baffles to slow and stir the air—as well as provide a large mucus-covered surface area over which air must pass before reaching the pharynx. The respiratory membrane produces copious quantities of mucus and possesses a rich blood supply, especially over the inferior conchae, which permits rapid warming and moistening of the dry inspired air. Mucous secretions provide the final "trap" where some of the remaining particulate matter from air is removed as it travels through the nasal passages. Fluid from the lacrimal glands (see Figure 17-19 on p. 525) and additional mucus produced in the paranasal sinuses also help trap particulate matter and moisten air passing through the nose.

In addition, the hollow sinuses act to lighten the bones of the skull and serve as resonating chambers for speech. Swirling of air by the middle and superior conchae over the olfactory epithelium makes the special sense of olfaction possible.

| QUICK CHECK |

1. What are the overall functions of the respiratory system? Which other body system is involved in accomplishing these functions?
2. Name the principal organs of the upper respiratory tract. Name the principal organs of the lower respiratory tract.
3. Describe the paranasal sinuses. What is their anatomical relationship to the nose?

Pharynx

STRUCTURE OF THE PHARYNX

Another name for the **pharynx** is the throat. It is a tubelike structure about 12.5 cm (5 inches) long that extends from the base of the skull to the esophagus and lies just anterior to the cervical vertebrae. It is made of muscle and is lined with mucous membrane.

The pharynx has three anatomical divisions. The **nasopharynx** is located behind the nose and extends from the posterior nares to the

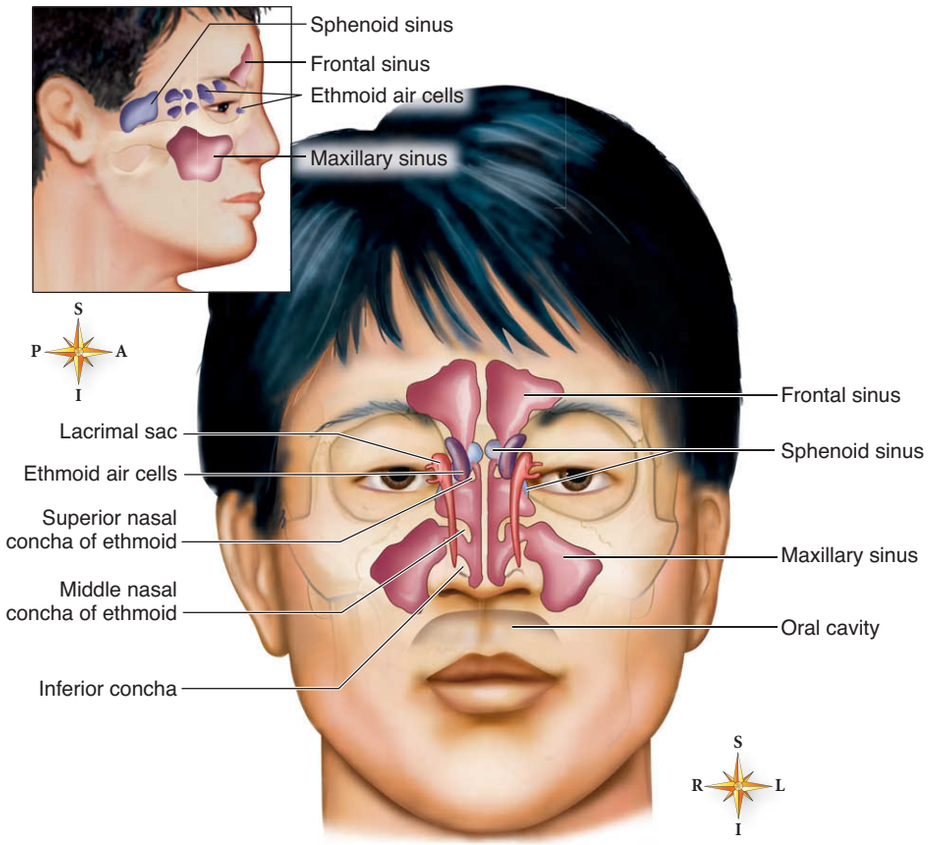


FIGURE 26-5

The paranasal sinuses. The anterior view shows the anatomical relationship of the paranasal sinuses to each other and to the nasal cavity. The inset is a lateral view of the position of the sinuses.

level of the soft palate. The **oropharynx** is located behind the mouth from the soft palate above to the level of the hyoid bone below. Finally, the **laryngopharynx** extends from the hyoid bone to the esophagus. Figure 26-3 shows the divisions of the pharynx.

Seven openings are found in the pharynx (see Figure 26-3):

- Right and left auditory (eustachian) tubes opening into the nasopharynx
- Two posterior nares opening into the nasopharynx
- The opening from the mouth, known as the fauces, into the oropharynx
- The opening into the larynx from the laryngopharynx
- The opening into the esophagus from the laryngopharynx

The **pharyngeal tonsils** are located in the nasopharynx on its posterior wall opposite the posterior nares. The pharyngeal tonsils are referred to as *adenoids* when they are enlarged. Although the cavity of the nasopharynx differs from the oral and laryngeal divisions in that it does not collapse, it still may become obstructed. If these tonsils enlarge to become adenoids, they may fill the space behind the posterior nares and make it difficult or even impossible for air to travel from the nose into the throat. You may want to review details of the structure and function of tonsils in Chapter 23.

Two pairs of organs are found in the oropharynx: the **palatine tonsils,** located behind and below the pillars of the fauces, and the **lingual tonsils,** located at the base of the tongue. The palatine tonsils are the ones most commonly removed in the procedure referred to as a tonsillectomy. Only rarely are the lingual tonsils also removed.

FUNCTIONS OF THE PHARYNX

The pharynx serves as a common pathway for the respiratory and digestive tracts, because both air and food must pass through this structure before reaching the appropriate tubes—the trachea (air) and esophagus (food). It also affects phonation (speech production). For example, only by changing the shape of the pharynx can the different vowel sounds of speech be formed.

Larynx

LOCATION OF THE LARYNX

The **larynx,** or voice box, lies between the root of the tongue and the upper end of the trachea just below and in front of the lowest part of the pharynx (see Figure 26-1). It might be described as a vestibule opening into the trachea from the pharynx. It normally extends between the third, fourth, fifth, and sixth cervical vertebrae but is often positioned somewhat higher in females and during childhood for both genders. The lateral lobes of the thyroid gland and the carotid artery within its covering sheath touch the sides of the larynx.

STRUCTURE OF THE LARYNX

The triangle-shaped larynx consists largely of cartilages that are attached to one another and to surrounding structures by muscles or

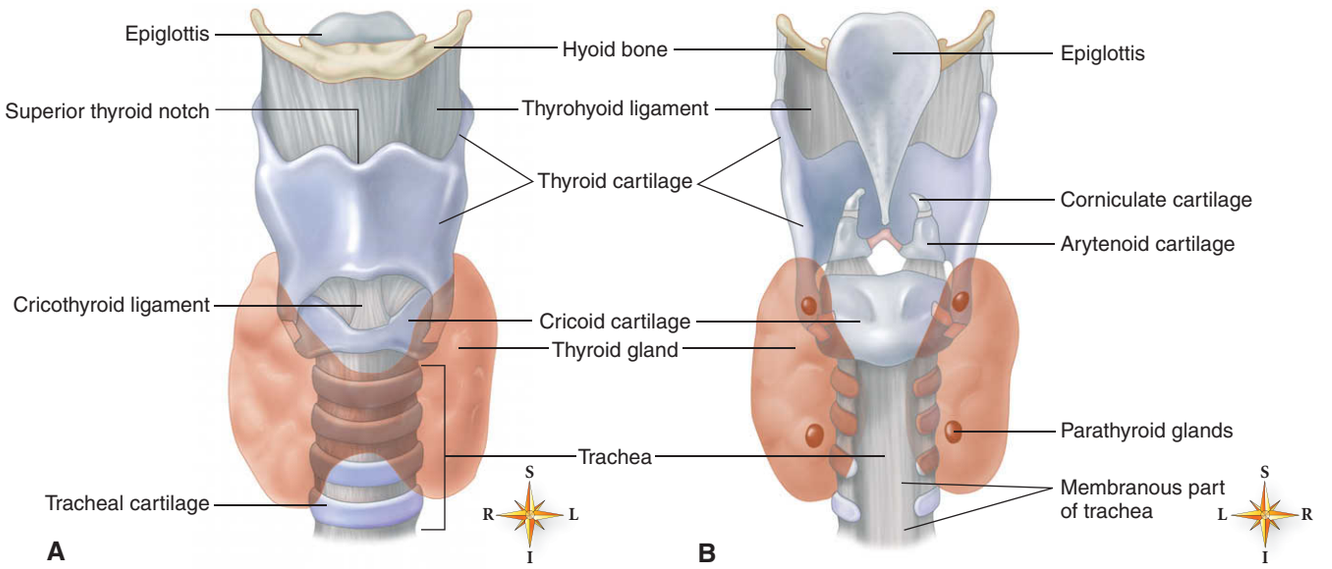


FIGURE 26-6

Laryngeal cartilages. Some softer tissues of the larynx and surrounding structures have been removed to make it possible to see the cartilages of the larynx. Note the position of the nearby thyroid gland. **A,** Anterior view. **B,** Posterior view.

by fibrous and elastic tissue components (Figure 26-6). It is lined by a ciliated mucous membrane. The cavity of the larynx extends from its triangle-shaped inlet at the epiglottis to the circular outlet at the lower border of the cricoid cartilage, where it is continuous with the lumen of the trachea (Figure 26-7).

The larynx is lined primarily with respiratory mucosa—pseudostratified ciliated columnar epithelium. The mucous membrane lining the larynx forms two pairs of lateral folds that jut inward into its cavity. The upper folds are called the **vestibular folds.** They are also sometimes called the *false vocal folds* for the rather obvious reason that they play no part in vocalization. The lower pair serves as the **vocal folds,** which produce sounds needed for speech and other vocalizations. The vocal folds are sometimes called the *true vocal folds* or simply *vocal cords.* Each vocal fold is covered with nonkeratinized stratified squamous epithelium and supported at its medial edge by a strong *vocal ligament.* The slitlike space between the left and right vocal folds, called the *rima glottidis,* is the narrowest part of the larynx.

The vocal folds and the space between them (rima glottidis) are together designated as the **glottis.** An endoscopic view of the vocal folds and related structures is shown in Figure 26-8, *B*.

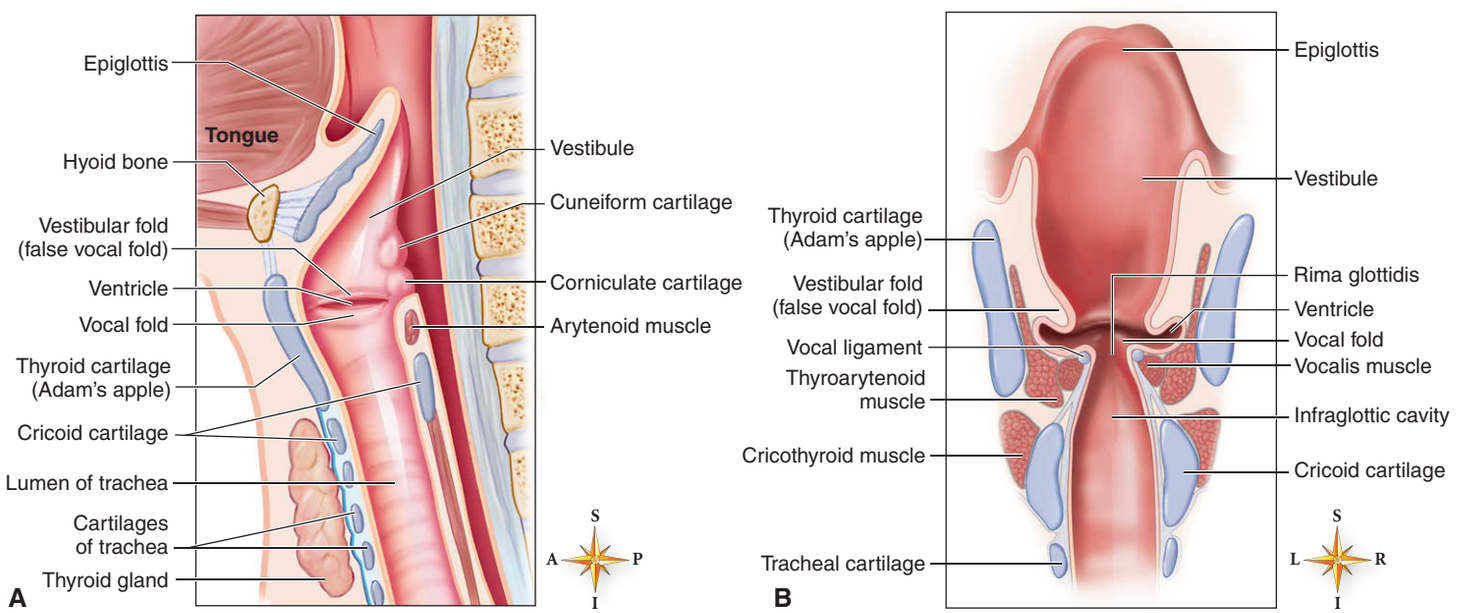


FIGURE 26-7

Larynx. These illustrations depict the mucosal lining of the larynx, with its folds and underlying muscles and ligaments visible. **A,** Sagittal section. **B,** Frontal section, viewed from behind.

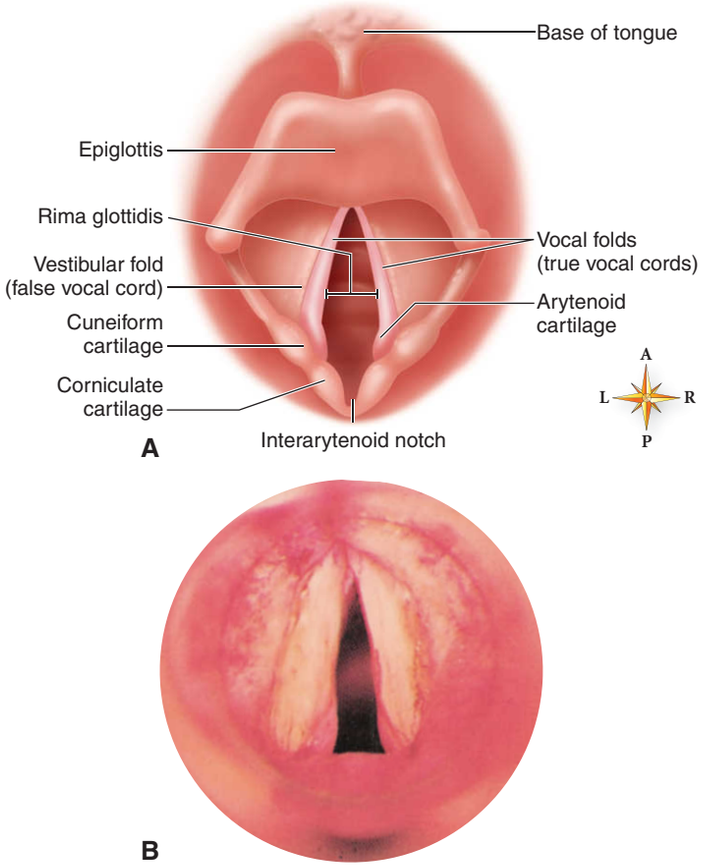


FIGURE 26-8

Vocal folds. A, Vocal folds viewed from above. **B,** Photograph taken with an endoscope showing the vocal folds in the open position.

The laryngeal cavity above the vestibular folds is called the **vestibule.** The very short middle portion of the cavity between the vestibular and vocal folds is the **ventricle** of the larynx, or *laryngeal ventricle.* The *infraglottic cavity* is the open space below the glottis.

CARTILAGES OF THE LARYNX

Nine cartilages form the framework of the larynx. The three largest—the thyroid cartilage, the epiglottis, and the cricoid cartilage—are single structures. The other six are three pairs of smaller accessory cartilages, namely, the arytenoid, corniculate, and cuneiform cartilages.

- The **thyroid cartilage** (Adam's apple) is the largest cartilage of the larynx and is the one that gives the characteristic triangular shape to its anterior wall. It is usually larger in men than in women and has less of a fat pad lying over it—two reasons that a man's thyroid cartilage protrudes more than a woman's.
- The **epiglottis** is a small leaf-shaped cartilage that projects upward behind the tongue and hyoid bone. It is attached below to the thyroid cartilage, but its free superior border can flex to move up and down during swallowing to prevent food or liquids from entering the trachea (see Figures 26-6 and 26-7). The epiglottis is covered with nonkeratinized stratified squamous epithelium.
- The pyramid-shaped **arytenoid** cartilages are the most important of the paired laryngeal cartilages. The base of each cartilage articulates with the superior border of the cricoid cartilage (see Figure 26-6). The anterior angles of these cartilages serve as points of attachment for the vocal folds.

MUSCLES OF THE LARYNX

The muscles of the larynx are often divided into intrinsic and extrinsic groups. Intrinsic muscles have both their origin and insertion on the larynx. They are important in controlling vocal fold length and tension and in regulating the shape of the laryngeal inlet. Extrinsic muscles insert on the larynx but have their origin on some other structure—such as the hyoid bone. Therefore, contraction of the extrinsic muscles actually moves or displaces the larynx as a whole. Muscles in both groups play important roles in respiration, vocalization, and swallowing. During swallowing, for example, contraction of the intrinsic aryepiglottic muscles (those that connect the arytenoid cartilages with the epiglottis) prevents entry of food or fluid into the trachea by squeezing the laryngeal inlet shut.

Two other pairs of intrinsic laryngeal muscles function to open and close the glottis by adducting or abducting the vocal folds. These events are crucial to both respiration and voice production. Certain other intrinsic muscles of the larynx function to influence the pitch of the voice by either lengthening and tensing or shortening and relaxing the vocal folds.

FUNCTIONS OF THE LARYNX

The larynx functions in respiration because it constitutes part of the vital airway to the lungs. This unique passageway, like the other components of the upper respiratory tract, is lined with a ciliated mucous membrane that helps in removal of dust particles and in warming and humidification of inspired air. In addition, it protects the airway against the entrance of solids or liquids during swallowing.

It also serves as the organ of voice production—hence its popular name, the *voice box.* Air being expired through the glottis, narrowed by partial adduction of the vocal folds, causes them to vibrate. Their vibration produces the voice. Several other structures besides the larynx contribute to the sound of the voice by acting as sounding boards or resonating chambers. Thus the size and shape of the nose, mouth, pharynx, and bony sinuses help determine the quality of the voice.

| A&P CONNECT |

Edema (swelling) of the mucosa covering the vocal folds and other laryngeal tissues can be a potentially lethal condition. Even a moderate amount of swelling can obstruct the glottis so much that air cannot get through and asphyxiation results. To find out more, check out ***Swollen Larynx*** online at ***A&P Connect.***

evolve

| QUICK CHECK |

4. What are the three main divisions of the pharynx?
5. Describe where the tonsils are located.
6. Distinguish between true and false vocal folds.

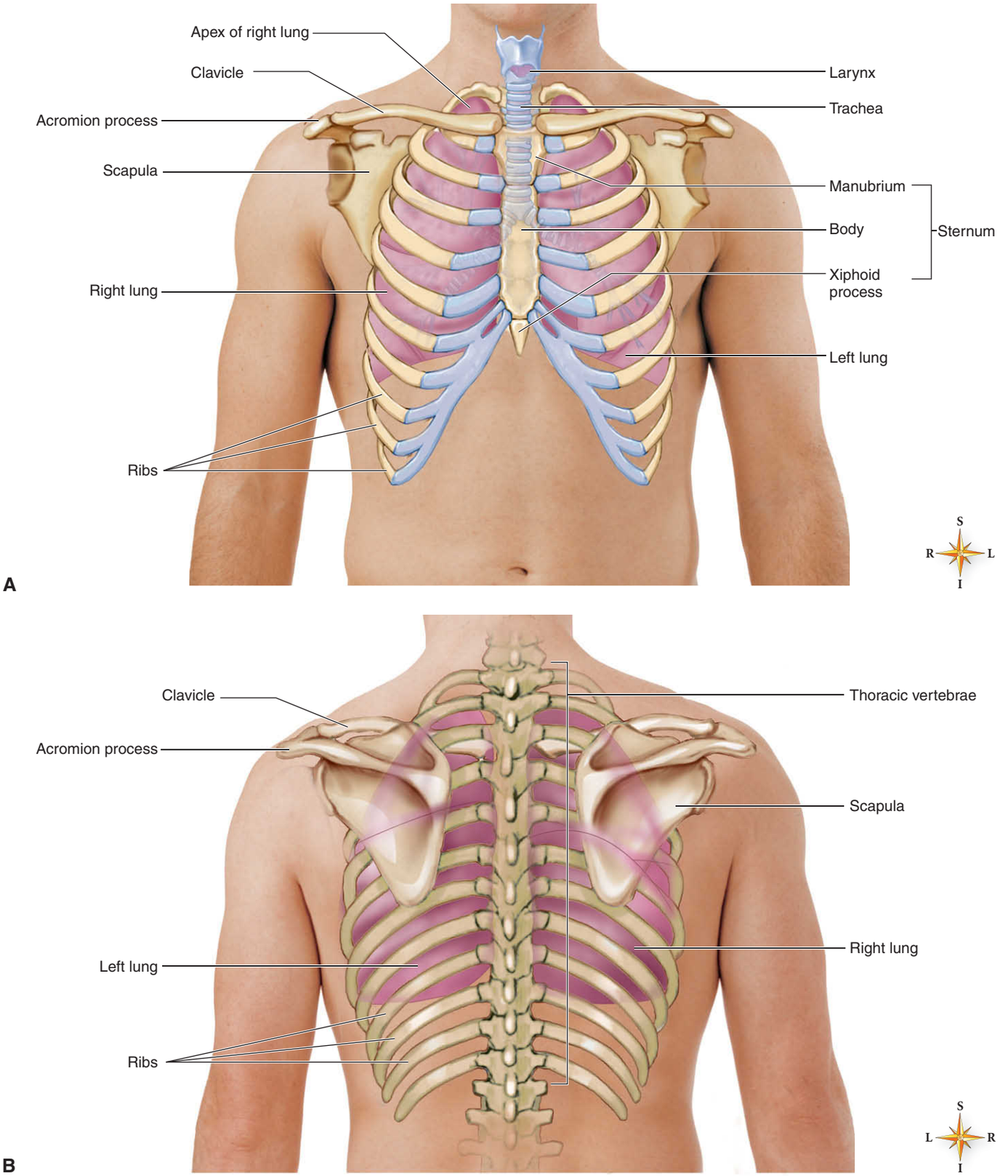


FIGURE 26-9

Bony structures of the chest. These structures form a protective and expandable cage around the lungs and heart. **A,** Anterior view. **B,** Posterior view.

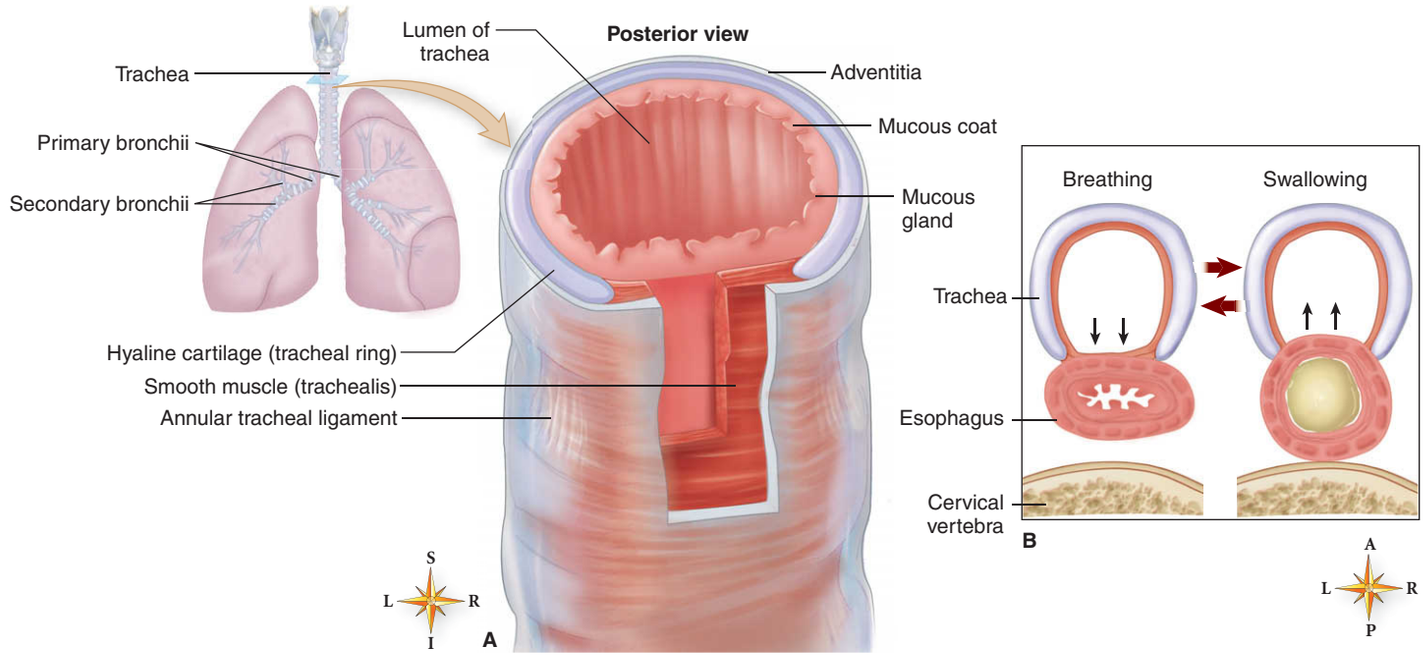


FIGURE 26-10

Cross section of the trachea. The inset at the top shows where the section was cut. **A,** Structure of the trachea. **B,** Incomplete tracheal rings and elasticity of posterior tracheal wall allow the esophagus to expand during swallowing.

LOWER RESPIRATORY TRACT

Trachea

STRUCTURE OF THE TRACHEA

The **trachea,** or windpipe, is a tube about 11 cm (4.5 inches) long that extends from the larynx in the neck to the primary bronchi in the thoracic cavity (Figure 26-9). Its diameter measures about 2.5 cm (1 inch).

The outside of the tracheal wall is covered in a fibrous *adventitia*. Smooth muscle, in which are embedded C-shaped rings of cartilage at regular intervals, makes up most of the wall of the trachea (Figure 26-10, A). The posterior wall also contains many elastic fibers.

The cartilaginous rings are incomplete on the posterior surface (look back at Figure 26-6, *B*). They give firmness to the wall and tend to prevent it from collapsing and shutting off the vital airway. The fact that the rings are incomplete allows the esophagus, which runs just posterior to the trachea, to expand as food moves toward the stomach during swallowing (Figure 26-10, *B*).

The trachea is lined with *respiratory mucosa*. This type of mucosa is characterized by pseudostratified ciliated columnar epithelium and is typical of the respiratory tract as a whole (Figure 26-11).

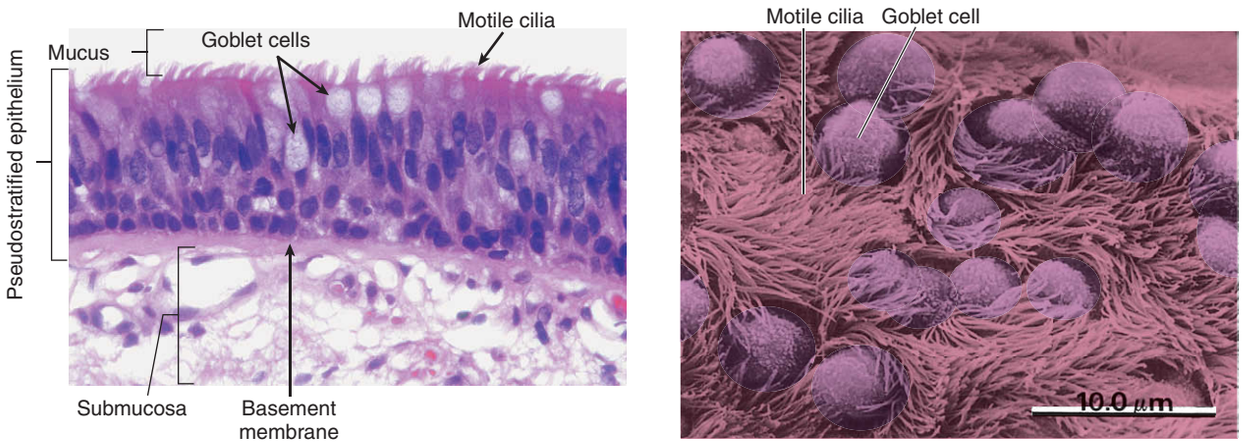


FIGURE 26-11

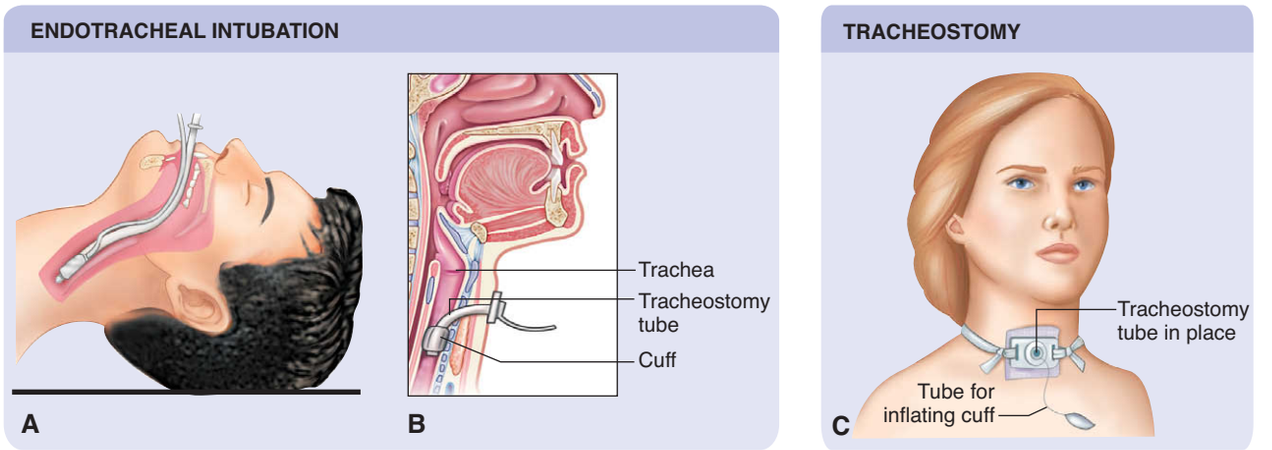
Respiratory mucosa. **A,** Light micrograph (×200) and **B,** Scanning electron micrograph (×2000) of respiratory mucosa. Note the numerous motile (moving) cilia and mucus-producing goblet cells.

Box 26-3 | HEALTH matters

Keeping the Trachea Open

Often, a tube is placed through the mouth, pharynx, and larynx into the trachea before patients leave the operating room, especially if they have been given a muscle relaxant. This procedure is called **endotracheal intubation.** The purpose of the tube is to ensure an open airway (see parts *A* and *B* of the figure). To ensure that the tube enters the trachea rather than the nearby esophagus (which leads to the stomach), anatomical landmarks such as the vocal folds are visualized. Likewise, the distinct feel of the V-shaped groove called the *interarytenoid notch* (see Figure 26-8, *A*) can help guide the proper insertion of the tube.

Another procedure done frequently in today's modern hospitals is a **tracheostomy,** that is, the cutting of an opening into the trachea (part *C* of the figure). A surgeon may perform this procedure so that a suction device can be inserted to remove secretions from the bronchial tree or so that mechanical ventilation can be used to improve ventilation of the lungs.



FUNCTION OF THE TRACHEA

The trachea performs a simple, but vital function—it furnishes part of the open passageway through which air can reach the lungs from the outside. Obstruction of this airway for even a few minutes causes death from asphyxiation (Box 26-3).

Bronchi and Alveoli

STRUCTURE OF THE BRONCHI

The trachea divides at its lower end into two **primary bronchi,** the right bronchus being slightly larger and more vertical than the left. This anatomical fact helps explain why aspirated foreign objects frequently lodge in the right bronchus.

In structure the bronchi resemble the trachea. The bronchi walls have incomplete cartilaginous rings in the sections superior to the lungs, but have complete rings in the sections within the lungs. Ciliated mucosa lines the bronchi, as it does the trachea.

Each primary bronchus enters the lung on its respective side and there immediately divides into smaller branches called **secondary bronchi.** The secondary bronchi continue to branch and form tertiary bronchi and then small **bronchioles.** The trachea and the two primary bronchi and their many branches resemble an inverted tree trunk with its branches and are therefore spoken of as the **bronchial tree** (Figure 26-12).

There are 23 levels of branching in the bronchial tree, producing a huge number of tiny bronchioles. As these bronchioles subdivide into smaller and smaller tubes, they eventually terminate in microscopic branches sometimes called *terminal bronchioles.* The terminal bronchioles are the last branches that serve solely to conduct air.

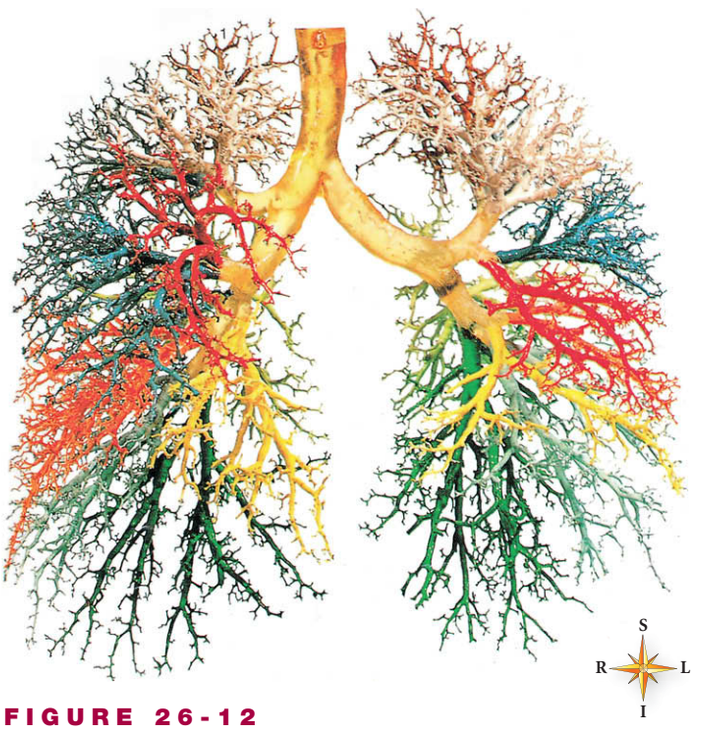


FIGURE 26-12

Plastic cast of air spaces of the lungs. The cast was prepared by pouring liquid plastic into the airways of a human lung—a different color for each bronchopulmonary segment supplied by its own tertiary bronchus. After the plastic hardened, the soft tissue was removed, leaving the branched form of the lower respiratory tract that is pictured here (compare with Figure 26-17).

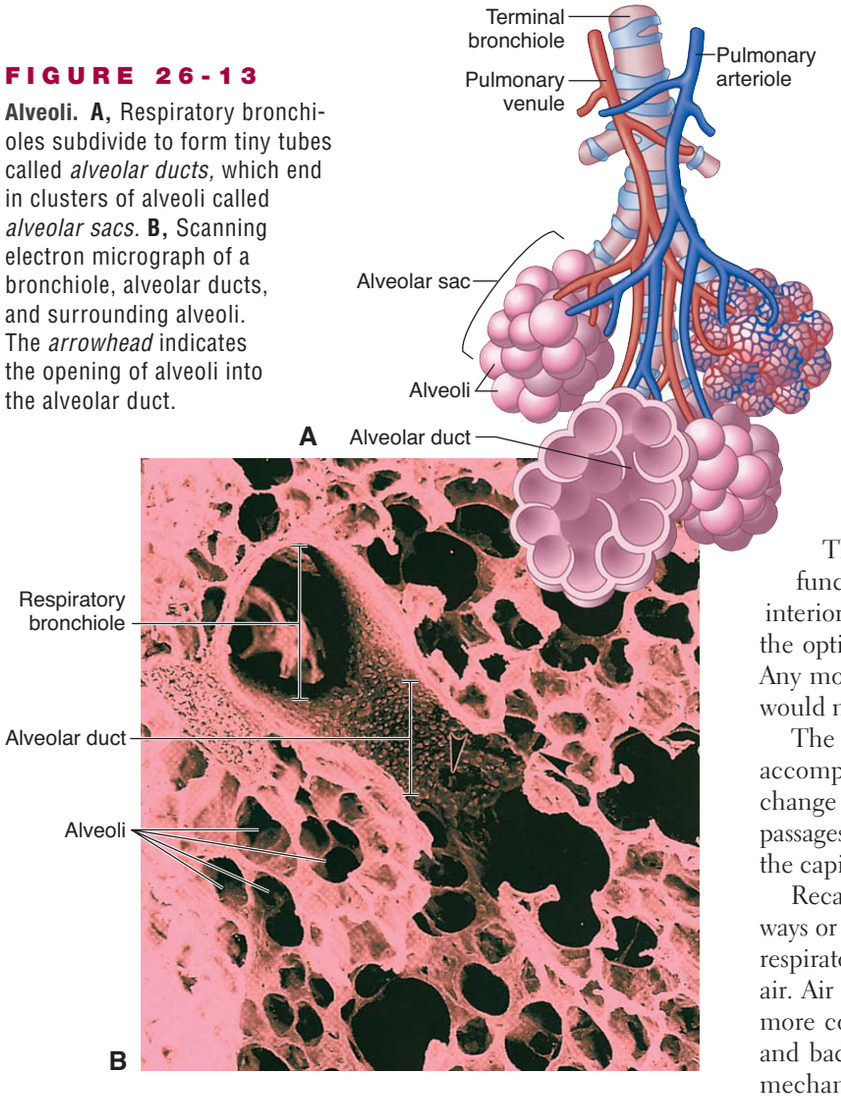


FIGURE 26-13

Alveoli. A, Respiratory bronchioles subdivide to form tiny tubes called *alveolar ducts,* which end in clusters of alveoli called *alveolar sacs.* **B,** Scanning electron micrograph of a bronchiole, alveolar ducts, and surrounding alveoli. The *arrowhead* indicates the opening of alveoli into the alveolar duct.

The terminal bronchioles divide into *respiratory bronchioles* that have thin, gas-exchanging walls. The respiratory bronchioles proceed onward into **alveolar ducts,** which end in one or more alveolar sacs, the walls of which consist of numerous **alveoli** grouped together like a bunch of hollow grapes (Figure 26-13; see also Figure 26-1). Some 300 million alveoli are estimated to be present in our two lungs.

The structure of the secondary and tertiary bronchi and bronchioles shows some modification of the primary bronchial structure. The cartilaginous rings become irregular and disappear entirely into the smaller bronchioles. By the time the branches of the bronchial tree dwindle to form the respiratory bronchioles, alveolar ducts and sacs, and the alveoli, only the internal surface layer of cells remains. In other words, the walls of these microscopic structures consist of a single layer of simple, squamous epithelial tissue (Figures 26-13 and 26-14). As we shall see, this structural fact makes it possible for them to perform their functions.

STRUCTURE OF THE ALVEOLI

The alveoli are the primary gas exchange structures of the respiratory tract (Figures 26-14 and 26-15). Alveoli are very effective in exchanging carbon dioxide (CO_2) and oxygen (O_2) because each alveolus is extremely thin walled, each alveolus lies in contact with blood capillaries, and there are millions of alveoli in each lung.

The barrier across which gases are exchanged between alveolar air and blood is called the **respiratory membrane** (see Figure 26-15, *inset*). The respiratory membrane consists of the alveolar epithelium, the capillary endothelium, and their joined basement membranes.

The surface of the respiratory membrane inside each alveolus is coated with a fluid containing **surfactant** produced by *type II cells* of the alveolar wall. Surfactant helps reduce surface tension—the force of attraction between water molecules—of the fluid. Thus it helps prevent each alveolus from collapsing and "sticking shut" as air moves in and out during respiration. In the next chapter, we explore this important role of surfactant further.

FUNCTIONS OF THE BRONCHI AND ALVEOLI

The tubes composing the bronchial tree perform the same function as the trachea—that of distributing air to the lung's interior. Calculations show that 23 levels of branching produce the optimum ability to transfer oxygen to the pulmonary blood. Any more or any fewer levels of branching in the bronchial tree would not be as efficient for oxygen exchange in the lungs.

The alveoli, enveloped as they are by networks of capillaries, accomplish the lung's main and vital function, that of gas exchange between air and blood. It has been observed that "the lung passages all serve the alveoli" just as "the circulatory system serves the capillaries."

Recall that in addition to serving as air distribution passageways or gas exchange surfaces, the anatomical components of the respiratory tract and lungs cleanse, warm, and humidify inspired air. Air entering the nose is generally contaminated with one or more common irritants; examples include insects, dust, pollen, and bacterial organisms. A remarkably effective air purification mechanism removes almost every form of contaminant before inspired air reaches the alveoli or terminal air sacs in the lungs.

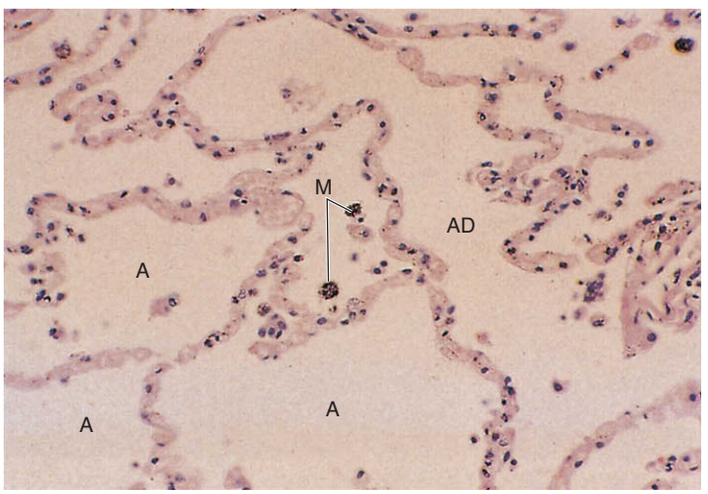


FIGURE 26-14

Micrograph of alveoli. Note the thin alveolar walls and open alveolar spaces **(A)**. An occasional macrophage **(M)**, which provides immune defense, can be seen in several of the alveolar spaces. **AD,** Alveolar duct.

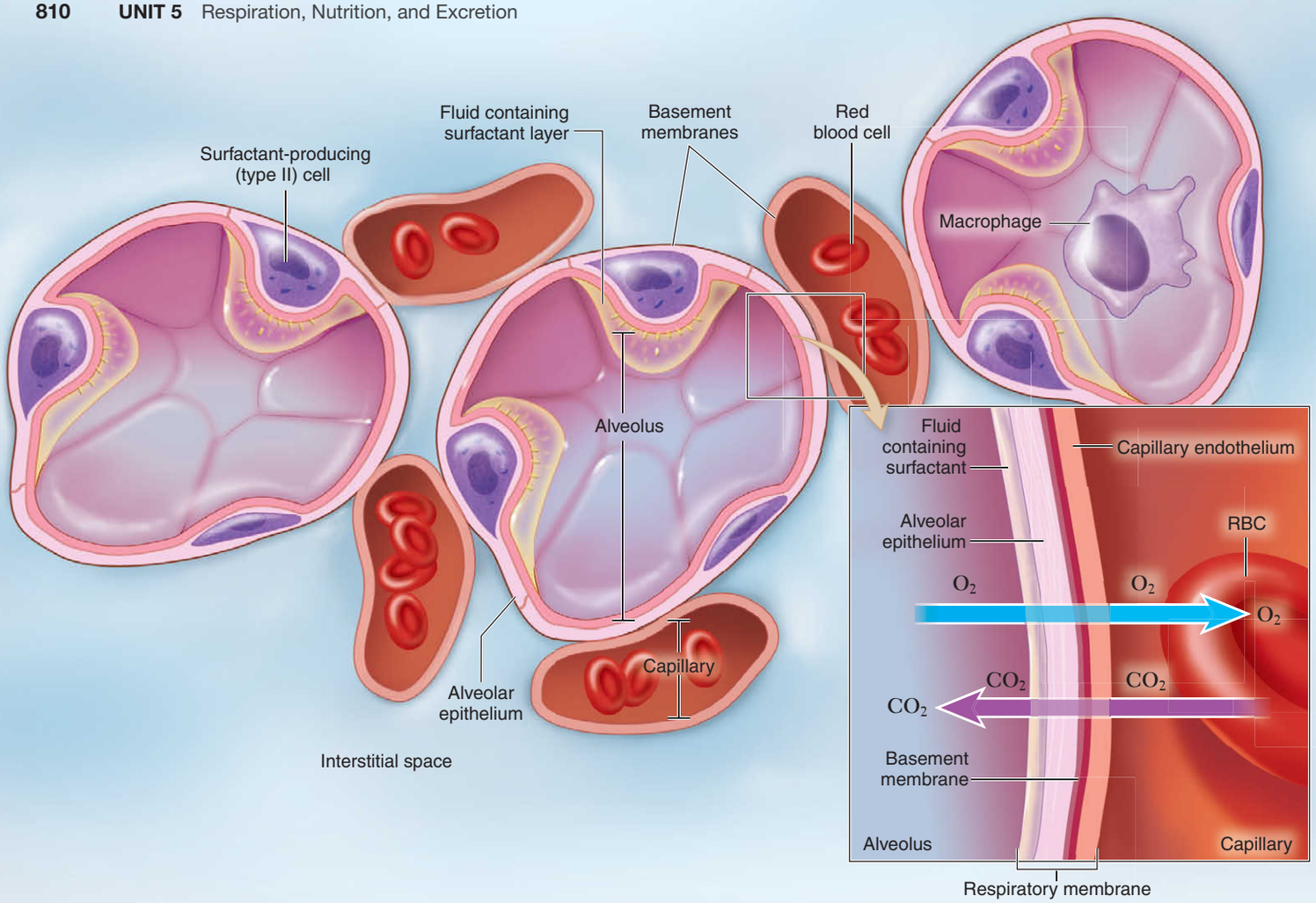


FIGURE 26-15

Gas exchange structures of the lung. Each alveolus is continually ventilated with fresh air. The inset shows a magnified view of the respiratory membrane composed of the alveolar wall (fluid coating, epithelial cells, and basement membrane), interstitial fluid, and the wall of a pulmonary capillary (basement membrane and endothelial cells). The gases—CO_2 (carbon dioxide) and O_2 (oxygen)—diffuse across the respiratory membrane.

The layer of protective mucus that covers a large portion of the membrane that lines the respiratory tree serves as the most important air purification mechanism. More than 125 ml of respiratory mucus is produced daily. It forms a continuous sheet, called a *mucus blanket*, that covers the lining of the air distribution tubes in the respiratory tree. This layer of cleansing mucus moves upward to the pharynx from the lower portions of the bronchial tree on millions of hairlike cilia that cover the epithelial cells in the respiratory mucosa (see Figure 26-11). The microscopic cilia that cover epithelial cells in the respiratory mucosa are motile, beating or moving in only one direction. The result is movement of mucus toward the pharynx—a mechanism sometimes called the *ciliary escalator*.

Respiratory cilia can "taste" bitter toxins and respond by moving more rapidly in an effort to clear the toxin molecules from the airway. Prolonged exposure to toxins, as with cigarette smoke, can paralyze the cilia. Eventually, the ciliary escalator begins to fail and accumulations of mucus trigger the typical smoker's cough, an effort to clear the secretions.

Additional information about the functional anatomy of each section of the respiratory tract can be found in Table 26-1.

| A&P CONNECT |

Because it is exposed to the external environment, the respiratory tract could be extremely vulnerable. Visualize how the respiratory tract defends itself in ***Protective Strategies of the Respiratory Tract*** online at ***A&P Connect.***

evolve

| QUICK CHECK |

7. How are the trachea and primary bronchi held open so that they do not collapse during inspiration?
8. What is meant by the term *bronchial tree?*
9. What characteristics of alveoli enable them to efficiently exchange gases with blood?

TABLE 26-1 Summary of Respiratory Tract Structures*

STRUCTURE	DESCRIPTION	FUNCTION
Upper respiratory tract	Portion of the respiratory tract outside the thoracic cavity	Processing of incoming air Conducts air to/from lungs Vocalization and phonation Olfaction
Nasal cavity	Lumen of nose, separated into left and right portions by nasal septum supported by cartilage, vomer, and perpendicular plate of ethmoid; supported laterally by nasal conchae	Conducts air between atmosphere (external environment) and pharynx Warms, humidifies, cleans inspired air
Anterior nares (external nares)	Nostrils External openings of nasal cavity	Boundary between external environment and nasal cavity
Vestibule	Extends from the anterior nares to the inferior meatus Supported by cartilage of septum and ala Lined with skin epidermis (keratinized stratified squamous epithelium) with vibrissae (hairs)	Conducts air between external environment and respiratory portion of nasal cavity Vibrissae prevent entry of large contaminants
Respiratory portion	Extends from vestibule to posterior nares Supported by bones of septum and nasal conchae, which curve to form meatuses Lined with highly vascular respiratory mucosa (pseudostratified ciliated columnar epithelium) Olfactory epithelium in superior lining contains numerous sensory receptors	Conducts air between vestibule and pharynx Meatuses create turbulence to assist processing of inspired air Mucosa warms, humidifies, and cleans inspired air Olfaction
Paranasal sinuses	Four pair of air-filled spaces within frontal, maxillary, ethmoid, and sphenoid bones of skull Lined with pseudostratified ciliated columnar epithelium Drain into the nasal cavity	Reduce weight of skull Help warm and humidify air
Posterior nares (internal nares)	Openings from the nasal cavity into the pharynx	Boundary between nasal cavity and pharynx
Pharynx	Throat Extends from posterior nares to the esophagus Supported by occipital bone and skeletal muscle Lined with mucous membrane (nonkeratinized stratified squamous epithelium)	Conducts air between nasal cavity and larynx
Nasopharynx	Segment of pharynx posterior to nasal cavity Pharyngeal tonsils in posterior wall	Conducts air between posterior nares and oropharynx
Oropharynx	Segment of pharynx posterior to oral cavity Pair of palatine tonsils in lateral walls Lingual tonsils in anterior wall, at base of tongue	Conducts air between nasopharynx and/or oral cavity and laryngopharynx
Laryngopharynx	Segment of pharynx posterior to opening of larynx and superior to opening of esophagus	Conducts air between oropharynx and larynx
Tonsils	Ring of individual aggregations of lymphoid nodules	Immune protection of respiratory and digestive mucosa (see Chapters 23 and 24)
Larynx	Voicebox Extends from laryngopharynx to trachea Supported by nine cartilages connected by muscle and ligaments Lined with mucosa (pseudostratified ciliated columnar epithelium, except epiglottis and vocal folds)	Conducts air between the pharynx and trachea Prevents food from entering lower airways Vocalization Ciliary escalator removes contaminants
Epiglottis	Flexible "lid" of larynx Covered/lined with nonkeratinized stratified squamous, transitioning through simple columnar to pseudostratified ciliated columnar epithelium at border with vestibule	Flexes during swallowing to cover larynx and prevent food from entering lower airways (see Chapter 29)
Vestibule	Extends from base of epiglottis to vestibular folds	Conducts air between pharynx and vestibular folds
Vestibular folds (false vocal folds)	Superior pair of lateral mucosal folds	Slow contaminants dripping toward lower airways
Ventricle (laryngeal ventricle)	Space between the vestibular folds and vocal folds	Conducts air between mucosal folds of larynx

*Listed in order of air flow during inspiration

(continued)

TABLE 26-1 Summary of Respiratory Tract Structures* *(continued)*

STRUCTURE	DESCRIPTION	FUNCTION
Upper respiratory tract (continued)		
Larynx *(continued)*		
Vocal folds (true vocal folds or vocal cords)	Inferior pair of lateral mucosal folds Each fold supported by skeletal muscle and strong *vocal ligament* at medial edge Covered with nonkeratinized stratified squamous epithelium Glottis: vocal folds and space between them (rima glottidis)	Prevent contaminants from entering lower airways Produce vibrations when pulled together during expiration (vocalization)
Infraglottic cavity	Segments below glottis, between vocal folds and trachea	Conducts air between vocal folds and trachea
Lower respiratory tract	Portion of respiratory tract within the thoracic cavity Also called *bronchial tree*	Conducts air to/from gas-exchange tissues of lungs
Trachea	Windpipe Extends from larynx to primary bronchi Supported by C-shaped cartilage rings Lined with respiratory mucosa (pseudostratified ciliated columnar epithelium)	Conduct air between the larynx and bronchi Ciliary escalator removes contaminants
Bronchi	Treelike branching of airways 23 levels of branching, producing a huge number of individual airways Supported by cartilage rings (incomplete outside lungs; complete inside lungs) Lined with respiratory mucosa (pseudostratified ciliated columnar epithelium)	Conduct air between trachea and lungs Ciliary escalator removes contaminants
Primary bronchi	Left and right branch from trachea, one to each lung	Conduct air to/from the lungs
Secondary bronchi (lobar bronchi)	Branches of the primary bronchi; three from the right, two from the left	Conduct air to/from the lobes of lungs
Tertiary bronchi (segmental bronchi)	Branches of the secondary bronchi	Conduct air to/from the various bronchopulmonary segments of lungs
Bronchioles	Smallest branches (20 levels of branching)	Conduct air to/from alveoli
Alveoli	Microscopic air spaces at terminals of bronchial tree Lined with simple squamous epithelium that joins with pulmonary capillary endothelium to form the respiratory membrane	Exchange of gases (CO_2, O_2) between air and pulmonary blood Surfactant lining alveoli prevents collapse of air spaces

*Listed in order of air flow during inspiration

Lungs

STRUCTURE OF THE LUNGS

The lungs are cone-shaped organs, large enough to fill the pleural portion of the thoracic cavity completely (see Figure 26-9). They extend from the diaphragm to a point slightly above the clavicles and lie against the ribs both anteriorly and posteriorly. The medial surface of each lung is roughly concave to allow room for the mediastinal structures and for the heart, but the concavity is greater on the left than on the right because of the position of the heart. The primary bronchi and pulmonary blood vessels (bound together by connective tissue to form what is known as the **root** of the lung) enter each lung through a slit on its medial surface called the **hilum.**

The broad inferior surface of the lung, which rests on the diaphragm, constitutes the **base,** whereas the pointed upper margin is the **apex** (Figure 26-16). Each apex projects above a clavicle (Figure 26-9, A). The **costal surface** of each lung lies against the ribs and is rounded to match the contours of the thoracic cavity.

Each lung is divided into lobes by fissures. The left lung is partially divided into two lobes (superior and inferior) and the

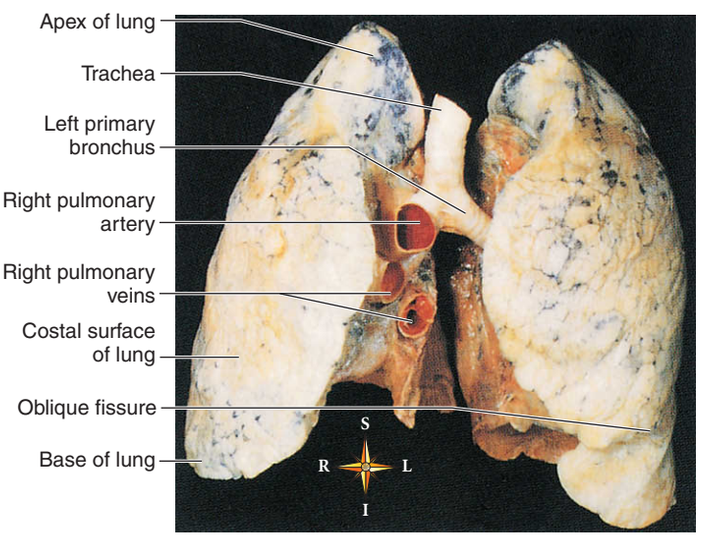


FIGURE 26-16

Anterior view of trachea, bronchi, and lungs. The lower respiratory tract has been dissected from a cadaver and its organs separated to show them clearly.

right lung into three lobes (superior, middle, and inferior). Note in Figure 26-17, *A*, that an **oblique fissure** is present in both lungs. In the right lung a **horizontal fissure** is also present that separates the superior from the middle lobe. After the primary bronchi enter the lungs, they branch into *secondary*, or *lobar*, bronchi that enter each lobe. Thus, in the right lung, three secondary bronchi are formed that enter the superior, middle, and inferior lobes. Each secondary bronchus is named for the lung lobe that it enters; for example, the superior secondary bronchus enters the superior lobe. The left primary bronchus divides into two secondary bronchi entering the superior and inferior lobes of that lung.

The lobes of the lung can be further subdivided into functional units called bronchopulmonary segments (see Figure 26-17, *B*). These segments may be called by their anatomically descriptive names (for example, *anterior segment of superior lobe*) or by Roman numerals. Both systems of naming the segments are shown in Figure 26-17, *B*.

Each bronchopulmonary segment is served by a separate *tertiary*, or *segmental*, bronchus. The interior of each bronchopulmonary segment consists of almost innumerable tubes of dwindling diameter that make up the bronchial tree and serve as air distributors. The smallest tubes terminate in the smallest, but

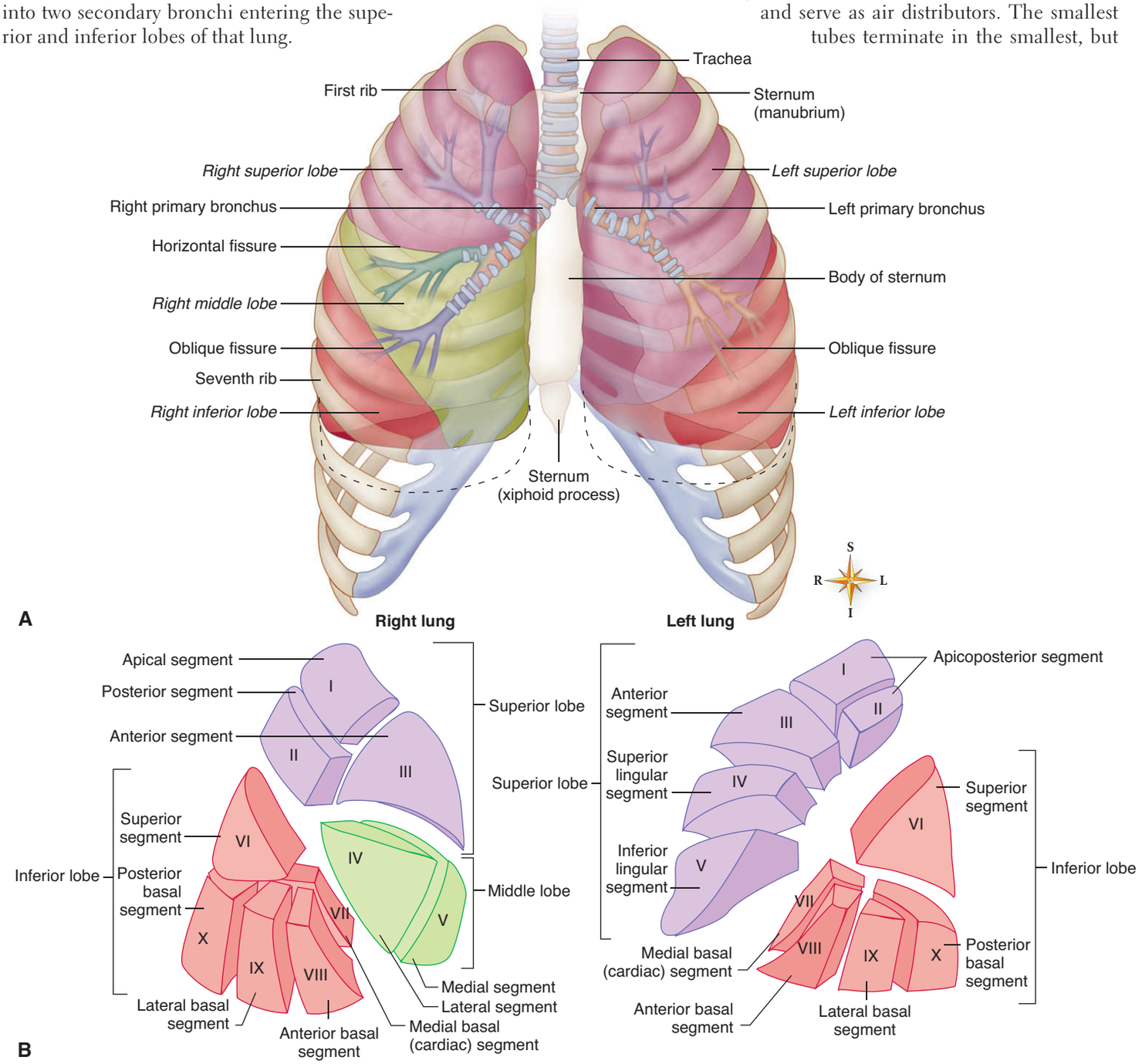


FIGURE 26-17

Lobes and segments of the lungs. **A,** Anterior view of the lungs, bronchi, and trachea. **B,** Expanded diagram showing the bronchopulmonary segments.

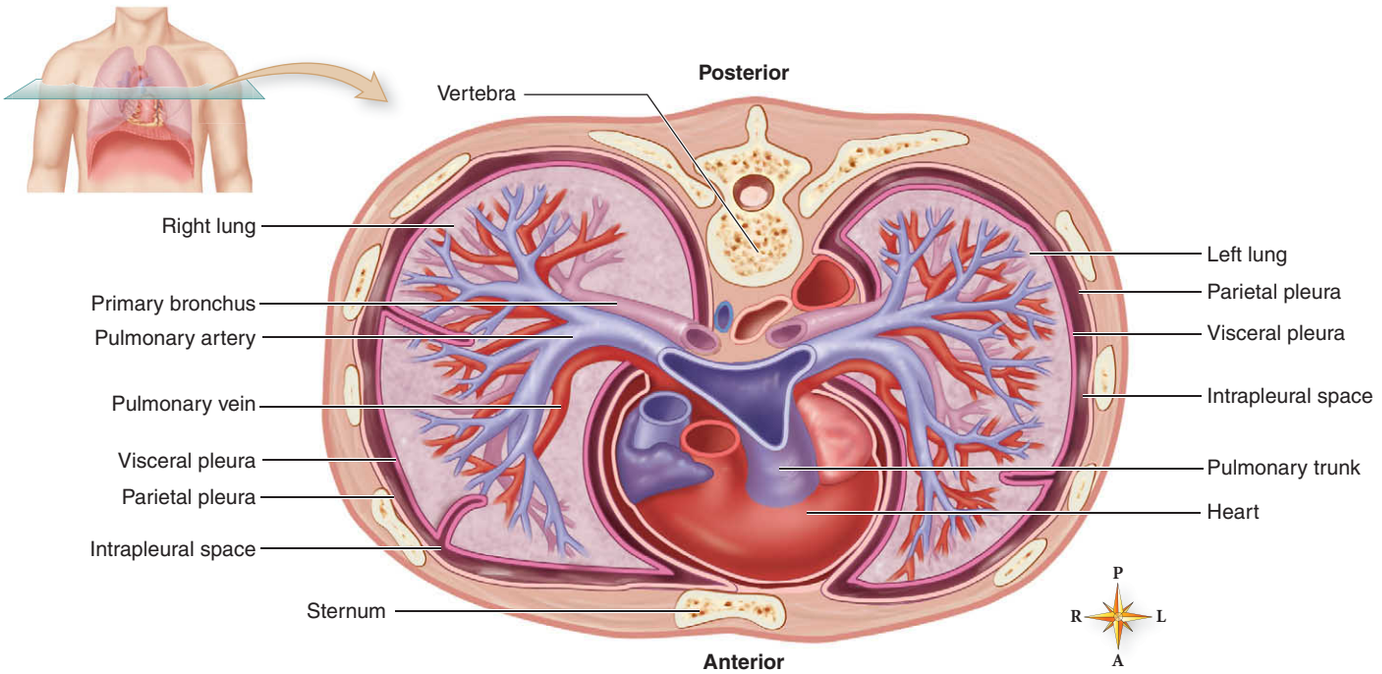


FIGURE 26-18

Lungs and pleura (transverse section). Note the parietal pleura lining the right and left pleural divisions of the thoracic cavity before folding inward near the bronchi to cover the lungs as the visceral pleura. The intrapleural space separates the parietal and visceral pleura. The heart, esophagus, and aorta are shown in the central mediastinum.

functionally most important, structures of the lung—the alveoli, or "gas exchangers."

Visceral pleura covers the outer surfaces of the lungs and adheres to them much as the skin of an apple adheres to the apple (Figure 26-18).

FUNCTIONS OF THE LUNGS

The lungs perform two functions—air distribution and gas exchange. Air distribution to the alveoli is the function of the tubes of the bronchial tree. Gas exchange between air and blood is the joint function of the alveoli and the networks of blood capillaries that envelop them. These two structures—one part of the respiratory system and the other part of the circulatory system—together serve as highly efficient gas exchangers. Why? Because together they provide an enormous surface area, the **respiratory membrane,** where the very thin-walled alveoli and equally thin-walled pulmonary capillaries come in contact (see Figures 26-14 and 26-15). This makes possible extremely rapid diffusion of gases between alveolar air and pulmonary capillary blood. It has been estimated that if the lungs' 300 million or so alveoli could be opened up flat, they would form a surface about the size of a tennis court, that is, about 85 square meters, or more than 40 times the surface area of the entire body! No wonder such large amounts of oxygen can be so quickly loaded into the blood while large amounts of carbon dioxide are rapidly unloaded from it.

Box 26-4 discusses the surgical removal of portions of the lung.

Thorax

STRUCTURE OF THE THORACIC CAVITY

As described in Chapter 1, the thoracic cavity has three divisions, separated from each other by partitions of **pleura.** The parts of the cavity occupied by the lungs are the *pleural divisions.* The space between the lungs occupied mainly by the esophagus, trachea, large blood vessels, and heart is the *mediastinum* (see Figure 26-18).

The **parietal pleura** lines the entire thoracic cavity. It adheres to the internal surface of the ribs and the superior surface of the diaphragm, and it partitions off the mediastinum. A separate pleural sac thus encases each lung. Because the outer surface of each lung is covered by the visceral layer of the pleura, the **visceral pleura** lies against the parietal pleura, separated only by a potential space (pleural space) that contains just enough pleural fluid for lubrication (see Figure 26-18). Thus, when the lungs inflate with air, the smooth, moist visceral pleura coheres to the smooth, moist parietal pleura. Friction is thereby avoided, and respirations are painless. In *pleurisy* (pleuritis), on the other hand, the pleura is inflamed and respirations become painful.

FUNCTIONS OF THE THORACIC CAVITY

The thorax plays a major role in respiration. Because of the elliptical shape of the ribs and the angle of their attachment to the spine, the thorax becomes larger when the chest is raised and smaller when it is lowered. Lifting up the chest raises the ribs so that they no longer slant downward from the spine, and because of their elliptical shape, both the depth (from front to back) and the width of

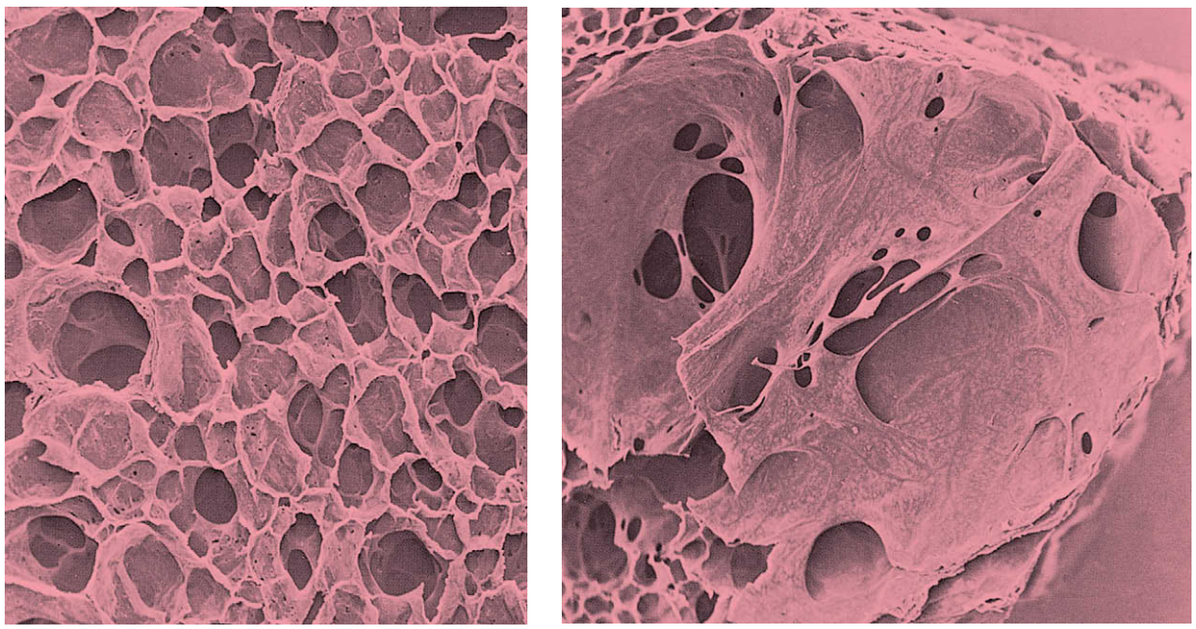
Box 26-4 | HEALTH matters

Lung Volume Reduction Surgery

Lung volume reduction surgery (LVRS) is a "treatment of last resort" for severe cases of emphysema. It involves the removal of 20% to 30% of each lung. Diseased tissue is generally removed from the upper or apical areas of the superior lobes. Evidence from a number of large clinical trials has now shown that the LVRS procedure may benefit or at least help stabilize selected emphysema patients whose lung function continues to decline despite aggressive pulmonary rehabilitation efforts and other more conservative forms of treatment.

More than 2 million Americans, most of whom are older than age 50 and are current or former smokers, have emphysema—a major cause of disability and death in the United States. Emphysema is one of a number of conditions discussed in Chapter 27 and classified as a **chronic obstructive pulmonary disease,** or **COPD.** Although lung damage caused by emphysema is irreversible, in some cases the disease may be halted or its progression slowed by LVRS. In the end stages of this chronic disease, breathing becomes labored as the lungs fill with large irregular spaces resulting from the enlargement and rupture of many alveoli (see illustration). The LVRS procedure removes part of the diseased lung tissue and increases available space in the pleural cavities. As a result, the diaphragm and other respiratory muscles can more effectively move air into and out of the remaining lung tissue, thereby improving pulmonary function and making breathing easier.

LVRS may reduce the need for lung transplantation procedures and augment the effectiveness of such supporting medical treatments as nutritional supplementation and exercise training in the treatment of selected late-stage emphysema patients. Newer and less invasive techniques involving smaller incisions and tiny video equipment inserted into the thoracic cavity (video-assisted thoracic surgery) are now being used for many LVRS procedures. As a result, the relatively long hospital stays and home recovery periods previously required after more traditional open-chest surgery have been shortened.



A B

Emphysema. A, Scanning electron micrograph (SEM) of normal lung with many small alveoli. **B,** SEM of lung tissue affected by emphysema. Alveoli have merged into large air spaces, thereby reducing the surface area available for gas exchange.

the thorax are enlarged. (If this does not sound convincing to you, examine a skeleton to see why it is so.) An even greater change in thoracic volume occurs when the diaphragm contracts and relaxes. When the diaphragm contracts, it flattens out and thus pulls the floor of the thoracic cavity downward—thereby enlarging the volume of the thorax. When the diaphragm relaxes, it returns to its resting, domelike shape—thus reducing the volume of the thoracic cavity. It is these changes in thorax size that bring about inspiration and expiration (discussed on pp. 828–830 in Chapter 27).

| QUICK CHECK |

10. What is meant by the term *lobe of the lung?* What is a bronchopulmonary segment?
11. How does the structure of the diaphragm enable it to participate in breathing movements?

Cycle of LIFE

Respiratory System

Respiration involves the exchange of O_2 and CO_2 between the organism and its environment. The exchange must occur between air in the lungs and blood and, then, between blood and every body cell. In addition to the structural components of the body through which the respiratory gases must pass, hemoglobin plays a vital role in the respiration process. Each component of the system may be affected by developmental defects, by age-related structural changes, or by loss of function during the life cycle.

Premature birth can cause potentially fatal respiratory problems. A very low–birth-weight baby may have inadequate blood flow to the lungs, an inability to ventilate properly, and inadequate quantities of surfactant. Other diseases that cause serious respiratory problems are also associated with specific age-groups. Examples include cystic fibrosis and asthma in children and certain types of obstructive pulmonary disease and emphysema in older adults. Pneumothorax occurs more frequently in young adult females.

Numerous age-related changes affect lung capacity, make ventilation difficult, or reduce the oxygen- or carbon dioxide–carrying capacity of blood. For example, in older adulthood the ribs and sternum tend to become more fixed and less able to expand during inspiration, the respiratory muscles are less effective, and hemoglobin levels are often reduced. The result is a general reduction in respiratory efficiency in old age.

the BIG picture

Anatomy of the Respiratory System

Understanding the relationship of structure to function is critical to an understanding of homeostasis in all of the body organ systems. The anatomy of the respiratory system components permits the distribution of air and the exchange of respiratory gases. This dual function ultimately allows for both exchange of gases between environmental air and blood in the lungs and, finally, gas exchange between blood and individual body cells. In addition to delivery of air to the tiny terminal air passageways and alveoli for gas exchange with blood, components of the upper respiratory tract effectively filter, warm, and humidify the air we breathe.

Respiratory functions are dependent on the structural organization of the system parts and on the interrelationship of those components with other body systems, including the nervous, cardiovascular, muscular, and immune systems. For example, nerves regulate the thoracic and abdominal muscles that drive breathing, as well as the smooth muscles that regulate airflow through the bronchial tree. The immune system guards against airborne pathogens and irritants. Understanding the proper functioning and regulation of the physiology of the respiratory system, discussed in Chapter 27, depends on your understanding of its structural components and their relationships to one another and to other body organ systems—the "big picture" of total-body homeostasis.

MECHANISMS of DISEASE

DISORDERS ASSOCIATED WITH RESPIRATORY ANATOMY

Disorders of the Upper Respiratory Tract

Inflammation and Infection

Any infection localized in the mucosa of the upper respiratory tract (nose, pharynx, and larynx) can be called an **upper respiratory infection (URI)** and is often named for the specific structure involved.

Rhinitis (from the Greek *rhinos*, "nose") is an inflammation of the mucosa of the nasal cavity. It is commonly caused by a viral infection, as in the common cold (caused by rhinoviruses) or flu (caused by influenza viruses). Rhinitis can also be caused by nasal irritants or an allergic reaction to airborne allergens. Allergic rhinitis, or "hay fever," occurs in sensitive people in a seasonal pattern, depending on the allergens involved (e.g., pollen). The excessive mucus production that results from the inflammatory response involved in rhinitis can cause fluid to drip down the pharynx and into the esophagus and lower respiratory tract. This dripping may cause sore throat, coughing, and upset stomach. Irritation of the **nasal mucosa** itself often triggers the sneeze reflex. Elimination of the causative factor, rest, and the use of antihistamines and decongestants usually relieve these symptoms.

Pharyngitis is inflammation or infection of the pharynx. Commonly referred to as a "sore throat," it is often due to viral invasion. Bacterial infection by *Streptococcus* bacteria is termed "strep throat." The common complaint is a sore throat, but redness and difficulty swallowing (dysphagia) often accompany it. Throat lozenges, rest, and fluid intake are encouraged, and antibiotics are prescribed for severe infections.

Laryngitis, or inflammation of the mucous lining of the larynx, is characterized by edema of the vocal folds, resulting in hoarseness (dysphonia) or loss of voice. Besides infections, inhalation of toxic or irritating fumes (i.e., smoking), endotracheal intubation, vocal abuse (i.e., public speaking), and alcohol ingestion can precipitate laryngitis. In children younger than 5 years, it may cause difficulty breathing, a condition often called **croup.** Conservative treatment, including limiting speech, is usually effective. A rare, but much more severe and rapidly progressing viral form of laryngeal edema called **epiglottitis** is always treated as a medical

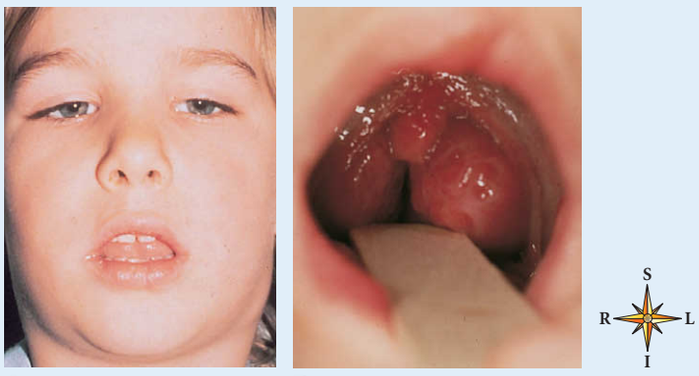
emergency because of the potential for airway obstruction (see ***Swollen Larynx*** online at ***A&P Connect***).

Tonsillitis is inflammation of one or more of the masses of lymphatic tissue embedded in the mucous membrane of the pharynx (see pp. 733–734). Most cases of tonsillitis result in inflammation and swelling of the palatine tonsils in the oropharynx and the pharyngeal tonsils or adenoids in the nasopharynx. Repeated episodes of infection and chronic swelling of these tonsillar tissues require aggressive antibiotic therapy and, in severe cases, even surgical removal.

However, **tonsillectomy,** the surgical procedure used to remove inflamed and/or enlarged tonsillar tissue, is no longer considered a "first-choice" treatment option in routine cases of tonsillitis. As a result, the number of tonsillectomies performed each year continues to decrease. Physicians now recognize the value of lymphatic tissue in the body's defense mechanism and delay tonsillectomy with its rare, but potentially serious complications—including severe hemorrhage—until more conservative treatment options have proved ineffective.

Occasionally, surgical removal may be required, especially in children, if adenoidal and tonsillar infection and hypertrophy do not respond to antibiotic therapy. In these cases, sleep disturbance, fatigue, and other potentially serious complications involving the heart and lungs can result from progressive upper airway obstruction over time. Figure 26-19, *A*, shows the fatigued facial appearance of a child with severely enlarged tonsils who must keep his mouth open to breathe. In Figure 26-19, *B*, note how the enlarged tonsils in this child have all but filled the pharynx and are nearly meeting in the midline, thus seriously limiting airflow.

Because the upper respiratory mucosa is continuous with the mucous lining of the sinuses, auditory or eustachian tube, middle ear, and lower respiratory tract, URIs have the unfortunate tendency to spread. It is not unusual to see a common cold progress to **sinusitis** (sinus infection) or **otitis media** (middle ear infection).



A B

FIGURE 26-19

Tonsillitis. A, Facial appearance of a child with marked enlargement of the tonsils and adenoids. He must keep his mouth open to breathe and shows signs of fatigue. **B,** Enlarged tonsils can be seen meeting in the midline of the pharynx.

Anatomical Disorders

Nasal obstruction can be caused by displacement of the nasal septum from the midline of the nasal cavity, called a **deviated septum.** Most individuals have a small amount of septal cartilage protruding into one nasal passage; however, some are born with a congenital defect that results in various degrees of blockage on one or both sides of the nasal cavity. Damage from injury or infection may also cause a deviated septum. If breathing is impaired, surgical intervention is required to correct the deformity.

A frequent problem associated with a deviated septum is snoring. Pronounced snoring may be a symptom of **sleep apnea.** In these individuals there is a transition during sleep from loud snoring to variable periods of complete cessation of breathing. These periods of apnea are characterized by restlessness and often end in a loud "snort" before a normal breathing pattern resumes. Sleep apnea may be repeated many times each night and cause excessive daytime sleepiness and other symptoms related to chronic lack of oxygen.

Trauma to the nose can occur because the nose projects some distance from the front of the head. Usually, however, common bumps and other injuries cause little, if any, serious damage. **Epistaxis,** or nosebleed, can be caused by violent sneezing or nose blowing, chronic infection or inflammation (as in rhinitis), hypertension, or a strong bump or blow to the nose. Immediate direct pressure with an ice pack will often slow or stop the bleeding.

Disorders of the Lower Respiratory Tract

A range of conditions can interfere with the lower respiratory tract functions of gas exchange and ventilation. Some of these disorders, such as restrictive and obstructive conditions, are discussed in Chapter 27. For now, we concentrate on infections and lung cancer.

| A&P CONNECT |

Bronchial and lung disorders are often detected and monitored by chest x-ray imaging. Find out more in ***Pulmonary Radiology*** online at ***A&P Connect.***

evolve

Lower Respiratory Infection

Acute bronchitis is a common condition characterized by acute inflammation of the tracheobronchial tree, most commonly caused by infection. Part of or preceded by an acute URI, it is most prevalent in winter. Predisposing factors include chilling, fatigue, malnutrition, and exposure to air pollutants. The protective functions of the bronchial epithelium are disturbed and excessive fluid accumulates in the bronchi. Acute bronchitis often begins with a nonproductive cough, but malaise, slight fever, back and muscle pain, and a sore throat occur if a URI is present. Rest is indicated until the fever subsides, and cough suppressants may be used if the cough is troublesome.

Pneumonia is a common condition characterized by acute inflammation of the lungs. Depending on the cause, the alveoli and bronchi become swollen and plugged with mucous secretions. In

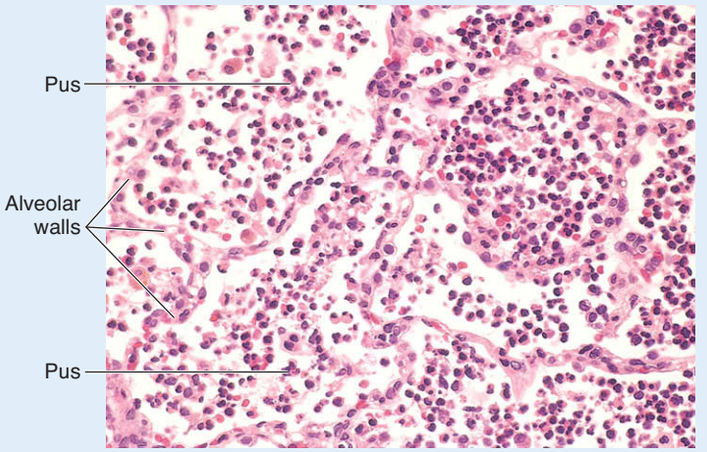


FIGURE 26-20

Acute bacterial pneumonia. The alveolar walls are thickened and the spaces filled with a fibrin exudate and neutrophils (pus)—a classic finding in acute pneumonia caused by bacterial infection.

bacterial pneumonia, a thick fibrin and neutrophil (pus)-containing exudate forms (Figure 26-20).

The vast majority of pneumonia cases result from infection by *Streptococcus pneumoniae* bacteria (see Figure 26-20), but pneumonia can also be caused by several other bacteria, viruses, and fungi. For example, **legionnaires' disease** is a form of bacterial pneumonia caused by infection with the *Legionella pneumophila* organism. Contaminated air conditioning cooling towers and whirlpool spas are sources of infection.

Viral infections can produce pneumonia as well. A dramatic example is the 2003 outbreak of *severe acute respiratory syndrome (SARS)* caused by the SARS-associated coronavirus (SARS-CoV). Unless treated very early, most SARS cases progress to pneumonia. SARS, like most viral infections responsible for pneumonia, is transmitted by close contact of individuals.

The term *aspiration pneumonia* is used to describe lung infections caused by the inhalation of vomit or other infective material. It is common in acute alcohol intoxication and as a complication of anesthesia.

Pneumonia is often associated with a high fever, chills, headache, cough, and chest pain. Increases in white blood cell (WBC) numbers (leukocytosis) and depressed blood oxygen levels (hypoxia) are common findings. The fact that each day over 10,000 liters of potentially contaminated air enters the respiratory system helps explain why pneumonia is such a common illness—especially in individuals with lowered resistance or impaired immune systems.

Types include *lobar pneumonia*, which typically affects an entire lobe of the lung (Figure 26-21), and *bronchopneumonia*, in which patches of infection are scattered along portions of the bronchial tree and generally involve more than one lobe (see Figure 26-20). Treatment involves antimicrobial drugs to control the infection and supportive therapy, including the administration of supplemental oxygen. Removal of tracheobronchial secretions may be necessary to maintain airway integrity.

Tuberculosis (TB) is a chronic bacillus infection caused by *Mycobacterium tuberculosis*. It is a highly contagious disease, transmitted by airborne mechanisms (i.e., inhalation of infectious

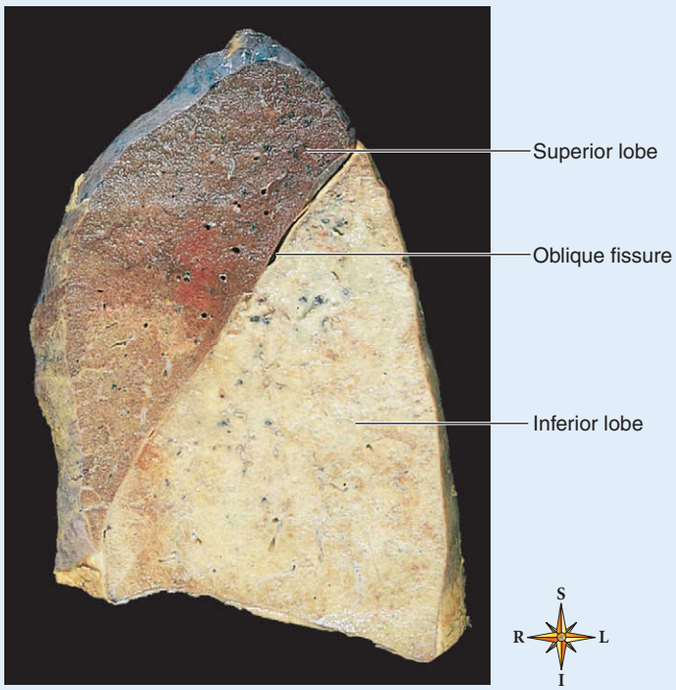


FIGURE 26-21

Lobar pneumonia. Exudate fills many of the alveoli and ducts of a single lobe of the left lung. Note the difference is texture and color of the affected inferior lobe. (See Figure 26-20.)

droplets). Inflammatory lesions called "tubercles" form around colonies of TB bacilli in the lung and produce the characteristic symptoms of cough, fatigue, chest pain, weight loss, and fever. As TB progresses, lung hemorrhage and dyspnea (labored breathing) may develop. If large areas of the lung are infected and tissue is destroyed, scar tissue may develop and cause reduced lung volume and restrictive lung disease. TB can invade other tissues or organs such as the lymphatic system, genitourinary system, and bone tissue. Because of the advancement of modern antimicrobial agents, the incidence of TB in the United States dropped dramatically in the last half century. However, various factors have allowed some highly resistant strains of TB to emerge once again as a major health threat in the United States. Although the incidence of TB has not yet reached epidemic proportions, health authorities in many large cities are working hard to prevent a major health crisis.

Lung Cancer

Lung cancer is a malignancy of pulmonary tissue that not only destroys the vital gas exchange tissues of the lungs, but like other cancers, may also invade other parts of the body (metastasis). Lung cancer most often develops in damaged or diseased lungs (see Figure 26-21). The most common predisposing condition associated with lung cancer is cigarette smoking (accounting for about 75% of lung cancer cases). In 1950, British epidemiologist Sir Richard Doll published the results of a groundbreaking scientific study that established for the first time the deadly link between smoking and lung cancer. His pioneering research was uniquely important in medical history. At the time of his death in 2005 at age 92, Doll was regarded as one of the most eminent scientists of his generation and one whose work will ultimately prevent tens of millions of

premature tobacco-related deaths around the world. Other factors thought to cause lung cancer include exposure to "second-hand" cigarette smoke, asbestos, chromium, coal products, petroleum products, rust, and ionizing radiation (as in radon gas).

Lung cancer may be arrested if detected early on routine chest x-ray films or by other diagnostic procedures such as bronchoscopy. Depending on the size, location, and exact type of malignancy involved, several strategies are available for treatment. Surgery is perhaps the most effective single treatment for most localized lung cancers. In a lobectomy, only the affected lobe of a lung is removed. **Pneumonectomy** is the surgical removal of an entire lung. Chemotherapy can also cause a cure or remission in selected cases, as can radiation therapy or concurrent (combination) chemotherapy and radiation treatment.

Unfortunately, in about 40% of patients diagnosed with the most common type of lung cancer, called "non–small cell" lung cancer, the disease has already spread, or metastasized, to lymph nodes and other organs by the time a diagnosis is made. Non–small cell lung cancer accounts for over 85% of cancer diagnoses in the United States.

Results of a National Cancer Institute study has shown that lobectomy combined with concurrent chemotherapy and radiation treatment can significantly increase survival time in cases of non–small cell lung cancer. Patients in the study who received either surgery or standard concurrent therapy—but not both—had less favorable survival rates 3 and 5 years after diagnosis.

So called "small cell" lung cancers usually appear first in the lining of the respiratory passageways. Curable if detected very early, this type of cancerous lesion is often treated by surgical removal, with **photodynamic therapy (PDT),** or both. This deadly form of the disease spreads very rapidly and is usually not effectively treated in its later stages with either standard concurrent radiation plus chemotherapy or by the standard treatment options followed by operation.

| A&P CONNECT |

Learn how light can be used to treat lung cancer! Check out ***Photodynamic Therapy*** online at ***A&P Connect.*** evolve

LANGUAGE OF SCIENCE *(continued from p. 798)*

hilum
(HYE-lum)
[*hilum* **least bit**] *pl.,* hila

horizontal fissure
(hor-i-ZON-tal FISH-ur)
[*fissur-* **cleft**]

laryngopharynx
(lah-ring-go-FAIR-inks)
[*laryng-* **voicebox (larynx),** *-pharynx* **throat**] *pl.,* laryngopharynges or laryngopharynxes

larynx
(LAIR-inks)
[*larynx* **voicebox**] *pl.,* larynges or larynxes

lingual tonsil
(LING-gwal TAHN-sil)
[*ling-* **tongue,** *-al* **relating to**]

lower respiratory tract
(RES-pih-rah-tor-ee)
[*re-* **again,** *-spir-* **breathe,** *-tory* **relating to,** *tractus* **trail**]

nasal mucosa
(NAY-zal myoo-KOH-sah)
[*nas-* **nose,** *-al* **relating to,** *mucus* **slime**] *pl.,* mucosae

nasopharynx
(nay-zoh-FAIR-inks)
[*naso-* **nose,** *-pharynx* **throat**] *pl.,* nasopharynges or nasopharynxes

oblique fissure
(oh-BLEEK FISH-ur)
[*obliqu-* **slanted,** *fissur-* **cleft**]

olfactory epithelium
(ohl-FAK-tor-ee ep-ih-THEE-lee-um)
[*olfact-* **smell,** *-ory* **relating to,** *epi-* **upon,** *-theli-* **nipple,** *-um* **thing**] *pl.,* epithelia

oropharynx
(or-oh-FAIR-inks)
[*oro-* **mouth,** *-pharynx* **throat**] *pl.,* oropharynges or oropharynxes

palatine tonsil
(PAL-ah-tine TAHN-sil)
[*palat-* **palate,** *-ine* **relating to**]

paranasal sinus
(pair-ah-NAY-zal SYE-nus)
[*para-* **beside,** *-nas-* **nose,** *-al* **relating to,** *sinus* **hollow**]

parietal pleura
(pah-RYE-i-tal PLOO-rah)
[*parie-* **wall,** *-al* **relating to,** *pleura* **rib**] *pl.,* pleurae

pharyngeal tonsil
(fah-RIN-jee-al TAHN-sil)
[*pharyng-* **throat,** *-al* **relating to**]

pharynx
(FAIR-inks)
[*pharynx* **throat**] *pl.,* pharynges or pharynxes

pleura
(PLOO-rah)
[*pleura* **rib**] *pl.,* pleurae

primary bronchus
(BRONG-kus)
[*prim-* **first,** *-ary* **relating to,** *bronchus* **windpipe**] *pl.,* bronchi

respiratory membrane
(RES-pih-rah-tor-ee)
[*re-* **again,** *-spir-* **breathe,** *-tory* **relating to,** *membran-* **thin skin**]

respiratory mucosa
(RES-pih-rah-tor-ee myoo-KOH-sah)
[*re-* **again,** *-spir-* **breathe,** *-tory* **relating to,** *mucus* **slime**]

respiratory portion
(RES-pih-rah-tor-ee POR-shun)
[*re-* **again,** *-spir-* **breathe,** *-tory* **relating to**]

root

secondary bronchus
(BRONG-kus)
[*second-* **second,** *bronchus* **windpipe**] *pl.,* bronchi

septum
(SEP-tum)
pl., septa

surfactant
(sur-FAK-tant)
[**combination of** *surf*(ace) *act*(ive) *a*(ge)*nt*]

thyroid cartilage
(THY-royd KAR-ti-lij)
[*thyr-* **shield,** *-oid* **like**]

trachea
(TRAY-kee-ah)
[*trachea* **rough duct**] *pl.,* tracheae or tracheas

turbinate
(TUR-bih-nayt)
[*turbin-* **top (spinning toy),** *-ate* **of or like**]

upper respiratory tract
(RES-pih-rah-tor-ee)
[*re-* **again,** *-spir-* **breathe,** *-tory* **relating to,** *tract-* **trail**]

ventricle
(VEN-tri-kul)
[*ventr-* **belly,** *-icle* **little**]

vestibular fold
(ves-TIB-yoo-lar)
[*vestibul-* **entrance hall,** *voca-* **voice,** *-al* **relating to**]

vestibule
(VES-tih-byool)
[*vestibul-* **entrance hall**]

vibrissa
(VYE-BRISS-ah)
[*vibrissa* **nostril hair**] *pl.,* vibrissae

visceral pleura
(VISS-er-al PLOO-rah)
[*viscer-* **internal organ,** *-al* **relating to,** *pleura* **rib**] *pl.,* pleurae

vocal fold
[*voca-* **voice,** *-al* **relating to**]

vomeronasal organ (VNO)
(voh-mer-oh-NAY-sal)
[*vomer-* **plowshare (vomer bone),** *nas-* **nose,** *-al* **relating to**]

LANGUAGE OF MEDICINE *(continued from p. 819)*

acute bronchitis
(ah-KYOOT brong-KYE-tis)
[*acut-* **sharp**, *bronch-* **windpipe**, *-itis* **inflammation**]

chronic obstructive pulmonary disease (COPD)
(KRON-ik ob-STRUK-tiv PUL-moh-nair-ee)
[*chron-* **time**, *-ic* **relating to**, *pulmon-* **lung**, *-ary* **relating to**]

cleft palate
(kleft PAL-ett)

croup
(kroop)
[*croup* **croak**]

deviated septum
(DEE-vee-ay-ted SEP-tum)
[*devia-* **turn aside**, *-ate* **process**, *septum* **partition**] *pl.,* septa

endotracheal intubation
(en-doh-TRAY-kee-al in-too-BAY-shun)
[*endo-* **within**, *-trache-* **rough duct**, *-al* **relating to**, *in-* **within**, *-tub-* **tube**, *-ation* **process**]

epiglottitis
(EPP-ih-glaw-tye-tis)
[*epi-* **upon**, *-glotti-* **tongue (glottis)**, *-itis* **inflammation**]

epistaxis
(ep-i-STAK-sis)
[*epi-* **upon**, *-staxis* **drip**]

laryngitis
(lar-in-JYE-tis)
[*laryng-* **voice box (larynx)**, *-itis* **inflammation**]

legionnaires' disease
(LEE-jen-airz)
[**named for American Legion convention, location of first diagnosed case**]

lung cancer
[*cancer* **crab or malignant tumor**]

otitis media
(oh-TYE-tis MEE-dee-ah)
[*oti-* **ear**, *-itis* **inflammation**, *media* **middle**]

pharyngitis
(fair-in-JYE-tis)
[*pharyng-* **throat (pharynx)**, *-itis* **inflammation**]

photodynamic therapy (PDT)
(foh-toh-dye-NAM-ik)
[*photo-* **light**, *-dynam-* **force**, *-ic* **relating to**]

pneumonectomy
(noo-moh-NEK-toh-mee)
[*pneumon-* **lung**, *-ec-* **out**, *-tom-* **cut**, *-y* **action**]

pneumonia
(noo-MOH-nee-ah)
[*pneumon-* **lung**]

rhinitis
(rye-NYE-tis)
[*rhin-* **nose**, *-itis* **inflammation**]

sinusitis
(sye-nyoo-SYE-tis)
[*sinus-* **hollow**, *-itis* **inflammation**]

sleep apnea
(APP-nee-ah)
[*a-* **not**, *-pnea* **breathe**]

tonsillectomy
(tahn-sih-LEK-toh-mee)
[*tonsil-* **tonsil**, *-ec-* **out**, *-tom-* **cut**, *-y* **action**]

tonsillitis
(tahn-sih-LYE-tis)
[*tonsil-* **tonsil**, *litis* **inflammation**]

tracheostomy
(tray-kee-OS-toh-mee)
[*trache-* **rough duct**, *-os-* **mouth or opening**, *-tom-* **cut**, *-y* **action**]

tuberculosis (TB)
(too-ber-kyoo-LOH-sis)
[*tuber-* **swelling**, *-cul-* **little**, *-osis* **condition**]

upper respiratory infection (URI)
(RES-pih-rah-tor-ee)
[*re-* **again**, *-spir-* **breathe**, *-tory* **relating to**, *infec-* **stain**, *-tion* **process**]

CASE study

Sharon looked away from her toddler for just a second. Her 2-year-old daughter, Zoe, was playing on the floor next to her desk. When Sharon glanced down again, Zoe was squirming, holding her throat and making little squeaking sounds. Zoe looked up at her Mom with scared eyes. "She's choking!" Sharon's voice screamed in her head. She first thought about performing the Heimlich maneuver on Zoe, but then remembered that was not the correct action because the child was still able to breathe a little (as evidenced by the squeaking sound). She didn't want to cause whatever had been swallowed to block Zoe's airway completely. Sharon grabbed the phone and dialed 911. The EMTs were there in minutes, but it seemed like hours. They took Zoe to the hospital. Based on Zoe's symptoms, the doctors immediately scheduled a bronchoscopy. In this procedure, a thin tube (with a camera) is inserted through the mouth and down the throat.

1. What is the correct sequence of structures through which the bronchoscope will pass?
   a. Nasopharynx, laryngopharynx, trachea, larynx
   b. Oropharynx, laryngopharynx, larynx, trachea
   c. Laryngopharynx, oropharynx, larynx, trachea
   d. Trachea, larynx, oropharynx, laryngopharynx

After finding nothing in the trachea, the doctor focused attention on the first tube to the right (after the trachea).

2. What is the name of this tube?
   a. Primary bronchiole
   b. Tracheal limb
   c. Primary bronchus
   d. Alveolar duct

3. What type of epithelium lines both this tube and the trachea?
   a. Stratified squamous
   b. Simple cuboidal
   c. Simple columnar
   d. Pseudostratified ciliated columnar

And there it was! Zoe had attempted to swallow a small magnetic ball, one of her older brother's toys. The toy had gone into her respiratory tract instead of her esophagus. The doctor inserted forceps through the bronchoscope, clamped onto the ball, and pulled it out.

4. What structure usually directs material into the esophagus when we swallow (instead of the air passages)?
   a. Epiglottis
   b. Glottis
   c. Concha
   d. Vocal fold



To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook, ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

STRUCTURAL PLAN OF THE RESPIRATORY SYSTEM

A. Structure determined by respiratory system functions of air distributor and gas exchanger—supplying oxygen and removing carbon dioxide from cells (Figure 26-1)
   1. Alveoli—sacs that serve as gas exchangers; all other parts of respiratory system serve as air distributors
   2. The respiratory system also warms, filters, and humidifies air
   3. Respiratory organs involved in speech, homeostasis of body pH, and olfaction

B. The respiratory system is divided into two structural divisions
   1. Upper respiratory tract—the organs are located outside the thorax and consist of the nose, nasopharynx, oropharynx, laryngopharynx, and larynx
   2. Lower respiratory tract—the organs are located within the thorax and consist of the trachea, the bronchial tree, and the lungs
   3. Accessory structures include the oral cavity, rib cage, and diaphragm

UPPER RESPIRATORY TRACT

A. Nose
   1. Structure of the nose—external portion consists of a bony and cartilaginous frame covered by skin containing sebaceous glands
      a. The two nasal bones meet and are surrounded by the frontal bone to form the root
      b. The nose is surrounded by the maxilla (Figure 26-2)
   2. Internal portion of the nose (nasal cavity) lies over the roof of the mouth, separated by the palatine bones
      a. Cleft palate—condition in which the palatine bones fail to unite completely and only partially separate the nose and the mouth, thereby producing difficulty swallowing
      b. Cribriform plate—separates the roof of the nose from the cranial cavity
      c. Septum—separates the nasal cavity into right and left cavities; it consists of four structures: the perpendicular plate of the ethmoid bone, the vomer bone, the vomeronasal cartilages, and the septal nasal cartilage
   3. Each nasal cavity is divided into three passageways: superior, middle, and inferior meatuses (Figure 26-3)
   4. Anterior (external) nares—external openings to the nasal cavities; open into the vestibule
   5. Sequence of airflow through the nose into the pharynx—anterior nares to the vestibule to all three meatuses simultaneously and then to the posterior (internal) nares
   6. Nasal mucosa
      a. Air passes over respiratory mucosa, which contains a rich blood supply (Figure 26-4)
      b. Olfactory epithelium—special sensory membrane containing many olfactory nerve cells and a rich lymphatic plexus
   7. Paranasal sinuses
      a. Four pairs of air-containing spaces that open or drain into the nasal cavity
      b. Each is lined with respiratory mucosa (Figure 26-5)
   8. Functions of the nose
      a. Provides a passageway for air traveling to and from the lungs
      b. Filters the air, aids speech, and makes possible the sense of smell

B. Pharynx (throat)
   1. Structure of pharynx
      a. Tubelike structure extending from the base of the skull to the esophagus
      b. Made of muscle and divided into three parts (Figure 26-3)—nasopharynx, oropharynx, and laryngopharynx
   2. Pharyngeal tonsils
      a. Located in the nasopharynx
      b. Called *adenoids* when they become enlarged
   3. Oropharynx contains two pair of organs—the palatine tonsils (most commonly removed in tonsillectomy) and the lingual tonsils (rarely removed)
   4. Functions of the pharynx—pathway for the respiratory and digestive tracts

C. Larynx (Figures 26-6 and 26-7)
   1. Location of larynx—positioned between the root of the tongue and the upper end of the trachea
   2. Structure of larynx
      a. Consists of cartilages attached to each other by muscle
      b. Lined by a ciliated mucous membrane, which forms two pairs of folds (Figure 26-8)—vestibular folds (false vocal folds) and vocal folds
   3. Cartilages (framework) of the larynx—formed by nine cartilages
      a. Single laryngeal cartilages—the three largest cartilages: the thyroid cartilage, the epiglottis, and the cricoid cartilages
      b. Paired laryngeal cartilages—three pairs of smaller cartilages: the arytenoid, the corniculate, and the cuneiform cartilages
   4. Muscles of the larynx
      a. Intrinsic muscles both insert and originate within the larynx
      b. Extrinsic muscles insert in the larynx but originate on some other structure
   5. Functions of the larynx—forms part of the airway to the lungs and produces the voice

D. Additional information is found in Table 26-1

LOWER RESPIRATORY TRACT

A. Trachea—often called "windpipe" (Figure 26-10)
   1. Structure of trachea
      a. Extends from the larynx to the primary bronchi
      b. Wall composed of (outer) adventitia, (middle) smooth muscle and C-shaped cartilage rings, (inner) respiratory mucosa; posterior wall is very elastic (Figure 26-11)

c. Incomplete rings and posterior elasticity allows esophagus to expand into trachea during swallowing
2. Functions of trachea—furnishes part of the open airway to the lungs; obstruction causes death

B. Bronchi and alveoli
1. Structure of bronchi
a. Lower end of the trachea divides into two primary bronchi, one on the right and one on the left; right one is larger and more vertical than left
b. Primary bronchi enter the lung and divide into secondary bronchi, which branch into bronchioles and eventually divide into alveolar ducts and alveoli
c. 23 levels of branching (Figure 26-12)
2. Structure of alveoli—the primary gas exchange structures
a. Respiratory membrane—the barrier between which gases are exchanged by alveolar air and blood (Figure 26-15)
b. Respiratory membrane consists of the alveolar epithelium, the capillary endothelium, and their joined basement membranes
c. Surfactant—a component of the fluid coating the respiratory membrane that reduces surface tension; produced by type II cells
3. Functions of bronchi and alveoli
a. Distribute air to the lung's interior; 23 levels of branching are optimal for oxygen transfer to the blood
b. Mucus blanket cleans the airways as it is moved upward by the ciliary escalator

C. Lungs
1. Structure of the lungs—cone-shaped organs extending from the diaphragm to above the clavicles (Figure 26-17)
a. Hilum—slit on the lung's medial surface where the primary bronchi and pulmonary blood vessels enter
b. Base—the inferior surface of the lung that rests on the diaphragm
c. Costal surface—lies against the ribs
d. Left lung is divided into two lobes—superior and inferior
e. Right lung is divided into three lobes—superior, middle, and inferior
f. Lobes are further divided into functional units—bronchopulmonary segments
(1) Ten segments in the right lung
(2) Eight segments in the left lung
2. Functions of the lungs—air distribution and gas exchange

D. Thorax (Figure 26-18)
1. Structure of the thoracic cavity—three divisions divided by the pleura
a. Pleural divisions—the part occupied by the lungs
b. Mediastinum—part occupied by the esophagus, trachea, large blood vessels, and heart
2. Functions of the thorax—brings about inspiration and expiration

E. Additional information is found in Table 26-1

CYCLE OF LIFE: RESPIRATORY SYSTEM

A. Respiration may be affected by developmental defects, age-related structural changes, or loss of function throughout the life cycle
B. Age-related changes affect lung capacity, make ventilation difficult, or reduce the oxygen- or carbon dioxide–carrying capacity of blood
C. Respiratory efficiency is reduced in old age as a result of changes in ribs, respiratory muscles, and hemoglobin levels

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Identify the major anatomical structures of the nose.
2. How are the conchae arranged in the nose? What are they?
3. Describe the draining of the paranasal sinuses.
4. What organs are found in the nasopharynx?
5. What tubes open into the nasopharynx?
6. The pharynx is common to what two systems?
7. List the divisions of the larynx.
8. What is the voice box? Of what is it composed? What is the Adam's apple?
9. What is the epiglottis? What is its function?
10. What are the vocal folds? What name is given to the opening between the folds?
11. Describe the structure and function of the trachea.
12. Discuss the component parts of the bronchial tree.
13. Make a diagram showing the termination of a bronchiole in an alveolar duct with alveoli.
14. How many lobes are in the right lung? The left? What are the bronchopulmonary segments?
15. Describe the changes in thorax size during respiration.
16. List the organs that are included in the upper respiratory tract. Do the same for the lower respiratory tract.
17. What is the role of the vomeronasal organ?

CRITICAL THINKING QUESTIONS

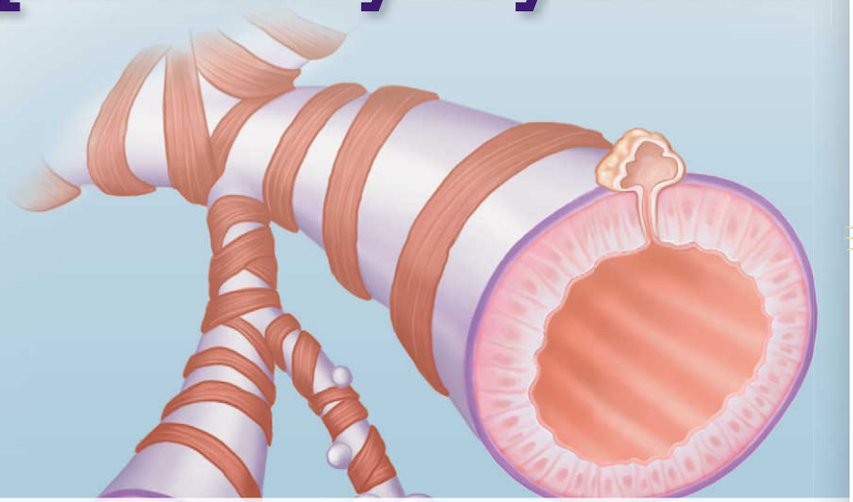


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. How would you describe the structure and function of the respiratory mucosa? Include the types of cells it contains and where these cells are located in the respiratory system.
2. Why do you think mucus production is especially important in the olfactory epithelium?
3. What are the features of the pharynx? Include in your answer the location of the openings in the pharynx, location of the tonsils, and the role of the pharynx in phonation.
4. Which of the paired laryngeal cartilages are the most important? What evidence can you cite to support your answer?
5. Identify which single cartilage is associated with a life-threatening condition in children. What are the symptoms of this condition?
6. In an earlier chapter the characteristic of water called *polarity* was described as the attraction water molecules have for each other. Why is this a problem in the respiratory system, and how is it solved?
7. Make the distinction between air distribution and gas exchange in the respiratory system. Identify the organs that serve as air distributors and gas exchangers.

Physiology of the Respiratory System

27



CHAPTER OUTLINE

HINT *Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.*

Respiratory Physiology, 824

Pulmonary Ventilation, 824
- Mechanism of Pulmonary Ventilation, 824
  - Inspiration, 828
  - Expiration, 830
- Pulmonary Volumes and Capacities, 831
  - Pulmonary Volumes, 831
  - Pulmonary Capacities, 834
  - Pulmonary Airflow, 837

Pulmonary Gas Exchange, 838
- Partial Pressure, 838
- Exchange of Gases in the Lungs, 839

How Blood Transports Gases, 841
- Hemoglobin, 842
- Transport of Oxygen, 844
- Transport of Carbon Dioxide, 844
  - Dissolved Carbon Dioxide, 844
  - Carbamino Compounds, 844
  - Bicarbonate, 844
  - Carbon Dioxide and pH, 846

Systemic Gas Exchange, 846

Regulation of Pulmonary Function, 848
- Respiratory Control Centers, 848
- Factors That Influence Breathing, 849
- Ventilation and Perfusion, 852

The Big Picture: Respiratory Physiology and the Whole Body, 853

Mechanisms of Disease, 854

Case Study, 857

LANGUAGE OF SCIENCE

HINT *Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.*

alveolar ventilation
(al-VEE-oh-lar ven-ti-LAY-shun)
[*alve-* **hollow**, *-ol-* **little**, *-ar* **relating to**, *vent-* **fan or create wind**, *-tion* **process**]

anatomical dead space
(an-ah-TOM-i-kal)
[*ana-* **apart**, *-tom-* **cut**, *-ical* **relating to**]

apneustic center
(ap-NYOO-stik)
[*a-* **not**, *-pneus-* **breathing**, *-ic* **relating to**]

arterial blood Po_2
(ar-TEER-ee-al)
[*arteri-* **airpipe (artery)**, *-al* **relating to**, *P* **pressure**, O_2 **oxygen**]

arterial blood pressure
(ar-TEER-ee-al)
[*arteri-* **airpipe (artery)**, *-al* **relating to**]

bicarbonate
(bye-KAR-boh-nayt)
[*bi-* **two**, *-carbon,* **coal (carbon)**, *-ate* **oxygen compound**]

Bohr effect (BOR)
[*Christian Bohr* **Danish physiologist**]

Boyle's law
(boils law)
[*Robert Boyle* **English scientist**]

carbaminohemoglobin
(kahr-bam-ih-no-hee-moh-GLOH-bin)
[*carb-* **coal (carbon)**, *-amino-* **ammonia compound (amino acid)**, *-hemo-* **blood**, *-glob-* **ball**, *-in* **substance**]

cerebral cortex
(seh-REE-bral KOR-teks)
[*cerebr-* **brain (cerebrum)**, *-al* **relating to**, *cortex* **bark**] *pl.*, cortices

Charles's law
(CHARLZ-ez law)
[*Jacques Alexandre César Charles* **French physicist**]

continued on p. 856

In Chapter 26 the anatomy of the respiratory system was presented as a basis for understanding the physiological principles that regulate air distribution and gas exchange. This chapter deals with ***respiratory physiology****—a complex series of interacting and coordinated processes that have a critical role in maintaining the stability, or constancy, of our internal environment. The proper functioning of the respiratory system ensures the tissues of an adequate oxygen supply and prompt removal of carbon dioxide. This process is complicated by the fact that control mechanisms must permit maintenance of homeostasis throughout a wide range of ever-changing environmental conditions and body demands. Adequate and efficient regulation of gas exchange between body cells and circulating blood under changing conditions is the essence of respiratory physiology. This complex function would not be possible without integration of numerous physiological control systems, including acid-base, water, and electrolyte balance, circulation, and metabolism.*

RESPIRATORY PHYSIOLOGY

Functionally, the respiratory system is composed of an integrated set of regulated processes that include the following:

- External respiration: pulmonary ventilation (breathing) and gas exchange in the pulmonary capillaries of the lungs
- Transport of gases by the blood
- Internal respiration: gas exchange in the systemic blood capillaries and cellular respiration
- Overall regulation of respiration

Figure 27-1 summarizes the essential processes of pulmonary function. We will use this set of processes as a general framework for this chapter. Cellular respiration has already been covered in Chapter 4 and will be reviewed again in greater detail in Chapter 30.

PULMONARY VENTILATION

Pulmonary ventilation is a technical term for what most of us call breathing. One phase of it, inspiration, moves air into the lungs and the other phase, expiration, moves air out of the lungs.

Mechanism of Pulmonary Ventilation

Air moves in and out of the lungs for the same basic reason that any fluid (a liquid or a gas) moves from one place to another—briefly, because its pressure in one place is different from that in the other place. Or stated differently, the existence of a pressure gradient (a pressure difference) causes fluids to move. A fluid always moves *down* its pressure gradient. This means that a fluid moves from the area where its pressure is higher to the area where its pressure is lower. When applied to the flow of air in the pulmonary airways, we can call this central idea the **primary principle of ventilation.**

Under standard conditions, air in the atmosphere exerts a pressure of 760 mmHg. Air in the alveoli at the end of one **expiration** and before the beginning of another **inspiration** also exerts a pressure of 760 mmHg. This explains why, at that moment, air is neither entering nor leaving the lungs. The mechanism that produces pulmonary ventilation is one that establishes a gas pressure gradient between the atmosphere and the alveolar air.

When atmospheric pressure is greater than pressure within the lung, air flows down this gas pressure gradient. Then air moves from the atmosphere into the lungs. In other words, inspiration occurs. When pressure in the lungs becomes greater than atmospheric pressure, air again moves down a gas pressure gradient. But this time, the air moves in the opposite direction. That is, air moves out of the lungs into the atmosphere. The pulmonary ventilation mechanism, therefore, must somehow establish these two gas pressure gradients—one in which alveolar pressure (P_A, pressure within the alveoli of the lungs) is lower than atmospheric pressure (or barometric pressure, P_B) to produce inspiration and one in which it is higher than atmospheric pressure to produce expiration. See Figures 27-2 and 27-3.

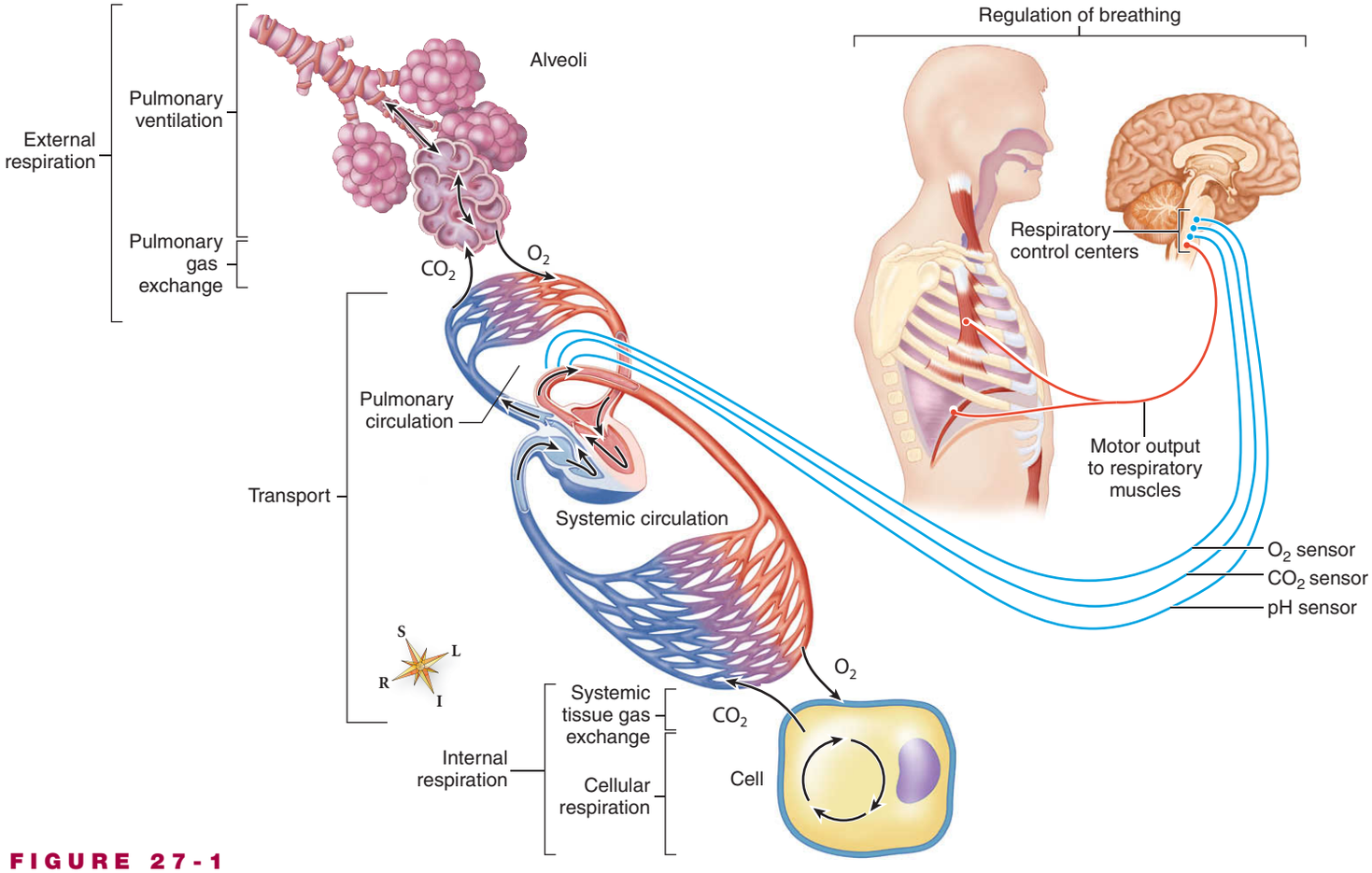


FIGURE 27-1

Overview of respiratory physiology. This chapter is organized around the principle that respiratory function includes external respiration (ventilation and pulmonary gas exchange), transport of gases by blood, and internal respiration (systemic tissue gas exchange and cellular respiration). Cellular respiration is discussed separately (see Chapters 4 and 30). Regulatory mechanisms centered in the brainstem use feedback from blood gas sensors to regulate ventilation.

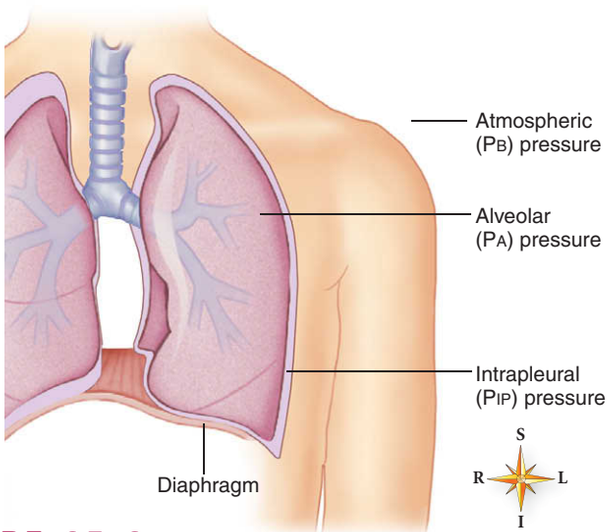


FIGURE 27-2

Pressures important in ventilation. This diagram shows the locations of pressures involved in the pressure gradients needed for ventilation (see Figure 27-3). Atmospheric pressure (P_B) is the air pressure of the atmosphere outside the body's airways. Alveolar pressure (P_A) is intrapulmonary pressure—the pressure at the far end of the internal airways. Intrapleural pressure (P_{IP}) is the fluid pressure of the pleural fluid between the parietal pleura and visceral pleura—or intrathoracic pressure (pressure in the thorax).

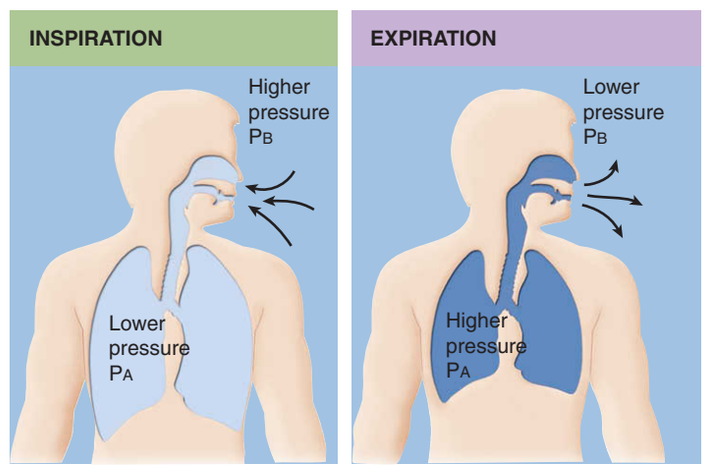


FIGURE 27-3

Primary principle of ventilation. Put simply, air moves down its pressure gradient—that is, it always moves from an area of high pressure to an area of lower pressure. To achieve inspiration, the higher pressure must be outside the body. To achieve expiration, the higher pressure must be inside the body's airways. P_B, Atmospheric [barometric] pressure; P_A, alveolar pressure. (See Figure 27-2.)

These pressure gradients are established by changes in the size of the thoracic cavity, which in turn are produced by contraction and relaxation of respiratory muscles. An understanding of *Boyle's law* is important for understanding the pressure changes that occur in the lungs and thorax during the breathing cycle. It is a familiar principle, stating that the volume of a gas varies inversely with pressure at a constant temperature (Box 27-1). One application of this principle is as follows: expansion of the thorax (increase in volume) results in a decreased intrapleural (intrathoracic) pressure. This leads to a decreased intraalveolar pressure that causes air to move from the outside into the lungs.

The mechanics of ventilation are often modeled using a balloon in a jar, as you can see in Figure 27-4. The bell-shaped jar represents the rib cage (thoracic cavity), and a rubber sheet across the open bottom of the bell jar represents the diaphragm. A balloon represents the lungs. The space between the balloon and the jar represents the intrapleural space. Expanding the thorax by pulling the diaphragm downward increases thoracic volume—thus decreasing intrapleural pressure (P_{IP}). Because the balloon is compliant (stretchable), the decrease in P_{IP} causes a similar decrease in the balloon pressure (alveolar pressure, P_A). This creates a pressure gradient that results in flow of air into the balloon. The opposite occurs when the elastic diaphragm recoils, decreasing

Box 27-1 | Gas Laws

A true understanding of respiratory function requires some familiarity with some of what physical scientists call the "gas laws." The gas laws are simply statements of what we have come to understand about the physical nature of gases. The gas laws are based on the concept of an **ideal gas,** that is, a gas whose molecules are so far apart that the molecules rarely collide with one another.

The gas laws are also based on the premise that gas molecules continually collide with the walls of their container and thus produce a force against it called the *gas pressure.* Pressure exerted by a gas depends on several factors. One factor is the frequency of collisions, which is proportional to the concentration of the gas: the higher the gas concentration, the higher the number of collisions with the wall of the container and thus the higher the gas pressure. **Boyle's law** sums up this principle very neatly by stating that a gas's volume is inversely proportional to its pressure (see figure, part *A*). When the volume of a container increases, the pressure of the gas inside it decreases, and when the volume decreases, the gas pressure increases. In this chapter, Boyle's law has been applied to ventilation: when thoracic volume increases, air pressure in the airways decreases (allowing air to move inward), and when thoracic volume decreases, air pressure in the airways increases (allowing air to move outward).

Another factor that affects an ideal gas is its temperature. Temperature is really a measurement of the motion of molecules. Thus an increase in temperature signals an increase in the average velocity of gas molecules. It follows that all other things remaining the same, an increase in the temperature of a gas will increase its pressure. However, if the container is expandable, as it is in part *B* of the figure, and thus the pressure is held constant, the volume increases. This principle is summed up in **Charles's law,** which states that volume is directly proportional to temperature ($V \propto T$) when pressure is held constant (see figure, part *B*). One could extend this notion to state that pressure is proportional to temperature ($P \propto T$) when volume is held constant. One can assume, then, that during inspiration, air expands in volume as it is warmed by the respiratory mucosa.

Dalton's law takes things a step further by stating the situation when the gas in question is actually a *mixture* of different kinds of gas molecules, as in air (part *C* of the figure). Dalton's law states that the total pressure exerted by a mixture of gases is the sum of the pressure of each individual gas. That is, the collision force created by all of one type of molecule accounts for only a part of the total pressure—the collision forces of all the other types of molecules in the mixture must be included to arrive at the total gas pressure. Dalton's law, also known as the **law of partial pressures,** is used to determine the partial pressure of oxygen (P_{O_2}) in air, for example. Because the partial pressure of a gas is determined by its relative concentration in the mixture of gases, partial pressure values can be used in much the same way as concentration values in determining the direction of net diffusion.

Another gas law, **Henry's law,** describes how the pressure of a gas relates to the concentration of that gas in a liquid solution (part *D* of the figure). If you have a beaker of water surrounded by air, which contains the oxygen, the concentration of oxygen dissolved in the water will be proportional by the partial pressure of oxygen in the air. Henry's law further states that the concentration of the gas in solution is also a function of the gas's **solubility,** or its relative ability to dissolve. Thus Henry's law states that the concentration of a gas in a solution depends on the partial pressure of the gas and the solubility of the gas, as long as the temperature remains constant. This principle explains how the plasma concentration of a gas such as oxygen relates to its partial pressure.

Also see Box 27-6, which discusses Fick's law.

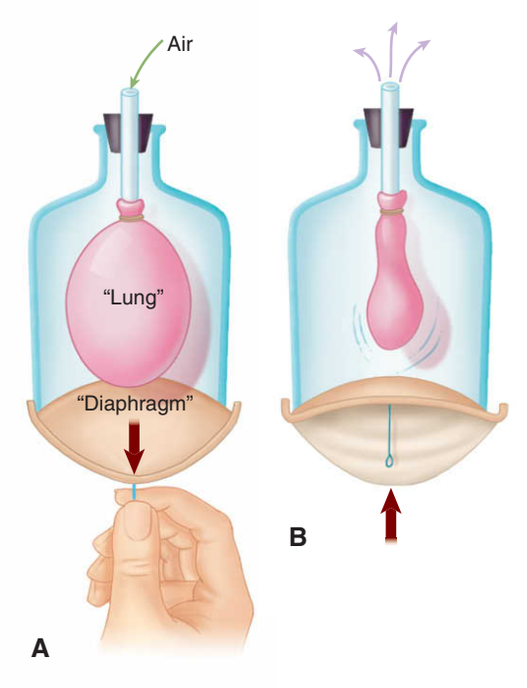
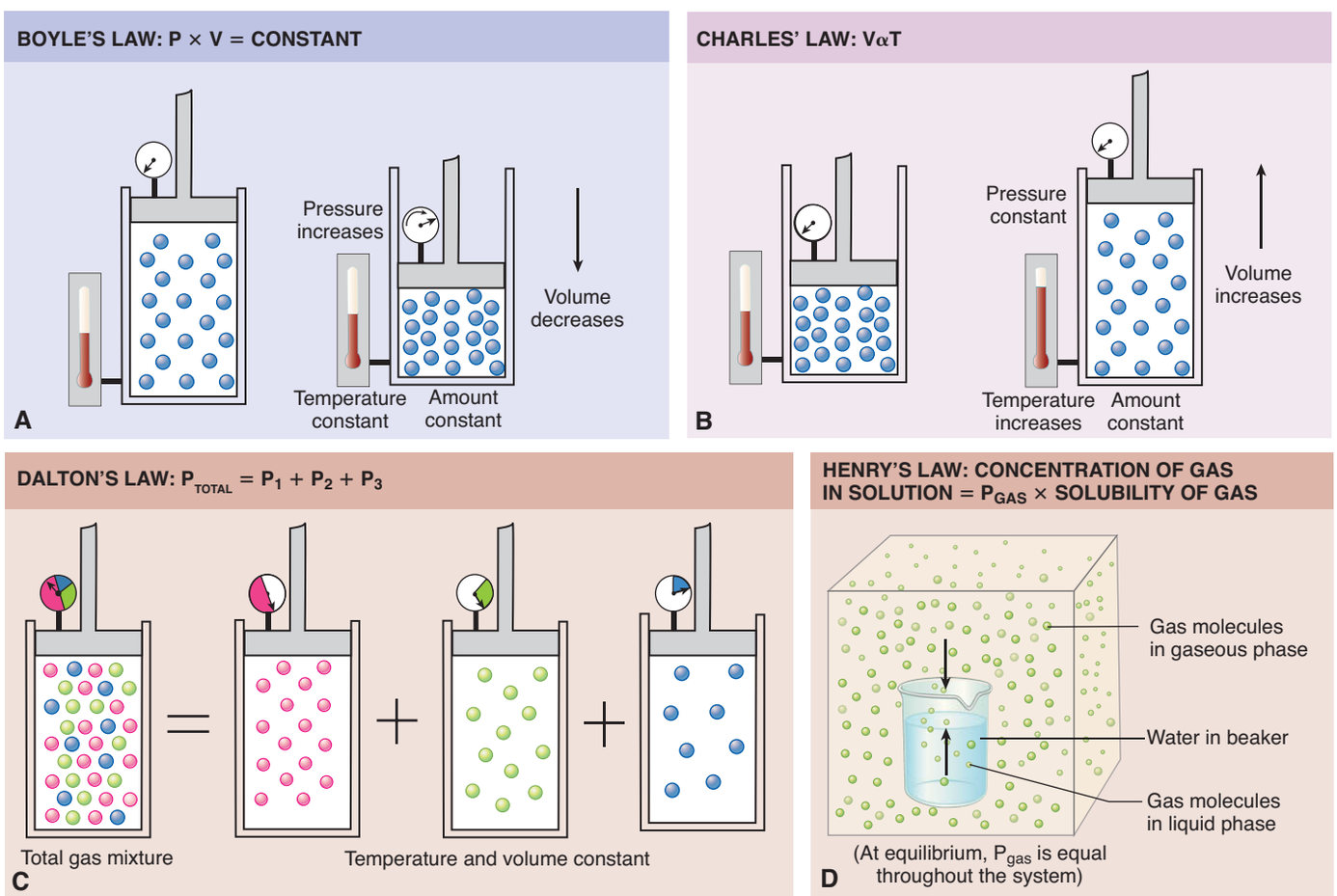


FIGURE 27-4

Balloon model of ventilation. The cartoons show a classic model in which a jar represents the rib cage (thoracic cavity), a rubber sheet represents the diaphragm, and a balloon represents the alveoli of the lungs. The space between the jar and balloon represents the intrapleural space. **A,** Inspiration, caused by downward movement of the diaphragm. **B,** Expiration, caused by elastic recoil of the diaphragm upward.



The gas laws. **A,** Boyle's law. **B,** Charles's law. **C,** Dalton's law. **D,** Henry's law.

internal air volumes (thus increasing internal air pressure) and forcing air out of the balloon.

Figure 27-5 applies the same principles of the balloon model to the human airways to demonstrate the mechanics of ventilation. The constant alternation between inspiration and expiration is called the **respiratory cycle.** The specific mechanics of the respiratory cycle are outlined in the following sections and in Table 27-1.

INSPIRATION

Contraction of the diaphragm alone, or contraction of both the diaphragm and the external intercostal muscles, produces quiet inspiration. As the diaphragm contracts, it descends, and this makes the thoracic cavity longer. Contraction of the external intercostal muscles pulls the anterior end of each rib up and out (Figure 27-6, *A*). This also elevates the attached sternum and enlarges the thorax from front to back and from side to side (Figure 27-6, *B*). In addition, contraction of the sternocleidomastoid, pectoralis minor, and serratus anterior muscles can aid in elevation of the sternum and rib cage during forceful inspiration.

As the size of the thorax increases, the intrapleural (intrathoracic) and alveolar pressure decreases (Boyle's law) and inspiration occurs.

At the beginning of each inspiration, intrapleural pressure (P_{IP}) is about 758 mmHg. Thus the P_{IP} is about 2 mmHg less than atmospheric pressure (frequently written −2 mmHg). During normal quiet inspiration, P_{IP} decreases further to 756 mmHg (−4 mmHg) or

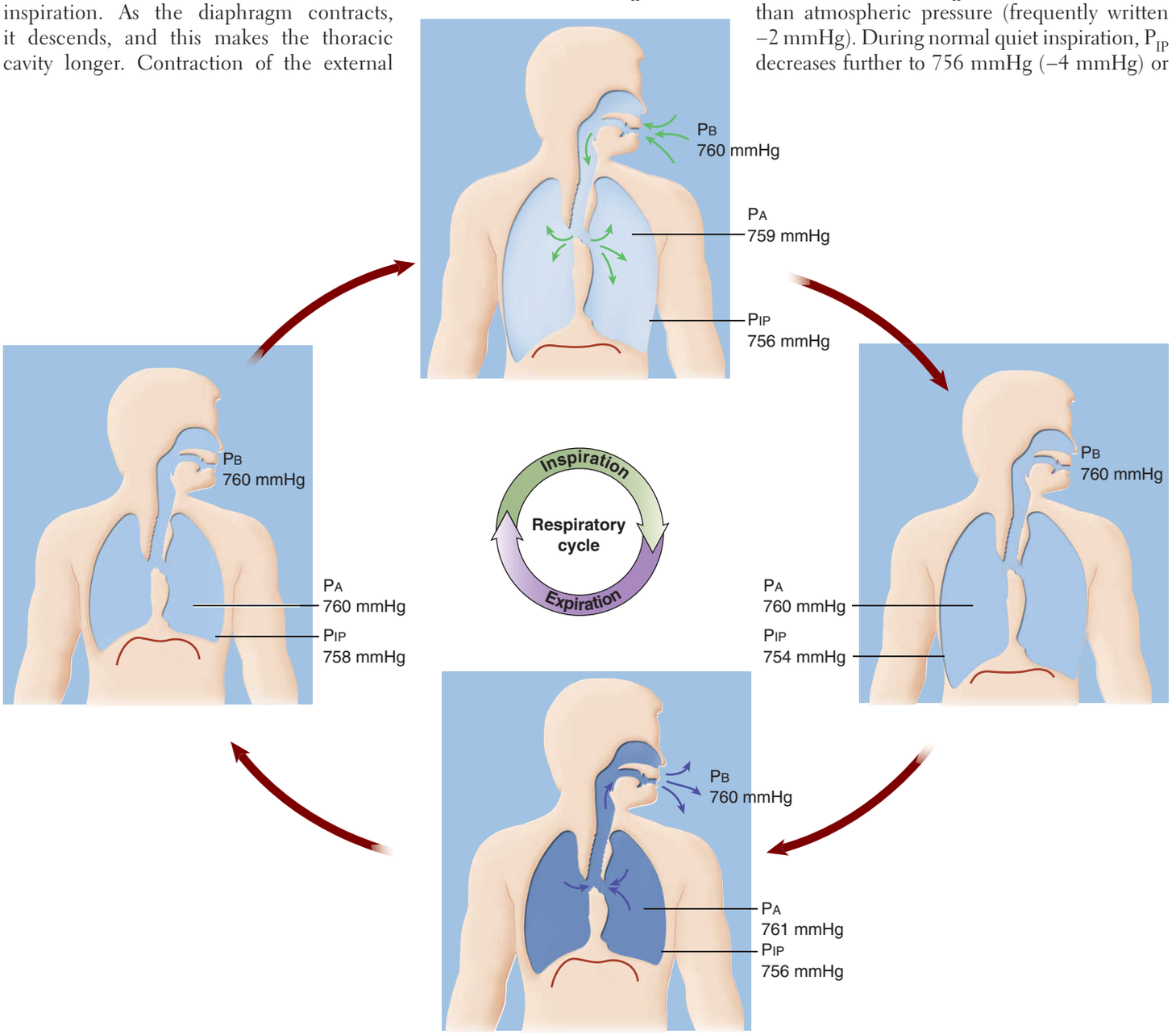


FIGURE 27-5

The respiratory cycle. During *inspiration,* the diaphragm contracts, increasing the volume of the thoracic cavity. This increase in volume results in a decrease in pressure, which causes air to rush into the lungs. During *expiration,* the diaphragm returns to an upward position, reducing the volume in the thoracic cavity. Air pressure thus increases, forcing air out of the lungs. See Table 27-1 for additional details. P_A, Alveolar pressure; P_B, barometric pressure; P_{IP}, intrapleural pressure.

TABLE 27-1 The Respiratory Cycle*

P_{IP}	P_A	P_B	DESCRIPTION
Inspiration			
758	760	760	The diaphragm is relaxed, putting the thoracic cavity at low volume. At the beginning of inspiration $P_{IP} < P_A$, keeping alveoli open. Since $P_A = P_B$, no air is flowing yet.
756	759	760	The diaphragm contracts, increasing the thoracic volume and reducing P_{IP}. A decrease in P_{IP} causes a decrease in P_A. Now $P_A < P_B$, and air flows down the pressure gradient (into the lungs).
754	760	760	Eventually, the alveoli fill with air and P_A equilibrates with P_B. Inward airflow stops. The cycle is now ready to shift to the expiration phase. Note that P_{IP} is still dropping but P_A has not yet "caught up" with the drop.
Expiration			
754	760	760	As expiration is about to begin, the diaphragm is contracted maximally. Since $P_A = P_B$, there is no airflow.
756	761	760	The diaphragm relaxes, and elastic recoil of the thoracic walls and alveoli increases P_{IP} and P_A. Now, $P_A > P_B$. Air moves (outward) down the pressure gradient.
758	760	760	The diaphragm eventually relaxes fully, so the decrease in volume stops. P_A equilibrates with P_B, and airflow ceases. The system is now ready for another inspiration phase.

*All P values are expressed in *mmHg* and are examples only.
P_{IP} = Intrapleural pressure (air pressure in the intrapleural space); P_A = alveolar pressure (air pressure inside the alveoli); P_B = atmospheric (barometric) pressure (air pressure of the external environment [atmosphere]).

less. As the thorax enlarges, it pulls the lungs along with it because of cohesion between the moist pleura covering the lungs and the moist pleura lining the thorax. Thus the lungs expand and the pressure in their tubes and alveoli necessarily decreases. Alveolar pressure decreases from an atmospheric level to a subatmospheric level—typically a drop of about 1 to 3 mmHg. The moment that alveolar pressure becomes less than atmospheric pressure, a pressure gradient exists between the atmosphere and the interior of the lungs. According to the primary principle of ventilation, air moves into the lungs. Eventually, enough air moves out of the lungs to establish a pressure equilibrium between the atmosphere and the alveoli—and the flow of air then stops.

The ability of the lungs and thorax to stretch, referred to as **compliance,** is essential to normal respiration. If the compliance

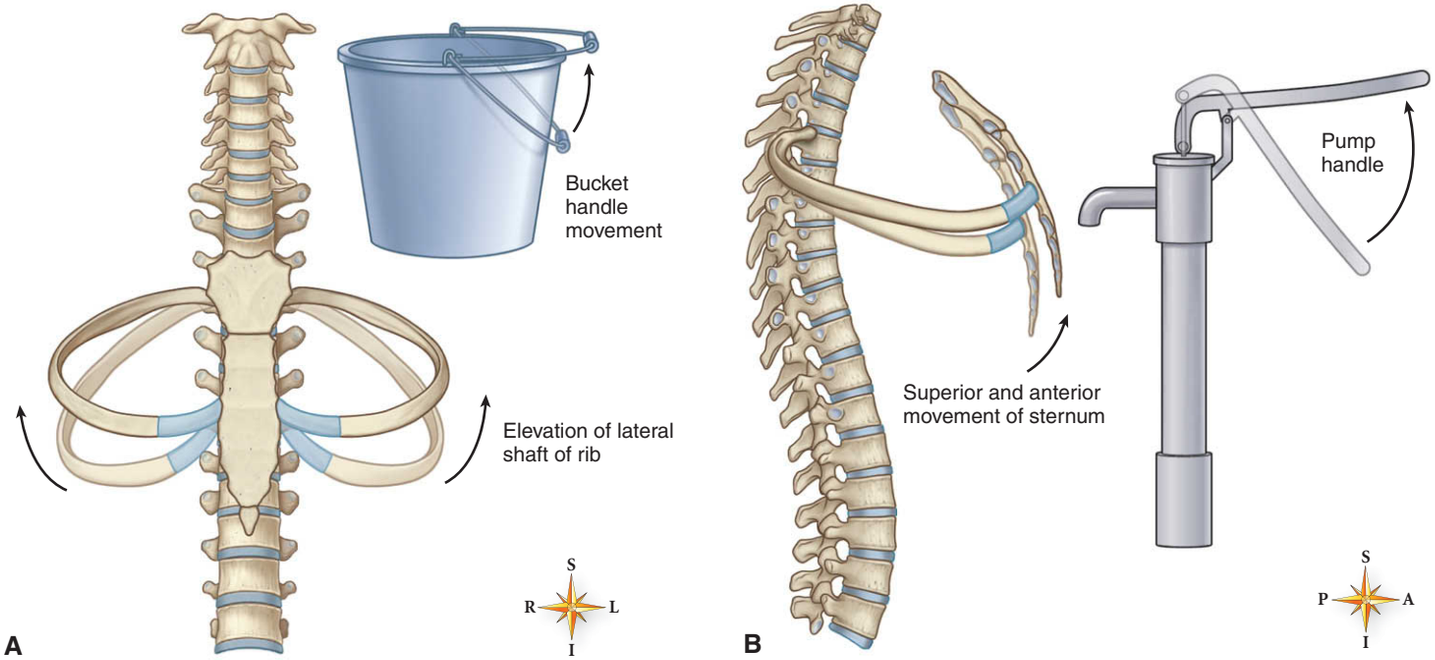


FIGURE 27-6

Movement of the rib cage during breathing. A, Inspiratory muscles pull the ribs upward and thus outward, as illustrated by lifting a bucket handle. **B,** Inspiratory muscles pull the sternum upward and thus outward, as when pulling upward on the handle of a water pump.

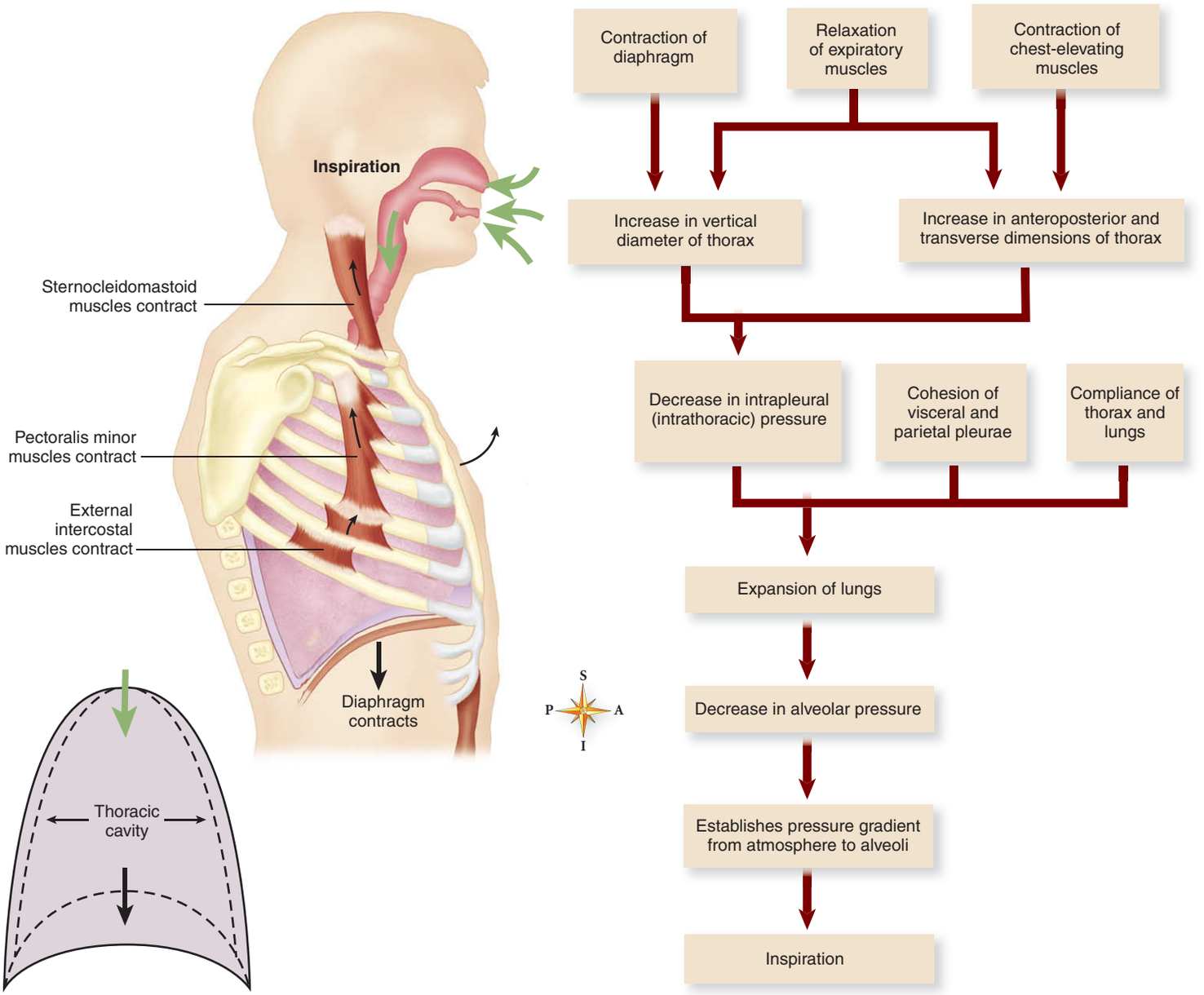


FIGURE 27-7

Mechanism of inspiration. Note the role of the diaphragm and the chest-elevating muscles (pectoralis minor and external intercostals) in increasing thoracic volume, which decreases pressure in the lungs and thus draws air inward.

of these structures is reduced by injury or disease, inspiration becomes difficult—or even impossible (Box 27-2 on p. 848).

For a summary of the mechanism of inspiration just described, see Figures 27-5 and 27-7.

EXPIRATION

Quiet expiration is ordinarily a passive process that begins when the pressure gradients that resulted in inspiration are reversed. The inspiratory muscles relax, causing a decrease in the size of the thorax and an increase in intrapleural pressure from about 754 mmHg (–6 mmHg) before expiration to about 756 mmHg (–4 mmHg) or more during respiration. It is important to understand that this pressure between the parietal and visceral pleura is always negative, that is, less than atmospheric pressure and less than alveolar pressure. The negative intrapleural pressure is required to overcome the so-called "collapse tendency of the lungs" caused by surface tension of the fluid lining the alveoli and the stretch of elastic fibers that are constantly attempting to recoil.

As alveolar pressure increases, a positive-pressure gradient is established from alveoli to atmosphere—and thus expiration occurs

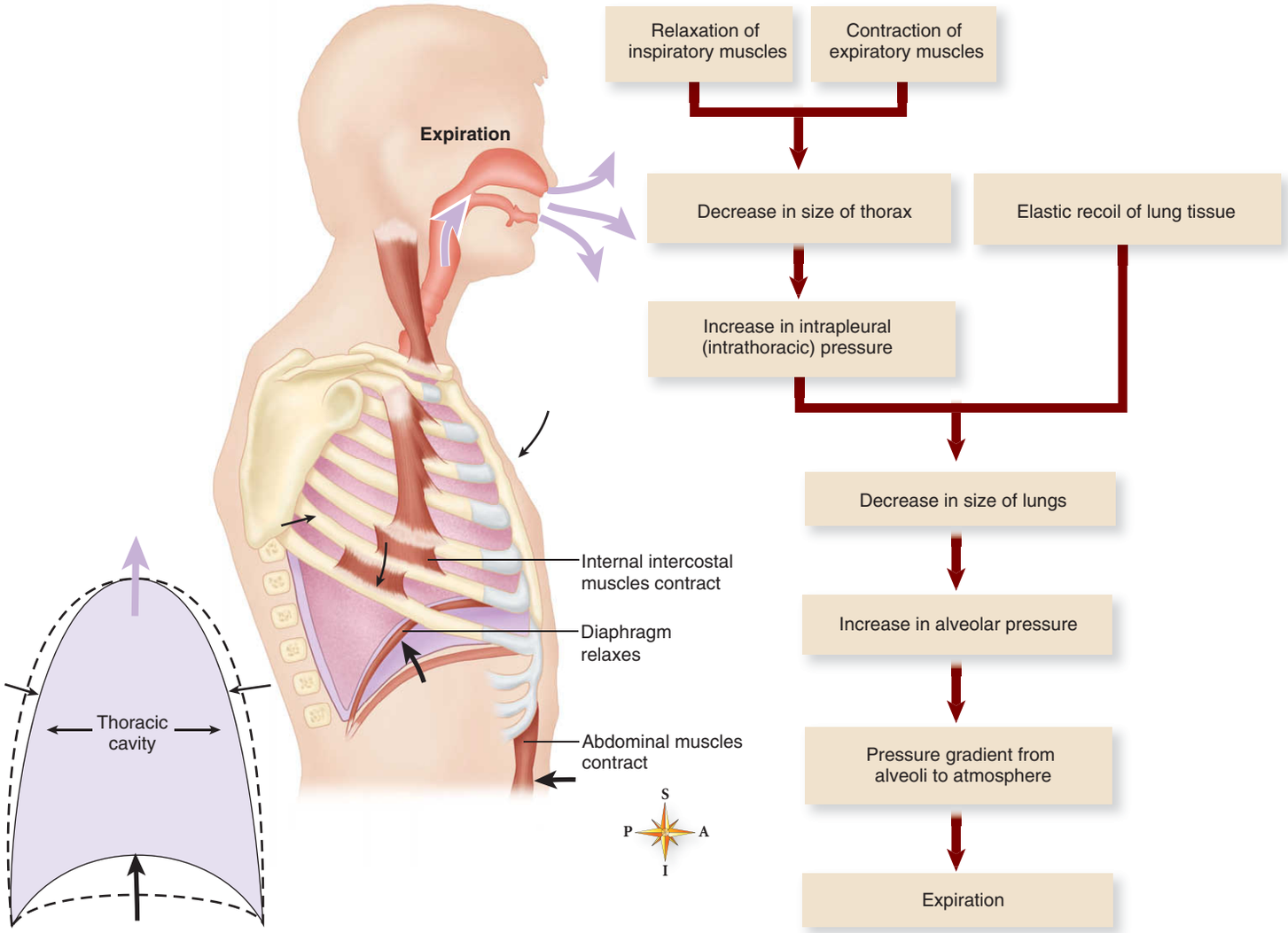


FIGURE 27-8

Mechanism of expiration. Note that relaxation of the diaphragm plus contraction of chest-depressing muscles (internal intercostals) reduces thoracic volume, which increases pressure in the lungs and thus pushes air outward.

as air flows outward through the respiratory passageways. In forced expiration, contraction of the abdominal and internal intercostal muscles can increase alveolar pressure tremendously—creating a very large air pressure gradient.

The tendency of the thorax and lungs to return to their preinspiration volume is a physical phenomenon called **elastic recoil.** If a disease condition reduces the elasticity of pulmonary tissues, expirations must become forced even at rest.

Figures 27-5 and 27-8 summarize the mechanism of expiration just described.

Look for a moment at Figure 27-9. This figure shows the repeating respiratory cycle mapped out as changes in pressures and volumes. Note that intrapleural pressure is always less than alveolar pressure. This difference ($P_{IP} - P_A$) is called the **transpulmonary pressure.** Intrapleural pressure is always "negative" with respect to alveolar pressure. Transpulmonary pressure must be negative to maintain inflation of the lungs, as stated previously.

| QUICK CHECK |

1. What is meant by the term *pulmonary ventilation?*
2. What effect does enlargement of the thoracic cavity have on the air pressure inside the lungs?
3. Which requires more expenditure of energy during normal, quiet breathing—inspiration or expiration?

Pulmonary Volumes and Capacities

The volumes of air moved in and out of the lungs and the volume remaining in them are matters of great importance. They must be normal so that normal exchange of oxygen and carbon dioxide can occur between alveolar air and pulmonary capillary blood.

PULMONARY VOLUMES

An apparatus called a **spirometer** is used to measure the volume of air exchanged in breathing (Figure 27-10). A graphic recording

Box 27-2 | Surfactant and Lung Compliance

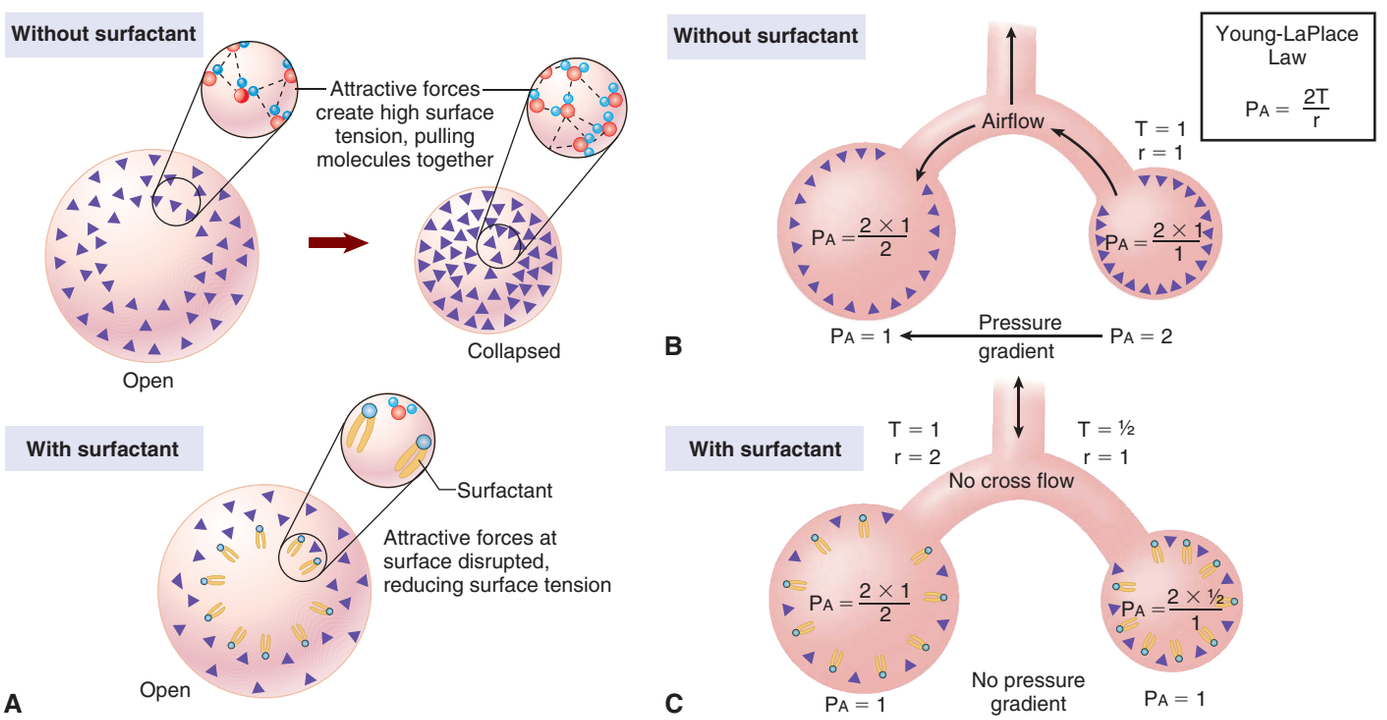
As we have discussed already, inspiration cannot occur without the lungs and thorax having the ability to stretch—a characteristic called *compliance.* Of course, the natural "stretchiness" of the alveolar walls is important in determining lung compliance. Conditions that cause thickening, or fibrosis, of lung tissues reduce the ease of stretch and thus reduce lung compliance. A greater impact on lung compliance is made by **surface tension** in the fluid film that lines the alveoli.

Surface tension in an aqueous (water-based) solution results from the attractive forces between water molecules in the solution. Recall from Chapter 2 that water molecules are polar and thus are electrically attracted to one another—as though they are weak magnets. Surface tension is high as the water molecules try to move toward one another, thereby contracting the fluid. The fluid lining of each alveolus would thus tend to collapse under this contracting force. However, as we discussed in Chapter 26 (see p. 809), the presence of surfactant prevents such collapse of alveoli. Surfactant is formed from the protein and phospholipid secretions of **type II cells** in the wall of each alveolus. Surfactant reduces surface tension and thus prevents fluid contraction and alveolar collapse. The role of surfactant in preventing alveolar collapse is illustrated in Figure *A.*

The pressure created by the force of surface tension is greater in smaller alveoli than in larger alveoli, according to the **Young-LaPlace law**. This means that smaller alveoli would tend to have a higher pressure (P_A) than larger alveoli would. Thus air would move from the smaller alveoli into larger alveoli. However, because the surfactant on the surface of the fluid that lines the smaller alveoli is more concentrated than that on larger alveoli, surface tension is reduced proportionally. In this way, the pressure in large alveoli is equal to that in smaller alveoli. In theory, all alveoli—no matter what their size—are ventilated equally. Figure *B* summarizes the Young-LaPlace law.

Surfactant is present in most newborns. However, because surfactant formation is not fully under way until the seventh or eighth month of prenatal development, premature infants often do not have enough surfactant. The deficiency of surfactant in premature infants is called **hyaline membrane disease (HMD).** Because lack of surfactant decreases lung compliance, a premature infant will try to inflate the alveoli by increasing effort of the inspiratory muscles. Such great effort is needed to maintain normal ventilation that the baby may die of exhaustion. The effects of such alveolar collapse and ventilation difficulty are collectively called **respiratory distress syndrome (RDS).** In infants, it is more specifically called *infant respiratory distress syndrome (IRDS).* See Figure *C.*

One way to treat IRDS is to use a special type of mechanical respirator with **continuous positive airway pressure** (**CPAP,** pronounced "SEE-pap"). The respirator artificially inflates the baby's lungs and then maintains enough pressure during expiration to prevent collapse—thus relieving the baby's inspiratory muscles. Synthetic surfactants are also used frequently to prevent or treat IRDS. The surfactant is delivered through a tube directly into the airways—a method called **intratracheal injection.**



A, Role of surfactant. The surface of the water that lines the small alveoli tends to contract because of its high surface tension, thereby collapsing the entire alveolus. Surfactant disrupts some of the attractive forces and thus reduces surface tension—and the risk of alveolar collapse. **B, Young-LaPlace law.** Also called the *law of LaPlace,* this principle states that alveolar pressure (P_A) is directly proportional to surface tension (T) and inversely proportional to the radius (r) of the alveolus. Without surfactant, the pressure gradient would cause air to flow from the small alveoli to the larger alveoli—thus triggering collapse of the smaller alveoli. When surfactant is present, the concentration of the surfactant is higher as the alveolus gets smaller. Because small alveoli have less surface tension than larger alveoli do (as a result of more concentrated surfactant), the effect of the Young-LaPlace law is counterbalanced. Because P_A thus remains about the same in all alveoli, regardless of size, ventilation is not disrupted. **C, Microscopic effects of respiratory distress syndrome (RDS).** The light micrograph on the left shows normal lung structure, with many open alveoli. The right image is from an infant who died of RDS. Note the collapse of the alveoli.

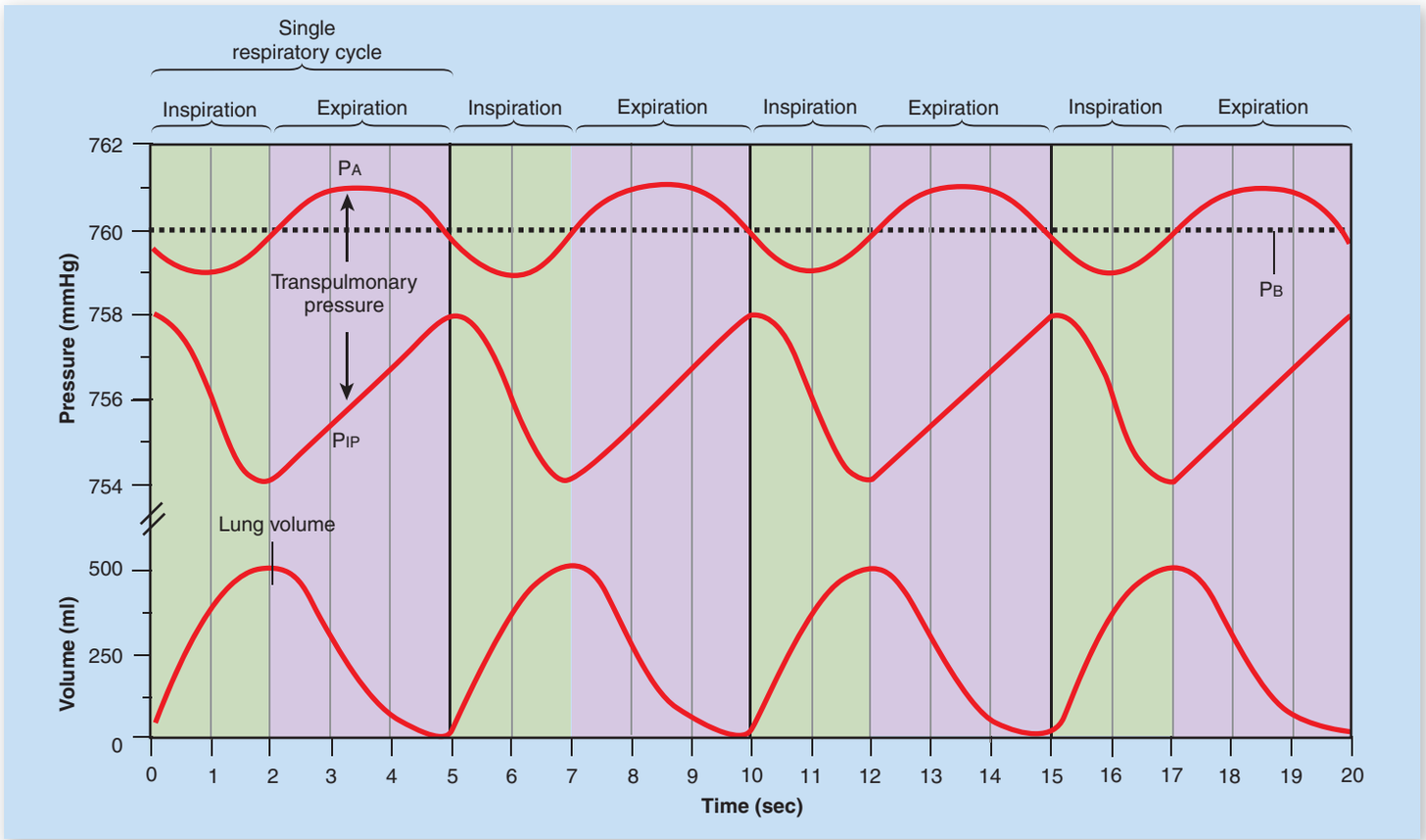


FIGURE 27-9

Rhythm of ventilation. Respiratory cycles repeat continuously in normal, quiet breathing. Notice the rhythmic rise and fall of the intrapleural pressure (P_{IP}) and alveolar pressure (P_A). You can easily see that P_{IP} is always lower than P_A (negative transpulmonary pressure), which helps keep the alveoli inflated. The lowest line shows the change in air volumes during the respiratory cycle.

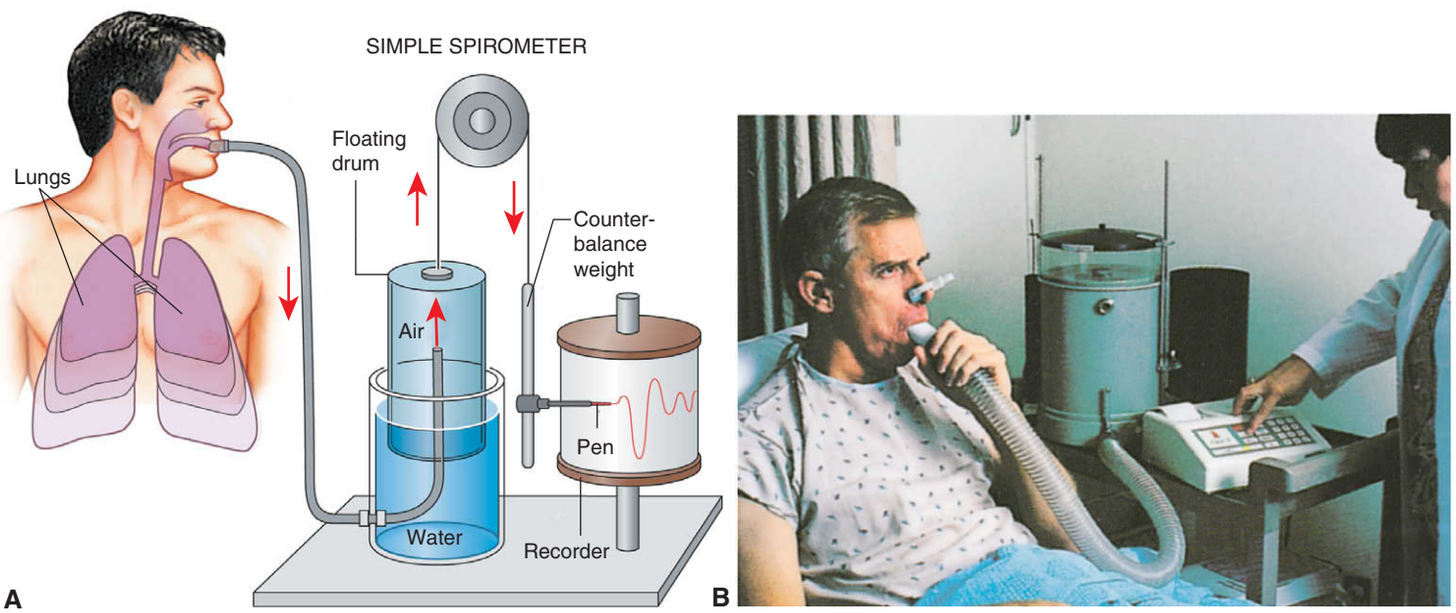


FIGURE 27-10

Spirometer. Spirometers are devices that measure the volume of gas that the lungs inhale and exhale, usually as a function of time. **A,** Diagram of a classic spirometer design showing how the volume of air exhaled and inhaled is recorded as a rising and falling line. **B,** A simple spirometer attached to a computerized recording device. This apparatus is used frequently for routine assessment of ventilation.

of the changing pulmonary volumes observed during breathing is called a **spirogram** (Figure 27-11, A). The volume of air exhaled normally after a typical inspiration is termed **tidal volume (TV).** As you can see in Figure 27-11, the normal volume of tidal air for an adult at rest is approximately 500 ml (or 0.5 L).

After expiration of tidal air, an individual can force still more air out of the lungs. The largest additional volume of air that one can forcibly expire after expiring tidal air is called the **expiratory reserve volume (ERV).** An adult, as Figure 27-11 shows, normally has an ERV of between 1000 and 1200 ml (1.0 to 1.2 L). **Inspiratory reserve volume (IRV)** is the amount of air that can be forcibly inspired over and above a normal inspiration. It is measured by having the individual exhale normally after a forced inspiration. The normal IRV is about 3300 ml (3.3 L). No matter how forcefully one exhales, one cannot squeeze all the air out of the lungs. Some of it remains trapped in the alveoli. This amount of air that cannot be forcibly expired is known as **residual volume (RV)** and amounts to about 1200 ml (1.2 L). Between breaths, an exchange of oxygen and carbon dioxide occurs between the trapped residual air in the alveoli and the blood. This process helps "level off" the amounts—or maintain the set point values—of oxygen and carbon dioxide in the blood during the breathing cycle. Have you ever had "the wind knocked out of you" by a sudden impact to the thorax or a series of deep coughs? In such a case, your expiratory reserve is forced out of your airways, as well as some of your residual volume. A few alveoli collapse as a result. It may take a moment or two, and some effort on your part, to reinflate the collapsed alveoli and reestablish normal breathing.

In *pneumothorax* (Box 27-3), the RV is eliminated when the lung collapses. Even after the RV is forced out, the collapsed lung has a porous, spongy texture and floats in water because of trapped air called the *minimal volume*, which is about 40% of the RV.

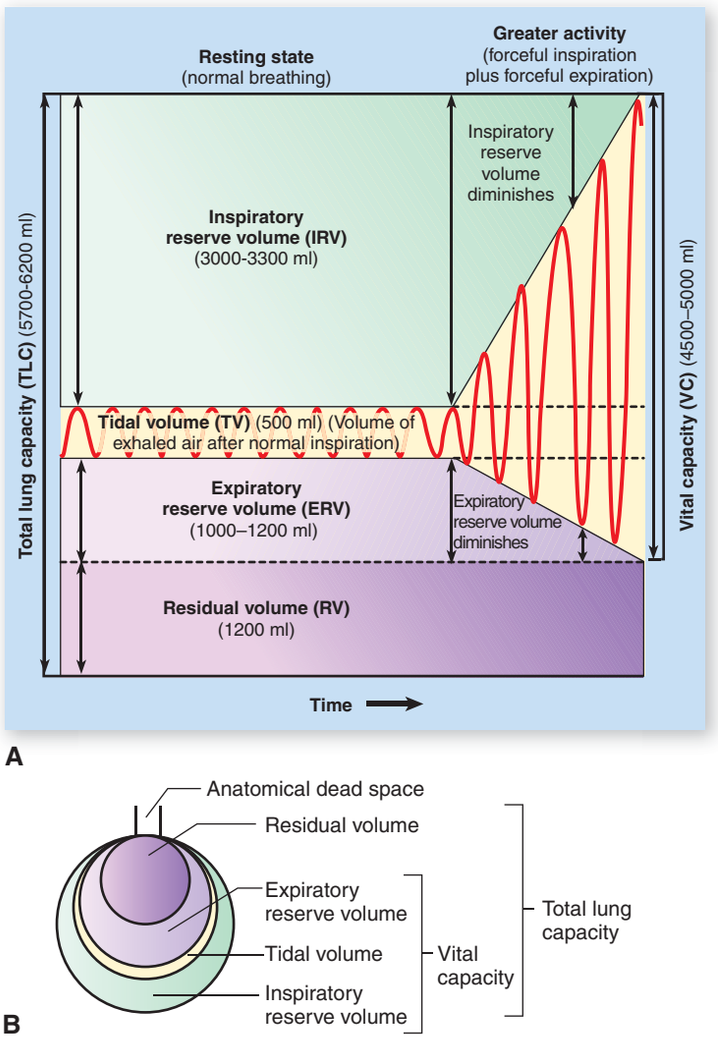


FIGURE 27-11

Pulmonary ventilation volumes and capacities. A, Spirogram. **B,** Pulmonary volumes (at rest) represented as relative proportions of an inflated balloon. During normal, quiet respirations, the atmosphere and lungs exchange about 500 ml of air (TV). With forcible inspiration, about 3300 ml more air can be inhaled (IRV). After a normal inspiration and normal expiration, approximately 1000 ml more air can be forcibly expired (ERV). Vital capacity is the amount of air that can be forcibly expired after a maximal inspiration and therefore indicates the largest amount of air that can enter and leave the lungs during respiration. Residual volume is the air that remains trapped in the alveoli.

PULMONARY CAPACITIES

A pulmonary "capacity" is the sum of two or more pulmonary "volumes." Notice in Figure 27-11 that **vital capacity (VC)** is the sum of:

$$IRV + TV + ERV$$

The vital capacity represents the largest volume of air an individual can move in and out of the lungs. It is determined by measuring the largest possible expiration after the largest possible inspiration. How large a vital capacity a person has depends on many factors—the size of the thoracic cavity, posture, and various other factors. In general, a larger person has a larger vital capacity than a smaller person does. An individual has a larger vital capacity when standing erect than when stooped over or lying down. The volume of blood in the lungs also affects the vital capacity. If the lungs contain more blood than normal, the alveolar air space is encroached on and vital capacity accordingly decreases. This becomes a very important factor in congestive heart disease.

Excess fluid in the pleural or abdominal cavities also decreases vital capacity. So, too, does the disease *emphysema*. In emphysema, the alveolar walls become stretched—that is, lose their elasticity—and are unable to recoil normally for expiration. This leads to an increased RV. In severe emphysema, the RV may increase so much that the chest occupies the inspiratory position even at rest. Excessive muscular effort is therefore necessary for inspiration, and because of the loss of elasticity of lung tissue, greater effort is required, too, for expiration.

In diagnosing lung disorders a physician may need to know the inspiratory capacity and the functional residual capacity of the patient's lungs. **Inspiratory capacity (IC)** is the maximal amount of air an individual can inspire after a normal expiration. From Figure 27-11, you can deduce that:

$$IC = TV + IRV$$

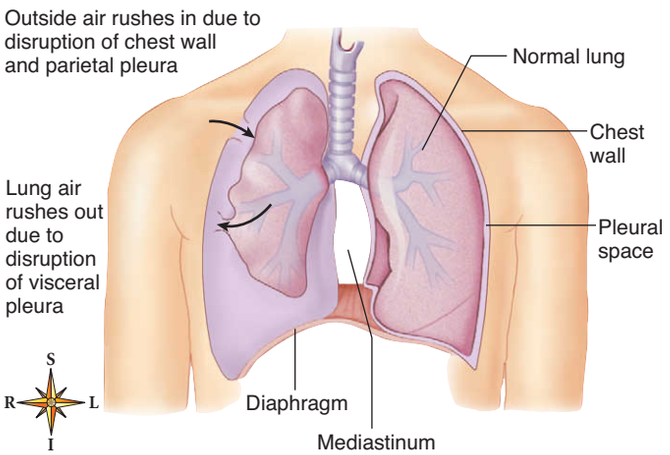
Box 27-3 | HEALTH matters

Pneumothorax

Air in the pleural space may accumulate when the visceral pleura ruptures and air from the lung rushes out or when atmospheric air rushes in through a wound in the chest wall and parietal pleura. In either case, the lung collapses and normal respiration is impaired. Air in the thoracic cavity is a condition known as **pneumothorax** (see figure). To apply some of the information you have learned about the respiratory mechanism, let us suppose that a surgeon makes an incision through the chest wall into the pleural space, as is done in one of the dramatic, modern open-chest operations. What change, if any, can you deduce takes place in respirations? Compare your deductions with those in the next paragraph.

Intrapleural pressure, of course, immediately increases from its normal subatmospheric level to the atmospheric level. More pressure than normal is therefore exerted on the outer surface of the punctured lung and causes it to collapse. It could even collapse the other lung. Why? Because the mediastinum is a mobile rather than a rigid partition between the two pleural sacs. This anatomical fact allows the increased pressure in the side of the chest that is open to push the heart and other mediastinal structures over toward the intact side, where they would exert pressure on the other lung. Pneumothorax can also result from disruption of the visceral pleura and the resulting flow of pulmonary air into the pleural space.

Pneumothorax results in many respiratory and circulatory changes. They are of great importance in determining medical and nursing care but lie beyond the scope of this book.



Pneumothorax. Diagram showing air entering the thoracic cavity, causing lung collapse.

Using the volumes given in the figure, how many milliliters is the IC? Check your answer in Table 27-2, which summarizes pulmonary volumes and capacities. **Functional residual capacity (FRC)** is the amount of air left in the lungs at the end of a normal expiration. Therefore, as Figure 27-11 implies,

$$FRC = ERV + RV$$

Using the volumes given, the functional residual capacity is 2200 to 2400 ml (2.2 to 2.4 L). The total volume of air a lung can hold is called the **total lung capacity (TLC).** It is, as Figure 27-11 indicates, the sum of all four lung volumes.

The term **alveolar ventilation** refers to the volume of inspired air that actually reaches, or "ventilates," the alveoli. Only this volume of air takes part in the exchange of gases between air and blood. (Alveolar air exchanges some of its oxygen for some of the blood's carbon dioxide.) With every breath we take, part of the entering air necessarily fills our air passageways—nose, pharynx, larynx, trachea, and bronchi. This portion of air does not descend into any alveoli and therefore cannot take part in gas exchange. In this sense, it is "dead air." Appropriately, the larger air passageways this air occupies are said to constitute the **anatomical dead space.** Figure 27-11, *B*, relates the volume of the anatomical dead space

TABLE 27-2 Pulmonary Volumes and Capacities

VOLUME	DESCRIPTION	TYPICAL VALUE	CAPACITY	FORMULA	TYPICAL VALUE
Tidal volume (TV)	Volume moved into or out of the respiratory tract during a normal respiratory cycle	500 ml (0.5 L)	Vital capacity (VC)	TV + IRV +ERV	4500-5000 ml (4.5-5.0 L)
Inspiratory reserve volume (IRV)	Maximum volume that can be moved into the respiratory tract after a normal inspiration	3000-3300 ml (3.0-3.3 L)	Inspiratory capacity (IC)	TV + IRV	3500-3800 ml (3.5-3.8 L)
Expiratory reserve volume (ERV)	Maximum volume that can be moved out of the respiratory tract after a normal expiration	1000-1200 ml (1.0-1.2 L)	Functional residual capacity (FRC)	ERV + RV	2200-2400 ml (2.2-2.4 L)
Residual volume (RV)	Volume remaining in the respiratory tract after maximum expiration	1200 ml (1.2 L)	Total lung capacity (TLC)	TV + IRV + ERV + RV	5700-6200 ml (5.7-6.2 L)

to the major pulmonary volumes. In disorders such as **chronic obstructive pulmonary disease (COPD)**, some alveoli are not able to perform gas exchange and are therefore also "dead space." The anatomical dead space plus any alveolar dead space together make up the **physiological dead space.**

One rule of thumb estimates the volume of air in the anatomical dead space to be the same number of milliliters as the individual's weight in pounds. Another generalization says that the anatomical dead space approximates 30% of the TV. TV – dead space volume = alveolar ventilation volume. Suppose you have a normal TV of 500 ml and that 30% of this, or 150 ml, fills the anatomical dead space. The amount of air reaching your alveoli—your alveolar ventilation volume—is then 350 ml per breath, or 70% of your TV.

Emphysema and certain other abnormal conditions, in effect, increase the amount of dead space air or physiological dead space. Consequently, alveolar ventilation decreases, and this in turn decreases the amount of oxygen that can enter blood and the amount of carbon dioxide that can leave it. Inadequate air-blood gas exchange, therefore, is the inevitable result of inadequate alveolar ventilation. Stated differently, the alveoli must be adequately ventilated for an adequate gas exchange to take place in the lungs.

Box 27-4 summarizes some abnormal breathing patterns seen in spirometry.

Box 27-4 | Types of Breathing

The alternate movement of air into and out of the lungs that we call breathing can occur in distinctive patterns that can be recognized and designated by name (see figure).

Eupnea is the term used to describe normal quiet breathing. During eupnea, the need for oxygen and carbon dioxide exchange is being met, and the individual is not usually conscious of the breathing pattern. Ventilation occurs spontaneously at the rate of 12 to 17 breaths per minute.

Hyperpnea means increased breathing that is regulated to meet an increased demand by the body for oxygen. During hyperpnea, there is always an increase in pulmonary ventilation. The hyperpnea caused by exercise may meet the need for increased oxygen by an increase in tidal volume alone or by an increase in both tidal volume and breathing frequency.

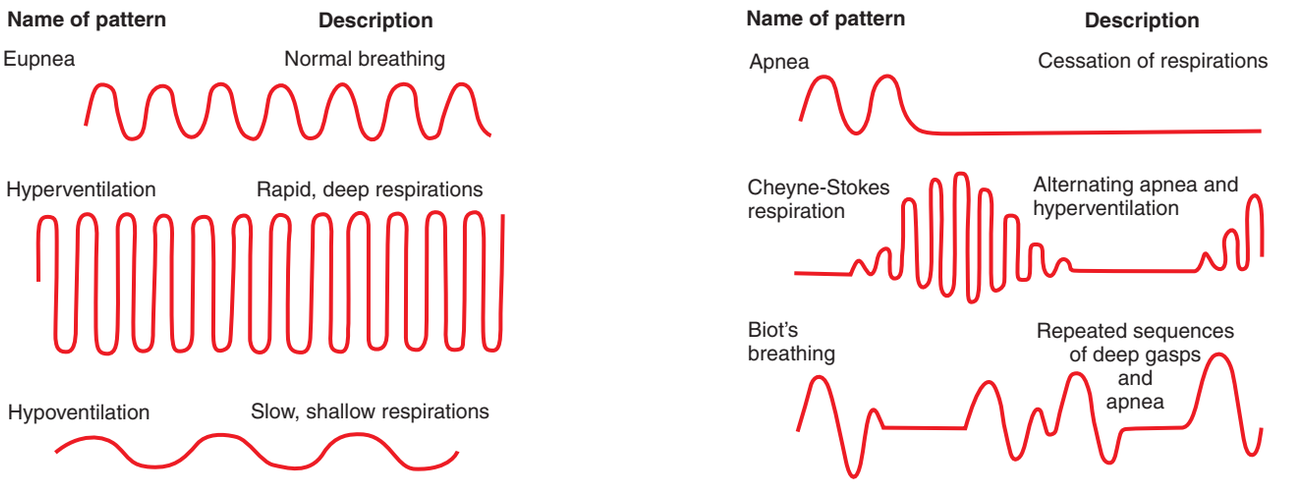
Hyperventilation is characterized by an increase in pulmonary ventilation in excess of the need for oxygen. It sometimes results from a conscious voluntary effort preceding exertion or from psychogenic factors (hysterical hyperventilation). **Hypoventilation** is a decrease in pulmonary ventilation that results in elevated blood levels of carbon dioxide.

Dyspnea refers to labored or difficult breathing and is often associated with hypoventilation. A person suffering from dyspnea is aware, or conscious, of the breathing pattern and is generally uncomfortable and in distress. **Orthopnea** refers to dyspnea while lying down. It is relieved by sitting or standing up. This condition is common in patients with heart disease.

Several terms are used to describe the cessation of breathing. **Apnea** refers to the temporary cessation of breathing at the end of a normal expiration. It may occur during sleep or when swallowing. **Apneusis** is the cessation of breathing in the inspiratory position. Failure to resume breathing following a period of apnea, or apneusis, is called **respiratory arrest.**

Cheyne-Stokes respiration is a periodic type of abnormal breathing often seen in terminally ill or brain-damaged patients. It is characterized by cycles of gradually increasing tidal volume for several breaths followed by several breaths with gradually decreasing tidal volume. These cycles repeat in a type of crescendo-decrescendo pattern.

Biot's breathing is characterized by repeated sequences of deep gasps and apnea. This type of abnormal breathing pattern is seen in individuals suffering from increased intracranial pressure.



Examples of breathing patterns and spirograms.

PULMONARY AIRFLOW

Various applications of spirometry can be used to generate additional information about airflow in an individual. For example, spirometry can be used to determine pulmonary airflow as the rate of pulmonary ventilation, or **total minute volume** (volume moved per minute). Tidal volume (ml/cycle) multiplied by respiration rate (cycles per minute) yields the total minute volume (ml/min). The total minute volume of a person at rest is about 6000 ml (500 ml/cycle × 12 cycles/min). Box 27-5 discusses the concept of *maximum oxygen consumption*.

Yet another application of spirometry is the **forced expiratory volume (FEV)** test. The FEV test can determine the presence of respiratory obstruction by measuring the volume of air expired per second during forced expiration. The volume forcefully expired during the first second, the FEV_1, is normally about 83% of the vital capacity (Figure 27-12). FEV_2, the total volume expired during the first 2 seconds, is about 94% of the VC. By the end of the third second, FEV_3, 97% of the vital capacity should have been expired. The FEV test is also sometimes called the *FVC (forced vital capacity) test.*

Some spirometers are capable of producing a graph called the **flow-volume loop.** This type of graph shows a forced expiration (forced vital capacity) as a loop rather than the peaks and valleys of the classic spirogram. In Figure 27-13 you can see that the top portion of the loop represents expiratory airflow (liters per second) along the vertical axis and expiratory volume (liters) along the horizontal axis. The inspiratory airflow and volume are represented by the bottom portion of the loop.

Notice in Figure 27-13 that the top of the flow-volume loop represents the peak expiratory flow, or more simply the *peak flow.* The peak flow is easy to measure even with simple hand-held spirometers. It is no wonder, then, that peak flow measurements are

Box 27-5 | SPORTS and FITNESS

Maximum Oxygen Consumption

Exercise physiologists use **maximum oxygen consumption** ($Vo_{2\ max}$) as a predictor of a person's capacity to do aerobic exercise. An individual's $Vo_{2\ max}$ represents the amount of oxygen taken up by the lungs, transported to the tissues, and used to do work. $Vo_{2\ max}$ is determined largely by hereditary factors, but aerobic (endurance) training can increase it by as much as 35%. Many endurance athletes are now using $Vo_{2\ max}$ measurements to help them determine and then maintain their peak condition.

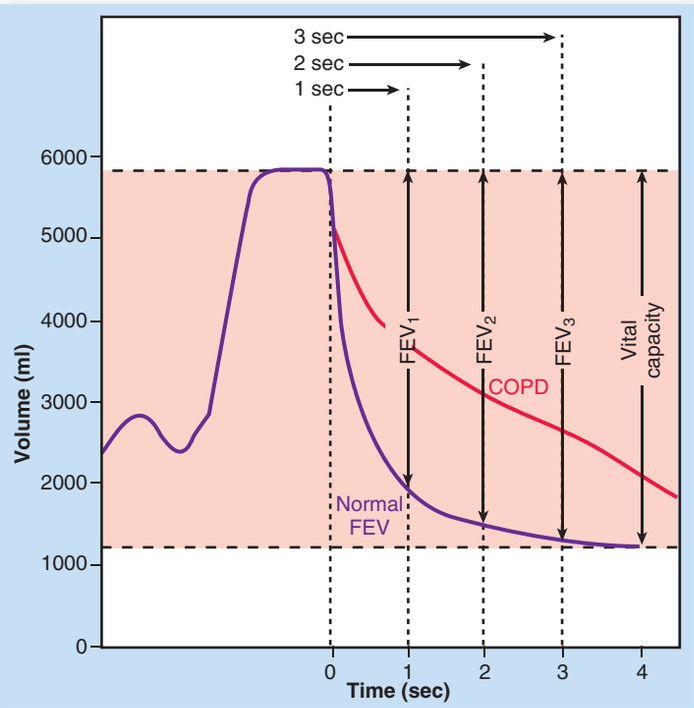


FIGURE 27-12

Forced expiratory volume (FEV). A normal individual forcefully exhales about 83% of the vital capacity (VC) during the first second, 94% at the end of 2 seconds, and 97% by the end of 3 seconds. The red line shows the results from a person with COPD (chronic obstructive pulmonary disease) who cannot forcefully exhale a large percentage of the vital capacity as quickly as a person without pulmonary obstruction.

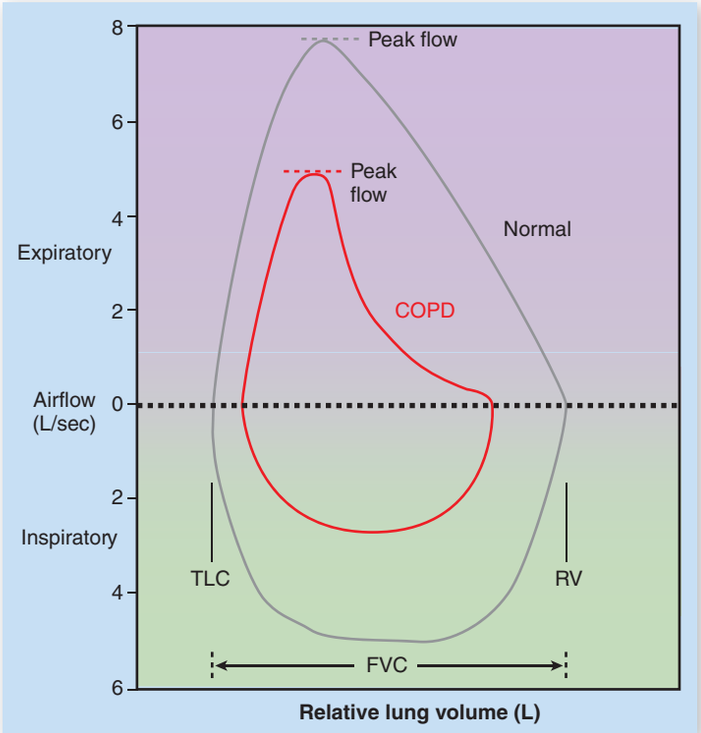


FIGURE 27-13

Flow-volume loops. The top of the loop represents expiratory flow (vertically) and volume (horizontally). The bottom of the loop represents inspiratory flow and volume. Notice that a person with COPD (chronic obstructive pulmonary disease) will produce a smaller loop with a "scooped-out" shape at the end of the expiratory curve. *FVC,* Forced vital capacity.

often used at home by asthma patients to keep a diary of airflow function. The flow-volume loop is especially useful in assessing such obstructive disorders because of the characteristic "scooped-out" shape of the expiratory part of the loop. In obstructive disorders, the inspiratory portion of the loop has a normal curve, but is smaller than normal.

| QUICK CHECK |

4. What is the difference between a pulmonary *volume* and a pulmonary *capacity?*
5. The volume of air that is expired after a normal inspiration during normal, quiet breathing is referred to by what name?
6. What is meant by the term *vital capacity?*
7. What is the *total minute volume?* How can it be calculated from a spirogram?

PULMONARY GAS EXCHANGE

Partial Pressure

Before discussing the exchange of gases across the respiratory membranes, we need to understand the law of partial pressures (Dalton's law). The term **partial pressure** means the pressure exerted by any one gas in a mixture of gases or in a liquid. According to the law of partial pressures, the partial pressure of a gas in a mixture of gases is directly related to the concentration of that gas in the mixture and to the total pressure of the mixture. Figure 27-14 shows how each gas in atmospheric air contributes to the total atmospheric pressure. The partial pressure of each gas is directly related to its concentration in the total mixture. Suppose we apply this principle to compute the partial pressure of oxygen in the atmosphere. The concentration of oxygen in the atmosphere is about 21%, and the total pressure of the atmosphere is 760 mmHg under standard conditions. Therefore:

$$\text{Atmospheric } P_{O_2} = 21\% \times 760 = 159.6 \text{ mmHg}$$

The symbol used to designate partial pressure is the capital letter *P* preceding the chemical symbol for the gas. Examples: alveolar air P_{O_2} is about 100 mmHg, arterial blood P_{O_2} is also about 100 mmHg, and venous blood P_{O_2} is about 37 mmHg. The word **tension** is often used as a synonym for the term *partial pressure*—oxygen tension means the same thing as P_{O_2}.

The partial pressure of a gas in a liquid is directly determined by the amount of that gas dissolved in the liquid, which in turn is determined by the partial pressure of the gas in the environment of the liquid. Gas molecules diffuse into a liquid from its environment and dissolve in the liquid until the partial pressure of the gas in solution becomes equal to its partial pressure in the environment of the liquid. Alveolar air constitutes the environment

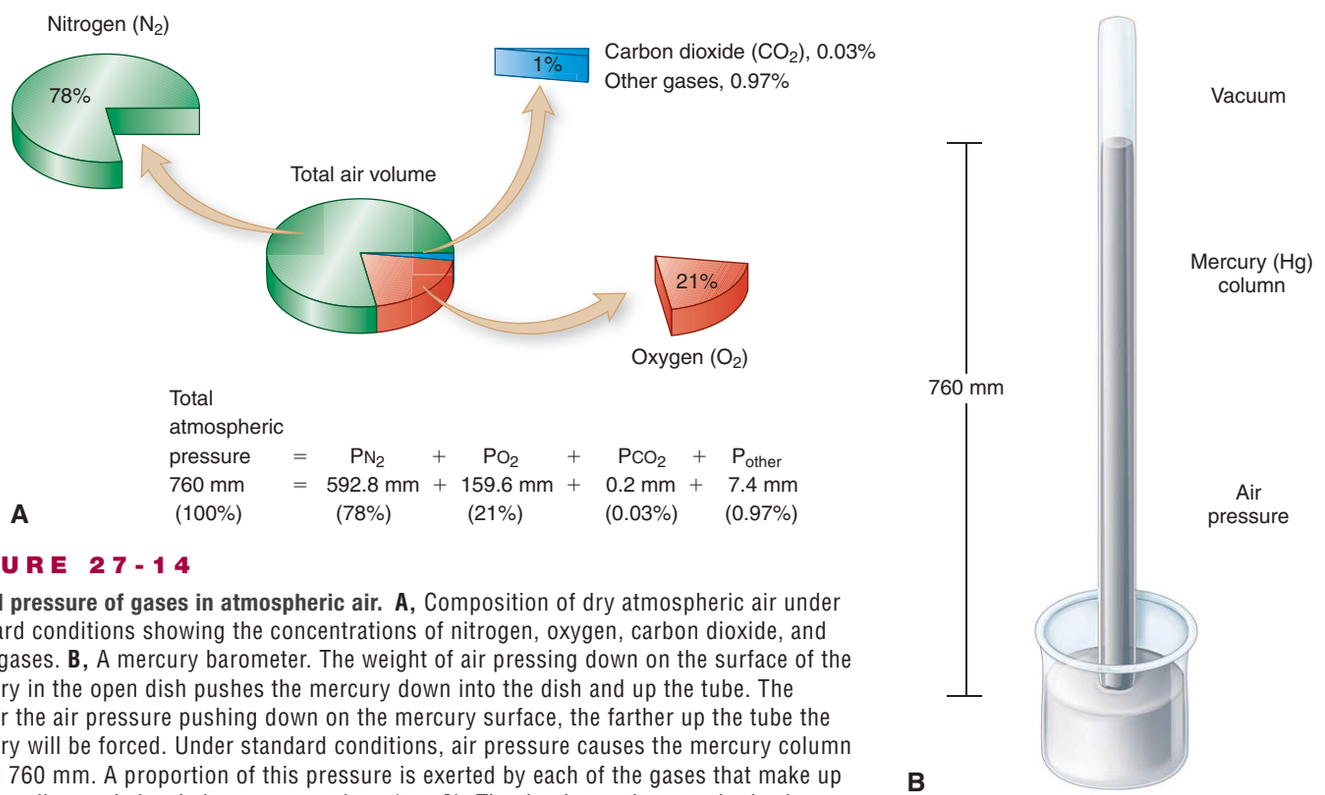


FIGURE 27-14

Partial pressure of gases in atmospheric air. A, Composition of dry atmospheric air under standard conditions showing the concentrations of nitrogen, oxygen, carbon dioxide, and other gases. **B,** A mercury barometer. The weight of air pressing down on the surface of the mercury in the open dish pushes the mercury down into the dish and up the tube. The greater the air pressure pushing down on the mercury surface, the farther up the tube the mercury will be forced. Under standard conditions, air pressure causes the mercury column to rise 760 mm. A proportion of this pressure is exerted by each of the gases that make up air, according to their relative concentrations (see **A**). That is, the total atmospheric air pressure is the sum of the partial pressures of nitrogen, oxygen, carbon dioxide, water vapor, and other gases.

TABLE 27-3 Oxygen and Carbon Dioxide Pressure Gradients*

	ATMOSPHERE	ALVEOLAR AIR	SYSTEMIC ARTERIAL BLOOD	SYSTEMIC VENOUS BLOOD
P_{O_2}	160	100	100	40
P_{CO_2}	0.2	40	40	46

*Values indicate approximate mmHg pressure under usual conditions.

surrounding blood moving through pulmonary capillaries. Standing between the blood and the air are only the very thin alveolar and capillary membranes, and both of these membranes are highly permeable to oxygen and carbon dioxide. By the time blood leaves the pulmonary capillaries as arterial blood, diffusion and approximate equilibration of oxygen and carbon dioxide across the membranes have occurred. Arterial blood P_{O_2} and P_{CO_2} therefore usually equal or very nearly equal alveolar P_{O_2} and P_{CO_2} (Table 27-3).

Exchange of Gases in the Lungs

Exchange of gases in the lungs takes place between alveolar air and blood flowing through lung capillaries. It is important to realize that physiologically speaking, air in the lung is not part of our body. That is, inspired air is not part of the internal environment. As Figure 27-15 shows, the airways are merely inward extensions of the external environment. Before oxygen can enter our internal environment, and before carbon dioxide can leave our internal environment, these gases must cross the barrier between the external world and the internal world.

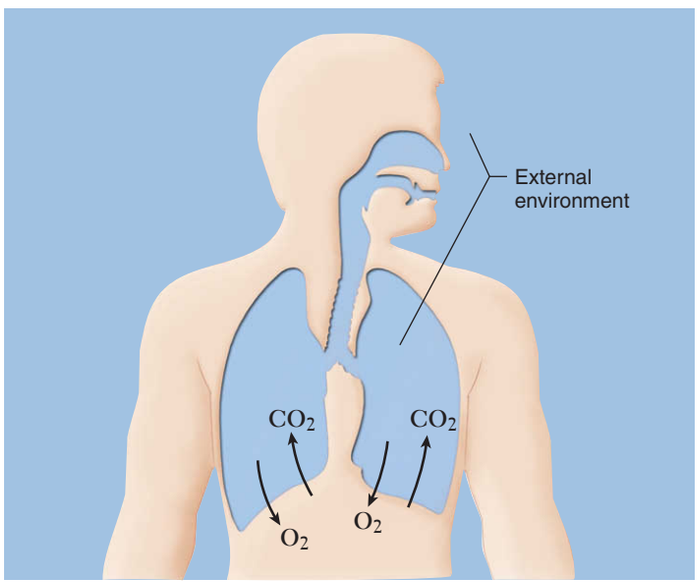


FIGURE 27-15

External-internal barrier. The respiratory membranes of the lung represent an interface or barrier that gases must cross to enter or exit the body's internal environment. The pulmonary airway is merely an extension of the external environment.

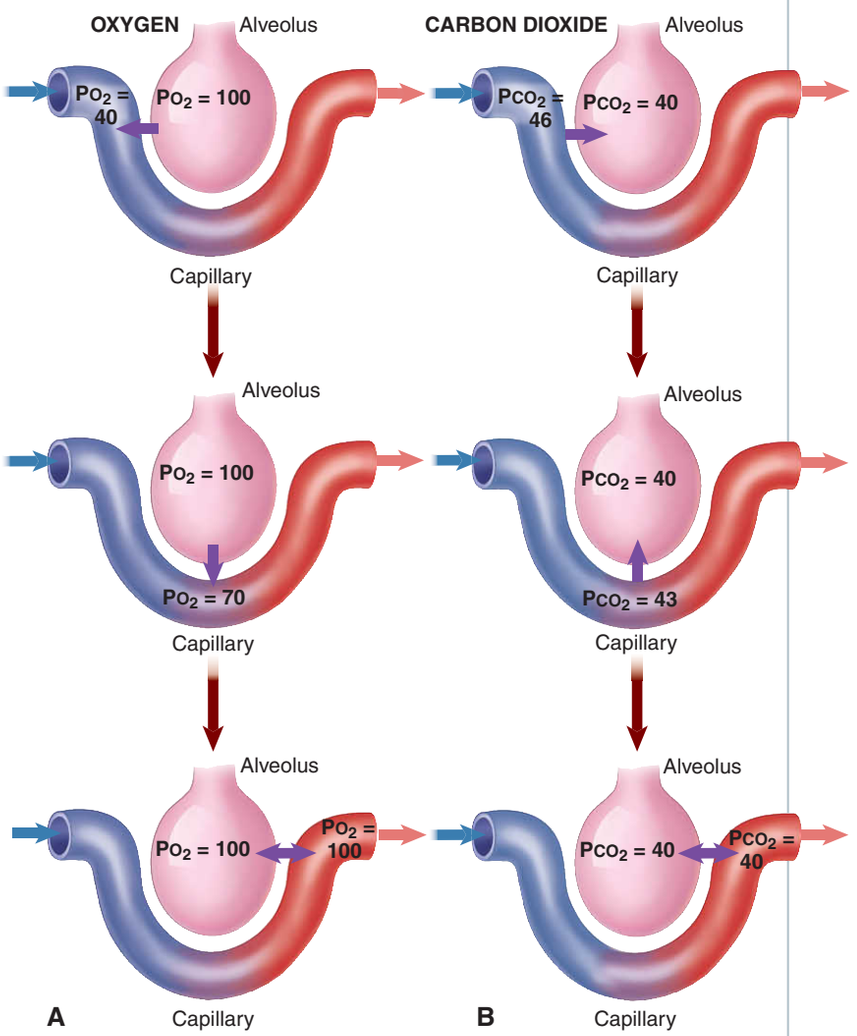


FIGURE 27-16

Pulmonary gas exchange. A, As blood enters a pulmonary capillary, oxygen diffuses down its pressure gradient (into the blood). Oxygen continues diffusing into the blood until equilibration has occurred (or until the blood leaves the capillary). **B,** As blood enters a pulmonary capillary, carbon dioxide diffuses down its pressure gradient (out of the blood). As with oxygen, carbon dioxide continues diffusing as long as there is a pressure gradient. P_{O_2} and P_{CO_2} remain relatively constant in a continually ventilated alveolus.

Gases move in both directions through the respiratory membrane (see Figure 26-15 on p. 810). Oxygen enters blood from the alveolar air because the P_{O_2} of alveolar air is greater than the P_{O_2} of incoming blood. Another way of saying this is that oxygen diffuses "down" its pressure gradient. Simultaneously, carbon dioxide molecules exit from the blood by diffusing down the carbon dioxide pressure gradient out into the alveolar air. The P_{CO_2} of venous blood is much higher than the P_{CO_2} of alveolar air. This two-way exchange of gases between alveolar air and pulmonary blood converts deoxygenated blood to oxygenated blood (Figure 27-16).

When you look at Figure 27-16, you might wonder why the partial pressures of gases in the alveoli remain constant, whereas

the partial pressures of gases in the blood change to equilibrate with alveolar partial pressures. The answer to this question lies in the fact that the alveoli are more or less continually ventilated. That is, there is always new air moving into the alveoli at a relatively low, stable velocity (Figure 27-17). Therefore, the average partial pressures of gases in the alveoli as a group are relatively constant.

The amount of oxygen that diffuses into blood each minute depends on several factors, notably the following four:

1. The oxygen pressure gradient between alveolar air and incoming pulmonary blood (alveolar Po_2 – blood Po_2)
2. The total functional surface area of the respiratory membrane
3. The respiratory minute volume (respiratory rate per minute times volume of air inspired per respiration)
4. Alveolar ventilation (discussed on p. 835)

All four of these factors bear a direct relation to oxygen diffusion. Anything that decreases alveolar Po_2, for instance, tends to decrease the alveolar-blood oxygen pressure gradient and therefore tends to decrease the amount of oxygen entering the blood. An application of this is as follows: Alveolar air Po_2 decreases as altitude increases, and thus less oxygen enters the blood at high altitudes. At a certain high altitude, alveolar air Po_2 equals the Po_2 of blood entering the pulmonary capillaries. How would this affect oxygen diffusion into blood?

Anything that decreases the total functional surface area of the respiratory membrane also tends to decrease oxygen diffusion into the blood (functional surface area is meant as that which is freely permeable to oxygen). An application of this is as follows: In emphysema the total functional area decreases and is one of the factors responsible for poor blood oxygenation in this condition. Surfactant disorders (Box 27-2) and pneumothorax (Box 27-3) can also decrease total functional area by collapsing alveoli.

Anything that decreases the respiratory minute volume also tends to decrease blood oxygenation. Application: Morphine slows respirations and therefore decreases the respiratory minute volume (volume of air inspired per minute) and tends to lessen the amount of oxygen entering the blood.

Several times we have stated the principle that structure determines function. This principle applies to gas exchange in the lungs. Several structural facts facilitate oxygen diffusion from the alveolar air into the blood in lung capillaries:

- The walls of the alveoli and the capillaries together form a very thin barrier for the gases to cross (estimated at not more than 0.004 mm thick—see Figure 26-15, p. 810).
- Alveolar and capillary surfaces are both extremely large (Box 27-6).

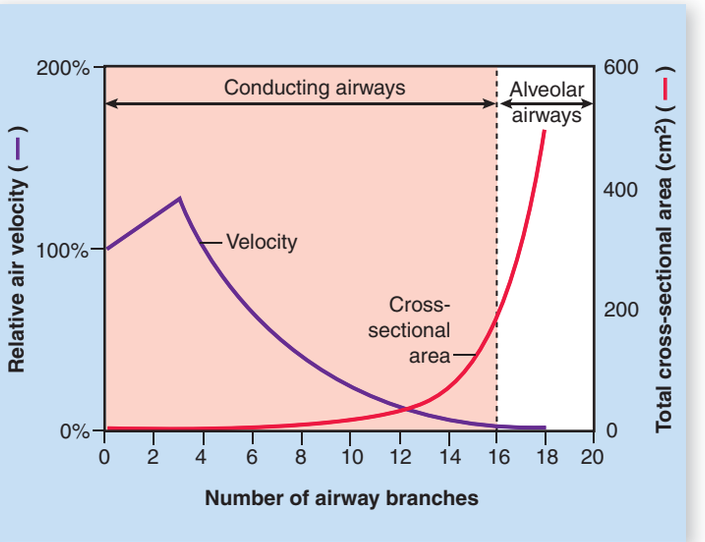


FIGURE 27-17

Airflow in airways. Air velocity (speed of flow) is high in the upper respiratory tract, where the total cross-sectional area is very low. As you can see on the left of the graph, however, the airflow slows down considerably in the alveolar airways because of the high total cross-sectional area of all of the alveoli. This accounts for the fact that ventilation of the alveoli is slow and relatively steady whereas ventilation of the upper airways is characterized by high-speed, alternating rushes of air.

- Lung capillaries accommodate a large amount of blood at one time. The lung capillaries of a small individual—one who has a body surface area of 1.5 square meters—contain about 90 ml of blood at one time under resting conditions (Figure 27-18).
- Blood is distributed through the capillaries in a layer so thin (equal only to the diameter of one red blood cell) that each red blood cell comes close to alveolar air.

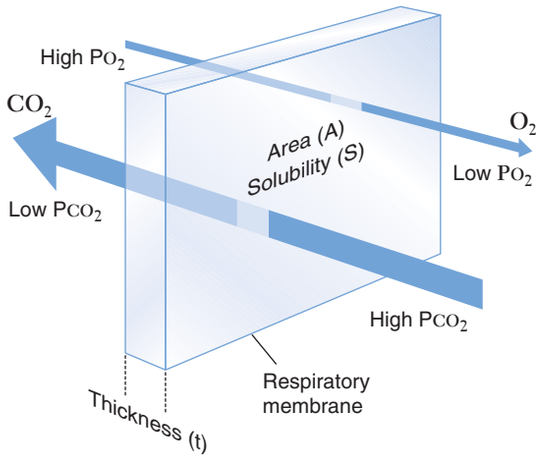
| QUICK CHECK |

8. How does the partial pressure of a gas relate to its concentration?
9. What determines the direction in which oxygen will diffuse across the respiratory membrane?
10. List two of the four major factors that influence how much oxygen diffuses into pulmonary blood per minute.

Box 27-6 | Fick's Law

Fick's law is a principle that describes the diffusion of carbon dioxide (CO_2) and oxygen (O_2) across the respiratory membrane, including the fluid film on the surface of the alveoli. As you can see in the figure, the principle illustrates common sense: each gas diffuses more efficiently (faster) if the surface area *(A)* is large, if the thickness of the membrane *(t)* is small, if the solubility of the gas *(S)* is high, and if the partial pressure *(Po_2* or *Pco_2)* gradient is high. Another way of stating Fick's law is that the net gas diffusion rate across a fluid membrane is proportional to the membrane surface area *(A)*, solubility of the gas in the membrane *(S)*, and partial pressure *(P)* difference—and inversely proportional to the membrane thickness *(t)*.

The human respiratory system takes advantage of this principle by improving what it can in the equation to maximize the rate of gas diffusion. The body builds its respiratory membrane of material with as much solubility to CO_2 and O_2 as possible and makes it as thin as possible. The large number of alveoli in a fractal-like arrangement ensure a very large surface area, and a high partial pressure gradient is maintained across the respiratory membrane.



Rate of diffusion of a gas through a membrane. According to Fick's law, the membrane diffusion rate is affected by surface area (A), solubility (S) of the gas, membrane thickness (t), and the partial pressure (P) gradient.

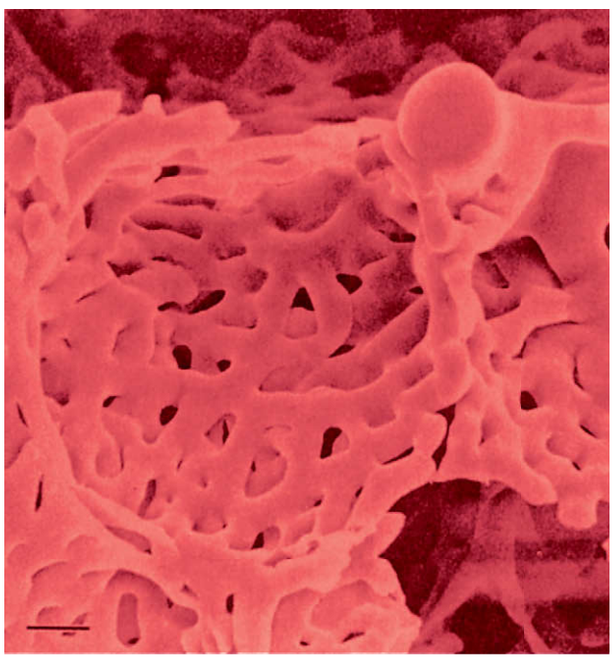


FIGURE 27-18

Alveolar blood supply. Scanning electron micrograph showing the rich blood supply to alveoli (which have been removed). The numerous, narrow branches ensure that each red blood cell is exposed to the alveolar air. (Black bar in lower left represents 10 μm.)

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HOW BLOOD TRANSPORTS GASES

Blood transports oxygen and carbon dioxide either as solutes or combined with other chemicals. Immediately on entering the blood, both oxygen and carbon dioxide dissolve in the plasma, but because fluids can hold only small amounts of gas in solution, most of the oxygen and carbon dioxide rapidly form a chemical union with some other molecule—such as hemoglobin, a plasma protein, or water. Once gas molecules are bound to another molecule, their plasma concentration decreases and more gas can diffuse into the plasma. In this way, comparatively large volumes of the gases can be transported.

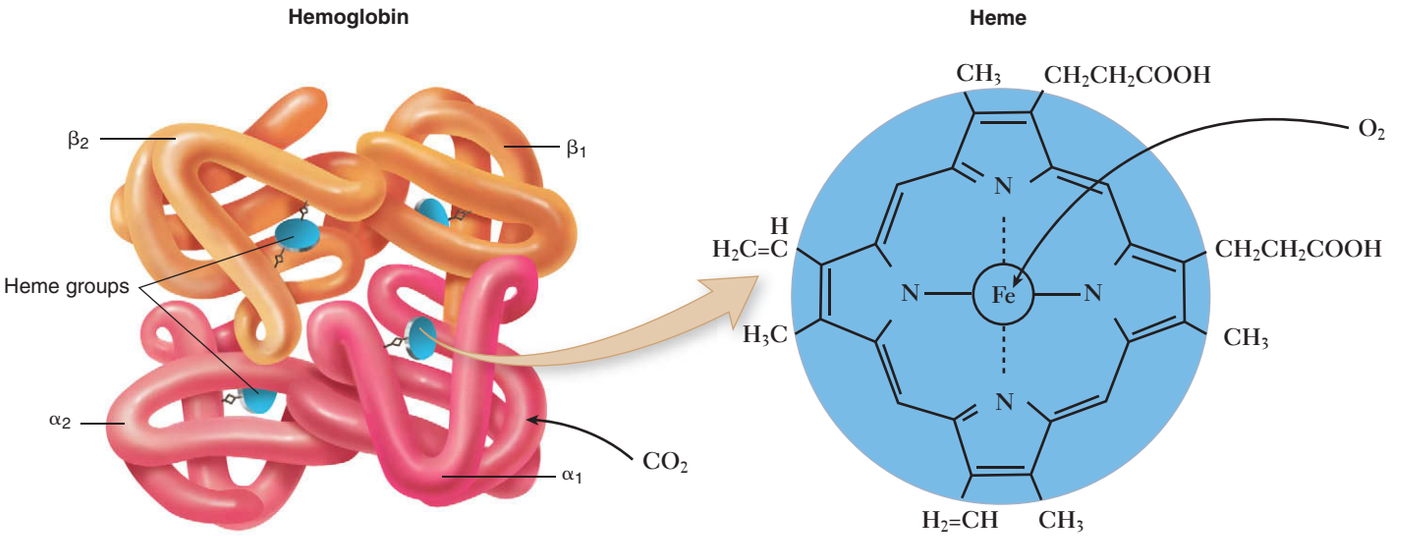


FIGURE 27-19

Hemoglobin. Sketch showing that hemoglobin is a quaternary protein consisting of four different tertiary (folded) polypeptide chains—two alpha (α) chains and two beta (β) chains. Each chain has an associated iron-containing heme group, as seen in detail in the inset. Oxygen (O_2) can bind to the iron (Fe) of the heme group, or carbon dioxide (CO_2) can bind to amine groups of the amino acids in the polypeptide chains.

Hemoglobin

Before we begin our discussion of transport of gases in the blood, we will pause and briefly review some facts about **hemoglobin (Hb)** (Figure 27-19). As we outlined in Chapter 20, hemoglobin is a reddish protein pigment found only inside red blood cells.

Hemoglobin is a quaternary protein made of four different polypeptide chains—two alpha chains and two beta chains—each associated with an iron-containing **heme group.** If you look at Figure 27-19, you will see that an oxygen molecule (O_2) can combine with the iron atom (Fe) in each heme group. Thus hemoglobin can act as a kind of oxygen sponge that chemically absorbs oxygen molecules from the surrounding solution. Notice also in this figure that carbon dioxide (CO_2) molecules can combine with the amino acids of the alpha and beta polypeptide chains. Thus hemoglobin can also act as a carbon dioxide sponge and absorb carbon dioxide molecules from a solution. Hemoglobin, then, has exactly the chemical characteristics needed to pick up and transport gases that enter the blood. As you will learn in the following paragraphs, hemoglobin also has the chemical characteristics needed to unload these gases. Box 27-7 explains how carbon monoxide interferes with hemoglobin's function.

Transport of Oxygen

Because oxygenated blood has a Po_2 of 100 mmHg, it contains only about 0.3 ml of dissolved O_2 per 100 ml of blood. Many times that amount, however, combines with the hemoglobin in 100 ml of blood to form **oxyhemoglobin.** Because each gram of hemoglobin can unite with 1.34 ml of oxygen, the exact amount of oxygen in blood depends mainly on the amount of hemoglobin present. Normally, 100 ml of blood contains about 15 grams of hemoglobin. If 100% of it combines with oxygen, 100 ml of blood will contain 15 × 1.34, or 20.1 ml, of oxygen in the form of oxyhemoglobin. Figure 27-20 shows how hemoglobin increases the oxygen-carrying capacity of blood.

Perhaps a more common way of expressing blood oxygen content is in terms of volume percent. Normal arterial blood, with a Po_2 of 100 mmHg, contains about 20 vol% O_2 (meaning 20 ml of oxygen in each 100 ml of blood).

Blood that contains more hemoglobin can, of course, transport more oxygen. Thus blood that contains less hemoglobin can transport less oxygen. Therefore hemoglobin deficiency anemia decreases oxygen transport and may produce marked cellular hypoxia (inadequate oxygen supply).

To combine with hemoglobin, oxygen must, of course, diffuse from plasma into the red blood cells where millions of hemoglobin molecules are located. Several factors influence the rate at which hemoglobin combines with oxygen in lung capillaries. For

Box 27-7 | Carbon Monoxide Poisoning

Gases other than O_2 and CO_2 can bind to the hemoglobin (Hb) molecule. **Carbon monoxide (CO)** is a molecule produced by incomplete combustion in furnaces, engines, and other circumstances. This invisible, odorless gas binds to Hb more than 200 times more strongly than O_2 does. That means that CO "knocks out" O_2 from HbO_2 and forms HbCO. As more and more HbCO is formed, less and less oxygen is being carried by your blood—a life-threatening situation. Because CO binds so strongly, it is hard to remove it from Hb. One strategy to remove CO is to place a person in a pressure chamber where the Po_2 can be driven so high that it "knocks off" the CO from the Hb, allowing O_2 to form HbO_2.

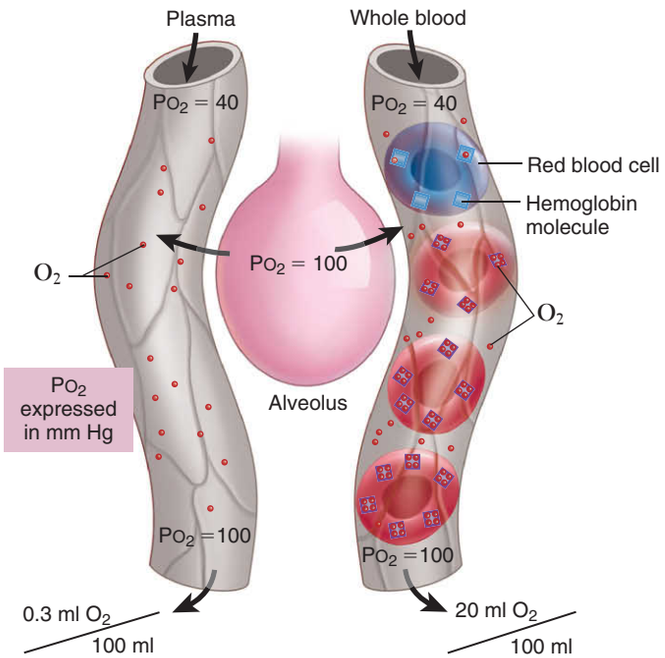


FIGURE 27-20

Oxygen-carrying capacity of blood. If blood consisted only of plasma, the maximum oxygen that could be transported would be only about 0.3 ml of O_2 per 100 ml of blood. Because the red blood cells contain hemoglobin molecules, which act as "oxygen sponges," the blood can actually carry up to 20 ml of dissolved O_2 per 100 ml of blood.

instance, as the following equation and the **oxygen-hemoglobin dissociation curve** (Figure 27-21) show, an increasing blood Po_2 accelerates hemoglobin association with oxygen:

$$Hb + O_2 \xrightarrow{\text{Increasing } Po_2} HbO_2$$

Decreasing Po_2, on the other hand, accelerates oxygen dissociation from oxyhemoglobin, that is, the reverse of the preceding equation. Oxygen associates with hemoglobin rapidly—so rapidly, in fact, that about 97% of the blood's hemoglobin has united with oxygen by the time the blood leaves the lung capillaries to return to the heart. In other words, the average oxygen saturation of hemoglobin in oxygenated blood is about 97%.

Summing up, we can say that oxygen travels in two forms: as dissolved O_2 in the plasma and as O_2 associated with hemoglobin (oxyhemoglobin). Of these two forms of transport, oxyhemoglobin carries the vast majority of the total oxygen transported by the blood.

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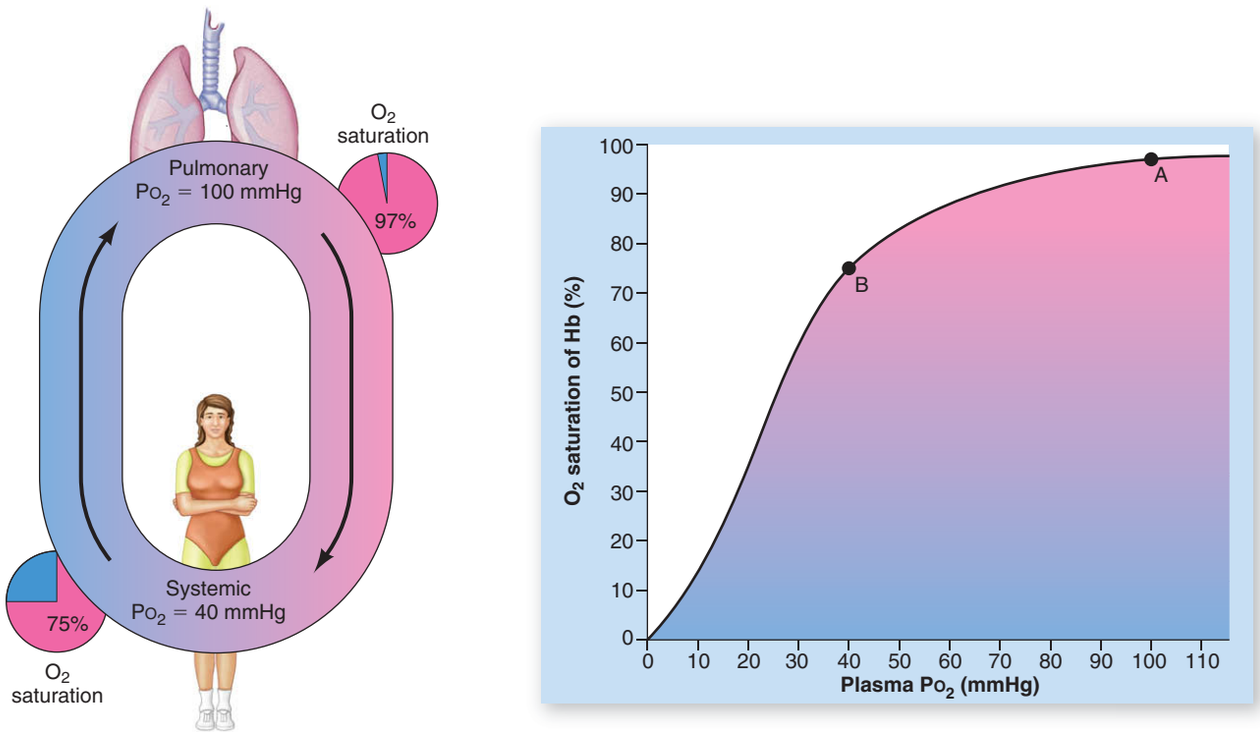


FIGURE 27-21

Oxygen-hemoglobin dissociation curve. The graph represents the relationship between Po_2 and O_2 saturation of hemoglobin (Hb-O_2 affinity). The inset shows how the graphed curve relates to oxygen transport by the blood. Notice that at high plasma Po_2 values (point *A*), hemoglobin (Hb) is fully loaded with oxygen. At low plasma Po_2 values (point *B*), Hb is only partially loaded with oxygen.

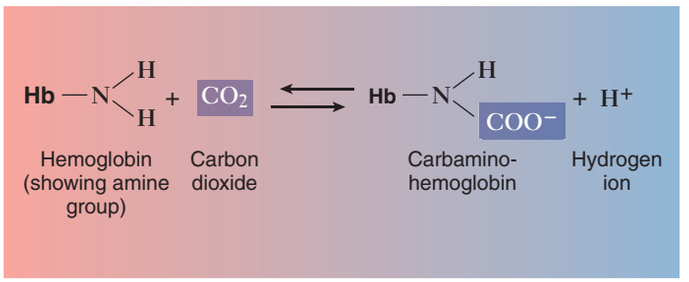


FIGURE 27-22

Carbon dioxide–hemoglobin reaction. Carbon dioxide can bind to an amine group (NH_2) in an amino acid within a hemoglobin (Hb) molecule to form carbaminohemoglobin ($HbNCOOH^-$) and a hydrogen ion. The highlighted areas show where the original carbon dioxide molecule is in each part of the equation.

Transport of Carbon Dioxide

Carbon dioxide is carried in the blood in several ways, the most important of which are described briefly in the following paragraphs.

DISSOLVED CARBON DIOXIDE

A small amount of CO_2 dissolves in plasma and is transported as a solute. About 10% of the total amount of carbon dioxide carried by the blood is carried in the dissolved form. It is this dissolved CO_2 that produces the P_{CO_2} of blood plasma.

CARBAMINO COMPOUNDS

One fifth to one quarter of the carbon dioxide in blood unites with the NH_2 (amine) groups of the amino acids that make up the polypeptide chains of hemoglobin and various plasma proteins. When carbon dioxide binds to amine groups, it forms *carbamino compounds*. Because hemoglobin is the main protein that combines with carbon dioxide, most carbamino molecules are formed and transported in the red blood cells. The compound formed when carbon dioxide combines with hemoglobin has a tongue-twisting name—**carbaminohemoglobin.** The following chemical equation, amplified in Figure 27-22, shows how carbon dioxide combines with amine (NH_2) in hemoglobin's polypeptide chains to produce carbaminohemoglobin (HbNCOOH) and H^+:

$$Hb{-}N\begin{matrix}H\\H\end{matrix} + CO_2 \rightleftharpoons Hb{-}N\begin{matrix}H\\COO^-\end{matrix} + H^+$$

Notice that the arrows in this equilibrium point in both directions. This means that under any given conditions, some carbon dioxide will be associated with hemoglobin and some will not—the reaction is moving in both directions at the same time. The rate of both forward and reverse reactions—carbon dioxide association with and dissociation from hemoglobin—can shift with changes in carbon dioxide concentration. This principle is sometimes called the **rate law** of chemistry. The addition of more carbon dioxide to blood, therefore, will increase the rate of formation of carbaminohemoglobin. Another way to state this principle is to say that the association of carbon dioxide with hemoglobin is accelerated by an increase in P_{CO_2} and is slowed by a decrease in P_{CO_2}. Figure 27-23, which shows the carbon dioxide dissociation curve, illustrates that the CO_2-carrying capacity of blood increases as plasma P_{CO_2} increases.

BICARBONATE

More than two-thirds of the CO_2 carried by blood is carried in the form of **bicarbonate** ions (HCO_3^-). When CO_2 dissolves in water (as in blood plasma), some of the CO_2 molecules associate with H_2O to form carbonic acid (H_2CO_3). Once formed, some of the H_2CO_3 molecules dissociate to form H^+ and bicarbonate (HCO_3^-) ions. This process, which is catalyzed by an enzyme present in red blood cells called *carbonic anhydrase (CA)*, is summarized by the following chemical equation:

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H + HCO_3$$

Figure 27-24 amplifies this equation. According to the rate law of chemistry we stated earlier, as more CO_2 is added to the plasma, more will be converted to carbonic acid. Because the carbonic anhydrase enzyme in the blood is facilitating the conversion of carbon dioxide and water to carbonic acid, this reaction occurs very rapidly as CO_2 is added to the plasma. Carbonic acid concentration increases as a result, "pulling" the system toward the bicarbonate side, thus increasing the rate of bicarbonate formation. The end result is that CO_2 molecules diffusing into plasma will continually be removed from the solution and converted into bicarbonate. This allows room for even more CO_2 to dissolve in the plasma—thus increasing the CO_2-carrying capacity of the blood.

Figure 27-25, which summarizes all three forms of CO_2 transport, shows that once bicarbonate ions are formed, they diffuse down their concentration gradient into the plasma. The exit of this negative ion (HCO_3^-) from the red blood cell is balanced by the inward transport of another negative ion, chloride (Cl^-). This countertransport of negative ions is often called the **chloride shift.**

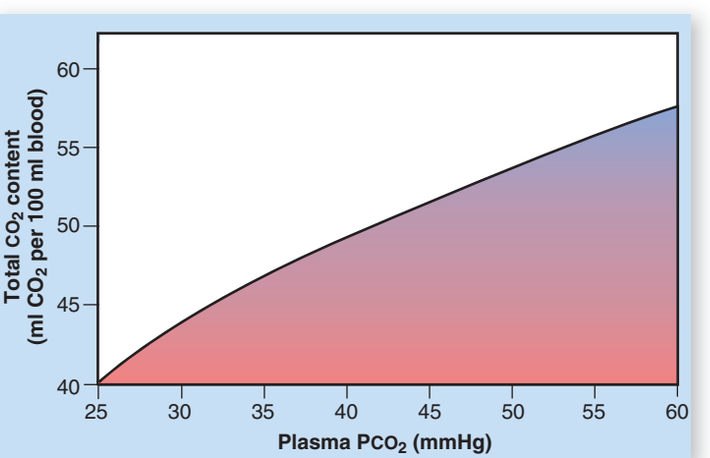


FIGURE 27-23

Carbon dioxide dissociation curve. The relationship between P_{CO_2} and total CO_2 content (ml CO_2 per 100 ml blood) is graphed as a nearly straight line. Notice that the CO_2-carrying capacity of blood increases as the plasma P_{CO_2} increases.

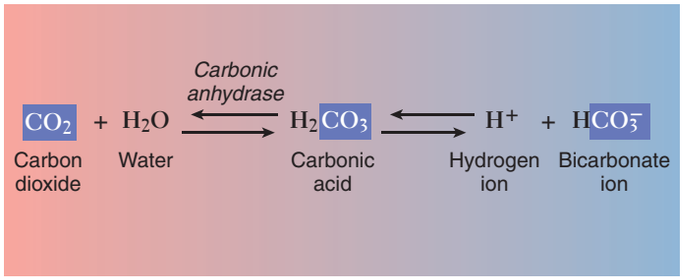


FIGURE 27-24

Formation of bicarbonate. Carbon dioxide can react with water to form carbonic acid, a reaction catalyzed by the red blood cell (RBC) enzyme carbonic anhydrase. Carbonic acid then dissociates to form bicarbonate and a hydrogen ion. The highlighted areas show where the original carbon dioxide molecule is in each part of the equation. The double arrows show that each reaction is reversible, the actual rate in each direction governed by the relative concentration of each molecule.

According to the rate law of chemistry described earlier, when CO_2 is removed from the plasma, the entire system, illustrated in Figures 27-24 and 27-25, shifts in the opposite direction. Thus the reaction that converts carbonic acid to free CO_2 becomes dominant. The declining concentration of carbonic acid then forces a shift in favor of the conversion of bicarbonate to carbonic acid. In short, CO_2 is unloaded from bicarbonate.

The relative proportions of the three different forms of carbon dioxide carried in the blood are summarized in Figure 27-26.

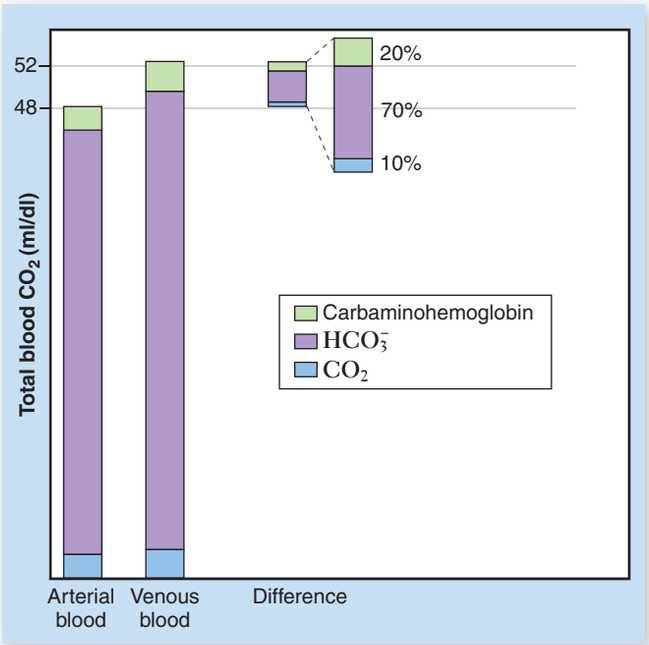
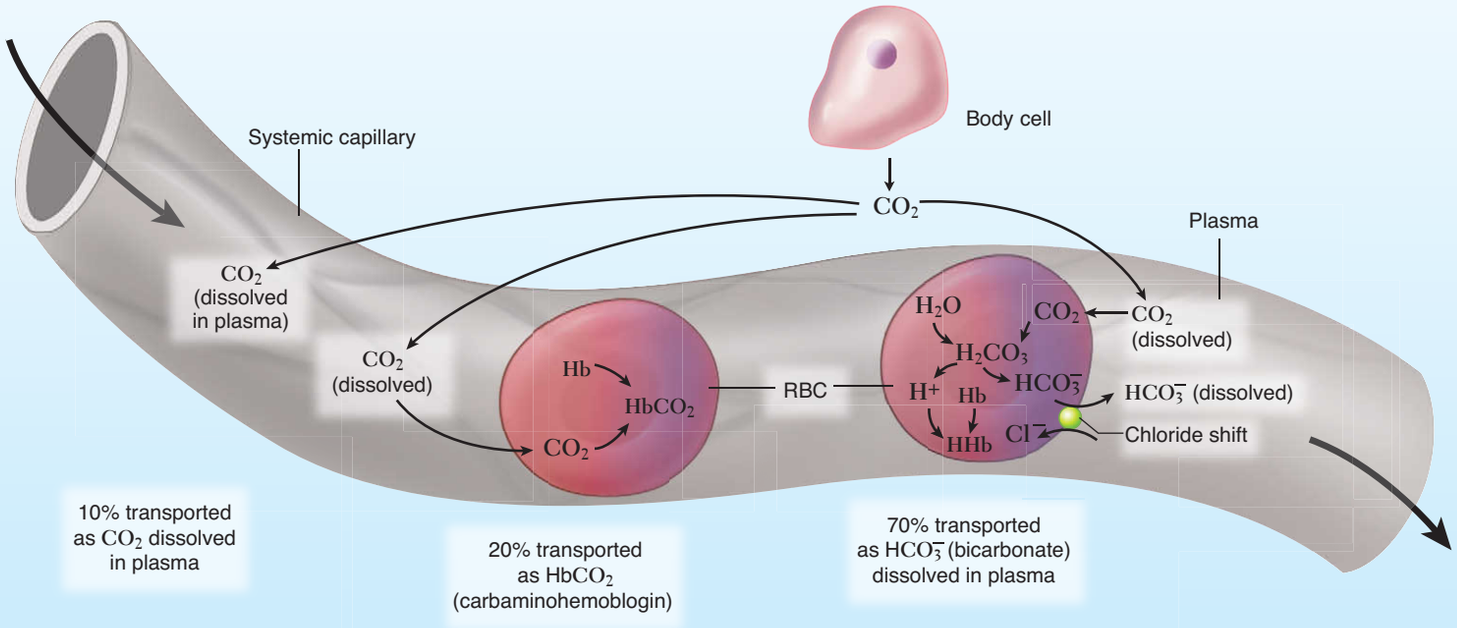


FIGURE 27-26

Proportions of carbon dioxide transported in the blood. This graph shows that systemic venous blood carries more carbon dioxide than systemic arterial blood does. The difference, shown in the upper left, represents the total amount of carbon dioxide loaded into the blood in the systemic tissues. Or it could be viewed as the total amount of carbon dioxide unloaded from the blood in the lungs. Note that most of the carbon dioxide is carried in the form of HCO_3^- (bicarbonate).

FIGURE 27-25

Carbon dioxide transport in the blood. As the illustration shows, CO_2 dissolves in the plasma. Some of the dissolved CO_2 enters red blood cells (RBCs) and combines with hemoglobin (Hb) to form carbaminohemoglobin ($HbCO_2$). Some of the CO_2 entering RBCs combines with H_2O to form carbonic acid (H_2CO_3), a process facilitated by the enzyme carbonic anhydrase (CA) present inside each cell. Carbonic acid then dissociates to form H^+ and bicarbonate (HCO_3^-). The H^+ combines with Hb, whereas the HCO_3^- diffuses down its concentration gradient into the plasma. As HCO_3^- leaves each RBC, Cl^- enters and prevents an imbalance in charge—a phenomenon called the *chloride shift,* which is discussed in Chapter 33.



CARBON DIOXIDE AND PH

You may have noticed by now that when carbon dioxide enters the blood, most of it is converted to carbaminohemoglobin and hydrogen ions (H^+) or to bicarbonate and hydrogen ions. In other words, have you noticed that increasing the carbon dioxide content of the blood also increases its H^+ concentration? Thus an increase in carbon dioxide in the blood causes an increase in the acidity, or a drop in pH, in the blood. This is a very important principle in understanding how and why respiration is regulated in the manner that it is. We will discuss these matters later in this chapter. This principle is also important to the understanding of acid-base balance in the body—a topic discussed thoroughly in Chapter 33.

| QUICK CHECK |

11. Most oxygen carried by the blood is transported in what form?
12. Most carbon dioxide carried by the blood is transported in what form?
13. What is oxyhemoglobin? What is carbaminohemoglobin?
14. How does carbon dioxide affect the pH of blood?

SYSTEMIC GAS EXCHANGE

Exchange of gases in tissues takes place between arterial blood flowing through tissue capillaries and cells (Figure 27-27). It occurs because of the principle already noted—that gases move down a gas pressure gradient. More specifically, in the tissue capillaries, oxygen diffuses out of arterial blood because the oxygen pressure gradient favors its outward diffusion (see Figure 27-27). Arterial blood P_{O_2} is about 100 mmHg, interstitial fluid P_{O_2} is considerably lower, and intracellular fluid P_{O_2} is still lower. Although interstitial fluid and intracellular fluid P_{O_2} are not definitely established, they are thought to vary considerably—perhaps from around 60 mmHg down to about 1 mmHg.

As activity increases in any tissue, its cells necessarily use oxygen more rapidly. This decreases intracellular and interstitial P_{O_2}, which in turn tends to increase the oxygen pressure gradient between blood and tissues and to accelerate oxygen diffusion out of the tissue capillaries. In this way, the rate of oxygen use by cells automatically tends to regulate the rate of oxygen delivery to cells. As dissolved oxygen diffuses out of arterial blood, blood P_{O_2} decreases, and this accelerates oxyhemoglobin dissociation to release more oxygen into the plasma for diffusion out to cells, as indicated in Figure 27-28 and the following equation:

$$HbO_2 \xrightarrow{\text{Decreasing } P_{O_2}} Hb + O_2$$

Because of oxygen release to tissues from tissue capillary blood, P_{O_2}, oxygen saturation, and total oxygen content are less in venous blood than in arterial blood, as shown in Table 27-4. Carbon dioxide exchange between tissues and blood takes place in the opposite direction from oxygen exchange. Catabolism produces large amounts of CO_2 inside cells. Therefore, intracellular and interstitial P_{CO_2} are higher than arterial blood P_{CO_2}. This means that the CO_2 pressure gradient causes diffusion of CO_2 from the tissues into the blood flowing along through tissue capillaries (see Figure 27-27). Consequently, the P_{CO_2} of blood increases in tissue capillaries from its arterial level of about 40 mmHg to its venous level of about 46 mmHg.

TABLE 27-4 Blood Oxygen

	SYSTEMIC VENOUS BLOOD	SYSTEMIC ARTERIAL BLOOD
P_{O_2}	40 mmHg	100 mmHg
Oxygen saturation	75%	97%
Oxygen content	15 ml O_2 per 100 ml blood	20 ml O_2 per 100 ml blood*

*Oxygen use by tissues = difference between the oxygen content of arterial and venous blood (20-15) = 5 ml O_2 per 100 ml blood circulated per minute.

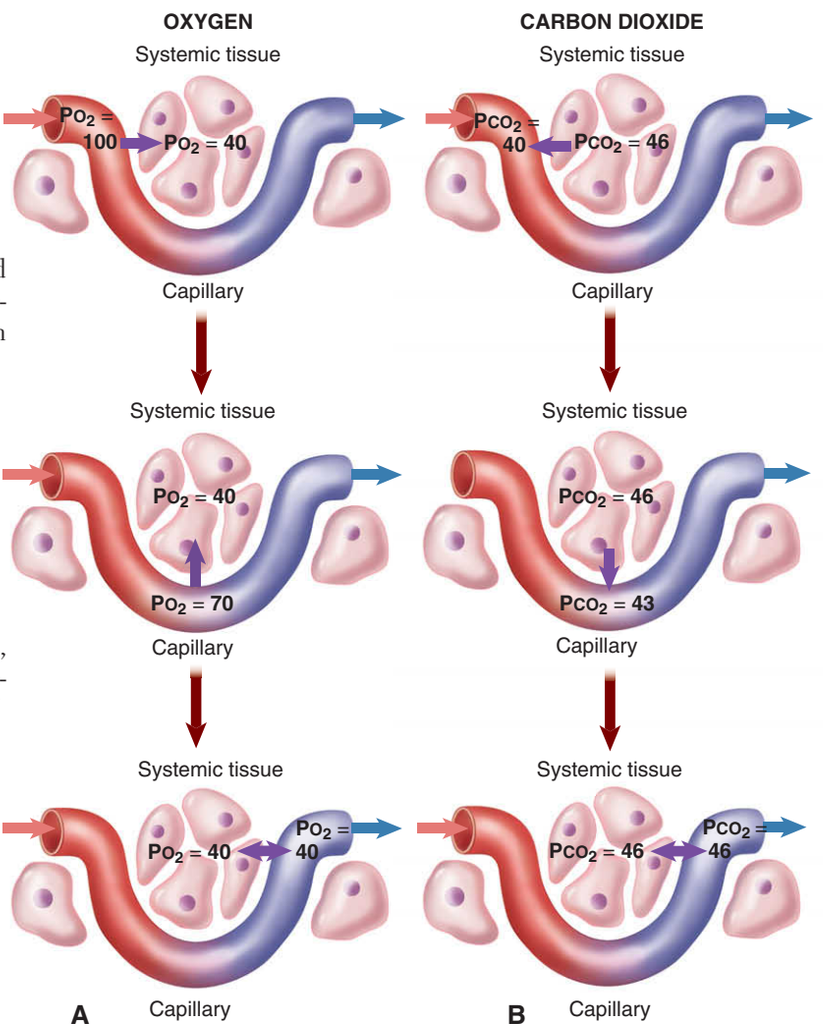


FIGURE 27-27

Systemic gas exchange. A, As blood enters a systemic capillary, O_2 diffuses down its pressure gradient (out of the blood). O_2 continues diffusing out of the blood until equilibration has occurred (or until the blood leaves the capillary). **B,** As blood enters a systemic capillary, CO_2 diffuses down its pressure gradient (into the blood). As with O_2, CO_2 continues diffusing as long as there is a pressure gradient.

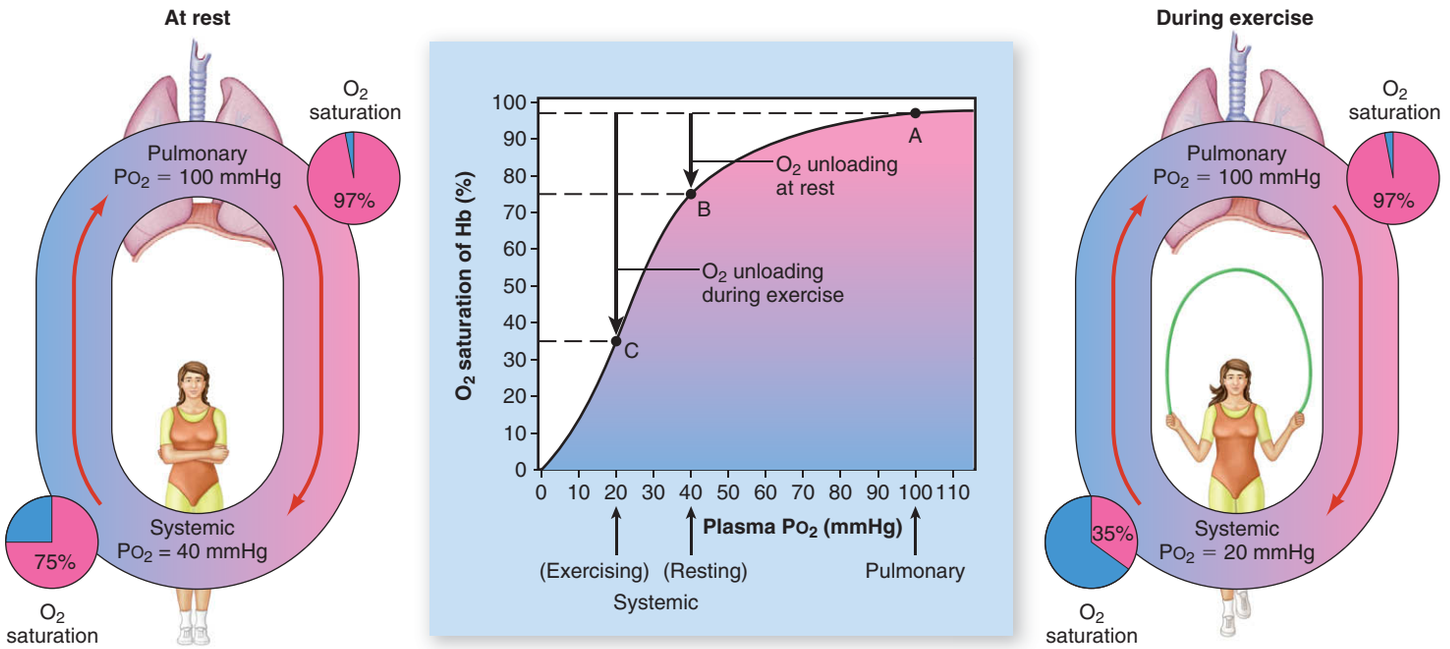


FIGURE 27-28

Oxygen unloading at rest and during exercise. At rest, fully saturated Hb unloads almost 25% of its O_2 load when it reaches the low-P_{O_2} (40 mmHg) environment in systemic tissues *(left inset)*. During exercise, the tissue P_{O_2} is even lower (20 mmHg)—thus causing fully saturated Hb to unload about 70% of its O_2 load *(right inset)*. As you can see in the graph, a slight drop in tissue P_{O_2}—from point *B* to point *C*—causes a large increase in O_2 unloading.

This increasing P_{CO_2} and decreasing P_{O_2} together produce two effects—they favor oxygen dissociation from oxyhemoglobin and carbon dioxide association with hemoglobin to form carbaminohemoglobin. This reciprocal interrelationship between oxygen and carbon dioxide transport mechanisms is contrasted in Figure 27-29. Note that increased P_{CO_2} decreases the affinity between hemoglobin and oxygen—this is called a "right shift." A right shift of the oxygen-hemoglobin dissociation curve resulting from increased P_{CO_2} is also known as the **Bohr effect,** named for Christian Bohr, who along with other scientists, discovered this phenomenon in 1904. A drop in plasma pH, which normally accompanies an increase in blood P_{CO_2}, also causes a right shift. The **Haldane effect** refers to the increased CO_2 loading caused by a decrease in P_{O_2}. This phenomenon is named for its discoverer John Scott Haldane.

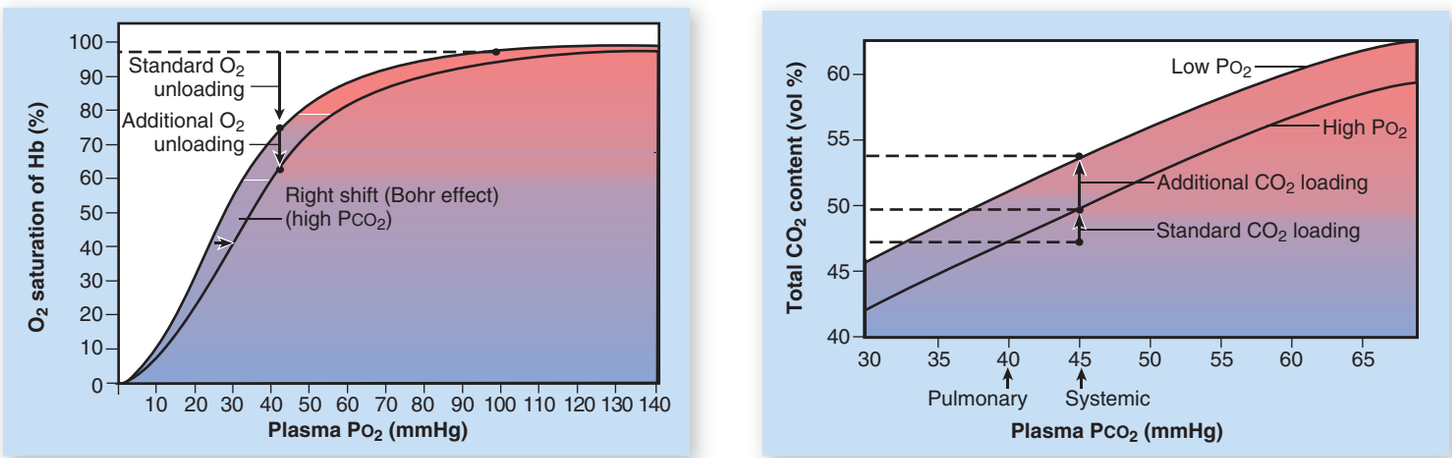


FIGURE 27-29

Interaction of P_{O_2} and P_{CO_2} on gas transport by the blood. A, The increased plasma P_{CO_2} in systemic tissues decreases the affinity between Hb and O_2, shown as a right shift of the oxygen-hemoglobin dissociation curve. This phenomenon is known as the *Bohr effect.* A right shift can also be caused by a decrease in plasma pH. **B,** At the same time, the decreased plasma P_{O_2} commonly observed in systemic tissues increases the CO_2 content of the blood, shown as a left shift of the CO_2 dissociation curve. This phenomenon is known as the *Haldane effect.*

| A&P CONNECT |

If you are having trouble visualizing the essential process of gas exchange, check out the simplified ***Summary of Gas Exchange*** online at ***A&P Connect.***

evolve

| QUICK CHECK |

15. What factors can cause the attraction between hemoglobin and oxygen to decrease?
16. What factors can cause an increase in the amount of carbon dioxide loaded into the systemic blood?

REGULATION OF PULMONARY FUNCTION

Respiratory Control Centers

Various mechanisms operate to maintain relative constancy of the blood P_{O_2} and P_{CO_2}. This homeostasis of blood gases is maintained primarily by means of changes in ventilation—the rate and depth of breathing. The main integrators that control the nerves that affect the inspiratory and expiratory muscles are located within the brainstem and are together simply called the *respiratory centers* (Figure 27-30).

The basic rhythm of the respiratory cycle of inspiration and expiration seems to be generated by the **medullary rhythmicity area.** This area of the medulla consists of two regions of interconnected control centers: the *dorsal respiratory group (DRG)* and the *ventral respiratory group (VRG)*. The VRG seems to be the basic rhythm generator in animal models and thus may also serve this function in human beings. Normal, quiet breathing rhythm is generated by alternating patterns of stimulation and inhibition of motor neurons that signal the muscles of the diaphragm. The DRG integrates information from chemoreceptors for P_{CO_2} and signals the VRG to alter the breathing rhythm to restore homeostasis.

A current hypothesis suggests that the basic breathing rhythm can be altered by different inputs to the medullary rhythmicity area. For example, input from the **apneustic center** in the pons regulates the length and depth of inspiration. Damage to the

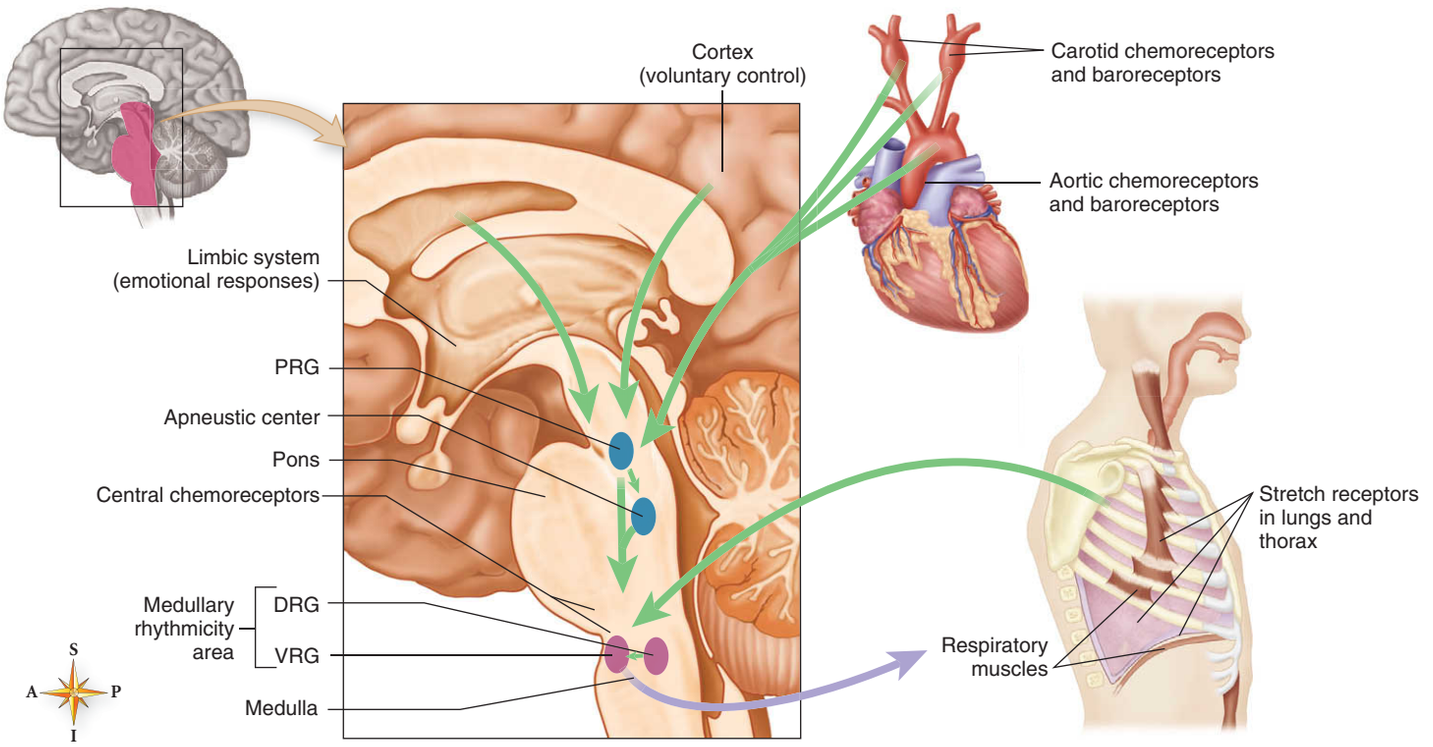


FIGURE 27-30

Regulation of breathing. The dorsal respiratory group (DRG) and ventral respiratory group (VRG) of the medulla represent the medullary rhythmicity area. The pontine respiratory group (PRG, or pneumotaxic center) and apneustic center of the pons influence the basic respiratory rhythm by means of neural input to the medullary rhythmicity area. The brainstem also receives input from other parts of the body; information from chemoreceptors, baroreceptors, and stretch receptors can alter the basic breathing pattern, as can emotional (limbic) and sensory input. Despite these subconscious reflexes, the cerebral cortex can override the "automatic" control of breathing to some extent to do such activities as sing or blow up a balloon. Green arrows show flow of information to the respiratory control centers. The purple arrow shows the flow of information from the control centers to the respiratory muscles that drive breathing.

Box 27-8 | FYI

Unusual Breathing Reflexes



The **cough reflex** is stimulated by foreign matter in the trachea or bronchi. The epiglottis and glottis reflexively close, and contraction of the expiratory muscles causes air pressure in the lungs to increase. The epiglottis and glottis then open suddenly, resulting in an upward burst of air that removes the offending contaminants—a cough.

The **sneeze reflex** is similar to the cough reflex, except that it is stimulated by contaminants in the nasal cavity. A burst of air is directed through the nose and mouth, forcing the contaminants (and mucus) out of the respiratory tract. Droplets from a sneeze can travel more than 161 km/hr (100 miles/hr) and travel 3 m (12 ft). Research suggests that many pathogenic microbes produce symptoms that trigger sneezing in order to spread themselves to other people. Scientists call this *altered host behavior* and identify it as a mechanism of microbes to efficiently spread themselves to additional human hosts.

The term **hiccup** is used to describe an involuntary, spasmodic contraction of the diaphragm. When such a contraction occurs, generally at the beginning of an inspiration, the glottis suddenly closes, producing the characteristic sound. Hiccups lasting for extended periods can be disabling. They may be produced by irritation of the phrenic nerve or the sensory nerves in the stomach or by direct injury or pressure on certain areas of the brain. Fortunately, most cases of hiccups last only a few minutes and are harmless.

A **yawn** is slow, deep inspiration through an unusually widened mouth. Yawns were once thought to be reflexes that increase ventilation when blood oxygen content is low, but newer evidence suggests that this is unlikely. A current theory states that we yawn for the same reason we occasionally stretch—to prepare our muscles and our circulatory system for action. Alternate hypotheses suggest that yawning cools the brain or otherwise regulates body temperature—or that yawning is triggered by neurotransmitters related to mood. The variety of hypotheses show one thing for certain: *we do not currently understand the physiology of yawning!*

A protective physiological response called the **diving reflex** is responsible for the astonishing recovery of apparent drowning victims—including some who may have been submerged for more than 40 minutes! Survivors are most often preadolescent children who have been immersed in water below 20° C (68° F). Apparently, the colder the water, the better the chance of survival. Victims initially appear dead when pulled from the water. Breathing has stopped; they have fixed, dilated pupils; they are cyanotic; and their pulse has stopped.

Studies have shown that when the head and face are immersed in ice-cold water, there is immediate shunting of blood to the core body areas with peripheral vasoconstriction and slowing of the heart (bradycardia). Metabolism is slowed, and tissue requirements for oxygen and nutrients decrease. The diving reflex is a protective response of the body to cold water immersion and is a function of such physiological and environmental parameters as water temperature, age, lung volume, and posture.

nerves from the apneustic center results in breathing characterized by abnormally long, deep inspirations, which is sometimes called "apneustic breathing." The **pontine respiratory group** (PRG; formerly called the *pneumotaxic center*), also in the pons, normally regulates both the apneustic center and the medullary rhythmicity area. Thus a network of interconnected centers in the brainstem regulates the rhythm of breathing. Box 27-8 discusses some unusual breathing reflexes such as coughing and sneezing.

Factors That Influence Breathing

Feedback information to the medullary rhythmicity area comes from sensors throughout the nervous system, as well as from other control centers. For example, changes in the P_{CO_2}, P_{O_2}, and pH of systemic arterial blood all influence the medullary rhythmicity area. The P_{CO_2} acts on chemoreceptors located in the medulla. Chemoreceptors, in this case, are cells that are sensitive to changes in the CO_2 and hydrogen ion concentration (pH) of arterial blood. The normal range for arterial P_{CO_2} is about 38 to 40 mmHg. When it increases even slightly above this value, it has a stimulating effect, mainly on *central chemoreceptors* (present throughout the brainstem).

Large increases in arterial P_{CO_2} also stimulate *peripheral chemoreceptors* in the carotid bodies and aorta. Stimulation of chemoreceptors by increased arterial P_{CO_2} results in faster breathing, with a greater volume of air moving in and out of

the lungs per minute. Figure 27-31 summarizes this negative feedback response. Decreased arterial P_{CO_2} produces opposite effects—it inhibits central and peripheral chemoreceptors, which leads to inhibition of the medullary rhythmicity area and slower respirations. In fact, breathing stops entirely for a few moments (apnea) when arterial P_{CO_2} drops moderately—to about 35 mmHg, for example. Recall that increases in the CO_2 content of plasma are accompanied by a proportional decrease in plasma pH. A decrease in arterial blood pH (increase in acid), within certain limits, has a stimulating effect on chemoreceptors located in the carotid and aortic bodies. Central chemoreceptors are more sensitive to changes in pH than are peripheral chemoreceptors. This increased sensitivity results from the fact that cerebrospinal fluid (CSF) and interstitial fluid (IF) of the brain is protected by the BBB (blood-brain barrier) from the buffers present in the blood. Thus, when blood P_{CO_2} increases in the blood, it is partially buffered in the blood—but the CO_2 is

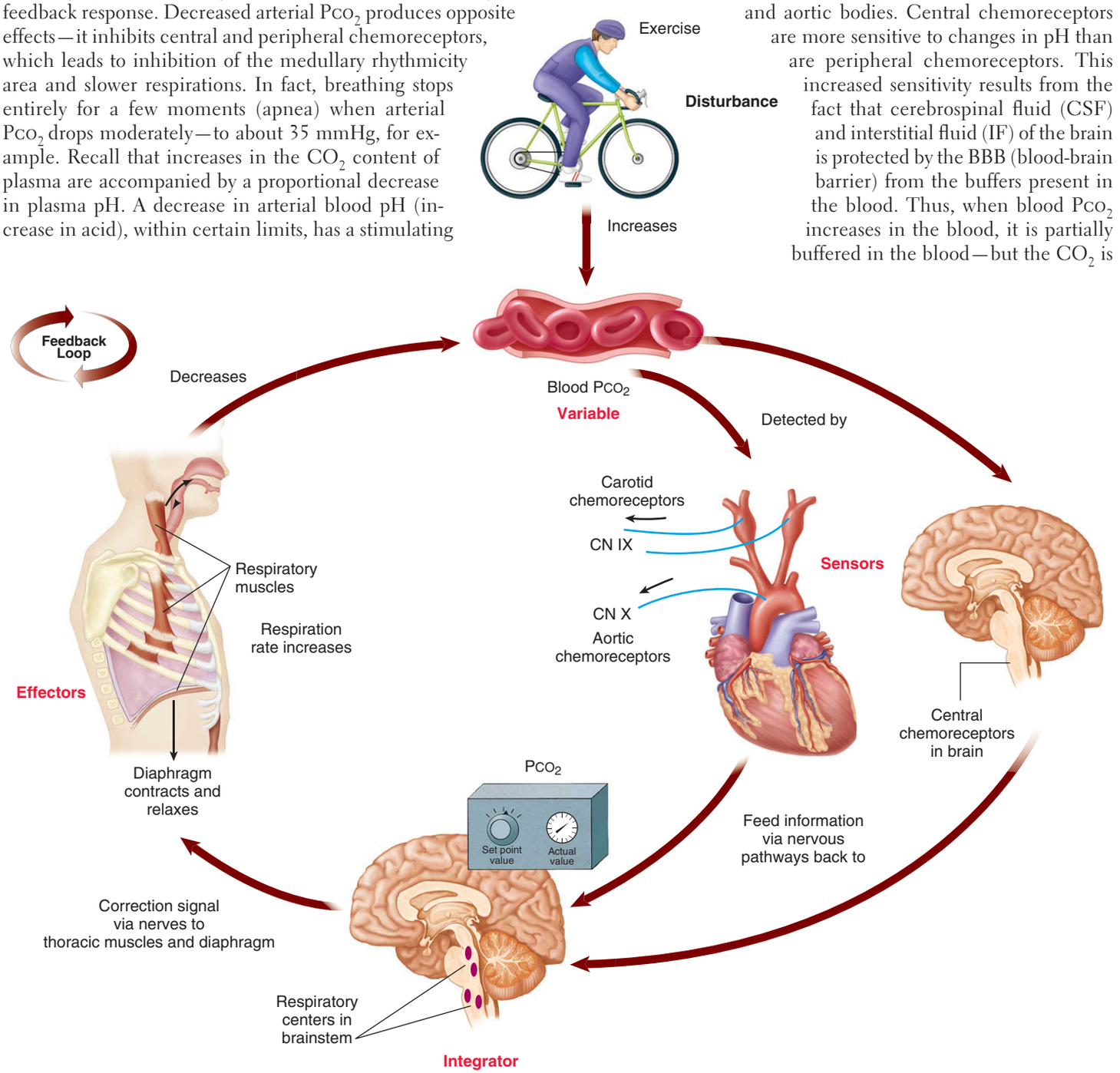


FIGURE 27-31

Negative feedback control of respiration. This diagram summarizes the feedback loop that operates to increase the respiratory rate in response to high plasma P_{CO_2}. Increased cellular respiration during exercise causes a rise in plasma P_{CO_2}—which is detected by central chemoreceptors in the brain and perhaps peripheral chemoreceptors in the carotid sinus and aorta. Feedback information is relayed to integrators in the brainstem that respond to the increase in P_{CO_2} above the set point value by sending nervous correction signals to the respiratory muscles, which act as effectors. The effector muscles increase their alternate contraction and relaxation, thus increasing the rate of respiration. As the respiration rate increases, the rate of CO_2 loss from the body increases and P_{CO_2} drops accordingly. This brings the plasma P_{CO_2} back to its set point value.

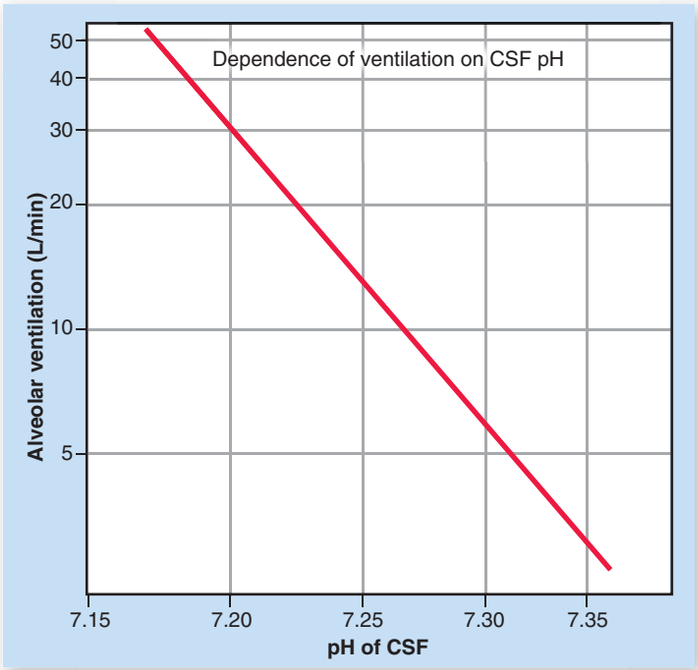


FIGURE 27-32

Regulatory effect of pH of cerebrospinal fluid. As P_{CO_2} of arterial blood increases, the pH of the cerebrospinal fluid (CSF) decreases, as does the brainstem's interstitial fluid (IF). As the graph shows, the lower the pH goes, the higher the ventilation rate rises. Higher ventilation results in increased rate of CO_2 loss from the body, eventually returning the body to a homeostatic balance.

not buffered in the brain's CSF and IF. The brain then senses unbuffered changes in pH (Figure 27-32).

The role of **arterial blood P_{O_2}** in controlling respirations is not entirely clear. Presumably, it has little influence as long as it stays above a certain level. But neurons of the respiratory centers, like all body cells, require adequate amounts of oxygen to function optimally. Consequently, if they become hypoxic, they become depressed and send fewer impulses to respiratory muscles. Respirations then decrease or fail entirely. This principle has important clinical significance. For example, the respiratory centers cannot respond to stimulation by an increasing blood CO_2 if, at the same time, blood P_{O_2} falls below a critical level—a fact that may become life or death important during anesthesia.

However, a decrease in arterial blood P_{O_2} below 70 mmHg, but not so low as the critical level, stimulates chemoreceptors in the carotid and aortic bodies and causes reflex stimulation of the inspiratory neurons of the medullary rhythmicity area. This constitutes an emergency respiratory control mechanism. It does not help regulate respirations under usual conditions when arterial blood P_{O_2} remains considerably higher than 70 mmHg, which is the level necessary to stimulate the chemoreceptors.

Arterial blood pressure helps control breathing through the respiratory pressoreflex mechanism. A sudden rise in arterial pressure, by acting on aortic and carotid baroreceptors, results in reflex slowing of respirations. A sudden drop in arterial pressure brings about a reflex increase in the rate and depth of respirations. The pressoreflex mechanism is probably not of great importance in the control of respirations. It is, however, of major importance in the control of circulation.

The **Hering-Breuer reflexes** also help control respirations, particularly their depth and rhythmicity when the tidal volume is high. It is believed they regulate the depth of respirations (extent of lung expansion)—and therefore the volume of tidal air—in the following way. Presumably, when a large tidal volume of air has been inspired, the lungs are expanded enough to stimulate stretch receptors located within them. The stretch receptors then send inhibitory impulses to the inspiratory neuron, relaxation of inspiratory muscles occurs, and expiration follows the Hering-Breuer expiratory reflex. Then, when a large tidal volume of air has been expired, the lungs are sufficiently deflated to inhibit the lung stretch receptors and allow inspiration to start again—the Hering-Breuer inspiratory reflex. Evidence suggests that these reflexes do not play a significant role in resting (low tidal volume) breathing, except perhaps in newborns.

The **cerebral cortex** also influences breathing. Impulses to the respiratory center from the motor area of the cerebrum may either increase or decrease the rate and strength of respirations. In other words, an individual may voluntarily speed up or slow down the breathing rate. This voluntary control of respirations, however, has certain limitations. For example, one may stop breathing and do so for a few minutes, but holding the breath results in an increase in the CO_2 content of the blood because it is not being removed by respirations. CO_2 is a powerful respiratory stimulant. So when arterial blood P_{CO_2} increases to a certain level, it stimulates the inspiratory neuron (directly and reflexively) to send motor impulses to the respiratory muscles, and breathing is resumed, even though the individual may still will contrarily.

Miscellaneous factors may also influence breathing. Among these are blood temperature and sensory impulses from skin thermal receptors and from superficial or deep pain receptors:

Sudden painful stimulation produces a reflex apnea, but continued painful stimuli cause faster and deeper respirations.

Sudden cold stimuli applied to the skin cause reflex apnea.

Stimulation of the pharynx or larynx by irritating chemicals or by touch causes a temporary apnea. This is the choking reflex, a valuable protective device. It operates, for example, to prevent aspiration of food or liquids during swallowing.

The major factors that influence breathing are summarized in Figure 27-30. Some factors that affect breathing during exercise are mentioned in Box 27-9.

Ventilation and Perfusion

Alveolar ventilation, as we already know, is airflow to the alveoli (see Figure 27-1). Alveolar perfusion is blood flow to the alveoli (see Figure 27-18). Matching ventilation and perfusion is important for efficient gas exchange in the lungs. If a poorly ventilated alveolus is well perfused, blood flow is being "wasted" on an inefficient alveolus. It is more efficient to detour some of the blood flow away from the poorly ventilated alveolus and toward a well-ventilated alveolus.

Figure 27-33 shows that perfusion can be matched—within very limited boundaries—to the ventilation status of individual groups of alveoli. As you have probably already deduced, this is accomplished through vasoconstriction (narrowing) of certain pulmonary arterioles to reduce perfusion to poorly ventilated alveoli. Such ventilation-perfusion matching in various regions of each lung can increase the overall efficiency of gas exchange.

| QUICK CHECK |

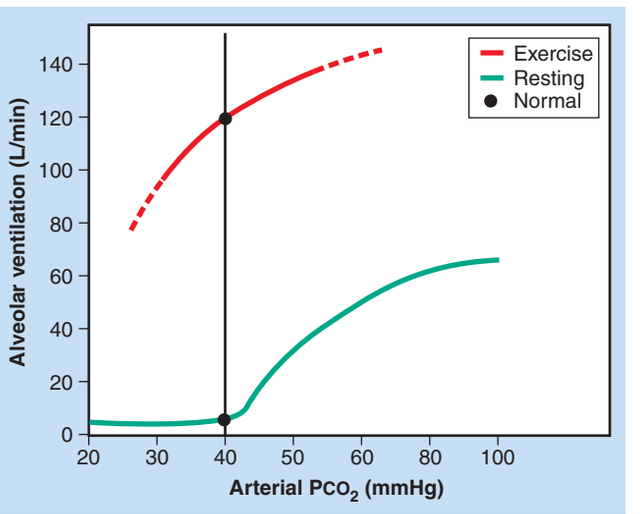
17. Where are the chief regulatory centers of the respiratory function located?
18. Name several factors that can influence the breathing rate of an individual; tell whether each triggers an increase or a decrease in breathing rate.



Box 27-9 | SPORTS and FITNESS

Control of Respirations During Exercise

Respirations increase abruptly at the beginning of exercise and decrease even more markedly as it ends. This much is known. The mechanism that accomplishes this increased ventilation rate, however, is not known. It is not identical to the one that produces moderate increases in breathing. Numerous studies have shown that arterial blood P_{CO_2}, P_{O_2}, and pH do not change enough during exercise to produce the degree of hyperpnea (faster, deeper respirations) observed. Presumably, many chemical and nervous factors and temperature changes operate as a complex, but still unknown, mechanism for regulating respirations during exercise.



Normal effects of maximum exercise in an athlete. This graph shows that the breathing rate (vertical axis) is much higher in an athlete exercising maximally than would be expected for any given blood carbon dioxide pressure (P_{CO_2}) (horizontal axis). As you can see at the normal points of a P_{CO_2} of 40 mmHg, the exercising athlete's breathing (ventilation) rate is 120 L/min. However, at rest the athlete's breathing rate is only about 5 or 6 L/min at the same P_{CO_2}—thus showing that P_{CO_2} is not the major factor causing an increased rate of breathing during exercise.

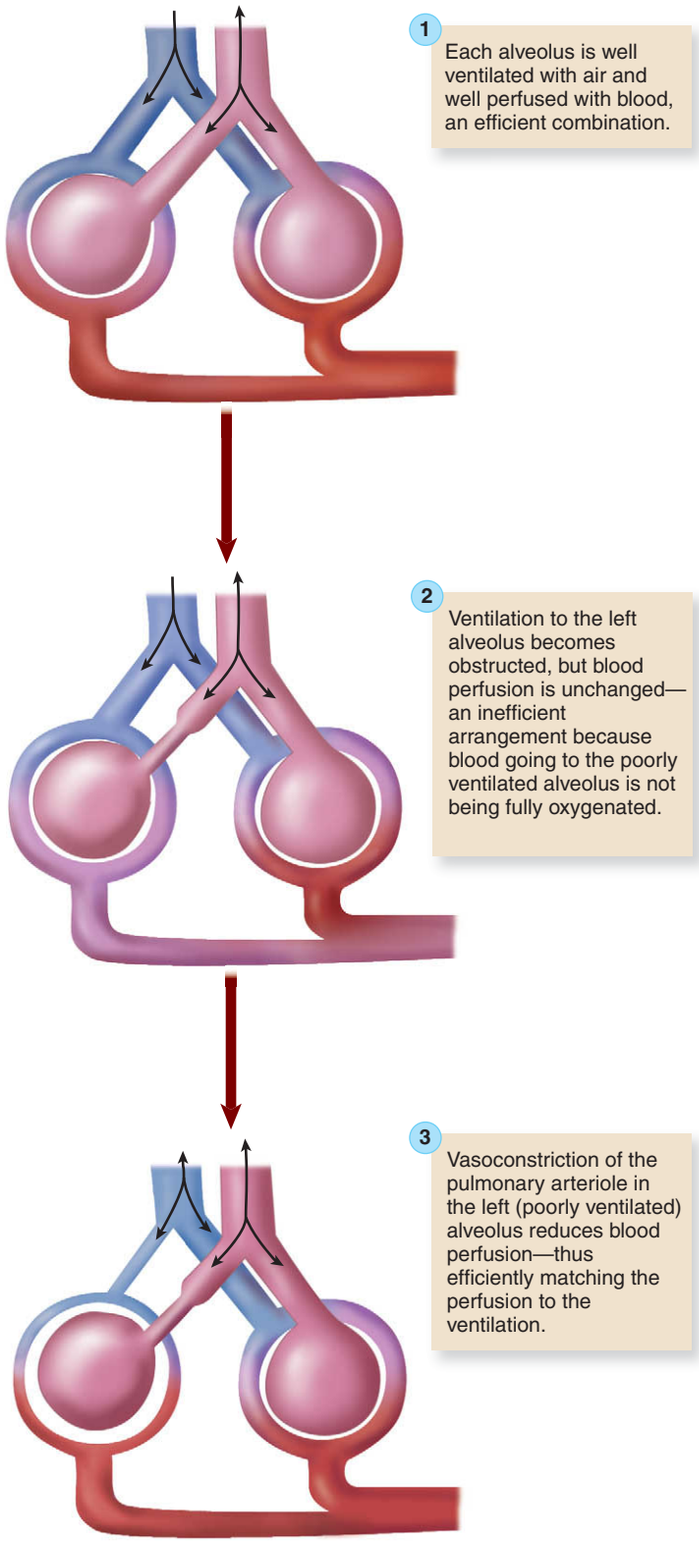


FIGURE 27-33

Ventilation and perfusion of the alveoli. Here, two alveoli represent typical alveoli in the lungs.

the BIG picture

Respiratory Physiology and the Whole Body

The homeostatic balance of the entire body, and thus the survival of each and every cell, depends on the proper functioning of the respiratory system. Because the mitochondria in each cell require oxygen for their energy conversions, and because each cell produces toxic carbon dioxide as a waste product of the very same energy conversions, the internal environment must continually acquire new oxygen and discard carbon dioxide. If each cell were immediately adjacent to the external environment—that is, atmospheric air—this would require no special system. However, because almost every one of the 100 trillion cells that make up the body are far removed from the outside air, another method of satisfying this condition must be employed—this is where the respiratory system comes in. By the process of ventilation, fresh external air continually flows less than a hair's breadth away from the circulating fluid of the body—the blood. By means of diffusion, oxygen enters the internal environment and carbon dioxide leaves. The efficiency of this process is enhanced by the presence of "oxygen sponges," called *hemoglobin molecules,* which immediately take oxygen molecules out of solution in the plasma so that more oxygen can rapidly diffuse into the blood. The blood, the circulating fluid tissue of the cardiovascular system, carries the blood gases throughout the body—picking up gases where there is an excess and unloading them where there is a deficiency. In this manner, each cell of the body is continually bathed in a fluid environment that offers a constant supply of oxygen and an efficient system for removing carbon dioxide.

Specific mechanisms involved in respiratory function show the interdependence between body systems observed throughout our study of the human body. For example, without blood and the maintenance of blood flow by the cardiovascular system, blood gases could not be transported between the gas exchange tissues of the lungs and the various systemic tissues of the body. Without regulation by the nervous system, ventilation could not be adjusted to compensate for changes in the oxygen or carbon dioxide content of the internal environment. Without the skeletal muscles of the thorax, the airways could not maintain the flow of fresh air that is so vital to respiratory function. The skeleton itself provides a firm outer housing for the lungs and has an arrangement of bones that facilitates the expansion and recoil of the thorax, which is needed to accomplish inspiration and expiration. Without the immune system, pathogens from the external environment could easily colonize the respiratory tract and possibly cause a fatal infection.

Even more subtle interactions between the respiratory system and other body systems can be found. For example, the language function of the nervous system is limited without the speaking ability provided by the larynx and other structures of the respiratory tract. The homeostasis of pH, which is regulated by a variety of systems, is influenced by the respiratory system's ability to adjust the body's carbon dioxide levels (and thus the levels of carbonic acid).

MECHANISMS of DISEASE

DISORDERS ASSOCIATED WITH RESPIRATORY FUNCTION

Many things can interfere with the functions of gas exchange and ventilation and cause respiratory failure. A few of the more important disorders are briefly described here.

Restrictive Pulmonary Disorders

Restrictive pulmonary disorders involve restriction of the alveoli, or reduced compliance, leading to decreased lung inflation. The hallmark of these disorders, regardless of their cause, is decreased lung volumes and capacities such as inspiratory reserve volume and vital capacity. Factors that restrict breathing can originate either within the lung or outside of it. Causes of restrictive lung disorders include alveolar fibrosis (scarring) secondary to occupational exposure to asbestos, toxic fumes, coal dust, or other contaminants; immunological diseases, as in rheumatoid lung; obesity; and metabolic disorders such as uremia. Restriction of breathing can also be caused by pain that accompanies pleurisy (inflammation of the pleurae) or mechanical injuries (such as a fractured or bruised rib). Patients with restrictive lung disease classically experience **dyspnea** (labored breathing) and are not able to tolerate increased activity, which reduces their ability to work or perform normal daily activities. Therapy involves eliminating the cause of the restriction, ensuring adequate gas exchange, and improving exercise tolerance.

Obstructive Pulmonary Disorders

A variety of conditions may cause obstruction of the airways. Exposure to cigarette smoke and other common air pollutants can trigger a reflexive constriction of bronchial airways. Obstructive disorders may obstruct inspiration and expiration, whereas restrictive disorders mainly restrict inspiration.

Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) is a broad term used to describe conditions of progressive irreversible obstruction of expiratory airflow. People with COPD have chronic difficulties with breathing, mainly emptying their lungs, and have visibly hyperinflated chests. Figures 27-12 and 27-13 (p. 837) show the effects of COPD compared to normal breathing patterns. Those with COPD often have a productive cough and intolerance of activity. The major disorders observed in people with COPD are chronic bronchitis and emphysema.

In North America, tobacco use is the primary cause of COPD, but air pollution, asthma, and respiratory infections also play a role. COPD is a leading cause of death—one that has been *increasing* over recent years! Until a few years ago, more men had COPD than women. However, the increase of smoking among women is thought to account for the fact that the rate for female COPD is growing rapidly.

Acute respiratory failure can occur when any of the disorders that produce COPD become intense. Heart failure resulting from the pulmonary disease and the vascular resistance that develops with COPD is another possible outcome. Although there is no cure for chronic obstructive respiratory conditions, limiting symptoms can improve quality of life. Bronchodilators and corticosteroids have been used to relieve some of the airway obstruction involved in COPD.

Acute obstruction of the airways, as when a piece of food blocks airflow, requires immediate action to avoid death from suffocation.

| A&P CONNECT |

Knowledge of the physical principles of ventilation can have lifesaving applications in medical emergencies involving acute airway obstruction caused by foreign material. Learn about how these procedures can help choking victims in ***Heimlich Maneuver*** online at ***A&P Connect.***

evolve

Bronchitis

In chronic **bronchitis,** the person produces excessive tracheobronchial secretions that obstruct airflow, and the bronchial mucous glands are enlarged (Figure 27-34, *B*). Risk factors include cigarette smoking (accounting for 80% to 90% of the risk of developing COPD), a normal decline in pulmonary function as a result of age, and environmental exposure to dust and chemicals. With impairment of the alveoli and loss of capillary beds, gas exchange is inefficient, which in turn produces hypoxia.

Emphysema

In **emphysema,** the air spaces distal to the terminal bronchioles are enlarged as a result of damage to lung connective tissue. As the bronchioles collapse and the alveoli enlarge, the alveolar walls rupture and fuse into large irregular spaces, and gas exchange units are destroyed (Figure 27-34, *D*). Although the etiology is not fully understood, this condition is believed to be caused by proteolytic enzymes that destroy lung tissue. Hypoxia often develops in emphysema victims.

Asthma

Asthma is an obstructive lung disorder characterized by recurring inflammation of mucous membranes and spasms of the smooth muscles in the walls of the bronchial air passages. The inflammation (edema and excessive mucus production) and contractions narrow airways, making breathing difficult (Figure 27-34, *C*). Initial onset of asthma can occur in children or adults. Acute episodes of asthma—so-called "asthma attacks"—can be triggered by stress, heavy exercise, infection, or exposure to allergens or other irritants such as dust, vapor, or fumes. Many patients with asthma have a family history of allergies.

Dyspnea is the major symptom of asthma, but hyperventilation, headaches, numbness, and nausea can occur. One way to treat asthma is by using inhaled or systemic bronchodilators that

reduce muscle spasms and thus open the airways. Other types of treatment involve the use of antiinflammatory medications including leukotriene modifiers to reduce the inflammation associated with asthma. (Recall from Chapter 24 that leukotrienes are cytokines released by immune cells to regulate the inflammation response.)

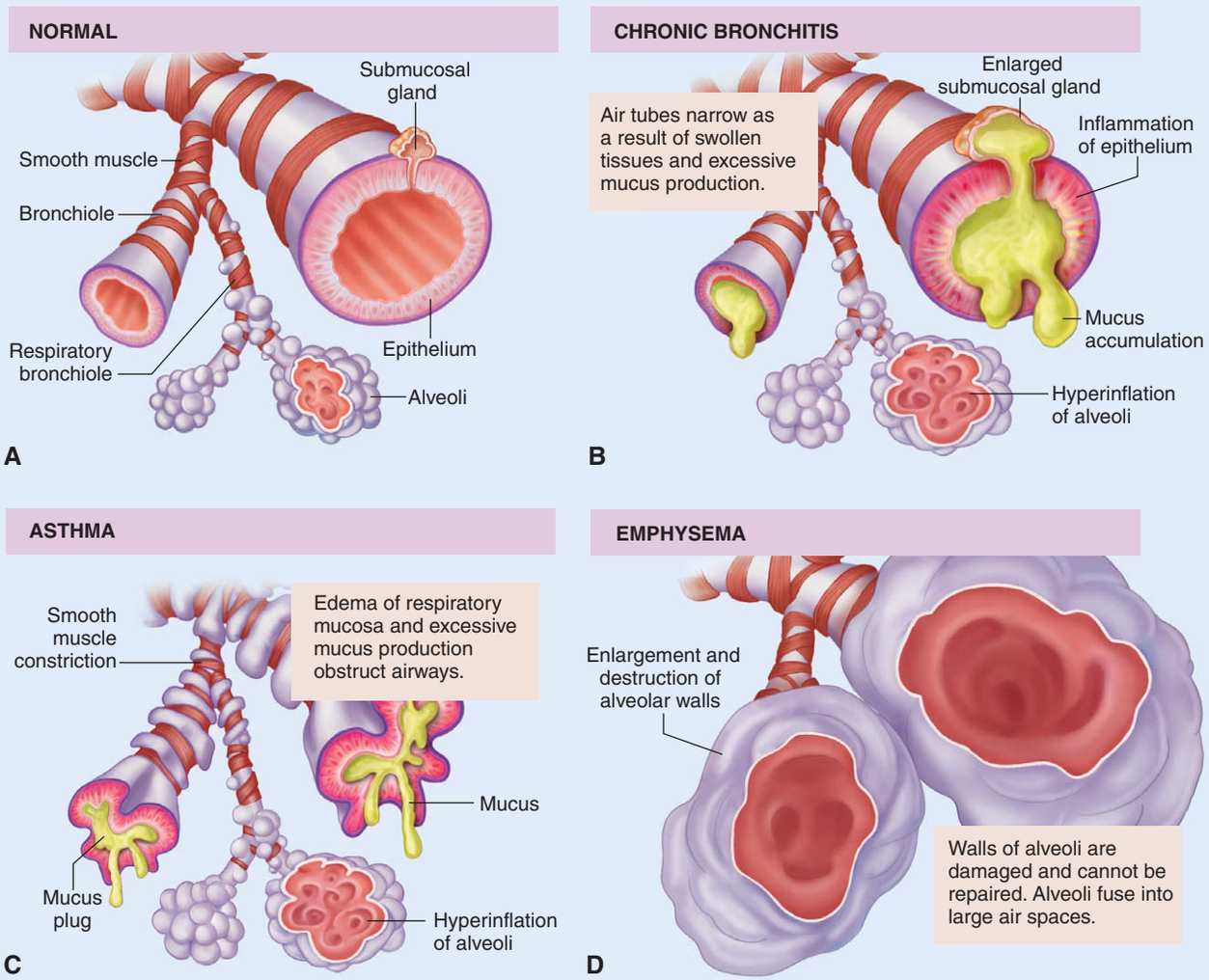


FIGURE 27-34

Obstructive pulmonary disorders. Examples of chronic disorders involving pulmonary obstruction.

HEALTH matters

Sudden Infant Death Syndrome (SIDS)

Sudden infant death syndrome (SIDS) is the third-ranking cause of infant death and accounts for about 1 in 9 of the nearly 30,000 infant deaths reported each year in the United States. Sometimes called "crib-death," SIDS occurs most frequently in babies with no obvious medical problems who are younger than 3 months of age. The exact cause of death can seldom be determined even after extensive testing and autopsy.

SIDS occurs at a higher rate in African-American and Native American babies than in white, Hispanic, or Asian infants, although the reasons remain a mystery. Regardless of infant ethnicity, data suggest that certain precautions, such as having babies sleep only on their backs and keeping cribs free of pillows or plush toys that might partially cover the nose or mouth, may reduce the incidence of SIDS. Also important is the elimination of smoking during pregnancy and protecting infants from exposure to "second-hand" cigarette smoke after birth.

Although the exact cause of SIDS remains unknown, genetic defects involving the structure and function of the respiratory system or unusual physiological responses to common flu or cold viruses may also play a role in this tragic problem.

LANGUAGE OF SCIENCE *(continued from p. 823)*

chloride shift
(KLOR-ide)
[*chlor-* **green**, *-ide* **chemical**]

compliance
[*compli-* **complete**, *-ance* **act of**]

Dalton's law
(DAL-tenz law)
[*John Dalton* **English chemist and physicist**]

elastic recoil
(eh-LAS-tik REE-koyl)
[*elast-* **drive or propel**, *-ic* **relating to**]

expiration
(eks-pih-RAY-shun)
[*ex-* **out**, *-pir-* **breathe**, *-tion* **process**]

flow-volume loop

Haldane effect
(HAWL-dayne)
[*John Scott Haldane* **Scots physiologist**]

heme group
(heem)
[*heme* **blood**]

hemoglobin (Hb)
(hee-moh-GLOH-bin)
[*hemo-* **blood**, *-glob-* **ball**, *-in* **substance**]

Henry's law
[*William Henry* **English chemist**]

Hering-Breuer reflex
(HER-ing BROO-er REE-fleks)
[*Heinrich E. Hering* **German physiologist**, *Joseph Breuer* **Australian physician**, *re-* **back or again**, *-flex* **bend**]

ideal gas

inspiration
(in-spih-RAY-shun)
[*in-* **in**, *-spir-* **breathe**, *-ation* **process**]

law of partial pressures

medullary rhythmicity area
(MED-eh-lair-ee rith-MIH-sih-tee)
[*medulla-* **middle**, *-ary* **relating to**, *rhythm-* **rhythm**, *-ic* **relating to**, *-ity* **condition**]

oxygen-hemoglobin dissociation curve
(AHK-sih-jen hee-moh-GLOH-bin)
[*oxy-* **sharp**, *-gen* **produce**, *hemo-* **blood**, *-glob-* **ball**, *-in* **substance**, *dis-* **reverse**, *-socia-* **unite**, *-ation* **process**]

oxyhemoglobin
(ahk-see-hee-moh-GLOH-bin)
[*oxy-* **sharp (oxygen)**, *-hemo-* **blood**, *-glob-* **ball**, *-in* **substance**]

partial pressure
(PAR-shal)

physiological dead space
(fiz-ee-oh-LOJ-i-kal)
[*physio-* **nature**, *-log-* **words (study)**, *-ical* **relating to**]

pontine respiratory group (PRG)
(pahn-TEEN RES-pih-rah-toh-ree groop)
[*pont-* **bridge (pons)**, *-ine* **relating to**]

primary principle of ventilation
(ven-tih-LAY-shun)
[*prim-* **first**, *-ary* **relating to**, *princip-* **foundation**, *vent-* **fan or create wind**, *-tion* **process**]

pulmonary ventilation
(PUL-moh-nair-ee ven-tih-LAY-shun)
[*pulmon-* **lung**, *-ary* **relating to**, *vent-* **fan or create wind**, *-tion* **process**]

rate law

respiratory cycle
(RES-pih-rah-tor-ee)
[*re-* **again**, *-spir-* **breathe**, *-tory* **relating to**]

respiratory physiology
(RES-pih-rah-tor-ee fiz-ee-OL-oh-jee)
[*re-* **again**, *-spir-* **breathe**, *-tory* **relating to**, *physio-* **nature**, *-log-* **words (study)**, *-y* **process**]

solubility
(sol-yoo-BIL-i-tee)
[*solubili-* **able to dissolve**, *-ity* **state**]

surface tension

tension

transpulmonary pressure
(trans-PUHL-mohn-air-ee)
[*trans-* **across**, *pulmon-* **lung**, *-ary* **relating to**]

type II cells
[*II* **Roman numeral two**]

Young-LaPlace law (law of LaPlace)
(yung lah-PLAHS)
[*Thomas Young* **English physician**, *Pierre Simon de LaPlace* **French physicist**]

LANGUAGE OF MEDICINE

apnea
(AP-nee-ah)
[*a-* **not**, *-pne-* **breathe**, *-a* **condition**]

apneusis
(ap-NYOO-sis)
[*a-* **not**, *-pneu-* **breathe**, *-sis* **condition**]

asthma
(AZ-mah)
[*asthma* **panting**]

Biot's breathing
(bee-OHS)
[*Camille Biot* **French physician**]

bronchitis
(brong-KYE-tis)
[*bronch-* **windpipe**, *-itis* **inflammation**]

carbon monoxide (CO)
(KAR-bon mon-OKS-ide)
[*mono-* **single**, *-ox-* **sharp (oxygen)**, *-ide* **chemical**]

Cheyne-Stokes respiration
(chain stokes res-pih-RAY-shun)
[*John Cheyne Scots* **physician**, *William Stokes* **Irish physician**]

chronic obstructive pulmonary disease (COPD)
(KRON-ik ob-STRUK-tiv PUL-moh-nair-ee)
[*chron-* **time**, *-ic* **relating to**, *pulmon-* **lung**, *-ary* **relating to**]

continuous positive airway pressure (CPAP)

cough reflex
[*re-* **back or again**, *-flex* **bend**]

diving reflex
[*re-* **back or again**, *-flex* **bend**]

dyspnea
(DISP-nee-ah)
[*dys-* **painful**, *-pne-* **breathe**, *-a* **condition**]

emphysema
(em-fi-SEE-mah)
[*em-* **in**, *-physema* **blowing or puffing up**]

eupnea
(YOOP-nee-ah)
[*eu-* **easily**, *-pne-* **breathe**, *-a* **condition**]

expiratory reserve volume (ERV)
(eks-PYE-rah-tor-ee)
[*ex-* **out of**, *-[s]pir-* **breathe**, *-tory* **relating to**]

forced expiratory volume (FEV)
(eks-PYE-rah-tor-ee)
[*ex-* **out of**, *-[s]pir-* **breathe**, *-tory* **relating to**]

functional residual capacity (FRC)

Heimlich maneuver
(HYME-lik mah-NOO-ver)
[*Henry J. Heimlich* **American physician**]

hiccup
(HIK-up)
[**imitation of hiccup sound**]

hyaline membrane disease (HMD)
(HYE-ah-lin)
[*hyal-* **glass**, *-ine* **of or like**]

hyperpnea
(hye-PERP-nee-ah)
[*hyper-* **excessive**, *-pne-* **breathe**, *-a* **condition**]

hyperventilation
(hye-per-ven-ti-LAY-shun)
[*hyper-* **excessive**, *-vent-* **fan or create wind**, *-tion* **process**]

hypoventilation
(hye-poh-ven-ti-LAY-shun)
[*hypo-* **under or below**, *-vent-* **fan or create wind**, *-tion* **process**]

inspiratory capacity (IC)
(in-SPY-rah-tor-ee kah-PASS-i-tee)
[*in-* **in**, *-spir-* **breathe**, *-tory* **relating to**]

inspiratory reserve volume (IRV)
(in-SPY-rah-tor-ee)
[*in-* **in**, *-spir-* **breathe**, *-tory* **relating to**]

intratracheal injection
(in-trah-TRAY-kee-al in-JEK-shun)
[*intra-* **within**, *-trache-* **rough duct**, *-al* **relating to**]

maximum oxygen consumption (Vo_2 max)
[*maximum* **greatest**, *oxy-* **sharp**, *-gen* **produce**, *con-* **with or in**, *-sum-* **take**, *-tion* **process**]

orthopnea
(or-THOP-nee-ah)
[*ortho-* **straight or upright**, *-pne-* **breathe**, *-a* **condition**]

pneumothorax
(noo-moh-THOH-raks)
[*pneumo-* **air or wind**, *-thorax* **chest**]

residual volume (RV)
(ree-ZID-yoo-al)

respiratory arrest
(RES-pih-rah-tor-ee ah-REST)
[*re-* **again**, *-spir-* **breathe**, *-tory* **relating to**]

respiratory distress syndrome (RDS)
(RES-pihrah- tor-ee di-STRESS SIN-drohm)
[*re-* **again**, *-spir-* **breathe**, *-tory* **relating to**, *syn-* **together**, *-drome* **running or (race)course**]

sneeze reflex
(sneez REE-fleks)
[*re-* **back or again**, *-flex* **bend**]

spirogram
(SPY-roh-gram)
[*spir-* **breathe**, *-gram* **drawing**]

spirometer
(spih-ROM-eh-ter)
[*spir-* **breathe**, *-meter* **measurement**]

tidal volume (TV)
(TYE-dal)
[*tid-* **time**, *-al* **relating to**]

total lung capacity (TLC)

total minute volume

vital capacity (VC)
(VYE-tal kah-PASS-i-tee)
[*vita-* **life**, *-al* **relating to**]

yawn
[*yawn* **gape**]

CASE study

After having surgery to remove a stomach tumor, Derrick woke up in the recovery room in extreme pain. It hurt to move; it hurt to blink; it hurt to take even a little breath, and here was this nurse demanding that he take a deep breath and cough. Was she crazy?

1. Which of these muscles would **not** contract when Derrick complied with his nurse's instructions?
   a. Diaphragm
   b. Serratus anterior
   c. Rectus abdominis
   d. External intercostals
2. Which statement best describes the "mechanics" of Derrick's inhalations?
   a. The thoracic cavity decreases in size, lowering the alveolar pressure, and air flows from high (atmosphere) pressure to low (alveolar) pressure.
   b. The thoracic cavity increases in size, lowering the alveolar pressure, and air flows from high (atmospheric) pressure to low (alveolar) pressure.
   c. Air flows from high (atmospheric) pressure to low (alveolar) pressure and expands the thoracic cavity.
   d. Air flows from high (intrapleural) pressure to low (alveolar) pressure and expands the thoracic cavity.

What Derrick didn't realize was that his shallow respirations were not getting rid of as much carbon dioxide as usual. As a result, the concentration of CO_2 in his bloodstream was building to a level that would negatively affect homeostasis.

3. This increased carbon dioxide will make Derrick's blood _____.
   a. More acidic
   b. More basic
   c. More neutral
   d. None of the above



4. How is carbon dioxide transported in Derrick's blood?
   a. Dissolved in the plasma
   b. Bound to hemoglobin
   c. In the form of bicarbonate
   d. All of the above

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook, **A&P Connect,** and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

RESPIRATORY PHYSIOLOGY (FIGURE 27-1)

A. Definition—complex, coordinated processes that help maintain homeostasis
B. External respiration
   1. Pulmonary ventilation (breathing)
   2. Pulmonary gas exchange
C. Transport of gases by the blood
D. Internal respiration
   1. Systemic tissue gas exchange
   2. Cellular respiration
E. Regulation of respiration

PULMONARY VENTILATION

A. Respiratory cycle (ventilation; breathing)
   1. Inspiration—moves air into the lungs
   2. Expiration—moves air out of the lungs
B. Mechanism of pulmonary ventilation
   1. Pulmonary ventilation mechanism must establish two gas pressure gradients (Figures 27-2 and 27-3)
      a. One in which the pressure within the alveoli of the lungs is lower than atmospheric pressure to produce inspiration
      b. One in which the pressure in the alveoli of the lungs is higher than atmospheric pressure to produce expiration
   2. Pressure gradients are established by changes in the size of the thoracic cavity that are produced by contraction and relaxation of muscles (Figures 27-4 and 27-5)
   3. Boyle's law—the volume of gas varies inversely with pressure at a constant temperature
   4. Inspiration—contraction of the diaphragm produces inspiration—as it contracts, it makes the thoracic cavity larger (Figures 27-6 and 27-7)
      a. Expansion of the thorax results in decreased intrapleural pressure (P_{IP}), leading to decreased alveolar pressure (P_A)
      b. Air moves into the lungs when alveolar pressure (P_A) drops below atmospheric pressure (P_B)
      c. Compliance—ability of pulmonary tissues to stretch, thus making inspiration possible
   5. Expiration—a passive process that begins when the inspiratory muscles are relaxed, which decreases the size of the thorax (Figures 27-8 and 27-9)
      a. Increasing thoracic volume increases the intrapleural pressure and thus increases alveolar pressure above the atmospheric pressure
      b. Air moves out of the lungs when alveolar pressure exceeds the atmospheric pressure
      c. Pressure between parietal and visceral pleura is always less than alveolar pressure and less than atmospheric pressure; the difference between P_{IP} and P_A is called *transpulmonary pressure*
      d. Elastic recoil—tendency of pulmonary tissues to return to a smaller size after having been stretched; occurs passively during expiration
C. Pulmonary volumes—normal exchange of oxygen and carbon dioxide depends on the presence of normal volumes of air moving in and out and the remaining volume (Figure 27-11)
   1. Spirometer—instrument used to measure the volume of air (Figure 27-10)
   2. Tidal volume (TV)—amount of air exhaled after normal inspiration
   3. Expiratory reserve volume (ERV)—largest volume of additional air that can be forcibly exhaled (between 1.0 and 1.2 liters is normal ERV)
   4. Inspiratory reserve volume (IRV)—amount of air that can be forcibly inhaled after normal inspiration (normal IRV is 3.3 liters)
   5. Residual volume—amount of air that cannot be forcibly exhaled (1.2 liters)
D. Pulmonary capacities—the sum of two or more pulmonary volumes
   1. Vital capacity (VC)—the sum of IRV + TV + ERV
   2. Minimal volume—the amount of air remaining after RV
   3. A person's vital capacity depends on many factors, including the size of the thoracic cavity and posture
   4. Inspiratory capacity (IC)—maximal amount of air that can be inspired after a normal expiration
   5. Functional residual capacity (FRC)—the amount of air at the end of a normal respiration
   6. Total lung capacity (TLC)—the sum of all four lung volumes—the total amount of air a lung can hold
   7. Alveolar ventilation—volume of inspired air that reaches the alveoli
   8. Anatomical dead space—passageways occupied by air that does not participate in gas exchange (Figure 27-6)
   9. Physiological dead space—anatomical dead space plus any alveoli not able to perform gas exchange (as in pulmonary disease)
   10. Alveoli must be properly ventilated for adequate gas exchange
E. Pulmonary airflow—rates of airflow into/out of the pulmonary airways
   1. Total minute volume—volume moved per minute (ml/min)
   2. Forced expiratory volume (FEV) or forced vital capacity (FVC)—volume of air expired per second during forced expiration (as a percentage of VC) (Figure 27-12)
   3. Flow-volume loop—graph that shows flow (vertically) and volume (horizontally), with the top of the loop representing expiratory flow-volume and the bottom of the loop representing inspiratory flow-volume relationships (Figure 27-13)

PULMONARY GAS EXCHANGE

A. Partial pressure of gases—pressure exerted by a gas in a mixture of gases or a liquid (Figure 27-14)
   1. Law of partial pressures (Dalton's law)—the partial pressure of a gas in a mixture of gases is directly related to the concentration of that gas in the mixture and to the total pressure of the mixture
   2. Arterial blood P_{O_2} and P_{CO_2} equal alveolar P_{O_2} and P_{CO_2}
B. Exchange of gases in the lungs—takes place between alveolar air and blood flowing through lung capillaries (Figures 27-15, 27-16, and 27-17)
   1. Four factors determine the amount of oxygen that diffuses into blood
      a. The oxygen pressure gradient between alveolar air and blood
      b. The total functional surface area of the respiratory membrane
      c. The respiratory minute volume
      d. Alveolar ventilation
   2. Structural facts that facilitate oxygen diffusion from the alveolar air to the blood
      a. The walls of the alveoli and capillaries form only a very thin barrier for gases to cross
      b. The alveolar and capillary surfaces are large
      c. The blood is distributed through the capillaries in a thin layer so that each red blood cell comes close to alveolar air (Figure 27-18)

HOW BLOOD TRANSPORTS GASES

A. Oxygen and carbon dioxide are transported as solutes and as parts of molecules of certain chemical compounds
B. Hemoglobin (Hb)
   1. Made up of four polypeptide chains (two alpha chains, two beta chains), each with an iron-containing heme group
   2. Carbon dioxide can bind to amino acids in the chains and oxygen can bind to iron in the heme groups (Figure 27-19)
C. Transport of oxygen
   1. Oxygenated blood contains about 0.3 ml of dissolved O_2 per 100 ml of blood
   2. Hemoglobin increases the oxygen-carrying capacity of blood (Figure 27-20)
   3. Oxygen travels in two forms: as dissolved O_2 in plasma and as being associated with hemoglobin (oxyhemoglobin)
      a. Increasing blood P_{O_2} accelerates hemoglobin association with oxygen (Figure 27-21)
      b. Oxyhemoglobin carries the majority of the total oxygen transported by blood
D. Transport of carbon dioxide
   1. A small amount of CO_2 dissolves in plasma and is transported as a solute (10%)
   2. Less than one-fourth of blood carbon dioxide combines with NH_2 (amine) groups of hemoglobin and other proteins to form carbaminohemoglobin (20%) (Figure 27-22)
   3. Carbon dioxide's association with hemoglobin is accelerated by an increase in blood P_{CO_2} (Figure 27-23)
   4. More than two-thirds of the carbon dioxide is carried in plasma as bicarbonate ions (70%) (Figures 27-24, 27-25, and 27-26)

SYSTEMIC GAS EXCHANGE

A. Exchange of gases in tissues takes place between arterial blood flowing through tissue capillaries and cells (Figure 27-27)
   1. Oxygen diffuses out of arterial blood because the oxygen pressure gradient favors its outward diffusion
   2. As dissolved oxygen diffuses out of arterial blood, blood P_{O_2} decreases, which accelerates oxyhemoglobin dissociation to release more oxygen to plasma for diffusion to cells (Figure 27-28)
B. Carbon dioxide exchange between tissues and blood takes place in the opposite direction from oxygen exchange
   1. Bohr effect—increased P_{CO_2} decreases the affinity between oxygen and hemoglobin (Figure 27-29, *A*)
   2. Haldane effect—increased carbon dioxide loading caused by a decrease in P_{O_2} (Figure 27-29, *B*)

REGULATION OF PULMONARY FUNCTION

A. Respiratory control centers—the main integrators controlling the nerves that affect the inspiratory and expiratory muscles are located in the brainstem (Figure 27-30)
   1. Medullary rhythmicity center—generates the basic rhythm of the respiratory cycle
      a. Consists of two interconnected control centers
         (1) Dorsal respiratory group (DRG)—integrates information from chemoreceptors to regulate the VRG pattern
         (2) Ventral respiratory group (VRG)—generates basic pattern of breathing rhythm
   2. The basic breathing rhythm can be altered by different inputs to the medullary rhythmicity center (Figure 27-30)
      a. Input from the apneustic center in the pons regulates the medullary rhythmicity area
      b. Pontine respiratory group (PRG, or pneumotaxic center)—in the pons—inhibits the apneustic center and medullary rhythmicity area to prevent overinflation of the lungs
B. Factors that influence breathing—sensors from the nervous system provide feedback to the medullary rhythmicity center (Figure 27-31)
   1. Changes in the P_{O_2}, P_{CO_2}, and pH of arterial blood influence the medullary rhythmicity area
      a. P_{CO_2} acts on central chemoreceptors throughout the brainstem—if it increases, the result is faster breathing; if it decreases, the result is slower breathing
      b. A decrease in blood pH stimulates peripheral chemoreceptors in the carotid and aortic bodies and, even more so, stimulates the central chemoreceptors (because they are surrounded by unbuffered fluid) (Figure 27-32)

   c. Arterial blood Po_2 presumably has little influence if it stays above a certain level
2. Arterial blood pressure controls breathing through the respiratory pressoreflex mechanism
3. Hering-Breuer reflexes help control respirations by regulating depth of respirations and the volume of tidal air
4. Cerebral cortex influences breathing by increasing or decreasing the rate and strength of respirations

C. Ventilation and perfusion (Figure 27-33)
1. Alveolar ventilation—airflow to the alveoli
2. Alveolar perfusion—blood flow to the alveoli
3. Efficiency of gas exchange can be maintained by limited ability to match perfusion to ventilation—for example, vasoconstricting arterioles that supply poorly ventilated alveoli and allow full blood flow to well-ventilated alveoli

THE BIG PICTURE: RESPIRATORY PHYSIOLOGY AND THE WHOLE BODY

A. The internal system must continually acquire new oxygen and rid itself of carbon dioxide because each cell requires oxygen and produces carbon dioxide as a result of energy conversion

B. Specific mechanisms involved in respiratory function
1. Blood gases need blood and the cardiovascular system to be transported between gas exchange tissues of the lungs and various systemic tissues of the body
2. Regulation by the nervous system adjusts ventilation to compensate for changes in oxygen or carbon dioxide in the internal environment
3. The skeletal muscles of the thorax aid the airways in maintaining the flow of fresh air
4. The skeleton houses the lungs, and the arrangement of bones facilitates the expansion and recoil of the thorax
5. The immune system prevents pathogens from colonizing the respiratory tract and causing infection

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Define respiratory physiology.
2. What is the main inspiratory muscle?
3. Identify the separate volumes that make up the total lung capacity.
4. Normally, about what percentage of the tidal volume fills the anatomical dead space?
5. Normally, about what percentage of the tidal volume is useful air, that is, ventilates the alveoli?
6. One gram of hemoglobin combines with how many milliliters of oxygen?
7. What factors influence the amount of oxygen that diffuses into the blood from the alveoli?
8. Identify the major factors that influence breathing.
9. Orthopnea is a symptom of what type of disease?
10. Dyspnea is often associated with what type of breathing?
11. Define the diving reflex and explain its physiological importance.
12. Describe four other unusual reflexes that indirectly affect breathing.
13. Describe the changes in respirations during a period of exercise.

CRITICAL THINKING QUESTIONS

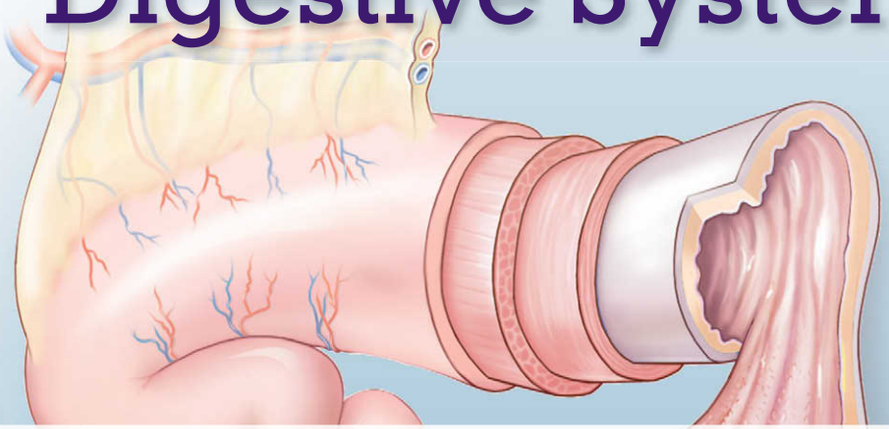


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. The proper functioning of the respiratory system allows what to occur in the body? What other control system has an impact on this function?
2. Can you identify the various processes that allow the respiratory system to accomplish its function?
3. What is pulmonary ventilation? What evidence can you find to describe whether the lungs are active or passive during this process?
4. How would you compare and contrast inspiration and expiration? Include the importance of elastic recoil and compliance to these processes.
5. How would you summarize the interaction of oxygen and carbon dioxide on gas transport in the blood? Include the Bohr and Haldane effects in your explanation.
6. Suppose your blood has a hemoglobin content of 15 grams/100 dl and an oxygen saturation of 97%. How many milliliters of oxygen would 100 ml of your arterial blood contain?
7. Compare and contrast infant and adult forms of respiratory distress syndrome.
8. After strenuous exercise, inexperienced athletes will quite often attempt to recover and resume normal breathing by bending over or sitting down. Using the mechanics of ventilation, how would you modify the recovery practices of these athletes?

Anatomy of the Digestive System

28



CHAPTER OUTLINE

HINT *Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.*

Organization of the Digestive System, 862
- Organs of Digestion, 862
- Wall of the GI Tract, 862
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LANGUAGE OF SCIENCE

HINT *Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.*

alimentary canal
(al-eh-MEN-tar-ee kah-NAL)
[*aliment-* **nourishment,** *-ary* **relating to**]

anal canal
(AY-nal kah-NAL)
[*an-* **ring (anus),** *-al* **relating to**]

ascending colon
(ah-SEND-ing KOH-lon)
[*colon* **large intestine**]

bile
(byle)

body

cardia
(KAR-dee-ah)
[*cardia* **heart**]

cheek

chief cell

colon
(KOH-lon)
[*colon* **large intestine**]

crown

deciduous teeth
(deh-SID-yoo-us)
[*decid-* **fall off,** *-ous* **relating to**]

deglutition
(deg-loo-TISH-un)
[*deglut-* **swallow,** *-tion* **process**]

descending colon
(dih-SEND-ing KOH-lon)
[*colon* **large intestine**]

digestion
(dye-JES-chun)
[*digest-* **break down,** *-tion* **process**]

duodenum
(doo-oh-DEE-num)
[**shortened from** *intestinum duodenum digitorum* **intestine of 12 finger-widths**] *pl.,* duodena or duodenums

continued on p. 895

This chapter deals with the anatomy of the digestive system. The organs of the digestive system together perform a vital function—that of preparing food for absorption and for use by the millions of body cells. Most food when eaten is in a form that cannot reach the cells (because it cannot pass through the intestinal mucosa into the bloodstream), nor could it be used by the cells even if it could reach them. It must therefore be modified in both chemical composition and physical state so that nutrients can be absorbed and used by the body cells. The complete process of altering the physical and chemical composition of ingested food material so that it can be absorbed and used by the body cells is called ***digestion.*** *This complex process is the function of both the digestive tract and accessory organs that make up the digestive system. The physiology of the digestive system is discussed in Chapter 29.*

ORGANIZATION OF THE DIGESTIVE SYSTEM

Organs of Digestion

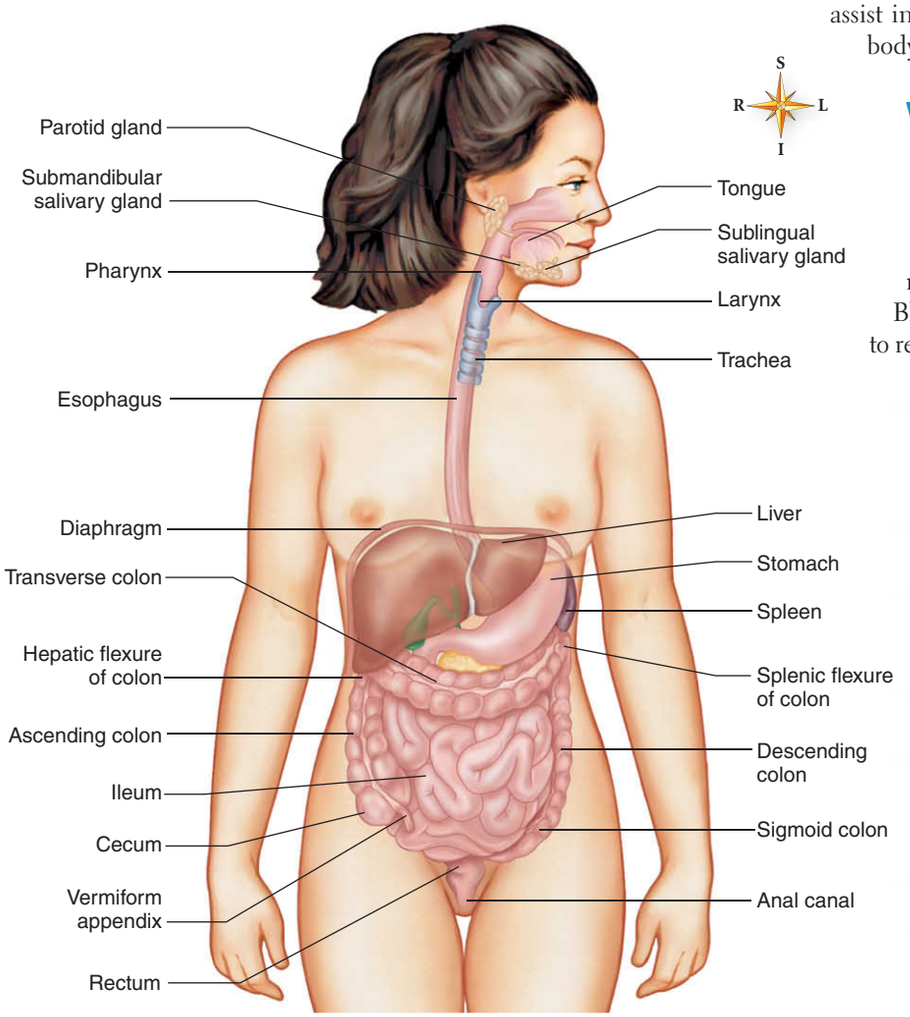
The main organs of the digestive system (Figure 28-1) form a tube that goes all the way through the ventral cavities of the body. It is open at both ends. This tube is usually referred to as the **alimentary canal** (tract). The term **gastrointestinal (GI) tract** refers only to the stomach and intestines but is sometimes used in reference to the entire alimentary canal.

It is important to realize that ingested food material passing through the lumen of the GI tract is actually outside the internal environment of the body, even though the tube itself is inside the ventral body cavity.

Box 28-1 lists the main organs of the digestive system, that is, the segments of the alimentary canal, and the accessory organs located in the main digestive organs or opening into them. Organs such as the larynx, trachea, diaphragm, and spleen are labeled in Figure 28-1, but they are not digestive organs. They are shown to assist in orienting the digestive organs to other important body structures.

Wall of the GI Tract

The GI tract is essentially a tube with walls fashioned of four layers of tissues: a mucous lining, a submucous coat of connective tissue in which are embedded the main blood vessels of the tract, a muscular layer, and a fibroserous layer (Figure 28-2). Blood vessels and nerves travel through the mesentery to reach the digestive tube throughout most of its length.



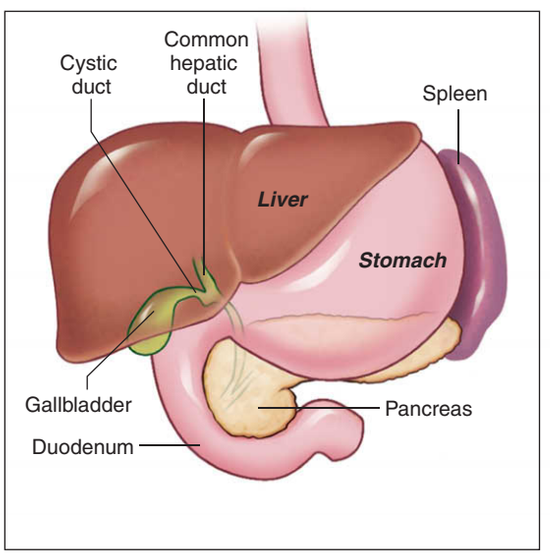


FIGURE 28-1
Location of the digestive organs.

MUCOSA

The innermost layer of the GI wall—the layer facing the lumen, or open space, of the tube—is called the **mucosa** or *mucous layer.* Note in Figure 28-2 that the mucosa is made up of three layers—an inner *mucous epithelium*, a layer of loose fibrous connective tissue called the *lamina propria*, and a thin layer of smooth muscle called the *muscularis mucosae*.

SUBMUCOSA

The **submucosa** layer of the digestive tube is composed of connective tissue that is thicker than the mucosal layer. It contains numerous small glands, blood vessels, and parasympathetic nerves that form the *submucosal plexus* (Meissner plexus).

MUSCULARIS

The **muscularis**—or *muscular layer*—is a thick layer of muscle tissue that wraps around the submucosa. This portion of the wall is characterized by an inner layer of circular and an outer layer of longitudinal smooth muscle. Like the submucosa, the muscularis contains nerves organized into a plexus called the *myenteric plexus* (Auerbach plexus). This plexus lies between the two muscle layers. Note in Figure 28-2 that the term **intramural plexus** is used to describe both plexuses. Together they play an important role in the regulation of digestive tract movement and secretion.

Box 28-1 | Organs of the Digestive System

Segments of the Gastrointestinal Tract

- Mouth
- Pharynx
- Esophagus
- Stomach
- Small intestine
  - Duodenum
  - Jejunum
  - Ileum
- Large intestine
  - Cecum
  - Colon
    - Ascending colon
    - Transverse colon
    - Descending colon
    - Sigmoid colon
  - Rectum
- Anal canal

Accessory Organs

- Salivary glands
  - Parotid
  - Submandibular
  - Sublingual
- Tongue
- Teeth
- Liver
- Gallbladder
- Pancreas
- Vermiform appendix

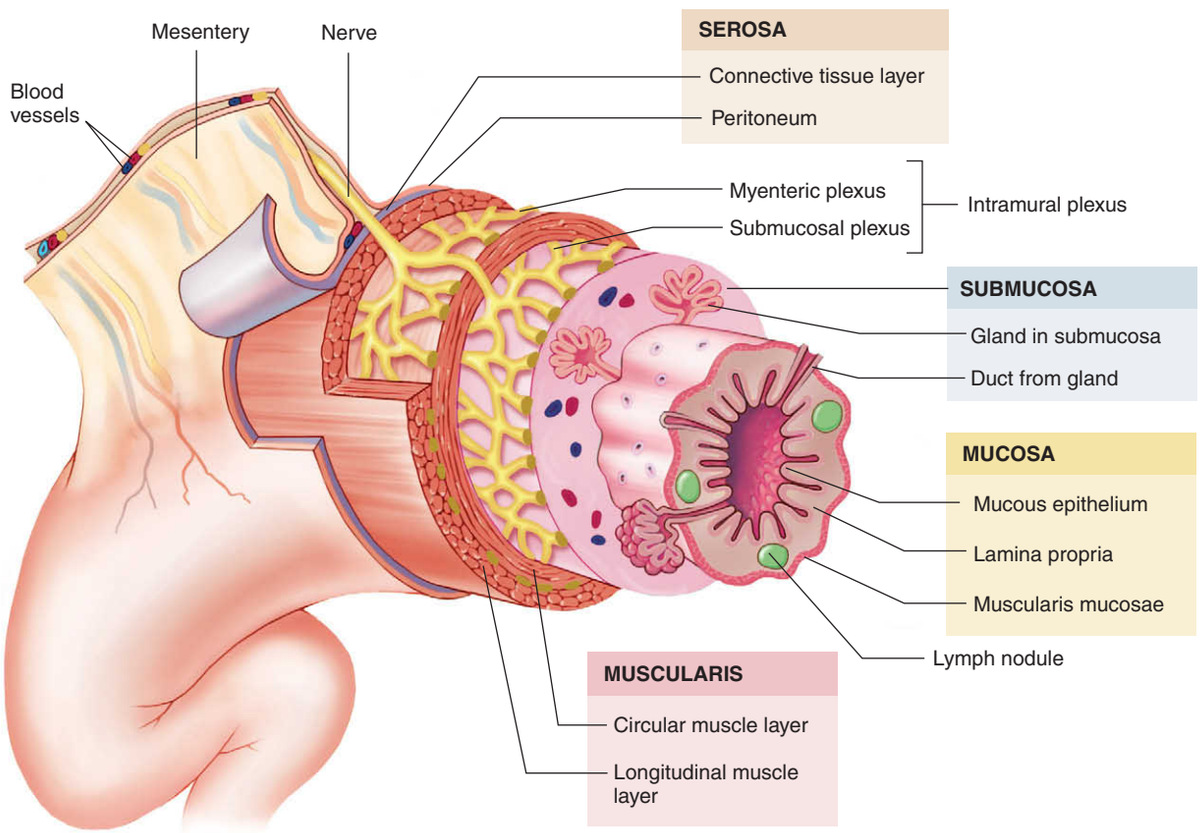


FIGURE 28-2

Wall of the GI tract. The wall of the gastrointestinal (GI) tract is made up of four layers, shown here in a generalized diagram of a segment of the GI tract. Notice that the serosa is continuous with a fold of serous membrane called a *mesentery.* Notice also that digestive glands may empty their products into the lumen of the GI tract by way of ducts.

SEROSA

The **serosa**—or *serous layer*—is the outermost layer of the GI wall. It is made up of serous membrane (see Figures 6-39 and 6-40 on pp. 639 and 640). The serosa is actually the *visceral layer* of the peritoneum—the serous membrane that lines the abdominopelvic cavity and covers its organs. The lining attached to and covering the walls of the abdominopelvic cavity is called the *parietal layer* of the peritoneum. The fold of serous membrane shown in Figure 28-2 that connects the parietal and visceral portions is called a *mesentery*.

MODIFICATIONS OF LAYERS

Although the same four tissue layers form the various organs of the GI tract, their structures vary in different regions of the tube throughout its length. Variations in the epithelial layer of the mucosa, for example, range from stratified layers of squamous cells that provide protection from abrasion in the upper part of the esophagus to the simple columnar epithelium, designed for absorption and secretion, which is found throughout most of the tract. Notice in Figure 28-2 that exocrine glands empty their secretions into the lumen of the GI tract through ducts. Some of these modifications are listed in Table 28-1; refer back to this table when each of these organs is studied in detail.

| QUICK CHECK |

1. What is another name for the digestive tract?
2. Name the four layers of the digestive tract wall.

MOUTH

Structure of the Oral Cavity

The mouth is also called the *oral cavity*. The following structures form the oral cavity *(buccal cavity)*: the lips, which surround the orifice of the mouth and form the anterior boundary of the oral cavity, the cheeks (side walls), the tongue and its muscles (floor), and the hard palate and soft palate (roof) (Figure 28-3).

LIPS

The **lips** are covered externally by skin and internally by mucous membrane that continues into the oral cavity and lines the mouth. The junction between skin and mucous membrane is highly sensitive and easily irritated. The upper lip is marked near the midline by a shallow vertical groove called the *philtrum*, which ends

TABLE 28-1 Modifications of Layers of the Digestive Tract Wall

ORGAN	MUCOSA	MUSCULARIS	SEROSA
Esophagus	Stratified squamous epithelium resists abrasion	Two layers—inner one of circular fibers and outer one of longitudinal fibers; striated muscle in the upper part and smooth muscle in the lower part of the esophagus and in the rest of the tract	Outer layer, fibrous (adventitia); serous around part of the esophagus in the thoracic cavity
Stomach	Arranged in flexible longitudinal folds called *rugae;* allow for distention; contains gastric pits with microscopic gastric glands	Has three layers instead of the usual two—circular, longitudinal, and oblique fibers; two sphincters—lower esophageal sphincter at the entrance of the stomach and pyloric sphincter at its exit, formed by circular fibers	Outer layer, visceral peritoneum; hangs in a double fold from the lower edge of the stomach over the intestines and forms an apronlike structure; greater omentum; lesser omentum connects the stomach to the liver
Small intestine	Contains permanent circular folds, plicae circulares Microscopic fingerlike projections, villi with brush border Crypts (of Lieberkühn) Microscopic duodenal (Brunner) mucous glands Aggregated lymphoid nodules (Peyer patches) Numerous single lymphoid nodules called *solitary nodules*	Two layers—inner one of circular fibers and outer one of longitudinal fibers	Outer layer, visceral peritoneum, continuous with the mesentery
Large intestine	Solitary lymph nodes Intestinal mucous glands Anal columns form in the anal region	Outer longitudinal layer condensed to form three tapelike strips (taeniae coli); small sacs (haustra) give the rest of the wall of the large intestine a puckered appearance; internal anal sphincter formed by circular smooth fibers; external anal sphincter formed by striated fibers	Outer layer, visceral peritoneum, continuous with mesocolon

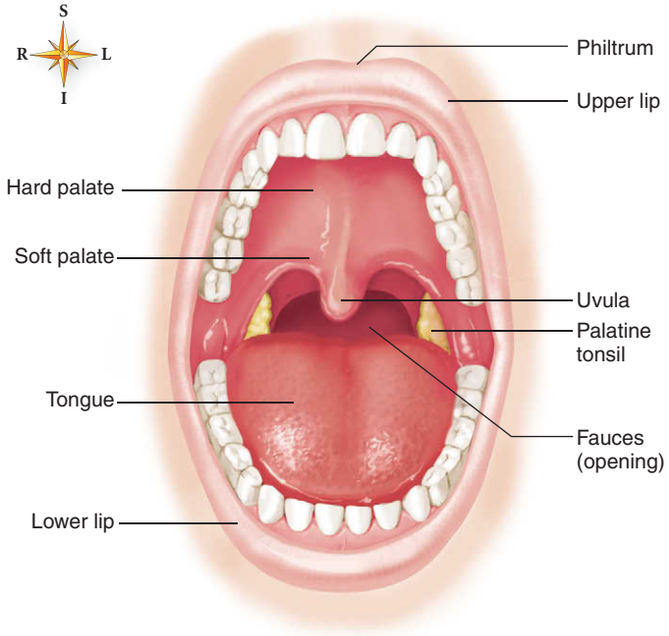


FIGURE 28-3
The oral cavity.

at the junction between skin and mucous membrane in a slight prominence called the *tubercle*. The term *fissure* is often used to describe a cleft or groove between or separating anatomical structures. Therefore, when the lips are closed, the line of contact between them is called the *oral fissure*. Besides keeping food in the mouth while it is being chewed, the lips help sense the temperature and texture of food before it enters the mouth. The lips are also needed to form many speech sounds (syllables).

CHEEKS

The **cheeks** form the lateral boundaries of the oral cavity. They are continuous with the lips in front and are lined by mucous membrane that is reflected onto the gingiva, or gums, and the soft palate. The cheeks are formed in large part by the buccinator muscle, which is sandwiched with a considerable amount of adipose, or fat, tissue between the outer skin and mucous membrane lining. Numerous small mucus-secreting glands are located between the mucous membrane and the buccinator muscle; their ducts open opposite the last molar teeth.

HARD PALATE AND SOFT PALATE

The **hard palate** consists of portions of four bones: two maxillae and two palatines (see Figure 8-5. *B* on p. 205). The **soft palate,** which forms a partition between the mouth and nasopharynx (see Figure 26-3), is fashioned of muscle arranged in the shape of an arch. The opening in the arch leads from the mouth into the oropharynx and is named the *fauces.* Suspended from the midpoint of the posterior border of the arch is a small cone-shaped process, the *uvula.*

TONGUE

The **tongue** is a solid mass of skeletal muscle components (intrinsic muscles) covered by a mucous membrane.

Note in Figure 28-4, A, that the tongue has a blunt *root*, a *tip*, and a central *body*. The upper, or dorsal, surface of the tongue is normally moist, pink, and covered by rough elevations, called *papillae* (Figure 28-4, *B*). Recall from Chapter 17 that papillae possess sensory organs called *taste buds.*

The four types of papillae—circumvallate, fungiform, foliate, and filiform—are all located on the sides or upper surface (dorsum) of the tongue. Note in Figure 28-4, A, that the large circumvallate papillae form an inverted V-shaped row extending from a

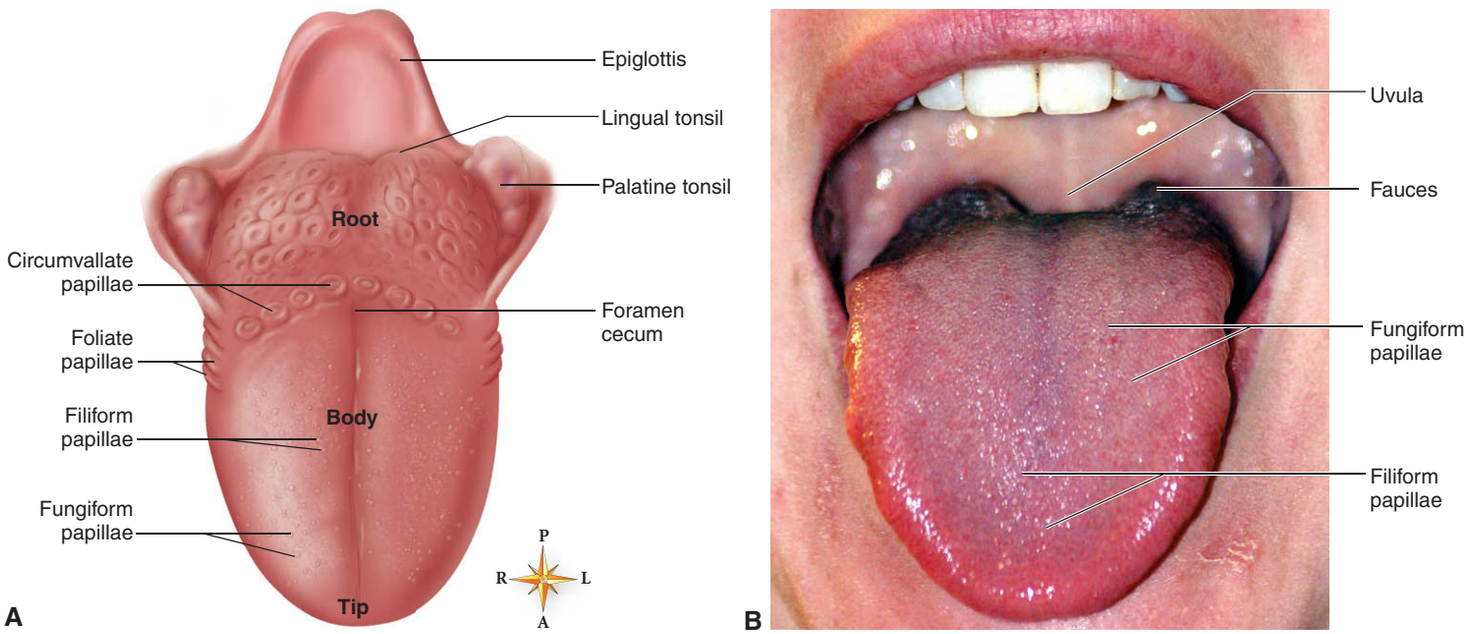


FIGURE 28-4
Dorsal surface of tongue. A, Sketch showing the three divisions of the tongue (see also Figure 17-8 on p. 516). **B,** Photograph showing rough texture of tongue produced by papillae.

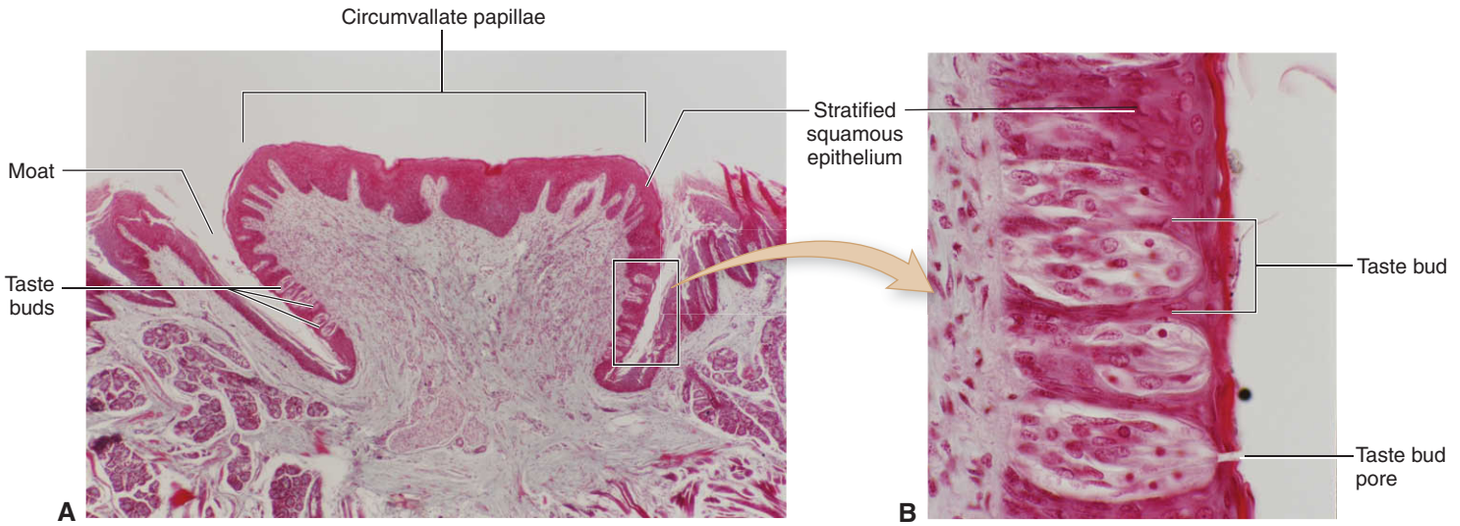


FIGURE 28-5

Circumvallate papillae on the surface of the tongue. A, Taste buds are located on the lateral surfaces of the papillae. Several taste buds can be seen opening into the moat from the sides of the papillae. (×35.) **B,** Enlargement of the photomicrograph of taste buds in **A.** The arrow points to a pore in the outer surface of the taste bud. (×40.) Compare to Figure 17-8 on p. 516.

median pit named the *foramen cecum* on the posterior part of the tongue. There are 10 to 14 of these large, mushroomlike papillae. You can readily distinguish them if you look at your own tongue. Figure 28-5 shows two micrographs of circumvallate papillae. To be tasted, a dissolved substance must enter a moatlike depression surrounding the papillae where it contacts taste buds located on the lateral surface.

Taste buds are also located on the sides of the fungiform papillae, which are found chiefly on the sides and tip of the tongue. Foliate papillae are leaflike ridges on the posterior, lateral edges of the tongue that also posses taste buds. The numerous filiform papillae are filamentous and threadlike in appearance. They have a whitish coloration and are distributed over the anterior two thirds of the tongue. Filiform papillae do not contain taste buds. Refer back to Chapter 17, p. 516, for more discussion of papillae and taste buds.

The *lingual frenulum* (Figure 28-6, A) is a fold of mucous membrane in the midline of the undersurface of the tongue that helps anchor the tongue to the floor of the mouth. If the frenulum is too short and hinders tongue movement—a congenital condition called *ankyloglossia*—the individual is said to be tongue-tied; this causes faulty speech (Figure 28-6, *B*).

A fold of mucous membrane called the *fimbriated fold* (or *plica fimbriata*) (see Figure 28-6, A) extends toward the apex of the tongue on either side of the lingual frenulum. The floor of the mouth and

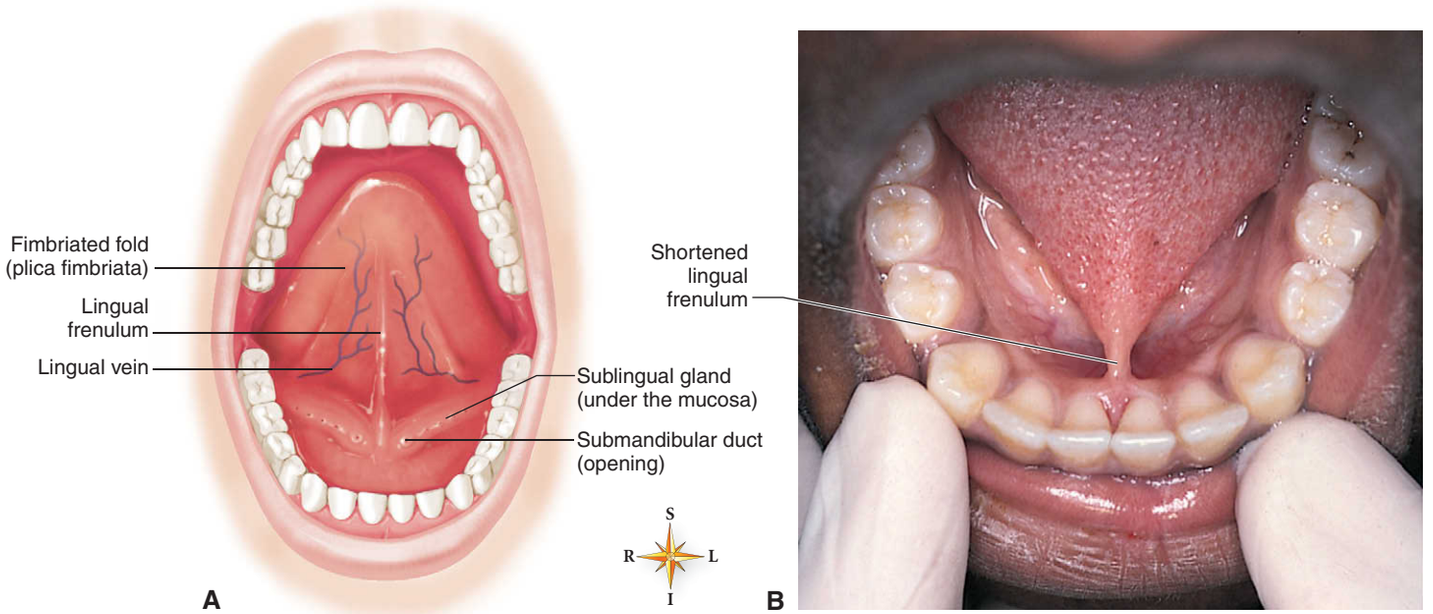


FIGURE 28-6

Floor of mouth. A, Floor of mouth and ventral surface of tongue. **B,** Photo showing ankyloglossia—characterized by an abnormally short lingual frenulum.

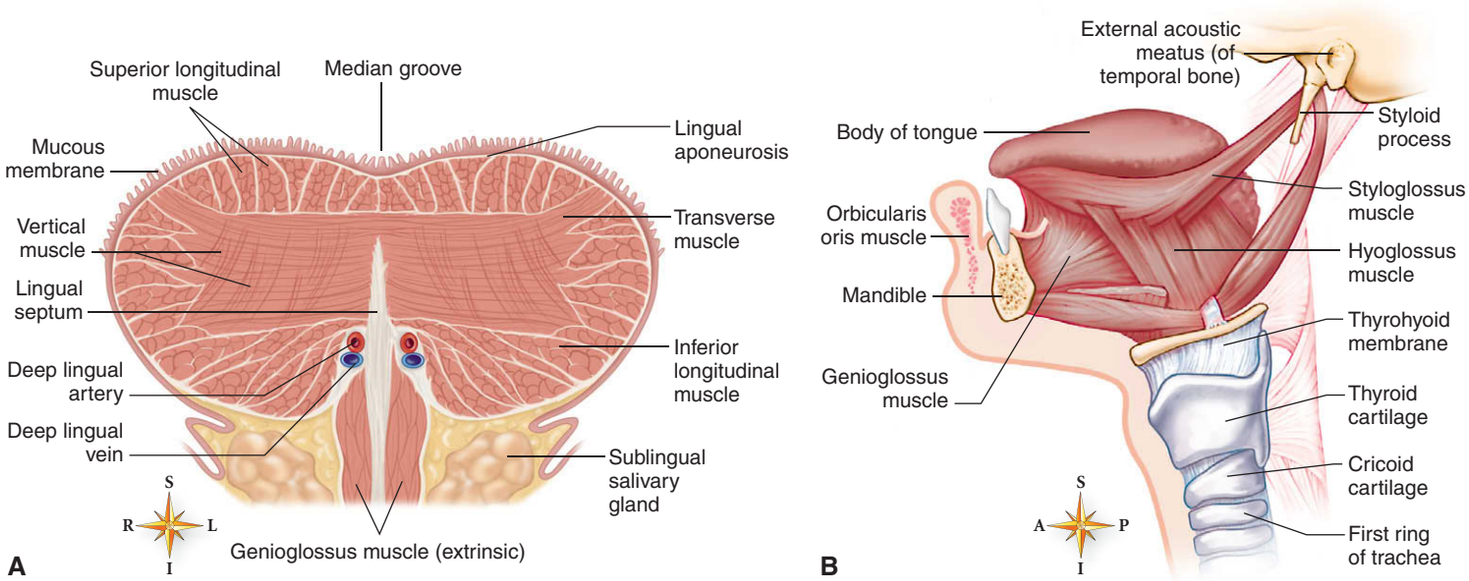


FIGURE 28-7

Muscles of the tongue. A, Intrinsic muscles of the tongue shown in a frontal section. **B,** Extrinsic muscles of the tongue.

undersurface of the tongue are richly supplied with blood vessels. The deep lingual vein can be seen (see Figure 28-6, *A*) shining through the mucous membrane between the lingual frenulum and fimbriated fold. In this region many vessels are extremely superficial and are covered only by a very thin layer of mucosa. Soluble drugs, such as aspirin or nitroglycerin used during a heart attack, are absorbed into the circulation rapidly if placed under the tongue.

The intrinsic muscles of the tongue have, by definition, both their origin and their insertion in the tongue itself. As you can see in Figure 28-7, *A*, intrinsic muscles have their fibers oriented in all directions, thus providing a basis for extreme maneuverability. Changes in the size and shape of the tongue caused by intrinsic muscle contraction assist in placement of food material between the teeth during **mastication** (chewing). Such movements are also necessary for forming speech syllables properly.

Extrinsic tongue muscles are those that insert into the tongue but have their origin on some other structure, such as the hyoid bone or one of the bones of the skull. Examples of extrinsic tongue muscles are the genioglossus, which protrudes the tongue, and the hyoglossus, which depresses it (see Figure 28-7, *B*). Contraction of the extrinsic muscles is important during **deglutition,** or swallowing, and speech.

Salivary Glands

The salivary glands are typical of the accessory glands associated with the digestive system. They are located outside the alimentary canal and convey their exocrine secretions by way of ducts from the glands into the lumen of the tract (Figure 28-8, *A*). The mucous and serous cells seen in the compound tubuloalveolar gland pictured in Figure 28-8, *B*, together secrete a mixture of fluids that are then

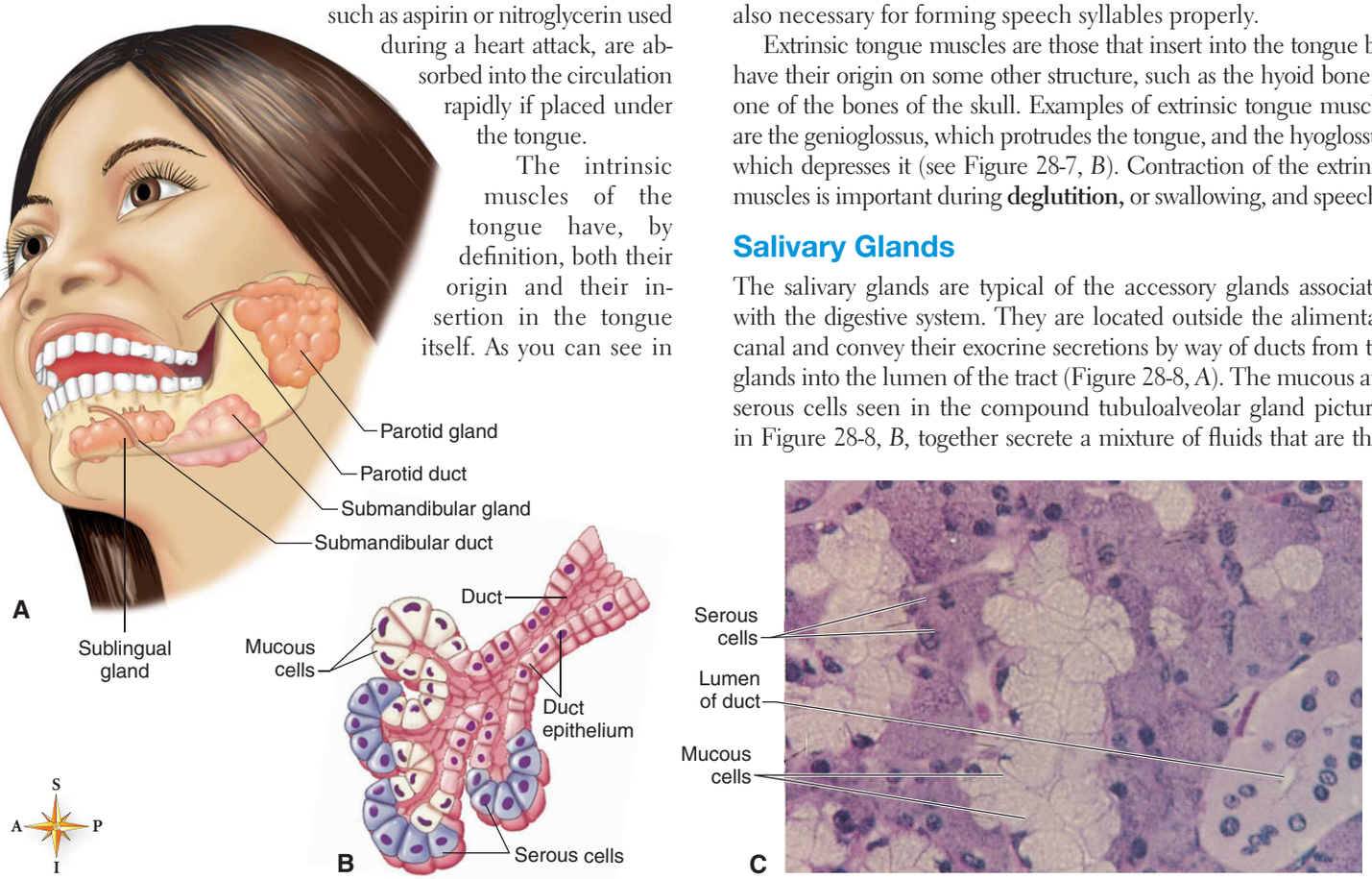


FIGURE 28-8

Salivary glands. A, Location of the salivary glands. **B** and **C,** Detail of submandibular salivary gland. This mixed- or compound-type gland produces mucus from mucous cells and enzymatic secretion from serous cells. Duct cross sections are also visible. (×140.)

modified by the duct cells on their way out of the salivary gland. The functions of saliva in the digestive process are discussed in Chapter 29.

Three pairs of major salivary glands (see Figure 28-8)—the parotid, submandibular, and sublingual glands—secrete a major amount (about 1 liter) of the saliva produced each day. The minor salivary glands (*buccal glands*) that occur in the mucosa lining the cheeks and mouth contribute less than 5% of the total salivary volume. Buccal gland secretion is important, however, to the hygiene and comfort of the mouth tissues.

PAROTID GLANDS

The pyramidal **parotids** are the largest of the paired salivary glands (see Figure 28-8, *A*). They are located between the skin and underlying masseter muscle in front of and below the external ear. The parotids produce a watery, or serous, type of saliva containing enzymes but not mucus. The parotid (Stensen) ducts are about 5 cm (2 inches) long. They penetrate the buccinator muscle on each side and open into the mouth through the *parotid papilla* opposite the upper second molars. Inflammation of the parotids is called **mumps** or **parotitis** and is caused by *paramyxovirus* (see Mechanisms of Disease, p. 888).

SUBMANDIBULAR GLANDS

Submandibular glands (see Figure 28-8, A) are called *mixed* or *compound glands* because they contain both serous (enzyme) and mucus-producing elements (see Figure 28-8, *B* and *C*). These glands are located just below the mandibular angle. You can feel the gland by placing your index finger on the posterior part of the floor of the mouth and your thumb medial to and just in front of the angle of the mandible. The gland is irregular in form and about the size of a walnut. The ducts of the submandibular glands (Wharton ducts) open into the mouth on either side of the lingual frenulum.

SUBLINGUAL GLANDS

Sublingual glands are the smallest of the main salivary glands (see Figure 28-8, A). They lie in front of the submandibular glands, under the mucous membrane covering the floor of the mouth. Each sublingual gland is drained by 8 to 20 ducts (ducts of Rivinus) that open into the floor of the mouth. Unlike the other salivary glands, the sublingual glands produce only a mucous type of saliva.

Teeth

The teeth are the organs of *mastication*, or chewing. They are designed to cut, tear, and grind ingested food so that it can be mixed with saliva and swallowed. During the process of mastication, food is ground into small bits. This increases the surface area that can be acted on by the digestive enzymes.

TYPICAL TOOTH

A typical tooth (Figure 28-9) can be divided into three main parts: crown, neck, and root. The **crown** is the exposed portion of a tooth. It is covered by enamel—the hardest and chemically most stable tissue in the body. Enamel consists of approximately 97% calcified (inorganic) material and only 3% organic material and water. It is ideally suited to withstand the very abrasive process of mastication. The *neck* of a tooth is the narrow portion shown in Figure 28-9 that is surrounded by the gingivae, or gums. It joins the crown of the tooth to the root. It is the **root** that fits into the socket of the alveolar process of either the upper or lower jaw.

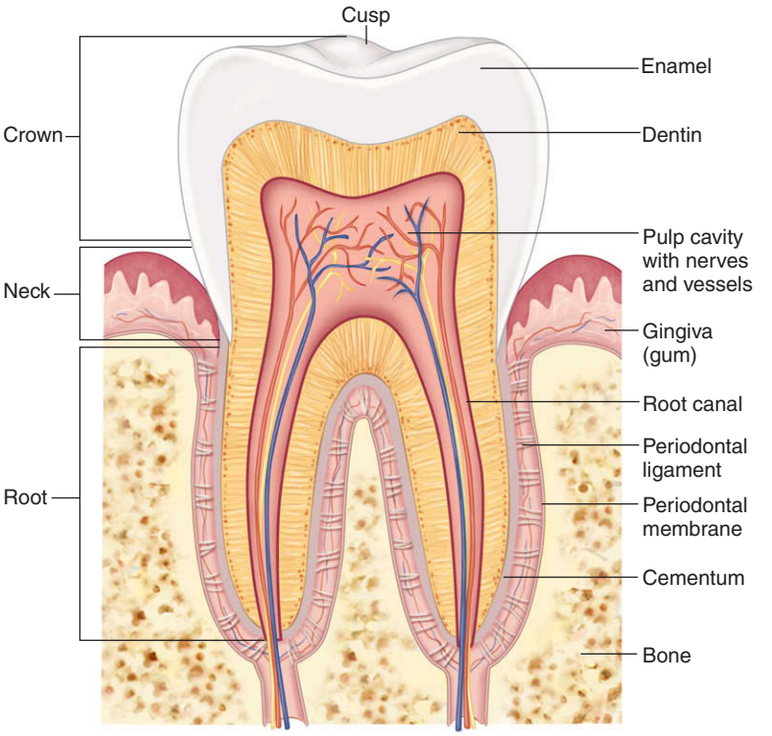


FIGURE 28-9

Typical tooth. A molar tooth sectioned to show its bony socket and details of its three main parts: crown, neck, and root. Enamel (over the crown) and cementum (over the neck and root) surround the dentin layer. The pulp contains nerves and blood vessels.

The root of a tooth may be a single peglike structure or consist of two or three separate conical projections. The root is not rigidly anchored to the alveolar process by cement but is suspended in the socket by the fibrous *periodontal membrane* (see Figure 28-9).

In addition to enamel, the outer shell of each tooth is composed of two additional dental tissues—*dentin* and *cementum* (see Figure 28-9). Dentin makes up the greatest proportion of the tooth shell. It is covered by enamel in the crown and by cementum in the neck and root area. The dentin contains a **pulp cavity** consisting of connective tissue, blood and lymphatic vessels, and sensory nerves.

TYPES OF TEETH

Dentition is the type, number, and arrangement of teeth in the jaws.

Twenty primary or **deciduous teeth,** or so-called *baby teeth,* appear early in life and are later replaced by 32 **permanent teeth** (Figure 28-10). The names and numbers of teeth in both sets are given in Table 28-2. The first deciduous tooth usually erupts at about 6 months of age. The remainder follow at the rate of one or more a month until all 20 have appeared. There is, however, great individual variation in the age at which teeth erupt. Deciduous teeth are generally shed between the ages of 6 and 13 years. The third molars (wisdom teeth) are the last to appear, and usually erupt sometime after 17 years of age.

Teeth in the upper jaw are called *maxillary teeth* because they are in the maxilla bone of the skull. Teeth in the lower jaw are called *mandibular teeth* because they are anchored in the mandible bone. Deciduous teeth are identified by either name or capital Roman letters (A, B, C, etc.) applied in a clockwise direction, as you can see in Figure 28-10. Permanent teeth are likewise identified by name or by Arabic numeral (1, 2, 3, etc.) in a clockwise direction.

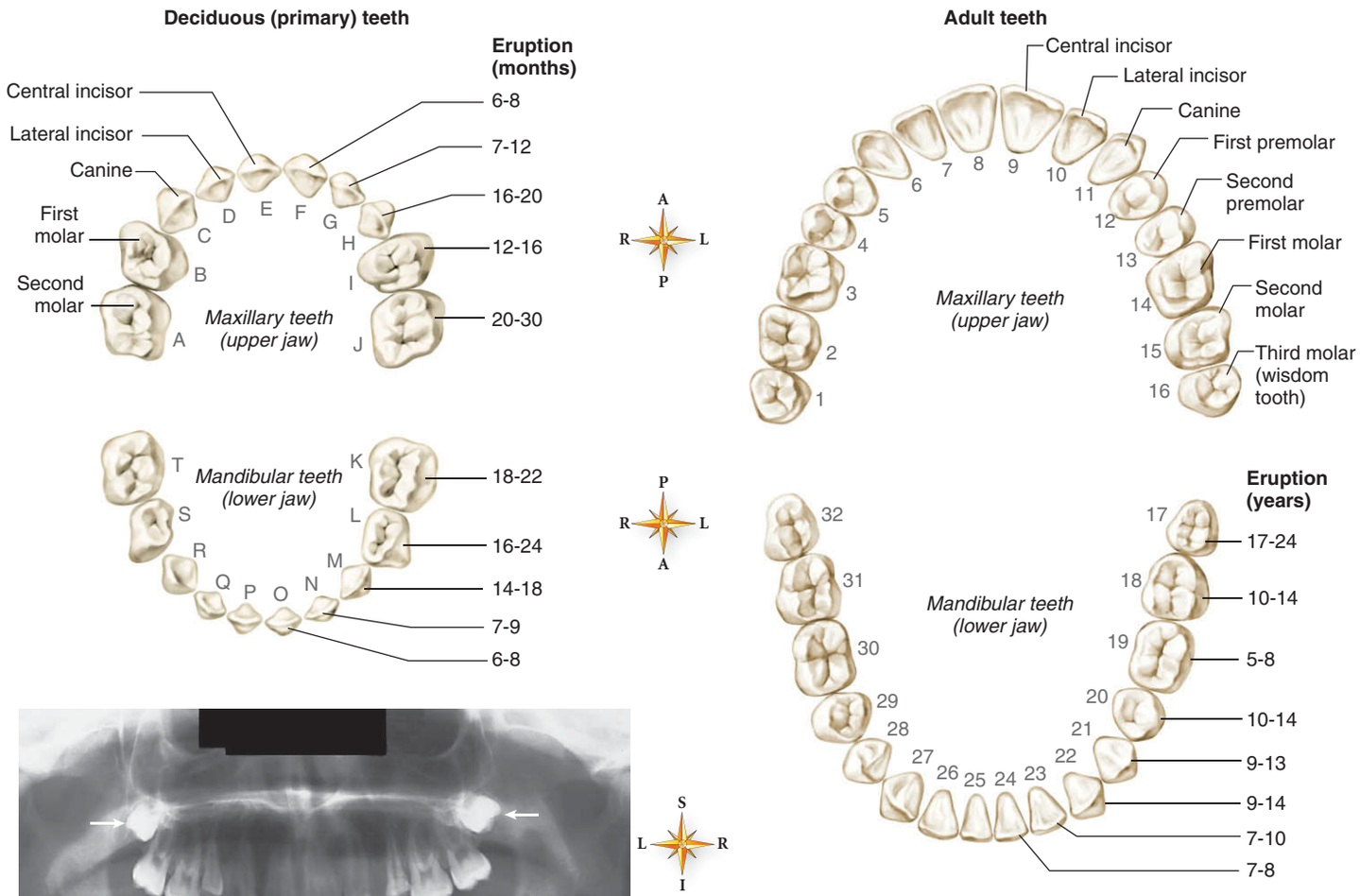


FIGURE 28-10

Dentition. In the deciduous set, where letters are used in place of numbers, there are no premolars and only two pairs of molars in each jaw. Generally, the lower teeth erupt before the corresponding upper teeth. The photo inset is a "Panorex" dental x ray. It displays the full dentition in a single "flattened-out" image. Arrows show the third molars or "wisdom teeth" that have not yet erupted.

| A&P CONNECT |

An epidemic of methamphetamine abuse has resulted in a number of health problems including "meth mouth." See an example of this disorder and learn about its causes in ***Meth Mouth*** online at ***A&P Connect.***

| QUICK CHECK |

3. What are the boundaries of the oral cavity?
4. Describe the location of the taste buds in the mouth.
5. What are the names of the three types of salivary glands?
6. How do the names of the salivary glands describe their locations?
7. What are the three main parts of a typical tooth?

TABLE 28-2 Dentition

	NUMBER PER JAW (UPPER OR LOWER)	
NAME OF TOOTH	DECIDUOUS SET	PERMANENT SET
Central incisors	2	2
Lateral incisors	2	2
Canines (cuspids)	2	2
Premolars (bicuspids)	0	4
First molars (tricuspids)	2	2
Second molars	2	2
Third molars (wisdom teeth)	0	2
TOTAL (per jaw)	10	16
TOTAL (per set)	20	32

PHARYNX

The act of swallowing, or **deglutition,** moves a rounded mass of food, called a *bolus*, from the mouth to the stomach. As the food bolus passes from the mouth, it enters the oropharynx by passing through a constricted, archlike opening called the *fauces*. The oropharynx is the second division of the pharynx (see Figure 26-3). During respiration, air passes through all three pharyngeal divisions. However, only the terminal portions of the pharynx serve the digestive system. Once a bolus has passed through the pharynx, it enters the digestive tube proper—the portion of the digestive tract that serves only the digestive system. The anatomy of the pharynx is discussed in more detail in Chapter 26 on pp. 802–803.

| A&P CONNECT |

The ring of tonsils in the pharynx defends both the digestive tract and respiratory tract from infection. Visualize the tonsils and review their defensive role in ***Protective Strategies of the Respiratory Tract*** online at ***A&P Connect.***

ESOPHAGUS

The **esophagus** (eh-SOFF-ah-gus), a collapsible, muscular, mucosa-lined tube about 25 cm (10 inches) long, extends from the pharynx to the stomach and pierces the diaphragm in its descent from the thoracic cavity to the abdominal cavity (Figure 28-11). It lies posterior to the trachea and heart and serves as a dynamic passageway for food, pushing the food toward the stomach. The short portion of the esophagus in the neck is called the *cervical part*, the portion in the thorax is called the *thoracic part*, and the short portion in the abdomen is called the *abdominal part*.

The esophagus is the first segment of the digestive tube proper, and the four layers that form the wall of the GI tract organs can be identified there (Figure 28-12, A). The esophagus is normally flattened, and thus the lumen is practically nonexistent in the resting state. The stratified squamous epithelium of the esophageal mucosa seen in Figure 28-12 provides a thick, abrasion-resistant lining that protects the esophagus from injury. The inner circular and outer longitudinal layers of the muscular layer are striated (voluntary) in the upper third, mixed (striated and smooth) in the middle third, and smooth (involuntary) in the lower third of the tube.

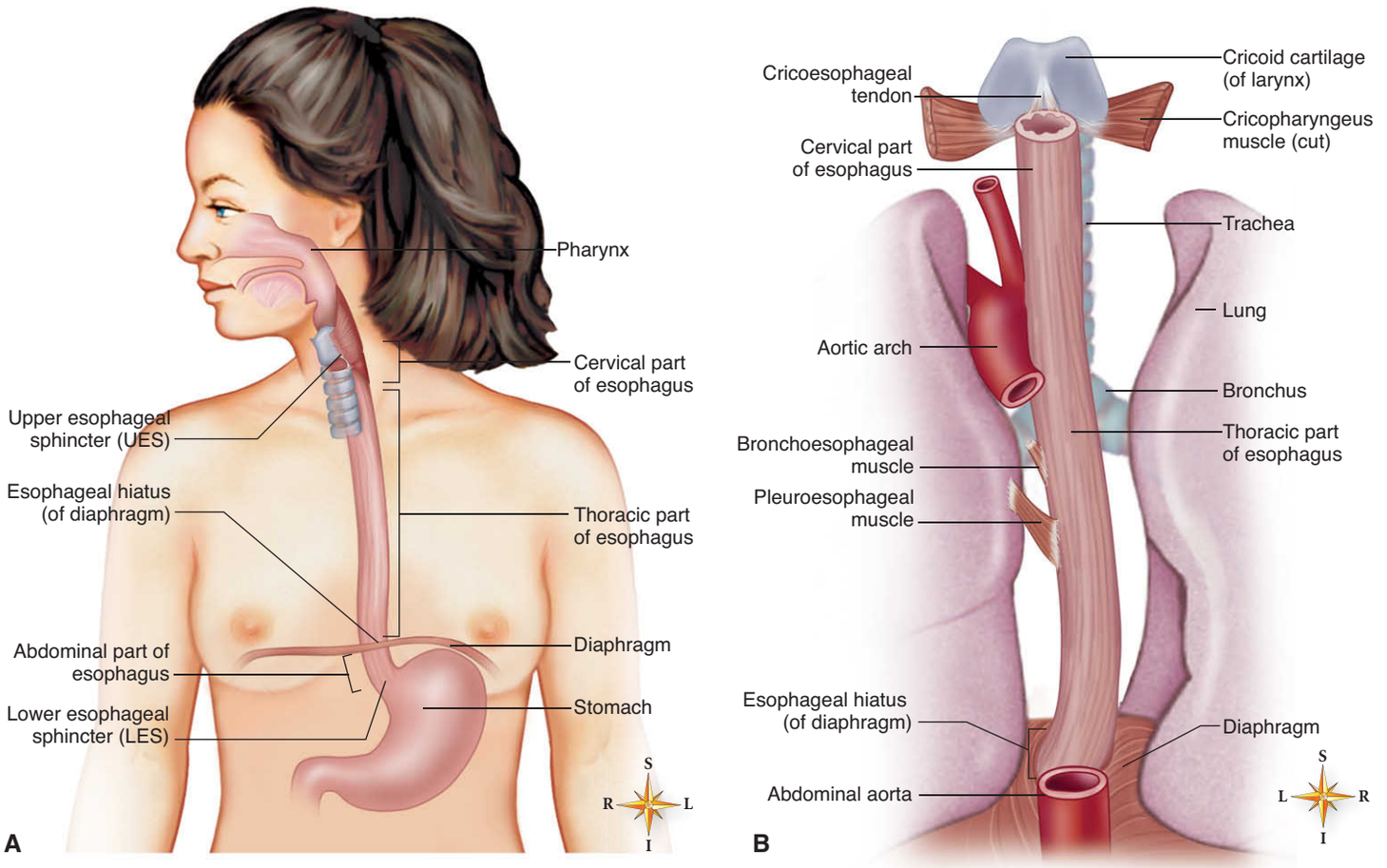


FIGURE 28-11

Esophagus. A, Diagram showing the major features of the esophagus. **B,** View of the muscular wall of the esophagus from behind, showing its position relative to other structures.

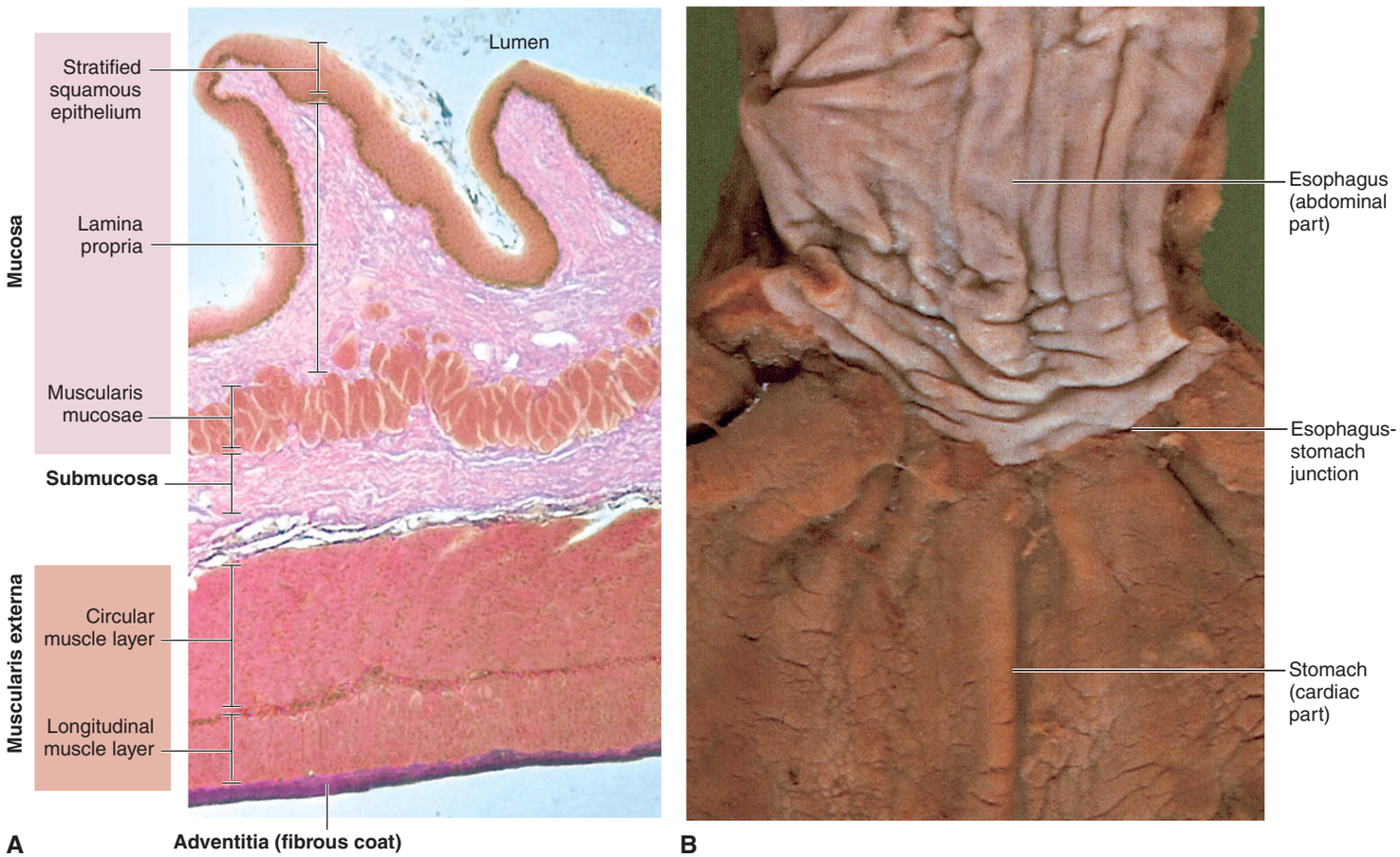


FIGURE 28-12

Wall of esophagus. A, The four layers of the gastrointestinal (GI) wall are easily identified in this microscopic cross section of the esophagus (see Table 28-1). **B,** Cadaver dissection photograph of the mucosal lining at the junction between the lower part of the esophagus and the stomach—a frequent site of irritation caused by reflux of acidic gastric secretions.

Each end of the esophagus is encircled by muscular sphincters that act as valves to regulate passage of material. The **upper esophageal sphincter (UES)** in the cervical part of the esophagus helps prevent air from entering the esophagus during respiration. The UES is made up of several muscles, but the *cricopharyngeus muscle* (see Figure 28-11, *B*) that wraps around the back of the cervical esophagus plays the primary role. Relaxation of the UES is what permits *belching* (or *burping*), which is the sudden escape of air trapped in the stomach and esophagus.

The **lower esophageal sphincter (LES)** is also called the *cardiac sphincter* or *cardial sphincter.* The intrinsic part of the LES is located at the junction with the stomach and is made up of layers of circular muscle that are thicker than in other parts of the esophagus. Slinglike oblique muscles from the stomach wall also form part of the LES, adding to its strength in containing the stomach contents while the stomach is full and churning. The muscles of the diaphragm at the *esophageal hiatus*—an opening in the diaphragm located near the junction between the terminal portion of the esophagus and the stomach—form the extrinsic part of the LES.

The esophageal hiatus in the diaphragm, which permits passage of the esophagus into the abdomen, may become stretched or otherwise enlarged. Such enlargement may permit bulging of the lower segment of the esophagus and intrinsic LES and part or even all of the stomach upward through the diaphragm and into the chest. The condition is called a **hiatal** (hye-AYT-al) **hernia.**

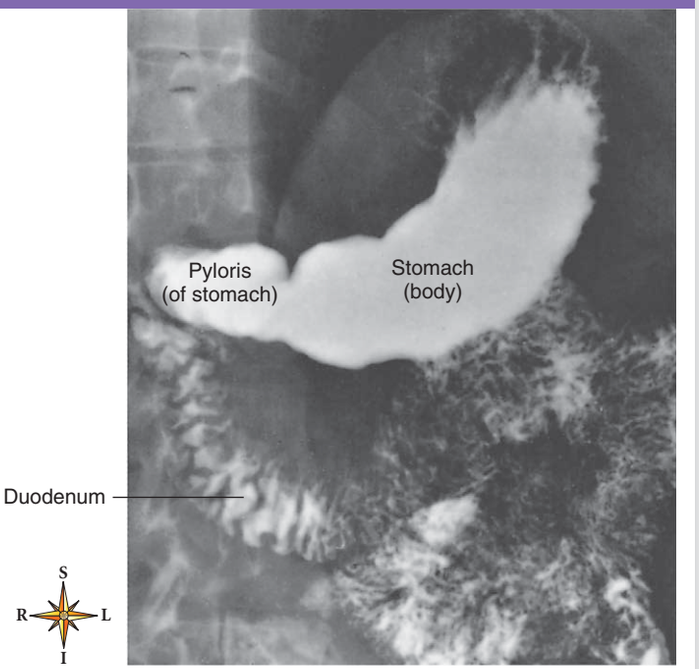
Gastroesophageal reflux disease, or **GERD,** is the term used to describe the backward flow of stomach acid up through the LES and into the lower part of the esophagus. It often causes a painful sensation called *heartburn.* Being a potentially serious medical condition, GERD is treated by elimination of the underlying causes, such as a hiatal hernia, by drugs to reduce excess

Box 28-2 | DIAGNOSTIC study

Upper Gastrointestinal X Ray Study

An upper GI (UGI) study consists of a series of x rays of the lower part of the esophagus, stomach, and duodenum, usually with barium sulfate used as the contrast medium. The test is used to detect ulcerations, tumors, inflammation, or anatomical malpositions such as *hiatal hernia* (distention of the diaphragm that allows the stomach to protrude). Obstruction of the upper GI tract is also easily detected.

In this test the patient is asked to drink a flavored liquid containing barium sulfate. As the contrast medium travels through the system, the lower portion of the esophagus, gastric wall, pyloric channel, and duodenum are each evaluated for defects. Benign peptic ulcer is a common pathological condition affecting these areas. Tumors, cysts, or enlarged organs near the stomach can also be identified by an anatomical distortion of the outline of the upper GI tract. Can you identify the outline of the stomach in the figure?



X ray film of the lower part of the esophagus, stomach, and duodenum.

stomach acid, or by surgery to reduce the lumen size or strengthen the LES (see Mechanisms of Disease on p. 890). Box 28-2 describes a method for imaging a hiatal hernia and other problems of the esophagus and stomach.

The junction between the lower part of the esophagus and stomach (see Figure 28-12, *B*) is an important site for a number of pathologic conditions, many associated with repeated exposure to acid gastric secretions. In the last 1- to 1.5-cm-long abdominal part of the esophagus below the diaphragm, stratified squamous epithelium is replaced by columnar epithelium. It is this area of transition that is often damaged by exposure to acid and digestive enzymes from the stomach. The area of transition between the lower part of the esophagus and stomach is clearly visible in Figure 28-12, *B*. The stratified squamous epithelial lining of the esophagus appears pale, whereas the columnar gastric epithelium appears brown.

STOMACH

Size and Position of the Stomach

Just below the diaphragm, the digestive tube dilates into an elongated pouchlike structure, the stomach (Figure 28-13), the size of which varies according to several factors, notably the amount of distention. For some time after a meal, the stomach is enlarged because of distention of its walls, but as food passes out of the stomach, the walls partially collapse, leaving the organ about the size of a large sausage. In adults, the stomach usually holds a volume of up to 1 to 1.5 liters.

The stomach lies in the upper part of the abdominal cavity under the liver and diaphragm, with approximately five sixths of its mass to the left of the median line (see Figure 28-1). In other words, it is described as lying in the *epigastrium* and left *hypochondrium* (see Figure 1-7, p. 14). Its position, however, alters frequently. For example, it is pushed downward with each inspiration and upward with each expiration. When it is greatly distended from an unusually large meal, its size interferes with descent of the diaphragm on inspiration, thereby producing the familiar feeling of *dyspnea* (breathing difficulty) that accompanies overeating. In this state, the stomach also pushes upward against the heart and may give rise to the sensation that the heart is being crowded.

Divisions of the Stomach

The **fundus, body,** and **pylorus** are the major divisions of the stomach. The fundus is the enlarged portion to the left and above the opening of the esophagus into the stomach. The body is the central part of the stomach, and the pylorus is its lower portion (see Figure 28-13). The small collar or margin of the stomach at its junction with the esophagus is often called the **cardia** or *cardiac part* (or *cardial part*).

Curves of the Stomach

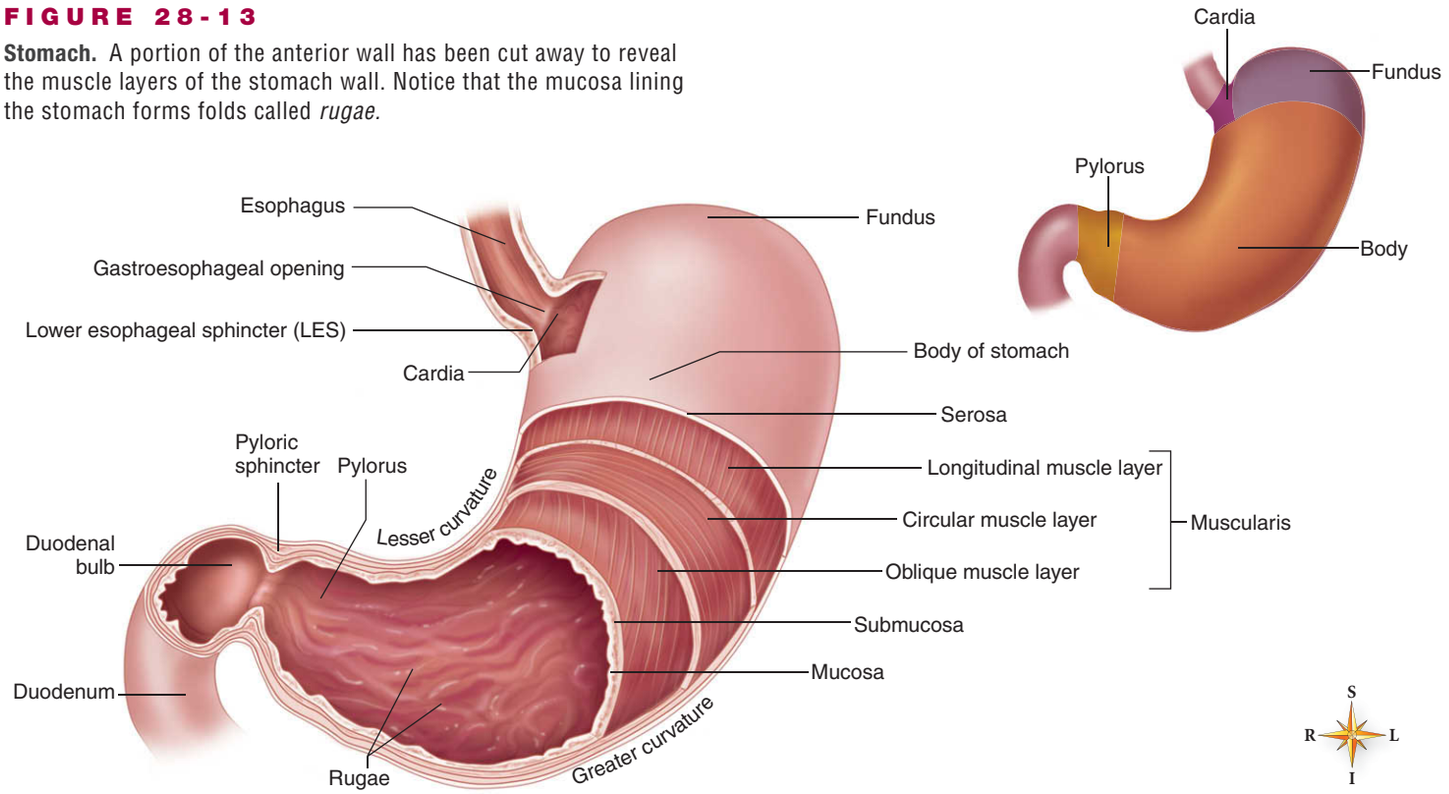
The curve formed by the upper right surface of the stomach is known as the *lesser curvature;* the curve formed by the lower left surface is known as the *greater curvature* (see Figure 28-13).

Sphincter Muscles

Sphincter muscles regulate passage of material at both stomach openings. A sphincter muscle, as you know, consists of circular fibers arranged to form an opening in the center of them (like the

FIGURE 28-13

Stomach. A portion of the anterior wall has been cut away to reveal the muscle layers of the stomach wall. Notice that the mucosa lining the stomach forms folds called *rugae.*



hole in a doughnut) when they are relaxed and no opening when they are fully contracted.

The *lower esophageal sphincter (LES)*, or *cardiac sphincter*, controls the opening of the esophagus into the stomach, and the **pyloric sphincter** controls the opening from the pyloric portion of the stomach into the first part of the small intestine (duodenum).

Stomach Wall

Each of the four layers of the stomach wall suits the function of this organ, as summarized in Table 28-1 (p. 863) and shown in Figures 28-13 and 28-14. Of particular interest are the modifications to the stomach mucosa and muscularis, both of which are briefly described below.

GASTRIC MUCOSA

The epithelial lining of the stomach is thrown into folds, called *rugae*, and marked by depressions called *gastric pits*. Numerous coiled

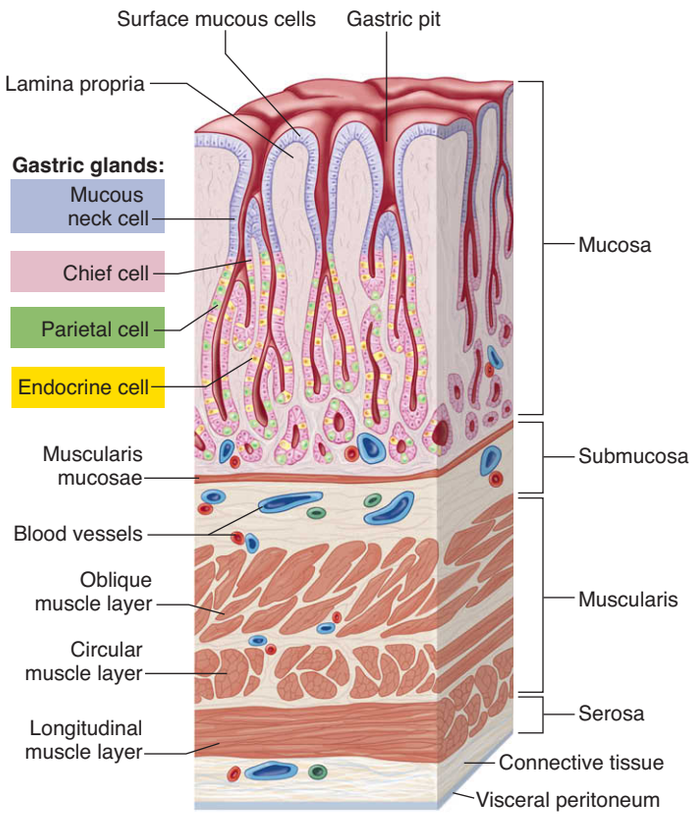


FIGURE 28-14

Gastric pits and gastric glands. Gastric pits are depressions in the epithelial lining of the stomach. At the bottom of each pit is one or more tubular *gastric glands.* Chief cells produce the enzymes of gastric juice, and parietal cells produce stomach acid. Endocrine cells secrete the appetite-boosting hormone ghrelin.

tubular-type glands, *gastric glands*, are found below the level of the pits, particularly in the fundus and body of the stomach. Figure 28-14 illustrates the anatomical relationship of the gastric pits and gastric glands. The glands secrete most of the gastric juice, a mucous fluid containing digestive enzymes and hydrochloric acid (HCl). Figure 28-15, *A*, a low-power micrograph of the mucosal lining in the body of the stomach, shows numerous gastric pits and a uniform underlying layer of coiled gastric glands. The mucosal lining is easily differentiated from the deeper submucosal layer in this section. Figure 28-15, *B*, shows an enlarged view of gastric pits and gastric glands isolated from the submucosa and surrounding tissues.

In addition to the mucus-producing cells that cover the entire surface of the stomach and line the pits, the gastric glands contain three major secretory cells—**chief cells, parietal cells,** and **endocrine cells** (see Figure 28-14). Chief cells (zymogenic cells) secrete the enzymes of gastric juice. Parietal cells secrete hydrochloric acid and are also thought to produce the important substance known as *intrinsic factor*. Intrinsic factor binds to vitamin B_{12} molecules to protect them from digestive juices until they reach the small intestine—and then facilitates the absorption of B_{12}. Endocrine cells secrete *ghrelin (GHRL)*—a hormone that stimulates the hypothalamus to secrete growth hormone and increase appetite—and *gastrin*, which influences digestive functions. The roles of the gastric secretory cells are explored further in Chapter 29.

GASTRIC MUSCLE

The thick layer of muscle in the stomach wall—the **muscularis**—is made of three distinct sublayers of smooth muscle tissue. As Figure 28-13 shows, there is the usual layer of longitudinal muscles and circular muscles, as well as an additional, underlying oblique layer. The crisscrossing pattern of smooth muscle fibers formed by this arrangement gives the stomach wall the ability to contract strongly at many angles—thus making the mixing action of this organ very efficient.

Functions of the Stomach

The stomach performs the following functions:

- Serves as a food reservoir, its main function; food is stored in the stomach until it can be partially digested and moved farther along the gastrointestinal tract.

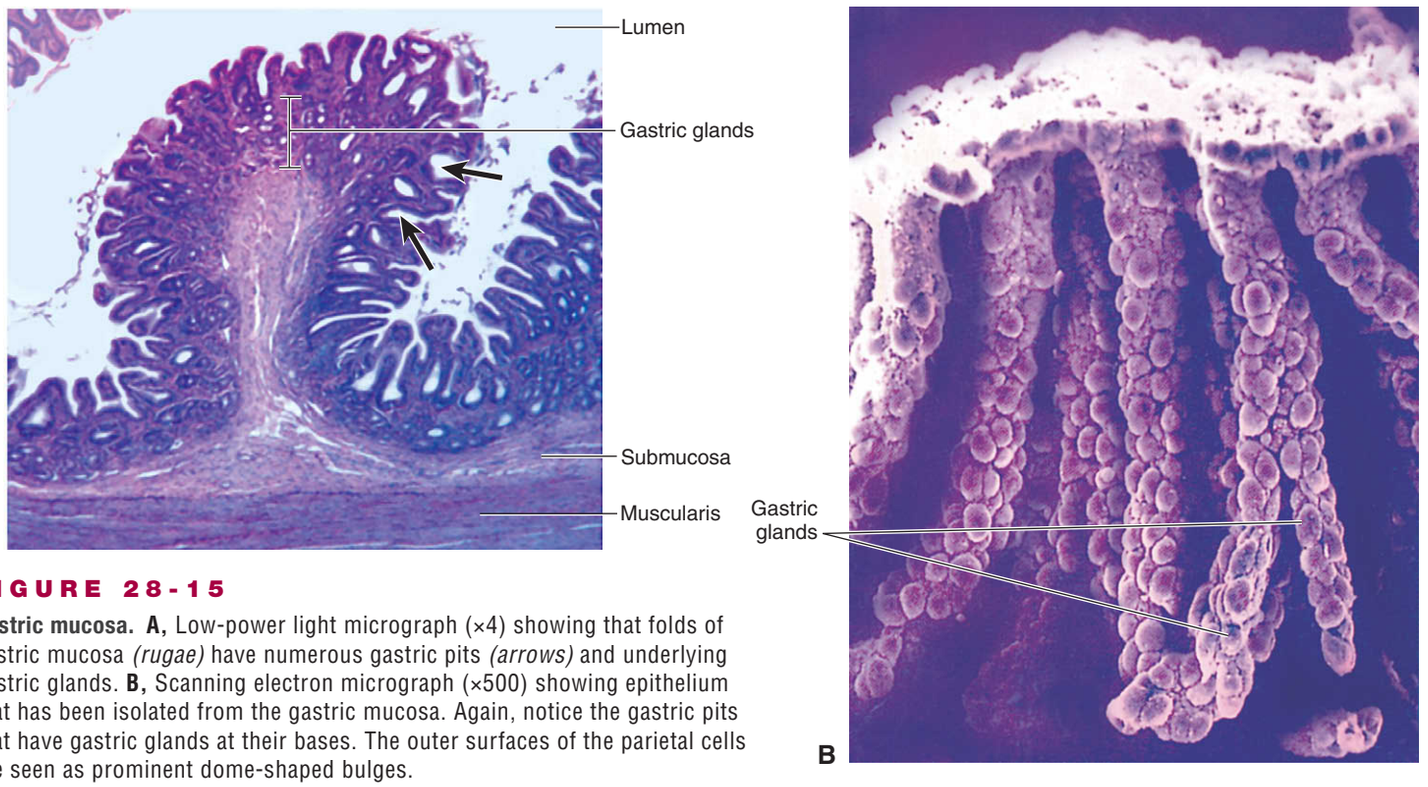


FIGURE 28-15

Gastric mucosa. A, Low-power light micrograph (×4) showing that folds of gastric mucosa *(rugae)* have numerous gastric pits *(arrows)* and underlying gastric glands. **B,** Scanning electron micrograph (×500) showing epithelium that has been isolated from the gastric mucosa. Again, notice the gastric pits that have gastric glands at their bases. The outer surfaces of the parietal cells are seen as prominent dome-shaped bulges.

- Secretes *gastric juice*, which contains acid and enzymes that aid in the digestion of food.
- Churns the food (by contractions of its muscular coat), breaking it into small particles and mixing them well with the gastric juice; in time, gastric contents are moved along into the duodenum.
- Secretes *intrinsic factor.*
- Performs a limited amount of absorption; absorbed substances include certain drugs, some water, alcohol, and some short-chain fatty acids found in butter or milk fat.
- Produces the hormones *gastrin*, which helps regulate digestive functions, and *ghrelin (GHRL)*, which increases appetite.
- Helps protect the body by destroying pathogenic bacteria swallowed with food or with mucus from the respiratory tract.

The digestive functions of the stomach are discussed further in Chapter 29.

| QUICK CHECK |

8. What is the primary digestive function of the pharynx?
9. Describe the location of the esophagus.
10. What are the three main divisions of the stomach?
11. What are gastric pits?

SMALL INTESTINE

Size and Position of the Small Intestine

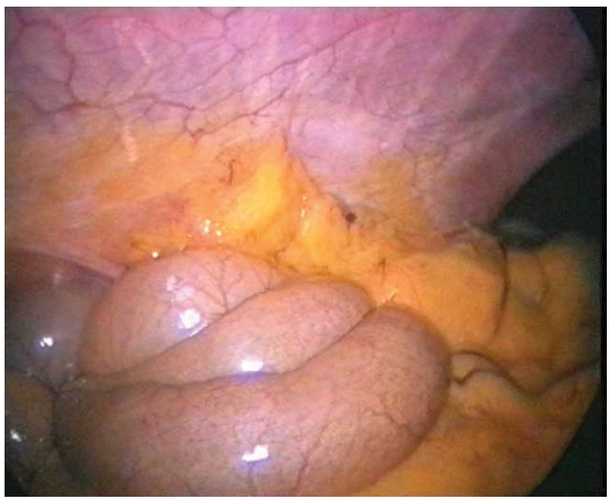
The small intestine is a tube measuring about 2.5 cm (1 inch) in diameter and 6 m (20 feet) in length. Its coiled loops fill most of the abdominal cavity (see Figures 28-1 and 28-16).

Divisions of the Small Intestine

The small intestine consists of three divisions: the duodenum, the jejunum, and the ileum. The **duodenum** is the uppermost division and the part to which the pyloric end of the stomach attaches. It is about 25 cm (10 inches) long and is shaped roughly like the letter C. The name *duodenum*, meaning "12 fingerbreadths," refers to the short length of this intestinal division. The duodenum becomes **jejunum** at the point where the tube turns abruptly forward and downward. The jejunal portion continues for approximately the next 2.5 m (8 feet), at the end of which it becomes the **ileum,** but without any clear line of demarcation between the two divisions. The ileum is about 3.5 m (12 feet) long.



A



B

FIGURE 28-16

Viewing the small intestine. A, Anteroposterior (AP) x ray image obtained during a contrast (barium-enhanced) study of the small intestine. The individual is lying supine on the x ray table. **B,** Laparoscopic view of the small intestine.

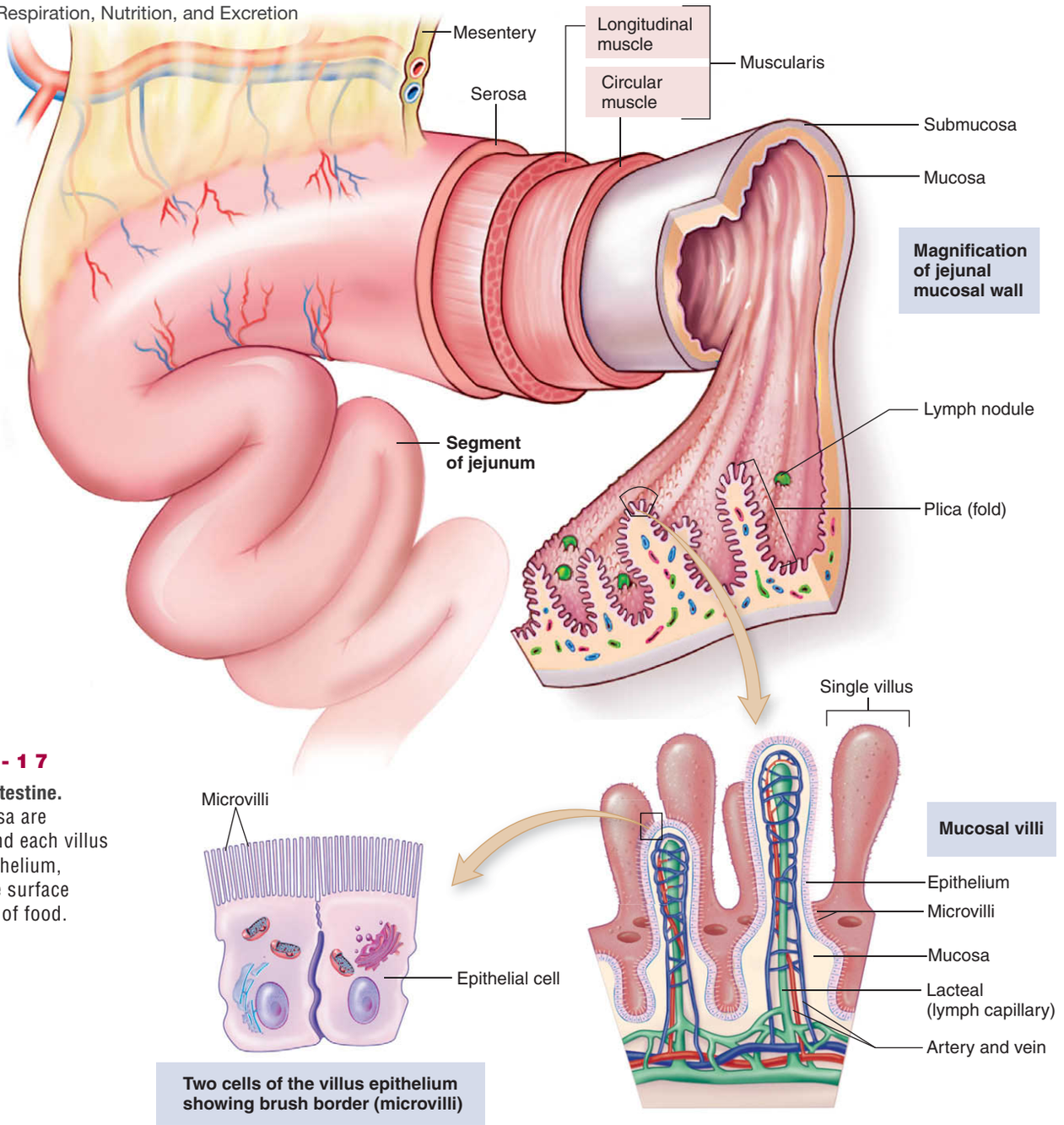


FIGURE 28-17

Wall of the small intestine. Note folds of mucosa are covered with villi and each villus is covered with epithelium, which increases the surface area for absorption of food.

Wall of the Small Intestine

Notice in Figure 28-17 that the intestinal lining has circular *plicae* (folds) that have many tiny projections called **villi.** Villi are important modifications of the mucosal layer of the small intestine. Millions of these projections, each about 1 mm in height, give the intestinal mucosa a velvety appearance. Each **villus** contains an arteriole, venule, and lymph vessel (lacteal) (see Figure 28-17). Box 28-3 identifies the fractal-like structure of the intestinal lining.

Absorptive epithelial cells called *enterocytes* on the surface of villi can be seen by microscopy to have a surface resembling a fine brush. This so-called *brush border* is formed by about 1700 ultrafine *microvilli* per cell. Intestinal digestive enzymes are imbedded in the brush border of these cells. The presence of villi and microvilli increases the surface area of the small intestine hundreds of times, thus making this organ the main site of digestion and absorption.

Box 28-3 | FYI

Fractal Geometry of the Body

Biologists are now applying the principles of the new field of **fractal geometry** to human anatomy. Specialists in fractal geometry often study surfaces with a seemingly infinite area, such as the lining of the small intestine. Fractal surfaces have bumps that have bumps that have bumps, and so on. The fractal-like nature of the intestinal lining is represented in Figure 28-17. The plicae (folds) have villi, the villi have microvilli, and even the microvilli have bumps that cannot be seen in the figure. Thus the absorptive surface area of the small intestine is almost limitless.

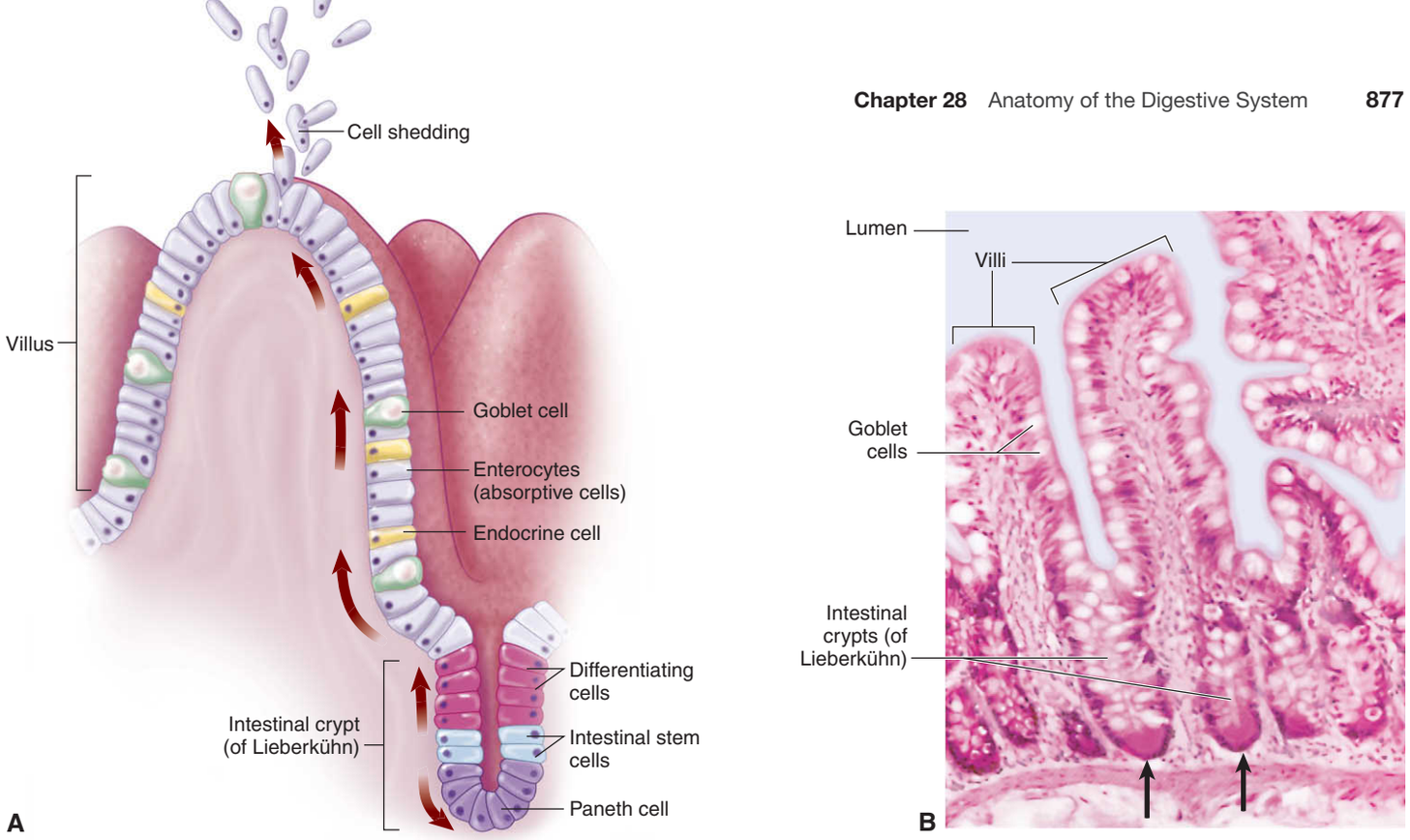


FIGURE 28-18

Intestinal villi and crypts. A, Stem cells near the bottom of each intestinal crypt divide to form daughter cells that move upward and differentiate into mucus-producing goblet cells, hormone-producing endocrine cells, and absorptive enterocytes. Eventually these cells are pushed to the top of the villus, where they are shed. Stem cells also produce Paneth cells, which move deeper into the crypt where they produce bactericidal secretions. **B,** This micrograph shows a section of the ileum wall with several villi and the intestinal crypts between them. Protective Paneth cells at the base of each crypt are marked by arrows.

Mucus-secreting goblet cells are found in large numbers on villi (Figure 28-18). Endocrine cells that produce intestinal hormones (to be discussed in Chapter 29) are also found in the villi.

Intestinal crypts serve as a site of rapid mitotic cell division. Stem cells near the bottom of each crypt keep the intestinal mucosa continuously supplied with fresh cells. New differentiating daughter cells are produced by the stem cells and pushed upward toward the mouth of the crypt. As they differentiate into enterocytes, goblet cells, and endocrine cells, the older cells are pushed up and out of each crypt, eventually moving to the distal end of a villus, where they are shed. Thus the intestinal mucosa is continually renewed. At the base of each crypt, protective *Paneth cells* produce enzymes and other molecules that inhibit bacterial growth in the small intestine. The location of the Paneth cells makes them especially useful in protecting the vital stem cells. See Table 28-1 and Figure 28-17 for more information on the layers of the small intestine.

| QUICK CHECK |

12. What are the three main divisions of the small intestine?
13. What are intestinal villi? What is their function?

LARGE INTESTINE

Size of the Large Intestine

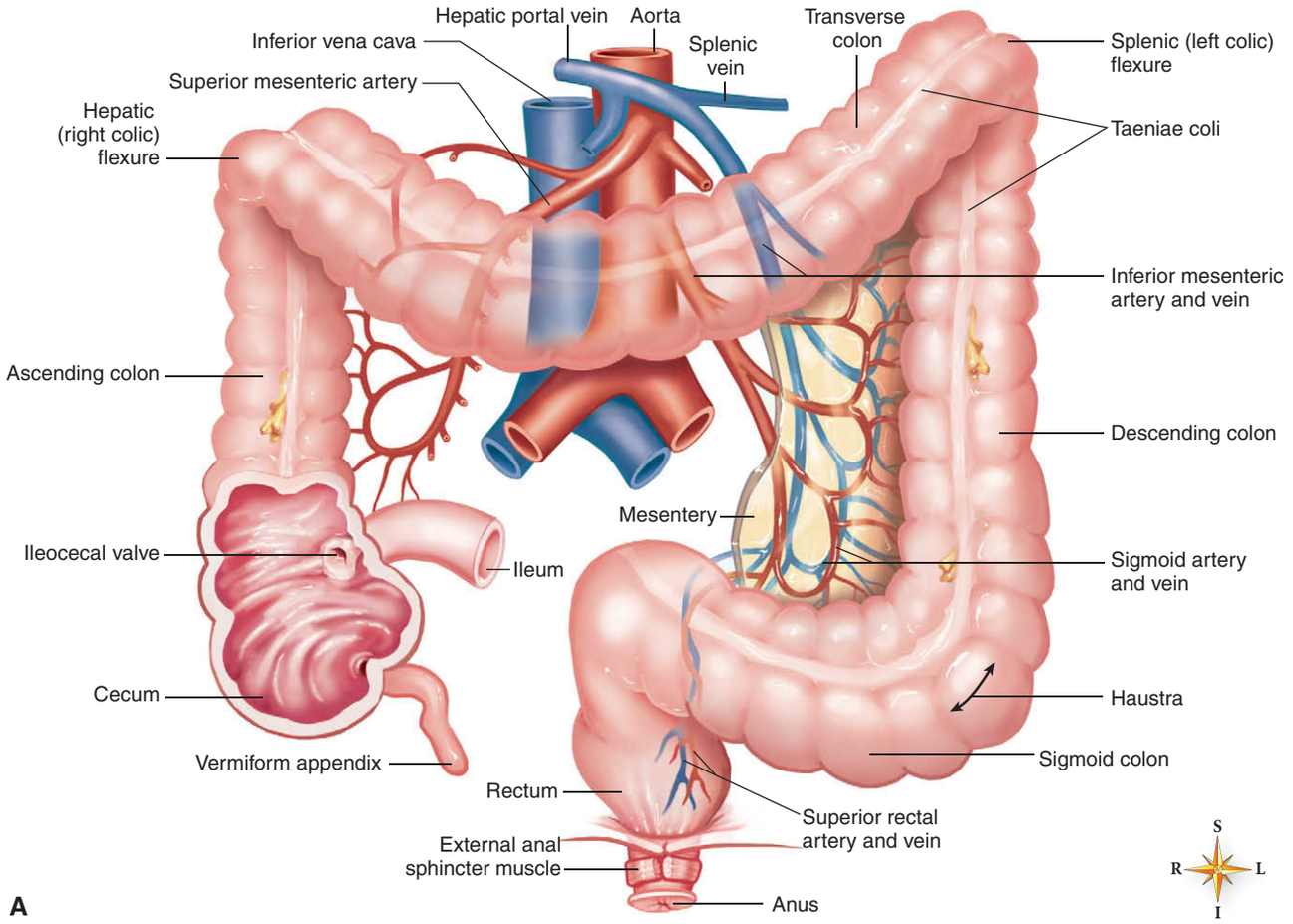
The lower part of the alimentary canal bears the name *large intestine* because its diameter is noticeably larger than that of the small intestine. Its length, however, is much less, being about 1.5 to 1.8 m (5 or 6 feet). Its average diameter is approximately 6 cm (2½ inches), but the diameter decreases toward the lower end of the tube. Box 28-4 describes a common method for imaging the large intestine.

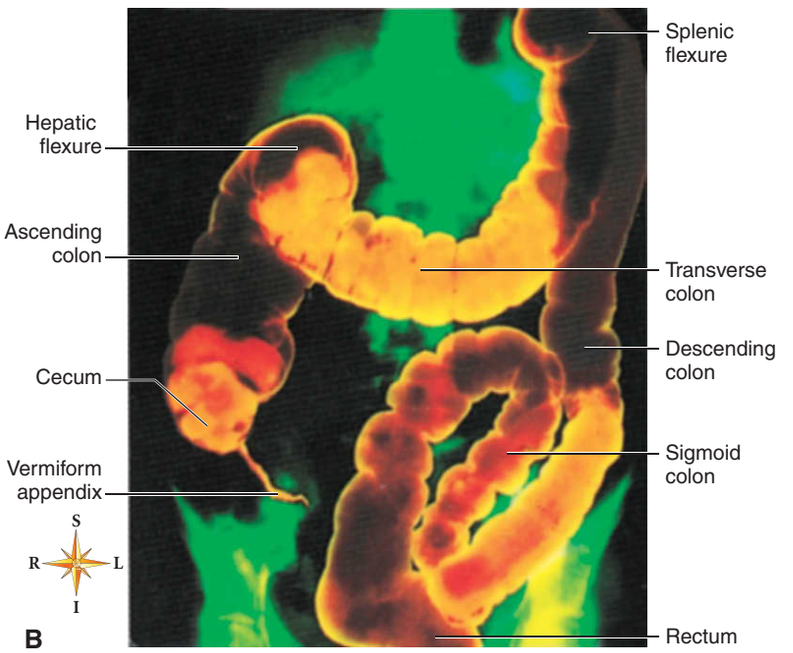
Box 28-4 | DIAGNOSTIC study

Barium Enema Study

The barium enema (BE) study, or lower GI series, consists of a series of x ray films of the colon that are used to detect and locate polyps, tumors, and diverticula (abnormal "pouches" in the lining of the intestine). Abnormalities in organ position can also be detected.

The test begins with the rectal instillation (enema) of approximately 500 to 1500 ml of fluid containing barium sulfate. The patient is placed in various positions, and the progress of the barium's flow through the intestine is monitored on a fluoroscope. Small polyps and early changes in ulcerative colitis are more easily detected with an *air-contrast barium enema study.* In this study, after the bowel is outlined with a thin coat of barium, air is added to enhance the contrast and outline of small lesions. After the x ray films are taken (see Figure 28-19), the patient is allowed to expel the barium.





Divisions of the Large Intestine

The large intestine is divided into the cecum, colon, and rectum (Figure 28-19).

CECUM

The first 5 to 8 cm (2 or 3 inches) of the large intestine is named the *cecum*. It is a blind pouch located in the lower right quadrant of the abdomen (see Figure 28-1).

COLON

The **colon** is divided into the following portions: ascending, transverse, descending, and sigmoid (see Figure 28-19).

- The **ascending colon** lies in a vertical position, on the right side of the abdomen, and extends up to the lower border of the liver. The ileum joins the large intestine

FIGURE 28-19

Divisions of the large intestine. A, Illustration showing divisions of the large intestine and adjacent vascular structures. **B,** Colorized x ray film taken after a barium enema (see Box 28-4).

at the junction of the cecum and ascending colon, the place of attachment resembling the letter T (see Figure 28-19). The *ileocecal valve* permits material to pass from the ileum into the large intestine, but not usually in the reverse direction.

- The **transverse colon** passes horizontally across the abdomen, below the liver, stomach, and spleen. Note that this part of the colon is above the small intestine (see Figure 28-1). The transverse colon extends from the *hepatic flexure* to the *splenic flexure*, the two points at which the colon bends on itself to form 90-degree angles.
- The **descending colon** lies in the vertical position, on the left side of the abdomen, and extends from a point below the stomach and spleen to the level of the iliac crest.
- The **sigmoid colon** is the portion of the large intestine that courses downward below the iliac crest. It is called *sigmoid* (meaning "S-shaped") because it forms an S-shaped curve. The lower part of the curve, which joins the rectum, bends toward the left, the anatomical reason for placing a patient on the left side when giving an enema. In this position, gravity aids the flow of enema fluid from the rectum into the sigmoid flexure.

RECTUM

The last 17 to 20 cm (7 or 8 inches) of the intestinal tube is called the **rectum** (Figure 28-20). Crescent-shaped *transverse rectal folds*, also called *rectal valves*, help slow down the flow of feces as it enters the rectum and hold the feces in place until defecation occurs. In an empty rectum, these folds may overlap and make it difficult to insert instruments during a **colonoscopy.**

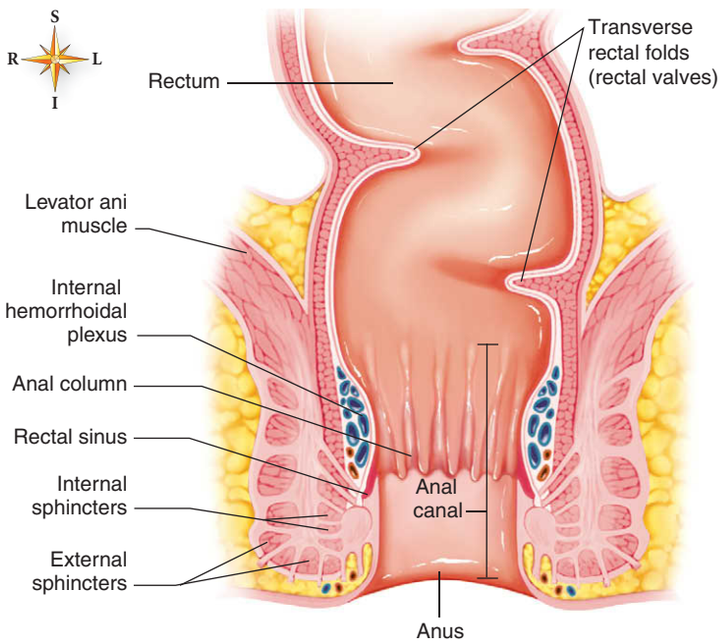


FIGURE 28-20
The rectum and anus.

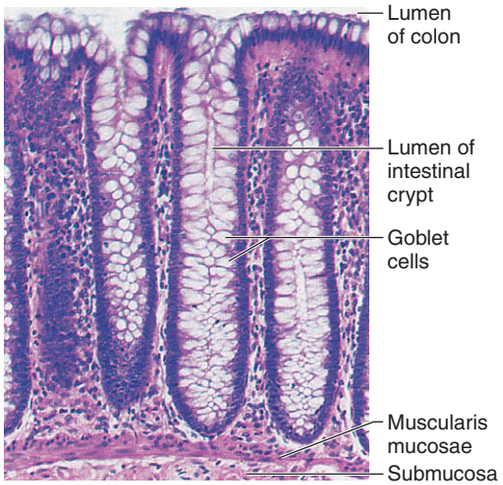


FIGURE 28-21
Wall of the colon. Note the straight nature of the intestinal glands of the colon. Many of the columnar epithelial cells are mucus-producing goblet cells.

The terminal inch of the rectum is called the **anal canal.** Its mucous lining is arranged in numerous vertical folds known as *anal columns*, each of which contains an artery and a vein. The opening of the canal to the exterior is guarded by two sphincter muscles—an internal one of smooth muscle and an external one of striated muscle. The opening itself is called the *anus*. The anus is directed slightly posteriorly and is therefore at almost a right angle to the rectum (see Figure 28-22).

Wall of the Large Intestine

Table 28-1 (see p. 863) summarizes modifications of the GI wall seen in the large intestine. One of the most notable of these modifications is the presence of intestinal mucous glands, which produce the lubricating mucus that coats the feces as they are formed (Figure 28-21). Although cells lining the large intestine have microvilli, the cells do not form villi like those that appear in the lining of the small intestine.

Another notable feature of the wall of the colon is the uneven distribution of fibers in the muscle layer. The longitudinal muscles are grouped into tapelike strips called *taeniae coli*, and the circular muscles are grouped into rings that produce pouchlike *haustra* between them (see Figure 28-19). In the rectum, rings of circular muscle form the rectal valves seen in Figure 28-20.

VERMIFORM APPENDIX

The **vermiform appendix** (from *vermis* "worm," *form* "shape") is, as the name implies, a wormlike tubular organ. It averages 8 to

10 cm (3 to 4 inches) in length and is most often found just behind the cecum or over the pelvic rim. The lumen of the appendix communicates with the cecum 3 cm (about 1 inch) below the ileocecal valve, thus making it an accessory organ of the digestive system (see Figure 28-19).

The appendix serves as a sort of "breeding ground" for the nonpathogenic intestinal bacteria found throughout the colon. The normal microbiome of the colon contributes to the digestive process by digesting unused nutrients and producing essential molecules such as vitamins K and B_7 (biotin). Some bacteria also produce gases that escape from the colon through the anus—a phenomenon called flatulence or *flatus*. Maintaining a normal intestinal microbiome also helps prevent pathogenic bacteria from becoming established. When the normal microbiome of the gut is disrupted by infection or antibiotics, for example, bacteria hidden away in the appendix can migrate into the colon to restore the normal ecological balance. The ecology of the human gut's microbiome is a very active field of research.

Lymph nodules appear in the wall of the appendix shortly after birth, become more prominent during the first 10 years of life, and then progressively disappear. The normal adult appendix shows only traces of lymphoid tissue. The function of lymphatic tissue present in the appendix of young children is not fully understood but may involve regulating the gut's microbial communities.

Inflammation of the appendix, or **appendicitis,** is a common and potentially very serious medical problem (see Mechanisms of Disease, pp. 893–894. The lifetime risk for appendicitis in the United States is 7%. A site on the surface of the anterior abdominal wall is often used to help in the diagnosis of appendicitis and to estimate the location of the appendix internally. It is called *McBurney's point* and is located in the right lower quadrant of the abdomen about a third of the way along a line from the right anterior superior iliac spine to the umbilicus. Extreme sensitivity and pain are common when the abdomen of persons with acute appendicitis is palpated over this point.

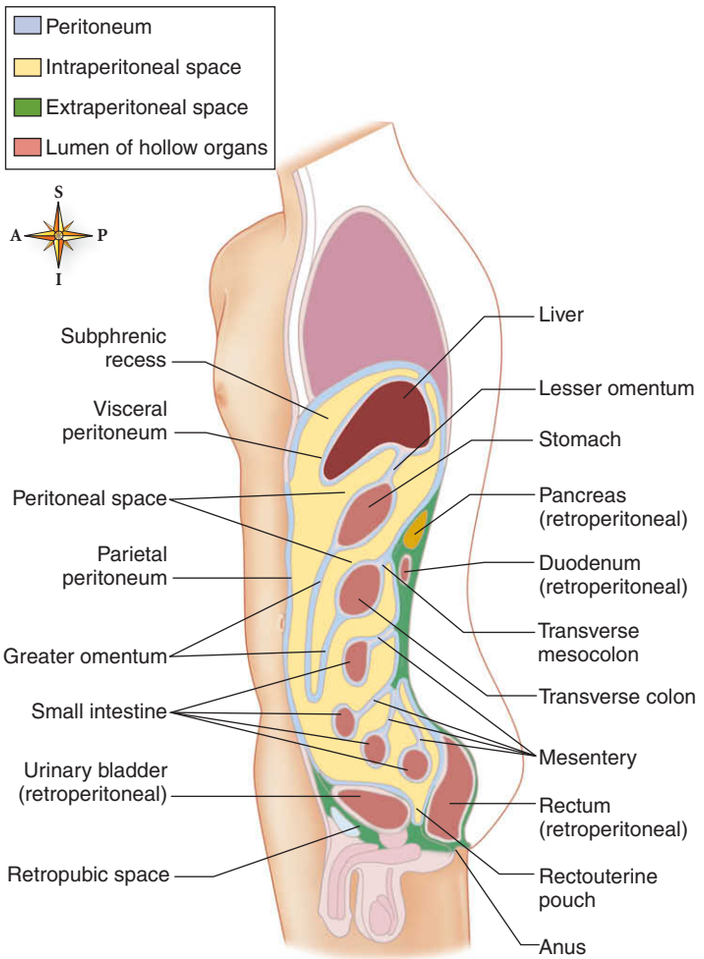


FIGURE 28-22

Peritoneum. Sagittal view of the abdomen showing the peritoneum and its reflections. *Intraperitoneal* spaces are shown in yellow and *extraperitoneal* spaces in green. The portion of the extraperitoneal space along the posterior wall of the abdomen is often called the *retroperitoneal space.*

PERITONEUM

Now that we have described the entire length of the digestive tube from one end to the other, let's focus on the membrane covering most of these organs and holding them loosely in place. The **peritoneum** is a large, continuous sheet of serous membrane. It lines the walls of the entire abdominal cavity (parietal layer) and also forms the serous outer coat of the organs (visceral layer) as you can see in Figure 28-22. All the space outside the parietal peritoneum is called *extraperitoneal space.* The extraperitoneal space along the posterior and bottom of the abdominopelvic cavity is most often identified as *retroperitoneal* ("behind the peritoneum"). Retroperitoneal organs include the pancreas (except the tail), kidneys and adrenal glands, ureters and bladder, aorta and inferior vena cava, part of the esophagus, part of the duodenum, ascending and descending colon, and the rectum.

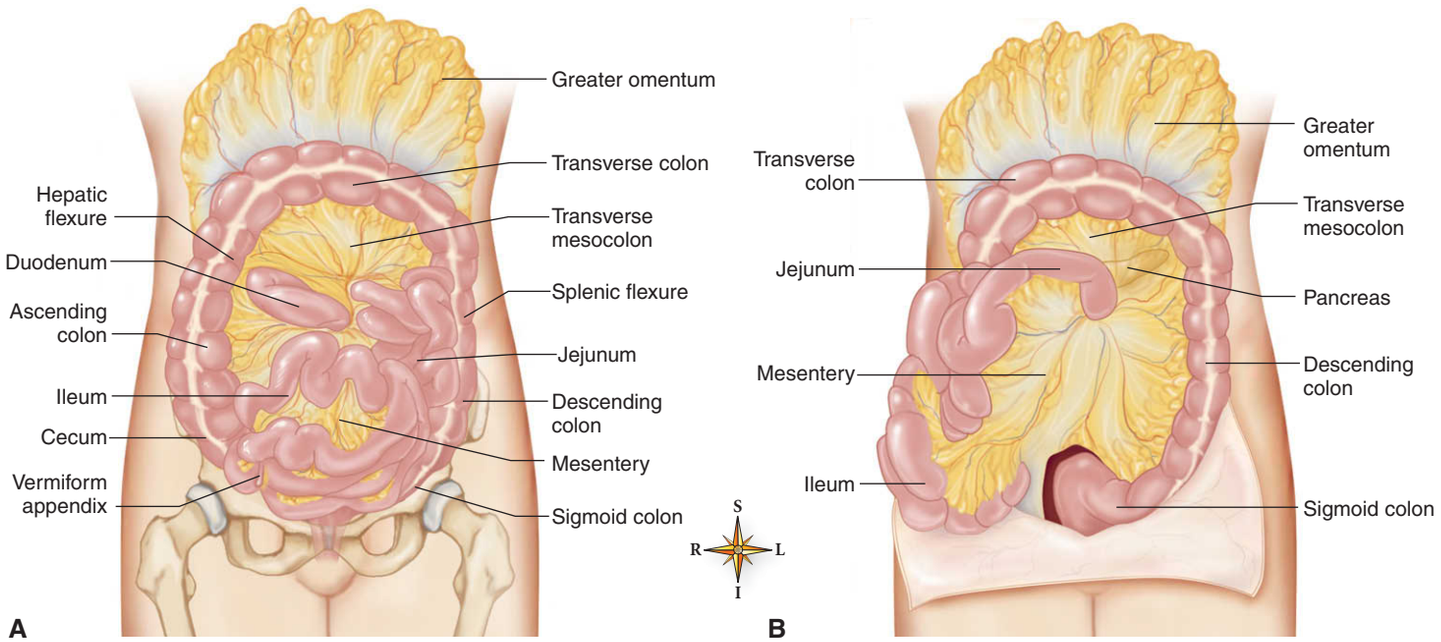


FIGURE 28-23

Projections of the peritoneum. A, Abdominal viscera from the front. The transverse colon and the greater omentum are elevated to reveal the flexures of the colon and the loops of the small intestine. **B,** The transverse colon and greater omentum are raised and the small intestine is pulled to the side to show the transverse mesocolon and mesentery.

In several places the peritoneum forms reflections, or extensions, that bind the abdominal organs together (Figures 28-22 and 28-23). The **mesentery** is a fan-shaped projection of the parietal peritoneum that extends from the lumbar region of the posterior abdominal wall. The attached posterior border of this great fan is just 15 to 20 cm (6 to 8 inches) long, yet the loose outer edge enclosing the jejunum and ileum is 6 m (over 9 feet) long. The mesentery allows free movement of each coil of the intestine and helps prevent strangulation of the long tube. A similar, but less extensive fold of peritoneum, called the **transverse mesocolon,** attaches the transverse colon to the posterior abdominal wall.

The **greater omentum** is a continuation of the serosa of the greater curvature of the stomach and the first part of the duodenum to the transverse colon. Spotty deposits of fat accumulate in the omentum and give it the appearance of a lace apron hanging down loosely over the intestines. In cases of localized abdominal inflammation such as appendicitis, the greater omentum envelops the inflamed area, walling it off from the rest of the abdomen. The **lesser omentum** attaches from the liver to the lesser curvature of the stomach and the first part of the duodenum. The falciform ligament extends from the liver to the anterior abdominal wall. Examine the relationships of peritoneal extensions in Figure 28-22.

| QUICK CHECK |

14. What are the four main divisions of the colon?
15. What are *haustra?*
16. Where is the vermiform appendix located?
17. Why is the greater omentum sometimes called the *lace apron?*

LIVER

Location and Size of the Liver

The liver is the largest gland in the body. It weighs about 1.5 kg (3 to 4 pounds), lies immediately under the diaphragm, and occupies most of the right hypochondrium and part of the epigastrium (see Figure 28-1).

Liver Lobes and Lobules

The liver consists of two lobes separated by the falciform ligament (Figure 28-24). The **left lobe** forms about one sixth of the liver, and the **right lobe** makes up the remainder. The right lobe has three parts designated the *right lobe proper*, the *caudate lobe* (a small oblong area on the posterior surface), and the *quadrate lobe* (a four-sided section on the undersurface). Each lobe is divided into numerous lobules by small blood vessels and by fibrous strands that form a supporting framework for them called the *perivascular fibrous capsule*. The perivascular fibrous capsule—also called *capsule of Glisson*—is an extension of the heavy connective tissue capsule that envelops the entire liver.

The **hepatic lobules** (Figure 28-25), the anatomical units of the liver, are tiny hexagonal or pentagonal cylinders about 2 mm high and 1 mm in diameter. A small branch of the hepatic vein extends through the center of each lobule. Around this central (intralobular) vein, in plates or irregular walls radiating outward, are arranged the hepatic cells. On the outer corners of each lobule, several sets of tiny tubes—branches of the hepatic artery, the portal vein (interlobular veins), and the hepatic duct (interlobular bile ducts)—are arranged. From these, irregular branches (sinusoids) of the interlobular veins extend between the radiating plates of hepatic cells to join the central vein. Minute bile canaliculi are formed by the spaces around each cell that collect bile secreted by the hepatic cells.

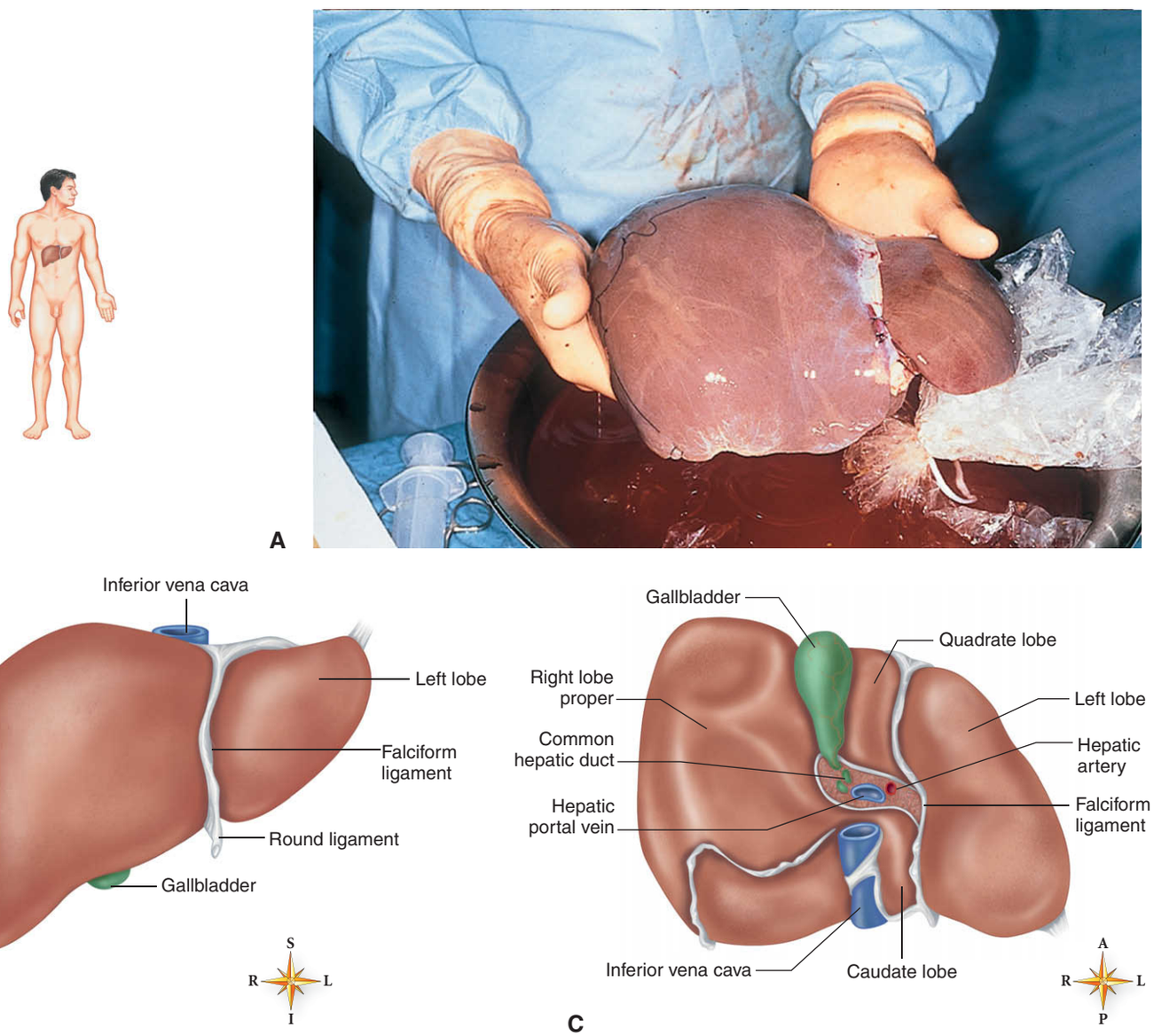


FIGURE 28-24

Gross structure of the liver. A, Normal liver prepared for organ transplantation. Diagrams of a normal liver—**B,** anterior view; **C,** inferior view.

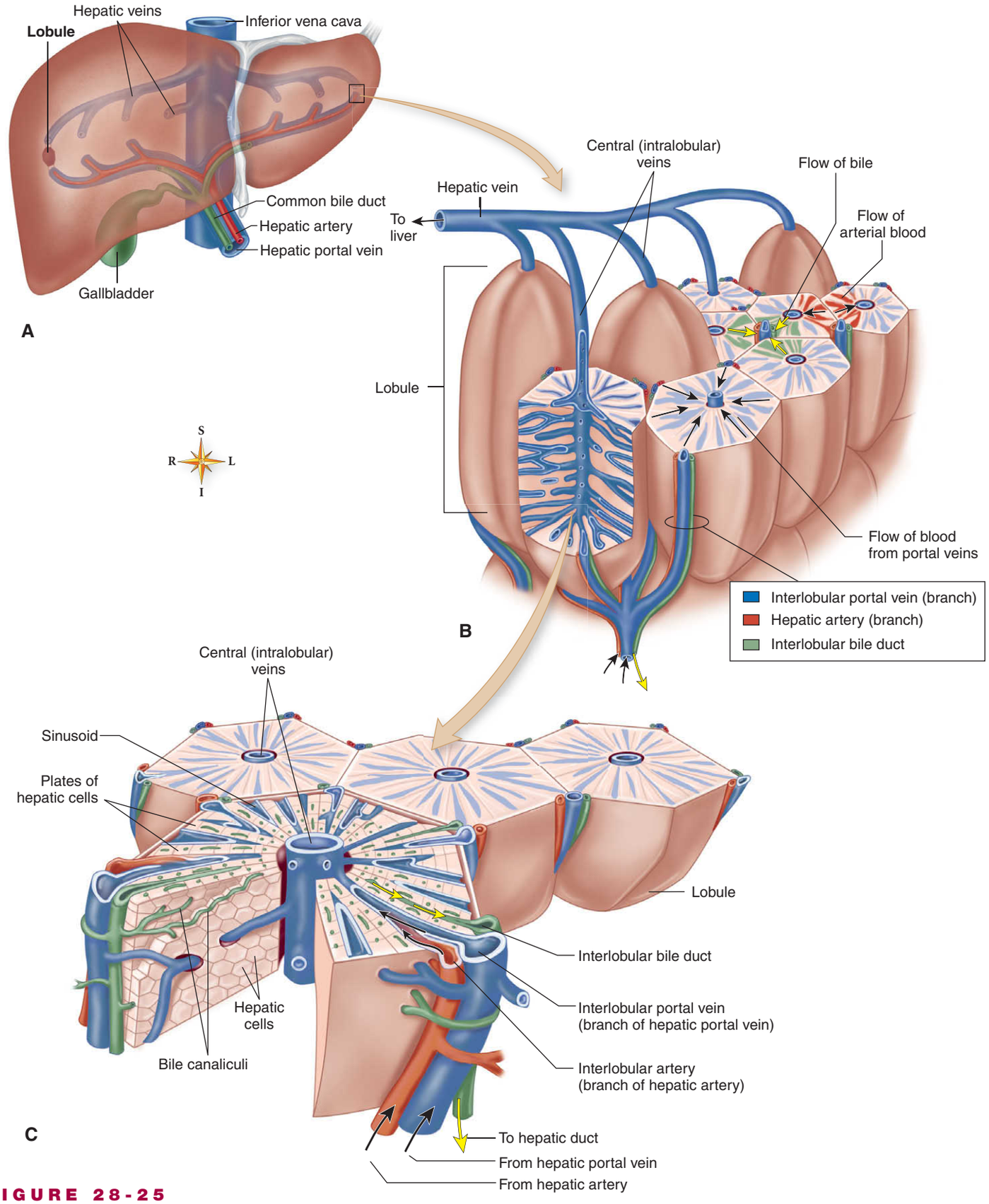


FIGURE 28-25

Microscopic structure of the liver. A, This diagram shows the location of liver lobules relative to the overall circulatory scheme of the liver. **B** and **C,** Enlarged views of several lobules show how blood from the hepatic portal veins and hepatic arteries flows through sinusoids and thus past plates of hepatic cells toward a central vein in each lobule *(black arrows)*. Hepatic cells form bile, which flows through bile canaliculi toward hepatic ducts that eventually drain the bile from the liver *(yellow arrows)*.

Consider the function of the hepatic lobule while carefully examining Figures 28-25 and 28-26. Blood enters a lobule from branches of the hepatic artery and portal vein. Arterial blood oxygenates the hepatic cells, whereas blood from the portal system simply passes through the liver for "inspection." Sinusoids in the lobule have many reticuloendothelial cells (mainly *Kupffer cells*) along their lining. These phagocytic cells can remove bacteria, worn red blood cells (RBCs), and other particles from the bloodstream. Ingested vitamins and other nutrients to be stored or metabolized by liver cells enter the hepatic cells that form radiating walls of the lobule. Dissolved toxins in the blood are also absorbed into hepatic cells, where they are detoxified (rendered harmless). Blood continues along the sinusoids to a vein at the center of the lobule. Such central, intralobular veins eventually lead to the main hepatic veins that drain into the inferior vena cava. **Bile** formed by hepatic cells passes through canaliculi to the periphery of the lobule to join small bile ducts.

Bile Ducts

The small bile ducts within the liver join to form two larger ducts that emerge from the undersurface of the organ as the *right* and *left hepatic ducts*. These ducts immediately join to form one common hepatic duct. The common hepatic duct merges with the *cystic duct* from the gallbladder to form the *common bile duct* (Figure 28-27), which opens into the duodenum in a small raised area called the *major duodenal papilla*. This papilla is located 7 to 10 cm (2 to 4 inches) below the pyloric opening from the stomach.

The inset in Figure 28-27 shows an x ray taken during a procedure with a tongue-twister name—*endoscopic cholangiography* (koh-lan-jee-OG-rah-fee). During this procedure, x rays are taken to visualize the gallbladder and ducts that carry bile. The process begins with passage of a flexible endoscope tube surrounding a hollow catheter and other laparoscopic instruments through the mouth, esophagus, and stomach into the duodenum. Once in the duodenum, the catheter is introduced into the major duodenal papilla, and contrast material is injected into the biliary tract. This procedure can also be used to fill the pancreatic duct and its branches with contrast material to obtain very high-quality x ray images.

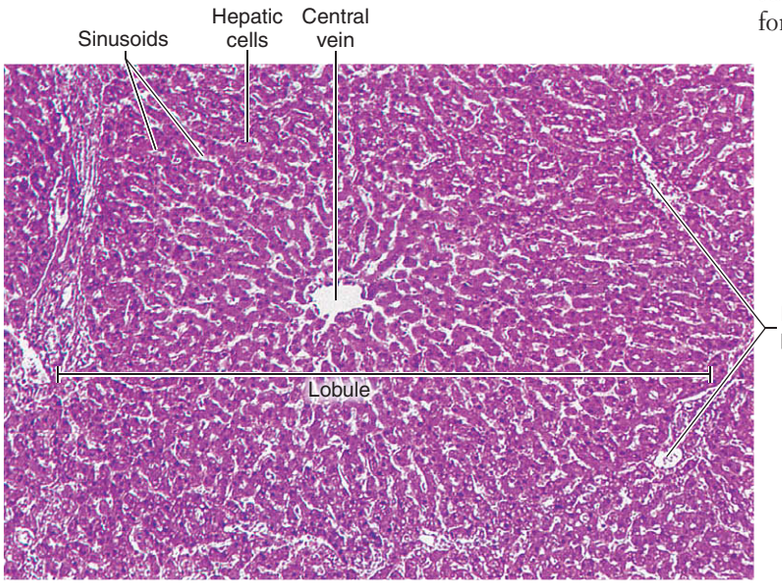


FIGURE 28-26

Liver tissue. This cross section of a hepatic lobule shows the sinusoids that permit passage of blood from the interlobular portal veins toward the central vein. The glandular epithelium (hepatic cells) forms plates between the sinusoids.

Functions of the Liver

The liver is one of the most vital organs of the body. Here, in brief, are its main functions:

- Liver cells detoxify various substances.
- Liver cells secrete approximately half a liter (about a pint) of bile a day.
- Liver cells carry on numerous important steps in the metabolism of all three kinds of foods—proteins, fats, and carbohydrates.
- Liver cells store several substances—iron, for example, and vitamins A, B_{12}, and D.
- The liver produces important plasma proteins and serves as a site of hematopoiesis (blood cell production) during fetal development.

DETOXIFICATION BY LIVER CELLS

Numerous poisonous substances enter blood from the intestines. They circulate to the liver, where, through a series of chemical reactions, they may be changed into nontoxic compounds. Ingested substances—alcohol, acetaminophen, and various other drugs, for example—and toxic substances formed in the intestines can be detoxified in the liver.

BILE SECRETION BY THE LIVER

The main components of bile are bile salts, bile pigments, and cholesterol. Bile salts (formed in the liver from cholesterol) are the most essential part of bile. They aid in the digestion and absorption of fats and then are themselves absorbed in the ileum. Eighty percent of bile salts are recycled in the liver to again become part of bile. Bile also serves as a pathway for elimination of certain breakdown products of RBCs. When aged and fragile erythrocytes are destroyed in the spleen, the heme portion of the released hemoglobin molecule is converted into bilirubin and transported by blood to the liver. Liver cells extract the bilirubin and excrete it into bile. Because it secretes bile into ducts, the liver qualifies as an exocrine gland.

LIVER METABOLISM

Although all liver functions are important for healthy survival, some of its metabolic processes are crucial for survival itself. A fairly detailed description of the role of the liver in metabolism is given in Chapter 30.

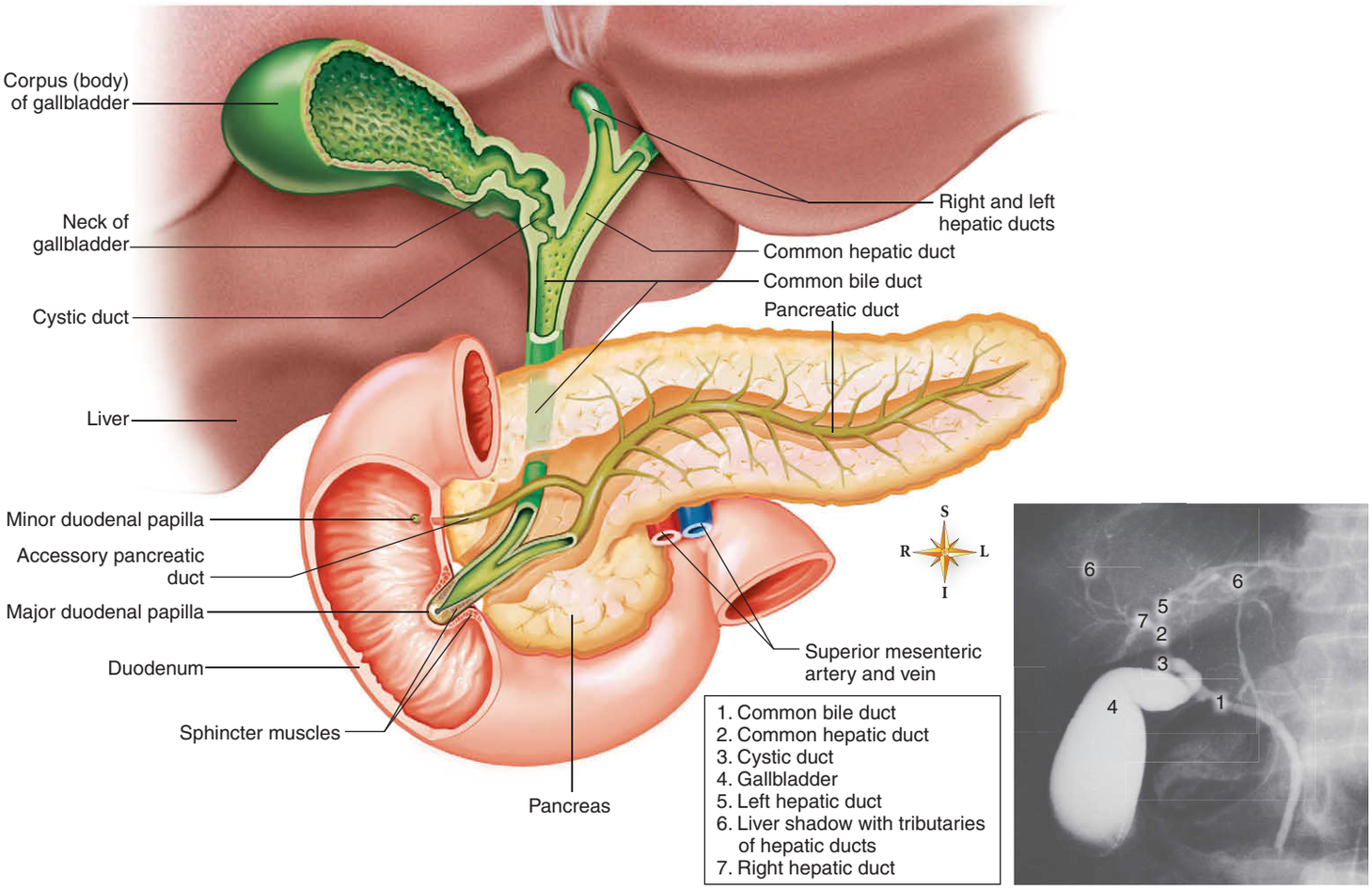


FIGURE 28-27

Ducts that carry bile from the liver and gallbladder. Bile exits the liver through the left and right hepatic ducts, which join to form the common hepatic duct. The common hepatic duct joins the cystic duct from the gallbladder to form the common bile duct, which enters the duodenum at the major duodenal papilla (regulated by sphincter muscles). When sphincter muscles contract, bile backs up into the gallbladder where it is stored and concentrated. Obstruction of either the common hepatic or the common bile duct by a stone or muscle spasm prevents bile from being ejected into the duodenum. The inset shows an x ray of the gallbladder and the ducts that carry bile taken during a procedure called *endoscopic cholangiography.*

GALLBLADDER

Size and Location of the Gallbladder

The gallbladder is a pear-shaped sac 7 to 10 cm (3 to 4 inches) long and 3 cm broad at its widest point (see Figure 28-27). The gallbladder lies on the undersurface of the liver and is attached there by areolar connective tissue.

Structure of the Gallbladder

Serous, muscular, and mucous layers compose the wall of the gallbladder. The mucosal lining is arranged in folds called *rugae*, similar in structure to those of the stomach. These rugae allow the gall bladder to expand as it receives bile that backs up into it when the sphincters of the major duodenal papilla contract. The gall bladder can hold 30 to 50 ml of bile.

Functions of the Gallbladder

The gallbladder stores bile that backs up into it. The gallbladder concentrates bile fivefold to tenfold as it is stored. When partially digested material exits the stomach, the gallbladder contracts and ejects the concentrated bile into the duodenum.

Jaundice, a yellow discoloration of the skin and mucosa, results when obstruction of bile flow into the duodenum occurs. Bile is thereby denied its normal exit from the body in feces. Instead, it is absorbed into the blood, and an excess of bile pigments with a yellow hue enters the blood and is deposited in tissues.

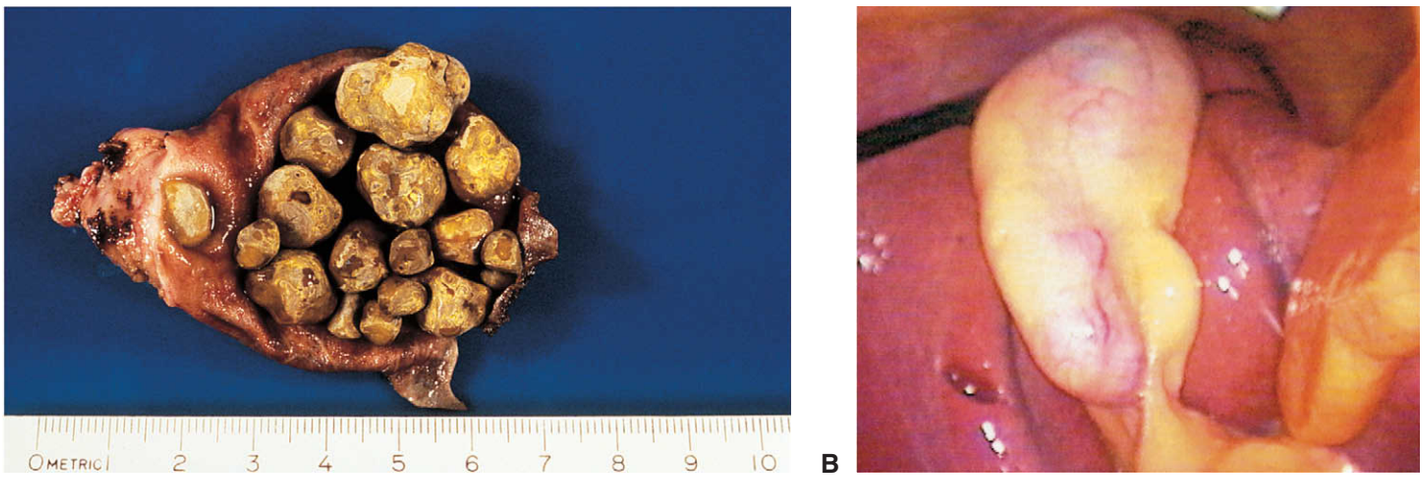


FIGURE 28-28

Gallbladder and gallstones. A, Gallbladder filled with yellow cholesterol gallstones. **B,** Laparoscopic view of the gallbladder before removal.

Inflammation of the gallbladder is called **cholecystitis** (koh-leh-sis-TYE-tis). It is often caused by gallstone formation or **cholelithiasis** (koh-leh-lih-THEE-ah-sis) (Figure 28-28, *A*). Inflammation and stone formation may require surgical removal in a procedure called **cholecystectomy** (koh-leh-sis-TEK-toh-mee). Surgical removal is now commonly performed laparoscopically, a procedure less invasive than traditional surgery (Figure 28-28, *B*). However, efforts to eliminate stones with drugs or nonsurgical methods, such as *ultrasound lithotripsy*, are often the treatment of choice initially.

| A&P CONNECT |

Did you know that the formation of gallstones may be related to weight loss and dieting? Find out how, and see some dramatic medical images, in ***Gallstones and Weight Loss*** online at ***A&P Connect.***

PANCREAS

Size and Location of the Pancreas

The pancreas is a grayish pink–colored gland about 12 to 15 cm (6 to 9 inches) long, weighing about 60 grams. It resembles a fish with its head and neck in the C-shaped curve of the duodenum, its body extending horizontally behind the stomach, and its tail touching the spleen (Figure 28-29; see Figure 28-1). According to an old anatomical witticism, the "romance of the abdomen" is the pancreas lying "in the arms of the duodenum."

Structure of the Pancreas

The pancreas is composed of two different types of glandular tissue, one exocrine and one endocrine. Most of the tissue is exocrine, with a compound acinar arrangement. The word *acinar* means that the cells are in a grapelike formation and that they release their secretions into a microscopic duct within each unit (see Figure 28-29, *B*). The word *compound* indicates that the ducts have branches. These tiny ducts unite to form larger ducts that eventually join the main pancreatic duct, which extends throughout the length of the gland from its tail to its head.

The pancreatic duct empties into the duodenum at the same point as the common bile duct at the *major duodenal papilla*. An accessory duct is frequently found extending from the head of the pancreas into the duodenum, opening at the *minor duodenal papilla* about 2 cm above the major papilla (see Figure 28-29, *A*).

Embedded between the exocrine units of the pancreas, like so many little islands, lie clusters of endocrine cells called **pancreatic islets** (see Figure 28-29). Although there are about a million of these tiny islands, they constitute only about 2% of the total mass of the pancreas. Special staining techniques have revealed that several kinds of cells—mainly alpha cells and beta cells—make up the islets. They are secreting cells, but their secretion passes into blood capillaries rather than into ducts. Thus the pancreas is a dual gland—an exocrine, or duct, gland because of the acinar units and an endocrine, or ductless, gland because of the pancreatic islets.

Functions of the Pancreas

The acinar units that comprise most of the pancreatic tissue secrete pancreatic juice. This digestive juice is made up mostly of water but also contains sodium bicarbonate ($NaHCO_3$) and various digestive enzymes. Hence the exocrine part of the pancreas plays an important part in digestion (Chapter 29).

The endocrine functions of the pancreas were introduced in Chapter 19 (see p. 581) and will be discussed further in subsequent chapters. Recall that *beta cells* of the pancreatic islets secrete **insulin,** a hormone that exerts a major control over carbohydrate metabolism (see Figure 28-29, *B*). *Alpha cells* secrete **glucagon.** It is interesting to note that glucagon, which is produced so close to where insulin is produced, has an opposite effect on carbohydrate metabolism.

| A&P CONNECT |

An abnormal decrease in insulin effects can have dramatic consequence for a person's health. To see a flowchart of how these effects create disease and possibly death, check out ***Diabetes Mellitus*** online at your ***A&P Connect.***

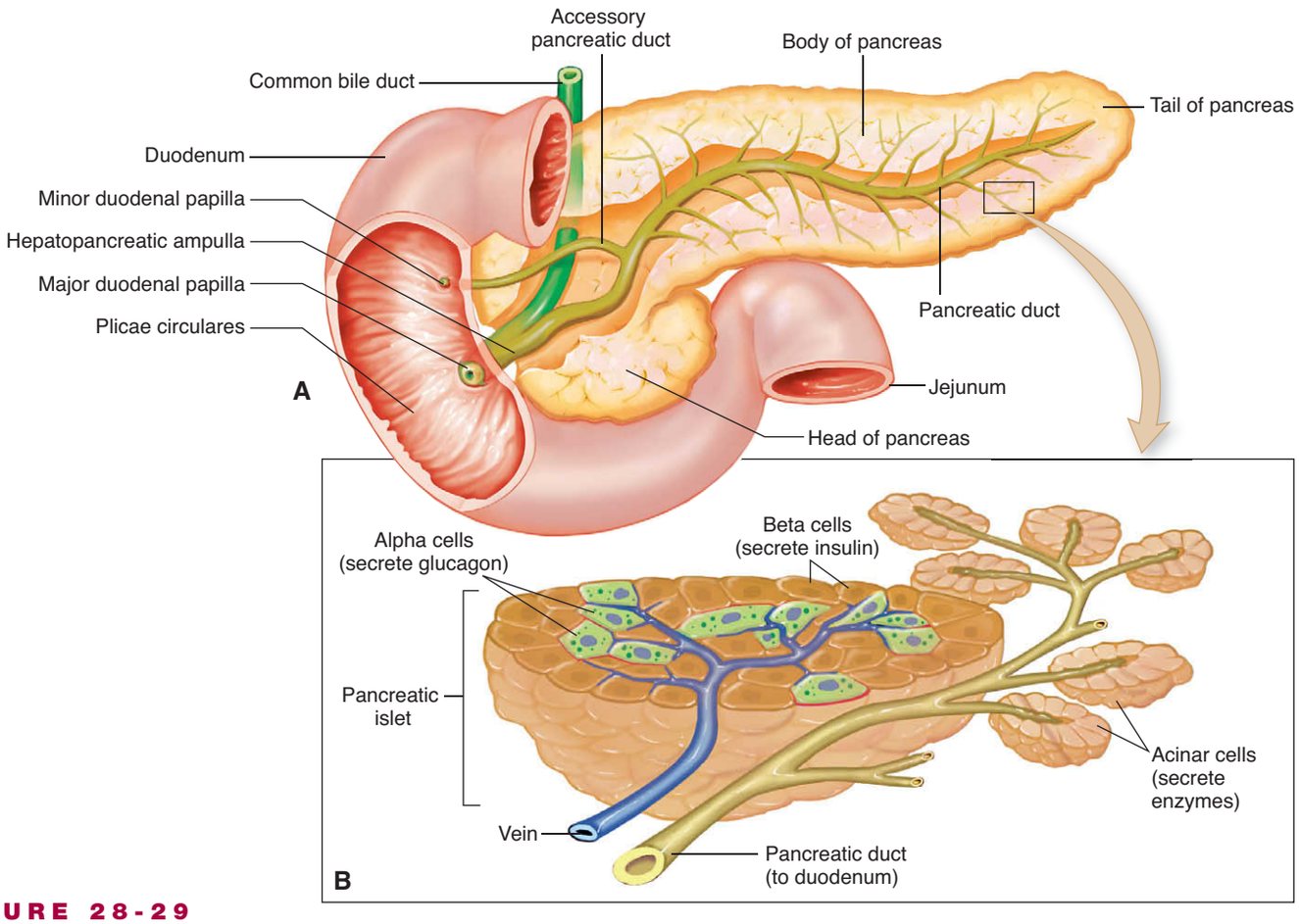


FIGURE 28-29

Pancreas. A, Pancreas dissected to show the main and accessory ducts. The main duct may join the common bile duct, as shown here, to enter the duodenum by a single opening at the major duodenal papilla (see Figure 28-27), or the two ducts may have separate openings. The accessory pancreatic duct is usually present and has a separate opening into the duodenum. **B,** Exocrine glandular cells (around small pancreatic ducts) and endocrine glandular cells of the pancreatic islets (adjacent to blood capillaries). Exocrine pancreatic cells secrete pancreatic juice, alpha endocrine cells secrete glucagon, and beta cells secrete insulin.

| QUICK CHECK |

18. Where is the liver located?
19. Name three of the many functions of the liver.
20. Trace the route of bile from the gallbladder to the duodenum.
21. What is the function of the acinar units of the pancreas?

Cycle of LIFE

Digestive System

Significant changes in both the structure and function of the digestive system can occur at different times in the human life cycle. Such changes result in numerous diseases or pathological conditions and may occur in any segment of the intestinal tract from the mouth to the anus. In addition, life cycle changes also involve the accessory organs of digestion, such as the teeth, salivary glands, liver, gallbladder, and pancreas.

Because of the immaturity of intestinal mucosa in young infants, some types of intact proteins can pass through the epithelial cells that line the tract. The result may be an early allergic response caused by the protein triggering the baby's immune system. Lactose intolerance is another age-related example of a common digestive system problem. Intestinal lactase, needed for the digestion of lactose, or milk sugar, is almost always present at the time of birth. Levels may rapidly diminish in some babies, however, and such individuals soon become unable to digest lactose.

Inflammation of the parotid salivary gland (mumps) is a common disease of children, whereas appendicitis occurs more frequently in adolescents. The incidence of appendicitis then decreases with age because the size of the opening between the appendix and the intestinal lumen decreases. Gallbladder disease and ulcers are primarily problems of middle age. In more elderly individuals, a decrease in volume of digestive fluids coupled with a slowing of peristalsis and reduced physical activity often results in constipation and diverticulosis.

the BIG picture

Anatomy of the Digestive System

The process of digestion, which is discussed in the next chapter, is structure dependent. It is the normal interrelationships of the anatomical components of the digestive system coupled with the functioning of other body organ systems that permit the highly regulated processes that result in digestion and absorption of nutrients. For example, breaking down of food involves not only the grinding action of the teeth but also the mechanical mixing of food as it passes through the GI tract. Nervous involvement in this process requires the conscious control of mastication and the parasympathetic regulation of smooth muscle contraction mediated through the intramural plexus. Furthermore, the structural adaptations of the GI tract that increase the surface area for better absorption (rugae, villi, brush borders) increase overall digestive efficiency. Involvement of the nervous, endocrine, circulatory, and muscular systems is obvious. Fluid balance, maintenance of core body temperature, numerous circadian rhythms, and regulation of pH, metabolic rates, and blood nutrient concentrations are less obvious, but nonetheless critically important components of the big picture as it relates to the anatomy of the digestive system.

MECHANISMS of DISEASE

DISORDERS OF THE DIGESTIVE SYSTEM

Disorders of the digestive system are described here rather than at the end of Chapter 29 because they will help you both apply the concepts of this chapter and prepare you for the concepts of the next chapter.

Disorders of the Mouth and Esophagus

Infections, cancer, congenital defects, and other disorders of the mouth and teeth can result in a variety of serious complications. Such conditions may cause pain or damage to the mouth and teeth that makes chewing and swallowing difficult. Mouth infections or cancer may also spread to nearby tissues: the nasal cavity (then on to the sinuses, middle ear, and brain) or pharynx (and on to the esophagus, larynx, and thoracic and other body organs).

Diseases of the salivary glands, including problems that affect their sympathetic and parasympathetic innervation, may alter both the chemical composition and the amount of saliva produced, about 1 liter per day on average. Inadequate saliva inhibits proper mixing and mastication of food, decreases production of salivary amylase (ptyalin) that initiates digestion in the mouth, and causes an imbalance in salivary pH (normally about 7.4).

Sjögren Syndrome

Sjögren syndrome is an autoimmune disease in which the body's immune system targets the salivary and tear glands for destruction. One to two million persons in the U.S. are affected. The condition results in a dramatic reduction in both the production of saliva, causing dry mouth (**xerostomia**), and tears, which produces dry eyes (**xerophthalmia**). Symptoms of dry mouth and dry eyes, which cause a feeling of irritation and grittiness, becomes progressively worse over time. The syndrome affects many more women than men and usually begins around age 50. Among other symptoms, the lack of saliva makes chewing and swallowing difficult and contributes to a higher incidence of tooth decay. Drugs used to treat the altered immune response and stimulate saliva production such as cyclosporine (Restasis) and the use of artificial tears and saliva help people with Sjögren syndrome cope with symptoms.

Mumps

Mumps is an acute viral disease characterized by swelling and inflammation of the parotid gland *(parotitis)*. Both parotid glands are involved in about 70% of individuals with mumps. It is caused by a paramyxovirus. Initial symptoms include fever, loss of appetite, and a generalized feeling of weakness and discomfort. Within a few hours, swelling of the parotid gland and spasm of the jaw muscles cause pain when the mouth is opened or during chewing movements. As swelling of the parotid gland becomes more pronounced, it extends over the ramus and fills the hollow behind the angle of the mandible to produce the classic "puffy" facial appearance of mumps (Figure 28-30). Another helpful diagnostic sign is redness of the parotid papilla on the inside of the cheek opposite the second molar tooth on one or both sides of the upper jaw.

Most of us think of mumps as a childhood disease because it most often affects children between the ages of 5 and 15 years. However, it can occur in adults—often producing a more severe infection. The mumps infection can affect other tissues in addition to the parotid gland, including the joints, pancreas, myocardium, and kidneys. In about 25% of infected men, mumps causes inflammation of the testes, or **orchitis.** Of the 25% of men in whom mumps-related orchitis develops, only about half experience atrophy of testicular tissue. Furthermore, since the problem is usually unilateral and involves only one testis, sterility rarely results, although some reduction in fertility may occur.



FIGURE 28-30

Mumps. This young boy with mumps has unilateral parotid swelling on the right side.

Tooth Decay

Tooth decay, or dental **caries** (KAIR-ees), is a common disease throughout the world. It is a disease of the enamel, dentin, and cementum of teeth that results in the formation of a permanent defect called a *cavity*. Most people living in the United States, Canada, and Europe are significantly affected by the disease.

Decay refers to demineralization of the hard tissues of the tooth caused by acids produced by *Streptococcus mutans* bacteria. These bacteria survive on sugars from food debris that collects around teeth, forming an acid-producing biofilm called *plaque*.

If the disease goes untreated, tooth decay results in infection, loss of teeth, and inflammation of the soft tissues in the mouth. Bacteria may also invade the paranasal sinuses or extend to the surface of the face and neck, causing even more serious complications.

Gingivitis (jin-ji-VYE-tis) is the general term for inflammation or infection of the gums. Most cases of gingivitis result from poor oral hygiene—inadequate brushing and no flossing. Gingivitis may also be a complication of other conditions such as diabetes mellitus, vitamin deficiency, or pregnancy.

Periodontitis (pair-ee-oh-don-TYE-tis) is inflammation of the periodontal membrane, or *periodontal ligament*, that anchors the tooth to the bone of the jaw. Periodontitis is often a complication of advanced or untreated gingivitis and may spread to the surrounding bony tissue. Destruction of periodontal membrane and bone results in loosening and eventually complete loss of teeth. Periodontitis is the leading cause of tooth loss in adults.

Leukoplakia (loo-koh-PLAY-kee-ah) of the mouth is a precancerous change in the mucous membrane characterized by thickened, white, and slightly raised patches of tissue. Leukoplakia often develops in the fold between the "cheek and gum" in users of smokeless tobacco. The condition, called *snuff dipper's pouch*, may lead to tooth and gum disease, as well as oral cancer.

Malocclusion

Malocclusion of the teeth occurs when missing teeth create wide spaces in the dentition, when teeth overlap, or when malposition of one or more teeth prevents correct alignment of the maxillary and mandibular dental arches (Figure 28-31, *A* and *B*). Malocclusion that results in protrusion of the upper front teeth so that they hang over the lower front teeth is called *overbite (A)*, whereas positioning of the lower front teeth outside the upper front teeth is called *underbite (B)*.

Dental malocclusion may cause chronic pain and significant problems in functioning of the temporomandibular joint, contribute to the generation of headaches, or complicate routine mastication of food. Fortunately, even severe malocclusion problems can be corrected by the use of braces and other dental appliances. **Orthodontics** (or-thoh-DON-tiks) is the branch of dentistry that deals with the prevention and correction of positioning irregularities of the teeth and malocclusion.





FIGURE 28-31

Malocclusion. A, Overbite. **B,** Underbite.

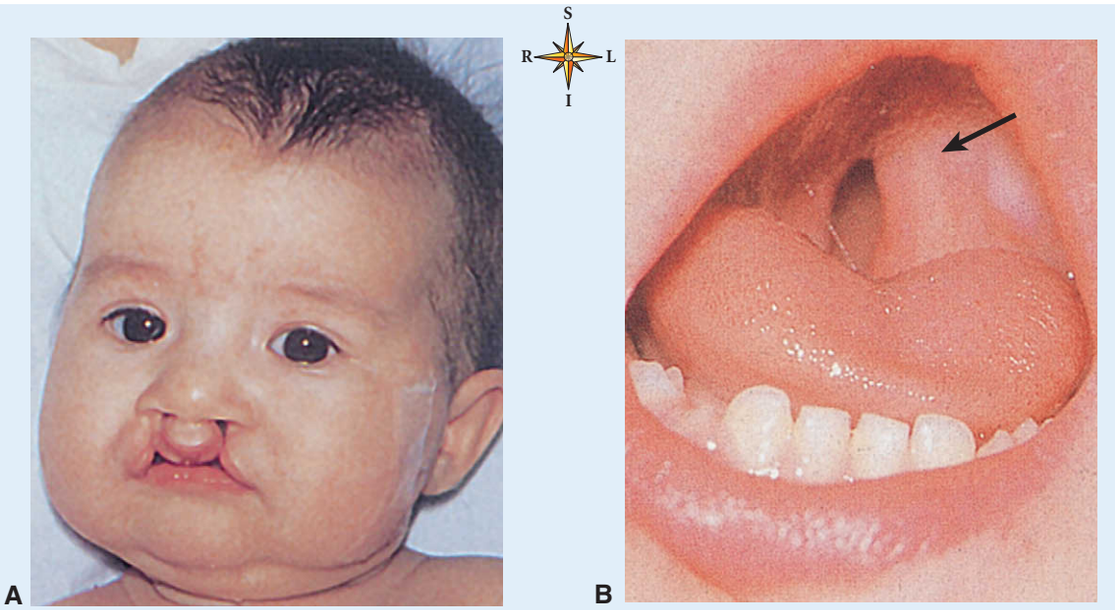


FIGURE 28-32

Congenital defects of the mouth. A, Bilateral cleft lip in an infant. **B,** Cleft palate (*arrow*). Modern reconstructive surgery techniques are extremely effective in minimizing the cosmetic, anatomical, and functional problems associated with these defects.

Cleft lip and *cleft palate* (Figure 28-32) are the most common *congenital defects* affecting the mouth. They may occur alone or together and are caused by failure of structures in the upper lip or palate to fuse or close properly during embryonic development. Cleft lip, which may occur on one or both sides, is typically repaired soon after birth. Surgical repair of cleft palate is usually done later—but generally in the first or second year of life.

Gastroesophageal Reflux Disease (GERD)

The terms *heartburn* or *acid indigestion* are often used to describe a number of unpleasant symptoms experienced by more than 60 million Americans each month. Backward flow of stomach acid up into the esophagus causes these symptoms, which typically include burning and pressure behind the breastbone. The term **gastroesophageal reflux disease (GERD)** is now used to better describe this common and sometimes serious medical condition.

In its simplest form, GERD symptoms are mild and occur only infrequently (twice a week or less). In these cases, avoiding problem foods or beverages, stopping smoking, or losing weight if needed may solve the problem. Additional treatment with over-the-counter antacids or nonprescription-strength acid-blocking medications called H_2-receptor antagonists (famotidine [Pepcid], others) may also be used. More severe and frequent episodes of GERD can trigger asthma attacks, cause severe chest pain, result in bleeding, or promote a narrowing (stricture) or chronic irritation of the esophagus called **erosive esophagitis** (Figure 28-33, *D*). In these cases, more powerful inhibitors of stomach acid production called *proton pump inhibitors* (esomeprazole [Nexium], others) may be added to the treatment prescribed. Drugs called *promotility agents*, which strengthen the lower esophageal sphincter and thus reduce backflow of stomach acid, are also used in moderate to severe cases of GERD.

Two minimally invasive procedures for treating serious cases of GERD are now available (Figure 28-33, *B* and *C*). One, called the *Stretta procedure*, uses radiofrequency energy emitted by a special electrode to produce small burns that tighten the muscular wall of the lower esophageal sphincter and reduce acid reflux from the stomach. The other procedure, called the *Bard endoscopic suturing system*, uses a miniature sewing machine–like device to place two or more stitches in the muscular wall of the lower esophageal sphincter, which are then pulled together to narrow the lumen. In both procedures, which are done on an outpatient basis, a flexible tube called an **esophageal endoscope** is used to insert and then remove the necessary electrode or suturing device required for treatment. As a last resort, a surgical procedure called *fundoplication* is performed to strengthen the sphincter. The procedure involves wrapping a layer of the upper stomach wall around the sphincter and terminal esophagus to lessen the possibility of acid reflux. If GERD is left untreated, serious pathological (precancerous) changes in the esophageal lining may develop—a condition called *Barrett esophagus*.

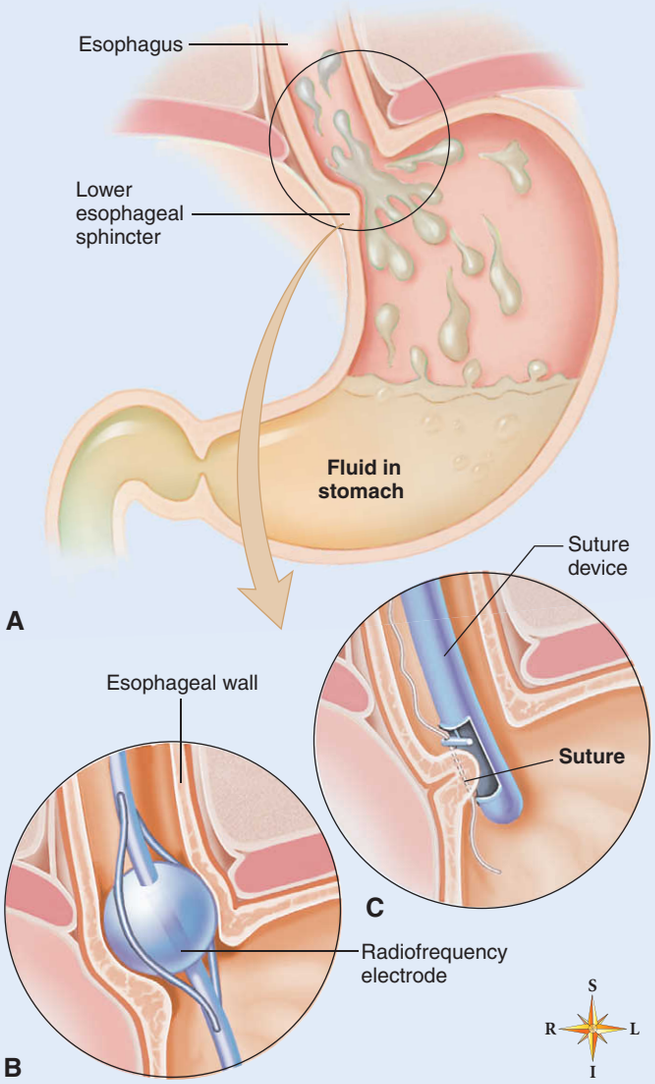


FIGURE 28-33

Gastroesophageal reflux disease (GERD). **A,** Reflux of gastric acid up into the esophagus through the lower esophageal sphincter. **B,** Stretta procedure. **C,** Bard endoscopic suturing system. **D,** Endoscopic view of esophageal inflammation *(esophagitis)* caused by "splashing back" of acids from the stomach in a patient with GERD.

Disorders of the GI Tract

Gastroenterology (gas-troh-en-ter-AHL-oh-jee) is the study of the stomach *(gastro-)* and intestines *(entero-)* and their diseases. The gastrointestinal tract is the potential site of numerous diseases and conditions, some of which are briefly described in this section. Many of these disorders, particularly those that primarily affect the stomach or duodenum, are characterized by one or more of the following signs and symptoms:

Gastroenteritis — stomach inflammation (gastritis) and intestinal inflammation (enteritis)

Anorexia — chronic loss of appetite

Nausea — unpleasant feeling that often leads to vomiting

Emesis — vomiting (Figure 28-34)

Diarrhea — elimination of liquid feces, perhaps accompanied by abdominal cramps

Constipation — decreased motility of colon, resulting in difficulty in defecation

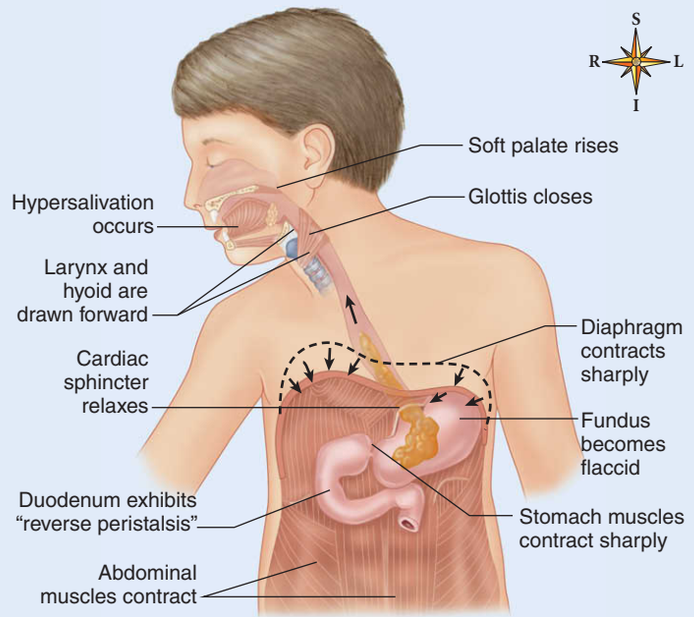


FIGURE 28-34

Emesis (vomiting). Summary of components of the vomiting reflex.

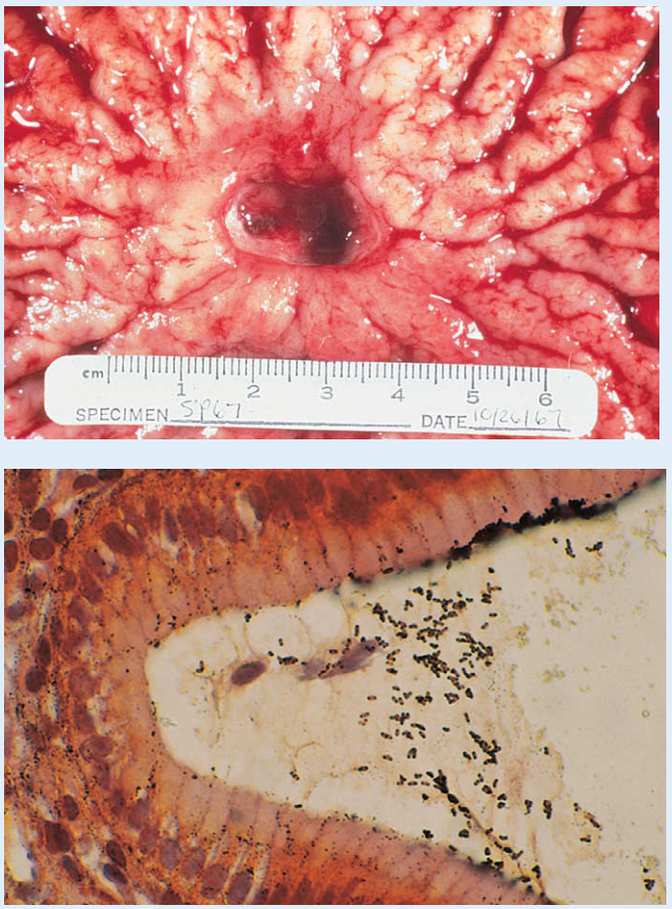


FIGURE 28-35

Ulcer. A, Gastric ulcer (actual size). **B,** Micrograph of *H. pylori (black particles)* infecting the stomach mucosa *(pink)*.

An **ulcer** is a craterlike wound or sore in a membrane caused by tissue destruction (Figure 28-35). Current statistics show that about 1 in 10 individuals in the United States will suffer from either a gastric (stomach) or duodenal ulcer in his or her lifetime. Ulcers cause disintegration, loss, and death of tissue as they erode the layers of the wall of the stomach or duodenum. These crater-like lesions cause gnawing or burning pain and may ultimately result in hemorrhage, perforation, widespread inflammation, scarring, and other very serious medical complications. Usually, perforation does not occur, but small, repeated hemorrhages over long periods can cause anemia.

Two Australian scientists, Dr. Barry Marshall (a microbiologist) and Dr. J. Robin Warren (a pathologist) were awarded the 2005 Nobel Prize in Physiology or Medicine for ulcer research. In 1979 they discovered that infection with a spiral-shaped bacterium called *Helicobacter pylori (H. pylori)*—and not excessive acid secretion—was the primary cause of most ulcers. The two scientists were quick to report the relationship they observed between inflammation, lack of protective mucus, and tissue erosion around areas of bacterial colonization by *H. pylori* in tissue biopsies obtained from many ulcer patients. However, many in the medical community were initially slow to accept their research results linking *H. pylori* to ulcer development as valid. At the time, it was difficult for many clinicians to accept that ulcers were caused by a bacterium and were, therefore, more like an infectious disease than an illness caused by excess acid. Initial skepticism decreased when Marshall publicly swallowed a culture of *H. pylori* and then developed a severe case of gastritis that was successfully treated with antibiotics!

Marshall and Warren not only identified a bacterium as the cause of ulcers, their work also suggested that the time-honored and traditional use of antacid treatment for ulcers be abandoned and replaced by antibiotic therapy. In awarding the Nobel, the committee described the research of Marshall and Warren as producing "one of the most radical and important changes in the last 50 years in the perception of a medical condition." What was once considered a radical new explanation for the cause of ulcers is now a proven fact. And, antibiotic treatment is now an important part of the accepted standard of care for most ulcer patients. *H. pylori* infection in ulcer patients can be diagnosed by biopsy, breath, or blood antibody tests.

Long-term use of certain pain medications such as aspirin and ibuprofen, called *nonsteroidal antiinflammatory drugs (NSAIDs)*, can also cause ulcers. These drugs interfere with prostaglandins that regulate the mucus lining of the GI tract. NSAID-induced ulcers can be treated by stopping NSAID use and taking acid-reducing drugs until the ulcer heals.

Stomach cancer (Figure 28-36) has been linked to *H. pylori* infection, excessive alcohol consumption, use of chewing tobacco, and eating smoked or heavily preserved food. Most stomach cancers, usually *adenocarcinomas*, have already metastasized before they are found because patients treat themselves for the early warning signs of heartburn, belching, and nausea. Later warning signs of stomach cancer include chronic indigestion, vomiting, anorexia, stomach pain, and blood in the feces. Surgical removal of the malignant tumors has been the most successful method of treating stomach cancer.

The pyloric sphincter is of clinical importance because **pylorospasm** is a fairly common condition in infants. The pyloric fibers do not relax normally to allow food to leave the stomach, and

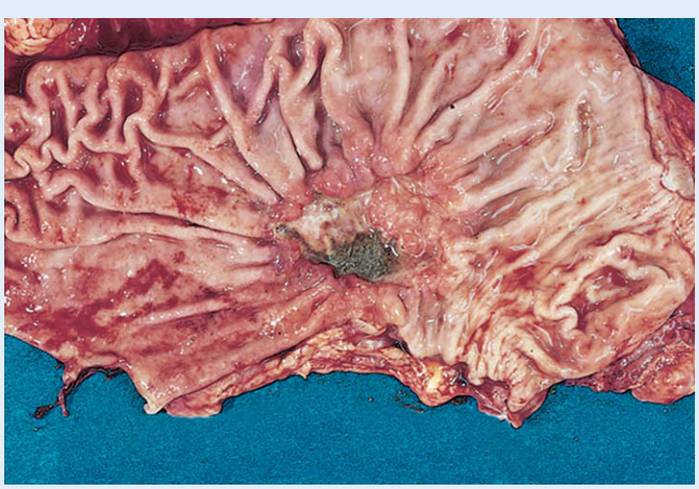


FIGURE 28-36

Stomach cancer. The abnormal tissue near the center of this opened stomach is gastric carcinoma, or "stomach cancer." Note the distinct, normal rugae (folds) that surround the tumor tissue.

consequently, the infant vomits food instead of digesting and absorbing it. The condition is relieved by the administration of a drug that relaxes smooth muscles. Another abnormality of the pyloric sphincter is **pyloric stenosis,** an obstructive narrowing of its opening.

Malabsorption syndrome is a general term referring to a group of symptoms resulting from the failure of the small intestine to absorb nutrients properly. These symptoms include anorexia, abdominal bloating, cramps, anemia, and fatigue. Numerous underlying conditions can cause malabsorption syndrome. For example, certain enzyme deficiencies can result in an absorption failure because there are no digested nutrients to absorb. Cystic fibrosis and other genetic conditions can also cause malabsorption syndrome.

Diverticulosis is the presence of abnormal saclike outpouchings of the intestinal wall called *diverticula* (Figure 28-37). Diverticula often develop in adults older than 50 years who eat low-fiber foods. Diverticulosis is usually asymptomatic. If the diverticula become inflamed, however, the condition is called **diverticulitis.** Diverticulitis is characterized by pain, tenderness, and fever.

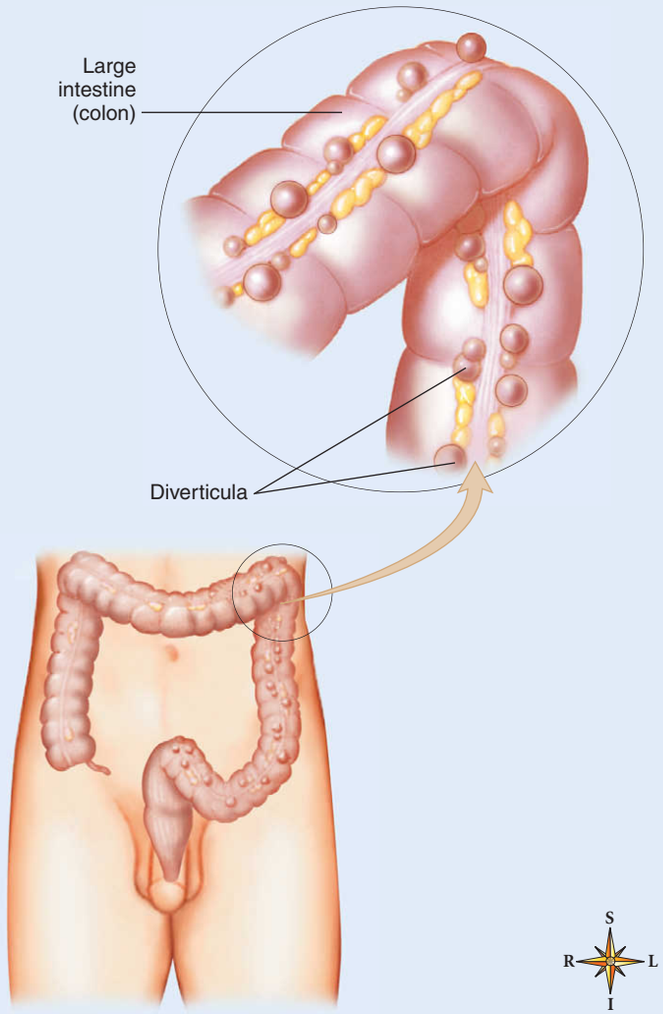


FIGURE 28-37

Diverticula. Abnormal outpouchings of the colon are called *diverticula.* When they become inflamed, the condition is called *diverticulitis.* Diverticula occur mainly in the descending colon and only very rarely in the transverse colon.

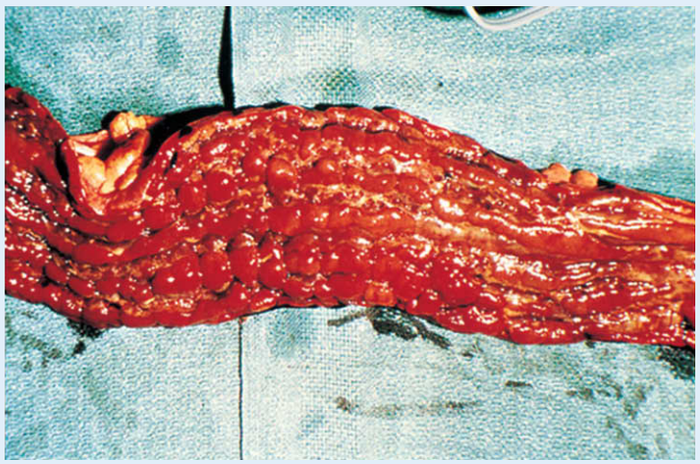


FIGURE 28-38

Crohn disease. Crohn disease, an autoimmune form of colitis, is characterized by severe inflammation that gives a sort of "cobblestone" appearance to the intestinal lining.

Colitis refers to any inflammatory condition of the large intestine. Symptoms of colitis include diarrhea and abdominal cramps or constipation. Some forms of colitis may also produce bleeding and intestinal ulcers. It may also result from an autoimmune disease, as in *ulcerative colitis.* Another type of colitis can occur in those with **Crohn disease.** Crohn disease results from an abnormal inflammatory response. Although it can occur in any part of the alimentary canal, it most often affects the small intestine and the colon (Figure 28-38). If more conservative treatments fail, colitis may be corrected by surgical removal of the affected portions of the colon.

Irritable bowel syndrome, or *spastic colon,* is a common chronic noninflammatory condition that is often caused by stress. Irritable bowel syndrome is characterized by diarrhea or constipation with or without pain.

Colorectal cancer is a malignancy, usually an *adenocarcinoma,* of the colon or rectum. Colorectal cancer occurs most often after the age of 50, and a low-fiber, high-fat diet and genetic predisposition are known risk factors. Early warning signs of this common type of cancer include changes in bowel habits, fecal blood, rectal bleeding, abdominal pain, unexplained anemia or weight loss, and fatigue. Screening for colorectal cancer may be done by checking for occult (hidden) blood in the feces or by examining the rectum and colon with a flexible scope during a *colonoscopy.*

If the mucous lining of the appendix becomes inflamed, the resulting condition is the well-known affliction **appendicitis.** As you can see in Figure 28-19, the appendix is very close to the rectal wall. For patients with suspected appendicitis, a physician often evaluates the appendix by performing a digital rectal examination.

The opening between the lumen of the appendix and the cecum is quite large in children and young adults—a fact of clinical significance because food, fecal material, or calcified, stonelike concrections called *appendicoliths* (ah-pen-DIK-oh-liths) may become trapped in the opening, block the lumen, and cause irritation and inflammation resulting in appendicitis. If calcification within the appendix is visible on an x ray in a patient with pain in the lower

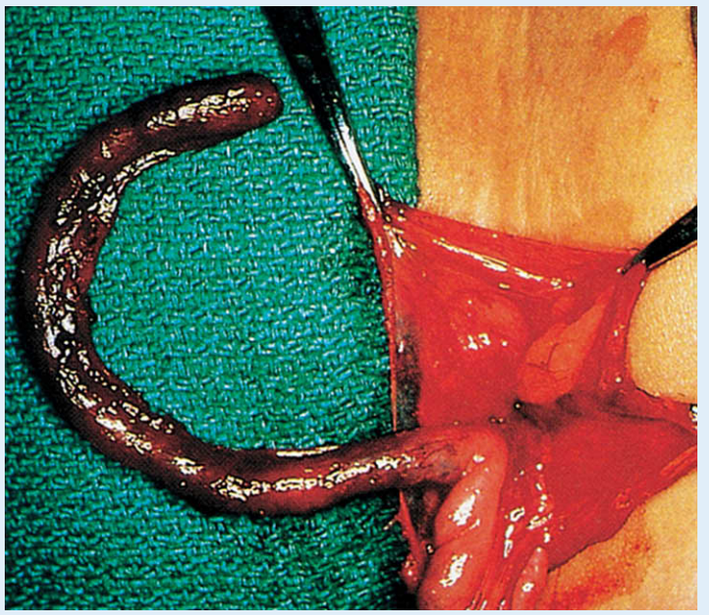


FIGURE 28-39

Acute appendicitis. Note the inflamed tissue surrounding the base of a gangrenous appendix.

right abdominal quadrant, there is an extremely high probability—physicians call it "clinical suspicion"—of acute appendicitis.

The opening between the appendix and the cecum is often completely obliterated in elderly persons, which explains the low incidence of appendicitis in this population.

If infectious material becomes trapped in an inflamed appendix (Figure 28-39), the appendix may rupture and release the material into the abdominal cavity. Infection of the peritoneum and other abdominal organs may result—with sometimes tragic consequences.

Rectal bleeding is a symptom that should always be investigated. Although it may signal a serious disease problem, such as cancer, most instances of this common problem are indicators of less serious and non–life-threatening conditions (Figure 28-40).

Hemorrhoids are dilated veins that result from direct irritation or from increases in venous pressure that often accompany pregnancy or result from constipation and the subsequent straining required to pass compact and hardened stools. Hemorrhoids most commonly develop near the anal opening or on the wall of the anal canal. Though often painful and irritating, hemorrhoids generally respond readily to treatment and are seldom a serious health concern.

Proctitis, or inflammation of the rectal mucosa, is another frequent cause of rectal bleeding and related symptoms such as mucus discharge or increased frequency of bowel movements. The condition may result from direct irritation or infection. In most cases, proctitis responds quickly to the administration of antiinflammatory drugs and treatment of the underlying problem.

Anal fissures are generally minor lacerations in the lining of the anus or anal canal that result in rectal bleeding. They are caused by direct irritation—often the result of passing a hardened stool. An **anal fistula** is a more serious problem that may require surgical repair. A fistula is a passageway that often develops between the rectal wall and the skin surrounding the anus. Fistulas occur in Crohn disease, an inflammatory bowel disease.

Disorders of the Liver and Pancreas

Hepatitis is a general term referring to inflammation of the liver. Hepatitis is characterized by jaundice (yellowish discoloration of body tissues), liver enlargement, anorexia, abdominal discomfort, gray-white feces, and dark urine. Various conditions can produce hepatitis. Alcohol, drugs, or other toxins may cause hepatitis. It may also be a complication of bacterial or viral infection or parasite infestation. *Hepatitis A,* for example, results from infection by the hepatitis A virus. Contaminated food is often a source of infection. Hepatitis A occurs commonly in young people and ranges in severity from mild to life threatening. Another viral hepatitis, *hepatitis B,* is usually more severe. It is also called *serum hepatitis* because it is often transmitted by contaminated blood serum (plasma). The *hepatitis C virus (HCV),* causes a viral form of hepatitis that can also be transmitted by contaminated blood. Although *hepatitis C* does not always produce symptoms or liver disease, it can in many individuals lead to various liver disorders. Other viral forms of hepatitis include the D, E, and G types.

Hepatitis, chronic alcohol abuse, malnutrition, infection, or *nonalcoholic fatty liver disease* may lead to a degenerative liver condition known as **cirrhosis.** The liver's ability to regenerate damaged tissue is well known, but it has its limits. For example, when the toxic effects of alcohol accumulate faster than the liver can regenerate itself, damaged tissue is replaced with fibrous scar tissue instead of normal tissue (Figure 28-41). *Cirrhosis* is the name given to such degeneration.

Besides the endocrine disorders such as diabetes mellitus discussed in Chapter 19, the pancreas may be involved in numerous other diseases. For example, **pancreatitis,** or inflammation of the

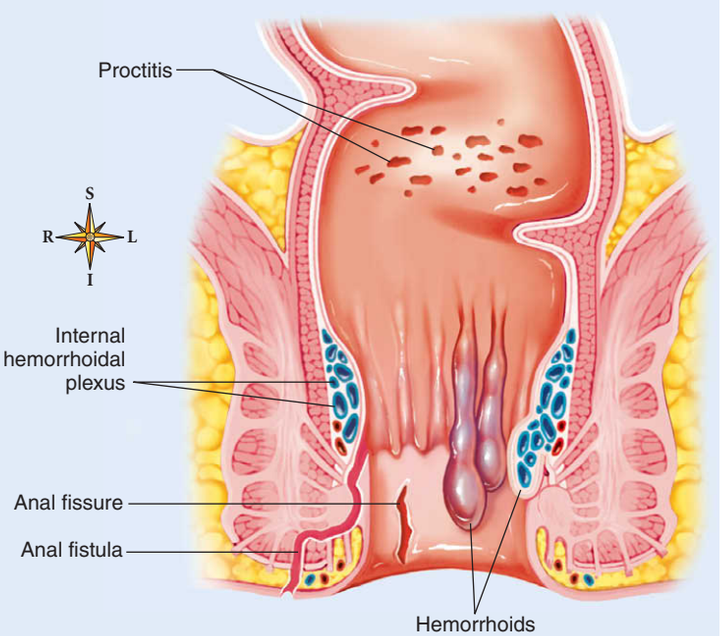


FIGURE 28-40

Causes of rectal bleeding.

pancreas, can be caused by various factors. *Acute pancreatitis* usually results from blockage of the pancreatic duct. The blockage causes pancreatic enzymes to "back up" into the pancreas and digest it. Another condition that blocks the flow of pancreatic enzymes is *cystic fibrosis (CF)*. You may recall from Chapter 4 that this inherited disorder disrupts cell transport and causes exocrine glands to produce excessively thick secretions. Thick pancreatic secretions may build up and block pancreatic ducts, disrupting the flow of pancreatic enzymes and damaging the pancreas.

Another serious pancreatic disorder is **pancreatic cancer.** Usually a form of *adenocarcinoma*, pancreatic cancer claims the lives of nearly all its victims within 5 years after diagnosis.

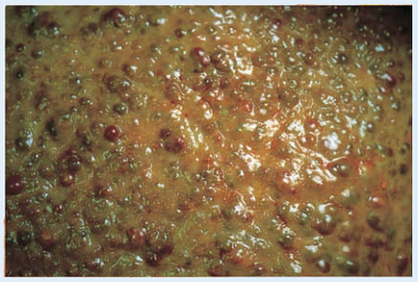


FIGURE 28-41

Cirrhosis. Alcoholic cirrhosis is characterized by hardness of the liver caused by fibrous tissue and by nodules—which can be seen clearly in this photograph of the surface of a cirrhotic liver.

LANGUAGE OF SCIENCE *(continued from p. 861)*

endocrine cell
(EN-doh-krin)
[*endo-* **within,** *-crin-* **secrete,** *cell* **storeroom**]

esophagus
(eh-SOF-ah-gus)
[*es-* **will carry,** *-phagus* **food**]
pl., esophagi

fractal geometry

fundus
(FUN-duss)
[*fundus* **bottom**] *pl.,* fundi

gastrointestinal (GI) tract
(gas-troh-in-TES-tin-ul)
[*gastr-* **stomach,** *-intestin-* **intestine,** *-al* **relating to,** *tractus* **trail**]

glucagon
(GLOO-kah-gon)
[*gluc-* **glucose,** *-agon* **drive**]

greater omentum
(oh-MEN-tum)
[*omentum* **fatty covering of intestines**] *pl.,* omenta

hard palate
(PAL-et)

hepatic lobule
(heh-PAT-ik LOB-yool))
[*hepa-* **liver,** *-ic* **relating to,** *lob-* **pod,** *-ule* **small**]

ileum
(IL-ee-um)
[*ileum* **groin or flank**] *pl.,* ilea

insulin
(IN-suh-lin)
[*insul-* **island,** *-in* **substance**]

intramural plexus
(in-trah-MYOO-ral PLEK-sus)
[*intra-* **within,** *-mura-* **wall,** *-al* **relating to,** *plexus* **network**]
pl., plexi or plexuses

jejunum
(jeh-JOO-num)
[*jejunus* **empty**]

left lobe

lesser omentum
(oh-MEN-tum)
[*omentum* **fatty covering of intestines**]

lip

lower esophageal sphincter (LES)
(eh-SOF-eh-JEE-ul SFINGK-ter)
[*es-* **will carry,** *-phag-* **food (eat),** *-al* **relating to,** *sphinc-* **bind tight,** *-er* **agent**]

mastication
(mas-ti-KAY-shun)
[*mastic-* **chew,** *-ation* **process**]

mesentery
(MEZ-en-tair-ee)
[*mes-* **middle,** *-enter-* **intestine**]

mucosa
(myoo-KOH-sah)
[*muc-* **slime,** *-osa* **relating to**]
pl., mucosae

muscularis
(mus-kyoo-LAIR-is)
[*mus-* **mouse,** *-cul-* **little,** *-aris* **relating to**] *pl.,* musculares

pancreatic islet
(pan-kree-AT-ik EYE-let)
[*pan-* **all,** *-crea-* **flesh,** *-ic* **relating to,** *islet* **island**]

parietal cell
(pah-RYE-i-tal sell)
[*paires-* **wall,** *-al* **relating to,** *cell* **storeroom**]

parotid
(peh-RAH-tid)
[*par-* **beside,** *-ot-* **ear,** *-id* **relating to**]

peritoneum
(pair-i-toh-NEE-um)
[*peri-* **around,** *-tone-* **stretched,** *-um* **thing**] *pl.,* peritonea

permanent teeth

pulp cavity
[*pulp* **flesh,** *cav-* **hollow,** *-ity* **condition**]

pyloric sphincter
(pye-LOR-ik SFINGK-ter)
[*pyl-* **gate,** *-or-* **to guard,** *-ic* **relating to,** *sphinc-* **bind tight,** *-er* **agent**]

pylorus
(pye-LOR-us)
[*pyl-* **gate,** *-orus* **guard**]

rectum
(REK-tum)
[*rect-* **straight,** *-um* **thing**]

right lobe

root

serosa
(see-ROH-sah)
[*ser-* **watery fluid,** *-osa* **relating to**]
pl., serosae

sigmoid colon
(SIG-moyd KOH-lon)
[*sigm-* **sigma (Σ or σ)18th letter of Greek alphabet (Roman S),** *-oid* **like,** *colon* **colon**]

soft palate
(PAL-et)

sublingual gland
(sub-LING-gwall)
[*sub-* **under,** *-lingua-* **tongue,** *-al* **relating to,** *gland* **acorn**]

submandibular gland
(sub-man-DIB-yoo-lar)
[*sub-* **under,** *-mandibul-* **chew (mandible or jawbone),** *-ar* **relating to,** *gland* **acorn**]

submucosa
(sub-myoo-KOH-sah)
[*sub-* **under,** *-muc-* **slime,** *-osa* **relating to**] *pl.,* submucosae

tongue

transverse colon
(trans-VERS KOH-lon)
[*trans-* **across,** *-vers-* **turn,** *colon* **large intestine**]

transverse mesocolon
(trans-VERS MEZ-oh-koh-lon)
[*trans-* **across,** *-vers-* **turn,** *meso-* **middle,** *-colon* **large intestine**]

upper esophageal sphincter (UES)
(eh-SOF-ah-JEE-ul SFINGK-ter)
[*es-* **will carry,** *-phag-* **food (eat),** *-al* **relating to,** *sphinc-* **bind tight,** *-er* **agent**]

vermiform appendix
(VERM-i-form ah-PEN-diks)
[*vermi-* **worm,** *-form* **shape,** *append-* **hang upon,** *-ix* **thing**]
pl., appendices

villus
(VIL-us)
[*villus* **shaggy hair**], *pl.,* villi

LANGUAGE OF MEDICINE *(continued from p. 895)*

anal fissure
(AY-nal FISH-ur)
[*an-* **ring (anus),** *-al* **relating to,** *fissur-* **cleft**]

anal fistula
(AY-nal FISS-tyoo-lah)
[*an-* **ring (anus),** *-al* **relating to,** *fistula* **pipe**] *pl.,* fistulae or fistulas

anorexia
(an-oh-REK-see-ah)
[*an-* **without,** *-orex-* **appetite,** *-ia* **condition**]

appendicitis
(ah-pen-di-SYE-tis)
[*appendic-* **hang upon,** *-itis* **inflammation**]

caries
(KAIR-ees)
[*caries* **decay**]

cholecystectomy
(koh-leh-sis-TEK-toh-mee)
[*chole-* **bile,** *-cyst-* **bag,** *-ec-* **out,** *-tom-* **cut,** *-y* **action**]

cholecystitis
(koh-leh-sis-TYE-tis)
[*chole-* **bile,** *-cyst-* **bag,** *-itis* **inflammation**]

cholelithiasis
(koh-leh-lih-THEE-ah-sis)
[*chole-* **bile,** *-lith-* **stone,** *-iasis* **condition**]

cirrhosis
(sih-ROH-sis)
[*cirrhos-* **yellow-orange,** *-osis* **condition**]

colitis
(koh-LYE-tis)
[*col-* **colon,** *-itis* **inflammation**]

colonoscopy
(koh-lon-AH-skah-pee)
[*colon* **large intestine,** *-scop-* **see,** *-y* **activity**]

colorectal cancer
(koh-loh-REK-tal KAN-ser)
[*colo-* **colon,** *-rect-* **straight,** *-al* **relating to,** *cancer* **crab or malignant tumor**]

constipation
(kon-sti-PAY-shun)
[*constipa-* **crowd together,** *-ation* **process**]

Crohn disease
(krohn)
[*Burrill B. Crohn* **American physician**]

diarrhea
(dye-ah-REE-ah)
[*dia-* **through,** *-rrhea* **flow**]

diverticulitis
(dye-ver-tik-yoo-LYE-tis)
[*diverticul-* **turn aside,** *-itis* **inflammation**]

diverticulosis
(dye-ver-tik-yoo-LOH-sis)
[*diverticul-* **turn aside,** *-osis* **condition**]

emesis
(EM-eh-sis)
[*emesis* **vomiting**]

erosive esophagitis
(eh-ROH-siv eh-SOF-ah-jye-tis)
[*es-* **will carry,** *-phag-* **food (eat),** *-itis* **inflammation**]

esophageal endoscope
(eh-sof-ah-JEE-ul EN-doh-skohp)
[*es-* **will carry,** *-phag-* **food (eat),** *-al* **relating to,** *endo-* **within,** *-scop-* **see**]

gastroenteritis
(gas-troh-en-ter-EYE-tis)
[*gastr-* **stomach,** *-enter-* **intestine,** *-itis* **inflammation**]

gastroenterology
(gas-troh-en-ter-AHL-oh-jee)
[*gastr-* **stomach,** *-entero-* **intestine,** *-o-* **combining form,** *-log-* **words (study of),** *-y* **activity**]

gastroesophageal reflux disease (GERD)
(gas-troh-eh-sof-eh-JEE-all REE-fluks)
[*gastro-* **stomach,** *-es-* **will carry,** *-phag-* **food (eat),** *-al* **relating to,** *re-* **again or back,** *-flux* **flow**]

gingivitis
(jin-ji-VYE-tis)
[*gingiv-* **gum,** *-itis* **inflammation**]

hemorrhoid
(HEM-eh-royd)
[*hemo-* **blood,** *- rrhoi-* **flow**]

hepatitis
(hep-ah-TYE-tis)
[*hepat-* **liver,** *-itis* **inflammation**]

hiatal hernia
(hye-AY-tal HER-nee-ah)
[*hiat-* **gap,** *-al* **relating to,** *hernia* **rupture**] *pl.,* herniae or hernias

irritable bowel syndrome
(IR-i-tah-bul BOW-uhl SIN-drohm)
[*irrita-* **tease,** *-ble* **able or tending to,** *bowel* **sausage,** *syn-* **together,** *-drome* **running or (race)course**]

jaundice
(JAWN-dis)
[*jaun-* **yellow,** *-ice* **state**]

leukoplakia
(loo-koh-PLAY-kee-ah)
[*leuko-* **white,** *-plak-* **flat area,** *-ia* **condition**]

malabsorption syndrome
(mal-ab-SORP-shun SIN-drohm)
[*mal-* **bad,** *-absorp-* **swallow,** *-tion* **process,** *syn-* **together,** *-drome* **running or (race)course**]

malocclusion
(mal-oh-CLEW-zhun)
[*mal-* **bad,** *-occlu-* **close up,** *-sion* **state**]

mumps
[*mumps* **grimace**]

nausea
(NAW-zee-ah)
[*nausea* **seasickness**]

orchitis
(or-KYE-tis)
[*orchi-* **testis,** *-itis* **inflammation**]

orthodontics
(or-thoh-DON-tiks)
[*ortho-* **straight or upright,** *-odont-* **tooth,** *-ic* **relating to**]

pancreatic cancer
(pan-kree-AT-ik KAN-ser)
[*pan-* **all,** *-creat-* **flesh,** *-ic* **relating to,** *cancer* **crab or malignant tumor**]

pancreatitis
(pan-kree-ah-TYE-tis)
[*pan-* **all,** *-creat-* **flesh,** *-itis* **inflammation**]

parotitis
(pair-oh-TYE-tis)
[*par-* **beside,** *-ot-* **ear (parotid salivary gland),** *-itis* **inflammation**]

periodontitis
(pair-ee-oh-don-TYE-tis)
[*peri-* **around,** *-odont-* **tooth,** *-itis* **inflammation**]

proctitis
(prok-TYE-tis)
[*proct-* **anus,** *-itis* **inflammation**]

pyloric stenosis
(pye-LOR-ik steh-NO-sis)
[*pyl-* **gate,** *-or-* **guard,** *-ic* **relating to,** *stenos-* **narrow,** *-osis* **condition**]
pl., stenoses

pylorospasm
(pye-LOHR-oh-spaz-um)
[*pyl-* **gate,** *-or-* **guard,** *-spasm* **twitch or involuntary contraction**]

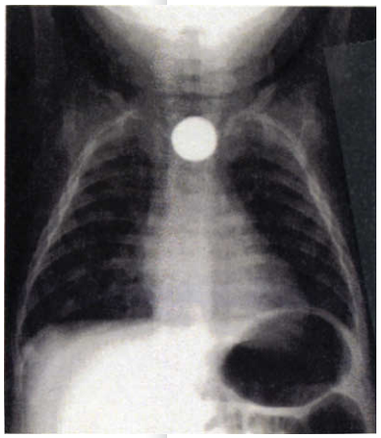
Sjögren syndrome
(SHOW-grin SIN-drohm)
[*Henrik S.C. Sjögren* **Swedish ophthalmologist,** *syn-* **together,** *-drome* **running or (race)course**]

ulcer
(UL-ser)
[*ulc-* **sore**]

xerophthalmia
(zee-rof-THAL-mee-ah)
[*xero-* **dryness,** *-opth-* **eye,** *-thalm-* **inner chamber,** *-ia* **condition**]

xerostomia
(zee-roh-STOH-mee-ah)
[*xero-* **dryness,** *-stom-* **mouth,** *-ia* **condition**]

CASE study



It only took 3 seconds. Sangetha turned away from her sewing basket to pick up her cell phone. When she looked back, she saw a handful of buttons disappear into her 24-month-old daughter's mouth. She quickly dropped down and removed the buttons from her daughter Jinder's mouth—but Sangetha had no way of knowing how many had gone in. Had any already gone down Jinder's throat? She was coughing slightly and drooling. Sangetha immediately took Jinder to the emergency department, thankfully a very short drive away, where they took x rays of Jinder's neck and chest. On the x ray film, they found one button in Jinder's upper esophagus.

1. With what layer of the esophageal lining would the button be in contact?
- a. Serosa
- b. Muscularis
- c. Submucosa
- d. Mucosa

Because the button was rounded, with no sharp points, the decision was made to let it "pass" through Jinder's system naturally.

2. As the button makes its way through Jinder's alimentary tract, it will go through which sequence of sphincters and valves?
- a. Lower esophageal, pyloric, ileocecal, anal
- b. Anal, pyloric, lower esophageal, ileocecal
- c. Lower esophageal, ileocecal, pyloric, anal
- d. Pyloric, ileocecal, anal, lower esophageal

3. Imagine a camera is attached to the button. As the button travels through Jinder's small intestines, the viewing monitor shows many tiny projections that look like gently moving brush bristles in the lining of the small intestine. What are these projections?
- a. Plicae
- b. Rugae
- c. Villi
- d. Crowns

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

ORGANIZATION OF THE DIGESTIVE SYSTEM

A. Organs of digestion (Figure 28-1)
   1. Main organs of the digestive system form the GI tract that extends through the abdominopelvic cavity
   2. Ingested food material passing through the lumen of the GI tract is outside the internal environment of the body

B. Wall of the GI tract (Figure 28-2)
   1. Mucosa—innermost layer
   2. Submucosa—contains numerous glands, blood vessels, and parasympathetic nerves
   3. Muscularis—thick layer of muscle tissue
   4. Serosa—outermost layer
   5. Modifications of layers—structure of layers varies in different regions throughout length of GI tract (Table 28-1)

MOUTH

A. Structure of the oral cavity (buccal cavity) (Figure 28-3)
   1. Lips
      a. Covered externally by skin and internally by mucous membrane
      b. Junction between skin and mucous membrane is highly sensitive
      c. Line of contact between closed lips forms the oral fissure
   2. Cheeks
      a. Lateral boundaries of the oral cavity, continuous with the lips and lined by mucous membrane
      b. Formed in large part by the buccinator muscle covered by adipose tissue
      c. Contain mucus-secreting glands
   3. Hard palate and soft palate
      a. Hard palate consists of portions of four bones: two maxillae and two palatines
      b. Soft palate forms the partition between the mouth and nasopharynx and is made of muscle arranged in an arch
      c. Suspended from the midpoint of the posterior border of the arch is the uvula
   4. Tongue—solid mass of skeletal muscle covered by a mucous membrane; extremely maneuverable
      a. Has three parts: root, tip, and body (Figure 28-4)

b. Papillae located on the dorsal and lateral surfaces of the tongue (Figure 28-5)
c. Lingual frenulum anchors the tongue to the floor of the mouth (Figure 28-6)
d. Intrinsic muscles important for speech and mastication; extrinsic muscles important for deglutition and speech (Figure 28-7)

B. Salivary glands
1. Three main pairs of compound tubuloalveolar glands (Figure 28-8)
a. Secrete approximately 1 liter of saliva each day
b. Additional small buccal glands contribute less than 5% of the total salivary volume but provide for hygiene and comfort of oral tissues
2. Parotid glands—largest of the paired salivary glands; produce watery saliva containing enzymes
3. Submandibular glands—compound glands that contain enzyme- and mucus-producing elements
4. Sublingual glands—smallest of the salivary glands; produce a mucous type of saliva

C. Teeth—organs of mastication
1. Typical tooth (Figure 28-9)
a. Crown—exposed portion of a tooth, covered by enamel; ideally suited to withstand abrasion during mastication
b. Neck—narrow portion that joins the crown to the root; surrounded by gingivae
c. Root—fits into the socket of the alveolar process; suspended by a fibrous periodontal membrane
d. Outer shell contains two additional tissues: dentin and cementum
(1) Dentin—greatest portion of the tooth shell; at the crown, covered by enamel, and at the neck and root, covered by cementum
(2) Pulp cavity—located in dentin, contains connective tissue, blood, and lymphatic vessels and sensory nerves
2. Types of teeth (Figure 28-10)
a. Deciduous teeth—20 baby teeth, which appear early in life
b. Permanent teeth—32 teeth, which replace the deciduous teeth

PHARYNX

A. Tube through which a food bolus passes when moved from the mouth to the esophagus by the process of deglutition
B. Air passes through all three divisions of the pharynx; only terminal portion involved in digestive system

ESOPHAGUS

A. Tube that extends from the pharynx to the stomach; first segment of the digestive tube (Figure 28-11)
B. Lined with stratified squamous epithelium (Figure 28-12)
C. Each end encircled by muscular sphincters

STOMACH

A. Size and position of the stomach
1. Size varies according to factors such as gender and amount of distention
a. When no food is in the stomach, it is about the size of a large sausage
b. In adults, its capacity ranges from 1.0 to 1.5 liters
2. Stomach location: upper part of the abdominal cavity under the liver and diaphragm

B. Divisions of the stomach (Figure 28-13)
1. Cardia—collarlike region at junction with esophagus
2. Fundus—enlarged portion to the left and above the opening of the esophagus into the stomach
3. Body—central portion of the stomach
4. Pylorus—lower part of the stomach

C. Curves of the stomach
1. Lesser curvature—upper right curve of the stomach
2. Greater curvature—lower left curve of the stomach

D. Sphincter muscles—circular fibers arranged so that there is an opening in the center when relaxed and no opening when contracted
1. Lower esophageal sphincter (LES), or cardiac sphincter, controls the opening of the esophagus into the stomach
2. Pyloric sphincter controls the outlet of the pyloric portion of the stomach into the duodenum

E. Stomach wall (Figure 28-14)
1. Gastric mucosa
a. Epithelial lining has rugae marked by gastric pits (Figure 28-15)
b. Gastric glands—found below the level of the pits; secrete most of the gastric juice
c. Chief cells—secretory cells found in the gastric glands; secrete the enzymes of gastric juice
d. Parietal cells—secretory cells found in the gastric glands; secrete hydrochloric acid; thought to produce intrinsic factor needed for vitamin B_{12} absorption
e. Endocrine cells—secrete gastrin and ghrelin
2. Gastric muscularis
a. Thick layer of muscle with three distinct sublayers of smooth muscle tissue arranged in a crisscrossing pattern
b. This pattern allows the stomach to contract strongly at many angles

F. Functions of the stomach
1. Reservoir for food until it is partially digested and moved further along the GI tract
2. Secretes gastric juice to aid in digestion of food
3. Breaks food into small particles and mixes them with gastric juice
4. Secretes intrinsic factor
5. Performs limited absorption
6. Produces gastrin and ghrelin
7. Helps protect the body from pathogenic bacteria swallowed with food

SMALL INTESTINE

A. Size and position of the small intestine
1. Tube approximately 2.5 cm in diameter and 6 m in length
2. Coiled loops fill most of the abdominal cavity (Figure 28-16)

B. Divisions of the small intestine
   1. Duodenum—uppermost division; approximately 25 cm long, shaped roughly like the letter C
   2. Jejunum—approximately 2.5 m long
   3. Ileum—approximately 3.5 m long
C. Wall of the small intestine (Figure 28-17)
   1. Intestinal lining has plicae with villi
   2. Villi—important modifications of the mucosal layer
      a. Each villus contains an arteriole, venule, and lacteal vessel
      b. Covered by a brush border made up of 1700 ultrafine microvilli per cell
      c. Villi and microvilli increase the surface area of the small intestine hundreds of times
   3. Crypts—located between villi; contain stem cells from which other cell types are produced and then migrate upward to cover the villi, where they eventually slough off (Figure 28-18)

LARGE INTESTINE

A. Size of the large intestine
   1. Average diameter, 6 cm
   2. Length, approximately 1.5 to 1.8 m
B. Divisions of the large intestine (Figure 28-19)
   1. Cecum—first 5 to 8 cm of the large intestine; blind pouch located in the lower right quadrant of the abdomen
   2. Colon
      a. Ascending colon—vertical position on the right side of the abdomen; the ileocecal valve prevents material from passing from the large intestine into the ileum
      b. Transverse colon—passes horizontally across the abdomen, above the small intestine; extends from the hepatic flexure to the splenic flexure
      c. Descending colon—vertical position on left side of the abdomen
      d. Sigmoid colon joins the descending colon to the rectum
   3. Rectum
      a. Last 7 or 8 inches of the intestinal tube
      b. Terminal inch is the anal canal with the opening called the *anus* (Figure 28-20)
C. Wall of the large intestine (Figure 28-21)
   1. Intestinal mucous glands produce lubricating mucus that coats feces as they are formed
   2. Uneven distribution of fibers in the muscle coat

VERMIFORM APPENDIX

A. Accessory organ of digestive system
B. 8 to 10 cm in length; communicates with the cecum
C. Serves as reservoir for beneficial gut bacteria

PERITONEUM

A. Large, continuous sheet of serous membrane (Figure 28-22)
   1. Many organs are covered with visceral peritoneum; parietal peritoneum then lines the wall of the abdominopelvic cavity
   2. Extraperitoneal space is outside the parietal layer of the peritoneum; retroperitoneal identifies the extraperitoneal space along the posterior and bottom of the abdominopelvic cavity.
B. Mesentery—projection of the parietal peritoneum; allows free movement of each coil of the intestine and helps prevent strangulation of the long tube (Figure 28-23)
C. Transverse mesocolon—extension of the peritoneum that supports the transverse colon

LIVER

A. Location and size of the liver (Figure 28-24)
   1. Largest gland in the body, weighs approximately 1.5 kg
   2. Lies under the diaphragm; occupies most of the right hypochondrium and part of the epigastrium
B. Liver lobes and lobules—two lobes separated by the falciform ligament
   1. Left lobe—forms about one sixth of the liver
   2. Right lobe—forms about five sixths of the liver; divides into right lobe proper, caudate lobe, and quadrate lobe
   3. Hepatic lobules—anatomical units of the liver; a small branch of the hepatic vein extends through the center of each lobule (Figures 28-25 and 28-26)
C. Bile ducts (Figure 28-27)
   1. Small bile ducts form right and left hepatic ducts
   2. Right and left hepatic ducts immediately join to form one hepatic duct
   3. Hepatic duct merges with the cystic duct to form the common bile duct, which opens into the duodenum
D. Functions of the liver
   1. Detoxification by liver cells—ingested toxic substances and toxic substances formed in the intestines may be changed to nontoxic substances
   2. Bile secretion by liver—bile salts are formed in the liver from cholesterol and are the most essential part of bile; liver cells secrete approximately 1 pint of bile per day
   3. Liver metabolism—carries out numerous important steps in metabolizing proteins, fats, and carbohydrates
   4. Storage of substances such as iron and some vitamins
   5. Production of important plasma proteins

GALLBLADDER

A. Size and location of the gallbladder
   1. Pear-shaped sac 7 to 10 cm long and 3 cm wide at its broadest point
   2. Lies on the undersurface of the liver (Figure 28-27)
B. Structure of the gallbladder
   1. Serous, muscular, and mucous layers compose the gallbladder wall
   2. The mucosal lining has rugae that expand to allow storage of bile; holds 30 to 50 ml of bile
C. Functions of the gallbladder
   1. Storage of bile
   2. Concentration of bile fivefold to tenfold
   3. Ejection of the concentrated bile into the duodenum
D. Gallstones—often made of cholesterol; can form when bile becomes concentrated (Figure 28-28)

PANCREAS

A. Size and location of the pancreas
   1. Grayish pink–colored gland; 12 to 15 cm long; weighs approximately 60 grams
   2. Runs from the duodenum, behind the stomach, to the spleen
B. Structure of the pancreas (Figure 28-29)—composed of endocrine and exocrine glandular tissue
   1. Exocrine portion makes up the majority of the pancreas; has a compound acinar arrangement; tiny ducts unite to form the main pancreatic duct, which empties into the duodenum
   2. Endocrine portion—embedded between exocrine units; called *pancreatic islets*; constitute only 2% of the total mass of the pancreas; made up of alpha cells and beta cells; pass secretions into capillaries
C. Functions of the pancreas
   1. Acinar units secrete digestive enzymes
   2. Beta cells secrete insulin
   3. Alpha cells secrete glucagon

CYCLE OF LIFE: DIGESTIVE SYSTEM

A. Changes in digestive function and structure are age related
   1. Result in diseases or pathological conditions
   2. May occur in any segment of the intestinal tract
   3. Changes involve accessory organs: teeth, salivary glands, liver, gallbladder, and pancreas
B. Infants have immature intestinal mucosa
   1. Intact proteins can pass through epithelial cells lining the tract and trigger an allergic response
   2. Lactose intolerance affects infants who lack the enzyme lactase
C. Mumps common in children; appendicitis more common in adolescents and then incidence decreases with advancing age
E. Ulcers and gallbladder disease common in middle age
F. Decreased digestive fluids, slowing of peristalsis, and reduced physical activity lead to constipation and diverticulosis in the elderly

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. List the component parts or segments of the GI tract and the accessory organs of digestion.
2. Name and describe the four tissue layers that form the wall of GI tract organs.
3. Identify the structures that form the mouth.
4. Define the following terms associated with the mouth and pharynx: *philtrum, oral fissure, hard palate and soft palate, fauces, uvula, foramen cecum, lingual frenulum.*
5. What is ankyloglossia?
6. Identify the types of tongue papillae. What is the relationship between papillae and taste buds?
7. List and give the location of the paired salivary glands. Identify by name the ducts that drain the saliva from these glands into the mouth.
8. What type of saliva is produced by the parotid glands? What is meant by the term *mixed* or *compound salivary gland?*
9. Describe a typical tooth. Name the specific types of teeth.
10. Compare and contrast deciduous and permanent teeth.
11. What is meant by the term *deglutition?*
12. List the divisions of the stomach. What is the difference between gastric pits and gastric glands?
13. Identify the three major cell types of the gastric glands. What cell type produces hydrochloric acid? Gastric enzymes? Gastrin? Ghrelin?
14. Describe the seven functions of the stomach.
15. List the divisions of the small intestine from proximal to distal.
16. In what area of the GI tract do you find villi? Haustra? Taeniae coli?
17. List the divisions of the large intestine.
18. What is believed to be the function of the vermiform appendix?
19. Discuss the peritoneum and its reflections.
20. Discuss the anatomy of a typical liver lobule.
21. Identify the ducts of the liver and gallbladder.
22. Explain the functions of the gallbladder.
23. Differentiate between endocrine and exocrine functions of the pancreas.
24. Identify the condition that can develop in men who are infected with mumps.
25. What is the difference between dental caries and periodontitis?
26. What is pyloric stenosis?
27. Define cholelithiasis.

CRITICAL THINKING QUESTIONS

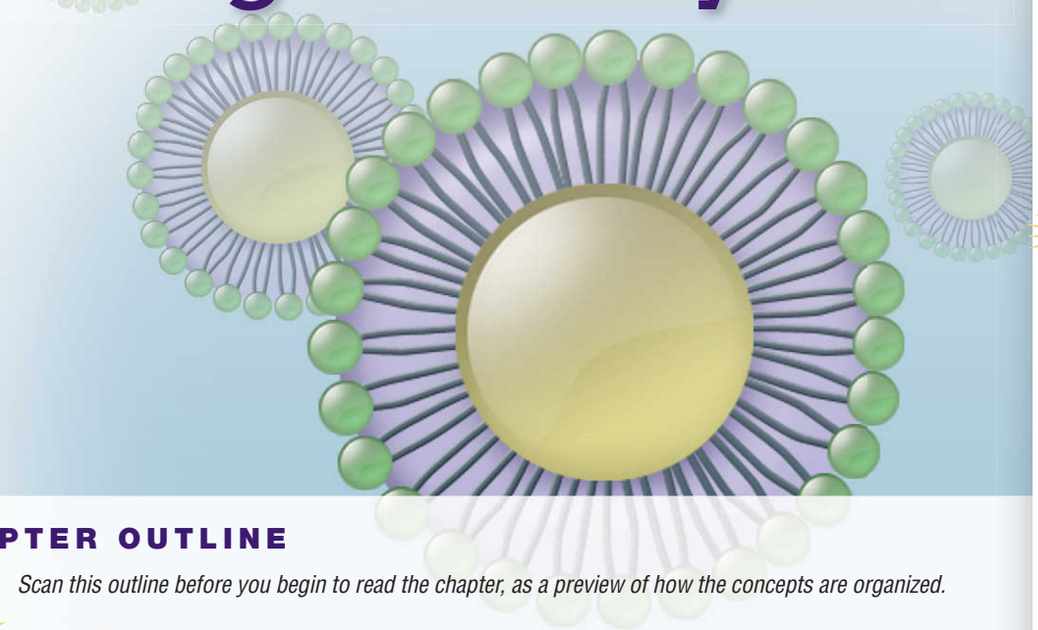


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Explain the role of the tongue's intrinsic and extrinsic muscles.
2. Describe the unique muscular layer of the esophagus.
3. Increasing the interior surface area of the small intestine allows it to absorb nutrients more efficiently. What examples can you find that add to the interior surface area of the small intestine?
4. Explain the x ray procedure used to diagnose a hiatal hernia. What procedure would be used to diagnose an intestinal diverticulum?
5. If an elderly patient had abdominal pain, why would it be unlikely that it is caused by appendicitis?

Physiology of the Digestive System

29



CHAPTER OUTLINE

HINT *Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.*

Overview of Digestive Function, 902

Digestion, 904
- Mechanical Digestion, 904
  - Mastication, 904
  - Deglutition, 904
  - Peristalsis and Segmentation, 905
  - Regulation of Motility, 906
  - Intestinal Motility, 907
- Chemical Digestion, 908
  - Digestive Enzymes, 908
  - Carbohydrate Digestion, 910
  - Protein Digestion, 910
  - Fat Digestion, 912
  - Residues of Digestion, 913

Secretion, 914
- Saliva, 914
- Gastric Juice, 914
- Pancreatic Juice, 916
- Bile, 916
- Intestinal Juice, 917

Control of Digestive Gland Secretion, 918
- Control of Salivary Secretion, 918
- Control of Gastric Secretion, 918
- Control of Pancreatic Secretion, 920
- Control of Bile Secretion, 920
- Control of Intestinal Secretion, 920

Absorption, 921
- Process of Absorption, 921
- Mechanisms of Absorption, 921

Elimination, 924

The Big Picture: Digestion and the Whole Body, 925

Case Study, 927

LANGUAGE OF SCIENCE

HINT *Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.*

absorption
(ab-SORP-shun)
[*absorp-* **swallow,** *-tion* **process**]

amylase
(AM-eh-layz)
[*amyl-* **starch,** *-ase* **enzyme**]

bile
(byle)

bile salt
(byle)

bilirubin
(bil-ih-ROO-bin)
[*bili-* **bile,** *-rub-* **red,** *-in* **substance**]

brush border

cephalic phase
(seh-FAL-ik fayz)
[*cephal-* **head,** *-ic* **relating to**]

chemical digestion

chief cell

cholecystokinin (CCK)
(koh-lee-sis-toh-KYE-nin)
[*chole-* **bile,** *-cyst-* **bladder,** *-kin-* **move,** *-in* **substance**]

chylomicron
(kye-loh-MYE-kron)
[*chylo-* **juice (chyle),** *-micro-* **small,** *-on* **particle**]

chyme
(kyme)
[*chym-* **juice**]

chymotrypsin
(kye-moh-TRIP-sin)
[*chymo-* **juice,** *-tryps-* **pound,** *-in* **substance**]

contact digestion
[*digest-* **break down,** *-tion* **process**]

defecation
(def-eh-KAY-shun)
[*de-* **remove,** *-feca-* **waste (feces),** *-tion* **process**]

continued on p. 926

Now that we are familiar with the structural organization of the digestive system (Chapter 28), we are ready to understand the physiological organization of this system. The primary function of the digestive system is to bring essential nutrients into the internal environment so that they are available to each cell of the body. This chapter lays out the essential processes of digestion and absorption. Later, in Chapter 30, you will learn about how the body manages the nutrients after they have been absorbed into the internal environment.

OVERVIEW OF DIGESTIVE FUNCTION

To accomplish the function of making nutrients available to each cell of the body, the digestive system uses various mechanisms (Table 29-1). For example, complex foods must first be taken in—a process called **ingestion.** Then, complex nutrients are broken down into simpler nutrients in the process that gives this system its name: **digestion.** To physically break large chunks of food into smaller bits and to move it along the tract, movement (or **motility**) of the gastrointestinal (GI) wall is required. Chemical digestion—that is, breakdown of large molecules into small molecules—requires **secretion** of digestive enzymes into the lumen of the GI tract. After being digested, nutrients are ready for the process of **absorption,** or movement through the GI mucosa into the internal environment. The material that is not absorbed must then be excreted to make room for more material—a process known as **elimination.** Of course, all these activities must be coordinated, which we have already learned is the process of *regulation*. Some of the major digestive processes are summarized in Figure 29-1. Digestive regulation is introduced in Box 29-1.

Note that Figure 29-1 also illustrates that from a functional perspective, the lumen of the alimentary canal is really a tubelike extension of the external environment that goes right through the middle of the body. Thus digested materials are not truly "part of the body" until they've been absorbed into the internal environment.

After we have explored the various mechanisms of the digestive process in this chapter, we will be ready for Chapter 30, which discusses the assimilation of nutrients after they have been absorbed.

TABLE 29-1 Primary Mechanisms of the Digestive System

MECHANISM	DESCRIPTION
Ingestion	Process of taking food into the mouth, starting it on its journey through the digestive tract
Digestion	A group of processes that break complex nutrients into simpler ones, thus facilitating their absorption; mechanical digestion physically breaks large chunks into small bits; chemical digestion breaks molecules apart
Motility	Movement by the muscular components of the digestive tube, including processes of mechanical digestion; examples include peristalsis and segmentation
Secretion	Release of digestive juices (containing enzymes, acids, bases, mucus, bile, or other products that facilitate digestion); some digestive organs also secrete endocrine hormones that regulate digestion or metabolism of nutrients
Absorption	Movement of digested nutrients through the gastrointestinal (GI) mucosa and into the internal environment
Elimination	Excretion of the residues of the digestive process (feces) from the rectum, through the anus; defecation
Regulation	Coordination of digestive activity (motility, secretion, etc.)

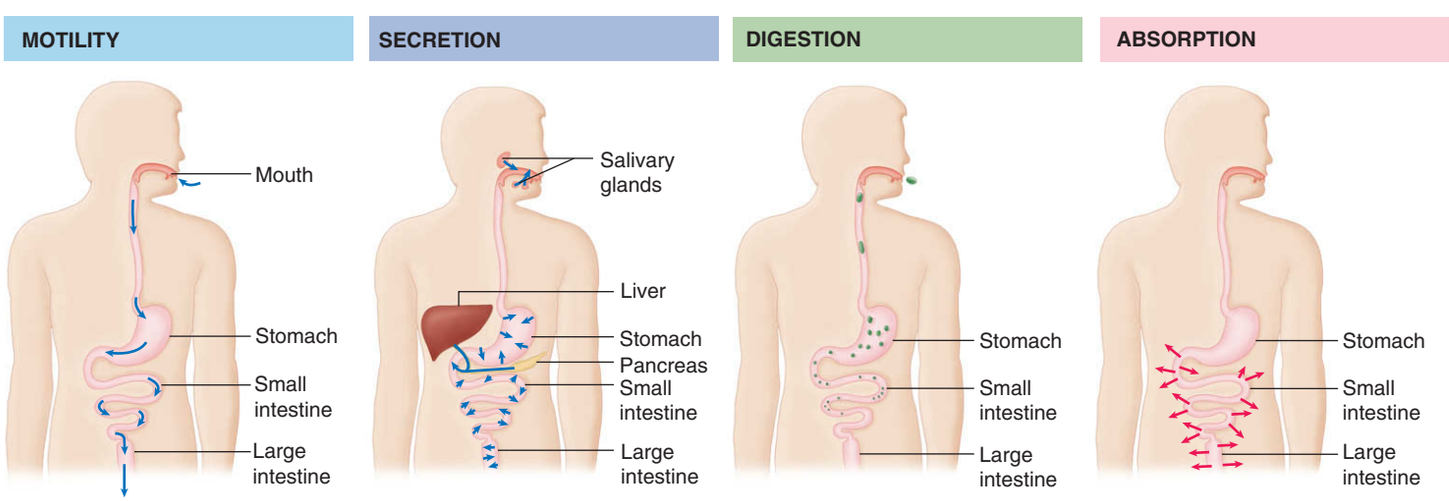


FIGURE 29-1

Overview of digestive functions. Several important digestive functions are summarized in these diagrams. Note that the digestive tract is an extension of the external environment—extending like a tunnel through the body.

Box 29-1 | The ENTERIC Nervous System

As we discussed in Chapter 28, the gastrointestinal (GI) wall includes an *intramural plexus* of nerve pathways. This complex arrangement of neurons is made up largely of the submucosal plexus (of Meissner) and the myenteric plexus (of Auerbach). Figure 28-2 on p. 863 clarifies the locations of these two structures and also shows that they are connected not only to each other but also to the CNS (central nervous system) and the GI muscles and mucous membrane. All of these structures work together in a coordinated system called the **enteric nervous system (ENS).**

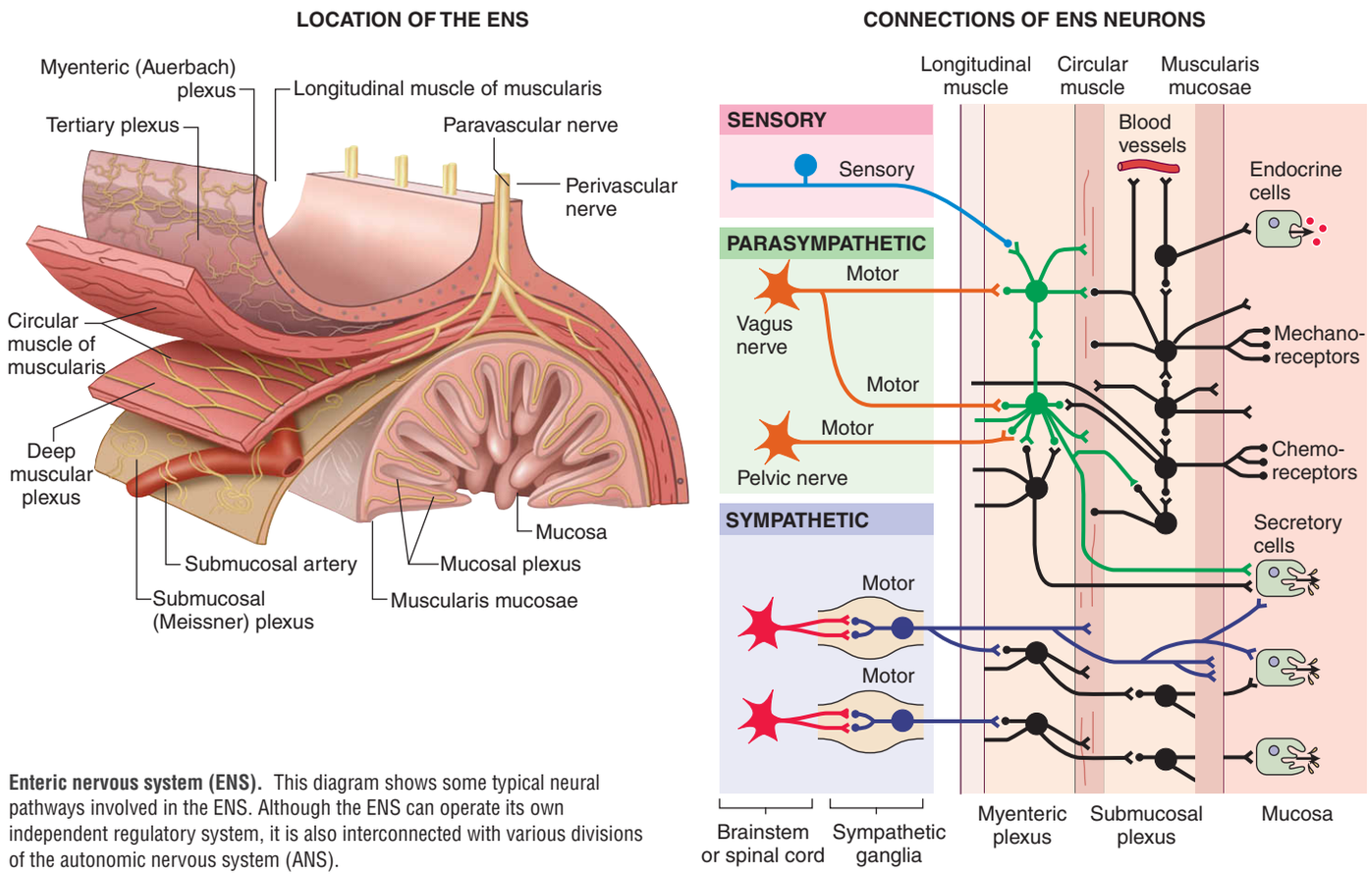
The ENS is often called a "mini brain" or "second brain" because it includes afferent neurons, interneurons, and efferent neurons that independently operate their own nervous reflexes. Thus the ENS can act as "its own brain" in many ways. However, the ENS is certainly influenced by the CNS—as you can see in the diagram here. Because it operates as an involuntary, autonomic system, many physiologists consider the ENS to be another division of the autonomic nervous system (ANS). As the diagram shows, there is certainly communication between the ENS and the various divisions of the ANS.

Operation of the ENS, like the brain, seems to involve the storage and retrieval of memories and the establishment of repeating patterns of response.

Of course, this "second brain" has a complete set of different neurotransmitters that help carry out the complex functions of coordinating enteric reflexes. The list of major ENS neurotransmitters includes some familiar names: acetylcholine (ACh), enkephalins, substance P, serotonin, and nitric oxide (NO). Also on the list is an important peptide neurotransmitter, vasoactive intestinal peptide (VIP). Like other peptide neurotransmitters, VIP helps modulate neuron function—in this case, involving inhibition of intestinal smooth muscle or stimulation of intestinal secretions.

The ENS also helps establish a nervous-immune connection (*neuroimmune* function). For example, neurotransmitters from the ANS and from the ENS can stimulate mast cells in the wall of the GI tract to release histamine and other regulatory molecules. Histamine, for example, stimulates acid secretion in the stomach, besides having the immune functions previously discussed (see Chapter 24).

As we shall see throughout this chapter, the ENS works with other divisions of the nervous system, with the endocrine system, and with local regulatory mechanisms to achieve the coordination of incredibly complex, finely tuned mechanisms of motility (movement), secretion, digestion, and other functions.



Enteric nervous system (ENS). This diagram shows some typical neural pathways involved in the ENS. Although the ENS can operate its own independent regulatory system, it is also interconnected with various divisions of the autonomic nervous system (ANS).

DIGESTION

After food is ingested (taken into the mouth), the process of digestion begins immediately. Digestion is the overall name for all the processes that chemically and mechanically break complex foods into simpler nutrients that can be easily absorbed. We begin our discussion with a brief overview of *mechanical digestion* and then move on to a discussion of *chemical digestion*.

Mechanical Digestion

Mechanical digestion consists of all movement (motility) of the digestive tract that brings about the following:

- Change in the physical state of ingested food from comparatively large solid pieces into minute particles, thereby facilitating chemical digestion
- Churning of the contents of the GI lumen in such a way that they become well mixed with the digestive juices and all parts of them come in contact with the surface of the intestinal mucosa, thereby facilitating absorption
- Propelling the food forward along the digestive tract, and finally eliminating the digestive wastes from the body

MASTICATION

Mechanical digestion begins in the mouth when the particle size of ingested food material is reduced by chewing movements, or **mastication.** The tongue, cheeks, and lips play an important role in keeping food material between the cutting or grinding surfaces of the teeth when a person is biting off or chewing food. In addition to reducing particle size, chewing movements serve to mix food with saliva in preparation for swallowing.

DEGLUTITION

The process of swallowing, or **deglutition,** involves three main steps, or stages, that may be divided into the formation and then movement of a food bolus from the mouth to the stomach (Figure 29-2):

1. Oral stage (mouth to oropharynx)
2. Pharyngeal stage (oropharynx to esophagus)
3. Esophageal stage (esophagus to stomach)

The first step, which is voluntary and under control of the cerebral cortex, involves the formation of a food bolus that is to be swallowed by means of a depression or groove in the middle of the tongue. During the oral stage, the bolus is pressed against the palate by the tongue and then moved back into the oropharynx. The pharyngeal and esophageal stages, both involuntary, consist of movement of food from the pharynx into the esophagus and, finally, into the stomach.

To propel food from the pharynx into the esophagus, three openings must be blocked: mouth, nasopharynx, and larynx. Continued elevation of the tongue seals off the mouth. The soft palate, including the uvula, is elevated and tensed, causing the nasopharynx to be closed off. Food is prevented from entering the larynx by muscle action that causes the epiglottis to block this opening. The mechanism involves raising of the larynx, a process easily noted by palpation of the thyroid cartilage during swallowing. As a result, the bolus slips over the back of the epiglottis to enter the laryngopharynx.

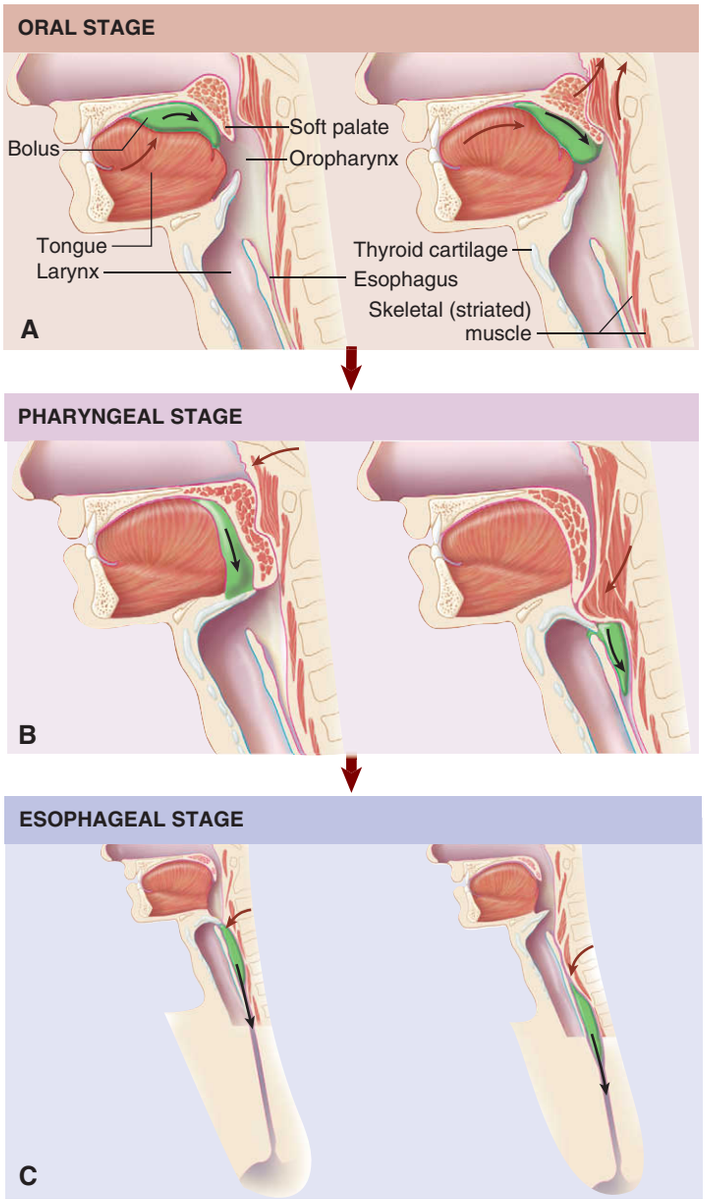


FIGURE 29-2

Deglutition. A, *Oral stage.* During this stage of deglutition (swallowing), a bolus of food is voluntarily formed on the tongue and pushed against the palate and then into the oropharynx. Notice that the soft palate acts as a valve that prevents food from entering the nasopharynx. **B,** *Pharyngeal stage.* After the bolus has entered the oropharynx, involuntary reflexes push the bolus down toward the esophagus. Notice that upward movement of the larynx and downward movement of the bolus close the epiglottis and thus prevent food from entering the lower respiratory tract. **C,** *Esophageal stage.* Involuntary reflexes of skeletal (striated) and smooth muscle in the wall of the esophagus move the bolus through the esophagus toward the stomach.

Contractions of the pharynx and esophagus compress the bolus into and through the esophageal tube. These steps are involuntary and under control of the *deglutition center* in the medulla. The presence of a bolus stimulates sensory receptors in the mouth and pharynx, thus initiating reflex pharyngeal contractions. Consequently, anesthesia of sensory nerves from the mucosa of the mouth and pharynx by a drug such as procaine makes swallowing difficult or impossible.

Swallowing is a complex process requiring the coordination of many muscles and other structures in the head and neck. The process must not only occur smoothly but also take place rapidly because respiration is inhibited for the 1 to 3 seconds required for food to clear the pharynx during each swallowing.

PERISTALSIS AND SEGMENTATION

After food enters the lower portion of the esophagus, smooth muscle tissue in the wall of the GI tract takes on primary responsibility for its movement (Box 29-2). The motility produced by smooth muscle is of two main types: peristalsis and segmentation.

Box 29-2 | Smooth Muscle Function in the GI Tract

Smooth muscle tissue in the wall of the gastrointestinal (GI) tract differs from other types of muscle tissue in a number of important ways. For example, smooth muscle is slow compared to skeletal muscle. Because the sliding of myofilaments proceeds at a much slower pace than in skeletal muscle, smooth muscle often exhibits a prolonged contraction phase. Because the same amount of energy is used for slow contraction as for fast contraction, GI muscle can sustain tension for long periods without fatigue—exactly what is needed for the long process of digestion.

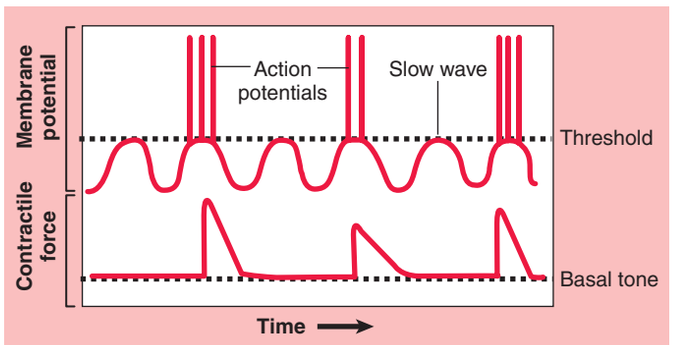
Another unique functional characteristic of smooth muscle is its ability to maintain *basal tone.* The basal tone is a continuous state of minimal contraction. Continuous tension is maintained in cells that have enough calcium ions free in the sarcoplasm to generate the contraction response. The force of contraction can increase above the basal tone by way of the effects of an action potential, which causes rapid influx of extracellular calcium.

Gastrointestinal *sphincter* muscles, as you recall from the previous chapter, are ringlike formations of smooth muscle in the GI wall that act as gateways or valves that regulate movement of chyme from one part of the tract to the next part. Sphincter muscles generally have a higher basal tone than does surrounding smooth muscle—thus constricting the lumen and "keeping the gate closed." Usually, stimuli in a section preceding the sphincter trigger a decrease in basal tone to allow material to pass through. Some of these reflexes are discussed later in this chapter.

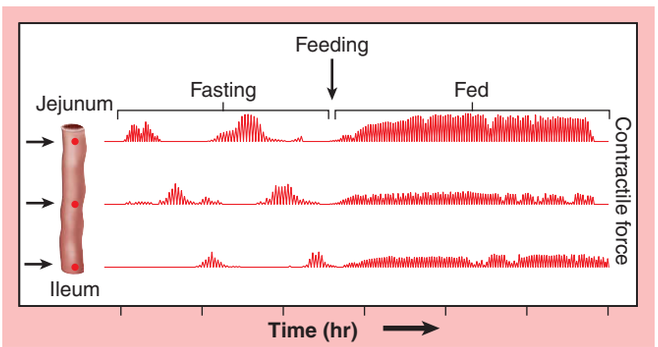
Most of the smooth muscles in the GI wall are electrically coupled by gap junctions—so-called *single-unit* muscles. Such electrical coupling allows for intrinsic control of smooth muscle contraction, as in cardiac muscle. Smooth muscle fibers exhibit an intrinsic, rhythmic fluctuation in membrane voltage that is sometimes called *basic electrical rhythm (BER).* As part *A* of the figure shows, the peaks of these slow waves sometimes reach the threshold potential—thus triggering bursts of action potentials. Because the fibers are electrically coupled, action potentials generated in one fiber spread rapidly to many surrounding fibers. This phenomenon is called *pacemaker* activity (as we have already seen in the heart with cardiac muscle fibers). Part *A* of the figure shows the effect of pacemaker activity on the force generated in a local area of the GI muscle. Between action potentials, the muscle cells exhibit the basal tone—but when stimulated by pacemaker potentials, the contractile force increases dramatically. The end result of pacemaker activity is a rather rhythmic increase and decrease in smooth muscle tension.

In part *B* of the figure, you can see that the small intestine shows an unusual pattern of this rhythmic pacemaker activity during the fasting state. In the fasting state, the electrical rhythm (and therefore the rhythm of contraction) is relatively quiet, except for a coordinated wave of motor activity every 1½ to 2 hours. Each wave of rhythmic contractions is called a **migrating motor complex (MMC).** One function of the MMC is thought to be that of clearing out any remaining material, such as larger, indigestible particles, bile and other secretions, bacteria, and sloughed off epithelial cells. The MMC pattern is largely triggered by the hormone **motilin** released from endocrine cells in the duodenum.

Once material enters a segment of the digestive tract, the slow basic rhythm of contraction changes to the rapid rhythms of *segmentation* (mixing actions) and *peristalsis* (progressive movement).



A



B

A, Pacemaker activity of smooth muscle. As the upper graph line shows, the membrane potential of smooth muscle exhibits a rhythmic fluctuation (the basic electrical rhythm). Occasionally, the fluctuating membrane potential reaches the threshold—triggering one or more action potentials that spread to surrounding muscle fibers. Smooth muscles are continually partially contracted (the basal tone), but the force of contraction increases dramatically with each burst of action potentials (bottom graph line). The more action potentials that occur in a short series, the stronger the force of contraction. **B, Migrating motor complex (MMC).** In the small intestine, the basal rhythm of smooth muscle contractions during the fasting state is characterized by occasional waves of motor activity called *migrating motor complexes (MMCs).* These waves of contraction slowly "sweep out" the intestinal lumen between active digestive periods (fed states). During the fed state, the MMC pattern disappears and is replaced by a more rapid, active pattern that includes peristalsis and segmentation.

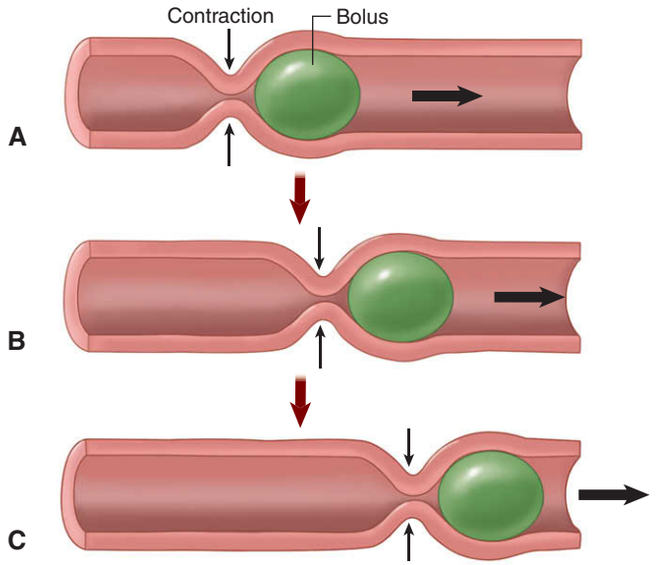


FIGURE 29-3

Peristalsis. Peristalsis is a progressive type of movement in which material is propelled from point to point along the gastrointestinal (GI) tract. **A,** A ring of contraction occurs where the GI wall is stretched, and the bolus is pushed forward. **B,** The moving bolus triggers a ring of contraction in the next region that pushes the bolus even farther along. **C,** The ring of contraction moves like a wave along the GI tract to push the bolus forward.

Peristalsis is often described as a wavelike ripple of the muscle layer of a hollow organ. The diagram in Figure 29-3 shows step by step how peristalsis occurs. A bolus stretches the GI wall, triggering a reflex contraction of circular muscle that pushes the bolus forward. This, in turn, triggers a reflex contraction in that location, pushing the bolus even farther. This process continues as long as the stretch reflex is activated by the presence of food. Peristalsis is a progressive kind of motility, that is, a type of motion that produces forward movement of ingested material along the GI tract. Figure 29-4 shows the effects of peristaltic contractions in the esophagus during deglutition.

Segmentation can be described simply as mixing movement. Segmentation occurs when digestive reflexes cause a forward and backward movement within a single region, or segment, of the GI tract (Figure 29-5). Such movement helps mechanically break down food particles, mixes food and digestive juices thoroughly, and brings digested food in contact with intestinal mucosa to facilitate absorption.

Peristalsis and segmentation can occur in an alternating sequence. When this happens, food is churned and mixed as it slowly progresses along the GI tract.

REGULATION OF MOTILITY

Gastric Motility

The process of emptying the stomach takes about 2 to 6 hours after a meal, depending on the amount and content of the meal. During its "storage time" in the stomach, food is churned with gastric juices to form a thick, milky material known as **chyme,** which is ejected about every 20 seconds into the duodenum. As

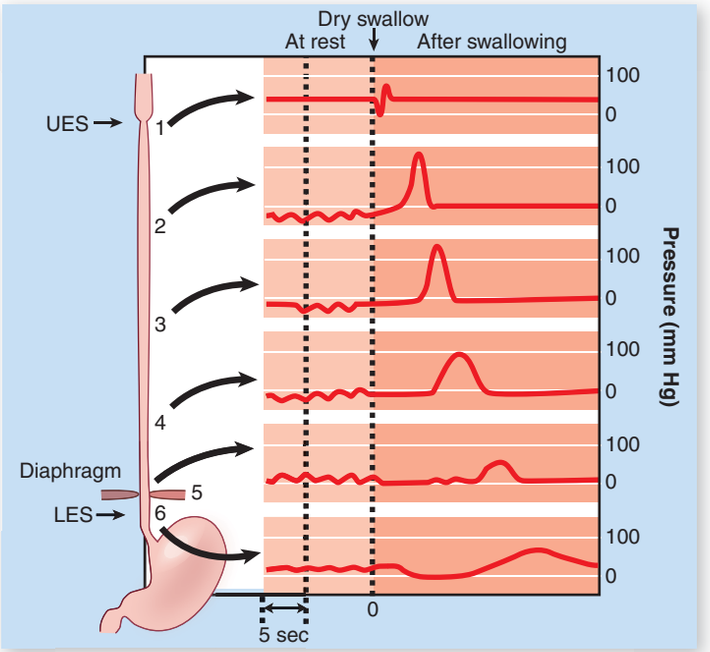


FIGURE 29-4

Pressure in the esophagus during swallowing. This diagram shows the changing pressure (mm Hg) inside the esophagus during the esophageal stage of deglutition (swallowing, see Figure 29-2). Note that an area of high pressure moves progressively down the esophagus—and eventually to the stomach. Note that during the rest period before swallowing, the smooth muscle exhibits a slow rhythm of weak contractions. *UES,* Upper esophageal sphincter; *LES,* lower esophageal [cardiac] sphincter.

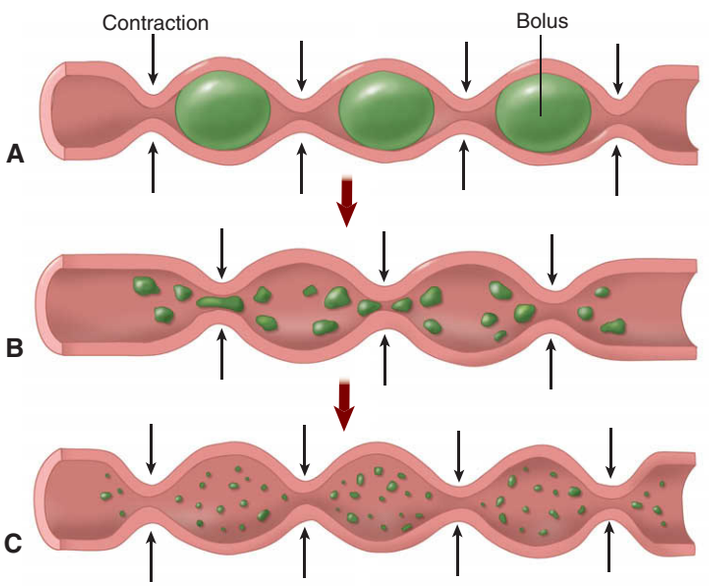


FIGURE 29-5

Segmentation. Segmentation is a back-and-forth action that breaks apart chunks of food and mixes in digestive juices. **A,** Ringlike regions of contraction occur at intervals along the gastrointestinal (GI) tract. **B,** Previously contracted regions relax and adjacent regions now contract, effectively "chopping" the contents of each segment into smaller chunks. **C,** The location of the contracted regions continues to alternate back and forth, chopping and mixing the contents of the GI lumen.

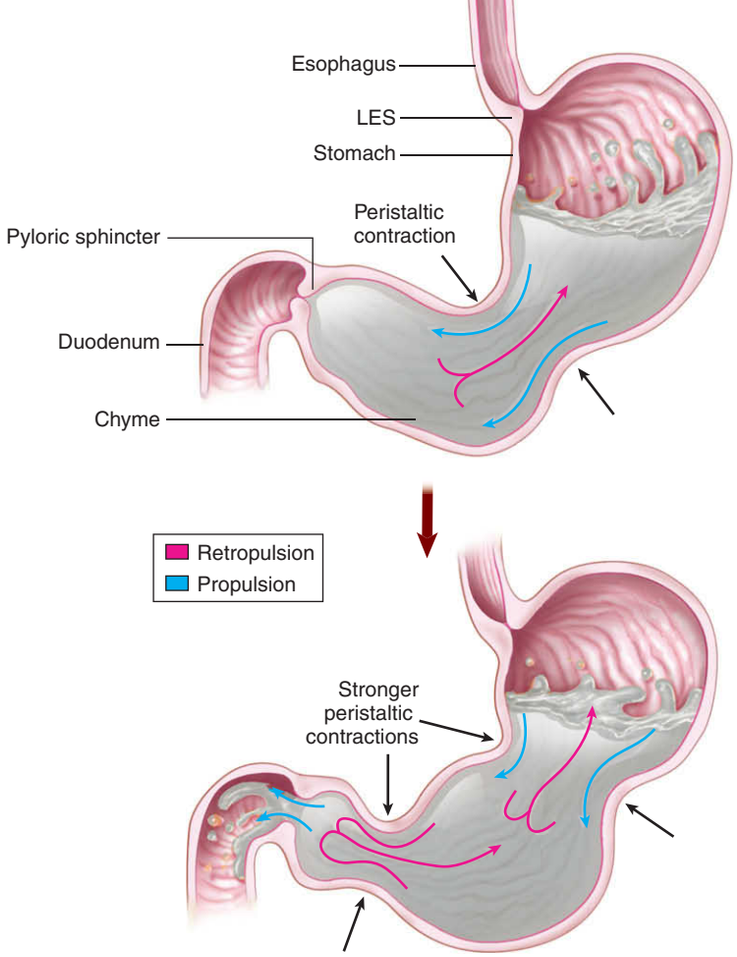


FIGURE 29-6

Gastric motility. Mixing actions in the stomach include both propulsion (forward movement) and retropulsion (backward movement). As peristaltic contractions become stronger, some of the liquid chyme squirts past the pyloric sphincter (which has decreased its muscle tone) and into the duodenum. The stomach continues to mix the chyme as it is gradually released into the duodenum.

you can see in Figure 29-6, while chyme is in the stomach, it is continually being pushed toward the pyloric sphincter by waves of peristaltic contractions—a process called **propulsion.** Because the pyloric sphincter remains closed most of the time, the chyme is forced to move backward—a process called **retropulsion.** Thus, because the chyme is temporarily "trapped," peristalsis creates a sort of "back-and-forth" movement that helps mix the chyme and gastric juice. Eventually, the contraction force of the pyloric sphincter decreases, allowing a little of the chyme to pass through to the duodenum.

Because the volume of the stomach is large and that of the duodenum is small, gastric emptying must be regulated to prevent overburdening of the duodenum. Such control occurs by way of two principal mechanisms—one hormonal and one nervous. Fats and other nutrients in the duodenum stimulate the intestinal mucosa to release a hormone called **gastric inhibitory peptide (GIP)** into the bloodstream. When it reaches the stomach wall via the circulation, GIP has an inhibitory effect on gastric muscle, decreasing its peristalsis and thus slowing passage of food into the duodenum. Nervous control results from receptors in the duodenal mucosa that are sensitive to the presence of acid and to distention. Sensory and motor fibers in the vagus nerve then cause a reflex inhibition of gastric peristalsis. This nervous mechanism is known as the **enterogastric reflex.**

Box 29-3 discusses one important application of concepts of gastric motility.

INTESTINAL MOTILITY

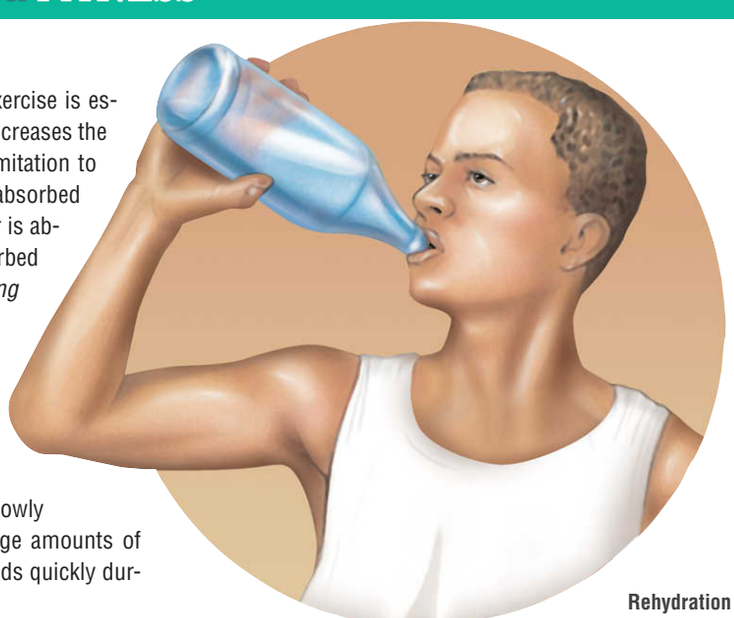
Intestinal motility includes both peristaltic contractions and segmentation. Segmentation in the duodenum and upper jejunum mixes the incoming chyme with digestive juices from the pancreas, liver, and intestinal mucosa. This mixing action also allows the products of digestion to contact the intestinal mucosa, where

Box 29-3 | SPORTS and FITNESS

Exercise and Fluid Uptake

Replacement of fluids lost through sweating during exercise is essential for maintaining homeostasis. Nearly everyone increases the intake of fluids during and after exercise. The main limitation to efficient fluid replacement is how quickly fluid can be absorbed rather than how much a person drinks. Very little water is absorbed until it reaches the intestines, where it is absorbed almost immediately. Thus the rate of *gastric emptying* into the intestine is critical.

Large volumes of fluid leave the stomach and enter the intestines more rapidly than small volumes do. However, having large volumes in the stomach may be uncomfortable during exercise. Cool fluids (8° to 13° C [46° to 55° F]) empty more quickly than warm fluids. Fluids with a high solute concentration empty slowly and may cause nausea or stomach cramps. Thus large amounts of cool, dilute, or isotonic fluids are best for replacing fluids quickly during exercise.



Rehydration after exercise.

they can be absorbed into the internal environment. Peristalsis continues as the chyme nears the end of the jejunum—moving the food through the rest of the small intestine and into the large intestine. After leaving the stomach, chyme normally takes about 5 hours to pass all the way through the small intestine.

Several mechanisms are involved in the control of intestinal motility. Peristalsis is regulated in part by the intrinsic stretch reflexes already described. It is also thought to be stimulated by the hormone **cholecystokinin (CCK),** which is secreted by endocrine cells of the intestinal mucosa when chyme is present.

A list of definitions of the different processes involved in mechanical digestion, along with the organs that accomplish them, is presented in Table 29-2.

| QUICK CHECK |

1. What is meant by the term *motility?*
2. Is deglutition a voluntary or involuntary process?
3. What is the purpose of peristalsis?
4. What triggers the *enterogastric reflex* to inhibit gastric emptying?

Chemical Digestion

Chemical digestion consists of all the changes in chemical composition that foods undergo in their travel through the digestive tract. These changes result from the hydrolysis of foods. **Hydrolysis** is a chemical process in which a compound unites with water and then splits into simpler compounds (see Chapter 2). Numerous enzymes in the various digestive juices catalyze the hydrolysis of foods.

DIGESTIVE ENZYMES

Overview of Digestive Enzymes

Enzymes were briefly introduced in Chapter 2 and their important functional roles were more fully discussed in Chapter 4 (see pp. 103–104). Although our interest until now has primarily concerned *intracellular enzymes*, our current discussion focuses on extracellular digestive enzymes. In the following paragraphs we briefly review enzymes in general and outline some characteristics of *digestive enzymes* in particular.

Recall that enzymes can be defined simply as "organic catalysts"; that is, they are organic compounds (proteins), and they accelerate chemical reactions without appearing in the final products of the reaction.

Recall the two systems used for naming enzymes: the suffix *-ase* is used with the root name of the substance whose chemical reaction is catalyzed (the substrate chemical, that is) or with the word that describes the kind of chemical reaction catalyzed. Thus, according to the first method, lipase is an enzyme that catalyzes a chemical reaction in which a lipid takes part. According to the second method, lipase might also be called a *hydrolase* because it catalyzes the hydrolysis of lipids. Enzymes investigated before these methods of nomenclature were adopted are still called by older names, such as **pepsin** and **trypsin**—both proteases (protein-digesting enzymes).

Enzymes can be classified as intracellular or extracellular, depending on whether they act within cells or outside of them in the surrounding medium. Most enzymes act intracellularly in the body; an important exception is the digestive enzymes. Digestive enzymes are classified as extracellular because they operate in the lumen of the digestive tract, outside any cells of the body. All

TABLE 29-2 Processes of Mechanical Digestion

ORGAN	MECHANICAL PROCESS	NATURE OF PROCESS
Mouth (teeth and tongue)	Mastication	Chewing movements—reduce size of food particles and mix them with saliva
	Deglutition	Swallowing—movement of food from mouth to stomach
Pharynx	Deglutition	See description above
Esophagus	Deglutition	See description above
	Peristalsis	Rippling movements that squeeze food downward in digestive tract; a constricted ring forms first in one section, then the next, and so on, causing waves of contraction to spread along entire canal
Stomach	Churning	Forward and backward movement (propulsion/retropulsion) of gastric contents, mixing food with gastric juices to form chyme
	Peristalsis	Wave starting in body of stomach that occurs about three times per minute and sweeps toward closed pyloric sphincter; at intervals, strong peristaltic waves press chyme past sphincter into duodenum
Small intestine	Segmentation (mixing contractions)	Forward and backward movement within segment of intestine; purpose is to mix food and digestive juices thoroughly and to bring all digested food into contact with intestinal mucosa to facilitate absorption; purpose of peristalsis, on the other hand, is to propel intestinal contents along digestive tract
	Peristalsis	
Large intestine		
Colon	Segmentation	Churning movements within haustral sacs
	Peristalsis	See description above
Descending colon	Mass peristalsis	Entire contents moved into sigmoid colon and rectum; occurs three or four times a day, usually after a meal
Rectum	Defecation	Emptying of rectum, so-called bowel movement

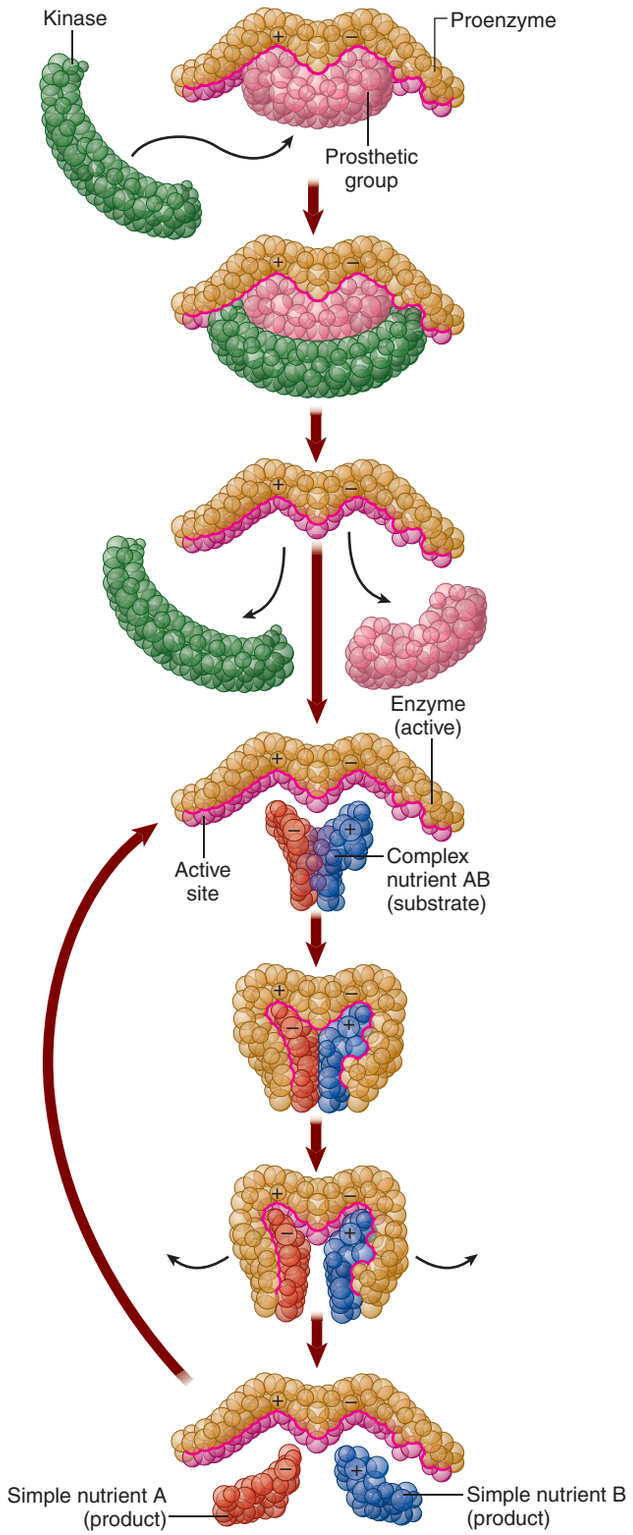


FIGURE 29-7

Model of digestive enzyme action. Enzymes are functional proteins whose molecular shape allows them to catalyze chemical reactions. First, an inactive proenzyme must be altered by an activating enzyme called a *kinase*. The kinase often accomplishes the activation by removing a prosthetic group from the proenzyme, exposing an active site. A complex nutrient molecule *AB* is acted on by the active digestive enzyme, yielding simpler nutrient molecules *A* and *B*. The active enzyme can then digest another complex nutrient molecule.

digestive enzymes are classified chemically as hydrolases because they catalyze the hydrolysis of food molecules—the breakdown of a molecule using water.

Properties of Digestive Enzymes

As with any type of enzyme, digestive enzymes are *specific in their action;* that is, they act only on a specific substrate. This is attributed to a "key-in-a-lock" kind of action, the configuration of the enzyme molecule fitting the configuration of some part of the substrate molecule (Figure 29-7).

Digestive enzymes *function optimally at a specific pH* and become inactive if the pH deviates beyond narrow limits (Figure 29-8). This effect occurs because changes in the hydrogen ion (H^+) concentration influence the chemical attractions that hold all protein molecules—including enzymes—in their complex, multidimensional shapes. In short, changing the pH changes the shape of an enzyme molecule—possibly rendering it inactive.

Different digestive enzymes require different H^+ concentrations in their environment for optimal functioning. This is because the H^+ concentration influences the shape of each enzyme molecule. Amylase, the main enzyme in saliva, functions best in the neutral to slightly acid pH range characteristic of saliva. It is gradually inactivated by the marked acidity of gastric juice. In contrast, pepsin, an enzyme in gastric juice, is inactive unless sufficient hydrochloric acid is present. Therefore, in diseases characterized by gastric hypoacidity, dilute hydrochloric acid is given orally before meals.

Most enzymes catalyze a chemical reaction in both directions, the direction and rate of the reaction being governed by the rate law (law of mass action). An accumulation of a product slows the reaction and tends to reverse it. A practical application of this fact is the slowing of digestion when absorption is interfered with and the products of digestion accumulate. However, digestive enzyme reactions do not ordinarily reverse themselves in the digestive tract.

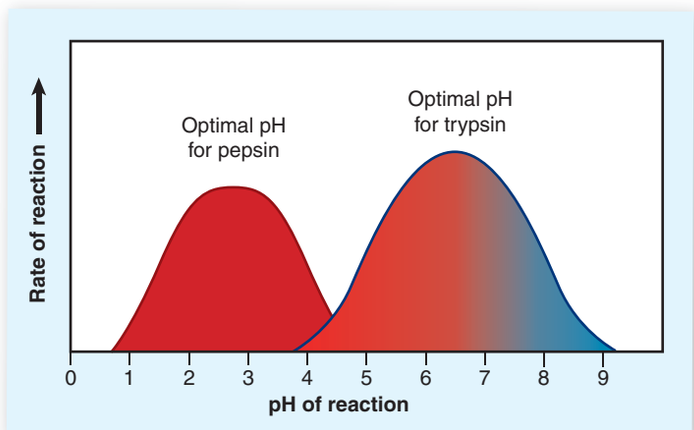


FIGURE 29-8

Effect of pH on digestive enzyme function. Digestive enzymes catalyze chemical reactions with greatest efficiency within a narrow range of pH. For example, *pepsin* (a protein-digesting enzyme in gastric juice) operates within a low pH range, whereas *trypsin* (a protein-digesting enzyme in pancreatic juice) operates within a higher pH range.

Digestive enzymes are continually being destroyed or eliminated from the body and therefore have to be continually synthesized, even though they are not used up in the reactions they catalyze.

Most digestive enzymes are synthesized and secreted as inactive **proenzymes** (see Figure 29-7). Enzymes that break apart proenzymes and thus convert them to active enzymes are often called *kinases*. For example, enterokinase is a kinase that changes inactive trypsinogen into active trypsin.

Although we eat six main types of chemical substances (carbohydrates, proteins, fats, vitamins, mineral salts, and water), only the first three have to be chemically digested to be absorbed.

CARBOHYDRATE DIGESTION

Carbohydrates are saccharide compounds. This means that their molecules contain one or more saccharide groups ($C_6H_{10}O_5$). Polysaccharides, notably starches and glycogen, contain many of these groups. Disaccharides (sucrose, lactose, and maltose) contain two of them, and monosaccharides (glucose, fructose, and galactose) contain only one. Polysaccharides are hydrolyzed to disaccharides by enzymes known as **amylases,** found in saliva and pancreatic juice (salivary amylase is sometimes called *ptyalin*). The enzymes that catalyze the final steps in carbohydrate digestion are *sucrase*, *lactase*, and *maltase* (Figure 29-9). These enzymes are located in the cell membrane of epithelial cells covering the villi and, therefore, lining the intestinal lumen. The substrates (disaccharides) bind onto the enzymes at the surface of the brush border, giving the name **contact digestion** to the process. The resulting end products of digestion, mainly glucose, are conveniently located at the site of absorption (and are not floating around somewhere in the lumen).

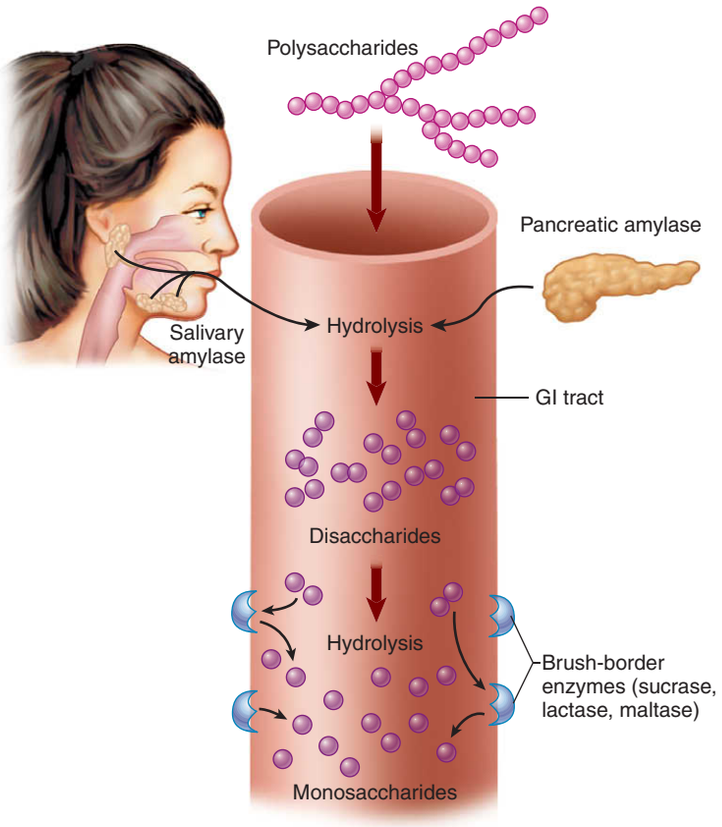


FIGURE 29-9

Carbohydrate digestion. Amylase in saliva and pancreatic juice hydrolyzes polysaccharides into disaccharides. Brush border disaccharidases in the lining of the small intestine then promote hydrolysis of the disaccharides into monosaccharides.

PROTEIN DIGESTION

Protein compounds have very large molecules made up of folded or twisted chains of amino acids, often hundreds in number. Enzymes called **proteases** catalyze the hydrolysis of proteins first into a variety of intermediate compounds called proteoses and peptides, which are simply shorter strands of amino acids. Then finally, proteases break these shorter molecules into individual amino acids (Figure 29-10).

The main proteases are **pepsin** in gastric juice, **trypsin** and **chymotrypsin** in pancreatic juice, and **peptidases** of the intestinal brush border (Box 29-4). Peptidases are also present within each intestinal cell where they break apart dipeptides and tripeptides absorbed into these cells. Each kind of protease catalyzes the breaking apart of a specific kind of peptide bond. Because different amino acid combinations within a protein or polypeptide can have slightly different kinds of peptide bonds holding them together, a whole arsenal of different proteases is needed for efficient protein digestion.

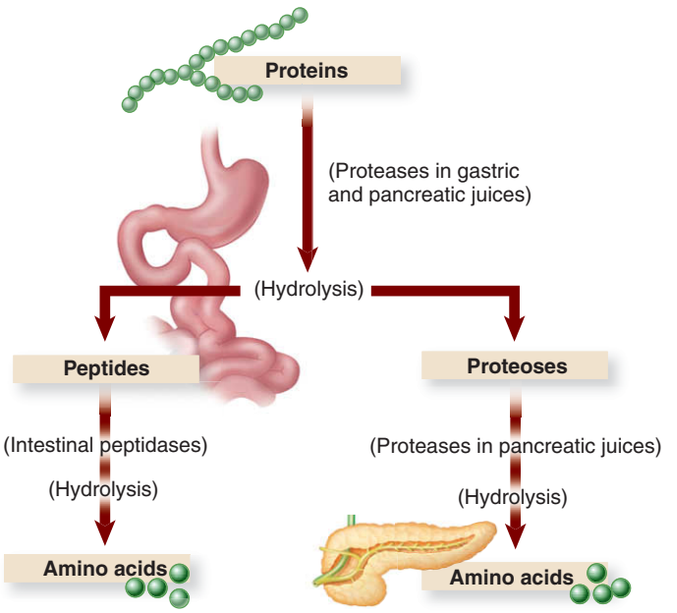


FIGURE 29-10

Protein digestion. Gastric juice protease (pepsin) and pancreatic juice protease (trypsin and chymotrypsin) hydrolyze proteins into proteoses and peptides. Protein digestion is then completed by pancreatic proteases, which hydrolyze proteoses into amino acids, and by intestinal peptidases, which hydrolyze peptides into amino acids.

Box 29-4 | The BRUSH BORDER

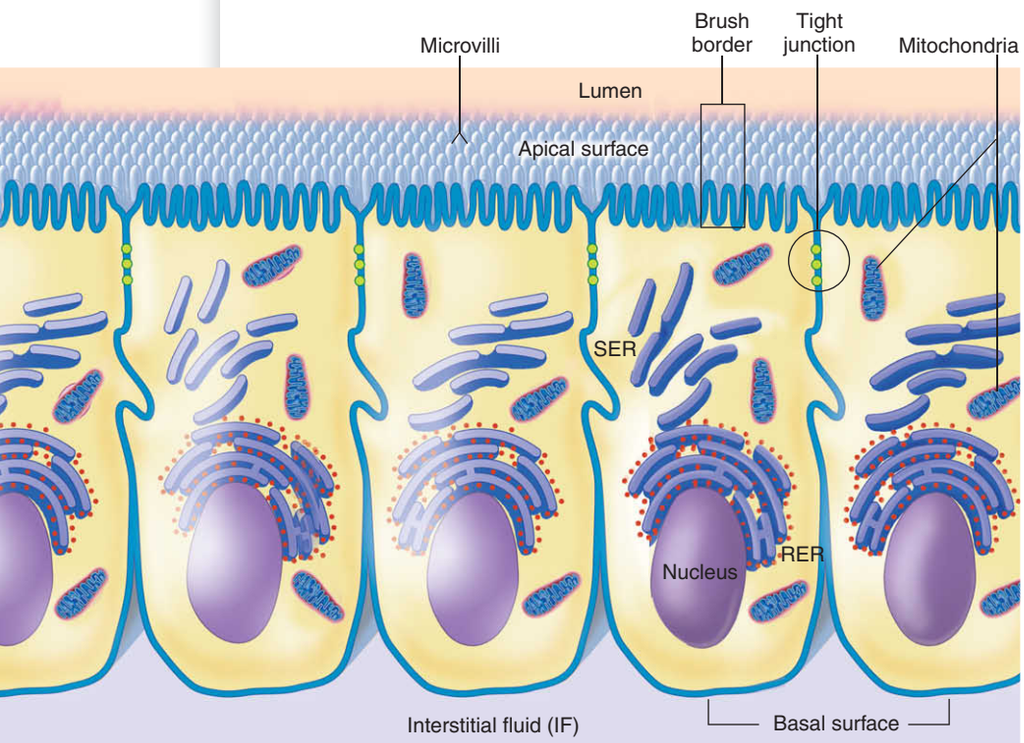
The term **brush border** refers to the microvilli on the epithelial mucous cells that line the small intestine, visible in the figures. These microvilli are on the apical surfaces of the epithelial cells—the surfaces that face the interior of the intestinal lumen. Because when viewed under high magnification the microvilli look like the bristles of a brush, the surface of the intestinal mucosa was nicknamed "brush border."

The brush border represents the boundary between the external environment (the lumen of the alimentary canal) and the internal environment of the body. It is across this border that molecules must pass if they are going to be absorbed into the body.

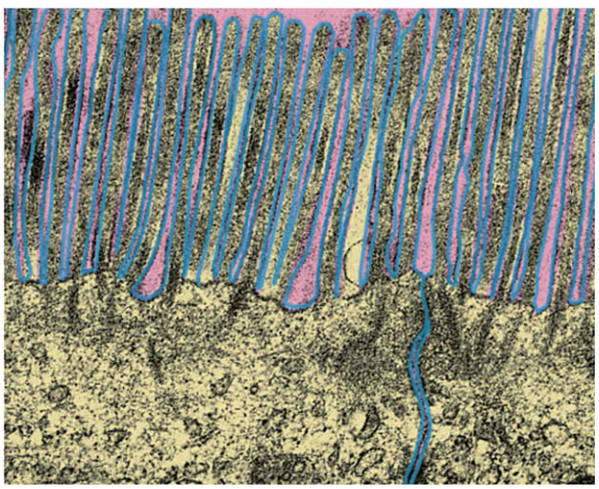
The brush border possesses an incredibly large surface area because the microvilli increase the apical surface area. There are usually 2000 to 3000 microvilli on each cell! Of course, the presence of intestinal villi, circular folds (plicae circulares), and numerous loops also adds to the intestinal surface area (see Figure 28-17 on p. 876).

The large surface area of the brush border provides sites for digestive enzymes on the plasma membranes of intestinal cells—the *brush border enzymes.* The efficiency of the last stages of digestion is thus enhanced by having more surface area for more digestive enzymes. Many of the brush border enzymes are on fine, branched filaments that extend from the surface of each microvillus and form a glycoprotein coat on the brush border called the *glycocalyx.* Because each substrate molecule must come in direct contact with a brush border enzyme before it can be digested, the process is called *contact digestion.*

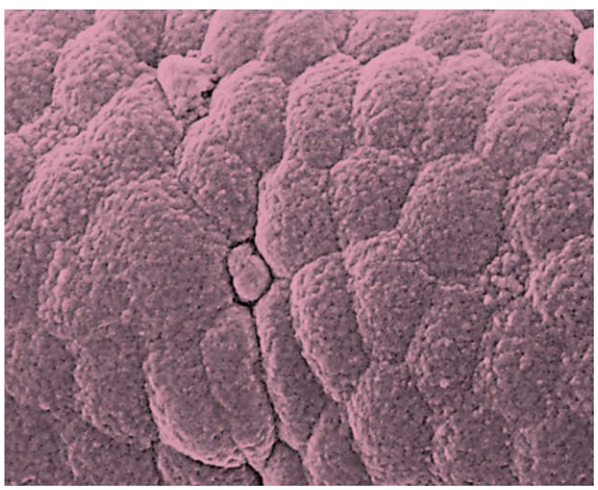
The large surface area also provides more opportunities for the absorption of digested nutrients. More surface area allows for more phospholipid bilayer to absorb fats and more carrier molecules to carry amino acids, peptides, monosaccharides, and other nutrients.



A



B



C

A, Intestinal epithelium. The diagram shows intestinal epithelial cells joined by tight junctions and covered with microvilli on their apical (lumen-facing) surfaces. *SER,* Smooth endoplasmic reticulum; *RER,* rough endoplasmic reticulum. **B, Cross section of the brush border.** A transmission electron micrograph shows microvilli, which resemble bristles of a brush. **C, Surface view of the brush border.** A scanning electron micrograph of the surface of an intestinal villus shows the epithelial cells joined by tight junctions. Note the brushy appearance of the surface caused by the presence of microvilli.

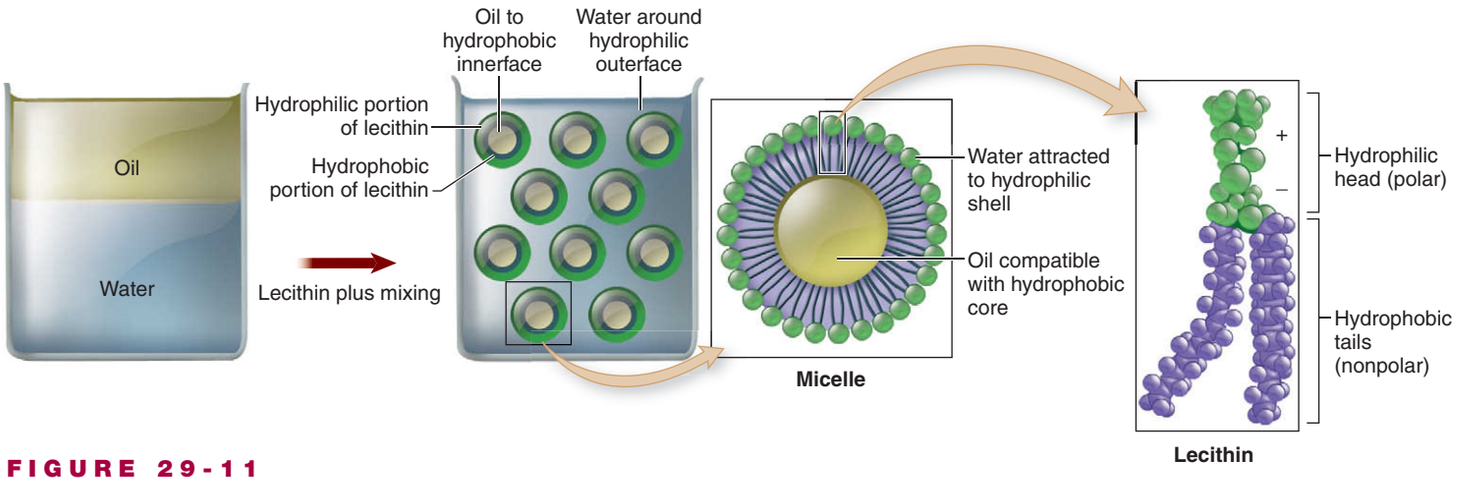


FIGURE 29-11

Formation of micelles by lecithin. Lecithin is a phospholipid in bile that mixes with oil and water to form micelles. Micelles are spherical shells formed by the orientation of lecithin molecules according to their solubility in water and lipids: the polar heads of lecithin face outward (toward water), and the nonpolar tails of lecithin face inward (toward lipid). Formation of micelles, a mechanical process called *emulsification,* breaks fat drops into small droplets and makes the droplets water soluble.

FAT DIGESTION

Because fats are insoluble in water, they must be **emulsified,** that is, dispersed into very small droplets, before they can be digested. Two substances found in bile, **lecithin** and **bile salts,** emulsify dietary oils and fats in the lumen of the small intestine. Bile is produced in the liver and stored and concentrated in the gallbladder. Bile is released into the lumen of the GI tract by way of the common bile duct.

Lecithin is a phospholipid similar to other phospholipids that make up the bulk of cellular membranes (see Figures 2-21 on p. 50 and 3-3 on p. 70). As Figure 29-11 shows, lecithin mixes with lipids and water, forming tiny spheres called **micelles.** In forming a micelle, lecithin molecules align to form a shell that surrounds the lipid. Alignment of lecithin molecules results from the fact that the polar heads of this molecule are attracted by polar water molecules and the nonpolar tails of lecithin are lipid soluble. Thus the hydrophilic (polar) heads form the outer face of the shell and the hydrophobic (nonpolar) tails form the inner face of the shell. Bile salts, which are derived from the lipid cholesterol, emulsify fats by forming micelles in the same manner.

The mechanical process of emulsification facilitates chemical digestion of fats by breaking large fat drops into small droplets. This process provides a greater contact area between fat molecules and pancreatic **lipases,** the main fat-digesting enzymes (Figure 29-12). Triglycerides, important dietary fats, are broken down by lipases to yield fatty acids, monoglycerides, and glycerol molecules. Other lipids are similarly broken down into their respective component chemical groups. For example, a phospholipid molecule can be chemically broken down by a lipase called *phospholipase* to yield one free fatty acid and one lysophosphatide (a phospholipid head with a single fatty acid tail).

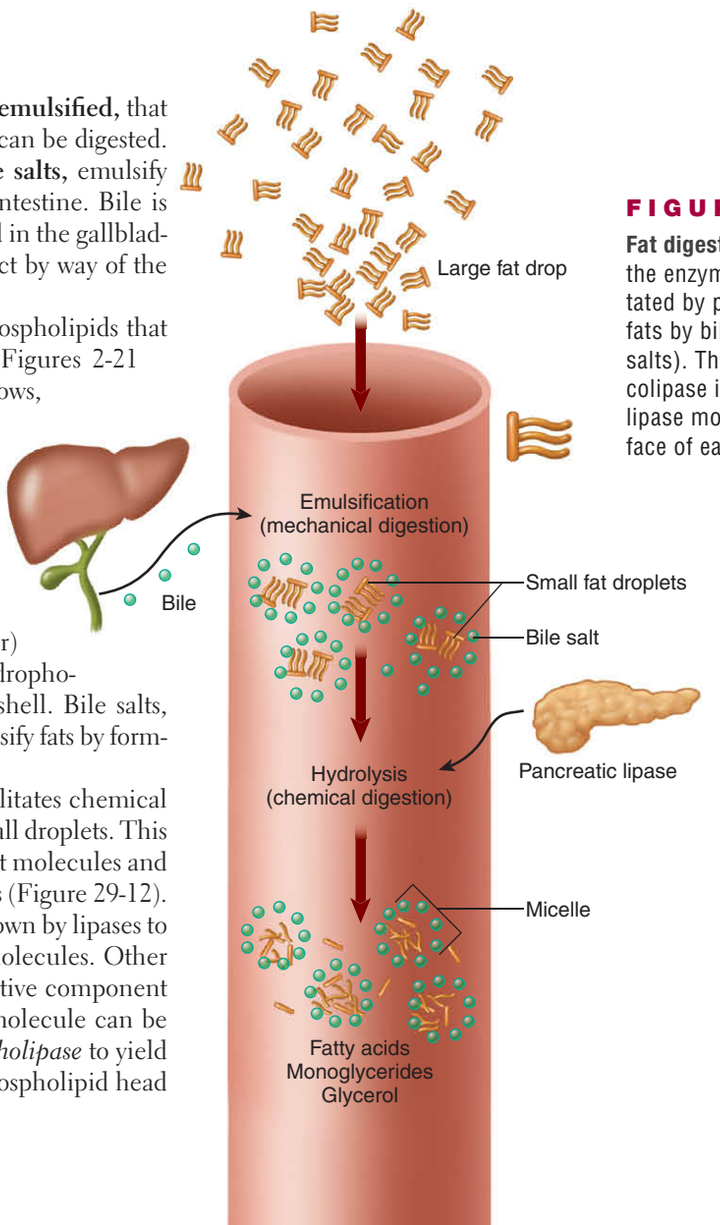
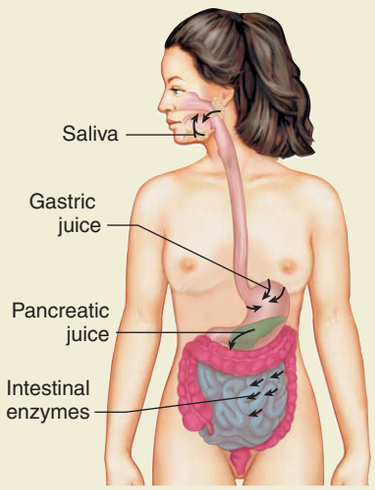


FIGURE 29-12

Fat digestion. Hydrolysis by the enzyme lipase is facilitated by prior emulsion of fats by bile (lecithin and bile salts). Though not pictured, colipase is needed to anchor lipase molecules to the inner face of each micelle.

TABLE 29-3 Chemical Digestion

DIGESTIVE JUICES AND ENZYMES		SUBSTANCE DIGESTED (OR HYDROLYZED)	RESULTING PRODUCT*
Saliva			
Amylase (ptyalin)		Starch (polysaccharide)	Maltose (disaccharide)
Gastric Juice			
Protease (pepsin)** plus hydrochloric acid		Proteins	Partially digested proteins
Pancreatic Juice			
Proteases (e.g., trypsin)†		Proteins (intact or partially digested)	Peptides and **amino acids**
Lipases		Fats emulsified by bile	**Fatty acids, monoglycerides,** and **glycerol**
Amylase		Starch	Maltose
Nucleases		Nucleic acids (DNA, RNA)	Nucleotides
Intestinal Enzymes‡			
Peptidases		Peptides	**Amino acids**
Sucrase		Sucrose (cane sugar)	**Glucose** and **fructose**§ (monosaccharides)
Lactase		Lactose (milk sugar)	**Glucose** and **galactose** (monosaccharides)
Maltase		Maltose (malt sugar)	**Glucose**
Nucleotidases and phosphatases		Nucleotides	Nucleosides



*Substances in **boldface type** are end products of digestion (that is, completely digested nutrients ready for absorption).
**Secreted in inactive form (pepsinogen); activated by low pH (hydrochloric acid).
†Secreted in inactive form (trypsinogen); activated by enterokinase, an enzyme in the intestinal brush border.
‡Brush-border enzymes.
§Glucose is also called *dextrose;* fructose is also called *levulose.*

The action of lipases is enhanced by a component of pancreatic juice called *colipase* (koh-LYE-payz). Colipase is a coenzyme molecule that anchors a lipase molecule to the inner face of a micelle. This positions the lipase for optimum hydrolysis of lipid molecules within the micelle.

For a summary of chemical digestion, see Table 29-3. Box 29-5 summarizes concepts of nucleic acid digestion and absorption.

RESIDUES OF DIGESTION

Certain components of food resist digestion and are eliminated from the intestines in the **feces.** Included among these *residues of digestion* are cellulose (a carbohydrate, also known as "dietary fiber") and undigested connective tissue from meat (mostly collagen). These substances remain undigested because humans lack the enzymes required to hydrolyze them. The residues of

Box 29-5 | FYI

Nucleic Acid Digestion and Absorption

Although they are not usually considered to be essential nutrients, the nucleic acids such as DNA and RNA found in cells of food material are digested, absorbed, and used by the body.

DNA and RNA strands released during mechanical digestion are still associated with proteins and so must first be hydrolyzed by proteases to break the proteins free from the DNA or RNA strand. **Nucleases** in pancreatic juice then break down each strand into individual nucleotides. Nucleotides are simple enough to be absorbed by intestinal cells. Many of the nucleotides, however, are first stripped of their phosphate groups by intestinal *phosphatases* and *nucleotidases.* A nucleotide thus stripped of its phosphate is called a *nucleoside.*

Although nucleotides can be absorbed, most nucleic acids are absorbed in the form of nucleosides. Both nucleotides and nucleosides are absorbed through the intestinal wall by a sodium cotransport process similar to that for glucose and amino acids. After absorption, the nucleosides have phosphates added to them by cellular enzymes and are thus restored to the nucleotide form.

Although a healthy body can make its own nucleotides, nucleotides from food help the body maintain a healthy pool of nucleotides available for making DNA and RNA. This external source of nucleotides is especially useful during rapid growth and development stages (as during infancy) and during certain disease or weakened states.

digestion also include undigested fats. Some fat molecules remain undigested because they have combined with dietary minerals such as calcium and magnesium, which render the fats indigestible. Box 29-6 discusses the fecal fat test used to detect abnormalities of fat absorption. In addition to these wastes, feces consist of bacteria, pigments, water, and mucus.

| QUICK CHECK |

5. What type of reaction do all digestive enzymes catalyze?
6. List some factors that alter the shape of an enzyme, thus altering its function.
7. Name the final digestive products of each of the following food molecules:
   a. Protein
   b. Carbohydrate
   c. Triglyceride

SECRETION

Digestive secretion generally refers to the release of various substances from the exocrine glands that serve the digestive system. For example, digestive secretion includes the release of saliva, gastric juice, bile, pancreatic juice, and intestinal juice. In the paragraphs that follow, we briefly summarize the major digestive juices. Later, we discuss how secretion is regulated.

Saliva

Saliva is the secretion of the salivary glands (see Figure 28-8 on p. 867). Saliva, as with all digestive secretions, is mostly water. Water helps mechanically digest food as it moves through the digestive tract by helping to liquefy the food. Liquefied food, called **chyme** after it enters the stomach, not only represents a physically broken-down form of food but also permits enzymes and other substances to mix freely with small chunks of food.

Mixed in the water is a combination of other important substances. **Mucus,** for example, is found not only in saliva but also in each of the other digestive juices. Mucus, you may recall, is a mixture of glycoproteins and related substances that is rather slippery to the touch. Mucus in intestinal juices has the primary functions of protecting the digestive mucosa and lubricating food as it passes through the alimentary canal.

Saliva, as with most other digestive juices, contains enzymes. Specifically, saliva contains **amylase**—a carbohydrate-digesting enzyme. Although salivary amylase (ptyalin) can chemically digest starches into smaller carbohydrates, the short time it has until it is destroyed by acids and enzymes in the stomach make this function relatively unimportant. Saliva also contains a small amount of **lipase,** which normally digests lipids. In the saliva, however, lipase is practically worthless because most ingested lipids must be emulsified before lipase can digest them easily.

Saliva also contains a small amount of sodium bicarbonate ($NaHCO_3$). Sodium bicarbonate dissociates in water to form sodium ions (Na^+) and bicarbonate ions (HCO_3^-). You may recall from Chapter 27 that bicarbonate can bind to hydrogen ions, thus taking the hydrogen ions out of solution and causing a decrease in acidity (increase in pH). This buffering mechanism keeps saliva close to neutral pH, which is optimum for amylase activity.

Gastric Juice

Gastric juice is secreted by exocrine *gastric glands*, which have ducts that lead to the gastric lumen by way of the gastric pits (see Figure 28-14 on p. 873). Gastric juice contains not only the basic water and mucus mixture of most other digestive juices but also a unique combination of other substances.

Chief cells in the gastric glands are also called **zymogenic cells** because they secrete the enzymes in gastric juice. The prefix *zymo-* refers to enzymes and *-genic* pertains to making something. Primary among the gastric enzymes is **pepsin,** which is secreted as the inactive proenzyme **pepsinogen.**

Pepsinogen is converted to pepsin by hydrochloric acid (HCl), which is produced by **parietal cells** of the gastric glands. Figure 29-13 shows how carbon dioxide and water form carbonic acid, which then dissociates to form the hydrogen ions needed to actively secrete hydrochloric acid. This is the very same chemical process that was outlined in Chapter 27, where we discussed carbon dioxide transport in the blood (see Figures 27-22, p. 874, and 27-24, p. 845). Notice here in Figure 29-13 that there is a *chloride*

Box 29-6 | DIAGNOSTIC study

Fecal Fat Test

Impaired fat absorption (malabsorption), prevalent in numerous diseases, produces large, greasy, and foul-smelling stools, or **steatorrhea.**

The fecal fat test measures the fat content in the stool. The total output of fecal fat per 24 hours in a 3- to 5-day stool collection provides the most reliable measurement. Each stool specimen throughout the period is collected in a clean, dry container and is sent immediately to the laboratory. The 3- to 5-day collection period is necessary to eliminate daily variations in the amount of fecal fat.

A standard fat content diet is begun 2 or 3 days before collection begins and continues until collection is done. Usually 100 grams of fat per day is suggested for adults. In children and infants who cannot eat 100 grams of fat per day, a fat retention coefficient is determined by using the following formula:

$$\frac{\text{Ingested fat} - \text{Fecal fat}}{\text{Ingested fat}} \times 100\%$$

If this fat retention coefficient is lower than 95%, the patient may have steatorrhea.

Analysis of fecal fat is useful in monitoring malabsorption in cystic fibrosis or in any condition characterized by malabsorption, maldigestion, or increased fecal fat.

shift similar to that discussed in regard to the respiratory system. In exchange for bicarbonate (also produced by dissociation of carbonic acid), chloride is shifted into the parietal cell where it can then diffuse into the duct of the gastric gland along with hydrogen ions. The end result of this process in parietal cells is that the contents of the stomach become more acidic, or drop in pH, and the contents of the blood become more basic, or increase in pH.

The ion pump in the membrane of gastric parietal cells that pumps H^+ ions into the gastric juice is often called the **H-K pump**—or more simply, a *proton pump* (see Figure 29-13). It is this pump that is targeted by drugs that inhibit gastric acid secretion, such as *omeprazole* (Prilosec). By inhibiting the H-K pumps of the stomach, these drugs reduce the overall acidity of the stomach contents.

The parietal cells have an interesting and important mechanism involved with secretion of ions. As Figure 29-14, *A*, shows, when the parietal cell is not actively secreting, it has a relatively small surface area and many internal vesicles. These vesicles have H-K pumps and ion channels and carriers embedded in their membranes. When the parietal cell becomes active, however, these vesicles move quickly to the apical surface (Figure 29-14, *B*). There, they fuse with the plasma membrane forming more microvilli and increasing the overall surface area by as much as 100 times! The pumps, carriers, and channels then begin the secretion process summarized in Figure 29-13.

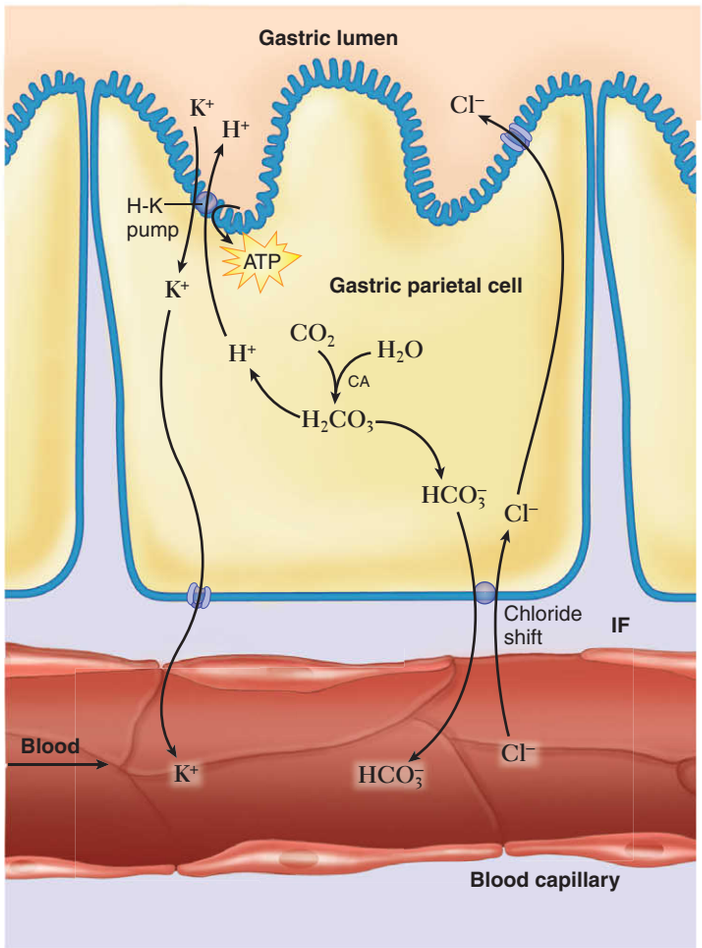


FIGURE 29-13

Acid secretion by gastric parietal cells. In this simplified diagram, you can see that hydrochloric acid (HCl) secretion by gastric parietal cells uses H^+ produced by the dissociation of carbonic acid (H_2CO_3). Recall that carbonic acid is produced by the reaction of water and carbon dioxide—a process enhanced by the enzyme carbonic anhydrase (CA). The chloride (Cl^-) of gastric HCl comes from a chloride shift into the cell in exchange for bicarbonate ions (HCO_3^-) produced by the same dissociation of carbonic acid that yielded the H^+. As Cl^- is shifted into the cell, the intracellular Cl^- concentration rises and produces a concentration gradient with the lumen of the gastric gland—forcing Cl^- to diffuse out of the parietal cell. The net effect is that active pumping of H^+ out of the cell by the H-K pump drives the concurrent shift of Cl^- into the cell from the blood and diffusion of Cl^- out of the cell and into the duct of the gastric gland. *IF,* Interstitial fluid.

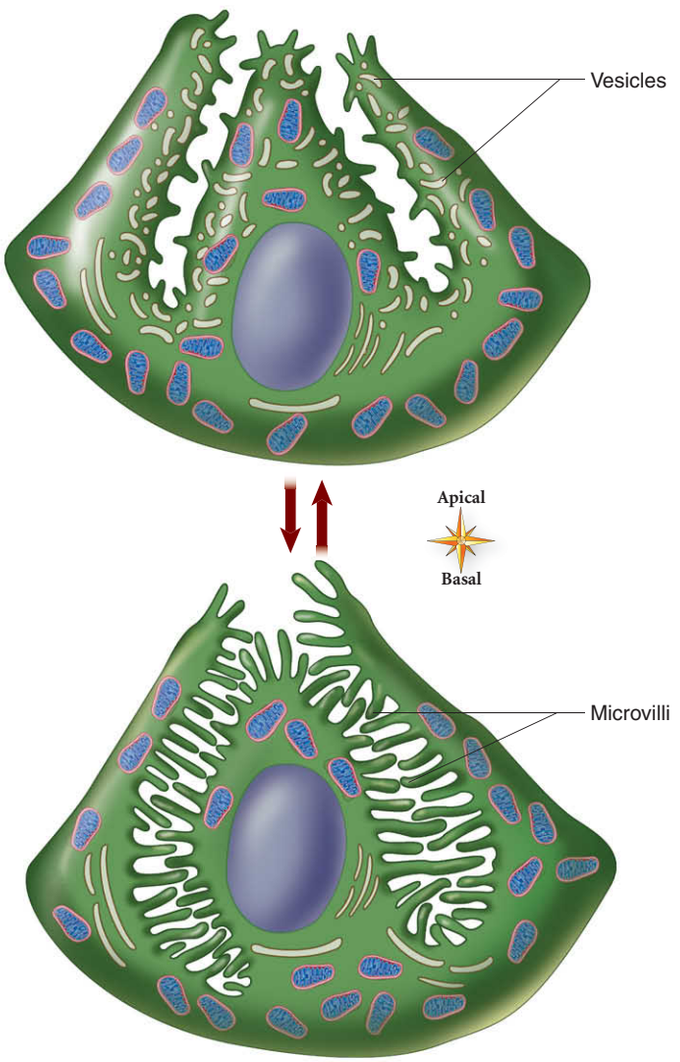


FIGURE 29-14

Parietal cell membrane surface. The surface of the resting parietal cell **(A)** can be enlarged by a factor of 100 when the cell becomes active and vesicles fuse to the apical surface of the cell **(B).** The vesicle membranes contain many ion pumps, carriers, and channels (Figure 29-13) that are thus added to the additional microvilli formed by fusion of the vesicle membrane to the plasma membrane.

Besides secreting acid, parietal cells also produce **intrinsic factor.** Intrinsic factor binds to molecules of vitamin B_{12}, protecting them from the acids and enzymes of the stomach. Intrinsic factor remains attached to B_{12} until it reaches the lower small intestine, where it facilitates the absorption of B_{12} across the intestinal wall (Figure 29-15). Vitamin B_{12}, you may recall, is essential for the production of new red blood cells. In pernicious anemia, caused by insufficient vitamin B_{12} in the body, the stomach may fail to make sufficient intrinsic factor (perhaps because of stomach cancer or ulcers). More frequently, however, an autoimmune mechanism produces antibodies that block the intrinsic factor from binding to vitamin B_{12}.

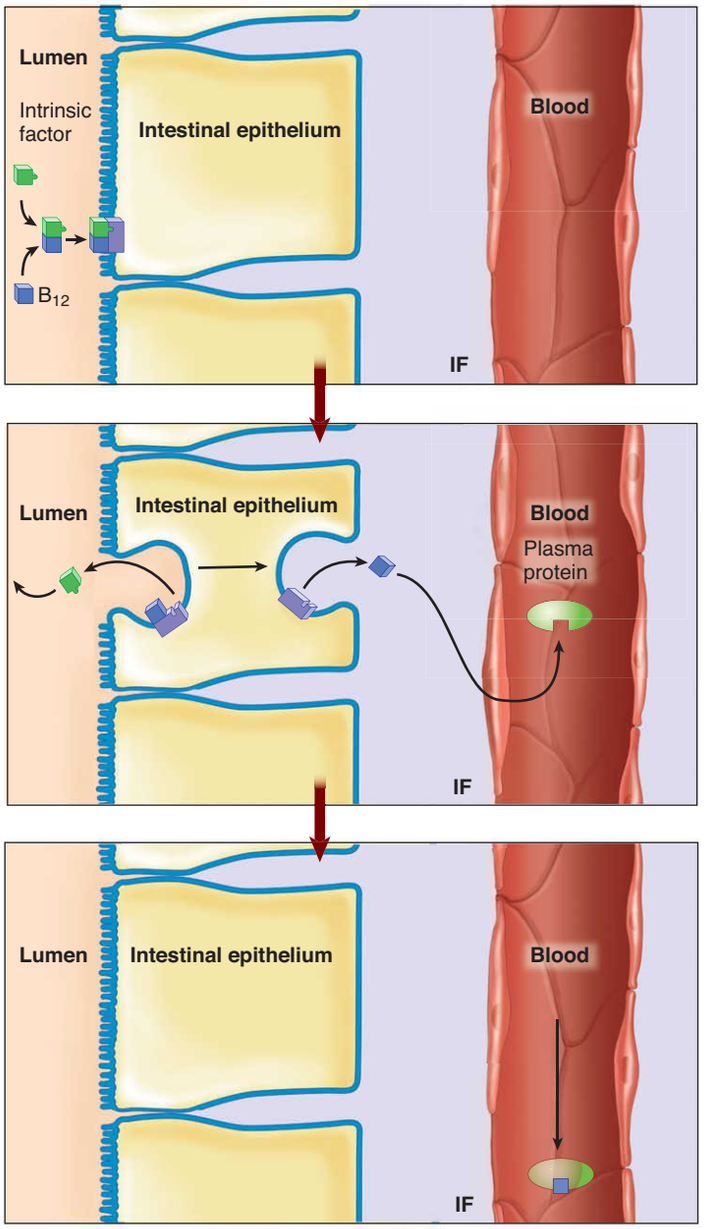


FIGURE 29-15

Role of intrinsic factor. As this series of sketches shows, intrinsic factor secreted from the stomach binds to vitamin B_{12}, which then permits the absorption of vitamin B_{12} into the bloodstream in the intestines. *IF,* Interstitial fluid.

Pancreatic Juice

Pancreatic juice is secreted by the exocrine *acinar cells* of the pancreas (see Figure 28-29 on p. 887). As with other digestive secretions, pancreatic juice is mostly water. In addition, pancreatic juice also contains various digestive enzymes. All of these enzymes are secreted as zymogens—inactive proenzymes. For example, protein-digesting **trypsin** is released as the zymogen **trypsinogen,** which is subsequently converted to active trypsin by **enterokinase** in the intestinal lumen. Enterokinase is an activating enzyme bound to the plasma membranes of cells that line the intestinal tract. After it is activated, trypsin can then activate other enzymes such as **chymotrypsin** (and other protein-digesting enzymes), various **lipases** (lipid-digesting enzymes), **nucleases** (RNA- and DNA-digesting enzymes), and **amylase** (a starch-digesting enzyme). Trypsin activates these molecules by an allosteric effect: it removes a specific sequence of amino acids from the proenzyme molecule, thus changing its shape to the active enzyme form. The advantage of this system is that the enzymes will not digest the cells that make them.

Cells along the exocrine ducts of the pancreas also have a secretory function. As Figure 29-16 shows, they produce sodium bicarbonate by more or less reversing the direction of the process described for acid secretion by gastric parietal cells and shown in Figure 29-13. In the pancreas, base (bicarbonate) is secreted into the GI lumen and acid is secreted into the blood—rather than the other way around, as in the stomach. This process thus provides a mechanism to neutralize the decreased pH of the chyme and the increased pH of the blood. As Figure 29-17 shows, the pH balance of the body is preserved and loss of homeostatic stability is avoided.

Bile

Bile is an interesting mixture of many different substances that is secreted by the liver and stored and concentrated by the gallbladder. As Figure 28-27 (on p. 885) shows, bile from the liver is conducted through the right and left hepatic ducts, which merge to form a common hepatic duct. The common hepatic duct, in turn, merges with the cystic duct from the gallbladder to form the common bile duct, which delivers bile to the duodenum through the major duodenal papilla.

Bile contains several substances that aid in digestion, specifically **lecithin** and **bile salts.** As we stated previously, both of these substances break down large drops of fat into smaller droplets, thus making the fats more easily digestible. Both lecithin and bile salts wrap a hydrophilic shell around the droplets, making them water soluble and therefore able to move freely through the watery chyme in the GI lumen. Bile also contains a small amount of sodium bicarbonate, which as with the sodium bicarbonate secreted by pancreatic duct cells, helps neutralize chyme.

Bile also contains several substances that are ultimately destined for removal from the body by becoming part of the feces that

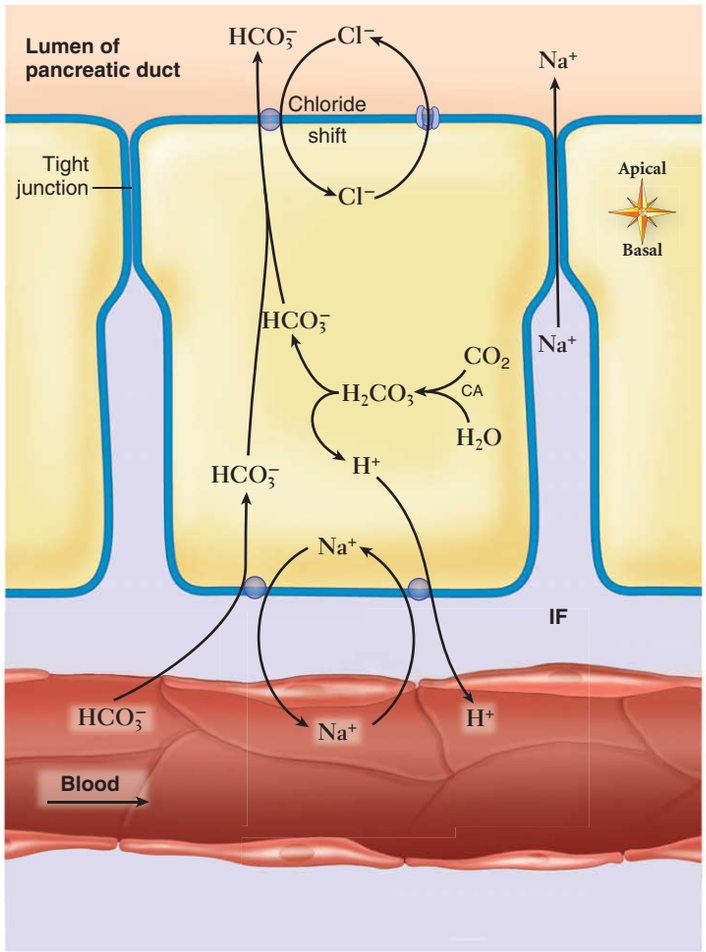


FIGURE 29-16

Bicarbonate secretion by pancreatic duct cells. In this simplified diagram, you can see that bicarbonate (HCO_3^-) secretion by cells of the pancreatic duct uses HCO_3^- produced by the dissociation of carbonic acid (H_2CO_3). Recall that carbonic acid is produced by the reaction of water and carbon dioxide—a process enhanced by the enzyme carbonic anhydrase (CA). Notice that a "reverse" chloride shift occurs as bicarbonate ions (HCO_3^-) are exchanged for Cl^- ions. The outward movement of negative bicarbonate ions into the lumen of the pancreatic ducts creates an electrical gradient that draws positive sodium ions (Na^+) from the IF (interstitial fluid), across the tight junctions, and into the pancreatic juice.

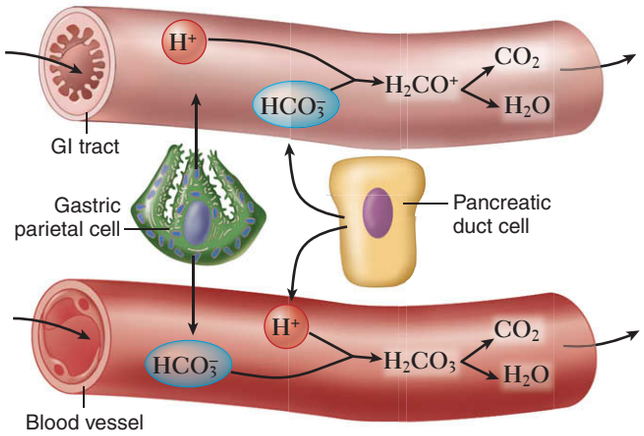


FIGURE 29-17

pH balance related to the digestive tract. Hydrochloric acid (HCl) secretion by gastric parietal cells moves H^+ into the gastrointestinal (GI) lumen, decreasing the pH of chyme. At the same time, gastric parietal cells shift bicarbonate ions (HCO_3^-) into the blood, increasing the pH of blood plasma. Eventually, this net loss of acid from the internal environment would cause alkalosis if not for the counterbalancing effects of bicarbonate secretion by the duct cells of the pancreas and other digestive glands such as the liver and intestinal glands. These cells secrete HCO_3^- into the GI lumen, increasing the pH of chyme, at the same time they move H^+ into the blood, decreasing the pH of blood back toward normal. This mechanism permits changes in the pH of chyme to facilitate the action of various enzymes without profoundly affecting the pH of the internal environment.

are eventually eliminated from the GI tract. It is therefore proper to state that these waste substances are actually *excretions*, a term that implies shedding waste, rather than *secretions*. Excreted substances in bile include cholesterol, products of detoxification, and bile pigments. The cholesterol in bile represents excess amounts of this lipid that have been picked up from body cells by lipoproteins and delivered to the liver for disposal in bile. Products of detoxification are formed in the liver as it renders toxic molecules harmless, a process called *detoxification*. Bile pigments, chiefly **bilirubin,** are products of hemolysis (the breakdown of old red blood cells) by the liver (see Figure 20-8 on p. 605). It is the bile pigments that are eventually eliminated from the GI tract that give feces its characteristic brownish color. Elimination of gray feces, therefore, can ordinarily be interpreted as a sign that bile secretion is abnormally low.

We discuss many functions of the liver further in the next chapter.

Intestinal Juice

The term **intestinal juice** refers to the sum total of intestinal secretions rather than to a premixed combination of substances that enters the GI lumen by way of a duct. Most intestinal cells produce a water-based solution of sodium bicarbonate. This adds to the buffering effect mentioned in previous paragraphs and illustrated in Figure 29-17. Goblet cells of the intestinal mucosa also produce a watery solution of mucus. Thus intestinal juice is a slightly basic, mucous solution that buffers and lubricates material in the intestinal lumen.

Intestinal juice is largely a product of the small intestine, but goblet cells in the mucosa of the large intestine produce some lubricating mucus.

TABLE 29-4 Digestive Secretions

DIGESTIVE JUICE	SOURCE	SUBSTANCE	FUNCTIONAL ROLE*
Saliva	Salivary glands	Mucus	*Lubricates bolus of food; facilitates mixing of food*
		Amylase (ptyalin)	**Enzyme; begins digestion of starches**
		Sodium bicarbonate	Increases pH (for optimum amylase function)
		Water	*Dilutes food and other substances; facilitates mixing*
Gastric juice	Gastric glands	Pepsin	**Enzyme; digests proteins**
		Hydrochloric acid	Denatures proteins; decreases pH (for optimum pepsin function)
		Intrinsic factor	**Protects and allows later absorption of vitamin B_{12}**
		Mucus	*Lubricates chyme; protects stomach lining*
		Water	*Dilutes food and other substances; facilitates mixing*
Pancreatic juice	Pancreas (exocrine portion)	Proteases (trypsin, chymotrypsin, collagenase, elastase, etc.)	**Enzymes; digest proteins and polypeptides**
		Lipases (lipase, phospholipase, etc.)	**Enzymes; digest lipids**
		Colipase	**Coenzyme; helps lipase digest fats**
		Nucleases	**Enzymes; digest nucleic acids (RNA and DNA)**
		Amylase	**Enzyme; digests starches**
		Water	*Dilutes food and other substances; facilitates mixing*
		Mucus	*Lubricates*
		Sodium bicarbonate	**Increases pH** (for optimum enzyme function)
Bile	Liver (stored and concentrated in gallbladder)	Lecithin and bile salts	*Emulsify lipids*
		Sodium bicarbonate	**Increases pH** (for optimum enzyme function)
		Cholesterol	Excess cholesterol from body cells, to be excreted with feces
		Products of detoxification	From detoxification of harmful substances by hepatic cells, to be excreted with feces
		Bile pigments (mainly bilirubin)	Products of breakdown of heme groups during hemolysis, to be excreted with feces
		Mucus	*Lubrication*
		Water	Dilutes food and other substances; facilitates mixing
Intestinal juice	Mucosa of small and large intestine	Mucus	*Lubrication*
		Sodium bicarbonate	**Increases pH** (for optimum enzyme function)
		Water	Small amount to carry mucus and sodium bicarbonate

***Boldface type** indicates a chemical digestive process; *italic type* indicates a mechanical process.

Table 29-4 lists various secretions of the digestive tract and their components.

| QUICK CHECK |

8. Name the primary components of saliva.
9. Name the components of gastric juice. Which type of cell produces each component?
10. Name as many pancreatic enzymes as you can.
11. What is excretion? What components of bile are excretions?

CONTROL OF DIGESTIVE GLAND SECRETION

Exocrine digestive glands secrete when food is present in the digestive tract or when it is seen, smelled, or imagined. Complicated nervous and hormonal reflex mechanisms control the flow of digestive juices in such a way that they appear in proper amounts when and for as long as needed.

Control of Salivary Secretion

As far as is known, only reflex mechanisms control the secretion of saliva. Chemical, mechanical, olfactory, and visual stimuli initiate afferent impulses to centers in the brainstem that send out efferent impulses to the salivary glands, stimulating them. Chemical and mechanical stimuli come from the presence of food in the mouth. Olfactory and visual stimuli come, of course, from the smell and sight of food.

Control of Gastric Secretion

Stimulation of gastric juice secretion occurs in three phases that are controlled by reflex and chemical mechanisms. Because stimuli that activate these mechanisms arise in the head, stomach, and intestines, the three phases are known as the cephalic, gastric, and

intestinal phases, respectively. As you read the description of each phase, glance at the diagrams shown in Figure 29-18.

The **cephalic phase** is also spoken of as the "psychic phase" because psychic (mental) factors activate the mechanism. For example, the sight, smell, taste, or even thought of food that is pleasing to an individual activates control centers in the medulla oblongata from which parasympathetic fibers of the vagus nerve conduct efferent impulses to the gastric glands. Vagal nerve impulses also stimulate the production of **gastrin,** a hormone secreted by endocrine *G cells* in the gastric mucosa.

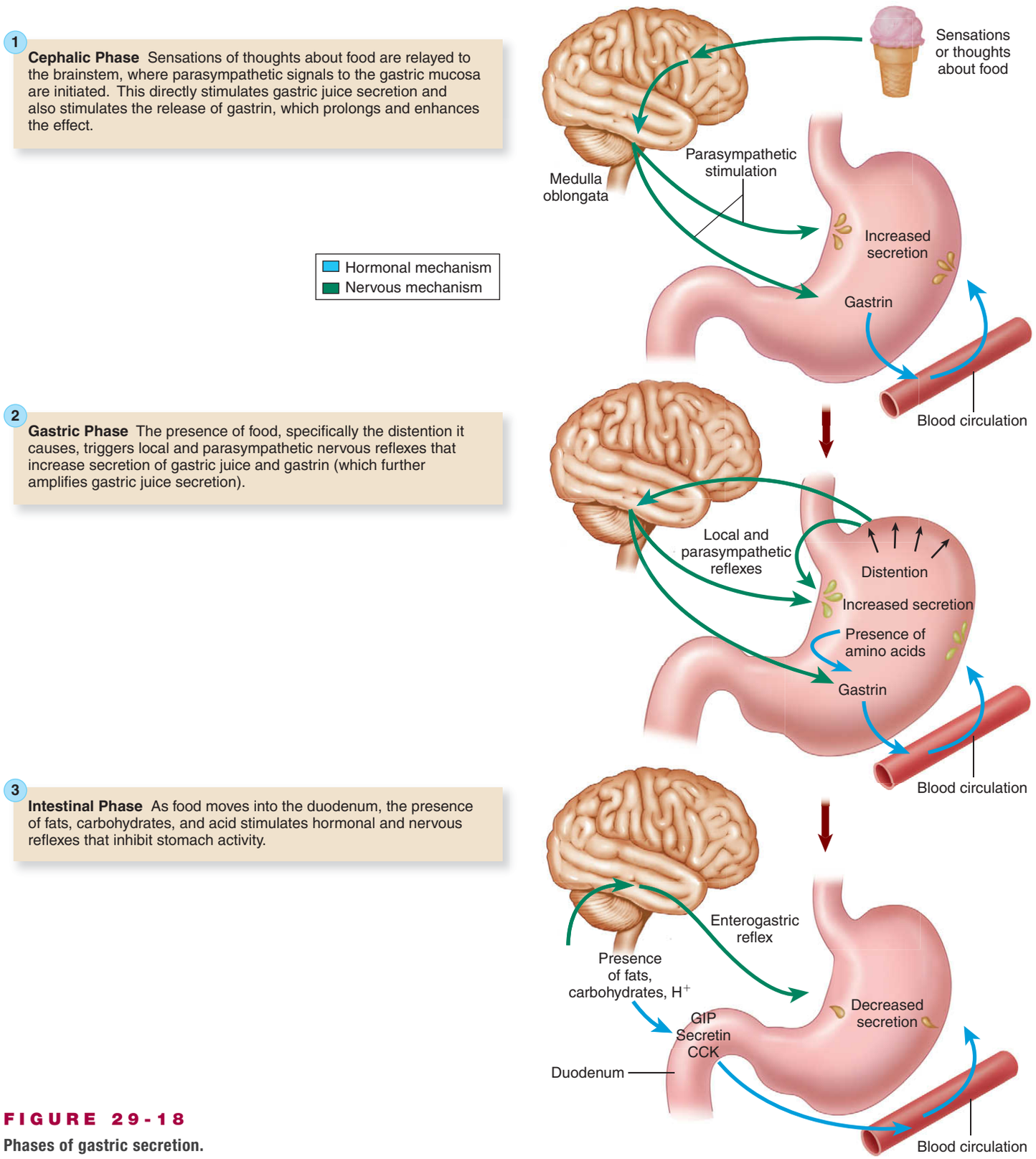


FIGURE 29-18
Phases of gastric secretion.

Gastrin stimulates gastric secretion, thus prolonging and enhancing the response.

During the **gastric phase** of gastric secretion, the following chemical control mechanism dominates. Products of protein digestion in foods that have reached the pyloric portion of the stomach stimulate its mucosa to release *gastrin* into the blood in stomach capillaries. When it circulates to the gastric glands, gastrin greatly accelerates their secretion of gastric juice, which has a high pepsinogen and hydrochloric acid content (Table 29-5). Hence, this seems to be a mechanism for ensuring that when food is in the stomach, there will be enough enzymes there to digest it. Gastrin release is also stimulated by distention of the stomach (caused by the presence of food), which activates local and parasympathetic reflexes in the pylorus.

The **intestinal phase** of gastric juice secretion is less clearly understood than the other two phases. Various different mechanisms seem to adjust gastric juice secretion as chyme passes to and through the intestinal tract. Experiments show that gastric secretions are inhibited when chyme containing fats, carbohydrates, and acid (low pH) is present in the duodenum. This probably occurs by means of endocrine reflexes that involve the hormones **gastric inhibitory peptide (GIP), secretin, CCK,** and perhaps several others. These hormones are secreted by endocrine cells in the mucosa of the duodenum. Gastric secretion may also be inhibited by the parasympathetic **enterogastric reflex.** We have discussed how this reflex inhibits gastric motility as food begins to fill the duodenum; now we see that it may inhibit gastric secretion as well.

In summary, we see that the rate of gastric secretion can be adjusted by nervous and endocrine reflex mechanisms in ways that improve the efficiency of the system. Anticipation of swallowing food causes the stomach to prepare itself by increasing its secretion of enzymes and acid. Thus food enters a stomach already partially filled with gastric juice. The rate of gastric secretion can then be adjusted according to the amount of food present and whether it contains proteins (the only food that can be chemically digested by gastric juice). Gastric secretion—and thus chemical digestion in the stomach—can be slowed when the duodenum becomes full. This prevents the stomach from finishing its task before the small intestine is ready to receive the chyme.

Control of Pancreatic Secretion

Several hormones released by the intestinal mucosa are known to stimulate pancreatic secretion. One of these hormones, *secretin*, evokes the production of pancreatic fluid low in enzyme content but high in bicarbonate (HCO_3^-). This alkaline fluid acts to neutralize the acid (chyme) entering the duodenum. As you might expect, the presence of acid in the duodenum serves as the most potent stimulator of secretin. (Additional control involving the same hormone is shown by the fact that fats in the duodenum also elicit secretin, which then influences the gallbladder to increase its ejection of the fat emulsifier bile.)

The other intestinal hormone, known as **CCK,** was originally thought to be two separate substances. It has now been identified as one chemical with several important functions: (1) it causes the pancreas to increase exocrine secretions high in enzyme content; (2) it opposes the influence of gastrin on gastric parietal cells, thus inhibiting hydrochloric acid secretion by the stomach; and (3) it stimulates contraction of the gallbladder so that bile can pass into the duodenum.

Control of Bile Secretion

Bile is secreted continually by the liver and is stored in the gallbladder until needed by the duodenum. The hormones secretin and CCK, as described, stimulate ejection of bile from the gallbladder (see Table 29-5).

Control of Intestinal Secretion

Relatively little is known about the regulation of intestinal exocrine secretions. Some evidence suggests that the intestinal mucosa, stimulated by hydrochloric acid and food products, releases hormones into the blood, including *vasoactive intestinal peptide* (VIP), which brings about increased production of intestinal juice. Intestinal secretions contain bicarbonate, which along with pancreatic bicarbonate, neutralizes acid from the stomach. Bicarbonate secretion is regulated by a reflex sensitive to changes in pH of the chyme. Presumably, neural mechanisms also help control the secretion of intestinal juice.

TABLE 29-5 Actions of Some Digestive Hormones Summarized

HORMONE	SOURCE	ACTION
Gastrin	Secreted by gastric mucosa in presence of partially digested proteins, when stimulated by the vagus nerve, or when the stomach is stretched	Stimulates secretion of gastric juice rich in pepsin and hydrochloric acid
Gastric inhibitory peptide (GIP)	Secreteded by intestinal mucosa in presence of glucose, fats, and perhaps other nutrients	Inhibits gastric secretion and motility; enhances insulin secretion by pancreas (see Chapter 30)
Secretin	Secreted by intestinal mucosa in presence of acid, partially digested proteins, and fats	Inhibits gastric secretion; stimulates secretion of pancreatic juice low in enzymes and high in alkalinity (bicarbonate); enhances effects of CCK
Cholecystokinin (CCK)	Secreted by intestinal mucosa in presence of fats, partially digested proteins, and acids	Stimulates ejection of bile from gallbladder and secretion of pancreatic juice high in enzymes; relaxes sphincters that regulate flow from the common bile duct; opposes the action of gastrin, raising the pH of gastric juice

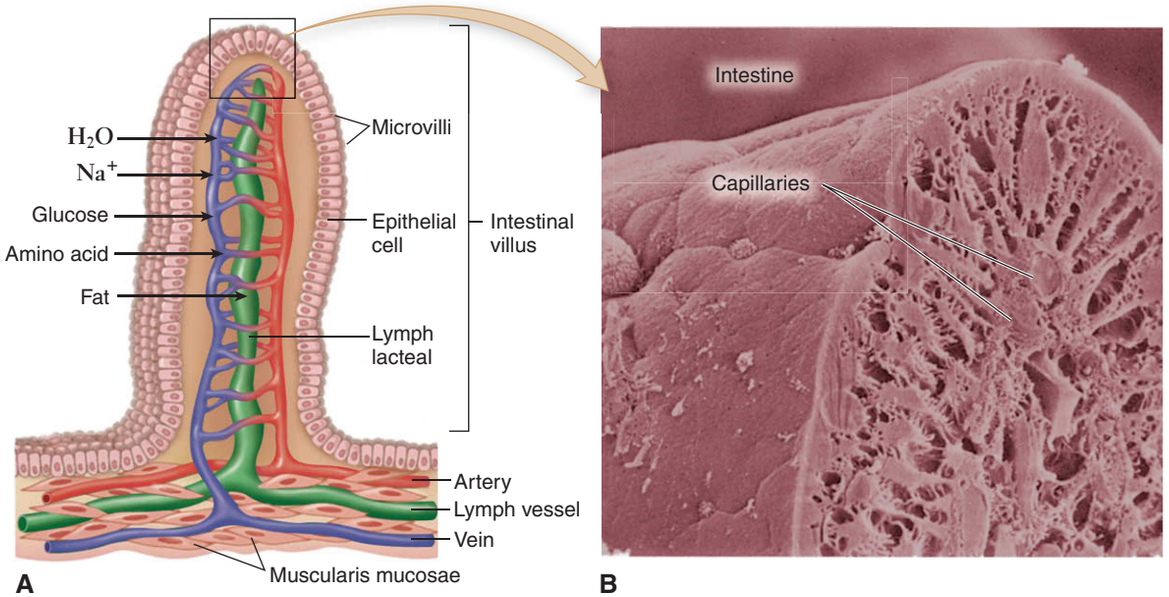


FIGURE 29-19

Intestinal villus. The presence of intestinal villi and microvilli increases the absorptive surface area of the intestinal mucosa. Most absorbed substances enter the blood in intestinal capillaries, with the exception of fat, which enters lymph by way of the intestinal lacteals.

| QUICK CHECK |

12. Name the three phases of gastric secretion.
13. What is the function of *gastric inhibitory peptide?*

ABSORPTION

Process of Absorption

Absorption is the passage of substances (notably digested foods, water, salts, and vitamins) through the intestinal mucosa into the blood or lymph. As stated earlier, most absorption occurs in the small intestine, where the large surface area provided by the intestinal villi and microvilli (Figure 29-19) facilitates this process.

Mechanisms of Absorption

Absorption of some substances, such as water, is simple and straightforward: diffusion, or more specifically, osmosis. However, some substances depend on more complex mechanisms to be absorbed. Sodium is a good example. Epithelial cells that form the outer wall of the villus (see Figure 29-19) constantly pump sodium from the GI lumen into the internal environment through a complex process called *secondary active transport* (see Box 4-3 on p. 93).

As Figure 29-20, A, shows, active transport carriers on the basal side, or "back side," of the cell continually pump Na^+ out of the cell. This mechanism maintains a low Na^+ concentration inside the cell. Thus it is likely that Na^+ in the GI lumen will diffuse

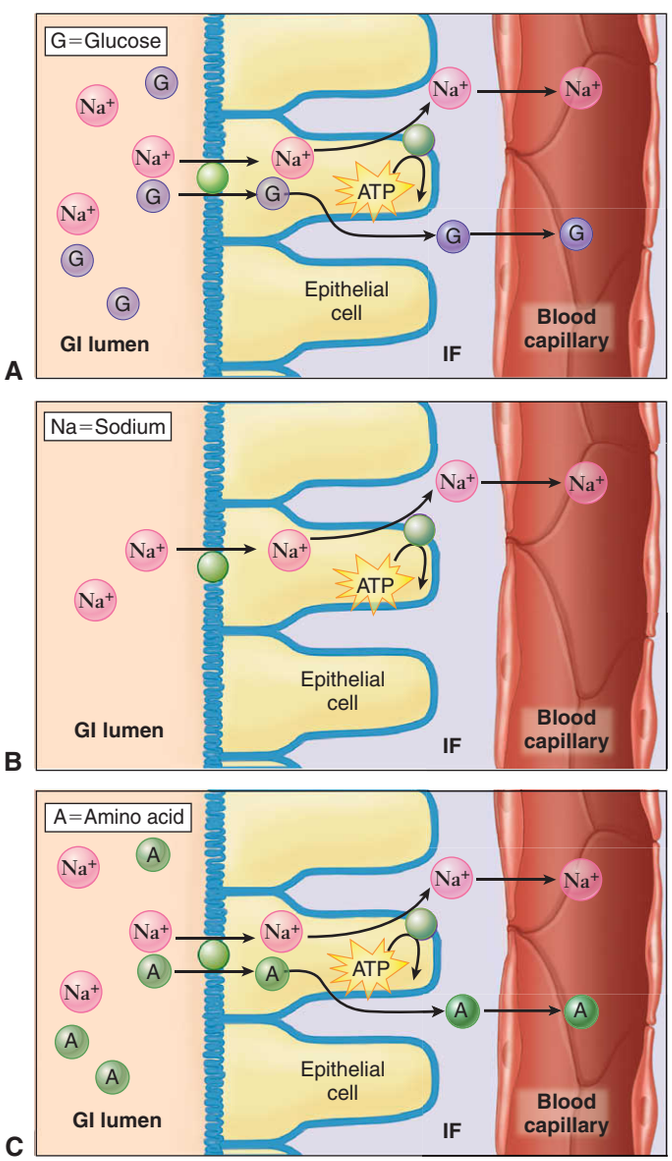


FIGURE 29-20

Absorption of glucose, sodium, and amino acids. Absorption of glucose **(A)**, sodium **(B)**, and amino acids **(C)** is a form of *secondary active transport* because each involves two carriers, one of which is active. The active carrier on the basal side of the epithelial cell maintains a sodium gradient, which facilitates passive transport of sodium, and perhaps another molecule, out of the gastrointestinal (GI) lumen via a passive carrier on the luminal side of the cell. *IF,* Interstitial fluid.

into the low-Na^+ cell. As Na^+ diffuses in through passive carriers in the cell's luminal surface, or "lumen side," it is removed by active transport pumps in the cell's basal membrane. In short, Na^+ moves out of the GI lumen only because it is being pumped from the other side of the intestinal cells.

Another good example of a complex transport process is that involving glucose. Though considered an "end product of digestion," glucose is a relatively large molecule and cannot pass freely through the brush border membrane of an intestinal mucosa cell. In addition to physical size, the lipid nature of the cell membrane (see Figure 3-3, p. 70) presents another barrier to glucose absorption. Molecules the size of glucose can pass freely (passively) through the lipid cell barrier only if they are lipid soluble (hydrophobic). Because glucose is too large physically and is hydrophilic (water soluble) in nature, it must be transported across the membrane by a carrier to enter the cell. In a process called **sodium cotransport** or coupled transport, carriers that bind both sodium ions and glucose molecules passively transport these molecules *together* out of the GI lumen (see Figure 29-20, *B*). However, this is another case of secondary active transport because this movement does not occur without the Na^+ concentration gradient maintained by the active transport of Na^+ out of the cell's basal membrane. Amino acids and several other compounds are thought to also be absorbed by such a secondary active transport mechanism (see Figure 29-20, *C*).

Other mechanisms of transporting glucose and amino acids across absorptive cells have also been proposed. One hypothesis suggests that these compounds are transported by passive carriers on both the apical surfaces (lumen side) and the basal surfaces of the absorptive cells. Another hypothesis suggests that the brush border enzymes also act as carriers. It should also be noted that some short polypeptides can diffuse by way of peptide carriers into absorptive cells where they are hydrolyzed into amino acids that can move into the blood.

Fatty acids and monoglycerides (products of fat digestion) and cholesterol are transported with the aid of lecithin and bile salts from fat droplets in the intestinal lumen to absorbing cells on villi. Lecithin and bile salts form microscopic spheres called **micelles,** which contain simple lipids (see Figure 29-12).

As Figure 29-21 shows, water-soluble micelles formed in the lumen of the intestine approach the brush border of absorbing cells. There, simple lipid molecules are released to pass through the plasma membrane (its phospholipid bilayer is receptive to lipids) by simple diffusion. After they are inside the cell, fatty acids are rapidly reunited with monoglycerides to form triglycerides (neutral fats). The final step in lipid transport by the intestine is the formation of **chylomicrons,** which are simply another type of micelle. Chylomicrons are formed by the Golgi apparatus of the absorptive cell. The water-soluble chylomicron allows fats to be transported through lymph and into the bloodstream (Table 29-6).

Vitamins A, D, E, and K, known as the "fat-soluble vitamins," also depend on bile salts for their absorption. Some water-soluble vitamins, such as certain of the B group, are small enough to be absorbed by simple diffusion; however, most require carrier-mediated transport. Many drugs (sedatives, analgesics, antibiotics) appear to be absorbed by simple diffusion because they are lipid soluble.

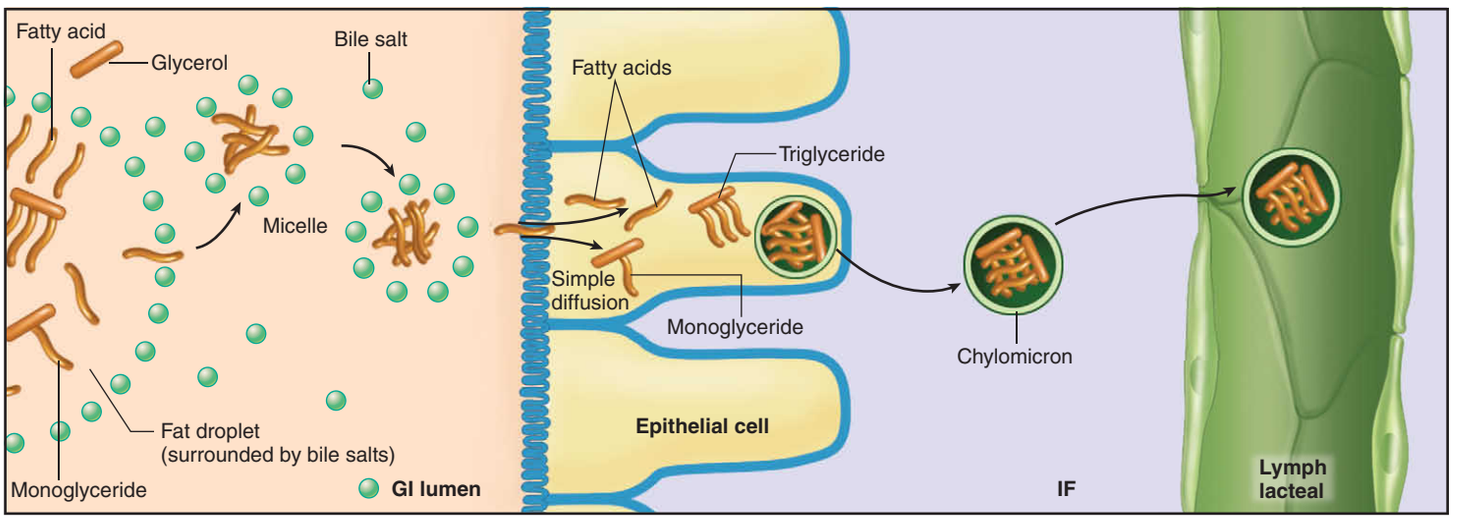


FIGURE 29-21

Absorption of fats. Fats such as triglycerides are chemically digested within emulsified fat droplets, yielding fatty acids, monoglycerides, and glycerol *(left).* Fatty acids and other lipid-soluble compounds (such as cholesterol) leave the fat droplets in small spheres coated with bile salts (micelles). When a micelle reaches the plasma membrane of an absorptive cell, individual fat-soluble molecules diffuse directly into the cytoplasm. The endoplasmic reticulum of the cell resynthesizes fatty acids and monoglycerides into triglycerides. A Golgi body within the cell packages the fats into water-soluble micelles called chylomicrons, which then exit the absorptive cell by exocytosis and enter a lymphatic lacteal. *IF,* Interstitial fluid.

TABLE 29-6 Food Absorption

FORM ABSORBED	STRUCTURES INTO WHICH ABSORBED	CIRCULATION
Protein—as amino acids Perhaps minute quantities of some short-chain polypeptides and whole proteins are absorbed; for example, some antibodies	Blood in intestinal capillaries	Portal vein, liver, hepatic vein, inferior vena cava to heart, and so on
Carbohydrates—as simple sugars	Same as amino acids	Same as amino acids
Fats		
Glycerol and monoglycerides	Lymph in intestinal lacteals	During absorption, that is, while in epithelial cells of intestinal mucosa, glycerol and fatty acids recombine to form microscopic packages of fats (chylomicrons); lymphatics carry them by way of thoracic duct to left subclavian vein, superior vena cava, heart, and so on; some fats are transported by blood in form of phospholipids or cholesterol esters
Fatty acids combine with bile salts to form water-soluble substance	Lymph in intestinal lacteals	
Some finely emulsified, undigested fats absorbed	Small fraction enters intestinal blood capillaries	

Note that after absorption, most nutrients do not pass directly into the general circulation. Lacteals conduct fats along a series of lymphatic vessels and through many lymph nodes before releasing them into the venous blood flowing through the left subclavian vein (see Figure 20-2, p. 600). Nutrients that are absorbed into the blood, such as amino acids and monosaccharides, first travel by way of the hepatic portal system to the liver (see Figure 21-32, p. 665). After absorption, blood entering the liver via the portal vein contains greater concentrations of glucose and other nutrients than does blood leaving the liver via the hepatic vein for the systemic circulation. Clearly, much of the excess of these food substances over and above normal blood levels has remained behind in the liver. What the liver does with them is part of the story of nutrition and metabolism, our topic for discussion in the next chapter.

The types of absorption discussed thus far involve *transcellular absorption*. In transcellular (meaning "across cells") absorption, particles are absorbed into the interior of the cell before moving out of the cell and into blood or lymph. Another type of absorption called *paracellular absorption* can also occur. In this type of absorption, small amounts of glucose, minerals, and even small peptides can move *between* the absorptive cells rather than through them. Paracellular absorption requires no energy expenditure by cells.

Figure 29-22 summarizes the locations where absorption of some important substances takes place. Notice that although the stomach can absorb a small amount of alcohol, almost all other absorption takes place in the intestines—particularly the small intestine.

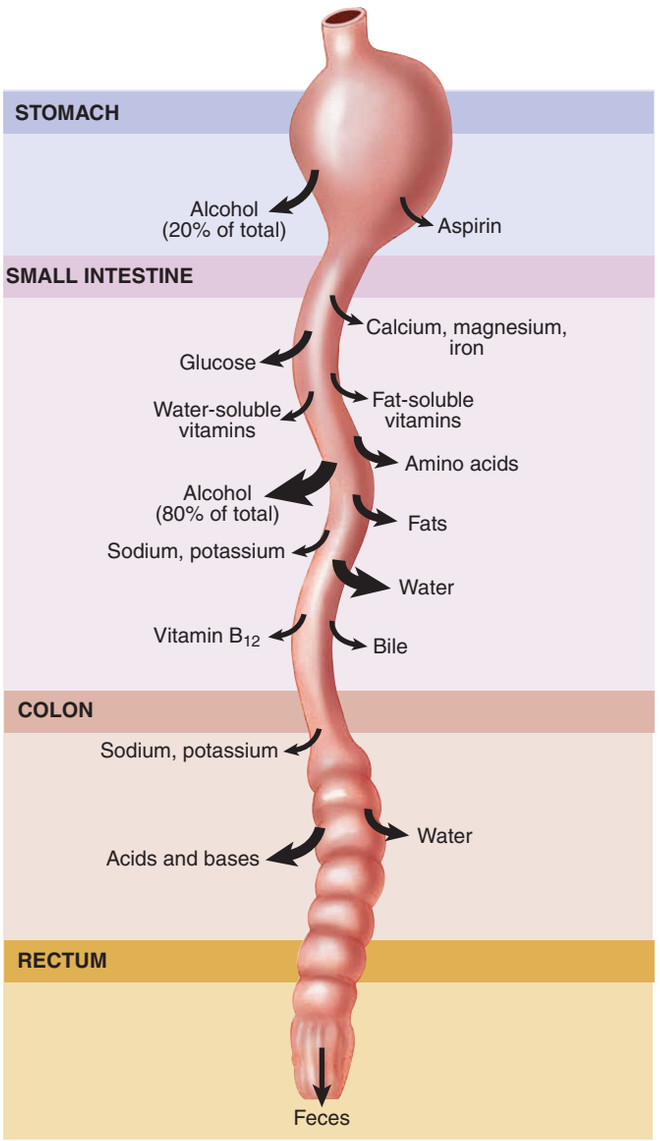


FIGURE 29-22

Absorption sites in the digestive tract. The size of the arrow at each site indicates the relative amount of absorption of a particular substance at that site. Notice that most absorption occurs in the intestines, particularly the small intestine.

ELIMINATION

The process of **elimination** is simply the expulsion of the residues of digestion—*feces*—from the digestive tract. Formation and storage of feces is the primary function of the colon. The act of expelling feces is called **defecation.**

Defecation is a reflex brought about by stimulation of receptors in the rectal mucosa. Normally, the rectum is empty until mass peristalsis moves fecal matter out of the colon into the rectum. This distends the rectum and produces the desire to defecate. Also, it stimulates colonic peristalsis and initiates reflex relaxation of the internal sphincter of the anus. Voluntary straining efforts and relaxation of the external anal sphincter may then follow as a result of the desire to defecate. Together, these several responses bring about defecation (Figure 29-23). Note that this is a reflex partly under voluntary control. If one voluntarily inhibits defecation, the rectal receptors soon become depressed and the urge to defecate does not usually recur until hours later, when mass peristalsis again takes place.

Constipation occurs when the contents of the distal part of the colon and rectum move at a rate that is slower than normal. What is normal can range from three times a day to three times a week, depending on a variety of factors such as the amount, type, and rate of food eaten. When motility in the distal colon and rectum slows significantly, extra water is absorbed from the fecal mass, producing a hardened stool.

Diarrhea may occur as a result of increased motility of the small intestine. Chyme moves through the small intestine too quickly, reducing the amount of absorption of water and electrolytes. Diarrhea may also result from bacterial toxins that damage the water reabsorption mechanisms of the intestinal mucosa. The large volume of material arriving in the large intestine exceeds the limited capacity of the colon for absorption, so a watery stool results. Prolonged diarrhea can be particularly serious, even fatal, in infants because they have a minimal reserve of water and electrolytes (Box 29-7).

| QUICK CHECK |

14. Explain the term *secondary active transport.*
15. Describe how fatty acids are absorbed by cells of the GI mucosa.
16. What triggers the defecation reflex?

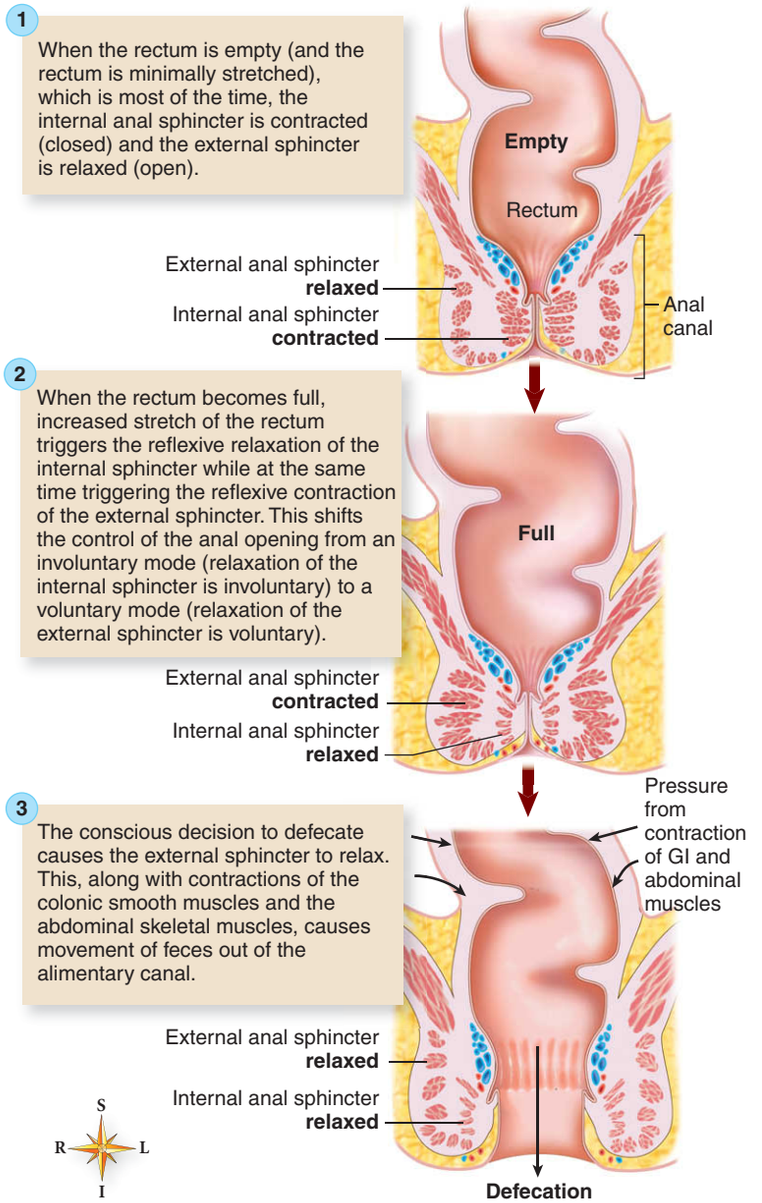


FIGURE 29-23

Defecation. The sketches show the role of the anal sphincters in defecation.

Box 29-7 | HEALTH matters

Infant Diarrhea

Severe diarrhea caused by a *rotavirus,* an intestinal infection, kills more than 600,000 infants and young children worldwide each year. Death results from severe dehydration caused by 20 or more episodes of diarrhea in a single day. More than 3 million U.S. children suffer symptoms of rotavirus intestinal infection annually and 65,000 require hospitalization. Good medical care in this country has limited the number of U.S. infant deaths caused by the disease each year to about 50. Unfortunately, in developing countries, rotavirus-induced diarrhea remains one of the leading causes of infant mortality. The first major attempt at a rotavirus vaccine provided good protection against the virus but was withdrawn from the world market at the close of the 20th century because of side effects. New rotavirus vaccines are now available and others are in the final stages of testing. Some have already been licensed outside the United States.

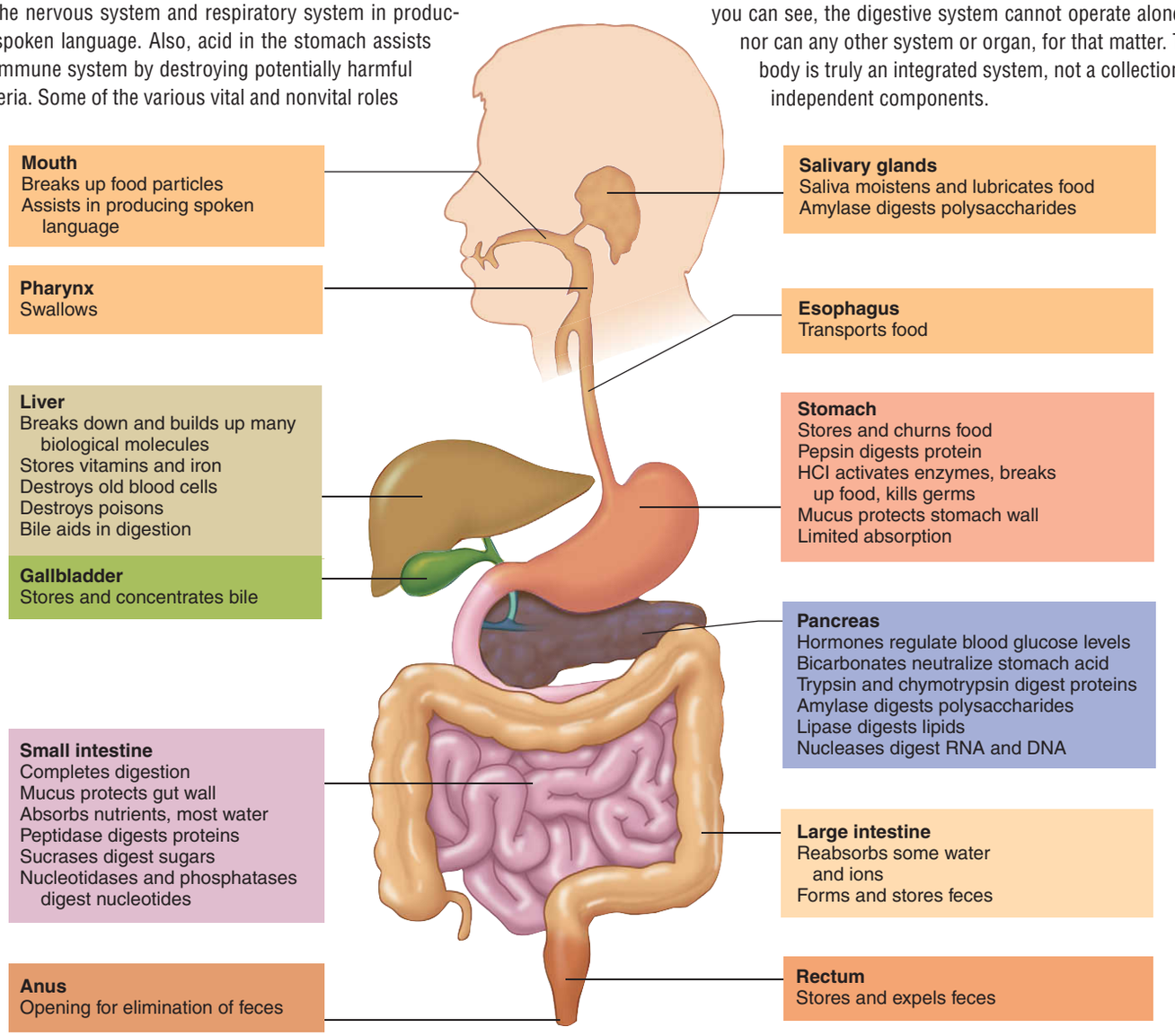
Until safe and effective vaccines become widely available, one of the best treatment options available in many areas of the world involves oral administration of liberal doses of a simple, easily prepared solution containing sugar and salt. Called **oral rehydration therapy (ORT),** the salt-sugar solution replaces nutrients and electrolytes lost in diarrheal fluid. Because the replacement fluid can be prepared from readily available and inexpensive ingredients, it is particularly valuable in the treatment of infant diarrhea in developing countries.

the BIG picture

Digestion and the Whole Body

The process of digestion, as with any other vital function, provides a means of survival for the entire body and also requires the function of other systems. The digestive system's primary contribution to overall homeostasis is its ability to maintain a constancy of nutrient concentration in the internal environment. It accomplishes this by breaking large, complex nutrients into smaller, simpler nutrients so they can be absorbed (see figure). The digestive system also provides the means of absorption—the cellular mechanisms that operate in the absorptive cells of the intestinal mucosa. The digestive system also provides some secondary, less vital functions. For example, the teeth and tongue aid the nervous system and respiratory system in producing spoken language. Also, acid in the stomach assists the immune system by destroying potentially harmful bacteria. Some of the various vital and nonvital roles played by the different organs that make up the digestive system are summarized in the "Summary of digestive function" figure.

To accomplish its functions, the digestive system requires functional contributions by other systems of the body. Regulation of digestive motility and secretion requires the active participation of both the nervous system and the endocrine system. The oxygen needed for digestive activity requires the proper functioning of both the respiratory system and the circulatory system. The body's framework (integumentary and skeletal systems) is required to support and protect the digestive organs. The skeletal muscles must function if ingestion, mastication, deglutition, and defecation are to occur normally. As you can see, the digestive system cannot operate alone—nor can any other system or organ, for that matter. The body is truly an integrated system, not a collection of independent components.



Summary of digestive function.

LANGUAGE OF SCIENCE *(continued from p. 901)*

deglutition
(deg-loo-TISH-un)
[*deglut-* **swallow**, *-tion* **process**]

digestion
[*digest-* **break down**, *-tion* **process**]

elimination
(ee-lim-i-NAY-shun)
[*e-* **out**, *-limen-* **threshold**, *-ation* **process**]

emulsified
(ee-MULL-seh-fyde)
[*e-* **out**, *-muls-* **milk**, *-i-* **combining form**, *-fy* **process**]

enteric nervous system (ENS)
(en-TER-ik)
[*enter-* **intestine**, *-ic* **relating to**]

enterogastric reflex
(en-ter-oh-GAS-trik)
[*entero-* **intestine**, *-gastr-* **stomach**, *-ic* **relating to**, *re-* **back or again**, *-flex* **bend**]

enterokinase
(en-ter-oh-KYE-nays)
[*entero-* **intestine**, *-kin-* **movement**, *-ase* **enzyme**]

enzyme
(EN-zyme)
[*en-* **in**, *-zyme* **ferment**]

feces
(FEE-seez)
[*feces* **waste**]

gastric inhibitory peptide (GIP)
(GAS-trik in-HIB-i-tor-ee PEP-tyde)
[*gastr-* **stomach**, *-ic* **relating to**, *inhibit-* **restrain**, *-ory* **relating to**, *pept-* **digest**, *-ide* **chemical**]

gastric juice
[*gastr-* **stomach**, *-ic* **relating to**]

gastric phase
[*gastr-* **stomach**, *-ic* **relating to**]

gastrin
(GAS-trin)
[*gastr-* **stomach**, *-in* **substance**]

H-K pump
[*H* **hydrogen**, *K* **potassium**]

hydrolysis
(hye-DROHL-i-sis)
[*hydro-* **water**, *-lysis* **loosening**]

ingestion
(in-JES-chun)
[*in-* **within**, *-gest-* **carry**, *-tion* **process**]

intestinal juice
(in-TES-ti-nal)
[*intestin-* **intestine**, *-al* **relating to**]

intestinal phase
(in-TES-ti-nal)
[*intestin-* **intestine**, *-al* **relating to**]

intrinsic factor
(in-TRIN-sik FAK-tor)
[*intr-* **inside or within**, *-insic* **beside**]

lecithin
(LES-i-thin)
[*lecith-* **yolk**, *-in* **substance**]

lipase
(LYE-pays)
[*lip-* **fat**, *-ase* **enzyme**]

mastication
(mas-ti-KAY-shun)
[*mastica-* **chew**, *-tion* **process**]

mechanical digestion
[*digest-* **break down**, *-tion* **process**]

micelle
(my-SELL)
[*mic-* **grain**, *-elle* **small**]

migrating motor complex (MMC)
[*migra-* **wander**, *-at-* **process**, *motor* **move**, *complex* **embrace**]

motilin
(moh-TIL-in)
[*mot-* **move**, *-il-* **relating to**, *-in* **substance**]

motility
(moh-TIL-i-tee)
[*mot-* **move**, *-il-* **relating to**, *-ity* **state**]

mucus
(MYOO-kus)
[*mucus* **slime**]

nuclease
(NOO-klee-ayz)
[*nucle-* **nut or kernel (nucleic acid)**, *-ase* **enzyme**]

pancreatic juice
(pan-kree-AT-ik)
[*pan-* **all**, *-creat-* **flesh**, *-ic* **relating to**]

parietal cell
(pah-RYE-i-tal)
[*pariet-* **wall**, *-al* **relating to**]

pepsin
(PEP-sin)
[*peps-* **digestion**, *-in* **substance**]

pepsinogen
(pep-SIN-oh-jen)
[*peps-* **digestion**, *-in* **substance**, *-o-* **combining form**, *-gen* **produce**]

peptidase
(PEP-tyd-ayz)
[*pept-* **digestion**, *-ide* **chemical**, *-ase* **enzyme**]

peristalsis
(pair-i-STAL-sis)
[*peri-* **around**, *-stalsis* **contraction**]

proenzyme
(pro-EN-zyme)
[*pro-* **first**, *-en-* **in**, *-zyme* **ferment**]

propulsion
(proh-PUL-shen)
[*pro-* **in front**, *-pul-* **drive**, *-sion* **process**]

protease
(PROH-tee-ayz)
[*prote-* **protein**, *-ase* **enzyme**]

retropulsion
(ret-roh-PUL-shen)
[*retro-* **backward**, *-pul-* **drive**, *-sion* **process**]

saliva
(sah-LYE-vah)

secretin
(seh-KREE-tin)
[*secret-* **separate**, *-in* **substance**]

secretion
(seh-KREE-shun)
[*secret-* **separate**, *-tion* **process**]

segmentation
(seg-men-TAY-shun)
[*segment-* **cut section**, *-ation* **process**]

sodium cotransport
(SOH-dee-um koh-TRANS-port)
[*sod-* **soda**, *-ium* **chemical ending**, *co-* **with**, *-trans-* **across**, *-port* **carry**]

trypsin
(TRIP-sin)
[*tryps-* **pound**, *-in* **substance**]

trypsinogen
(trip-SIN-oh-gen)
[*tryps-* **pound**, *-in* **substance**, *-o-* **combining form**, *-gen* **produce**]

zymogenic cell
(zye-moh-JEN-ik)
[*zym-* **ferment (enzyme)**, *-o-* **combining form**, *-gen-* **produce** *-ic* **relating to**]

LANGUAGE OF MEDICINE

constipation
(kon-sti-PAY-shun)
[*constipa-* **crowd together**, *-tion* **process**]

diarrhea
(dye-ah-REE-ah)
[*dia-* **through**, *-rrhea* **flow**]

oral rehydration therapy (ORT)
(OR-al ree-hye-DRAY-shun THER-ah-pee)
[*or-* **mouth**, *-alis* **relating to**, *re-* **back again**, *-hydra-* **water**, *-ation* **process**]

steatorrhea
(stee-eh-tah-REE-ah)
[*steat-* **fat**, *-o-* **combining form**, *-rrhea* **flow**]

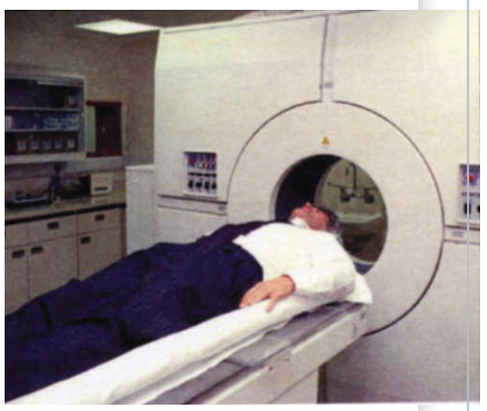
CASE study

Clarence had been cooking all day, getting Thanksgiving dinner ready for the whole family. After dinner, he bent over to pick up a serving dish and felt a sharp, stabbing pain in the right upper back just below his shoulder blade. The pain was so intense, he could hardly breathe. It lasted for about 20 minutes, then slowly dissipated to a dull ache. Having a history of back pain, he thought he had injured the same area again.

The following Monday, Clarence's doctor scheduled an MRI (magnetic resonance image) to look at his spine. The test results showed nothing wrong with the skeletal system—no misalignment in the spine. There was also no change in the pain with movement. The dull ache in Clarence's back remained constant, regardless of whether he was moving about or sitting still. A urinalysis came back normal.

Over the next few days, the pain receded considerably. Then one night not long after, Clarence had fried chicken and gravy for dinner. About 10 minutes after eating, the stabbing pain returned. At this point, he remembered that he had eaten a lot of gravy at Thanksgiving too. Both types of gravy were very high in fat content.

1. Taking all the information into account, what system do you think may be malfunctioning to cause the pain?
   a. Skeletal system
   b. Muscular system
   c. Digestive system
   d. Urinary system
2. Which of the following hormones is NOT released in response to fatty, acidic chyme entering the duodenum?
   a. Gastrin
   b. CCK
   c. Secretin
   d. GIP
3. After eating foods high in fat, Clarence's body may increase the production and release of bile. Bile is stored in which organ?
   a. Liver
   b. Pancreas
   c. Stomach
   d. Gallbladder



HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

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OVERVIEW OF DIGESTIVE FUNCTION

A. Primary function of the digestive system—to bring essential nutrients into the internal environment so that they are available to each cell of the body
B. Mechanisms used to accomplish the primary function of the digestive system (Figure 29-1)
   1. Ingestion—food is taken in
   2. Digestion—breakdown of complex nutrients into simple nutrients
   3. Motility of the GI wall—physically breaks down large chunks of food material and moves food along the tract
   4. Secretion—digestive enzyme secretion facilitates chemical digestion
   5. Absorption—movement of nutrients through the GI mucosa into the internal environment
   6. Elimination—excretion of material that is not absorbed
   7. Regulation—coordination of the various functions of the digestive system
C. The digestive tract is functionally an extension of the external environment—material does not truly enter the body until it is absorbed into the internal environment

DIGESTION

A. Mechanical digestion—movements of the digestive tract
   1. Change ingested food from large particles into minute particles, facilitating chemical digestion
   2. Churn contents of the GI lumen to mix with digestive juices and ensure contact with the surface of the intestinal mucosa, facilitating absorption
   3. Propel food along the alimentary tract, eliminating digestive waste from the body
   4. Mastication—chewing movements
      a. Reduces size of food particles
      b. Mixes food with saliva in preparation for swallowing
   5. Deglutition—process of swallowing; complex process requiring coordinated and rapid movements (Figure 29-2)
      a. Oral stage (mouth to oropharynx)—voluntarily controlled; formation of a food bolus in the middle of

the tongue; tongue presses bolus against the palate and food is then moved into the oropharynx
b. Pharyngeal stage (oropharynx to esophagus)—involuntary movement; to propel bolus from the pharynx to the esophagus, the mouth, nasopharynx, and larynx must be blocked; a combination of contractions and gravity move bolus into esophagus
c. Esophageal stage (esophagus to stomach)—involuntary movement; contractions and gravity move bolus through esophagus and into stomach

6. Peristalsis and segmentation—two main types of motility produced by the smooth muscle of the GI tract; can occur together, in an alternating fashion
a. Peristalsis—wavelike ripple of the muscle layer of a hollow organ; progressive motility that produces forward movement of matter along the GI tract (Figures 29-3 and 29-4)
b. Segmentation—mixing movement; digestive reflexes cause a forward-and-backward movement with a single segment of the GI tract; helps break down food particles, mixes food and digestive juices, and brings digested food in contact with intestinal mucosa to facilitate absorption (Figure 29-5)

7. Regulation of motility
a. Gastric motility
(1) Food in the stomach is churned (propulsion and retropulsion) and mixed with gastric juices to form chyme
(2) Chyme is ejected about every 20 seconds into the duodenum; emptying the stomach takes approximately 2 to 6 hours
b. Gastric emptying controlled by hormonal and nervous mechanisms (Figure 29-6)
(1) Hormonal mechanism—fats in duodenum stimulate the release of gastric inhibitory peptide, which acts to decrease peristalsis of gastric muscle and slows passage of chyme into duodenum
(2) Nervous mechanism—enterogastric reflex; receptors in the duodenal mucosa are sensitive to presence of acid and to distention; impulses over sensory and motor fibers in the vagus nerve cause a reflex inhibition of gastric peristalsis

8. Intestinal motility—includes peristalsis and segmentation
a. Segmentation in duodenum and upper jejunum mixes chyme with digestive juices from the pancreas, liver, and intestinal mucosa
b. Peristalsis rate picks up as chyme approaches end of jejunum, moving it through small intestine into the large intestine
c. After leaving stomach, passage of chyme all the way through the small intestine takes approximately 5 hours
d. Peristalsis regulated in part by intrinsic stretch reflexes; stimulated by cholecystokinin (CCK)

B. Chemical digestion—all changes in chemical composition of food as it travels through the digestive tract

1. Chemical changes result from hydrolysis—process in which compound unites with water and breaks down further
2. Digestive enzymes—extracellular, organic (protein) catalysts
a. Operate in lumen of digestive tract, outside of any body cells
b. Properties of digestive enzymes
(1) Specific in their action (Figure 29-7)
(2) Function optimally at a specific pH (Figure 29-8)
(3) Most enzymes catalyze a chemical reaction in both directions
(4) Enzymes are continually being destroyed or eliminated from the body and must continually be synthesized
(5) Most digestive enzymes are synthesized as inactive proenzymes

3. Carbohydrate digestion (Figure 29-9)
a. Carbohydrates are saccharide compounds
b. Polysaccharides are hydrolyzed by amylases to form disaccharides
c. Final steps of carbohydrate digestion are catalyzed by sucrase, lactase, and maltase, found in the cell membrane of epithelial cells covering the villi that line the intestinal lumen

4. Protein digestion (Figure 29-10)
a. Protein compounds are made up of twisted chains of amino acids
b. Proteases catalyze hydrolysis of proteins into intermediate compounds and, finally, into amino acids
c. Main proteases: pepsin in gastric juice, trypsin in pancreatic juice, peptidases in intestinal brush border

5. Fat digestion (Figure 29-12)
a. Fats must be emulsified by bile in small intestine before being digested (Figure 29-11)
b. Pancreatic lipase is the main fat-digesting enzyme

6. Residues of digestion—some compounds of food resist digestion and are eliminated as feces

SECRETION

A. Saliva—secreted by salivary glands
1. Mucus lubricates food and, with water, facilitates mixing
2. Amylase—an enzyme that begins digestion of starches
a. A small amount of salivary lipase is released; function uncertain
b. Sodium bicarbonate increases the pH for optimum amylase function

B. Gastric juice—secreted by gastric glands
1. Pepsin (secreted as inactive pepsinogen by chief cells)—a protease that begins the digestion of proteins
2. Hydrochloric acid (HCl, secreted by parietal cells)
a. HCl decreases the pH of chyme for activation and optimum function of pepsin (Figure 29-13)
b. Released actively into the gastric juice by H-K pumps (proton pumps)
c. Vesicles in the resting parietal cell move to the apical surface when the cell becomes active—thus increasing

the surface area for the process of secretion (Figure 29-14)
3. Intrinsic factor (secreted by parietal cells) protects vitamin B_{12} and later facilitates its absorption (Figure 29-15)
4. Mucus and water lubricate, protect, and facilitate mixing of chyme (Table 29-4)

C. Pancreatic juice—secreted by acinar and duct cells of the pancreas
1. Proteases (e.g., trypsin and chymotrypsin)—enzymes that digest proteins and polypeptides
2. Lipases—enzymes that digest emulsified fats
3. Nucleases—enzymes that digest nucleic acids such as DNA and RNA
4. Amylase—an enzyme that digests starches
5. Sodium bicarbonate increases the pH for optimum enzyme function; its manufacture also helps restore normal pH of blood (Figures 29-16 and 29-17)

D. Bile—secreted by the liver; stored and concentrated in the gallbladder
1. Lecithin and bile salts emulsify fats by encasing them in shells to form tiny spheres called *micelles*
2. Sodium bicarbonate increases pH for optimum enzyme function
3. Cholesterol, products of detoxification, and bile pigments (e.g., bilirubin) are waste products excreted by the liver and eventually eliminated in the feces

E. Intestinal juice—secreted by cells of intestinal exocrine cells
1. Mucus and water lubricate and aid in continued mixing of chyme
2. Sodium bicarbonate increases pH for optimum enzyme function

CONTROL OF DIGESTIVE GLAND SECRETION

A. Salivary secretion
1. Only reflex mechanisms control the secretion of saliva
2. Chemical and mechanical stimuli come from the presence of food in the mouth
3. Olfactory and visual stimuli come from the smell and sight of food

B. Gastric secretion—three phases (Figure 29-18)
1. Cephalic phase—"psychic phase," because mental factors activate the mechanism; parasympathetic fibers in branches of the vagus nerve conduct stimulating efferent impulses to the glands; stimulate production of gastrin (by G cells in the stomach)
2. Gastric phase—when products of protein digestion reach the pyloric portion of the stomach, they stimulate release of gastrin; gastrin accelerates secretion of gastric juice, ensuring enough enzymes are present to digest food
3. Intestinal phase—various mechanisms seem to adjust gastric secretion as chyme passes to and through the intestinal tract; endocrine reflexes involving gastric inhibitory peptide, secretin, and CCK inhibit gastric secretions

C. Pancreatic secretion—stimulated by several hormones released by intestinal mucosa
1. Secretin evokes production of pancreatic fluid low in enzyme content but high in bicarbonate
2. CCK—several functions
   a. Causes increased exocrine secretion from the pancreas
   b. Opposes gastrin, thus inhibiting gastric HCl secretion
   c. Stimulates contraction of the gallbladder so that bile is ejected into the duodenum

D. Bile secretion—bile secreted continually by the liver; secretin and CCK stimulate ejection of bile from the gallbladder

E. Intestinal secretion—little known about how intestinal secretion is regulated; suggested that the intestinal mucosa is stimulated to release hormones that increase the production of intestinal juice

ABSORPTION

A. Process of absorption
1. Passage of substances through the intestinal mucosa into the blood or lymph (Figure 29-19)
2. Most absorption occurs in the small intestine

B. Mechanisms of absorption
1. For some substances such as water, absorption occurs by simple diffusion or osmosis
2. Other substances are absorbed through more complex mechanisms (Figures 29-20 and 29-21)
   a. Secondary active transport—how sodium is transported
   b. Sodium cotransport (coupled transport)—how glucose and amino acids are transported
   c. Fatty acids, monoglycerides, and cholesterol are transported with the aid of bile salts from the lumen to absorbing cells of the villi
3. Transcellular absorption moves nutrient particle *through* cells (as described above) and paracellular absorption moves particles *between* cells
4. After food is absorbed, it travels to the liver via the portal system
5. In summary, most absorption occurs in the small intestine (Figure 29-22)

ELIMINATION

A. Definition—expulsion of feces from the digestive tract; referred to as *defecation*

B. Defecation—results from a reflex brought about by stimulation of receptors in the rectal mucosa that is produced when the rectum is distended (Figure 29-23)

C. Constipation—contents of the lower part of the colon and rectum move at a slower than normal rate; extra water is absorbed from the feces, resulting in a hardened stool

D. Diarrhea—result of increased motility of the small intestine, causing decreased absorption of water and electrolytes and a watery stool

THE BIG PICTURE: DIGESTION AND THE WHOLE BODY

A. Primary contribution of the digestive system to overall homeostasis is to provide a constant nutrient concentration in the internal environment
B. Secondary roles of digestive system
   1. Absorption of nutrients
   2. Teeth and tongue, along with respiratory and nervous system, are important in producing spoken language
   3. Gastric acids aid the immune system by destroying potentially harmful bacteria
C. To accomplish its functions, digestive system needs other systems to contribute
   1. Regulation of digestive motility and secretion requires the nervous system and endocrine system
   2. Oxygen for digestive activity is dependent on proper functioning of the respiratory and circulatory systems
   3. Integumentary and skeletal systems support and protect the digestive organs
   4. Muscular system is needed for ingestion, mastication, deglutition, and defecation to occur normally

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. List four of the mechanical processes that occur during digestion.
2. List the three steps, or stages, in deglutition.
3. Discuss the function of the deglutition center in the medulla.
4. How does gastric inhibitory peptide influence emptying of the stomach? What is the enterogastric reflex?
5. Discuss the functional roles of gastric juice.
6. What is chyme?
7. Describe the classification of digestive enzymes.
8. Discuss three important properties of digestive enzymes.
9. What substances chemically digest proteins? Carbohydrates? Fats?
10. What is meant by the term *cephalic phase* of gastric secretion? *Gastric phase? Intestinal phase?*
11. What digestive functions does the pancreas perform?
12. Describe the absorption of glucose from the lumen of the small intestine.
13. What vitamins depend on bile salts for their absorption?
14. Name each hormone that controls ejection of bile, stimulation of gastric enzymes, inhibition of gastric emptying, secretion of alkaline fluid from pancreas, and secretion of pancreatic enzymes.
15. Discuss responses that collectively result in defecation.
16. Describe the treatment called *oral rehydration therapy.*

CRITICAL THINKING QUESTIONS

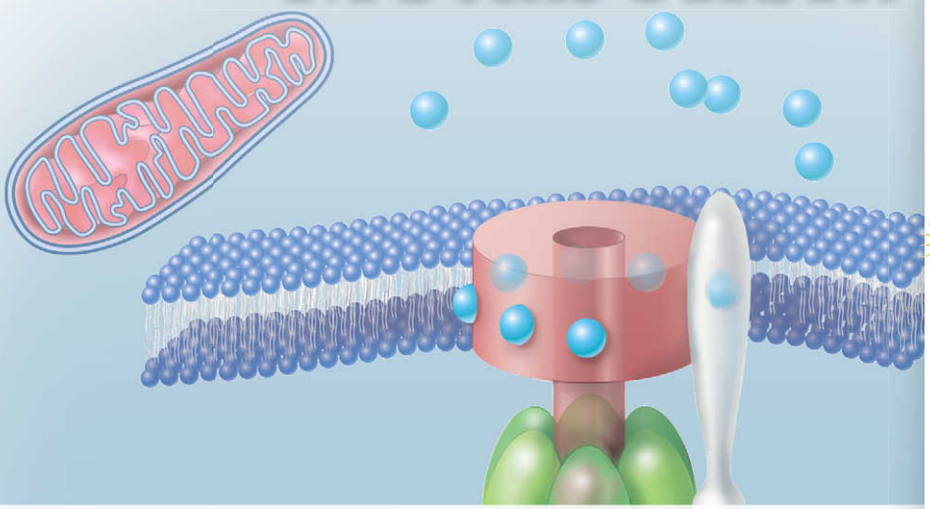


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. In terms of homeostatic balance in the body, what is the function of the digestive system?
2. Explain the two types of processes within the digestive system.
3. Describe the two types of motility within the intestine.
4. What distinction is there between trypsin and pepsin, protein and peptides, and polysaccharides and monosaccharides? Explain how one pair is different from the other two.
5. What is the relationship between hydrochloric acid production by the stomach and bicarbonate production by the pancreas?
6. Because fats are not soluble in water, what process is used by the digestive system to emulsify fats?
7. How is emulsification an example of mechanical digestion rather than chemical digestion?
8. Compare and contrast carbohydrate and protein absorption with fat absorption. Include an explanation of basal active transport.

Nutrition and Metabolism

30



CHAPTER OUTLINE

HINT *Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.*

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  - Glucose Transport and Phosphorylation, 935
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Cycle of Life: Nutrition and Metabolism, 960

The Big Picture: Nutrition, Metabolism, and the Whole Body, 960

Mechanisms of Disease, 961

Case Study, 965

LANGUAGE OF SCIENCE

HINT *Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.*

aerobic respiration
(air-OH-bik res-pi-RAY-shun)
[*aero-* **air,** *-b-* **(from** *-bio-***) life,** *-ic* **relating to,** *re-* **again,** *-spir-* **breathe,** *-tion* **process**]

amino acid
(ah-MEE-no)
[*amino* **NH_2,** *acid* **sour**]

anabolism
(ah-NAB-oh-liz-em)
[*anabol-* **build up,** *-ism* **action**]

anaerobic pathway
(an-air-OH-bik)
[*an-* **without,** *-aero-* **air,** *-b-* **(from** *-bio-***) life,** *-ic* **relating to**]

anorexigenic effect
(an-oh-rek-sih-JEN-ik)
[*an-* **without,** *-orex-* **appetite,** *-gen-* **produce,** *-ic* **relating to**]

antioxidant
(an-tee-OK-seh-dent)
[*anti-* **against,** *-oxi-* **sharp (oxygen),** *-ant* **agent**]

appetite center

assimilation
(ah-sim-i-LAY-shun)
[*assimila-* **make alike,** *-tion* **process**]

ATP synthase
(SIN-thays)
[*ATP* **adenosine triphosphate,** *syn-* **together,** *-ase* **enzyme**]

basal metabolic rate (BMR)
(BAY-sal met-ah-BAHL-ik)
[*bas-* **basis,** *-al* **relating to,** *metabol-* **change,** *-ic* **relating to**]

calcitriol
(kal-SIT-ree-ol)
[*calci-* **lime (calcium),** *-tri-* **three,** *-ol* **alcohol (after** *1,25-D_3* **or** *1,25-dihydroxycholecalciferol***)**]

continued on p. 964

The previous chapter (Chapter 29) explains the processes of getting nutrients into the internal environment. This chapter takes the story further by discussing how the body manages the nutrients after they are absorbed—how they are stored and how they are used by the cells of the body. Before beginning this chapter, you may want to review the story of metabolism summarized in Chapters 4 and 5, beginning on p. 102.

OVERVIEW OF NUTRITION AND METABOLISM

Nutrition and *metabolism* are words that are often used together—but what do they mean? **Nutrition** refers to the foods that we eat and the nutrients they contain. The Council on Food and Nutrition of the American Medical Association defines nutrition broadly as "the science of food; the nutrients and the substances therein; their action, interaction, and balance in relation to health and disease; and the process by which the organism (i.e., body) ingests, digests, absorbs, transports, utilizes, and excretes food substances."

Healthy nutrition requires a balance of different nutrients in healthy amounts. *Malnutrition* is a deficiency or imbalance in the consumption of food, vitamins, and minerals. As a matter of convenient communication, many nutrition experts divide the essential (required) nutrients into two major categories:

1. **Macronutrients**—usually include those nutrients that we need in large amounts, such as carbohydrates, fats, and proteins. Sometimes water is included because we need to ingest a large amount of water each day to remain healthy. Minerals that we need in large quantities to remain in good health are also often included among the macronutrients. For example, sodium, chloride, potassium, calcium, magnesium, and phosphorus are often considered to be macronutrients. This group of minerals can also be more specifically called *macrominerals*. Macronutrients are also sometimes called *bulk nutrients* because we need them in bulk quantities to survive.
2. **Micronutrients**—usually include nutrients that we need in very small amounts, such as vitamins and some minerals. Minerals in this group include iron, iodine, zinc, manganese, cobalt, and a few others. Mineral micronutrients can also be called *microminerals* or *trace elements*.

We have already stated that healthy nutrition requires a balance of nutrients in the proper amounts. What do we mean by "proper balance" of nutrients? That is a puzzle that scientists continue to work on unraveling. The answer to the puzzle will certainly be complicated because we now know that a complex interaction of slight differences in individual genetic codes and individual lifestyles and environments affect how nutrients affect our bodies. Until this puzzle is completely solved, if it ever is, we fortunately have some advice that we can rely on to help us make healthy choices. For example, the United States government makes use of an individually customized food plate as a general nutrition guide (Figure 30-1). The Canadian government uses a food rainbow to advise eating a healthy, balanced diet (Figure 30-2).

As we proceed through this chapter, we will discuss most of the major nutrients in more detail and their roles in maintaining the body.

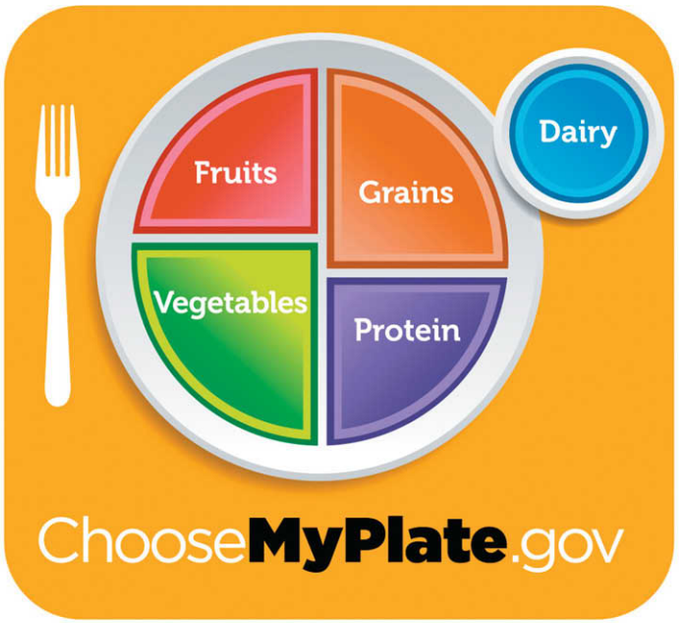


FIGURE 30-1

United States Food Guide Plate. Simple diagrams such as "My Plate" help educate the public on building a diet with a balance of foods from different categories illustrated in the diagram. This is an abbreviated version of the comprehensive food guide that can be found at ChooseMyPlate.gov. The full version includes detailed nutrition advice.

Metabolism refers to the complex, interactive set of chemical processes that make life possible. A good phrase to remember in connection with the word metabolism is "use of foods" because basically this is what metabolism is—the use the body makes of foods after they have been digested, absorbed, and circulated to cells.

Your body cells use nutrients from food in several ways: as fuel (energy), as material for growth and maintenance, and for regulation of body functions. Before they can be used in these different ways, nutrients have to be assimilated. **Assimilation** occurs when nutrient molecules enter cells and undergo many chemical changes.

Metabolism is a complex process made up of many other processes. Two of the major metabolic processes are **catabolism** and **anabolism.** Each of these processes, in turn, consists of a series of enzyme-catalyzed chemical reactions known as *metabolic pathways.*

Catabolism breaks food molecules down into smaller molecular compounds and, in so doing, releases energy from them. Anabolism does the opposite. It builds nutrient molecules up into larger molecular compounds and, in so doing, uses energy. Catabolism is a decomposition process. Anabolism is a synthesis

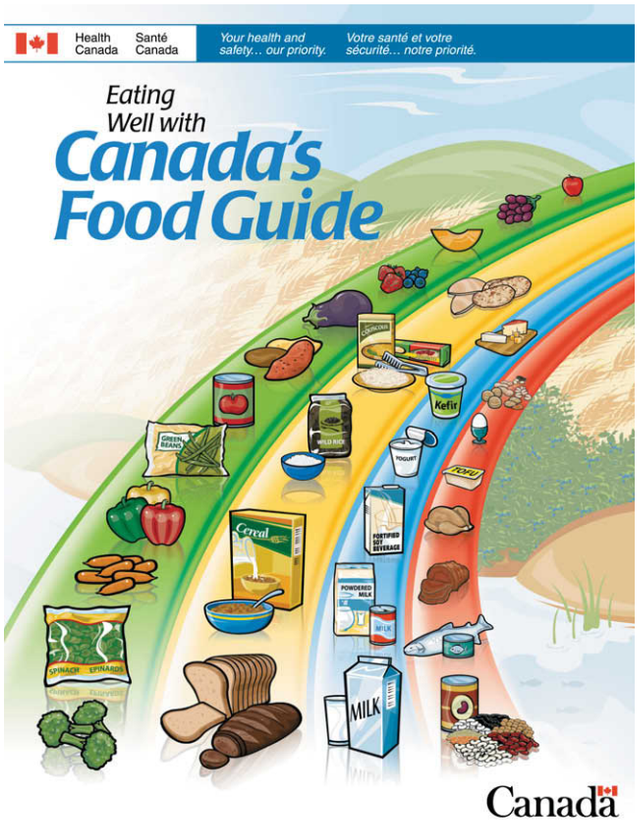


FIGURE 30-2

Canadian Food Rainbow. This is an abbreviated version of the comprehensive food guide found at hc-sc.gc.ca/fn-an/food-guide-aliment/index-eng.php. The full version includes additional nutrition advice.

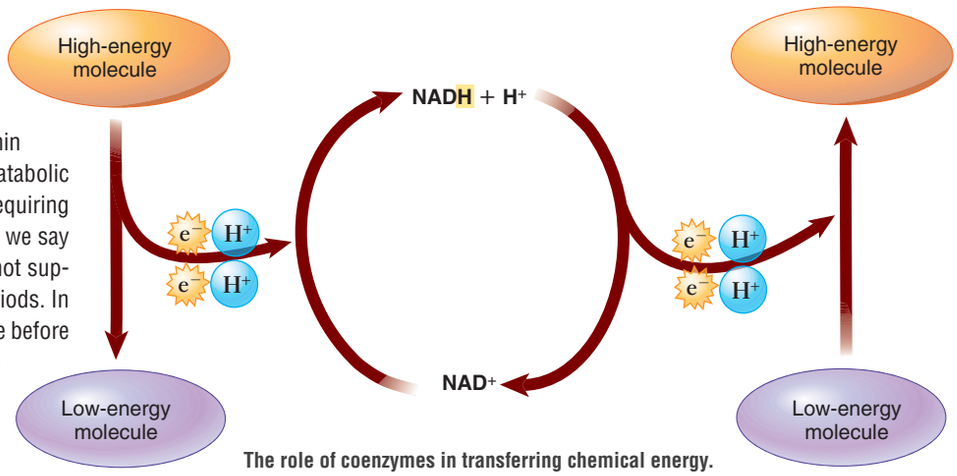
process. Both catabolism and anabolism take place inside cells. Both processes go on continually and concurrently.

Catabolism releases energy in two forms: heat and chemical energy. The amount of heat generated is relatively large—so large, in fact, that it would hard-boil cells if it were released in one large burst. Fortunately, this does not happen. Catabolism releases heat in frequent, small bursts. Heat is practically useless as an energy source for cells because they cannot use it to do their work. However, this heat is important in maintaining the homeostasis of body temperature. In contrast, chemical energy released by catabolism is more obviously useful. It cannot, however, be used directly for biological reactions. First, it must be transferred to the high-energy molecule of adenosine triphosphate (ATP) (Box 30-1).

ATP is one of the most important compounds in the world. Why? It supplies energy directly to the energy-using reactions of all cells in all kinds of living organisms, from one-celled plants to trillion-celled humans. ATP functions as the universal biological

Box 30-1 | Transferring Chemical Energy

The ability to transfer energy from molecule to molecule is, as you might imagine, essential to life. We have already discussed the critical role played by the nucleotide adenosine triphosphate (ATP) in transferring energy within living cells. ATP can accept energy from catabolic reactions and transfer that energy to energy-requiring anabolic reactions (see Figure 30-3). Although we say that ATP is an "energy storage molecule," do not suppose that the energy is stored for very long periods. In fact, an ATP molecule exists for only a brief time before its last phosphate group is broken off and its energy is transferred to another molecule in some metabolic pathway. Long-term storage of energy can be accomplished only by nutrient molecules such as glucose, glycogen, and triglycerides.



The role of coenzymes in transferring chemical energy.

In addition to ATP, various other energy transfer molecules are essential to human life. When atoms in a molecule absorb energy, some of their electrons may move outward to a higher energy level (shell). Electrons often become so energized that they leave the atom completely. As this occurs, pairs of "high-energy" electrons can be picked up and transferred to another molecule by an electron carrier such as **flavin adenine dinucleotide (FAD)** or **nicotinamide adenine dinucleotide (NAD).** The figure shows how NAD^+ (oxidized NAD) picks up a pair of energized electrons to become NADH. It should be noted here that electrons always travel with a proton (H^+) in the metabolic pathways described in this chapter. The electrons do not stay with the electron carrier for long, however. They are immediately transferred to molecules in another metabolic pathway, as the figure shows. In the cell, pairs of electrons (and their energy) can thus be transferred from pathway to pathway by NAD and FAD.

NAD and FAD, though very similar in function, do have their differences. One difference is that after NAD drops off its pair of high-energy electrons, three ATP molecules are generated and when FAD drops off its pair of electrons, only two ATP molecules are generated.

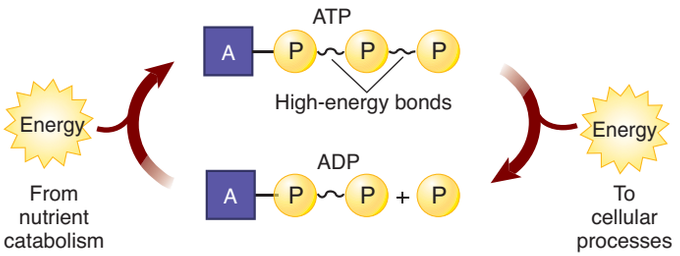


FIGURE 30-3

The role of ATP in metabolism. Adenosine triphosphate (ATP) temporarily stores energy in its last high-energy phosphate bond. When water is added and phosphate breaks free, energy is released to do cellular work. The adenosine diphosphate (ADP) and phosphate groups that result can be resynthesized into ATP, capturing additional energy from nutrient catabolism. This cycle is called the *ATP/ADP system.*

currency. It pays the energy bills for all cells and is as important in the world of cells as money is in the world of contemporary society.

Look now at Figure 30-3. The structural formula at the top of the diagram shows three phosphate groups attached to the rest of the ATP molecule, two of them by high-energy bonds. Adding water to ATP yields a phosphate group (P), adenosine diphosphate (ADP), and energy, which, as the diagram indicates, is used for anabolism and other cell work. The diagram also shows that P and ADP then use energy released by catabolism to recombine and form ATP. This cycle is called the *ATP/ADP system.*

Metabolism is not identical in all cells. It differs mainly with regard to rate and the kind of products synthesized by anabolism. More active cells have a higher metabolic rate than do less active cells. Anabolism in different kinds of cells produces different compounds. In liver cells, for example, anabolism synthesizes various blood protein compounds. Not so in beta cells of the pancreas. Anabolism there produces a different compound—insulin.

The bulk of this chapter discusses concepts related to the many and varied metabolic pathways of the human body. Our attempt here is to build on what you learned in previous chapters, but not to cover the subject of metabolism in its entirety—if that is even possible. Our goal, therefore, is to underscore the *basic* concepts of nutrition and metabolism. It is important to note that our discussion, as well as the diagrams that accompany the discussion, have been simplified to facilitate understanding of these basic concepts.

CARBOHYDRATES

Dietary Sources of Carbohydrates

Carbohydrates are found in most of the foods that we eat. *Complex carbohydrates*—polysaccharides such as starches in vegetables, grains, and other plant tissues—are broken down into simpler carbohydrates before they are absorbed.

Cellulose, a major component of most plant tissues, is an important exception to this principle. Because humans do not

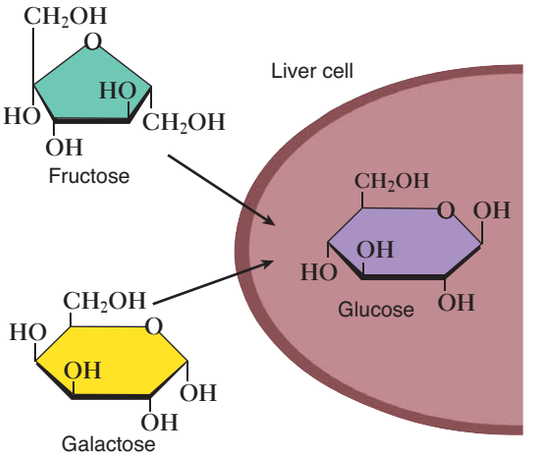


FIGURE 30-4

Conversion of monosaccharides. Monosaccharides fructose and galactose are usually converted to glucose by liver cells. Although simplified in this diagram, conversion to glucose requires several steps. Glucose is the carbohydrate used universally by all cells in the body.

make enzymes that chemically digest this complex carbohydrate, it passes through our system without being broken down. Also called *dietary fiber* or "roughage," cellulose and other indigestible polysaccharides keep chyme thick enough for the digestive system to push it easily. They also help mix chyme, much like the ball inside a can of spray paint. Most biologists believe that a high-fiber diet reduces the risk of many forms of cancer, including colorectal cancer.

Disaccharides such as those in refined sugar must also be chemically digested before they can be absorbed. Monosaccharides in fruits and some "diet foods" are already in an absorbable form, so they can move directly into the internal environment without initially being processed. The monosaccharide *glucose* is the carbohydrate that is most useful to the typical human cell. As Figure 30-4 shows, other important monosaccharides, *fructose* and *galactose*, are usually converted by liver cells into glucose for use by other cells of the body.

| QUICK CHECK |

1. Name the two types of metabolism and distinguish between them.
2. Why must energy in nutrient molecules be transferred to ATP?

Carbohydrate Metabolism

The body metabolizes carbohydrates by both catabolic and anabolic processes. Because many human cells use carbohydrates—mainly glucose—as their first or preferred energy fuel, they catabolize most of the carbohydrate absorbed and anabolize a

relatively small portion of it. When the amount of glucose entering cells is inadequate for their energy needs, they may make more use of an alternative pathway and catabolize fats or proteins.

We first discussed carbohydrate metabolism in Chapter 4 when we discussed basic concepts of cell metabolism (see pp. 102–104). The subject came up again in Chapter 12 when we discussed energy production in muscle tissue (see pp. 356–359). You may want to flip back to those passages and review the material before proceeding further with this chapter.

As you read through the following sections that briefly describe the process of carbohydrate metabolism, remember the ultimate result of catabolism: the transfer of energy from a nutrient molecule to ATP. It is the continued production of ATP, the energy currency of the cell, that makes nutrient catabolism so incredibly vital to the overall process of life itself.

GLUCOSE TRANSPORT AND PHOSPHORYLATION

Carbohydrate metabolism begins with the movement of glucose through cell membranes. Immediately on reaching the interior of a cell, glucose reacts with ATP to form glucose-6-phosphate. This step, named **glucose phosphorylation,** prepares glucose for further metabolic reactions. **Phosphorylation** (fos-for-i-LAY-shun) is the process of adding a phosphate group to a molecule. In most cells of the body, glucose phosphorylation is an irreversible reaction. However, in a few cells—namely, those of the intestinal mucosa, liver, and renal cortex—glucose phosphorylation is reversible. These cells contain phosphatase, an enzyme that splits phosphate off from glucose-6-phosphate. This reverse glucose phosphorylation reaction forms glucose, which then moves out of the cells into the blood. (Glucose-6-phosphate cannot pass through cell membranes.) Depending on their energy needs of the moment, cells either catabolize (break apart) or anabolize (bind together) glucose-6-phosphate.

| A&P CONNECT |

Nutritionists often talk about the "energy value" of food—that is, how much energy the body can get from that food. Do you know what it means when a label states that food energy in calories? Do you know the difference between a *calorie* and a *Calorie?* Or a calorie and a *joule* or *kilojoule?* Find answers to these questions, and also learn the energy values of major nutrients and the amount of energy expended by different physical activities in ***Measuring Energy*** online at ***A&P Connect.***

evolve

GLYCOLYSIS

Glycolysis is the first step in the process of carbohydrate catabolism. It breaks apart one glucose molecule to form two pyruvic acid molecules. (A glucose molecule contains six carbon atoms, and a pyruvic acid molecule contains three carbon atoms. See Figure 30-6.) Glycolysis consists, as Figure 30-5 shows, of a series of chemical reactions. A specific enzyme catalyzes each of these

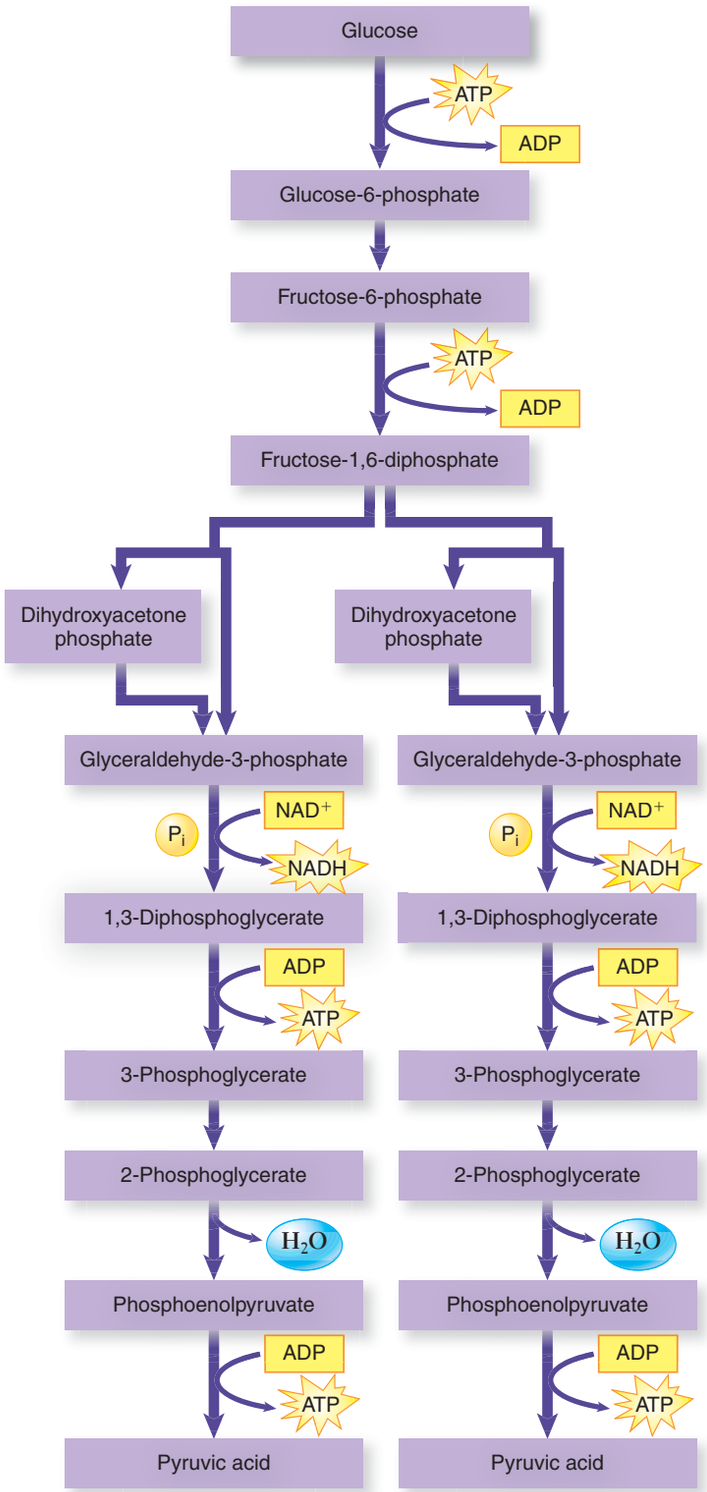


FIGURE 30-5

Glycolysis. The series of enzyme-catalyzed reactions that make up the portion of the catabolic pathway for carbohydrates is called *glycolysis. ADP,* Adenosine diphosphate; *ATP,* adenosine triphosphate; *NAD+,* oxidized nicotinamide adenine dinucleotide; *NADH,* reduced nicotinamide adenine dinucleotide.

reactions. Probably the most important facts for you to remember about glycolysis are the following:

- Glycolysis occurs in the cytoplasm of all human cells.
- Glycolysis is an *anaerobic* process, that is, it does not use oxygen. It is the only process that provides cells with energy when their oxygen supply is inadequate or even absent.
- Glycolysis breaks the chemical bonds in glucose molecules and thereby releases about 5% of the energy stored in them. Much of the released energy appears as heat, but some of it is transferred to the high-energy bonds of ATP molecules. For every molecule of glucose undergoing glycolysis, a net of two molecules of ATP is formed. About 8 kilocalories (kcal) of energy (under normal physiological conditions) is stored in the high-energy bonds that bind phosphate to ADP to form 1 mole (6.02 × 1023 molecules) of ATP.
- Glycolysis is an essential process because it prepares glucose for the second step in catabolism, namely, the **citric acid cycle.** Glucose itself cannot enter the cycle but must first be converted to pyruvic acid, then to a compound called *acetyl CoA (coenzyme A).*

CITRIC ACID CYCLE

As stated previously, for every glucose molecule that enters the catabolic pathway described here, two pyruvic acid molecules are produced. Before each pyruvic acid molecule can proceed into the citric acid cycle, it must be converted into an acetyl group (acetate), releasing a carbon dioxide molecule and being carried into the citric acid cycle by **coenzyme A (CoA).** Essentially, the citric acid cycle converts the two acetyl molecules to four carbon dioxide and six water molecules. But many chemical reactions intervene. Figure 30-6 shows that one glucose molecule is changed by glycolysis to two pyruvic acid molecules, which, by means of the citric acid cycle, yield six carbon dioxide molecules. Figure 30-7 shows the details of the citric acid cycle.

Glycolysis takes place in the cytoplasm of cells, whereas the citric acid cycle occurs in their mitochondria. Some of the enzymes needed for the many steps of the citric acid cycle are dissolved in the matrix of the mitochondrion, and some are attached to the inner membrane of the mitochondrion.

Before it can enter the citric acid cycle, each pyruvic acid molecule combines with coenzyme A (see Figure 30-7) after splitting off CO_2 and a pair of high-energy electrons (with their accompanying protons, H^+) from pyruvic acid, thus forming acetyl CoA. Coenzyme A then detaches from acetyl CoA, leaving a two-carbon acetyl group, which enters the citric acid cycle by combining with

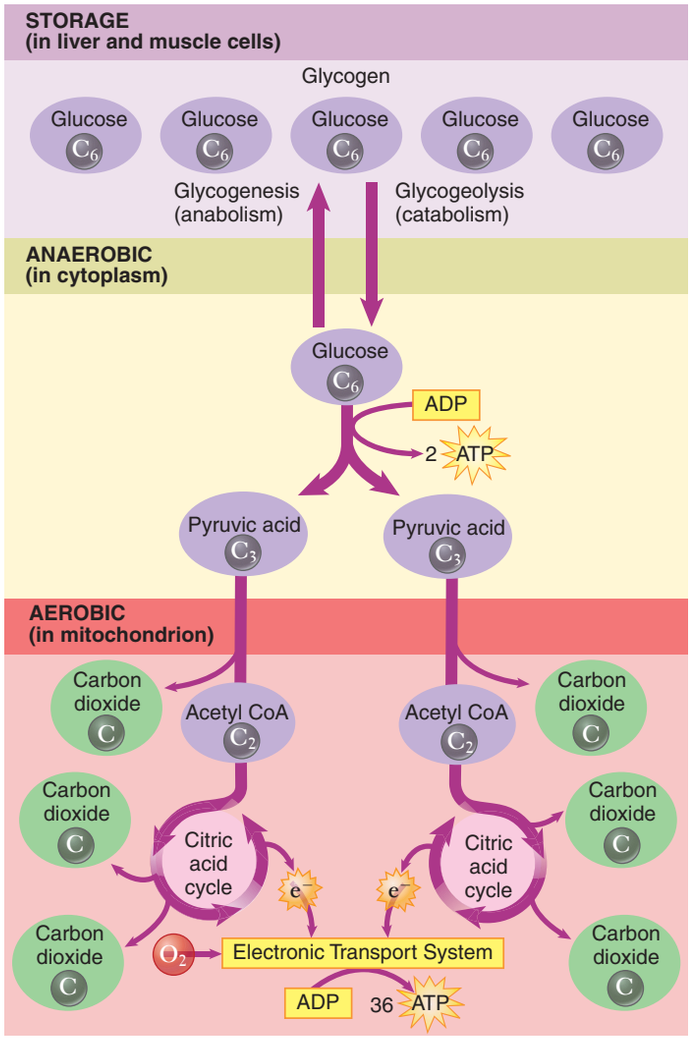


FIGURE 30-6

Catabolism of glucose. Glucose may be stored in the liver and other tissues as the polymer glycogen, which can then later be hydrolyzed to form individual glucose molecules. Glycolysis splits one molecule of glucose (six carbon atoms) into two molecules of pyruvic acid (three carbon atoms each). The glycolytic pathway does not require oxygen, so it is termed *anaerobic.* A transition reaction removes a carbon dioxide molecule, converting each pyruvic acid molecule into a two-carbon acetyl group that is escorted by coenzyme A (CoA) into the citric acid cycle. There, two more carbon dioxide molecules (one carbon atom each) are released. The carbon and oxygen atoms in the original glucose molecule are thus released as waste products. However, the real metabolic prize is energy, which is released as the molecule is broken down. Because this part of the pathway requires oxygen, it is termed *aerobic.* More detailed depictions of this process are included later in this chapter.

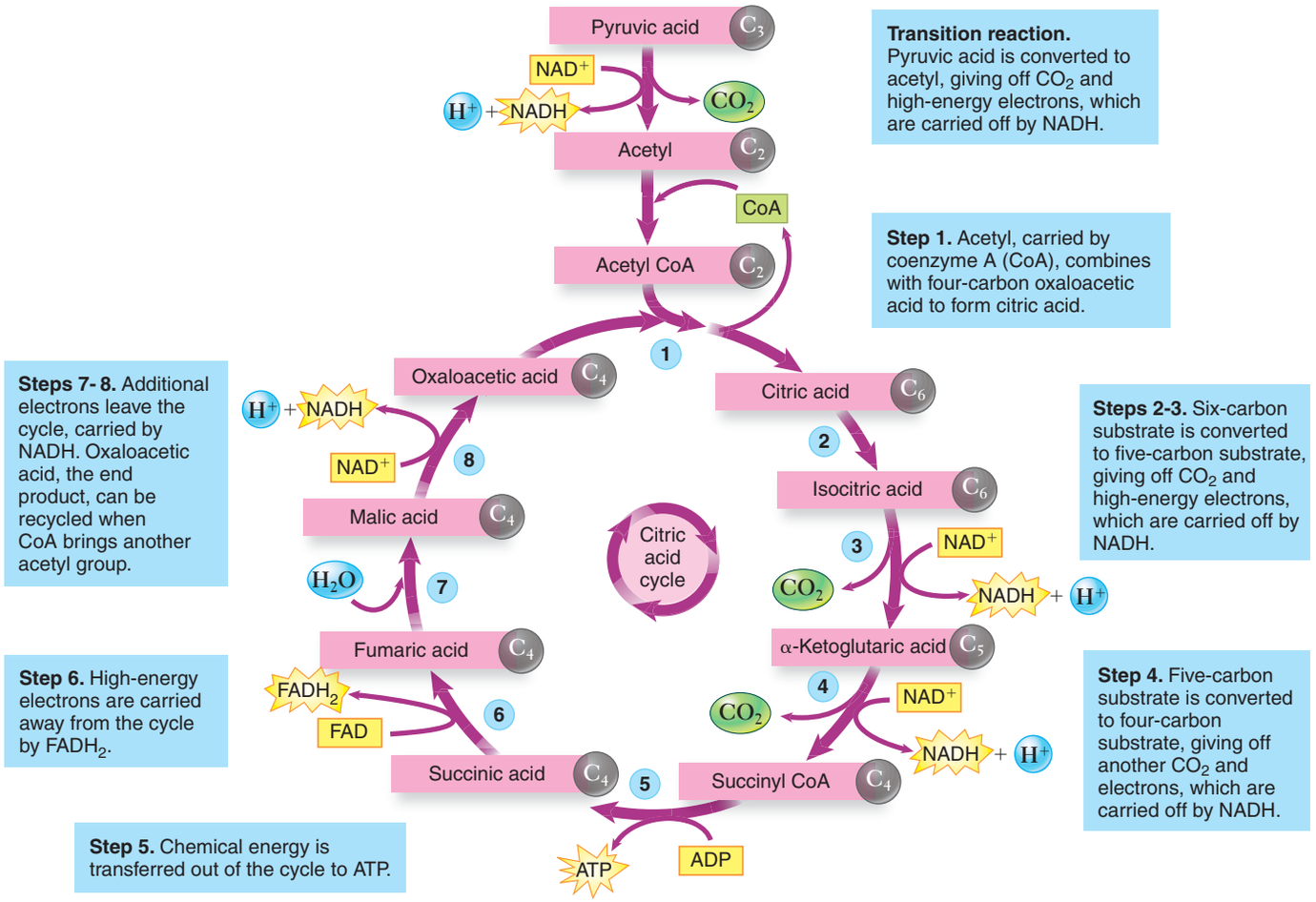


FIGURE 30-7

Citric acid cycle. Each pyruvic acid molecule is prepared to enter the citric acid cycle by the transition reaction, which yields a pair of high-energy electrons and a CO_2 molecule. The acetyl group that is thus formed is picked up by coenzyme A (CoA) and led into the citric acid cycle proper, which is described here as a recurring series of eight steps.

oxaloacetic acid to form citric acid. This is what gives the citric acid cycle its name. The cycle is also called the **tricarboxylic acid (TCA) cycle** because citric acid is also called *tricarboxylic acid*. For many years this cycle was called the **Krebs cycle** after Sir Hans Krebs, whose brilliant work in discovering this metabolic pathway earned him the 1953 Nobel Prize.

You probably do not need to memorize the names of the intermediate products formed during the citric acid cycle, but notice that all of them are acids. You should note that a little bit of ATP is directly generated by the citric acid cycle (in step 5). In step 5, energy is transferred first to GTP (guanosine triphosphate), a nucleotide similar to ATP, and then finally to ATP.

Observe, too, that for each pyruvic acid molecule entering this pathway, three CO_2 molecules are formed and that certain reactions yield high-energy electrons. Most of the energy leaving the citric acid cycle is in these high-energy electrons. The next section describes how these high-energy electrons are used to generate ATP.

ELECTRON TRANSPORT SYSTEM AND OXIDATIVE PHOSPHORYLATION

High-energy electrons removed during the citric acid cycle enter a chain of carrier molecules, which is embedded in the inner membrane of mitochondria and is known as the **electron transport system (ETS).** Figure 30-8 shows that high-energy electrons (along with their accompanying protons, H^+) are carried to the electron transport system by NAD and FAD. The electrons quickly move down the chain, from one membrane protein complex to the next, eventually to their final acceptor, oxygen.

As the electrons are transported, some of their energy is used to pump their accompanying protons (H^+) to the intramembrane

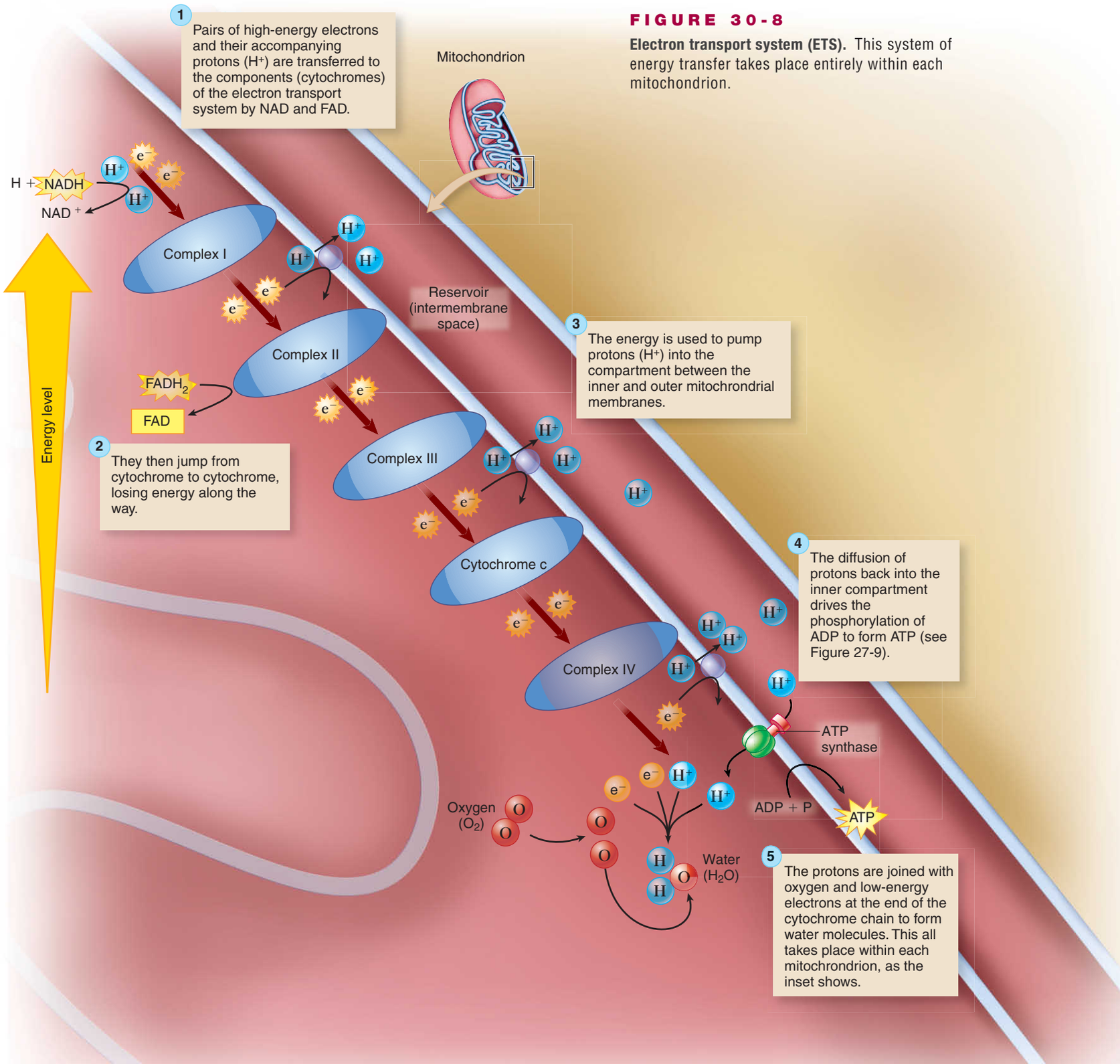


FIGURE 30-8

Electron transport system (ETS). This system of energy transfer takes place entirely within each mitochondrion.

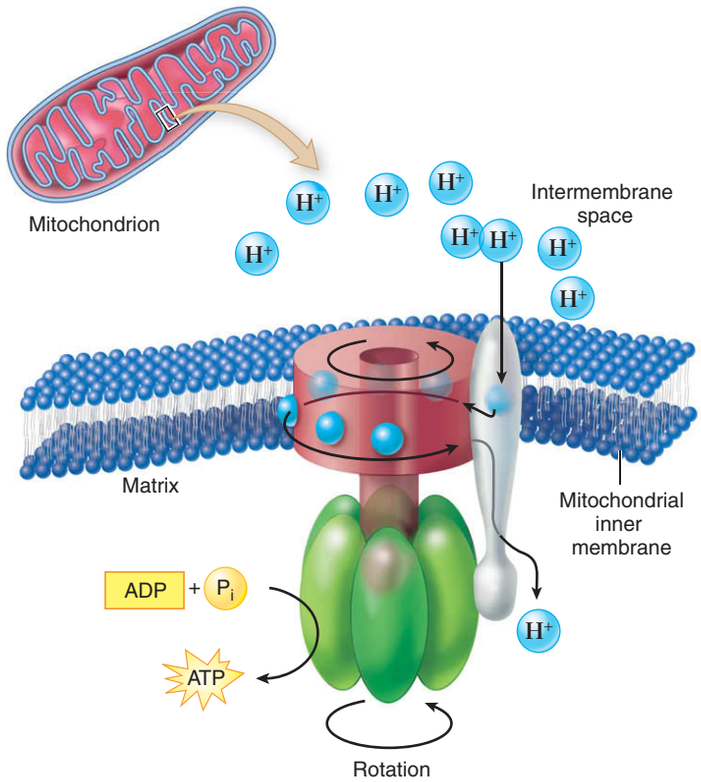


FIGURE 30-9

Generation of ATP by ATP synthase. This simplified model of the proton wheel in the mitochondrial inner membrane shows how protons (H^+) moving down their concentration gradient drive the rotation of a molecular machine. The energy of rotation then phosphorylates (adds phosphate to) adenosine diphosphate (ADP) to become adenosine triphosphate (ATP).

space between the inner and outer membranes of the mitochondrion. This creates a concentration gradient of protons, and the intermembrane space thus becomes a virtual reservoir of protons. As with water behind a dam, the reservoir of protons temporarily stores energy. As in a dam possessing water wheels that convert energy, the inner membrane has "proton wheels" built into it—in the form of **ATP synthase.** Figure 30-9 shows how protons move down their concentration gradient and into the ATP synthase structure, turning a molecular wheel that transfers energy by synthesizing ATP from ADP and phosphate.

At this time, the low-energy electrons (e^-) and their protons (H^+) join oxygen, forming water. As you can see, although oxygen is not needed until the very last step of aerobic respiration, its role is vital. Without oxygen to oxidize the hydrogen into water, the energy generation pathway would stop.

Oxidative phosphorylation refers to this oxygen-requiring joining of a phosphate group to ADP to form ATP—a reaction whose importance can scarcely be overemphasized.

The arrangement of catabolic "machinery" within the cell, as currently viewed, is shown in Figure 30-10. Glycolytic enzymes in the cytoplasm catalyze the production of pyruvic acid, which diffuses into mitochondria. The enzymes of the citric acid cycle have been localized mostly to the matter (matrix) inside the inner mitochondrial membrane. The high-energy electrons and their accompanying protons are then carried to the cristae of the inner membrane, where the electron transport carriers and mechanism for phosphorylation are found. Because so many of the cell's energy-releasing enzymes are located within the mitochondria, these tiny structures are aptly described as the "power plants" of the cell.

The breakdown of ATP molecules, of course, provides virtually all the energy that does cellular work. Therefore, the process that produces some 90% of the ATP formed during carbohydrate

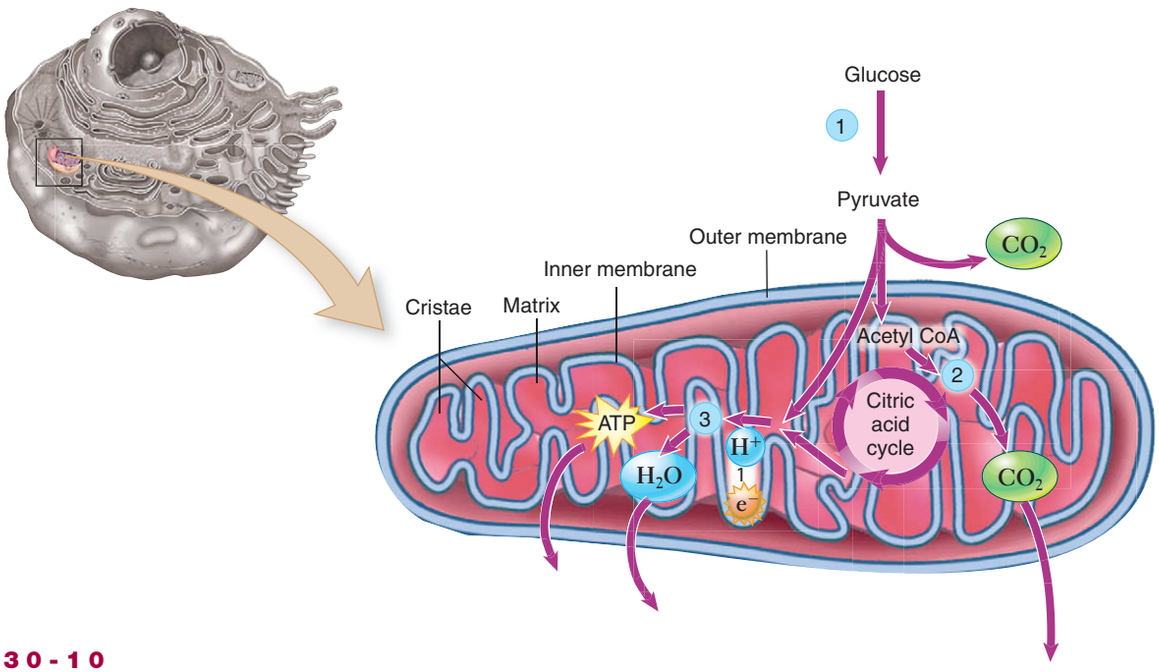


FIGURE 30-10

Cell machinery for glucose catabolism. 1, Glycolysis occurs in cytoplasm. **2,** Citric acid cycle takes place mostly in the mitochondrial matrix. **3,** Electron transport and oxidative phosphorylation occur on the inner membrane of mitochondria.

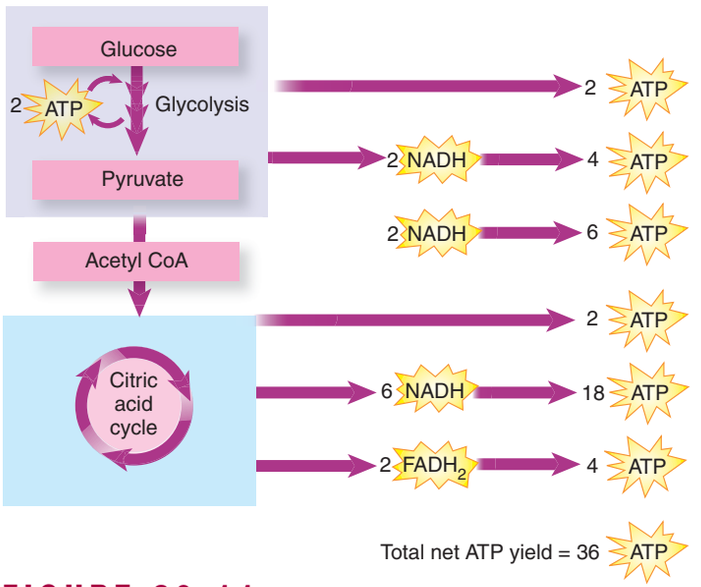


FIGURE 30-11

Energy extracted from glucose. Energy released from the breakdown of glucose is released mostly as heat, but some of it is transferred to a usable form—the high-energy bonds of adenosine triphosphate (ATP). In most human cells, one glucose molecule produces enough usable chemical energy to synthesize or "charge up" 36 ATP molecules. Some cells, such as heart and liver cells, shuttle electrons more efficiently and may be able to synthesize up to 38 ATP molecules. This represents an energy conversion efficiency of 38% to 44%, much better than the 20% to 25% typical of most machines.

catabolism, namely, oxidative phosphorylation, is the crucial part of catabolism (Figure 30-11). This vital process depends on cells receiving an adequate oxygen supply. Why? Briefly, because only when oxygen is present in cells to serve as the final acceptor of electrons and hydrogen ions can electrons then continue moving down the electron transport chain. If oxygen becomes unavailable, the movement of electrons and hydrogen ions stops. Cessation of ATP formation by oxidative phosphorylation necessarily follows. All too soon, cells have an inadequate energy supply—a lethal condition if it persists for more than a few minutes.

We can summarize the long series of chemical reactions in glucose catabolism with one short equation:

$$C_6H_{12}O_6 + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O + 36\ (\text{or } 38)\ \text{ATP} + \text{Heat}$$

| QUICK CHECK |

3. What is glycolysis? How much energy is transferred to ATP through this process?
4. What happens to a nutrient molecule as it proceeds through the citric acid cycle?
5. What is the purpose of the electron transport system?

ANAEROBIC PATHWAY

What if there is an inadequate amount of oxygen to operate the electron transport system and oxidative phosphorylation? You may recall from Chapter 12 that this often occurs in skeletal muscle cells, especially during strenuous exercise. You may remember that another pathway for the catabolism of glucose exists. It is sometimes called the **anaerobic pathway** because it transfers energy to ATP using only glycolysis—a process that does not require oxygen.

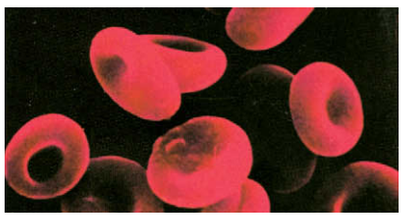
As Figure 30-12 shows, there are two main pathways that glucose or its derivatives can take. One is the pathway that ends with oxidative phosphorylation of ATP. This pathway, described in the previous sections, is called the *aerobic pathway*, or **aerobic respiration,** because it requires the presence of oxygen (Box 30-2). If enough oxygen is not available to operate this pathway, the cell will rely solely on glycolysis to produce ATP. Even though this process does not extract the maximum amount of energy from a glucose molecule, it is the only ATP-producing process that can operate under anaerobic conditions. Because the pyruvic acid molecule produced by glycolysis cannot enter the citric acid cycle, it is converted to *lactic acid* rather than acetyl CoA. Lactic acid cannot enter the citric acid cycle.

The production of lactic acid does something very important—it converts the NADH (reduced nicotinamide adenine dinucleotide) produced by glycolysis to NAD. As glycolysis proceeds, NAD is converted to NADH. If you look at Figure 30-5 carefully, you will see that there is no reaction in the glycolytic pathway to turn NADH back into NAD again. This is no problem if the aerobic pathway is in operation—NADH is converted back to NAD in the electron transport system. After a short period of anaerobic activity, however, glycolysis will turn all of the cell's NAD into NADH and thus glycolysis will have to shut down because of a lack of free NAD. The production of lactic acid solves this biochemical dilemma because this reaction also converts NADH back to NAD.

Box 30-2 | FYI

Anaerobic Body Cells

Some body cells, specifically the red blood cells (see photo), do not have the cellular organelles and enzymes required to carry out aerobic respiration. These cells must rely solely on glycolysis for their adenosine triphosphate (ATP) production. Red blood cells produce lactic acid continually, which diffuses into the plasma and is carried to liver cells for conversion back to pyruvic acid and then to glucose and glycogen (see Figure 30-12).



Red blood cells (RBCs). This color-enhanced scanning electron micrograph shows several RBCs, which are unable to perform aerobic respiration because of a lack of mitochondria. They rely solely on anaerobic glycolysis for their ATP, producing lactic acid as a metabolic waste product.

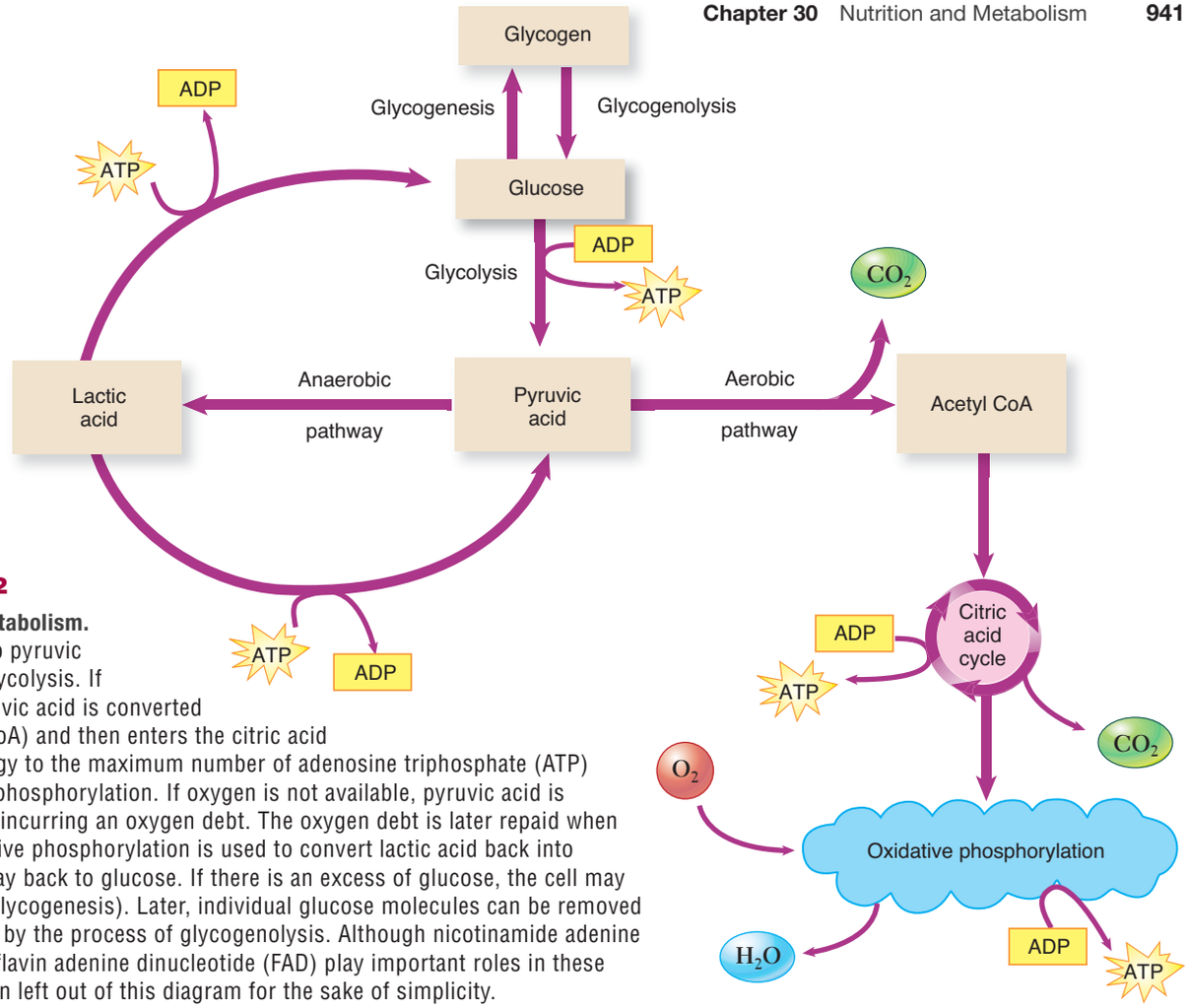


FIGURE 30-12

Summary of glucose metabolism. Glucose is catabolized to pyruvic acid in the process of glycolysis. If oxygen is available, pyruvic acid is converted to acetyl coenzyme A (CoA) and then enters the citric acid cycle and transfers energy to the maximum number of adenosine triphosphate (ATP) molecules via oxidative phosphorylation. If oxygen is not available, pyruvic acid is converted to lactic acid, incurring an oxygen debt. The oxygen debt is later repaid when ATP produced via oxidative phosphorylation is used to convert lactic acid back into pyruvic acid or all the way back to glucose. If there is an excess of glucose, the cell may convert it to glycogen (glycogenesis). Later, individual glucose molecules can be removed from the glycogen chain by the process of glycogenolysis. Although nicotinamide adenine dinucleotide (NAD) and flavin adenine dinucleotide (FAD) play important roles in these pathways, they have been left out of this diagram for the sake of simplicity.

Once oxygen becomes available again in cells that ordinarily rely on aerobic respiration, some of the lactic acid is converted back to pyruvic acid by the cell (see Figure 30-12). Notice that such reconversion requires energy from ATP. Thus reconversion in muscle cells, for example, can occur only when phosphorylation has resumed and produced enough ATP to allow reconversion to occur. Once it is converted to pyruvic acid, the molecule can follow the aerobic pathway and become completely catabolized.

Much of the lactic acid produced during anaerobic glycolysis diffuses into the blood and is removed by the liver. Inside liver cells, ATP produced by oxidative phosphorylation is used to convert the lactic acid back into glucose. The glucose may then be stored as glycogen in the liver or be returned through the bloodstream for use by other cells. Figure 30-13 summarizes this cycle during anaerobic glycolysis by skeletal muscles. This cycle is often called the **Cori cycle** after its discoverers, Carl and Gerty Cori.

Because anaerobic glycolysis requires the later use of ATP molecules produced by oxidative phosphorylation, we can say that an oxygen debt is incurred. This oxygen debt is repaid when oxygen becomes available to form the extra ATP needed to convert lactic acid back into pyruvic acid or glucose.

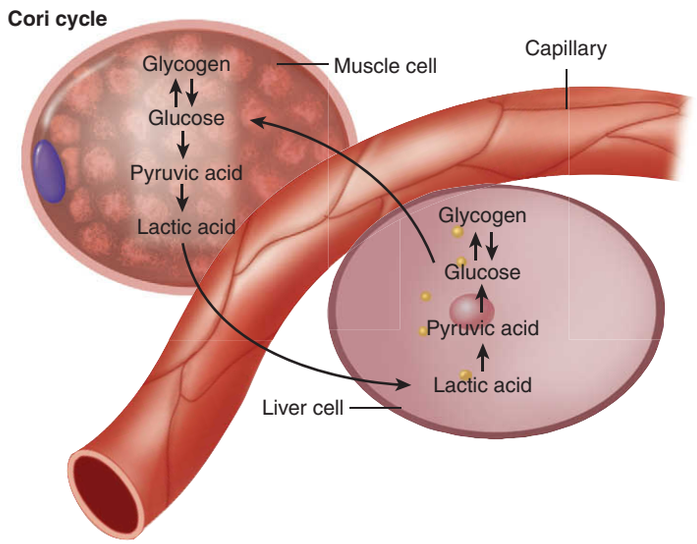


FIGURE 30-13

Cori cycle. Lactic acid produced by anaerobic glycolysis in skeletal muscles is carried to liver cells, where it is converted back to glucose and stored as liver glycogen or returned to the bloodstream, where the glucose may be taken up by muscle cells and used for respiration or stored as muscle glycogen.

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There is more to the oxygen debt than first meets the eye! Discover more about this important process in ***The Oxygen Debt*** online at ***A&P Connect.***

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GLYCOGENESIS

Imagine what happens in a cell if glucose catabolism is proceeding at maximum rate. What do you do if you see a traffic jam ahead with no possible way to get through it? Probably take an alternative route, if available. Similarly, if glycolytic pathways are "saturated" because of high levels of glucose entering the cell, a "traffic jam" of glucose-6-phosphate will result. Unable to enter glycolysis, glucose-6-phosphate will begin an alternative route; that is, it will enter the anabolic pathway of glycogen formation. The process of glycogen formation, called **glycogenesis** (see Figure 30-12), is a series of chemical reactions in which glucose molecules are joined together to form a structure made of a branched strand of stored glucose "beads" (Figure 30-14). The huge glycogen polymer molecules settle out of solution and therefore do not upset the osmotic balance of the cell—which would happen if a large quantity of individual glucose molecules is kept in the cell.

Glycogen polymers can be made by any cell but only two types of cells store a large quantity of glycogen: muscle fibers and liver cells. Astrocytes in the brain store more glycogen than most cells, but not nearly as much as muscle fibers and liver cells. However, that small amount of glycogen may be enough to protect the brain for a short time when glucose availability is low. It is mainly the liver that acts as the glycogen reservoir for the body.

The process of glycogenesis is part of a homeostatic mechanism that operates when the blood glucose level increases above the midpoint of its normal range. The normal range of glucose in a fasting person is about 80 to 90 mg/dl of blood. Soon after a meal high in carbohydrates, while glucose is being absorbed rapidly, the blood glucose may shoot up to 120 to 140 mg/dl or more. Recall that blood from the digestive tract is detoured directly to the liver via the portal system before being returned to the heart (see Figure 21-32 on p. 664). In the liver, the action of the pancreatic hormone *insulin* causes a great many glucose molecules to leave the blood for storage in hepatic cells as glycogen. As a result of glycogenesis, the blood glucose level decreases, ordinarily enough to reestablish its normal level. Figure 30-15 summarizes this role of glycogenolysis in maintaining homeostasis of blood glucose.

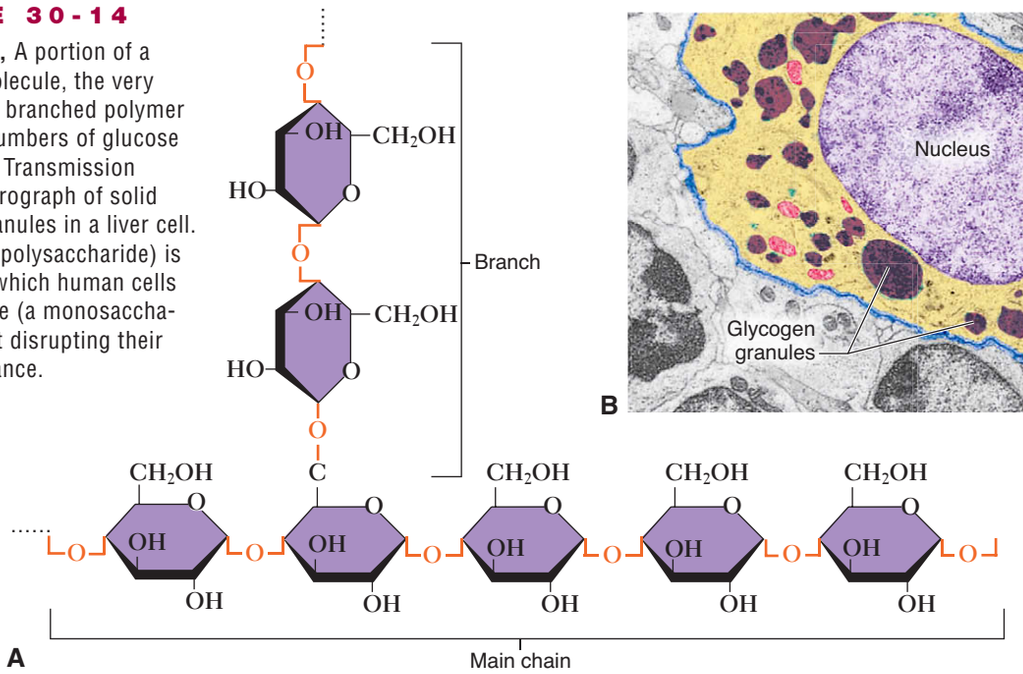
GLYCOGENOLYSIS

Glycogen molecules do not remain in the cell permanently but are eventually broken apart (hydrolyzed). This process of "splitting glycogen" is called **glycogenolysis** (Figure 30-16; see Figure 30-12). It is, in essence, a reversal of glycogenesis. What are the products of glycogenolysis? The answer depends on the cell. Although all cells presumably have the enzymes to break glycogen down to glucose-6-phosphate, only a few cell types (liver, kidney, intestinal mucosa) have the enzyme phosphatase, which allows free glucose to form and possibly leave the cell.

So the term *glycogenolysis* means different things in different cells. In muscles, glucose-6-phosphate is the product, which then undergoes glycolysis. But liver glycogenolysis (see Figure 30-16) results in free glucose that can leave the cell and increase the blood glucose level. Accordingly, liver glycogenolysis acts as a part of the homeostatic mechanism to maintain the blood glucose level. Example: A few hours after a meal, when the blood glucose level decreases (see Figure 30-15), the pancreatic hormone *glucagon* stimulates accelerated liver glycogenolysis. However, glycogenolysis alone can probably maintain homeostasis of blood glucose concentration for only 12 to 16 hours because the body can store only small amounts of glycogen.

FIGURE 30-14

Glycogen. A, A portion of a glycogen molecule, the very large, highly branched polymer of varying numbers of glucose subunits. **B,** Transmission electron micrograph of solid glycogen granules in a liver cell. Glycogen (a polysaccharide) is the form in which human cells store glucose (a monosaccharide) without disrupting their osmotic balance.



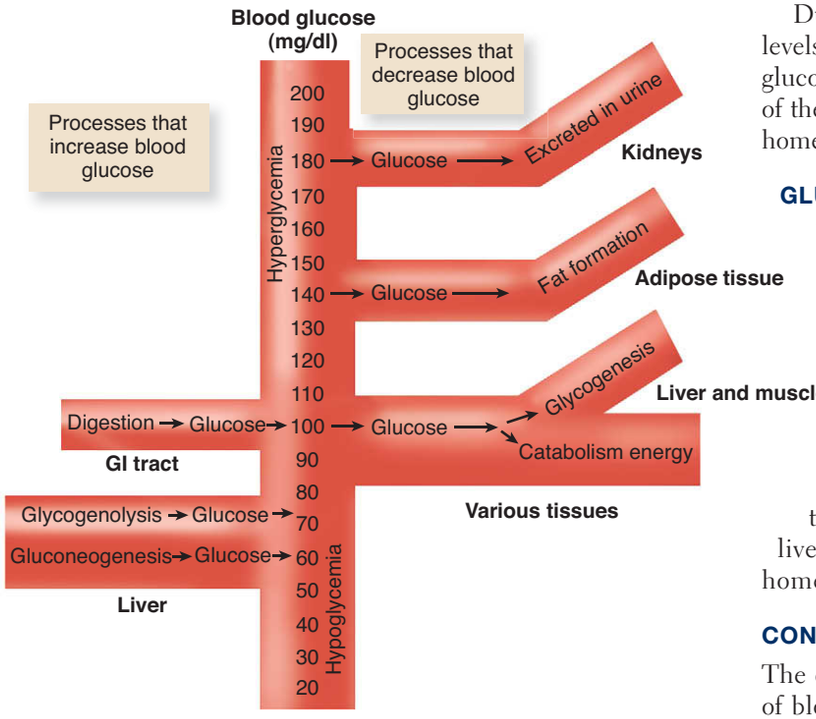


FIGURE 30-15

Homeostasis of blood glucose level. When blood glucose level starts to decrease below its normal range of about 80 to 90 mg/dl (fasting), liver cells increase the rate at which they convert glycogen, amino acids, and glycerol to glucose (glycogenolysis and gluconeogenesis) and release it into blood. But when blood glucose level increases, liver cells increase the rate at which they remove glucose molecules from blood and convert them to glycogen for storage (glycogenesis). At still higher levels, glucose leaves blood for liver cells to be converted into fat and, at still higher levels, is excreted in the urine. Hormones regulate the processes shown (see Figure 30-19).

During a stress response, elevated *epinephrine* and *cortisol* levels can stimulate glycogenolysis. This action elevates blood glucose levels, which may prove useful for the muscular activity of the "fight" or "flight" needed to resist or avoid a threat to the homeostatic balance of the body.

GLUCONEOGENESIS

Literally, **gluconeogenesis** means the formation of "new" glucose—"new" in the sense that it is made from proteins or, less frequently, from the glycerol of fats—not from carbohydrates. The process occurs chiefly in the liver. It consists of many complex chemical reactions. The new glucose produced from proteins or fats by gluconeogenesis (Figure 30-17) diffuses out of liver cells into the blood. Gluconeogenesis can therefore add glucose to the blood when needed. So, too, can the process of liver glycogenolysis. Obviously, then, the liver is a very important organ for maintaining blood glucose homeostasis.

CONTROL OF GLUCOSE METABOLISM

The complex mechanism that normally maintains homeostasis of blood glucose concentration consists of hormonal and neural devices. At least five endocrine glands—pancreatic islets, anterior pituitary gland, adrenal cortex, adrenal medulla, and thyroid gland—and at least eight hormones secreted by these glands function as key elements of the glucose homeostatic mechanism. As you read through the following paragraphs, keep in mind that each of the hormones listed have many different kinds of regulatory effects in the body—not just their effects on glucose metabolism.

Beta cells of the pancreatic islets secrete the most well-known sugar-regulating hormone of all—**insulin.** Insulin decreases blood glucose level by moving glucose molecules out of the blood

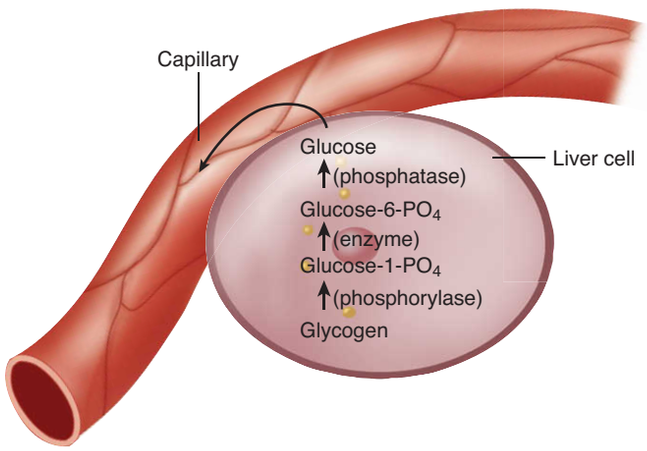


FIGURE 30-16

Glycogenolysis in a liver cell.

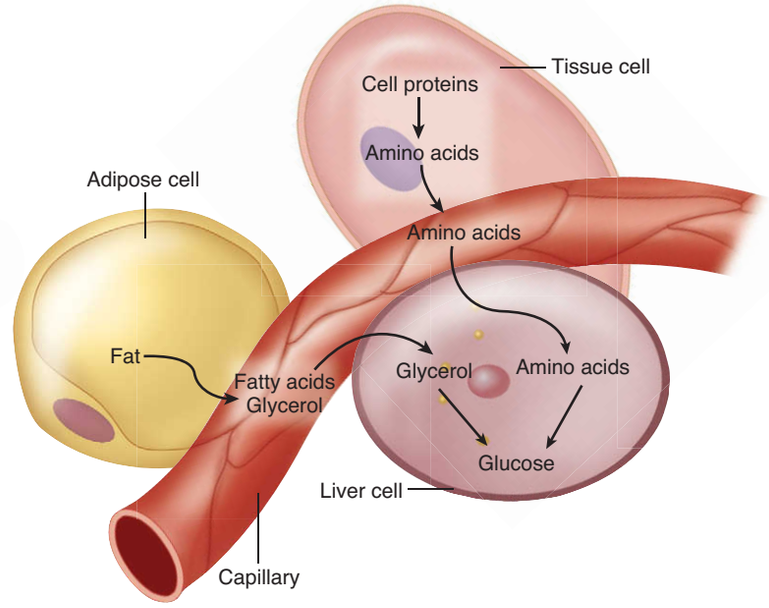


FIGURE 30-17

Gluconeogenesis. Liver cells can form glucose from mobilized tissue proteins and fats.

and into cells (Figure 30-18, *A*). Although the exact details of its mechanism of action are still being worked out, insulin is known to accelerate glucose transport through cell membranes. It also increases the activity of the enzyme glucokinase. Glucokinase catalyzes glucose phosphorylation, the reaction that must occur before either glycogenesis or glucose catabolism can take place. Insulin thus moves glucose into cells and increases glycogenesis and increased catabolism of glucose—all of which decrease blood glucose levels. Figure 30-18, *B*, demonstrates the blood-glucose lowering effects of insulin after ingesting glucose.

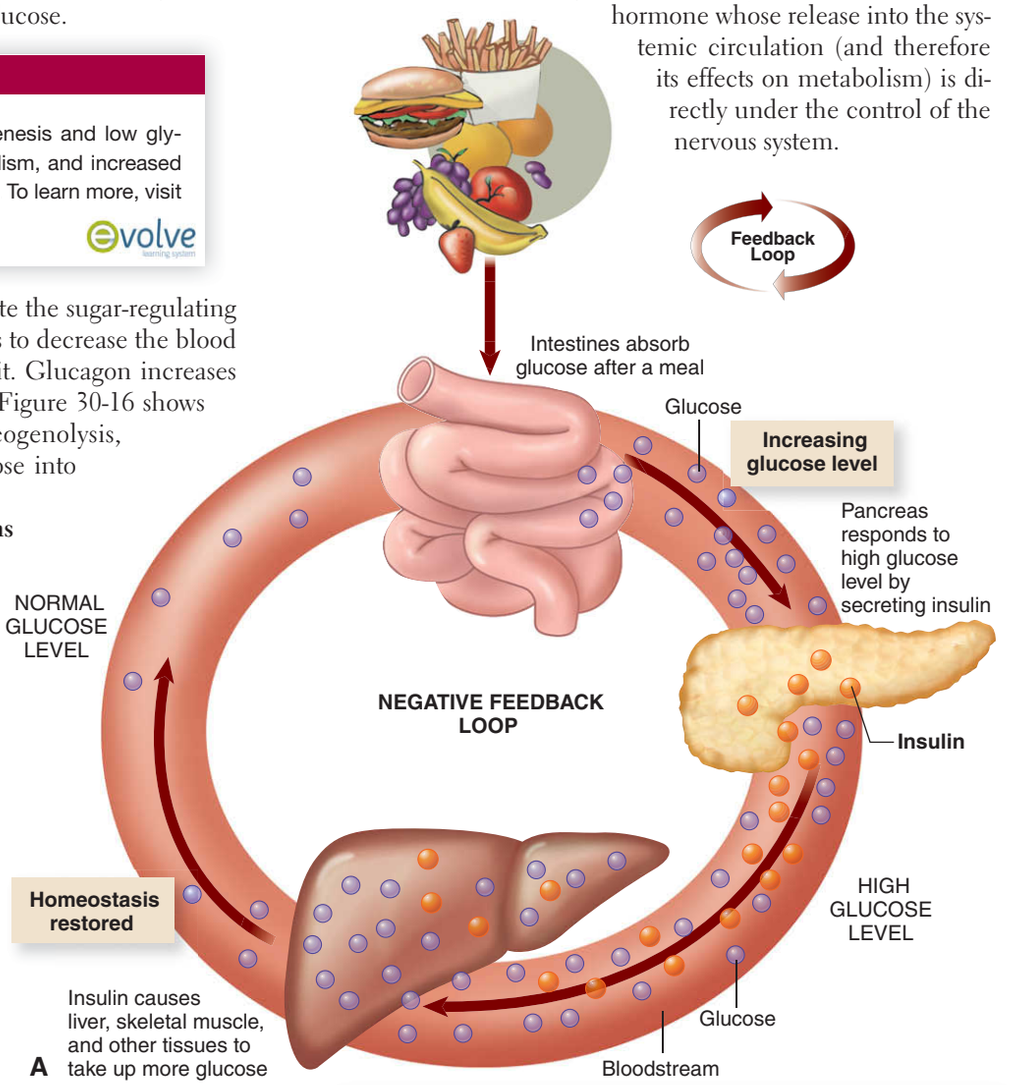
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Insulin deficiency can cause slow glycogenesis and low glycogen storage, decreased glucose catabolism, and increased blood glucose, as in diabetes mellitus (DM). To learn more, visit ***Diabetes Mellitus*** online at ***A&P Connect.***

Alpha cells of the pancreatic islets secrete the sugar-regulating hormone **glucagon.** Whereas insulin tends to decrease the blood glucose level, glucagon tends to increase it. Glucagon increases the activity of the enzyme phosphorylase. Figure 30-16 shows that phosphorylase promotes liver glycogenolysis, thereby causing the release of more glucose into the bloodstream.

Hormones collectively called **incretins** act to increase the amount of insulin released from the pancreatic beta cells and decrease the amount of glucagon released from pancreatic alpha cells. Thus incretins tend to decrease blood glucose levels. Incretins may also reduce the rate of gastric emptying and decrease desire for more food. Incretins are released by endocrine gastrointestinal (GI) cells in response to the presence of glucose and can increase insulin release even before blood glucose levels begin to rise after a meal. Incretins include *glucagon-like peptide 1 (GLP-1)* and *gastric inhibitory peptide (GIP)*. Because of its role as an incretin, GIP is also called *glucose-dependent insulinotropic peptide (GIP)*. Because of their insulin-elevating effects, incretin mechanisms are being investigated as possible treatments for diabetes mellitus (DM).

Epinephrine is a hormone secreted in large amounts by the adrenal medulla in times of emotional or physical stress. Like glucagon, epinephrine increases phosphorylase activity. This makes glycogenolysis occur at a faster rate. Epinephrine accelerates both liver and muscle glycogenolysis, whereas glucagon accelerates only liver glycogenolysis. Both hormones increase the blood glucose level. Epinephrine is the only hormone whose release into the systemic circulation (and therefore its effects on metabolism) is directly under the control of the nervous system.



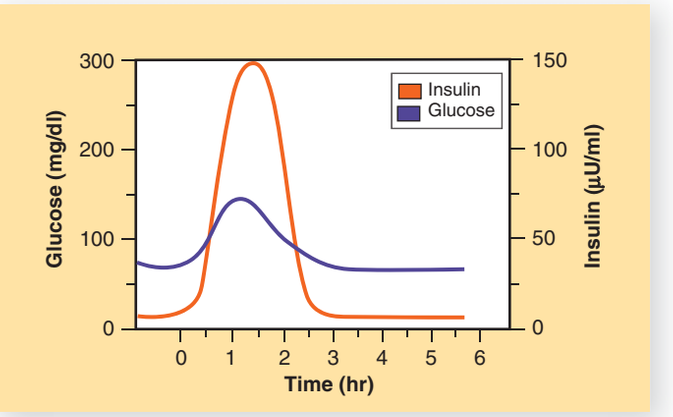


FIGURE 30-18

Role of insulin. Insulin operates in a negative feedback loop **(A)** that prevents blood glucose concentration from increasing too far above the normal range. Insulin promotes uptake of glucose by all cells of the body, enabling them to catabolize and/or store it. The liver and skeletal muscles are especially well adapted for storage of glucose as glycogen. Thus excess glucose is removed from the bloodstream, as the graph **(B)** demonstrates. If the glucose level falls below the normal range, hormones such as glucagon promote the release of glucose from storage into the bloodstream (see Figure 30-19).

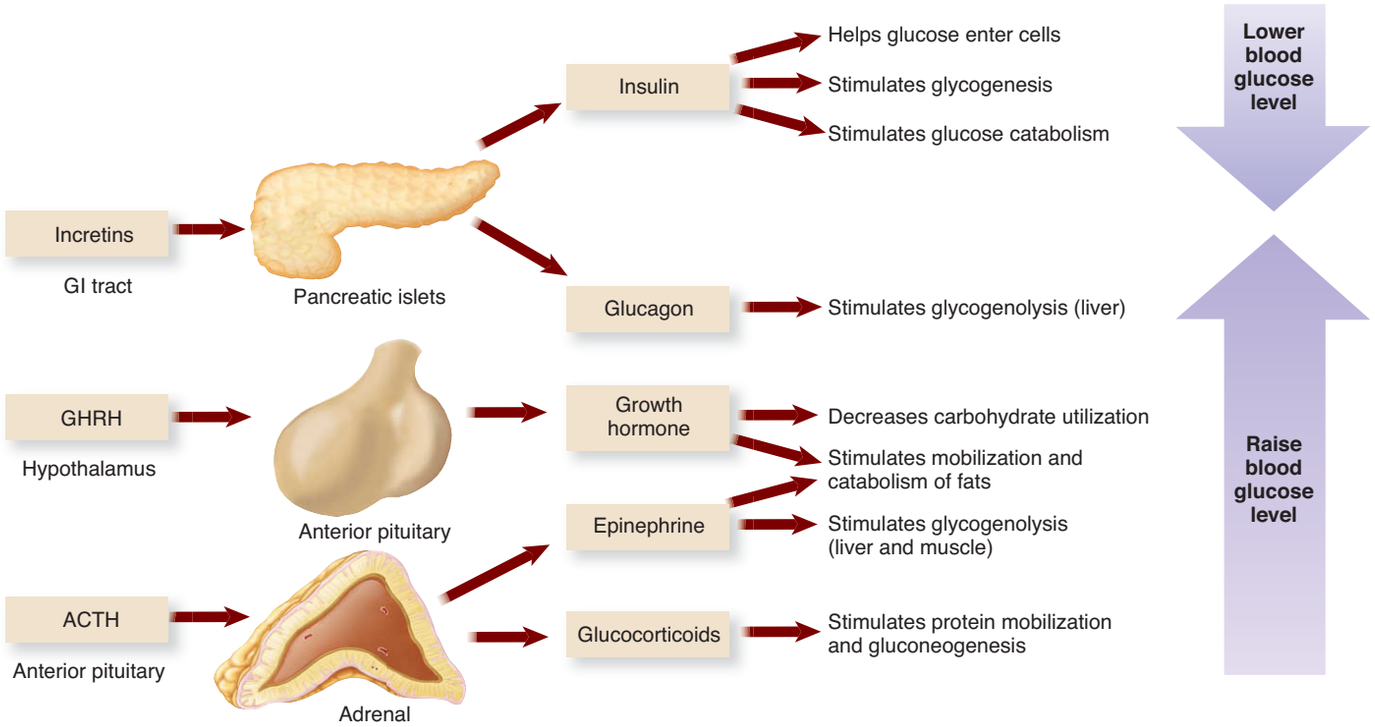


FIGURE 30-19

Hormonal control of blood glucose level. Simplified view of some of the major glucose-regulating hormones. Insulin lowers blood glucose level and is therefore hypoglycemic. Most hormones shown here raise blood glucose level and are called *hyperglycemic,* or *anti-insulin, hormones.* Figure 30-15 shows how the regulated processes change blood glucose levels.

Adrenocorticotropic hormone (ACTH) and *glucocorticoids* (e.g., cortisone) are two more hormones that increase blood glucose concentration. ACTH stimulates the adrenal cortex to increase its secretion of glucocorticoids. Glucocorticoids accelerate gluconeogenesis. They do this by mobilizing proteins, that is, the breakdown, or hydrolysis, of tissue proteins to amino acids. More amino acids enter the circulation and are carried to the liver. Liver cells step up their production of "new" glucose from the mobilized amino acids. Glucocorticoids help here, too, by stimulating enzymatic reversal of glycolysis and thus helping the cell in its effort to manufacture more glucose. The glucose streams out of liver cells into the blood and adds to the blood glucose level.

Growth hormone (GH), made by the anterior pituitary, also increases blood glucose level, but by a different mechanism. GH causes a shift from carbohydrate to fat catabolism. It does this by limiting the storage of fat in fat depots. Instead, more fats are mobilized and catabolized. In this way, GH "spares" carbohydrates from catabolism, and the level of glucose in the bloodstream is increased.

Thyroid-stimulating hormone (TSH) from the anterior pituitary gland and its target secretion, *thyroid hormone* (T_3 and T_4), have complex effects on metabolism. Some of these raise, and some lower, the glucose level. One of the effects of thyroid hormone is to accelerate catabolism, and because glucose is the body's "preferred fuel," the result may be a decrease in blood glucose level.

The summary of hormone control shown in Figure 30-19 indicates that most hormones cause the glucose blood level to rise. These hormones are called *hyperglycemic* because they tend to promote a high blood glucose concentration. The one notable exception is insulin, which is *hypoglycemic* (tends to decrease the blood glucose level). See Box 30-3 for more discussion of blood glucose problems.

Box 30-3 | FYI

Abnormal Blood Glucose Concentration

The term **hyperglycemia,** which literally means "condition of too much sugar in the blood," is used to describe any blood glucose concentration that is higher than the normal set point level. Hyperglycemia is most often associated with untreated diabetes mellitus, but it can occur in newborns when too much intravenous glucose is given or in other similar situations. If untreated, the excess glucose leaves the blood in the kidney—literally "spilling over" into the urine. This increases the osmotic pressure of urine, drawing an abnormally high amount of water into the urine from the bloodstream. Thus hyperglycemia causes loss of glucose in the urine and its accompanying loss of water—potentially threatening the fluid balance of the body. Dehydration of this sort can ultimately lead to death.

Hypoglycemia occurs when the blood glucose concentration dips below the normal set point level. Hypoglycemia can occur in various conditions, including starvation, hypersecretion of insulin by the pancreatic islets, or injection of too much insulin. Symptoms of hypoglycemia include weakness, hunger, headache, blurry vision, anxiety, and personality changes—perhaps leading to coma and death if untreated.

| QUICK CHECK |

6. Why might a cell switch to the anaerobic pathway as its major source of usable energy?
7. What is meant by the term *oxygen debt?*
8. Distinguish between glycogenesis and glycogenolysis. Under what circumstances might each occur?
9. List three of the hormones that affect glucose metabolism.

LIPIDS

Dietary Sources of Lipids

Recall from Chapter 2 that **lipids** are a class of organic compounds that includes fats, oils, and related substances. The most common lipids in the diet are **triglycerides,** which are composed of a *glycerol* subunit to which are attached three *fatty acids.* Other important dietary lipids include *phospholipids* and *cholesterol.* Dietary fats are often classified as either **saturated** or **unsaturated.** Saturated fats contain fatty acid chains in which there are no double bonds—that is, all available bonds of its hydrocarbon chain are filled (saturated) with hydrogen atoms (see Figure 2-19, p. 49). Saturated fats are usually solid at room temperature. Unsaturated fats contain fatty acid chains, of which there are some double bonds, meaning that not all sites for hydrogen are filled. Unsaturated fats are usually liquid at room temperature.

Triglycerides are found in nearly every food that we eat. However, the amount of triglycerides in each type of food varies considerably, as does the proportion of saturated to unsaturated types. Phospholipids are also found in nearly all foods because they

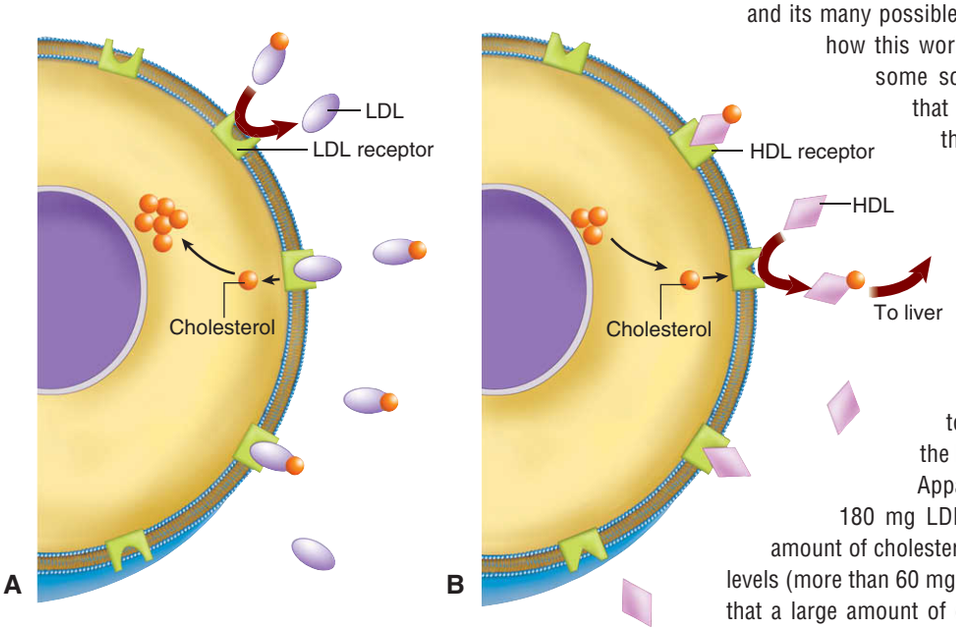
Box 30-4 | Lipoproteins

As stated in the text, high blood concentrations of low-density lipoproteins (LDLs) are associated with a high risk for atherosclerosis. Atherosclerosis is a form of "hardening of the arteries" that occurs when lipids accumulate in cells lining the blood vessels and promote the development of a plaque that eventually impedes blood flow and may trigger clot formation. Atherosclerosis may also weaken the wall of a blood vessel to the point that it ruptures. In any case, a person with atherosclerosis of the coronary arteries risks a heart attack when blood flow to cardiac muscle is impaired. If vessels in the brain are affected, there is risk of a *cerebrovascular accident (CVA),* or "stroke."

Part *A* of the figure is a simplified version of a concept of LDL function first proposed by Nobel laureates Michael Brown and Joseph Goldstein at the University of Texas. According to their model, LDL delivers cholesterol to cells for use in synthesizing steroid hormones and stabilizing the plasma membrane. Most, if not all, cells have many LDL receptors embedded in the outer surface of their plasma membranes. These receptors attract cholesterol-bearing LDL. Once the LDL molecule binds to the receptor, specific mechanisms operate to release the cholesterol it carries into the cell. Excess cholesterol is stored in droplets near the center of the cell. It seems that, in some individuals at least, cells have so few LDL receptors that they accumulate too much cholesterol in the blood. Some mechanism in endothelial cells moves this excess LDL into the wall of blood vessels. This has been proposed as a cause for the lipid accumulation characteristic of atherosclerosis.

High blood concentrations of high-density lipoproteins (HDLs) have been associated with a low risk of developing atherosclerosis and its many possible complications. Although the exact details of how this works have yet to be worked out or confirmed, some scientists have made some progress toward that end. Jack Oram, a cell biologist working at the University of Washington, has proposed the mechanism illustrated in part *B* of the figure. According to his model, HDL molecules are attracted to HDL receptors embedded in the plasma membranes. Once they bind to their receptors, the cell is stimulated to release some of its cholesterol from storage. The released cholesterol migrates to the plasma membrane, where it may attach to the HDL molecule and be whisked away to the liver for excretion in bile.

Apparently, high blood LDL levels (more than 180 mg LDL per 100 ml of blood) signify that a large amount of cholesterol is being delivered to cells. High blood HDL levels (more than 60 mg HDL per 100 ml of blood) apparently indicate that a large amount of cholesterol is being removed from cells and delivered to the liver for excretion from the body. Currently, researchers are using this information to develop treatments that may prevent—or even cure—atherosclerosis and the disorders it causes.



Role of blood lipoproteins. A, Simplified diagram of the role of low-density lipoprotein *(LDL)* in delivering cholesterol to cells. **B,** Proposed role of high-density lipoprotein *(HDL)* in removing cholesterol from cells.

make up the cellular membranes in and around each cell of all living organisms. Cholesterol, however, is found only in foods of animal origin. Cholesterol concentration also varies. For example, it is particularly high in liver and the yolks of eggs.

Transport of Lipids

Lipids are transported in blood as chylomicrons, lipoproteins, and free fatty acids. **Chylomicrons** are small fat droplets found in blood soon after fat absorption has occurred. Fatty acids and monoglyceride products of fat digestion combine during absorption to again form fats (triglycerides, or triacylglycerols). These triglycerides plus small amounts of cholesterol and phospholipids compose the chylomicrons. During fat absorption, the so-called *absorptive state*, blood may contain so many of these fat droplets that it appears turbid or even yellowish in color. But during the *postabsorptive state*—usually within about 4 hours after a meal—few, if any chylomicrons remain in the blood. Their contents have moved mostly into adipose tissue cells.

In the postabsorptive state, when chylomicrons are virtually absent from the circulation, some 95% of the lipids in blood are transported in the form of lipoproteins. **Lipoproteins** are produced mainly in the liver, and as their name suggests, they consist of lipids (triglycerides, cholesterol, and phospholipids) and protein. At all times, blood contains three types of lipoproteins, namely, very-low-density lipoproteins, low-density lipoproteins, and high-density lipoproteins. Usually, they are designated by their abbreviations: VLDL, LDL, and HDL. Diets high in saturated fats and cholesterol tend to produce an increase in blood LDL concentration, which in turn is associated with a high incidence of coronary artery disease (CAD) and atherosclerosis (Figure 30-20 and Box 30-4). A high blood HDL concentration, in contrast, is associated with a low incidence of heart disease. One might therefore think of the LDLs as the "bad lipoproteins" and the HDLs as the "good lipoproteins." Considerable evidence indicates that exercise tends to elevate HDL concentration. This may partially account for the beneficial effects of exercise.

Fatty acids, on entering the blood from adipose tissue or other cells, combine with albumin to form the so-called **free fatty acids (FFAs).** Fatty acids are transported from cells of one tissue to those of another in the form of free fatty acids. Whenever the rate of fat catabolism increases—as it does in starvation or diabetes—the free fatty acid content of blood increases markedly.

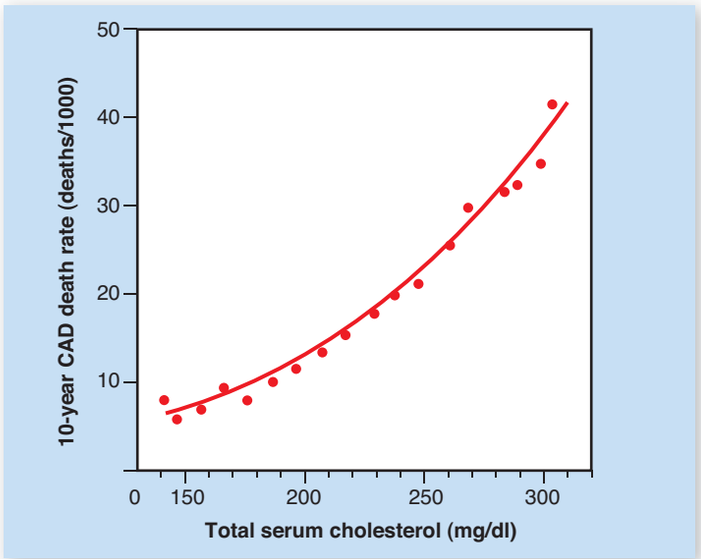


FIGURE 30-20

Cholesterol and heart disease. The graph shows a relationship between the total serum (blood plasma) cholesterol level and coronary artery disease (CAD).

Lipid Metabolism

LIPID CATABOLISM

Lipid catabolism, like carbohydrate catabolism, consists of several processes. Each of these processes, in turn, consists of a series of chemical reactions. Triglycerides are first hydrolyzed to yield fatty acids and glycerol. Glycerol is then converted to glyceraldehyde-3-phosphate, which may then be converted to glucose or it may enter the glycolysis pathway directly (see Figure 30-5). Fatty acids, as Figure 30-21 shows, are broken down by a process called *beta-oxidation* into two-carbon pieces, the familiar acetyl CoA. These molecules are then catabolized via the citric acid cycle. The final process of lipid catabolism therefore consists of the same reactions as does carbohydrate catabolism. Catabolism of lipids, however, yields considerably more energy than does catabolism of carbohydrates. Whereas catabolism of 1 gram of carbohydrates yields only 4.1 kcal of heat, catabolism of 1 gram of fat yields 9 kcal. It is not surprising, then, that lipids are the preferred energy source for muscle tissue.

When fat catabolism occurs at an accelerated rate, as in diabetes mellitus

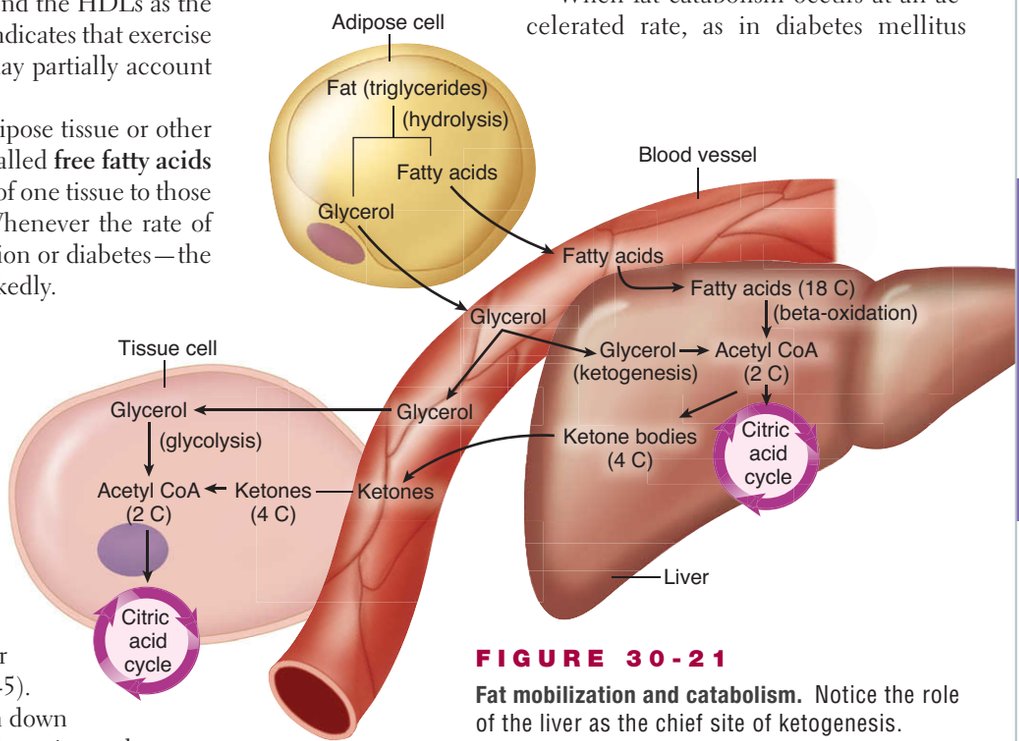


FIGURE 30-21

Fat mobilization and catabolism. Notice the role of the liver as the chief site of ketogenesis. Numbers of carbon atoms are in parentheses.

(when glucose cannot enter cells) or fasting, excessive numbers of acetyl CoA units are formed. Liver cells then temporarily condense acetyl CoA units together to form four-carbon acetoacetic acid. Acetoacetic acid is classified as a *ketone body* and can be converted to two other types of ketone bodies, namely, acetone and beta-hydroxybutyric acid—hence the name **ketogenesis** for this process (Box 30-5). Liver cells oxidize a small portion of the ketone bodies for their own energy needs, but most of them are transported by the blood to other tissue cells for the change back to acetyl CoA and oxidation via the citric acid cycle (see Figure 30-21).

LIPID ANABOLISM

Lipid anabolism, also called **lipogenesis,** consists of the synthesis of various types of lipids, notably *triglycerides*, *cholesterol*, *phospholipids*, and *prostaglandins*. Triglycerides and structural lipids (e.g., phospholipids) are synthesized from fatty acids and glycerol or from excess glucose or amino acids. So it is possible to "get fat" from foods other than fat. Triglycerides are stored mainly in adipose tissue cells. These fat deposits constitute the body's largest reserve energy source—often too large, unfortunately. Almost limitless pounds of fat can be stored. In contrast, only a few hundred grams of carbohydrates can be stored as liver and muscle glycogen.

Most fatty acids can be synthesized by the body. A certain number of the unsaturated fatty acids must be provided by the diet and are thus called **essential fatty acids.** Some of the essential fatty acids serve as a source within the body for synthesis of an important group of lipids called *prostaglandins*. These hormone-like compounds, first discovered in the 1930s in semen, have gained increasing recognition for their occurrence in various tissues, where they support a wide spectrum of biological activity (see Chapter 18). Certain essential fatty acids are also necessary for manufacturing the phospholipids in cell membranes (Chapter 3) and the myelin in nerve tissue (Chapter 13).

CONTROL OF LIPID METABOLISM

Lipid metabolism is controlled mainly by the following hormones:

- Insulin
- ACTH
- Growth hormone
- Glucocorticoids

You probably recall from our discussion of these hormones in connection with carbohydrate metabolism that they regulate fat metabolism in such a way that the rate of fat catabolism is inversely related to the rate of carbohydrate catabolism. If some condition such as diabetes mellitus causes carbohydrate catabolism to decrease below energy needs, increased secretion of growth hormone, ACTH, and glucocorticoids soon follows. These hormones, in turn, bring about an increase in fat catabolism. But, when carbohydrate catabolism equals energy needs, fats are not mobilized out of storage and catabolized (Box 30-6). Instead, they are spared and stored in adipose tissue. "Carbohydrates have a 'fat-sparing' effect," so says an old physiological maxim. Or stating this truth more descriptively: "Carbohydrates have a 'fat-storing' effect."

Research has shown that hormonal control of lipid metabolism is very complex—and still not well understood. One intriguing line of research involves the hormone **leptin.** Leptin is secreted by fat-storing cells and seems to regulate *satiety* (feeling of hunger/fullness) and how fat is metabolized. Researchers studying the complex interaction of leptin and other hormones and their receptors hope to find effective treatments for obesity, diabetes, and other fat-storage afflictions.



Box 30-5 | HEALTH matters

Ketosis

Large amounts of ketone bodies may be present in the blood of a person with uncontrolled diabetes mellitus. This condition is known as **ketosis.** Signs of it are acetone breath and *ketonuria* (high number of ketone bodies in the urine).

Box 30-6 | PPARs and Fat Metabolism

A class of proteins called *peroxisome proliferator–activated receptors,* or *PPARs,* may hold some keys as to how the body metabolizes fats. PPARs are molecules attached to the DNA molecules of cells. PPARs combine with other proteins to form a complex that regulates genes that determine how the cell takes in and breaks down fat. Initial research shows that chemicals that affect different PPARs can influence fat storage in the body. With more than 60% of the U.S. population being overweight and therefore at risk for heart disease, diabetes, cancer, and other health problems, it is no wonder that scientists are scrambling to find out more about how PPARs regulate fat metabolism and how we can influence them to reduce obesity-related health risks.

| QUICK CHECK |

10. In what forms are lipids transported to cells?
11. How can glycerol and fatty acids enter the citric acid cycle?
12. Which fatty acids cannot be made by the body?

PROTEINS

Sources of Proteins

Recall from Chapter 2 that proteins are very large molecules composed of chemical subunits called **amino acids** (see Figure 2-26, p. 53). Proteins are assembled from a pool of many different kinds of amino acids. If any one type of amino acid is deficient, vital proteins cannot be synthesized—a serious health threat. One way your body maintains a constant supply of amino acids is by

synthesizing them from other compounds already present in the body. Only about half of the required types of amino acids can be made by the body, however. The remaining types of amino acids must be supplied in the diet. Nutritionists often refer to the amino acids that must be in the diet as essential, or indispensable, amino acids. Table 30-1 lists amino acids according to whether they are considered essential in the diet or nonessential (dispensable) in the diet (synthesized by the body). Box 30-7 mentions the link between blood levels of amino acids and disease.

Proteins are obtained in the diet from various sources. Muscle meat and other animal tissues particularly high in proteins contain the essential amino acids. Food from a single plant or other nonanimal source does not usually contain an adequate amount of all the essential amino acids. Therefore, it is important to include meat in the diet or a mixture of different vegetables that provide all the amino acids needed by the body. Plant tissues that are particularly high in protein content include cereal grains, nuts, and legumes such as peas and beans.

Protein Metabolism

In protein metabolism, anabolism is primary and catabolism is secondary. In carbohydrate and fat metabolism, the opposite is true—catabolism is primary and anabolism is secondary. Proteins are primarily tissue-building foods. Carbohydrates and fats are primarily energy-supplying foods.

PROTEIN ANABOLISM

Protein anabolism is the process by which proteins are synthesized by the ribosomes of all cells. The specific mechanisms of protein anabolism were first discussed in Chapter 2 (see pp. 41–42) and further explained in Chapter 5 (see pp. 119–120). We review the basic idea of protein anabolism here.

Every cell synthesizes its own structural proteins and its own enzymes. In addition, many cells, such as liver and glandular cells, synthesize special proteins for export. For example, liver cells manufacture the plasma proteins found in blood. The cell's genes, under the influence of signaling mechanisms, determine the specific proteins to be synthesized. Protein anabolism is truly "big business" in the body. Consider, for instance, that protein anabolism constitutes the major process of growth, reproduction, tissue repair, and the replacement of cells destroyed by daily wear and tear. Red blood cell replacement alone amounts to millions of cells per second!

TABLE 30-1 Amino Acids

ESSENTIAL (INDISPENSABLE)	NONESSENTIAL (DISPENSABLE)
Histidine (His)*	Alanine (Ala)
Isoleucine (Ile)	Arginine (Arg)
Leucine (Leu)	Asparagine (Asn)
Lysine (Lys)	Aspartic acid (Asp)
Methionine (Met)	Cysteine (Cys)
Phenylalanine (Phe)	Glutamic acid (Glu)
Threonine (Thr)	Glutamine (Gln)
Tryptophan (Trp)	Glycine (Gly)
Valine (Val)	Proline (Pro)
	Selenocysteine (Sec)
	Serine (Ser)
	Tyrosine (Tyr)†

*Essential in infants and, perhaps, adult males.
†Can be synthesized from phenylalanine; therefore nonessential as long as phenylalanine is in the diet.

Box 30-7 | HEALTH matters

Amino Acids and Disease

The balance of amino acids circulating in the blood is associated with various diseases. High blood levels of homocysteine, one of several alternate forms of the amino acid cysteine (see Table 30-1), have been linked to heart disease, stroke, and dementias such as Alzheimer disease. Whether such abnormalities in homocysteine levels are the direct cause of these conditions is uncertain. Despite this uncertainty, many physicians recommend lowering abnormally high blood homocysteine levels to reduce the possible risk for these devastating conditions. Homocysteine can be reduced to normally low blood levels when there is adequate vitamin B_6, B_{12}, or B_9 (folic acid) in the diet.

PROTEIN CATABOLISM

The first step in protein catabolism takes place in liver cells. Called **deamination,** it consists of the splitting off of an amino (NH_2) group from an amino acid molecule to form a molecule of ammonia and one of keto acid (e.g., alpha-ketoglutaric acid). Most of the ammonia is converted by liver cells to *urea* and later excreted in the urine. The keto acid may be oxidized via the citric acid cycle (see Figure 30-7) or may be converted to glucose via gluconeogenesis (Figure 30-22) or to fat (lipogenesis). Both

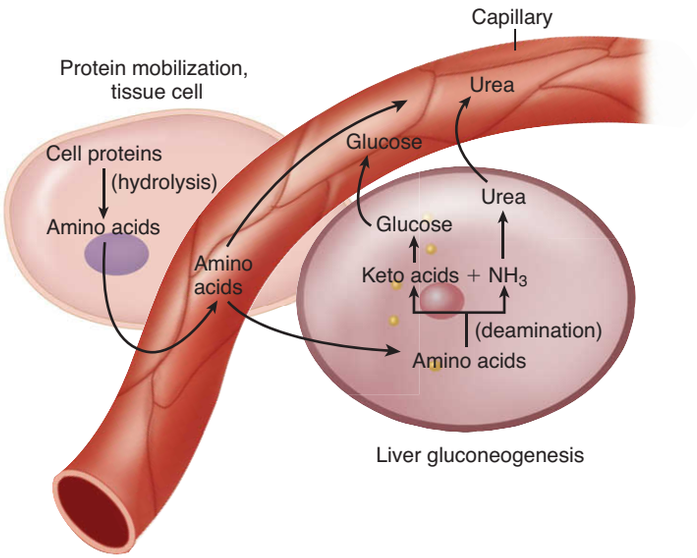


FIGURE 30-22

Protein mobilization and catabolism. Glucocorticoids tend to accelerate these processes and are therefore classified as protein catabolic hormones.

protein catabolism and anabolism go on continually. Only their rates differ from time to time. With a protein-deficient diet, for example, protein catabolism exceeds protein anabolism. Various hormones, as we shall see, also influence the rates of protein catabolism and anabolism.

PROTEIN BALANCE AND NITROGEN BALANCE

Usually a state of **protein balance** exists in the normal healthy adult body; that is, the rate of protein anabolism equals or balances the rate of protein catabolism. When the body is in protein balance, it is also in a state of **nitrogen balance** because the amount of nitrogen taken into the body (in protein foods) equals the amount of nitrogen in protein catabolic waste products excreted in the urine, feces, and sweat.

It is important to realize that there are two kinds of protein, or nitrogen, imbalance. When protein catabolism exceeds protein anabolism, the amount of nitrogen in the urine exceeds the amount of nitrogen in the protein foods ingested. The individual is then said to be in a state of **negative nitrogen balance,** or in a state of "tissue wasting"—because more of the tissue proteins are being catabolized than are being replaced by protein synthesis. Protein-poor diets, starvation, and wasting illnesses, for example, produce a negative nitrogen balance. A **positive nitrogen balance** (nitrogen intake in foods greater than nitrogen output in urine) indicates that protein anabolism is occurring at a faster rate than protein catabolism. A state of positive nitrogen balance therefore characterizes any condition in which large amounts of tissue are being synthesized, such as during growth, pregnancy, and convalescence from an emaciating illness.

CONTROL OF PROTEIN METABOLISM

Protein metabolism, like that of carbohydrates and fats, is controlled largely by hormones rather than by the nervous system. Growth hormone and the male hormone testosterone both have a stimulating effect on protein synthesis, or anabolism. For this reason, they are referred to as *anabolic* hormones. The protein *catabolic* hormones of greatest consequence are glucocorticoids. They speed up tissue protein mobilization, that is, the hydrolysis of cell proteins to amino acids, their entry into the blood, and their subsequent catabolism (see Figure 30-22). ACTH functions indirectly as a protein catabolic hormone because of its stimulating effect on glucocorticoid secretion.

Thyroid hormone is necessary for and tends to promote protein anabolism and therefore growth when plenty of carbohydrates and fats are available for energy production. On the other hand, under different conditions, for example, when the amount of thyroid hormone is excessive or when the energy foods are deficient, this hormone may then promote protein mobilization and catabolism.

Some of the facts about metabolism set forth in the preceding sections are summarized in Table 30-2 and Figure 30-23.

| QUICK CHECK |

13. What is meant by the term *essential amino acid?*
14. What happens when an amino acid is deaminated?
15. What is the purpose of the process of amino acid deamination?
16. What is meant by the term *nitrogen balance?*

TABLE 30-2 Metabolism

NUTRIENT	ANABOLISM	CATABOLISM	
Carbohydrates	Temporary excess changed into glycogen by liver cells in presence of insulin; stored in liver and skeletal muscles until needed and then changed back to glucose True excess beyond body's energy requirements converted into adipose tissue; stored in various fat depots of body	Oxidized, in presence of insulin, to yield energy (4.1 kcal per g) and wastes (carbon dioxide and water) $C_6H_{12}O_6 \times 6\ O_2 \longrightarrow$ Energy + 6 CO_2 + 6 H_2O	
Fats	Built into adipose tissue; stored in fat depots of body	Fatty acids ↓ (beta-oxidation) Acetyl CoA $\rightleftharpoons$ Ketones ↓ (tissues; citric acid cycle) Energy (9.3 kcal/g) + CO_2 + H_2O	Glycerol ↓ (glycolysis) Acetyl CoA
Proteins	Synthesized into tissue proteins, blood proteins, enzymes, hormones, etc.	Deaminated by liver, forming ammonia (which is converted to urea) and keto acids (which are either oxidized or changed to glucose or fat)	

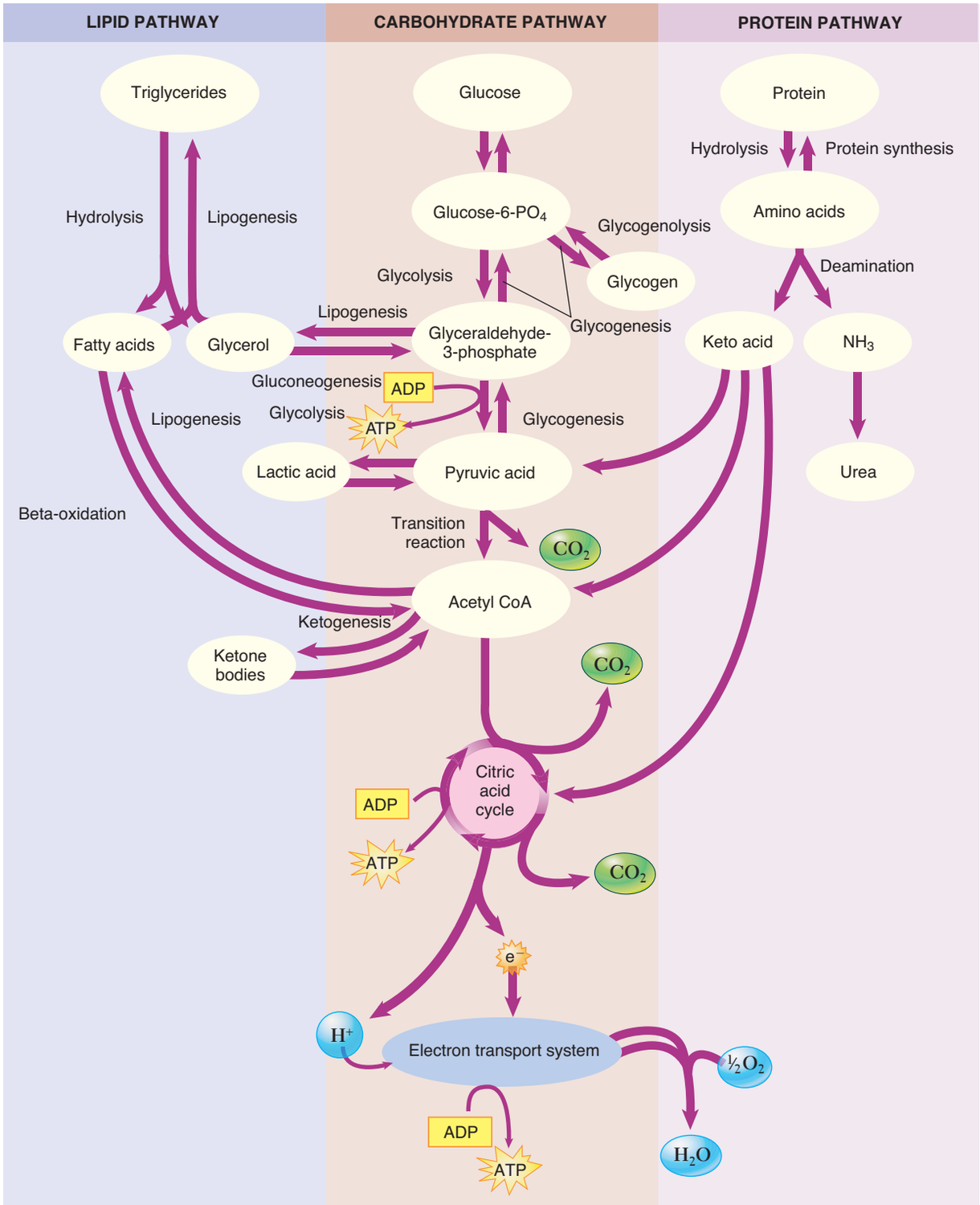


FIGURE 30-23

Summary of metabolism. Notice the central role played by the citric acid cycle and electron transport system. Notice also how different molecules can be converted to forms that may enter other pathways. *ADP,* Adenosine diphosphate; *ATP,* adenosine triphosphate; *CoA,* coenzyme A.

VITAMINS AND MINERALS

One glance at the label of any packaged food product reveals the importance we place on vitamins and minerals. We know that carbohydrates, fats, and proteins are used by our bodies to build important molecules and to provide energy. So why do we need vitamins and minerals?

Vitamins

Vitamins are organic molecules needed in small quantities for normal metabolism throughout the body (Box 30-8). The first vitamins were discovered in the early twentieth century at the University of Wisconsin by Marguerite Davis and Elmer Vernon McCollum. Earlier, vitamins were hypothesized to be amines so they were originally called vitamines, later shortened to vitamins. However, Davis and McCollum discovered two fat-soluble, nonamine substances that fit the proposed function of a vitamin and they named these factors fat-soluble A and fat-soluble B. This not only began a system of naming vitamins with letters but also spurred the whole science of nutrition.

Most vitamin molecules attach to enzymes or coenzymes and help them work properly. **Coenzymes** are organic, nonprotein catalysts that often act as "molecule carriers." Many enzymes or coenzymes are totally useless without the appropriate vitamins to attach to them and thus give them the shape that allows them to function properly. For example, coenzyme A (CoA), an important carrier molecule associated with the citric acid cycle, has *pantothenic acid* (vitamin B_5) as one of its major components.

Not all vitamins are involved directly with enzymes and coenzymes. Vitamins A, D, and E play a variety of different, but no less important, roles in the chemistry of the body. The form of vitamin A called *retinal*, for example, plays an important role in detecting light in sensory cells of the retina. Vitamin D can

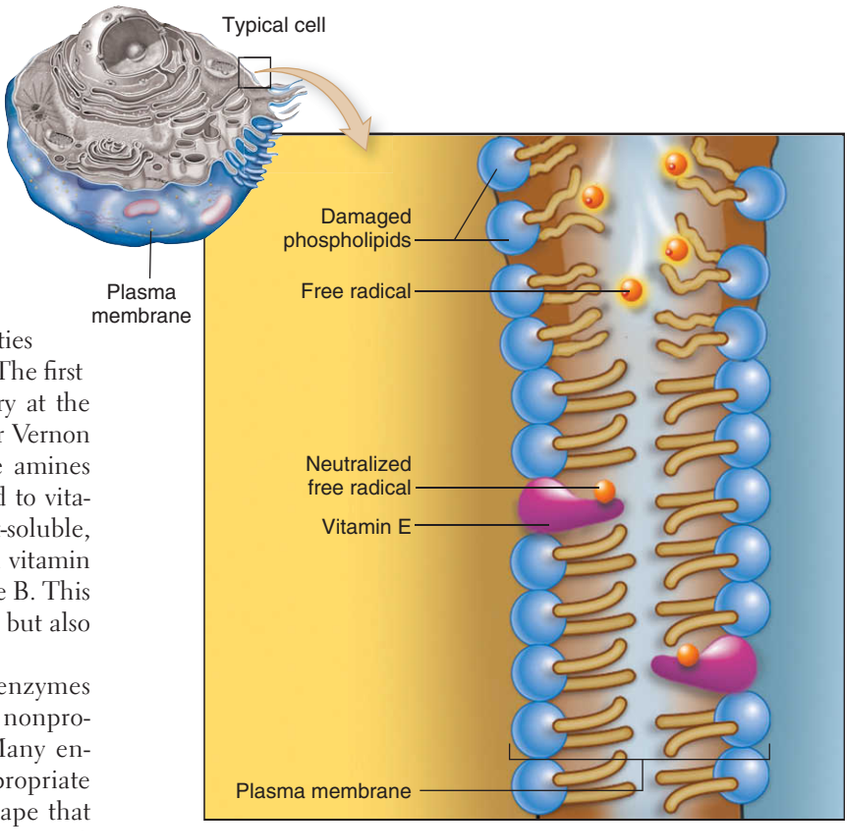


FIGURE 30-24

Role of vitamin E. Vitamin E can act as an antioxidant, attracting and neutralizing molecules with unpaired electrons. For example, free radicals are highly reactive molecules with an electron-seeking behavior that tends to damage electron-dense areas of the cell such as membrane phospholipids and DNA molecules. Vitamin E embedded among phospholipids in cell membranes can have a protective effect as it attracts and neutralizes free radicals that would otherwise destroy the membrane. Vitamin C has a similar antioxidant effect.

Box 30-8 | SPORTS and FITNESS

Vitamin Supplements for Athletes

Because a deficiency of vitamins *(avitaminosis)* can cause poor athletic performance, many athletes regularly consume vitamin supplements. However, research suggests that vitamin supplementation has little or no effect on a person's athletic performance. A reasonably well balanced diet supplies more than enough vitamins for even the elite athlete. The use of vitamin supplements therefore has fueled controversy among exercise experts. Opponents of vitamin supplements cite the cost and the possibility of liver damage associated with some forms of *hypervitaminosis,* whereas supporters cite the benefit of protecting against vitamin deficiency.

be converted to the hormone **calcitriol,** which plays a role in the regulation of calcium homeostasis in the body. One role of vitamin E is to serve as an **antioxidant** that prevents electron-seeking molecules such as free radicals from damaging electron-dense molecules in the cell membranes and DNA molecules. Figure 30-24 illustrates this function of vitamin E. Vitamin C may also serve as an antioxidant.

All but one vitamin, vitamin D, cannot be made by the body itself. Bacteria living in the colon make two more: vitamin K and biotin. We must eat vitamins, or molecules we can convert into vitamins, in our food to get the rest. The body can store fat-soluble vitamins—A, D, E, and K—in the liver for later use. Because the body cannot store significant amounts of water-soluble vitamins such as B vitamins and vitamin C, they must be continually supplied in the diet. Table 30-3 lists some of the better-known vitamins, their sources and functions, and symptoms of deficiency.

Minerals

Minerals are at least as important as vitamins in our diet. Minerals are inorganic elements or salts that are found naturally in the earth. Like vitamins, mineral ions can attach to enzymes or other organic molecules and help them work. Of course, minerals such as sodium, chloride, and potassium are essential in relatively large amounts for maintaining the fluid/ion composition of the internal fluid environment (see Chapter 29).

Minerals also function in various other vital chemical reactions. For example, sodium, calcium, and other minerals are required for nerve conduction and for contraction in muscle fibers. Without these minerals, the brain, heart, and respiratory tract would cease to function. Iron is needed to manufacture hemoglobin in red blood cells, and iodine is needed to make thyroid hormones T_3 and T_4. Calcium, phosphorus, and magnesium are required to build the strong structural components of the skeleton.

TABLE 30-3 Major Vitamins

VITAMIN	DIETARY SOURCE	FUNCTIONS	SYMPTOMS OF DEFICIENCY
Vitamin A	Green and yellow vegetables, dairy products, and liver	Maintains epithelial tissue and produces visual pigments	Night blindness and flaking skin
B-complex vitamins			
B_1 (thiamine)	Grains, meat, and legumes	Helps enzymes in the citric acid cycle	Nerve problems (beriberi), heart muscle weakness, and edema
B_2 (riboflavin)	Green vegetables, organ meats, eggs, and dairy products	Aids enzymes in the citric acid cycle	Inflammation of skin and eyes
B_3 (niacin)	Meat and grains	Helps enzymes in the citric acid cycle	Pellagra (scaly dermatitis and mental disturbances) and nervous disorders
B_5 (pantothenic acid)	Organ meat, eggs, and liver	Aids enzymes that connect fat and carbohydrate metabolism	Loss of coordination (rare), decreased gut motility
B_6 (pyridoxine)	Vegetables, meats, and grains	Helps enzymes that catabolize amino acids	Convulsions, irritability, and anemia
B_9 (folic acid)	Vegetables	Aids enzymes in amino acid catabolism and blood production	Digestive disorders and anemia
B_{12} (cyanocobalamin)	Meat and dairy products	Involved in blood production and other processes	Pernicious anemia
Biotin (vitamin H)	Vegetables, meat, and eggs	Helps enzymes in amino acid catabolism and fat and glycogen synthesis	Mental and muscle problems (rare)
Vitamin C (ascorbic acid)	Fruits and green vegetables	Helps in manufacture of collagen fibers; antioxidant	Scurvy and degeneration of skin, bone, and blood vessels
Vitamin D (calciferol)	Dairy products and fish liver oil	Aids in calcium absorption	Rickets and skeletal deformity
Vitamin E (tocopherol)	Green vegetables and seeds	Protects cell membranes from being destroyed; antioxidant	Muscle and reproductive disorders (rare)

TABLE 30-4 Major Minerals

MINERAL	DIETARY SOURCE	FUNCTIONS	SYMPTOMS OF DEFICIENCY
Calcium (Ca)	Dairy products, legumes, and vegetables	Helps blood clotting, bone formation, and nerve and muscle function	Bone degeneration and nerve and muscle malfunction
Chlorine (Cl)	Salty foods	Aids in stomach acid production and acid-base balance	Acid-base imbalance
Cobalt (Co)	Meat	Helps vitamin B_{12} in blood cell production	Pernicious anemia
Copper (Cu)	Seafood, organ meats, and legumes	Involved in extracting energy from the citric acid cycle and in blood production	Fatigue and anemia
Iodine (I)	Seafood and iodized salt	Required for thyroid hormone synthesis	Goiter (thyroid enlargement) and decrease in metabolic rate
Iron (Fe)	Meat, eggs, vegetables, and legumes	Involved in extracting energy from the citric acid cycle and in blood production	Fatigue and anemia
Magnesium (Mg)	Vegetables and grains	Helps many enzymes	Nerve disorders, blood vessel dilation, and heart rhythm problems
Manganese (Mn)	Vegetables, legumes, and grains	Helps many enzymes	Muscle and nerve disorders
Phosphorus (P)	Dairy products and meat	Aids in bone formation and is used to make ATP, DNA, RNA, and phospholipids	Bone degeneration and metabolic problems
Potassium (K)	Seafood, milk, fruit, and meats	Helps muscle and nerve function	Muscle weakness, heart problems, and nerve problems
Selenium (Se)	Nuts, grains, meat, fish, mushrooms, eggs	Needed to make some amino acids; cofactor for enzymes	Heart muscle damage, cartilage degeneration, hypothyroidism
Sodium (Na)	Salty foods	Aids in muscle and nerve function and fluid balance	Weakness and digestive upset
Zinc (Zn)	Many foods	Helps many enzymes	Inadequate growth

Information about some of the more important minerals is summarized in Table 30-4. Like vitamins, minerals are beneficial only when taken in the proper amounts. Some of the minerals listed in Table 30-4 are required in large amounts and some only in trace amounts. Any intake of minerals beyond or below the recommended amount may become unhealthy—perhaps even life threatening.

Recommended *adequate intakes (AIs)* of minerals can change over the life span. For example, Figure 30-25 shows that calcium intake should increase throughout childhood and remain high throughout adulthood. However, the same figure shows that actual intake of calcium among females in the United States tends to fall short during adulthood—thereby increasing the risk for osteoporosis and other disorders.

Figure 30-26 shows the requirement for iron over the life span for both men and women. Although both males and females require a large amount of iron during the spurt of growth in the teenage years, the iron requirement remains high only in women during the rest of adulthood. This difference is explained by the fact that adult women must continually replace the iron lost in

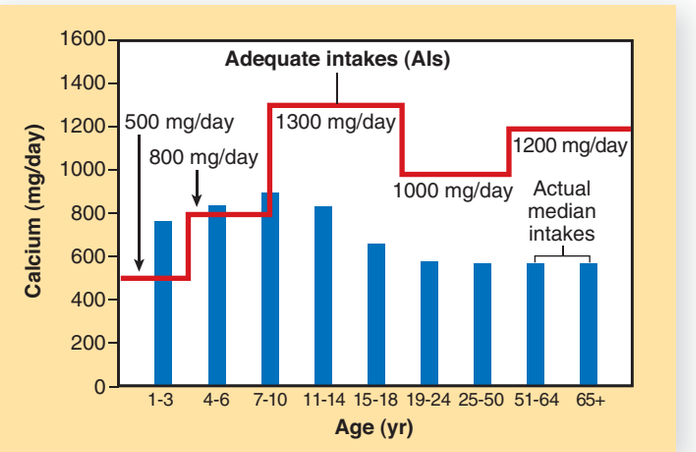


FIGURE 30-25

Calcium intake in women. The chart compares the recommended adequate intake (AIs) of calcium for women over the life span with the actual median intake of calcium among females in the United States.

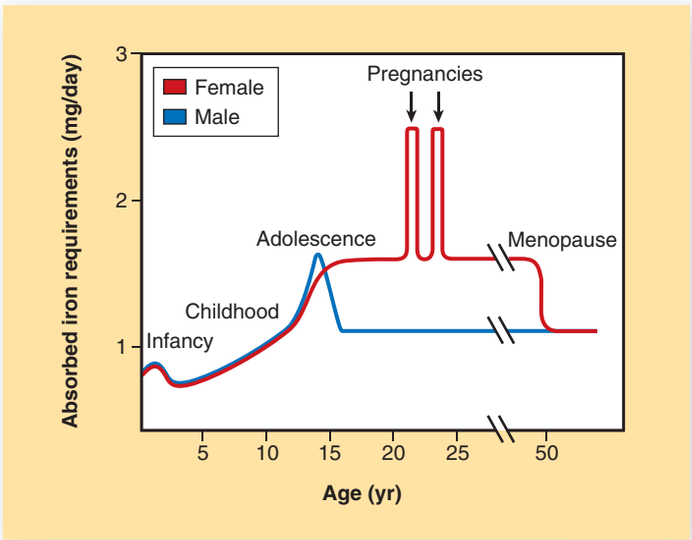


FIGURE 30-26

Iron intake requirements. The chart compares male and female absorbable iron requirements over the life span.

the menstrual flow. Notice that female iron requirements drop to the level of males after menopause. Notice also that the iron requirement peaks during pregnancies—when fetal blood development requires large amounts of iron.

| QUICK CHECK |

17. What is a vitamin?
18. List two functions of minerals in the body.

| A&P CONNECT |

One of the hottest areas in the field of nutrition today is that of *functional foods.* Find out what they are and why you may want to include them in your diet in ***Functional Foods*** online at ***A&P Connect.***

evolve

METABOLIC RATES

Metabolic rate refers to the amount of energy released in the body in a given time by catabolism. It is the energy that must be expended to accomplish various kinds of work. In short, metabolic rate is the catabolic rate, or the rate of energy release.

Metabolic rates are expressed in either of two ways: (1) in terms of the number of kilocalories of heat energy expended per hour or per day or (2) as normal or as a definite percentage above or below normal.

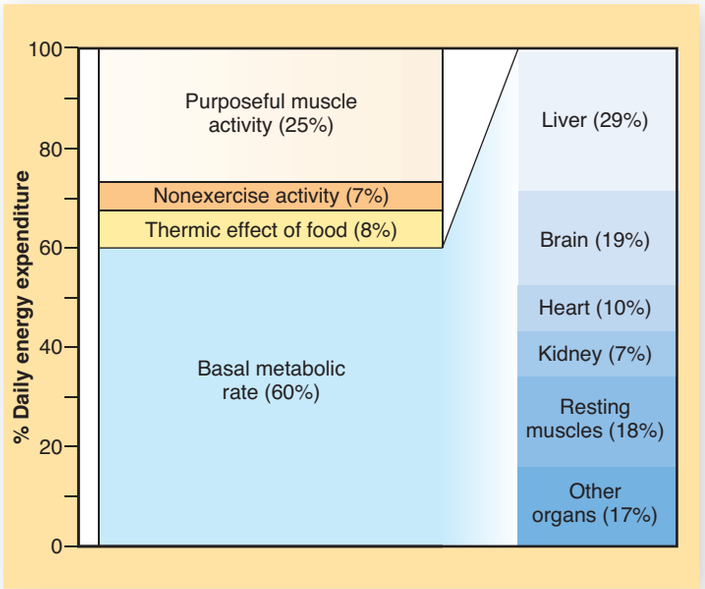


FIGURE 30-27

Daily energy expenditure. The left bar shows the total energy expenditure of the body as a combination of the basal metabolic rate (BMR), the thermic effect of food, everyday tasks, and purposeful exercise. The right bar shows the organs of the body that contribute to the basal metabolic rate.

Basal Metabolic Rate

The **basal metabolic rate (BMR)** is the body's rate of energy expenditure under "basal conditions," namely, when the individual is:

- Awake but resting, that is, lying down and, as far as possible, not moving a muscle.
- In the postabsorptive state (12 to 18 hours after the last meal).
- In a comfortably warm environment (the so-called *thermoneutral zone*, a temperature range at which metabolism is independent of ambient temperature).

Note that the BMR is not the minimum metabolic rate. It does not indicate the smallest amount of energy that must be expended to sustain life. It does, however, indicate the smallest amount of energy expenditure that can sustain life and also maintain the waking state and a normal body temperature in a comfortably warm environment.

FACTORS INFLUENCING BASAL METABOLIC RATE

The BMR is not identical for all individuals because of the influence of various factors (Figures 30-27 and 30-28), some of which are described in the following paragraphs (Box 30-9).

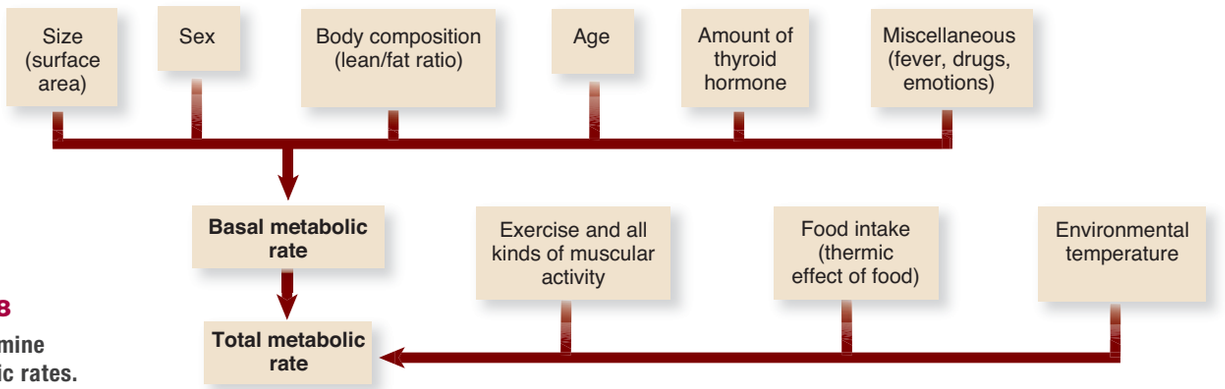


FIGURE 30-28
Some factors that determine basal and total metabolic rates.

Box 30-9 | How BMR Is Determined

Basal metabolic rate (BMR) can be determined by a method called **indirect calorimetry.** The rationale underlying this method is that BMR (expressed as the number of kilocalories of heat produced per unit of time) can be calculated from the amount of oxygen consumed in a given time (part *B* of the figure). BMR can then be expressed as normal, or as a definite percentage above or below normal, by dividing the actual kilocalorie rate by the known average kilocalorie rate for normal individuals of the same size, sex, and age.

Statistical tables, based on research, list estimated normal BMRs. (If BMR was calculated to be 10% above normal, for example, it would be reported as +10.) Are you curious to know the average BMR for a person of your size, sex, and age? If so, take the following steps:

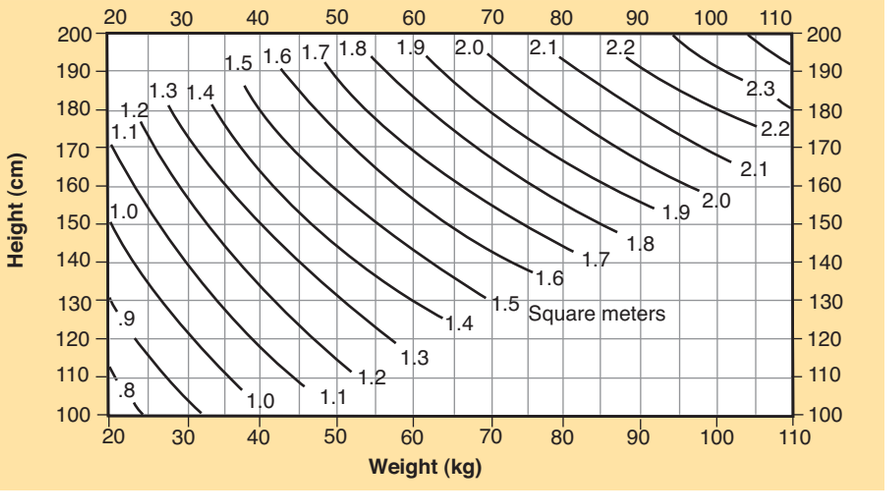
1. Start with your weight in kilograms and your height in centimeters. (Convert pounds to kilograms by dividing pounds by 2.2. Convert inches to approximate centimeters by multiplying inches by 2.5.) For example, 110 pounds = 50 kg; 5 feet, 3 inches = 158 cm.
2. Convert your weight and height to square meters by using the chart shown here (part *B* of the figure). For example, a weight of 50 kg and height of 158 cm = about 1.5 square meters of body surface area.
3. Find your age and sex in Table 30-5 and then multiply the number of kilocalories per square meter per hour given there by your square meters of surface area and then by 24. For example, the average BMR per day for a 25-year-old woman with a weight of 110 pounds and height of 5 feet, 3 inches = 1332 kcal (37 × 1.5 × 24).

A quick rule of thumb for estimating a young woman's BMR in kcal/hr is to multiply her weight in pounds by 12.

A



B



Measuring BMR. A, Indirect calorimetry calculates the rate of metabolism by measuring the rate at which oxygen is consumed. **B,** BMR estimate chart.

TABLE 30-5 Basal Metabolism

	KILOCALORIES PER HOUR PER SQUARE METER BODY SURFACE	
AGE (YR)	MALE	FEMALE
10-12	51.5	50.0
12-14	50.0	46.5
14-16	46.0	43.0
16-18	43.0	40.0
18-20	41.0	38.0
20-30	39.5	37.0
30-40	39.5	36.5
40-50	38.5	36.0
50-60	37.5	35.0
60-70	36.5	34.0

Size

In computing the BMR, size is usually indicated by the amount of the body's surface area. It is computed from the individual's height and weight. A large individual has the same BMR as a small person per square meter of body surface, if other conditions are equal. However, because a large individual has more square meters of surface area, the BMR is greater than that of a small individual. For example, the BMR for a man in his 20s is about 40 kcal per square meter of body surface per hour (Table 30-5). However, a large man with a body surface area of 1.9 square meters would have a BMR of 76 kcal per hour, whereas a smaller man with a surface area of perhaps 1.6 square meters would have a BMR of only 64 kcal per hour. The average surface area for American adults is 1.6 square meters for women and 1.8 square meters for men.

Body Composition

Lean tissue is mostly "working tissue" that uses energy at a faster rate than does storage tissue or fat tissue. Therefore, the higher the ratio of lean tissue to fat tissue in a person, the higher the BMR.

Gender

Men oxidize their food approximately 5% to 7% faster than women do. Therefore their BMRs are about 5% to 7% higher for a given size and age. A man 5 feet, 6 inches tall weighing 140 pounds, for example, has a 5% to 7% higher BMR than a woman of the same height, weight, and age. This gender difference in BMR probably results from the difference in the proportion of body fat, which is determined by sex hormones. Women tend to have a higher percentage of body fat (and thus a lower total lean mass) than men do (Figure 30-29). Fat tissue is less metabolically active than lean tissues such as muscle. Differences in total lean mass not related to gender also affect the BMR. The relationship of BMR to sex and age is illustrated in Figure 30-30.

Age

That the fires of youth burn more brightly than those of age is a physiological and a psychological fact. In general, the younger the individual, the higher the BMR for a given size and sex (see Table 30-5). Exception: the BMR is slightly lower at birth than it is a few years later. That is to say, the rate increases slightly during the first 3 to 6 years, then starts to decrease and continues to do so throughout life.

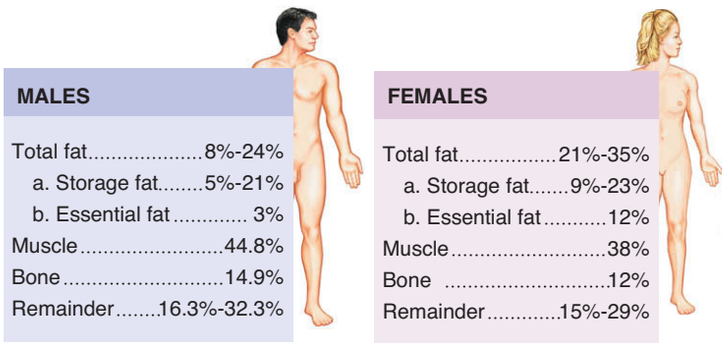


FIGURE 30-29

Body composition. Estimated values in healthy men and women.

Thyroid Hormone

Thyroid hormone (T_3 and T_4) stimulates basal metabolism. Without a normal amount of this hormone in the blood, a normal BMR cannot be maintained. When an excess of thyroid hormone is secreted, foods are catabolized faster, much as wood in a fireplace is burned faster when the draft is open. Deficient thyroid secretion, on the other hand, slows the rate of metabolism.

Body Temperature

Fever increases the BMR. For every degree Celsius increase in body temperature, metabolism increases about 13%. A decrease in body temperature (hypothermia) has the opposite effect. Metabolism decreases, and because it does, cells use less oxygen than they normally do. This knowledge has been applied clinically by using hypothermia in certain situations—for example, in open-heart surgery. Because circulation is reduced or interrupted during this

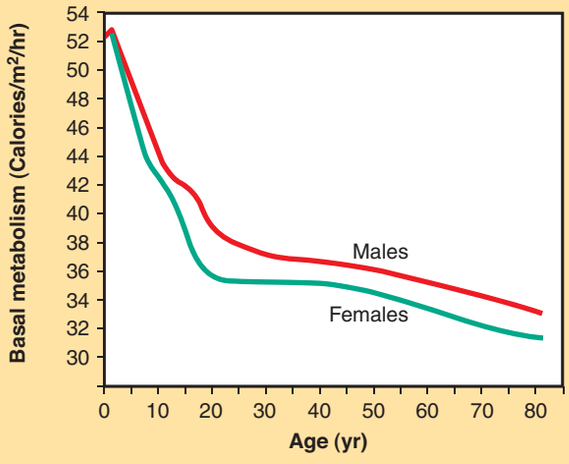


FIGURE 30-30

Basal metabolic rates over the life span. The chart shows normal basal metabolic rates (BMRs) as function of age for each sex.

procedure, oxygen supply necessarily decreases. Cells can tolerate this decreased oxygen supply reasonably well if their oxygen need has also decreased. Induced hypothermia decreases their rate of metabolism and thereby decreases their use of oxygen.

Drugs

Certain drugs, such as caffeine, amphetamine, and levothyroxine, increase the BMR.

Other Factors

Other factors, such as *emotions*, *pregnancy*, and *lactation* (milk production), also influence basal metabolism. All of these factors increase the BMR.

Total Metabolic Rate

Total metabolic rate is the amount of energy used or expended by the body in a given time. It is often expressed in kilocalories per hour or per day. Most of the factors that determine the total metabolic rate are shown in Figures 30-27 and 30-28. Of these, the main direct determinants are as follows.

Factor 1—the basal metabolic rate, that is, the energy used to do the work of maintaining life under the basal conditions previously described. Basal metabolic rate usually constitutes about 55% to 60% of the total metabolic rate.

Factor 2—the energy used to do all kinds of skeletal muscle work. This encompasses the simplest activities such as feeding oneself or sitting up in bed to the most strenuous kind of physical labor or exercise.

Factor 3—the *thermic effect* of foods. The metabolic rate increases for several hours after a meal, apparently because of the energy needed for metabolizing foods. Carbohydrates and fats have a thermic effect of about 5%. Proteins have a much higher thermic effect, about 30%. This means that for every 100 kcal of protein, 30 kcal are used for processes such as deamination and oxidation of the protein, leaving just 70 kcal available for other cell work. For this reason, proteins are "worth" fewer calories.

Energy Balance and Body Weight

When we say that the body maintains a state of energy balance, we mean that its energy input equals its energy output. Energy input per day equals the total calories (kilocalories) in the food ingested per day. Energy output equals the total metabolic rate expressed in kilocalories. You may be wondering what energy intake, output, and balance have to do with body weight. "Everything" would be a fairly good one-word answer. Or, to be somewhat more explicit, the following basic principles describe the relationships between these factors:

- Body weight remains constant (except for possible variations in water content) when the body maintains energy balance—when the total calories in the food ingested equals the total metabolic rate. Example: If you have a total metabolic rate of 2000 kcal per day and if the food you eat per day yields 2000 kcal, your body will be maintaining energy balance and your weight will stay constant.
- Body weight increases when energy input exceeds energy output—when the total calories of food intake per day is greater than the total calories of the metabolic rate. A small amount of the excess energy input is used to synthesize glycogen for storage in the liver and muscles. The rest is used for synthesizing fat and storing it in adipose tissue. If you were to eat 3000 kcal each day for a week and if your total metabolic rate were 2000 kcal per day, you would gain weight. How much you would gain you can discover by doing a little simple arithmetic:

  Total energy input for week = 21,000 kcal

  Total energy output for week= −14,000 kcal

  Excess energy input for week = 7000 kcal

  Approximately 3500 kcal are used to synthesize 1 pound of adipose tissue. Hence, at the end of this 1 week of "overeating"—of eating 7000 kcal over and above your total metabolic rate—you would have gained about 2 pounds.

- Body weight decreases when energy input is less than energy output—when the total number of calories in the food eaten is less than the total metabolic rate. Suppose you were to eat only 1000 kcal a day for a week and that you have a total metabolic rate of 2000 kcal per day. By the end of the week, your body would have used a total of 14,000 kcal of energy for maintaining life and doing its many kinds of work. All 14,000 kcal of this actual energy expenditure had to come from catabolism of foods because this is the body's only source of energy. Catabolism of ingested food supplied 7000 kcal, and catabolism of stored food supplied the remaining 7000 kcal. That week your body would not have maintained energy balance, nor would it have maintained weight balance. It would have incurred an energy deficit paid out of the energy stored in approximately 2 pounds of body fat. In short, you would have lost about 2 pounds.

Foods are stored primarily as glycogen and fats. Many cells catabolize them preferentially in this order: carbohydrates, then fats. (Skeletal muscle cells, however, seem to put fat first in their order of preference.) If there is no food intake, almost all of the glycogen is estimated to be used up in a matter of 1 or 2 days (Figure 30-31). Then, with no more carbohydrate to act as a fat sparer, fat is catabolized. How long it takes to deplete all of this reserve food depends, of course, on how much adipose tissue the individual has when starting the starvation diet. Finally, with no more fat available, tissue proteins are catabolized (see Figure 30-31). Because significant amounts of protein are not "stored" for use in catabolism, important structural and functional proteins are quickly depleted. Thus death soon ensues.

MECHANISMS FOR REGULATING FOOD INTAKE

Mechanisms for regulating food intake are still not clearly established. That the hypothalamus plays a part in these mechanisms, however, seems certain. Numerous studies seem to indicate that a cluster of neurons in the lateral hypothalamus function as an **appetite center**—meaning that impulses from them bring about increased appetite. This effect is often called an **orexigenic effect** (meaning an "appetite-producing" effect).

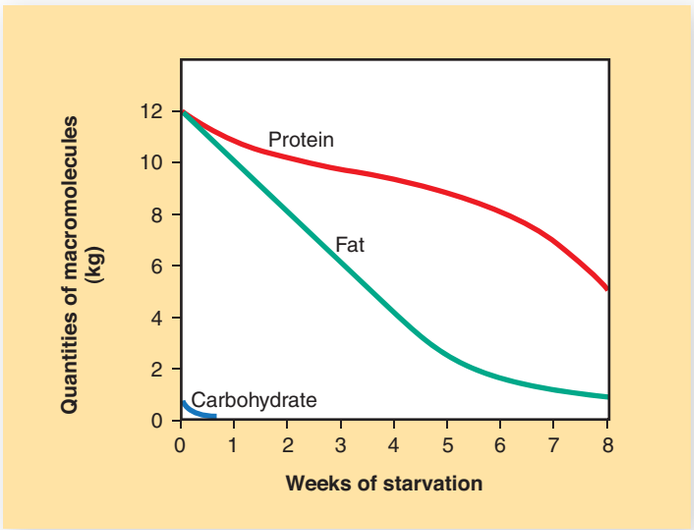


FIGURE 30-31

Effects of starvation on the body. Three major macromolecules serve as primary energy sources: carbohydrates, fats, and proteins. During starvation, the carbohydrate stores (glycogen) are rapidly depleted. However, stored lipids can mobilize and provide much of our energy needs for several weeks. Eventually, lipid stores run low and the body starts using proteins as a major source of energy—causing the breakdown of muscle and other protein-rich tissues. Muscle damage during starvation usually leads to death.

Additional data suggest that a group of neurons in the ventral medial nucleus of the hypothalamus functions as a **satiety center**—meaning that impulses from these neurons decrease appetite so that we feel sated, or satisfied. This effect is often called an **anorexigenic effect** (meaning "producing an appetite loss" effect).

What acts directly on both of these feeding centers to stimulate or depress them is still being worked out by researchers.

One factor is the temperature of the blood circulating to the hypothalamus. A moderate decrease in blood temperature stimulates the appetite center (and inhibits the satiety center). Result: The individual has an appetite, wants to eat, and probably does. An increase in blood temperature produces the opposite effect, a depressed appetite **(anorexia).** One well-known instance of this effect is the loss of appetite in persons who have a fever.

Another factor is blood glucose concentration and the rate of glucose use. A low blood glucose concentration or low glucose use stimulates the appetite center, whereas a high blood glucose concentration inhibits it. This may be the action of a group of hormones called **orexins** or *hypocretins* produced in the hypothalamus in response to low blood glucose levels.

More recently, a variety of hormones and other regulators have been identified that have a profound impact on the feeding centers of the brain. The hypothalamus itself produces several hormones and neurotransmitters that affect the feeding centers, as you can see in Table 30-6. In addition, appetite-altering factors (hormones and neurotransmitters) are produced in many other organs such as

TABLE 30-6 Examples of Appetite-Regulating Factors*

OREXIGENIC FACTORS (STIMULATE APPETITE)	ANOREXIGENIC FACTORS (INHIBIT APPETITE)	SOURCE
	Leptin Interleukin 18 (IL-18)	Adipose tissue
Cortisol		Adrenal cortex
Ghrelin (GHRL)	Cholecystokinin (CCK) Glucagon-like peptide-1 (GLP-1) Oxyntomodulin (OXM) Peptide YY_{3-36} (PYY_{3-36})	GI tract
Endogenous opioid peptides (EOP) Galanin (GAL) Gamma-aminobutyric acid (GABA) Neuropeptide Y (NPY) Norepinephrine (NE) Orexins	Alpha-melanocyte–stimulating hormone (α-MSH) Cocaine- and amphetamine-regulated transcript (CART) Corticotropin-releasing hormone (CRH)	Hypothalamus
	Glucose	Liver
Emotions Environmental stimuli Food sensations Internal stimuli (e.g., blood temperature, glucose) Lifestyle choices and habits	Emotions Environmental stimuli Food sensations Internal stimuli (e.g., blood temperature, glucose) Lifestyle choices and habits	Nervous system†
	Insulin Pancreatic polypeptide (PP)	Pancreas

*Hormones, neurotransmitters, and other factors that affect feeding centers in the hypothalamus.
†Nervous factors not specifically hypothalamic in origin. *GI,* Gastrointestinal.

the liver, adipose tissue, pancreas, GI tract, and autonomic nerve pathways (especially the vagal nerve). Of course, factors such as daily eating habits or patterns, emotional responses, the sensations of food, and many others must also be involved in regulating or affecting appetite.

Unquestionably, many factors operate together as a complex mechanism for regulating food intake—a mechanism that is still incompletely understood.

| QUICK CHECK |

19. Give one of the two ways in which metabolic rates can be expressed.
20. Name three of the factors that influence basal metabolic rate.
21. Distinguish between basal metabolic rate and total metabolic rate.
22. In which division of the brain would you find the control centers for regulating food intake?

Cycle of LIFE

Nutrition and Metabolism

The importance of proper nutrition to an individual's well-being begins at the moment of conception and continues until death. In the womb, various nutrients must be obtained from the mother's blood in sufficient quantity to ensure normal growth and development.

One critical nutrient during fetal development, infancy, and childhood is protein. Sufficient proteins, containing all the essential amino acids, are required to permit normal development of the nervous system, muscle tissues, and other vital structures.

Another critical nutrient during the early years of life is the mineral calcium. Large quantities of calcium are needed by a growing body to maintain normal development of the skeleton and other tissues. In the womb, a steady supply of calcium in the mother's blood is maintained by increased levels of the parathyroid hormone (PTH). Recall from Chapter 19 that PTH increases blood calcium levels by removing it from storage in the bones.

Unless a pregnant woman consumes enough calcium to replace this calcium lost from bones, she may suffer from the bone-softening effects of calcium deficiency. If proteins, calcium, or other necessary nutrients are in short supply anytime before the beginning of adulthood, the consequences may be permanent. For example, bone deformities resulting from a lack of calcium during childhood could become permanent if not corrected or compensated for before the skeleton ossifies completely.

In late adulthood, the number of food calories needed declines because the metabolic rate declines. This metabolic decline is thought to result largely from age-related changes in the balance of metabolic hormones such as thyroid hormones (T_3 and T_4). Even though the number of required food calories declines, the overall balance of nutrients consumed must be maintained to preserve proper metabolic function. Some nutrients, such as calcium, may be needed in greater quantity in older adults to compensate for (or avoid) age-related bone loss or other conditions.

the BIG picture

Nutrition, Metabolism, and the Whole Body

Of all the topics we have discussed so far, the topic of nutrition and metabolism has the most easily seen role in the "big picture" of human body function. Every cell in the body must maintain the operation of its metabolic pathways to ensure its survival. Anabolic pathways are required to build the various structural and functional components of the cells. Catabolic pathways are required to convert energy to a usable form. Catabolic pathways are also needed to degrade large molecules into small subunits that can be used in anabolic pathways. Of course, the basic nutrient molecules—carbohydrates, fats, and proteins of the correct type—must be available to each cell to carry out these metabolic processes. Besides the basic nutrient molecules, cells also require small amounts of specific vitamins and minerals needed to produce the structural and functional components necessary for cellular metabolism.

Various body systems operate to make sure that essential nutrients reach the cells as needed to maintain metabolism in a manner that preserves relative constancy of the internal environment. For example, the nervous, skeletal, and muscular systems make it possible for us to take in complex foods from our external environment. The digestive system reduces these complex nutrients to simpler, more usable nutrients—then provides the mechanisms that allow us to absorb them into the internal environment. The circulatory system—both the cardiovascular and the lymphatic circulations—transports the absorbed nutrients to the individual cells for immediate use or to the liver or other organs for temporary storage. The endocrine system regulates the balance between immediate use and storage. The respiratory system, working with the cardiovascular system, provides the oxygen needed for oxidative phosphorylation—that is, using the citric acid cycle and electron transport system to transfer energy to ATP. These two systems also provide a mechanism for removing waste carbon dioxide (CO_2) generated by the catabolism of nutrient molecules. Likewise, the urinary system provides a mechanism for removing waste urea generated by protein catabolism. Even the integumentary system becomes involved, by producing vitamin D in the presence of sunlight.

Metabolism, with all the physiological mechanisms that support it, could be described as the essential process of life. It is, after all, the sum total of all the biochemical processes that distinguish a living organism from a nonliving object.

MECHANISMS of DISEASE

METABOLIC AND NUTRITIONAL DISORDERS

Disorders characterized by a disruption or imbalance of normal metabolism can be caused by several different factors. For example, **inborn errors of metabolism** are a group of genetic conditions involving a deficiency or absence of a particular enzyme. Specific enzymes are required by cells to carry out each step of every metabolic reaction. Although an abnormal genetic code may affect the production of only a single enzyme, the resulting abnormal metabolism may have widespread effects. Specific diseases resulting from inborn errors of metabolism, such as **phenylketonuria,** are discussed in Chapter 37.

A number of metabolic disorders are complications of other conditions. For example, you may recall from Chapter 19 that both hyperthyroidism and hypothyroidism have profound effects on the basal metabolic rate. Diabetes mellitus affects metabolism throughout the body when an insulin deficiency limits the amount of glucose available for use by the cells.

Some metabolic disorders result from normal mechanisms in the body that maintain homeostasis. For example, the body has several mechanisms that maintain a relatively constant level of glucose in the blood—glucose required by cells for life-sustaining catabolism. As mentioned earlier in this chapter, during starvation or as a result of certain eating disorders, these mechanisms are taken to the extreme as they attempt to maintain blood glucose homeostasis. A few of the more well known eating and nutrition disorders are briefly described later in Mechanisms of Disease.

Body Mass Index (BMI)

The **body mass index (BMI)** is a measure of a person's proportion of body weight to height. The BMI was developed in the late twentieth century as a way for researchers to easily assess body-fat percentages in large populations so they could track trends in obesity and other health conditions.

To calculate a BMI, simply divide weight (in kilograms) by the square of height (in meters): BMI = kg/m^2. To determine kilogram weight, divide the number of pounds by 2.2. To determine meter height, divide total inches by 39.4. Thus the BMI can quickly tell individuals whether they are above or below their ideal weight, and by approximately how much.

As discussed in the following sections and illustrated in Figure 30-32, a BMI that is too high or too low is associated with an increased risk of death. However, remember that BMI is most useful when looking at trends in a population as a whole and not as useful in individual risk assessments. Factors such as gender, age, and genetics play a role in such health assessments, so BMI alone is not sufficient. Measurements of waist or thigh circumference and body fat percentages (see Box 6-4 p. 147) are often used along with BMI to give a more complete picture.

Metabolic Syndrome

Metabolic syndrome is a collection of risk factors for coronary artery disease, stroke, and type-2 diabetes. One of the risk factors that occurs in metabolic syndrome is large waist circumference—the "apple-shaped" central obesity previously described in Box 1-1 on p. 18. Another important factor is *insulin resistance*. As target cells respond less efficiently to insulin, glucose cannot enter cells and the body must move triglycerides and other lipids into the blood to supply energy needs. Thus, *hyperlipidemia* (elevated blood lipids, such as high triglyceride and LDL cholesterol) are also risk factors included in this syndrome. Other risk factors included are low HDL cholesterol, hypertension, increased blood clotting, elevated inflammation mediators, and related factors. Metabolic syndrome can be treated with diet, exercise, cholesterol-lowering therapy, and other strategies to reduce central obesity.

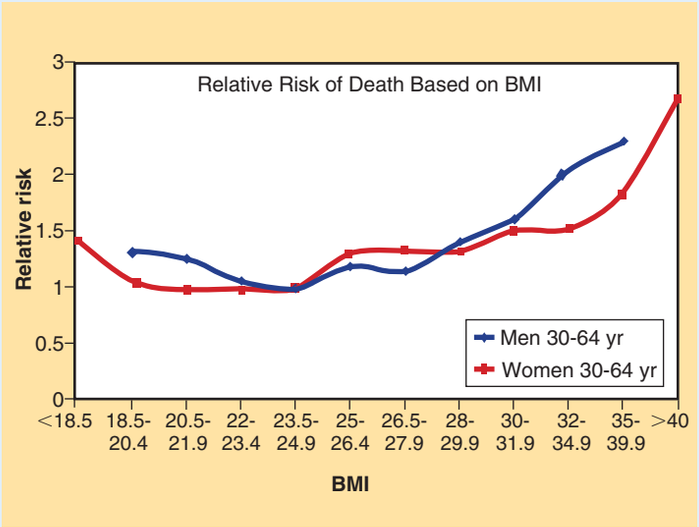


FIGURE 30-32

Body mass index (BMI) and risk of death. Mortality (death) risk is higher in individuals with a high or low BMI.

Eating Disorders

Eating disorders have been a part of the medical literature for many years, but interest and concern regarding these disorders are growing because the number of reported cases has increased dramatically. The two most common eating disorders are called *anorexia nervosa* and *bulimia*. Neither illness is completely understood, and successful treatment is often varied and sometimes controversial.

Anorexia Nervosa

Anorexia nervosa is primarily a disease of young adults. Most individuals affected are female (90% to 95%) and from 12 to 25 years of age. As many as 4% of college-aged students suffer from this condition to some degree. These individuals have a disturbed body image and an intense fear of obesity and therefore diet with a vengeance. They almost always develop unusual eating rituals

and scrupulously monitor and restrict their food intake. Anorexic individuals literally starve themselves and, as a result, suffer serious medical complications. The illness is characterized by a 20% to 25% loss of body mass, accompanied by slowed or impaired intellectual functioning. People affected are usually involved in excessive exercise and pursue ultimate thinness, regardless of their health. In women, menstruation ceases (amenorrhea), and the basal metabolic rate is decreased as a result of starvation. These individuals suffer from many skin abnormalities and an assortment of psychological, cardiovascular, and hormonal problems. They are at increased risk for sudden death from complications directly related to excessive weight loss and nutritional deficiency. Treatment is directed at resolution of both medical and psychological problems. In addition to psychotherapy and weight stabilization, pharmacological treatment with antidepressants has been used to improve mood and self-image.

Bulimia

Bulimia is an illness characterized by an eating and vomiting, or purging, cycle. It is sometimes referred to as **binge-purge syndrome.** The disease is said to affect about 1% of college-aged students. Most people who have bulimia are relatively young, single, white females. The mean age is 25, but the age of patients appears to be increasing. People suffering from bulimia have an uncontrollable urge for food that leads to massive overeating (binging) that is followed by repeated forced vomiting and laxative abuse (purging). Loss of gastric and intestinal contents often leads to serious fluid and electrolyte imbalance. The result is often the development of neurological problems such as convulsions, tetany, and seizures. Vomiting may also cause aspiration pneumonia, erosion of tooth enamel, trauma of the mouth and esophagus, and infection of the salivary glands. The longer the disease is allowed to continue without treatment, the greater the increase in mortality from medical complications. Many people who have bulimia suffer from major depression and have concomitant social problems such as alcohol abuse. About a fourth of people with bulimia are chemically dependent, and many have been victims of sexual abuse. They are especially prone to self-mutilation and suicide attempts. Nutritional counseling, psychotherapy, and treatment with antidepressants help bulimic patients cope with stress and break the binge/purge cycle.

Obesity

Obesity is not an eating disorder itself but may be a symptom of chronic overeating behavior. Like anorexia nervosa and bulimia, eating disorders characterized by chronic overeating usually have an underlying emotional cause. Obesity may also result from metabolic disorders. Obesity is defined as an abnormal increase in the proportion of fat in the body. Usually, a person with a BMI over 30 is considered moderately obese. A person with a BMI over 40 is considered to be extremely obese. Most of the excess fat is stored in the subcutaneous tissue and around the viscera. Obesity is a risk factor in various life-threatening diseases, including many forms of cancer, diabetes, and heart disease (see Figure 30-32).



FIGURE 30-33

Protein-calorie malnutrition (PCM). PCM is an abnormal condition resulting from a deficiency of calories in general and protein in particular. Here, two forms of advanced PCM, marasmus **(A)** and kwashiorkor **(B),** are shown.

Nutritional Disorders

Protein-Calorie Malnutrition

Protein-calorie malnutrition (PCM) is an abnormal condition resulting from a deficiency of calories in general and protein in particular. PCM is likely to result from reduced intake of food, but may also be caused by increased nutrient loss or increased use of nutrients by the body. Mild cases occur frequently in those with illness; as many as one in five patients admitted to the hospital are significantly malnourished. More severe cases of PCM are likely to occur in parts of the world where food, especially protein-rich food, is relatively unavailable. There are two forms of advanced PCM: **marasmus** and **kwashiorkor** (kwah-shee-OR-kor) (Figure 30-33). Marasmus results from an overall lack of calories and proteins, such as when sufficient quantities of food are not available. Marasmus is characterized by progressive wasting of muscle and subcutaneous tissue accompanied by fluid and electrolyte imbalances. Kwashiorkor results from a protein deficiency in the presence of sufficient calories, as when a child is weaned from milk to low-protein foods. At the same time, a child affected with kwashiorkor is also likely to have an underlying infection that further increases calorie and protein needs. Like marasmus, kwashiorkor also causes wasting of tissues, but unlike marasmus, it also causes pronounced ascites (abdominal bloating) and flaking dermatitis. The ascites results from a deficiency of plasma proteins, which changes the osmotic balance of the blood and thus promotes osmosis of water from the blood into the peritoneal space.

Vitamin Disorders

Vitamin deficiency, or **avitaminosis** (ay-vye-tah-mi-NO-sis), can lead to severe metabolic problems. For example, *avitaminosis C* (vitamin C deficiency) can lead to scurvy. Scurvy results from the inability of the body to manufacture and maintain collagen fibers. As you may have gathered from your studies thus far, collagen fibers compose the connective tissues that hold most of the body together. In scurvy, the body literally falls apart in the same way that a neglected house eventually falls apart (Figure 30-34). Other details about scurvy and other types of avitaminosis are given in Table 30-3.

Some forms of **hypervitaminosis**—or vitamin excess—can be just as serious as a deficiency of vitamins. For example, chronic *hypervitaminosis A* can occur if large amounts of vitamin A—more than 10 times the recommended dietary allowance (RDA)—are consumed daily over a period of 3 months or more (Figure 30-35). This condition is first manifested as dry skin, hair loss, anorexia (appetite loss), and vomiting. However, it may progress to severe headaches and mental disturbances, liver enlargement, and occasionally cirrhosis. Acute hypervitaminosis A, characterized by vomiting, abdominal pain, and headache, can occur if a massive overdose is ingested. Excesses of the fat-soluble vitamins (A, D, E, and K) are generally more serious than excesses of the water-soluble vitamins (B complex and C).



FIGURE 30-34

Scurvy. In scurvy, lack of vitamin C impairs the normal maintenance of collagen-containing connective tissues, causing bleeding and ulceration of the skin, gums, and other tissues, as these lesions on the skin **(A)** and inflamed gingiva **(B)** show.

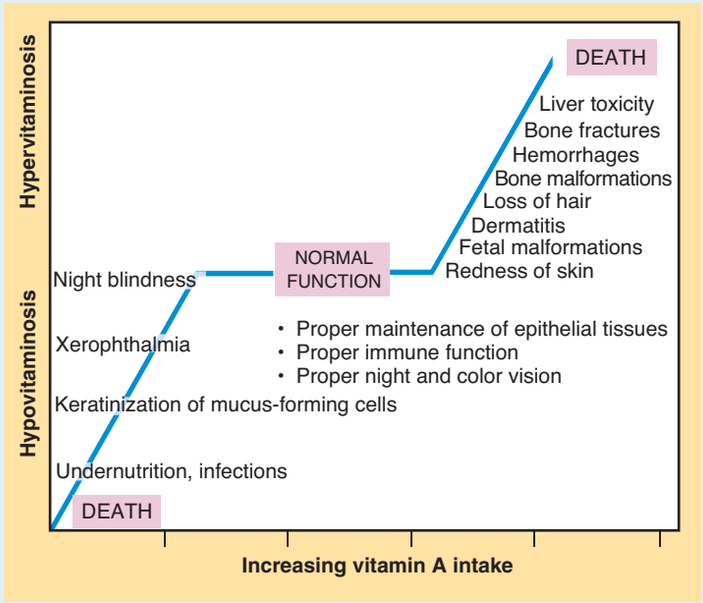


FIGURE 30-35

Vitamin A intake. This chart shows how changing the amount of vitamin A in the diet can lead to hypovitaminosis A or hypervitaminosis A. In extreme, either can lead to death.

LANGUAGE OF SCIENCE *(continued from p. 931)*

catabolism
(kah-TAB-oh-liz-em)
[*catabol-* **break down,** *-ism* **action**]

cellulose
(SEL-yoo-lohs)
[*cell-* **storeroom (cell),** *-ul-* **small,** *-ose* **carbohydrate**]

chylomicron
(kye-loh-MYE-kron)
[*chylo-* **juice (chyle),** *-micro-* **small,** *-on* **particle**]

citric acid cycle
(SIT-rik)
[*citr-* **citron tree,** *-ic* **relating to,** *acidus* **sour,** *kyklos* **circle**]

coenzyme
(koh-EN-zyme)
[*co-* **together,** *-en-* **in,** *-zyme* **ferment**]

coenzyme A (CoA)
(koh-EN-zyme)
[*co-* **together,** *-en-* **in,** *-zyme* **ferment,** *A* **first letter of Roman alphabet**]

Cori cycle
(KOR-ee)
[*Carl Ferdinand Cori* **and** *Gerty Theresa Radnitz Cori* **Czech-born American biochemists,** *cycl-* **circle**]

deamination
(dee-am-i-NAY-shun)
[*de-* **undo,** *-amin-* **ammonia compound,** *-ation* **process**]

electron transport system (ETS)
[*electr-* **electric,** *-on* **unit,** *trans-* **across,** *-port* **carry**]

essential fatty acid
[*acid* **sour**]

flavin adenine dinucleotide (FAD)
(FLAY-vin AD-en-een dye-NOO-klee-oh-tyde)
[*flav-* **yellow,** *-in* **substance,** *aden-* **gland,** *-ine* **chemical,** *di-* **two,** *nucleo-* **kernel (nucleus),** *-t-* **combining form,** *-ide* **chemical**]

free fatty acid (FFA)
[*acidus* **sour**]

glucagon
(GLOO-kah-gon)
[*gluca-* **sweet (glucose),** *-agon* **lead or bring**]

gluconeogenesis
(gloo-koh-nee-oh-JEN-eh-sis)
[*gluco-* **sweet (glucose),** *-neo-* **new,** *-gen-* **produce,** *-esis* **process**]

glucose phosphorylation
(GLOO-kohs fos-for-i-LAY-shun)
[*gluco-* **sweet,** *-ose* **carbohydrate (sugar),** *phos-* **light,** *-phor-* **carry,** *-yl-* **chemical,** *-ation* **process**]

glycogenesis
(glye-koh-JEN-eh-sis)
[*glyco-* **sweet,** *-gen-* **produce,** *-esis* **process**]

glycogenolysis
(glye-koh-jeh-NOL-ih-sis)
[*glyco-* **sweet (glucose),** *-gen-* **produce,** *-o-* **combining form,** *-lysis* **loosening**]

glycolysis
(glye-KOHL-i-sis)
[*glyco-* **sweet (glucose),** *-o* **combining form,** *-lysis* **loosening**]

incretin
(IN-kre-tin)
[*in-* **in,** *-cret-* **secrete,** *-in* **substance**]

insulin
(IN-suh-lin)
[*insul-* **island,** *-in* **substance**]

ketogenesis
(kee-toh-JEN-eh-sis)
[*keto-* **acetone,** *-gen-* **produce,** *-esis* **process**]

Krebs cycle
[*Sir Hans Adolf Krebs* **British biochemist,** *cycl-* **circle**]

leptin
(LEP-tin)
[*lept-* **thin,** *-in* **substance**]

lipid
(LIP-id)
[*lip-* **fat,** *-id* **form**]

lipogenesis
(lip-oh-JEN-eh-sis)
[*lipo-* **fat,** *-gen-* **produce,** *-esis* **process**]

lipoprotein
(lip-oh-PROH-teen)
[*lipo-* **fat, protein**]

macronutrients
(MAK-roh-NOO-tree-ents)
[*macro-* **large,** *nutri-* **nourish,** *-ent* **agent**]

metabolic rate
(met-ah-BOL-ik)
[*metabol-* **change,** *-ic* **relating to**]

metabolic syndrome
(met-ah-BOL-ik SIN-drohm)
[*metabol-* **change,** *-ic* **relating to,** *syn-* **together,** *-drome* **running or (race)course**]

metabolism
(meh-TAB-oh-liz-em)
[*metabol-* **change,** *-ism* **process**]

micronutrients
(MYE-kroh-NOO-tree-ents)
[*micro-* **small,** *nutri-* **nourish,** *-ent* **agent**]

negative nitrogen balance
(NEG-ah-tiv NYE-troh-jen)
[*nitro-* **soda,** *-gen* **produce**]

nicotinamide adenine dinucleotide (NAD)
(nik-oh-TIN-ah-myde AD-eh-neen dye-NOO-klee-oh-tyde)
[*Jacque Nicot* **French diplomat (brought tobacco to France),** *-in-* **substance (after plant genus** *Nicotiana***),** *-am-* **ammonia,** *-ide* **chemical,** *aden-* **gland,** *-ine* **derived substance,** *di-* **two,** *nucleo-* **kernel (nucleus),** *-t-* **combining form,** *-ide* **chemical**]

nitrogen balance
(NYE-troh-jen)
[*nitro-* **soda,** *-gen* **produce**]

nutrition
(noo-TRIH-shun)
[*nutri-* **nourish,** *-tion* **process**]

orexigenic effect
(oh-rek-sih-JEN-ik)
[*orex-* **appetite,** *-gen-* **produce,** *-ic* **relating to**]

orexin
(oh-REK-sin)
[*orex-* **appetite,** *-in* **substance**]

oxidative phosphorylation
(ahk-si-DAY-tiv fos-for-i-LAY-shun)
[*oxi-* **sharp (oxygen),** *-id-* **chemical (***-ide***),** *-at-* **action of** *(-ate),* *-ive* **relating to,** *phos-* **light,** *-phor-* **carry,** *-yl-* **chemical,** *-ation* **process**]

phosphorylation
(fos-for-i-LAY-shun)
[*phos-* **light,** *-phor-* **carry,** *-yl-* **chemical,** *-ation* **process**]

positive nitrogen balance
(POZ-it-iv NYE-troh-jen)
[*nitro-* **soda,** *-gen* **produce**]

protein balance
(PROH-teen)

satiety center
(sah-TYE-eh-tee)
[*sati-* **enough,** *-ety* **state**]

saturated
(SACH-yoo-ray-ted)

total metabolic rate
(met-ah-BOL-ik)
[*metabol-* **change,** *-ic* **relating to**]

tricarboxylic acid (TCA) cycle
(try-kar-bok-SIL-ik)
[*tri-* **three,** *-carbo-* **carbon,** *-oxy-* **sharp (oxygen),** *-yl-* **chemical,** *-ic* **relating to,** *acid* **sour,** *cyclo-* **circle**]

triglyceride
(try-GLI-ser-ide)
[*tri-* **three,** *-glycer-* **sweet,** *-ide* **chemical**]

unsaturated
(un-SATCH-yoo-ray-ted)

vitamins
(VYE-tah-mins)
[*vita-* **life,** *-amin-* **ammonia compound**]

LANGUAGE OF MEDICINE

anorexia nervosa
(an-oh-REK-see-ah ner-VOH-sah)
[*an-* **without**, *-orex-* **appetite**, *-ia* **condition**, *nerv-* **nerve**, *-osa* **relating to**]

avitaminosis
(ay-vye-tah-mi-NO-sis)
[*a-* **without**, *-vita-* **life**, *-amin-* **ammonia compound**, *-osis* **condition**]

binge-purge syndrome
[*syn-* **together**, *-drome* **running or (race)course**]

body mass index (BMI)

bulimia
(boo-LEE-mee-ah)
[*bu-* **ox**, *-lim-* **hunger**, *-ia* **condition**]

hyperglycemia
(hye-per-gly-SEEM-ee-ah)
[*hyper-* **above**, *-glyc-* **sweet (glucose)**, *-emia* **blood condition**]

hypervitaminosis
(hye-per-vye-tah-mih-NO-sis)
[*hyper-* **excessive**, *-vita-* **life**, *-amin-* **ammonia compound**, *osis* **condition**]

hypoglycemia
(hye-poh-gly-SEE-mee-ah)
[*hypo-* **under or below**, *-glyc-* **sweet (glucose)**, *-emia* **blood condition**]

inborn errors of metabolism
(meh-TAB-ohl-iz-em)
[*metabol-* **change**, *-ism* **action**]

indirect calorimetry
(in-dir-EKT kal-oh-RIM-eh-tree)
[*in-* **not, direct**, *calor-* **heat**, *-metr-* **measuring**, *-y* **process**]

ketosis
(kee-TOH-sis)
[*keto-* **acetone**, *-osis* **condition**]

kwashiorkor
(kwah-shee-OR-kor)
[*kwashiorkor* **one who is displaced (from the breast)**]

marasmus
(mah-RAZ-mus)
[*marasmus* **a wasting**]

obesity
(oh-BEES-i-tee)
[*obes-* **fatness**, *-ity* **state**]

phenylketonuria
(fen-il-kee-toh-NOO-ree-ah)
[*phen-* **shining (phenol)**, *-yl-* **chemical**, *-keton-* **acetone**, *-ur-* **urine**, *-ia* **condition**]

protein-calorie malnutrition (PCM)
(PROH-teen KAHL-ah-ree mal-noo-TRISH-un)
[*mal-* **poor**, *-nutri-* **nourish**, *-tion* **process**]

CASE study

Walter had heard that pizza was a complete meal because it contained all the major macronutrients. Maybe he could invent the "pizza diet," he thought. He went over the macronutrients in his head, "carbohydrates, lipids . . . ."



1. Which item doesn't belong in Walter's list?
   a. Protein
   b. Lipid
   c. Vitamin C
   d. Carbohydrate

Walter continued his list. "Then, there are the macrominerals—sodium, carbon, potassium . . . ."

2. Which of the minerals Walter listed is NOT considered a macromineral?
   a. Sodium
   b. Carbon
   c. Potassium
   d. All are considered macrominerals
3. The olive oil on pizza crust is mostly triglyceride lipids containing monounsaturated fatty acids. What is the first step in catabolizing the triglycerides in the olive oil?
   a. Conversion to glycerol and three fatty acids
   b. Glycolysis
   c. Lipogenesis
   d. Deamination
4. Walter is so busy writing his new diet book that he forgets to eat! His body has already run low on stored carbohydrates and his blood sugar level (glucose concentration) is low. Which of the following processes will restore glucose availability in the blood stream?
   a. Glycolysis
   b. Glycogenesis
   c. Oxidative phosphorylation
   d. Gluconeogenesis

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

OVERVIEW OF NUTRITION AND METABOLISM

A. Nutrition refers to the food (nutrients) we eat
   1. Malnutrition—a deficiency in the consumption of food, vitamins, and minerals
   2. Categories of nutrients
      a. Macronutrients—nutrients that the body needs in large amounts (bulk nutrients)
         (1) Macromolecules such as carbohydrates, fats (lipids), proteins
         (2) Water
         (3) Macrominerals—minerals needed in large quantity; for example, sodium, chloride, calcium
      b. Micronutrients—nutrients needed in very small amounts
         (1) Vitamins
         (2) Microminerals (trace elements)—minerals that are needed only in very small quantities, such as iron, iodine, and zinc
   3. Balance of nutrients is required for good health (Figures 30-1 and 30-2)

B. Metabolism—the use of nutrients—a process made up of many chemical processes (Figure 30-23)
   1. Catabolism breaks food down into smaller molecular compounds and releases two forms of energy—heat and chemical energy
   2. Anabolism—a synthesis process
   3. Both processes take place inside of cells continuously and concurrently
   4. Chemical energy released by catabolism must be transferred to ATP, which supplies energy directly to the energy-using reactions of all cells (Figure 30-3)

CARBOHYDRATES

A. Dietary sources of carbohydrates
   1. Complex carbohydrates
      a. Polysaccharides—starches; found in vegetables and grains; glycogen is found in meat
      b. Cellulose—a component of most plant tissue; passes through the system without being broken down
      c. Disaccharides—found in refined sugar; must be broken down before they can be absorbed
      d. Monosaccharides—found in fruits; move directly into the internal environment without being processed directly
         (1) Glucose—carbohydrate most useful to the human cell
         (2) Other monosaccharides can be converted into glucose (e.g., fructose and galactose) (Figure 30-4)

B. Carbohydrate metabolism—human cells catabolize most of the carbohydrate absorbed and anabolize a small portion of it
   1. Glucose transport and phosphorylation—glucose reacts with ATP to form glucose-6-phosphate
      a. This step prepares glucose for further metabolic reactions
      b. This step is irreversible except in the intestinal mucosa, liver, and kidney tubules
   2. Glycolysis—the first process of carbohydrate catabolism; consists of a series of chemical reactions (Figure 30-5)
      a. Occurs in the cytoplasm of all human cells
      b. Only process that provides cells with energy under conditions of inadequate oxygen—an anaerobic process
      c. Breaks down chemical bonds in glucose molecules and releases about 5% of the energy stored in them
      d. Prepares glucose for the second step in catabolism—the citric acid cycle
   3. Citric acid cycle
      a. Two pyruvic acid molecules from glycolysis are converted to two acetyl molecules in a transition reaction, losing one carbon dioxide molecule per pyruvic acid molecule converted
      b. By end of transition reaction and citric acid cycle, two pyruvic acids have been broken down to six carbon dioxide and six water molecules (Figures 30-6 and 30-7)
      c. Citric acid cycle also called the *tricarboxylic acid (TCA) cycle* because citric acid is also called *tricarboxylic acid*
      d. Citric acid cycle once called Krebs cycle after Sir Hans Krebs, who discovered this process
   4. Electron transport system (Figure 30-8)
      a. High-energy electrons (along with their protons) removed during the citric acid cycle enter a chain of molecules embedded in the inner membrane of the mitochondria
      b. As electrons move down the chain, they release small bursts of energy to pump protons between the inner and outer membrane of the mitochondrion
      c. Protons move down their concentration gradient, across the inner membrane, driving ATP synthase (Figure 30-9)
   5. Oxidative phosphorylation—the joining of a phosphate group to ADP to form ATP by the action of ATP synthase (Figure 30-10 and 30-11)
   6. Anaerobic pathway—a pathway for the catabolism of glucose; transfers energy to ATP using only glycolysis; ultimately ends with the oxidative phosphorylation of ATP (paying the "oxygen debt") (Figure 30-12)
   7. Cori cycle—circular pathway in which lactic acid produced by anaerobic glycolysis in skeletal muscles is carried to liver cells, where it is converted back to glucose and stored as liver glycogen or returned to the bloodstream, where the glucose may be taken up by muscle cells and used for respiration or stored as muscle glycogen (Figure 30-13)

8. Glycogenesis—a series of chemical reactions in which glucose molecules are joined to form a strand of glucose beads; a process that operates when the blood glucose level increases above the midpoint of its normal range (Figures 30-14 and 30-15)
9. Glycogenolysis (Figure 30-16)—the reversal of glycogenesis; it means different things in different cells; can be stimulated by glucagon hours after a meal when blood glucose declines or by epinephrine and cortisol during a stress response to provide extra blood glucose
10. Gluconeogenesis (Figure 30-17)—the formation of new glucose, which occurs chiefly in the liver
11. Control of glucose metabolism—hormonal and neural devices maintain homeostasis of blood glucose concentration (Figures 30-18 and 30-19)
    a. Insulin—secreted by beta cells to decrease blood glucose level (Figure 30-18)
    b. Glucagon increases the blood glucose level by increasing the activity of the enzyme phosphorylase
    c. Incretins—GI hormones that, in the presence of glucose in the gut, stimulate insulin release from pancreas, thereby decreasing blood glucose levels; examples: GLP-1 and GIP
    d. Epinephrine—hormone secreted in times of stress; increases phosphorylase activity
    e. Adrenocorticotropic hormone stimulates the adrenal cortex to increase its secretion of glucocorticoids
    f. Glucocorticoids accelerate gluconeogenesis
    g. Growth hormone increases blood glucose level by shifting from carbohydrate to fat catabolism
    h. Thyroid-stimulating hormone has complex effects on metabolism
12. Hormones that cause the blood glucose level to rise are called *hyperglycemic*
13. Insulin is hypoglycemic because it causes the blood glucose level to decrease

LIPIDS

A. Dietary sources of lipids
   1. Triglycerides—the most common lipids—composed of a glycerol subunit that is attached to three fatty acids
   2. Phospholipids—an important lipid found in all foods
   3. Cholesterol—an important lipid found only in animal foods
   4. Dietary fats
      a. Saturated fats contain fatty acid chains in which there are no double bonds
      b. Unsaturated fats contain fatty acid chains in which there are some double bonds

B. Transport of lipids—transported in blood as chylomicrons, lipoproteins, and fatty acids
   1. In the absorptive state, many chylomicrons are present in the blood
   2. Postabsorptive state—95% of lipids are in the form of lipoproteins
      a. Consist of lipids and protein; formed in the liver
         (1) Blood contains three types of lipoproteins: very low density, low density, and high density
         (2) Cholesterol lipoproteins associated with heart disease (Figure 30-20)
      b. Fatty acids transported from cells of one tissue to cells of another in the form of free fatty acids

C. Lipid metabolism
   1. Lipid catabolism
      a. Triglycerides are hydrolyzed to yield fatty acids and glycerol
      b. Glycerol is converted to glyceraldehyde-3-phosphate, which enters the glycolysis pathway
      c. Fatty acids are broken down by beta-oxidation and then catabolized through the citric acid cycle (Figure 30-21)
   2. Lipid anabolism consists of the synthesis of triglycerides, cholesterol, phospholipids, and prostaglandins
   3. Control of lipid metabolism is through the following hormones
      a. Insulin
      b. Growth hormone
      c. ACTH
      d. Glucocorticoids

PROTEINS

A. Sources of proteins
   1. Proteins assembled from a pool of many different amino acids
   2. The body synthesizes amino acids from other compounds in the body
   3. Only about half the necessary types of amino acids can be produced by the body; remainder supplied through diet—found in both meat and vegetables

B. Protein metabolism—anabolism is primary and catabolism is secondary
   1. Protein anabolism—process by which proteins are synthesized by the ribosomes of the cells
   2. Protein catabolism—deamination takes place in the liver cells and forms an ammonia molecule, which is converted to urea and excreted in urine, and a keto acid molecule, which is oxidized or converted to glucose or fat (Figure 30-22)
   3. Protein balance—rate of protein anabolism balances rate of protein catabolism
   4. Nitrogen balance—amount of nitrogen taken in equals nitrogen in protein catabolic waste
   5. Two kinds of protein or nitrogen imbalance
      a. Negative nitrogen balance—protein catabolism exceeds protein anabolism; more tissue proteins are catabolized than are replaced by protein synthesis
      b. Positive nitrogen balance—protein anabolism exceeds protein catabolism
   6. Control of protein metabolism—achieved by hormones

VITAMINS AND MINERALS

A. Vitamins (Table 30-3)—organic molecules necessary for normal metabolism; many attach to enzymes and help them work or have other important biochemical roles (Figure 30-24)
   1. Most of the necessary vitamins not produced by the body; must be obtained through diet
      a. The body stores fat-soluble vitamins, but not water-soluble vitamins

B. Minerals (Table 30-4)—inorganic elements or salts found in the earth
   1. They attach to enzymes and help them work and function in chemical reactions
   2. Essential to the fluid/ion balance of the internal fluid environment
   3. Involved in many processes in the body such as muscle contraction, nerve function, hardening of bone, etc.
   4. Too large or too small an amount of some minerals may be harmful
   5. Recommended mineral intakes may vary over the life span (Figures 30-25 and 30-26)

METABOLIC RATES

A. Metabolic rate means the amount of energy released by catabolism

B. Metabolic rates expressed in two ways
   1. The number of kilocalories of heat energy expended per hour or per day
   2. As normal or as a percentage above or below normal

C. Factors influencing basal metabolic rate—the rate of energy expended under basal conditions
   1. BMR not identical for all individuals because of influence of various factors
   2. Factors: size, body composition, gender, age, thyroid hormone, body temperature, drugs, other factors (Figures 30-27 through 30-30)

D. Total metabolic rate (Figure 30-27)
   1. Amount of energy used in a given time
   2. Main determinants
      a. Factor 1—basal metabolic rate
      b. Factor 2—energy used to do skeletal muscle work
      c. Factor 3—thermic effect of foods

E. Energy balance and body weight
   1. The body maintains a weight (state of energy balance) when the total calories in the food ingested equals the total metabolic rate
   2. Body weight increases when energy input exceeds energy output
   3. Body weight decreases when energy output exceeds energy input
   4. In starvation, the carbohydrates are used up first, then fats, then proteins (Figure 30-31)

MECHANISMS FOR REGULATING FOOD INTAKE (TABLE 30-6)

A. The hypothalamus plays a part in food intake

B. Feeding centers in the hypothalamus exert primary control over appetite
   1. Appetite center
      a. Cluster of neurons in the lateral hypothalamus that if stimulated brings about increased appetite
      b. Orexigenic effects—factors that trigger appetite
   2. Satiety center
      a. Group of neurons in the ventral medial nucleus of the hypothalamus that if stimulated brings about decreased appetite
      b. Anorexigenic effects—factors that suppress appetite (anorexia is loss of appetite)

THE BIG PICTURE: NUTRITION, METABOLISM, AND THE WHOLE BODY

A. Every cell in the body needs the maintenance of the metabolic pathways to stay alive

B. Anabolic pathways build the various structural and functional components of the cells

C. Catabolic pathways convert energy to a usable form and degrade large molecules into subunits used in anabolic pathways

D. Cells require appropriate amounts of vitamins and minerals to produce structural and functional components necessary for cellular metabolism

E. Other body mechanisms operate to ensure that nutrients reach the cells

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. What is metabolism? Nutrition?
2. What two processes make up the process of metabolism?
3. Does the body digest dietary fiber? Why or why not?
4. Briefly describe glycolysis, the first process of carbohydrate catabolism.
5. Where does glycolysis occur?
6. Describe the process of "splitting glycogen."
7. How are dietary fats classified?
8. Explain how lipids are transported in blood.
9. List the hormones involved in the control of lipid metabolism.
10. What are the essential amino acids?

11. What does the term *metabolic rate* mean?
12. List the various factors that influence basal metabolic rate.
13. Describe various factors that influence the amount of food a person eats.
14. Define the term *calorie*.

CRITICAL THINKING QUESTIONS

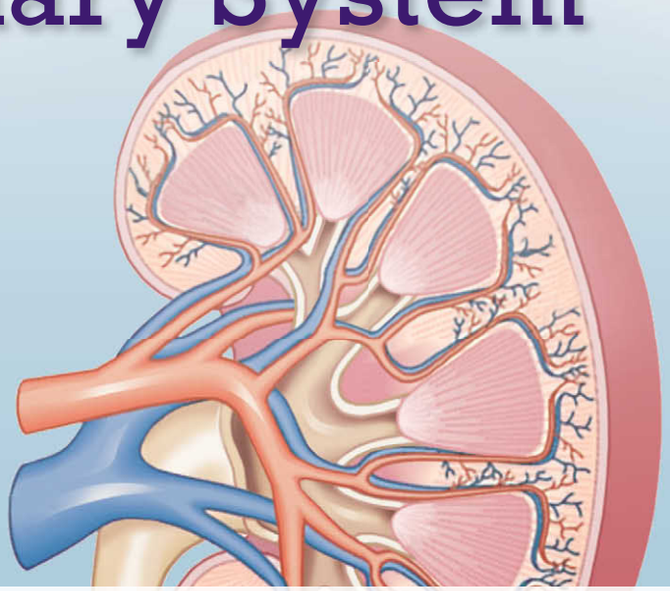


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. How would you state or interpret, in your own words, the process of carbohydrate catabolism known as the citric acid cycle? Draw a picture to illustrate what you mean.
2. How would you describe the mitochondria, and why do you think they are referred to as the "power plants" of the cells?
3. Compare anaerobic and aerobic pathways. What important role does lactic acid play in the anaerobic pathway?
4. Identify and explain the processes and hormones involved in maintaining the homeostatic level of glucose in the blood.
5. State in your own words the process of lipid catabolism. How is it similar to the carbohydrate pathway? How does this process generate ketone bodies?
6. Describe protein catabolism in your own words. How is this process related to a negative nitrogen balance?
7. How would you compare and contrast the functions of proteins, carbohydrates, and fats?
8. What is the function of most vitamins in the body? What examples can you find that do not have this function? What functions do these vitamins have?
9. What is the difference between basal and total metabolic rates?
10. What would be the predicted basal metabolism rate in kilocalories per day of a 22-year-old man who is 6 feet tall and weighs 176 pounds?
11. A man went on a 7-day vacation. Since he planned to be more active than normal, he thought he would not have to be concerned about his diet. During the 7 days, he burned 17,500 kcal. He ate 26,500 kcal. What was the approximate difference in his body weight before and after his vacation?
12. Why do you think high blood concentrations of low-density lipoproteins may lead to atherosclerosis?

31

Urinary System



LANGUAGE OF SCIENCE



Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

atrial natriuretic hormone (ANH)
(AY-tree-al nay-tree-yoo-RET-ik HOR-mohn)
[*atrium* **entrance courtyard (atrium of heart),** *natri-* **sodium,** *-ure-* **urine,** *-ic* **relating to,** *hormon-* **excite**]

Bowman capsule
(BOH-men KAP-sul)
[*William Bowman* **English anatomist**]

calyx
(KAY-liks)
[*calyx* **cuplike**] *pl.,* calyces

collecting duct (CD)

cortical nephron
(KOHR-ti-kal NEF-ron)
[*cortic-* **bark (cortex),** *-al* **relating to,** *nephro-* **kidney,** *-on* **unit**]

countercurrent mechanism
[*counter-* **against,** *-current* **flow**]

detrusor muscle
(dee-TROO-sor)
[*detrus-* **thrust,** *-or* **agent**]

distal convoluted tubule (DCT)
(DIS-tall KON-vo-LOO-ted TOO-byool)
[*dist-* **distance,** *-al* **relating to,** *con-* **together,** *-volut-* **roll,** *tub-* **tube,** *-ul-* **little**]

filtration
(fil-TRAY-shun)
[*filtr-* **strain,** *-ation* **process**]

glomerular capsular membrane
(gloh-MER-yoo-lar KAP-soo-lahr MEM-brayne)
[*glomer-* **ball,** *-ul-* **little,** *-ar* **relating to,** *caps-* **box,** *-ula-* **little,** *-ar* **relating to,** *membran-* **thin skin**]

glomerular filtration rate (GFR)
(gloh-MER-yoo-lar fil-TRAY-shun)
[*glomer-* **ball,** *-ul-* **little,** *-ar* **relating to,** *filtr-* **strain,** *-ation* **process**]

continued on p. 998

CHAPTER OUTLINE



Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

Anatomy of the Urinary System, 971
- Gross Structure, 971
  - Kidney, 971
  - Ureter, 973
  - Urinary Bladder, 974
  - Urethra, 975
- Microscopic Structure, 976
  - Nephron, 977
  - Collecting Duct, 980
  - Blood Supply of the Nephron, 980
  - Types of Nephrons, 981

Physiology of the Urinary System, 982
- Overview of Kidney Function, 982
- Filtration, 982
  - Mechanism of Filtration, 982
  - Glomerular Filtration Rate, 983
- Reabsorption, 984
  - Reabsorption in the Proximal Convoluted Tubule, 984
  - Reabsorption in the Henle Loop, 986
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- Tubular Secretion, 989
- Regulation of Urine Volume, 989
- Urine Composition, 992

Cycle of Life: Urinary System, 993

The Big Picture: Urinary System and the Whole Body, 993

Mechanisms of Disease, 994

Case Study, 999

We often think of the urinary system primarily as a "urine producer," which it certainly is. However, a better description of the system is that of "blood plasma balancer." Each kidney processes incoming blood plasma in ways that allow it to leave the kidney in better condition. The water content is adjusted so that the body does not have too much or too little water to maintain constancy of the internal environment. Likewise, the blood content of important ions such as sodium and potassium is adjusted to match set point levels. Even the pH of the blood can be altered to match the set point level. In these ways, the urinary system regulates the content of blood plasma so that the homeostasis, or "dynamic constancy," of the entire internal fluid environment can be maintained within normal limits.

This chapter explores the basic principles of urinary structure and function. The next two chapters look more closely at the role of the kidneys and other organs in fluid and ion homeostasis (Chapter 32) and pH homeostasis (Chapter 33).

ANATOMY OF THE URINARY SYSTEM

Gross Structure

The principal organs of the urinary system are the **kidneys,** which process blood and form urine as a waste to be excreted—that is, removed from the body (Box 31-1). The excreted urine travels from the kidneys to the outside of the body via accessory organs: the *ureters*, *urinary bladder*, and *urethra*.

KIDNEY

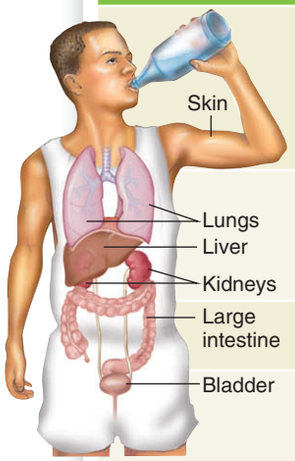
The kidneys resemble lima beans in shape, that is, roughly oval with a medial indentation (Figure 31-1, *A*). An average-sized

Box 31-1 | FYI

Excretion

The urinary system's chief function is to regulate the volume and composition of body fluids and excrete unwanted material, but it is not the only system in the body that is able to excrete unneeded substances.

The table below compares the excretory functions of several systems. Although all of these systems contribute to the body's effort to remove wastes, only the urinary system can finely adjust the water and electrolyte balance to the degree required for normal homeostasis of body fluids.



SYSTEM	ORGAN	EXCRETION
Urinary	Kidney	Nitrogen compounds Toxins Water Electrolytes
Integumentary	Skin—sweat glands	Nitrogen compounds Electrolytes Water
Respiratory	Lung	Carbon dioxide Water
Digestive	Intestine	Digestive wastes Bile pigments Salts of heavy metals

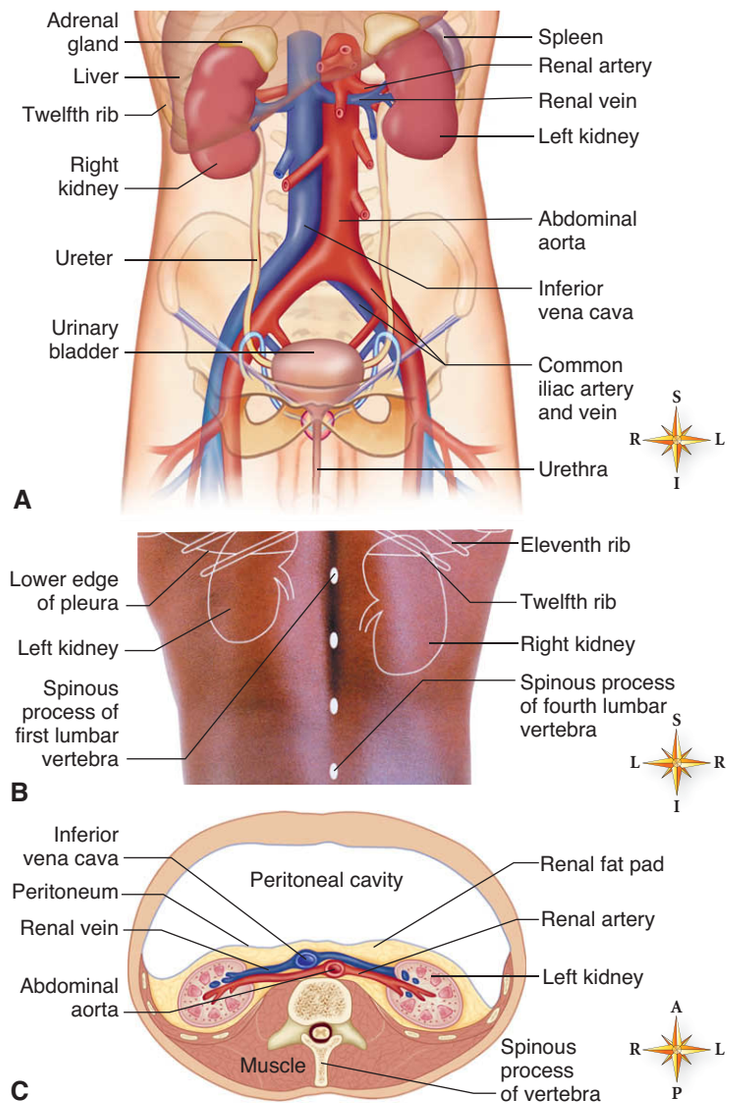


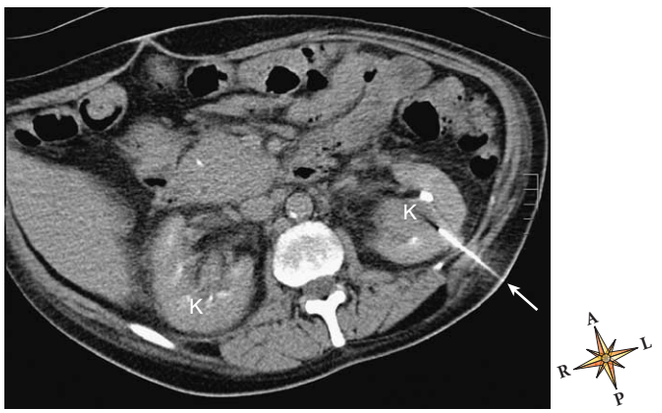
FIGURE 31-1

Location of urinary system organs. A, Anterior view of the urinary organs with the peritoneum and visceral organs removed. **B,** Surface markings of the kidneys, eleventh and twelfth ribs, spinous processes of L1 to L4, and lower edge of the pleura (posterior view). **C,** Horizontal (transverse) section of the abdomen showing the retroperitoneal position of the kidneys.

Box 31-2 | HEALTH matters

Kidney Biopsy

Suspected disease of the kidney, such as renal cancer, often requires a *needle biopsy* to confirm the diagnosis. In these procedures a hollow needle is inserted through the skin surface and then guided into the diseased organ to withdraw a tissue sample for analysis. In a renal biopsy, tissue is removed from the lower rather than the upper or superior end of the diseased kidney. This avoids the possibility of the biopsy needle damaging the pleura and thereby causing a pneumothorax (see Box 27-3 on p. 835).



Needle biopsy of kidney. Magnetic resonance image (MRI) of biopsy needle *(arrow)* inserted into the left kidney to remove tissue. *K,* Kidney.

kidney measures approximately 11 cm by 7 cm by 3 cm (4.3 by 2.7 by 1.2 inches). The left kidney is often slightly larger than the right. The kidneys lie in a *retroperitoneal* position, meaning posterior to the parietal peritoneum, against the posterior wall of the abdomen (Figure 31-1, *C*). They are located on either side of the vertebral column and extend from the level of the last thoracic vertebra (T12) to just above the third lumbar vertebra (L3). Note in Figure 31-1, *B*, that the superior or upper portions (poles) of both kidneys extend above the level of the twelfth rib and the lower edge of the thoracic parietal pleura. This anatomical relationship has important clinical implications (Box 31-2). Usually the right kidney is a little lower than the left, presumably because the liver takes up some of the space above the right kidney.

A heavy cushion of fat—the *renal fat pad*—normally encases each kidney and holds it in position. Connective tissue, the renal fasciae, anchors the kidneys to surrounding structures and also helps maintain their normal positions.

The medial surface of each kidney has a concave notch called the **hilum.** Renal blood vessels and other structures enter or leave the kidney through this notch. A tough, white fibrous capsule encases each kidney (Figure 31-2).

The coronal section of the right kidney shown in Figure 31-2 depicts the major internal structures of the kidney. Identify the **renal cortex,** or outer region, and the **renal medulla,** or inner region. A dozen or so distinct triangular wedges, the **renal pyramids,** make up much of the medullary tissue. The *base* of each pyramid faces outward, and the narrow *papilla* of each faces toward the hilum. Each renal papilla has multiple openings that release urine. Notice that the cortical tissue dips into the medulla between the pyramids, forming areas known as **renal columns.**

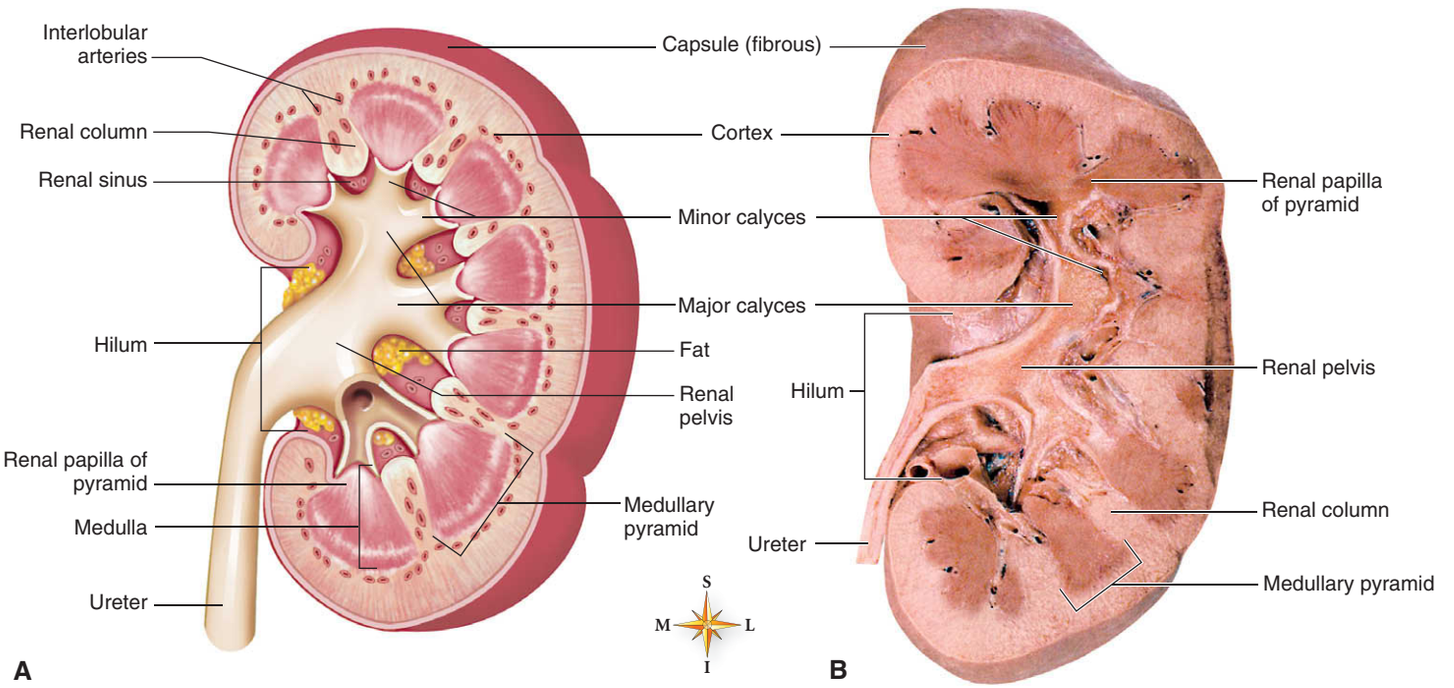


FIGURE 31-2

Internal structure of the kidney. A, Coronal section of the right kidney in an artist's rendering. **B,** Photo of a coronal section of a preserved human kidney.

Each renal papilla (point of a pyramid) juts into a cuplike structure called a **calyx.** The calyces are considered the beginnings of the "plumbing system" of the urinary system, for it is here that urine leaving the renal papilla is collected for transport out of the body. The cups that drain the renal papillae directly are called *minor calyces.* These minor calyces are stemlike branches that join together to form larger branches called *major calyces.* The major calyces join together to form a large collection basin called the **renal pelvis.** The pelvis of the kidney narrows as it exits the hilum to become the ureter. Pelvis is Latin for "basin" and, like a lavatory basin, it collects fluid and quickly drains it away through a channel.

Blood Vessels of the Kidneys

The kidneys are highly vascular organs (Figure 31-3). Every minute about 1200 ml of blood flows through them. Stated another way, approximately one fifth of all the blood pumped by the heart per minute goes to the kidneys. From this fact one might guess, and correctly so, that the kidneys process the blood in important ways before returning it to the general circulation. A large branch of the abdominal aorta—the *renal artery*—brings blood into each kidney. As it nears the kidney, it divides into *segmental arteries,* which divide to become *lobar arteries.* Between the pyramids of the kidney's medulla, the lobar arteries branch to form *interlobar arteries* that extend out toward the cortex, then arch over the bases of the pyramids to form the *arcuate arteries.* From the arcuate arteries, *interlobular arteries* penetrate the cortex. Because they radiate through the cortex, the interlobular arteries are sometimes called the *cortical radiate arteries.*

Branches of the interlobular arteries called *afferent arterioles* carry blood directly to the tiny functional units of the kidney called *nephrons.* We discuss the structure and function of nephrons later in this chapter, where we will resume outlining the path of blood flow—this time at a microscopic level.

| A&P CONNECT |

Knowing the pathway of blood flow in the kidney is important for understanding how the kidney works. We continue the story later in the chapter. We put all the pieces together in an overview in ***Tracing Blood Flow in the Kidney*** online at ***A&P Connect.***

evolve

| QUICK CHECK |

1. Name the accessory organs of the urinary system.
2. What is the general function of the urinary system?
3. Distinguish between the renal cortex and the renal medulla.
4. What proportion of the body's blood flow goes to the kidney?

URETER

The **ureters,** about 28 to 34 cm in length, are the two tubes that actively convey urine from the kidneys to the urinary bladder (see Figure 31-1, *A*). They begin on each side at the narrow outlet of the renal pelvis on a level with the first lumbar vertebra (L1). Each ureter is retroperitoneal and courses into the pelvis until it reaches the bladder, where it attaches to the bottom of the bladder

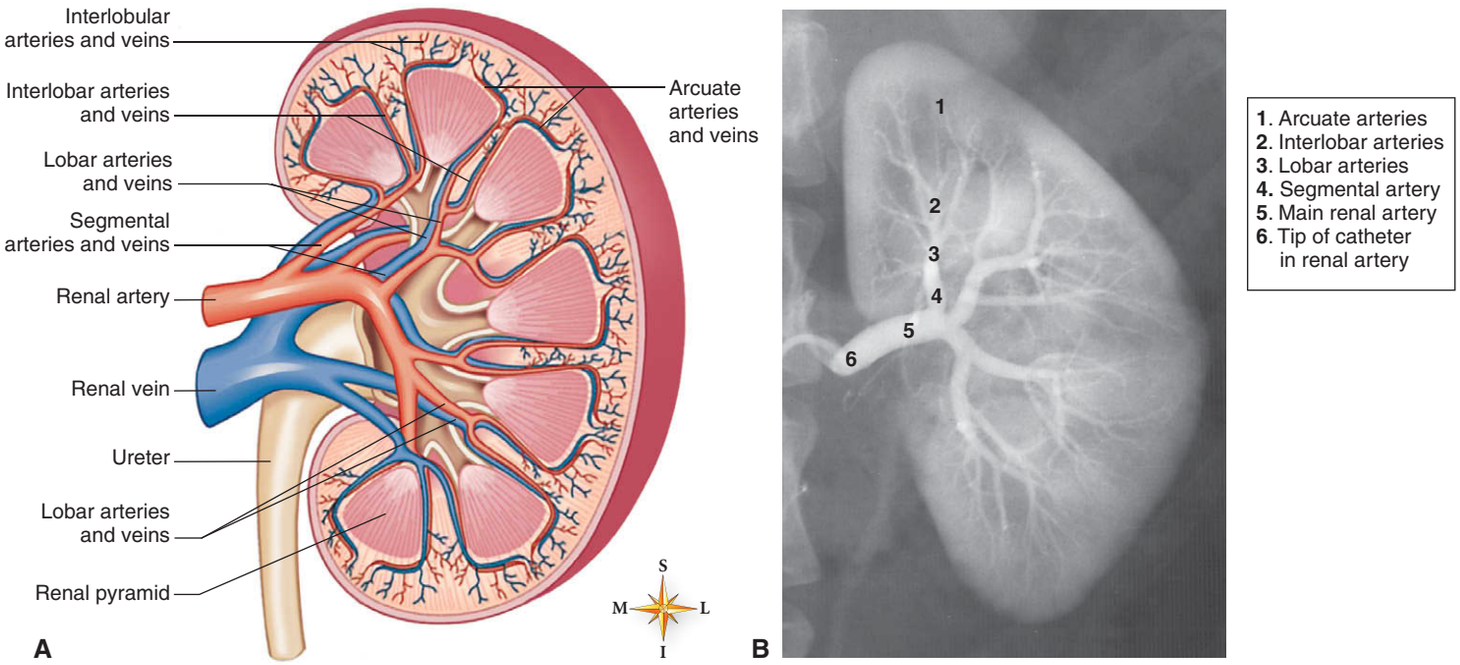


FIGURE 31-3

Circulation of blood through the kidney. A, Diagram showing the major arteries and veins of the renal circulation. **B,** Renal arteriogram. Arcuate arteries (1) are seen near the junction of the cortex and medulla, interlobar arteries (2) are present between the medullary pyramids, and lobar arteries (3) and segmental arteries (4) are seen branching from the main renal artery (5). Note the tip of the catheter used to inject contrast material (6) into the proximal part of the main renal artery.

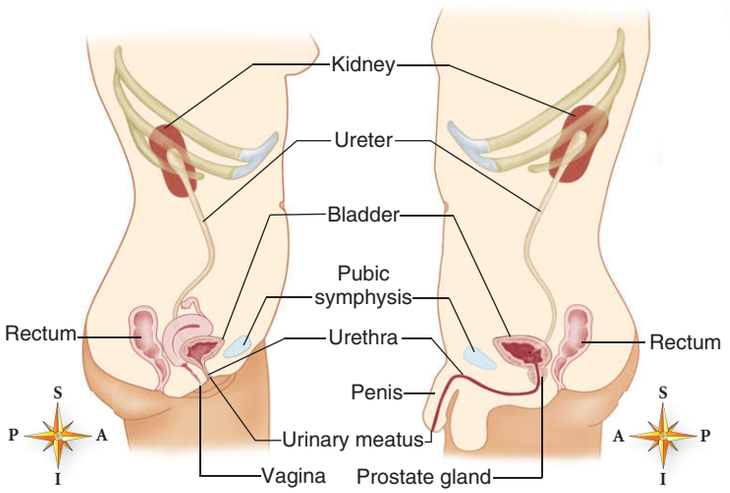


FIGURE 31-4

Sagittal view of urinary tract. Female urinary system is shown on the reader's left and the male urinary system on the reader's right, each showing a distended (stretched) bladder.

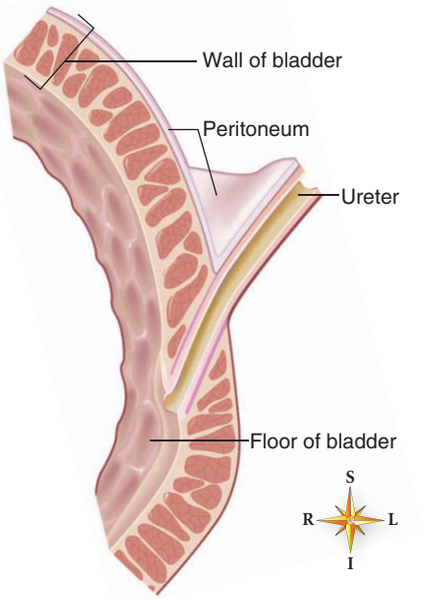


FIGURE 31-6

Ureter-bladder junction. The oblique path of the ureter through wall of the bladder, seen here in frontal section, permits the junction to act as a valve—reducing flow into the bladder as it becomes full.

(Figure 31-4). It then runs at an angle for about 2 cm through the bladder wall and opens at the lateral angles of the trigone (floor) of the bladder (Figure 31-5). Because of its oblique course through the bladder wall, the ends of the tube close and act as valves when the bladder is full, thus preventing backflow of urine (Figure 31-6).

The ureter is lined with transitional epithelium, which permits stretching without damage to the epithelial lining. This feature permits either high or low rates of flow through the ureters.

In females, the ureters are in close proximity to the ovaries and cervix of the uterus and, in males, in close proximity to the seminal vesicles and near the prostate gland (see Figure 31-4). Each ureter is composed of three layers of tissue: a mucous lining, a muscular middle layer, and a fibrous outer layer (Figure 31-7). The muscular layer is composed of smooth muscle, which propels the urine by peristalsis. The rate and strength of peristalsis increase with increasing urine volume.

URINARY BLADDER

The urinary bladder is a muscular, collapsible bag that is located directly behind the pubic symphysis and in front of the rectum (see Figure 31-4). It lies below the parietal peritoneum, which covers only its superior surface (see Figure 31-5). The remainder of the bladder surface is covered by a fibrous adventitia. In women it sits on the anterior of the vagina and in front of the uterus, whereas in men, it rests on the prostate.

The wall of the bladder is made mostly of smooth muscle tissue (see Figure 31-5). Often called the **detrusor muscle,** the muscle layer is formed by a network of crisscrossing bundles of smooth muscle fibers. The bundles run in all directions: circular, oblique, and lengthwise. The bladder is lined with mucous transitional epithelium that forms folds called *rugae* (see Figure 31-5). Because of the folds and the extensibility of transitional epithelium, the bladder can distend considerably. There are three openings

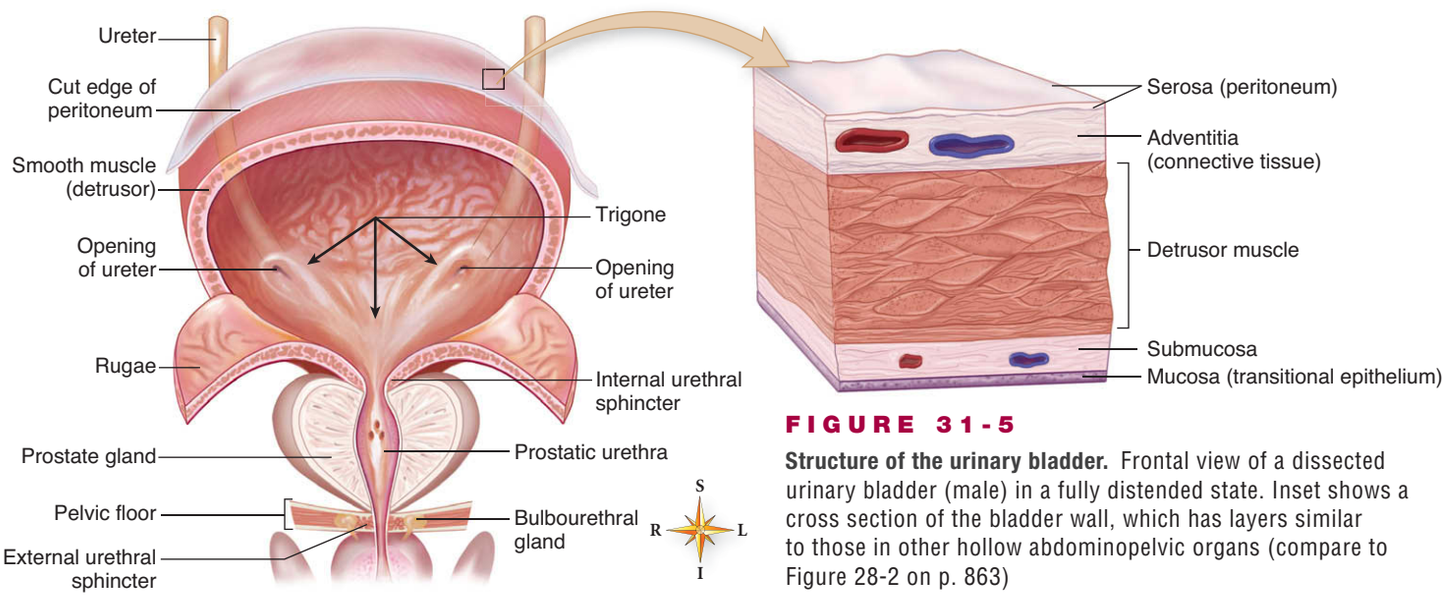


FIGURE 31-5

Structure of the urinary bladder. Frontal view of a dissected urinary bladder (male) in a fully distended state. Inset shows a cross section of the bladder wall, which has layers similar to those in other hollow abdominopelvic organs (compare to Figure 28-2 on p. 863)

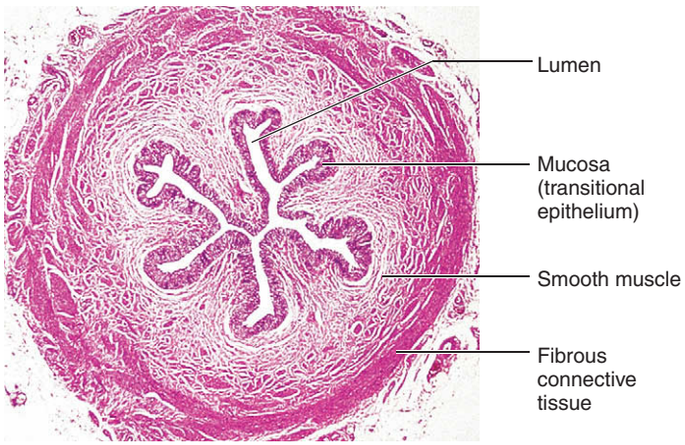


FIGURE 31-7

Ureter (cross section). Low power micrograph. Note the convoluted folds, covered by a transitional mucous lining, that almost fill the lumen. The thick muscular layer is surrounded by a tough fibrous coat.

in the floor of the bladder—two from the ureters and one into the **urethra.** The ureter openings lie at the posterior corners of the triangle-shaped floor—the **trigone**—and the urethral opening lies at the anterior, lower corner.

The bladder performs two major functions:

1. It serves as a reservoir for urine before it leaves the body.
2. Aided by the urethra, it expels urine from the body.

URETHRA

The urethra is a small tube lined with mucous membrane (transitional epithelium) that leads from the floor of the bladder *(trigone)* to the exterior of the body. In females, it lies directly behind the pubic symphysis and anterior to the vagina as it passes through the muscular floor of the pelvis (Figure 31-8). It extends down and forward from the bladder for a distance of about 3 cm (1.2 inches) and ends at the external urinary meatus (see Figure 31-4). The functional importance of the relationship of the urethra and vagina to the muscular pelvic floor, especially after vaginal delivery of a baby, will be discussed in Chapter 35. The male urethra, on the other hand, extends along a winding path for about 20 cm (7.9 inches) (see Figure 31-4). The male urethra passes through the center of the *prostate gland* just after leaving the bladder. Within the prostate, it is joined by two *ejaculatory ducts.* After leaving the prostate, the urethra extends down, forward, then up to enter the base of the penis. It then travels through the center of the penis and ends as a *urinary meatus* at the tip of the penis.

Because the male urethra is joined by the ejaculatory ducts, it serves as a pathway for *semen* (fluid containing sperm) as it is ejaculated out of the body through the penis. Thus we can say that the male urethra is a part of two different systems: the urinary system (when it is used to void urine) and the reproductive system (when it is used to ejaculate semen). Urine is prevented from mixing with semen during ejaculation by a reflex closure of sphincter muscles guarding the bladder's opening. The female urethral tract is separate from the lower reproductive tract (vagina), which lies just behind the urethra (see Figure 31-8).

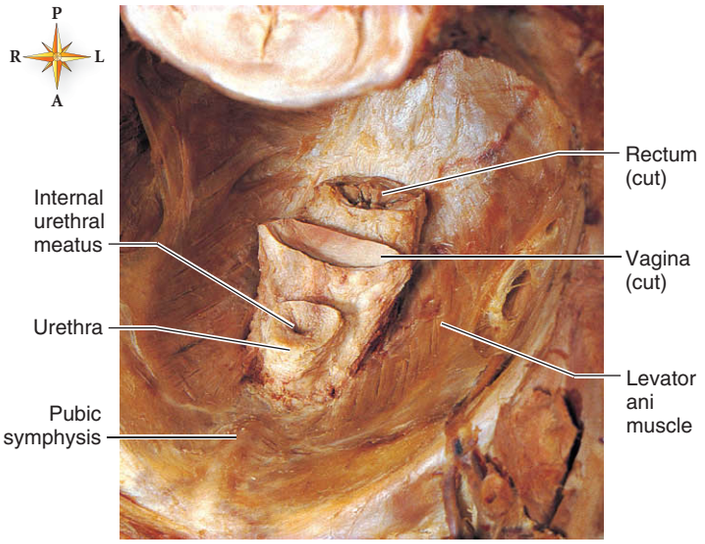


FIGURE 31-8

Female urethra piercing the muscular pelvic floor. The urethra is posterior to the pubic symphysis and anterior to the vagina. Some of the muscles of the pelvic floor act as an external urethral sphincter. (See also text discussion in Chapter 35, pp. 1071–1072.)

Micturition

The mechanism for urinating begins with involuntary contractions of the detrusor muscle of the bladder wall (see Figure 31-5). Urination is also called *voiding* the bladder or *micturition.* Figure 31-9 shows that as the pressure of urine

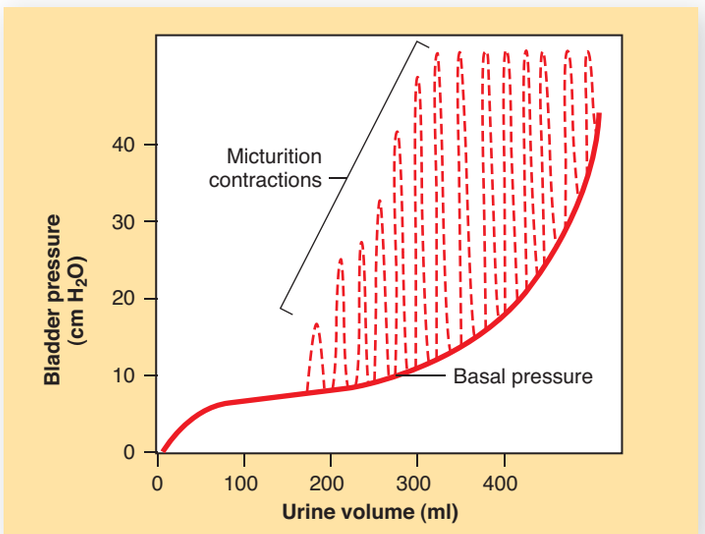


FIGURE 31-9

Micturition reflex. Increased volume of urine in the bladder causes increased internal bladder pressure. This triggers reflexive parasympathetic stimulation of micturition contractions of the detrusor muscles in the bladder wall. As these contractions get stronger, nerve signals to the internal sphincters (Figure 31-5) cause them to relax. *ml,* Milliliters; *cm H_2O,* centimeters of water (unit of pressure equal to about 0.73 mmHg).

against the inside of the bladder wall increases with urine volume, involuntary micturition contractions develop. This rapid succession of involuntary contractions triggered by a parasympathetic reflex get stronger and stronger as the bladder fills and the urine volume and pressure increase. The parasympathetic reflex also causes the *internal urethral sphincter* muscles to relax at the same time. The internal urethral sphincters include a ringlike part of the detrusor muscle of the bladder wall, as you can see in Figure 31-5. The relaxation of these internal sphincters along with the micturition contractions of the bladder wall can force urine out of the bladder and through the urethra.

Thankfully, most people learn how to consciously regulate voluntary contraction of the *external urethral sphincter* muscles to stop voiding—that is, until a suitable time. Figure 31-5 shows that the skeletal muscles of the pelvic floor, including the *levator ani* muscle, act as external urethral sphincters (see also Figure 11-15 on p. 321). Voluntary control of *micturition* (voiding, or urination) is possible only if the nerves supplying the pelvic floor, the projection tracts of the central nervous system (CNS), and the motor areas of the brain are all intact and functioning properly. Learning this function is not possible until the nervous system matures sufficiently—making voluntary control of urination impossible during infancy and very early childhood.

Injury to any of these parts of the nervous system, by a cerebral hemorrhage or a spinal cord injury, for example, results in involuntary emptying of the bladder at intervals. Involuntary micturition is called *incontinence* (see Mechanisms of Disease, p. 994). In the average bladder, 250 ml of urine causes a moderately distended sensation and therefore the desire to void.

| QUICK CHECK |

5. Where does the ureter enter the bladder? Why is its angle through the wall significant?
6. What type of mucous epithelium lines most of the urinary tract? What is the functional advantage of this type of epithelium?
7. What are the two major functions of the bladder?

Microscopic Structure

Over a million microscopic functional units named **nephrons** make up the bulk of each kidney. The shape of the nephron is unusual, unmistakable, and uniquely suited to its function of blood plasma processing and urine formation (Figure 31-10). It resembles a tiny funnel with a long, winding stem about 3 cm (1.2 inches) long.

As Figure 31-10 shows, each nephron is made up of two main regions: the *renal corpuscle* and the *renal tubule*. Fluid is filtered out of the blood in the renal corpuscle, then the filtrate flows through the renal tubule and collecting duct—where much of the filtrate is returned to the blood. The remaining filtrate leaves the collecting duct as urine. We will come back to the processing of filtrate later. For now, we explore the structure of the nephron and collecting duct. Here are the main structures we explore, listed in the order in which fluid flows through them:

Nephron
- Renal corpuscle
  - —Glomerulus (capillaries)
  - —Bowman capsule (glomerular capsule)
- Renal tubule
  - —Proximal convoluted tubule
  - —Henle loop (nephron loop)
  - —Distal convoluted tubule

Collecting duct

As you read the brief description of each of these microscopic structures, refer often to Figure 31-10, which shows a schematic diagram of a complete nephron.

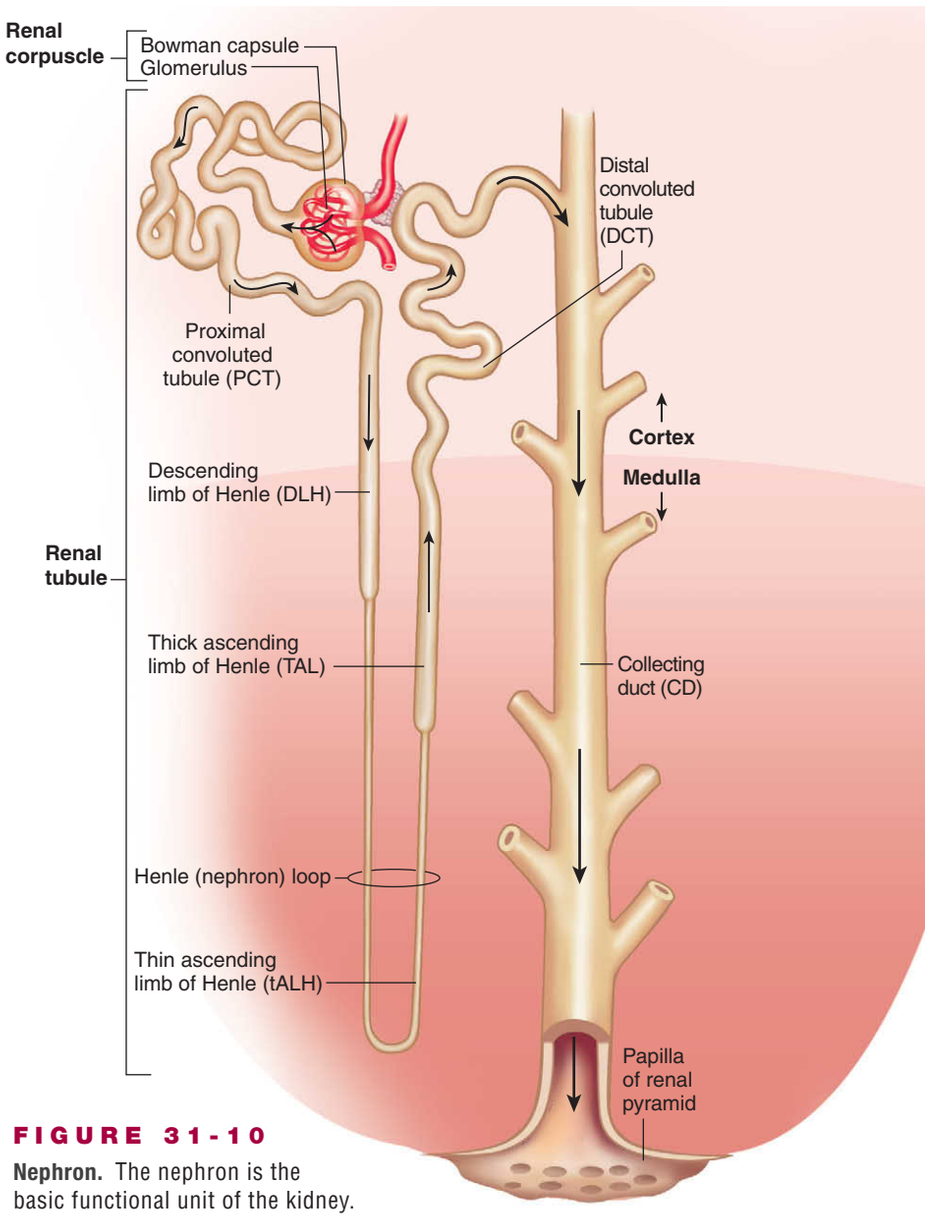


FIGURE 31-10

Nephron. The nephron is the basic functional unit of the kidney. *Arrows* show the direction of flow within the nephron.

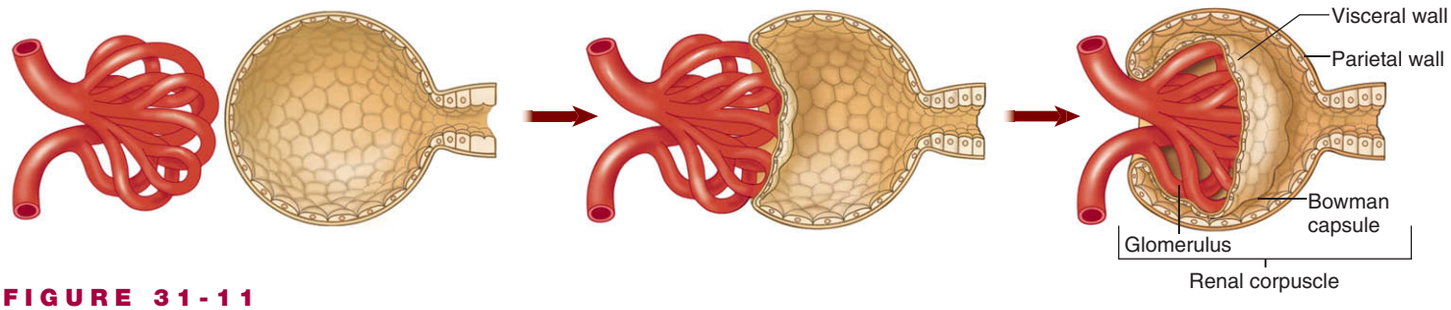


FIGURE 31-11

Overview of the renal corpuscle. Note that as the glomerular tuft of capillaries pushes into the inflated balloonlike structure representing a Bowman capsule, the visceral layer of the capsule adheres to the outer surface of the epithelial cells of the glomerular capillaries to become the visceral layer lining the capsular space. The outer layer of cells constitutes the parietal layer of a Bowman capsule. Glomerular filtrate enters the space between the parietal and visceral layers of the Bowman capsule before entering the tubular segments of the nephron.

| A&P CONNECT |

For our purposes, the simplified scheme of microscopic renal anatomy shown in Figure 31-10 works well. However, some renal biologists prefer the more elaborate scheme sketched out in a ***Detailed Map of Nephron*** online at ***A&P Connect.***

evolve

NEPHRON

Renal Corpuscle

The **renal corpuscle** is the first part of the nephron and is made up of the Bowman capsule and glomerulus. Formation of a renal corpuscle is sometimes compared to pushing your fist into the end of an inflated balloon. The mechanism is shown in Figure 31-11. Note that as the glomerular tuft of capillaries pushes into the balloon, it becomes surrounded by a double-walled cup with parietal (outer) and visceral (inner) walls—the Bowman capsule (Figure 31-12).

Fluid from the blood first filters out of the glomerulus and then into the Bowman capsule. We begin our discussion with the Bowman capsule first, however, because it will then make it easier to understand the structure and function of the glomerulus.

Bowman Capsule

The **Bowman capsule** is the cup-shaped mouth of a nephron. It is sometimes called the *glomerular capsule*. The capsule is formed by two layers of epithelial cells with a space, called the *capsular space (Bowman space)*, between them (Figure 31-13). Fluids, waste products, and electrolytes that pass through the porous glomerular capillaries and enter this space constitute the *filtrate*, which will be processed in the nephron to form urine.

The parietal, or outer, wall is composed of simple squamous epithelium. It plays no role in the production of glomerular filtrate. The visceral (inner) wall, however, is quite different. It is composed of special epithelial cells called *podocytes* (meaning "cells with feet"). The scanning electron micrograph in

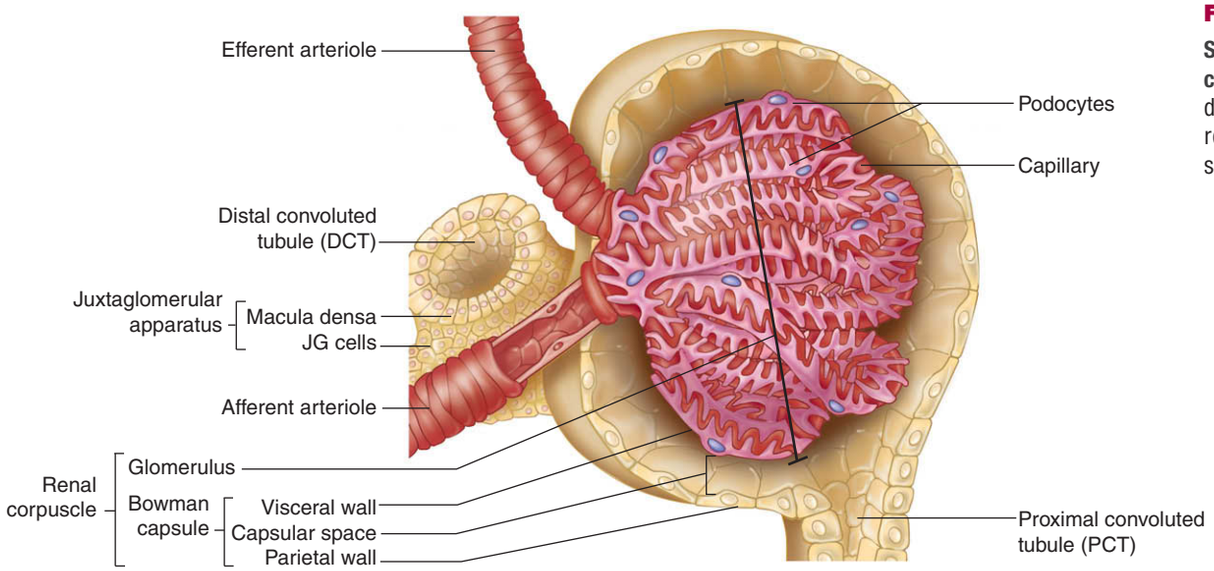


FIGURE 31-12

Structure of the renal corpuscle. Detailed diagram showing relationships to nearby structures.

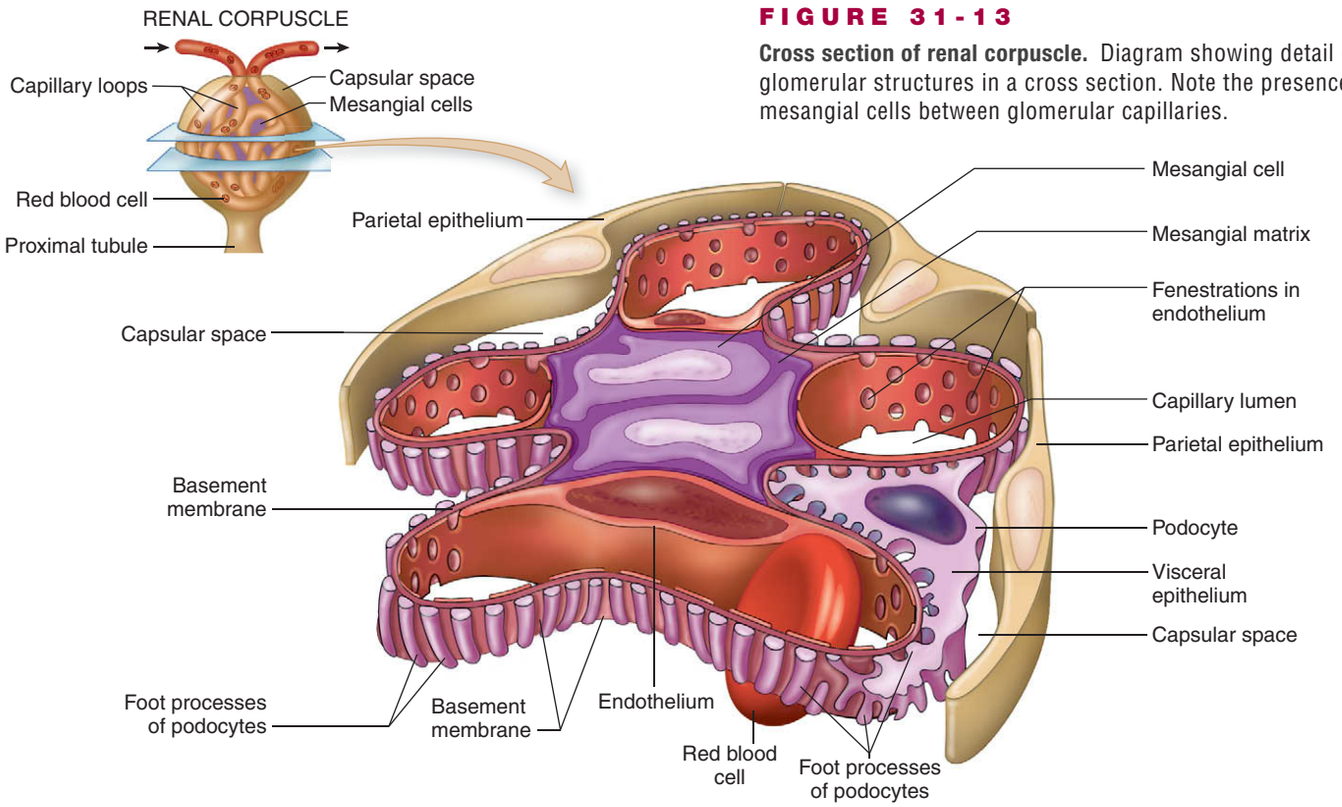


FIGURE 31-13

Cross section of renal corpuscle. Diagram showing detail of glomerular structures in a cross section. Note the presence of mesangial cells between glomerular capillaries.

Figure 31-14 reveals the odd shapes of podocytes. Notice that the primary branches extending from the cell bodies divide into a network of branches that terminate in little "feet" called *pedicels*. The pedicels are packed so closely together that only narrow slits of space lie between them. These spaces are called *filtration slits*. The slits are not merely open spaces, however. Within them is a mesh of fine connective tissue fibers called the *slit diaphragm* that prevents the slits from enlarging under pressure while still maintaining permeability of the slit. The slit diaphragm is an important component of the filter mechanism because it prevents many large macromolecules, such as proteins, from passing through.

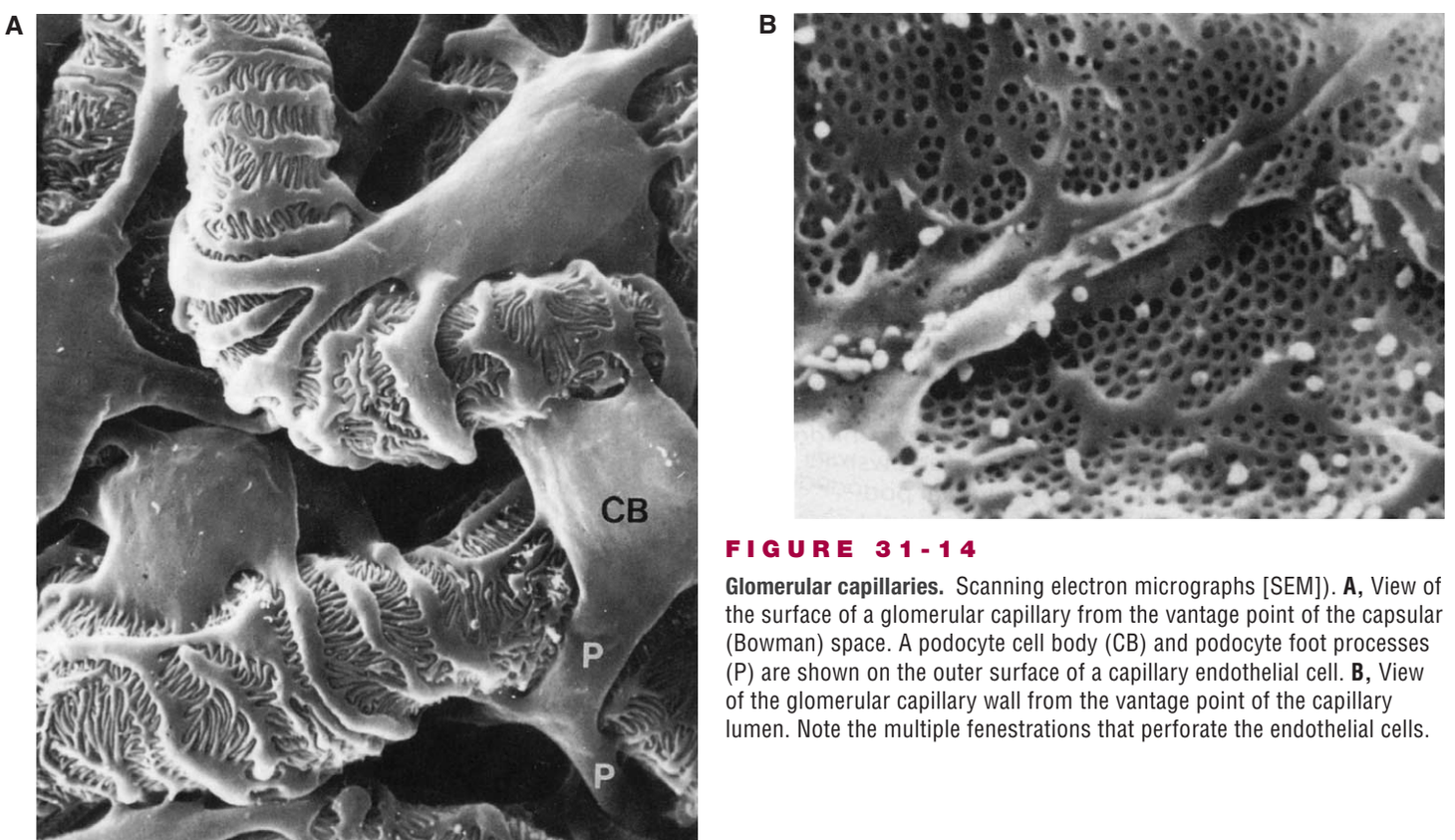


FIGURE 31-14

Glomerular capillaries. Scanning electron micrographs [SEM]). **A,** View of the surface of a glomerular capillary from the vantage point of the capsular (Bowman) space. A podocyte cell body (CB) and podocyte foot processes (P) are shown on the outer surface of a capillary endothelial cell. **B,** View of the glomerular capillary wall from the vantage point of the capillary lumen. Note the multiple fenestrations that perforate the endothelial cells.

Glomerulus

The **glomerulus** is probably the body's most well known capillary network and is surely one of its most important ones for survival. Its relationship to the Bowman capsule is clearly visible in Figures 31-11 and 31-12. Notice in both Figures that an afferent arteriole leads into the glomerular network and an efferent arteriole leads out.

Like all capillaries, glomerular capillaries have thin, membranous walls that are composed of a single layer of endothelial cells. Many pores, or *fenestrations* (meaning "windows"), are present in the glomerular endothelium (see Figure 31-14, *B*). These pores are not present in regular capillaries (see Figure 21-16 on p. 645). This increased porosity is necessary for filtration to occur at the rate required for normal kidney function. The relationship between fenestration size and the rate of glomerular filtration is yet another example of the connection between form and function.

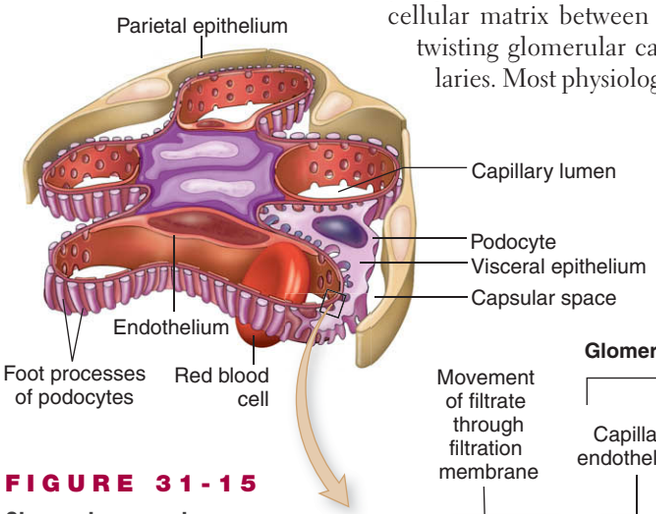
Mesangial cells (see Figure 31-13) are unique to renal corpuscles. They are irregular in shape, have numerous cytoplasmic processes, and are scattered in an apparently haphazard way in an extracellular matrix between the twisting glomerular capillaries. Most physiologists believe they serve a support and phagocytic function, similar in some ways to microglia and other types of glia cells found in the nervous system (see Chapter 13, p. 383). However, the presence of myosin-like filaments and angiotensin II receptors in their cytoplasm also suggests a possible role in control of blood flow through the glomerular loop. Mesangial cells are currently the subject of considerable research interest and may well have other important functions or play an important role in human glomerular disease.

Between a glomerulus and its Bowman capsule lies a basement membrane (basal lamina). It consists of a thin layer of fine fibrils embedded in a matrix of glycoprotein. The visceral layer of Bowman capsule contacts the basement membrane by means of countless pedicels ("feet") of the podocytes (see Figure 31-14, *A*). The glomerular endothelium, the basement membrane, and the visceral layer of Bowman capsule constitute the **glomerular capsular membrane,** a structure well suited to its function of filtration (Figure 31-15).

Renal Tubule

The renal tubule is a winding, hollow tube with walls largely made up of simple cuboidal and simple squamous epithelium. The epithelial cells each possess a single, *primary cilium* that acts as a sensory receptor that monitors the chemical makeup and rate of flow of the fluid flowing through the lumen of the tubule. Thus, renal tubule cells are able to respond to changes in the composition and flow of fluid to regulate the growth and functioning of the tubule. You can review the sensory role of primary cilia in the body on p. 83.

The renal tubule extends from the renal corpuscle to the end of the nephron, where it joins a collecting duct shared in common with other nearby nephrons. The renal tubule is divided into



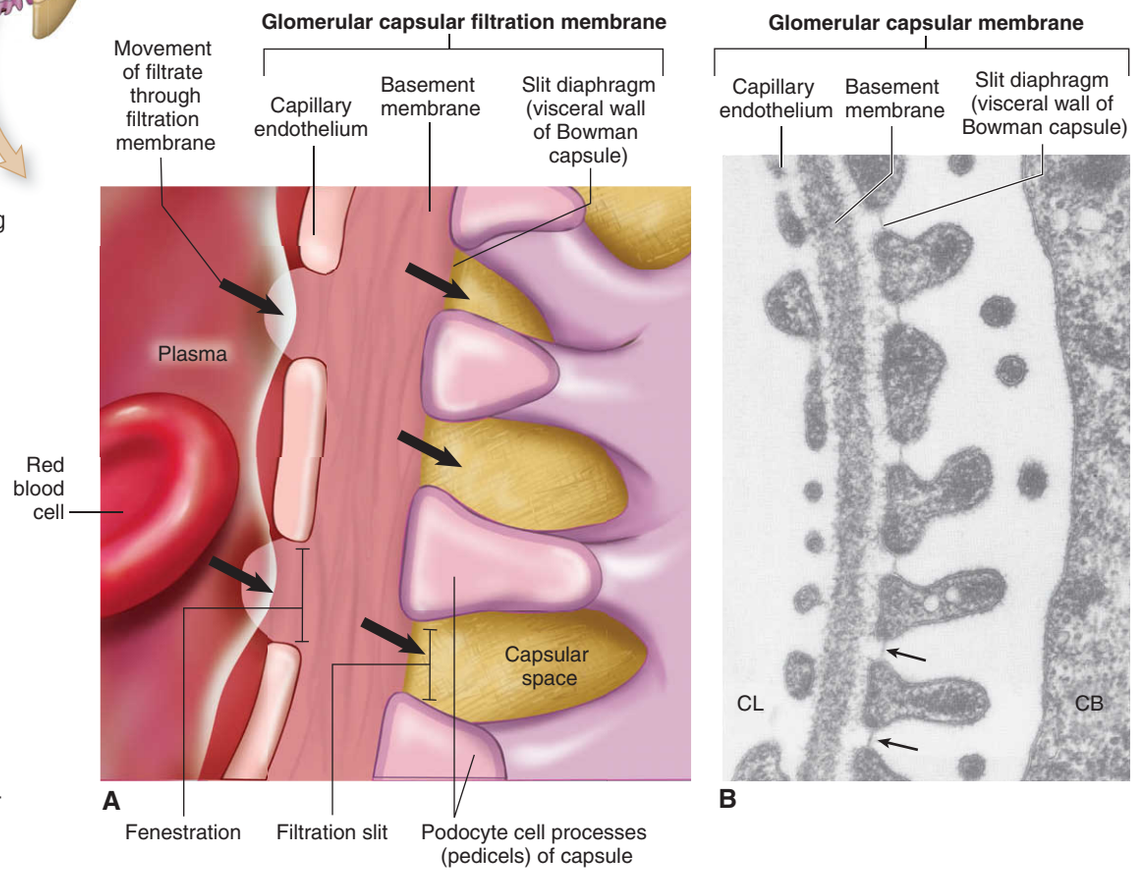


FIGURE 31-15

Glomerular capsular membrane. A, Artist's rendering of a transmission electron micrograph (TEM) showing the filtration membrane formed when footlike extensions (pedicels) of cells forming the visceral wall of the Bowman capsule share a basement membrane with the fenestrated endothelial cells that form the wall of glomerular capillaries. **B,** TEM of the glomerular capsular membrane. Note from left to right, the capillary lumen (CL), fenestrations in the capillary endothelium, and multiple podocyte foot processes separated by slit diaphragms (arrows) extending into the capsular (Bowman) space. A portion of an overarching podocyte cell body (CB) is visible on the right.

different regions: the proximal convoluted tubule, the Henle loop, and the distal convoluted tubule. Follow along in Figure 31-10 as we briefly explore these regions.

Proximal Convoluted Tubule

The **proximal convoluted tubule (PCT)**, or more simply *proximal tubule*, is the second part of the nephron but the first part of the *renal tubule*. As its name suggests, the proximal convoluted tubule is the segment proximal, or nearest, to the Bowman capsule. Because it follows a winding, convoluted course, it is called a *convoluted* tubule. Its wall consists of one layer of epithelial cells that have a brush border facing the lumen of the tubule. Thousands of microvilli form the brush border and greatly increase its luminal surface area—a structural fact of importance to its function, as we shall see.

Henle Loop

The **Henle loop,** or *nephron loop*, is the segment of renal tubule just beyond the proximal tubule. It consists of a thin *descending limb*, a sharp turn, and an *ascending limb*. Note in Figure 31-10 that the ascending limb has two regions of different wall thickness: the *thin ascending limb [of Henle] (tALH)* and the *thick ascending limb (TAL)*. The length of the Henle loop is important in the production of highly concentrated or very dilute urine.

Distal Convoluted Tubule

The **distal convoluted tubule (DCT),** or simply *distal tubule*, is a convoluted portion of the tubule beyond (distal to) the Henle loop. The distal convoluted tubule conducts filtrate out of the nephron and into a collecting duct.

The **juxtaglomerular apparatus** (meaning "structure near the glomerulus") is found at the point where the afferent arteriole brushes past the distal convoluted tubule (see Figure 31-12). Also called the *juxtaglomerular complex*, this structure is important in maintaining homeostasis of blood flow because it reflexively secretes **renin** when blood pressure in the afferent arteriole drops. Recall from Chapter 22 that renin triggers a mechanism that produces *angiotensin*, a substance that causes vasoconstriction and the resulting increase in blood pressure (see Figure 31-27 on p. 990).

The unique cells of the juxtaglomerular apparatus represent a modification of cells in the walls of both the distal convoluted tubule and the afferent arteriole at the point where they touch one another. Large smooth muscle cells in the wall of the afferent arteriole—called **juxtaglomerular (JG) cells**—contain renin granules. These cells are sensitive to increased pressure in the arteriole and are considered functional *mechanoreceptors*. Modified distal convoluted tubule cells in the juxtaglomerular apparatus form a dense, tightly packed structure called the **macula densa.** Cells in the macula densa are *chemoreceptors* that can sense the concentration of solute materials in the fluid passing through the tubule. Acting together, both cell types in the juxtaglomerular apparatus contribute to homeostasis of renal function by influencing the ability of the kidney to produce concentrated urine.

COLLECTING DUCT

The **collecting duct (CD)** is formed by the joining of renal tubules of several nephrons. All the collecting ducts of one renal pyramid converge at a renal papilla and release urine through their openings into one of the minor calyces (Figure 31-16). Bowman capsules and both convoluted tubules lie entirely within the cortex of the kidney, whereas the Henle loops and collecting ducts extend into the medulla (see Figure 31-10).

BLOOD SUPPLY OF THE NEPHRON

Earlier in this chapter, we traced renal blood flow through the renal artery and its branches to the afferent arteriole. Blood flows from the afferent arteriole into the glomerular capillaries and then exits through an *efferent arteriole* (Figure 31-17). The efferent arteriole then enters another capillary network that runs alongside the renal tubule. These capillaries are called **peritubular capillaries.** Some of the blood from the efferent arteriole flows through long hairpin-shaped loops that follow the nephron loop. These long, looping arterioles are called the **vasa recta** (*singular*, vas rectum) or *straight arterioles*. Blood flows very slowly through the vasa recta, a fact that plays an important role in the function of these vessels.

As you can see in Figure 31-17, blood flows through the efferent arteriole to the peritubular capillaries and vasa recta—the *peritubular blood supply*—then back toward the heart through *interlobular veins* and *arcuate veins* that head toward the large *renal veins*.

| A&P CONNECT |

Review the overall plan of renal blood flow in ***Tracing Blood Flow in the Kidney*** online at ***A&P Connect.***

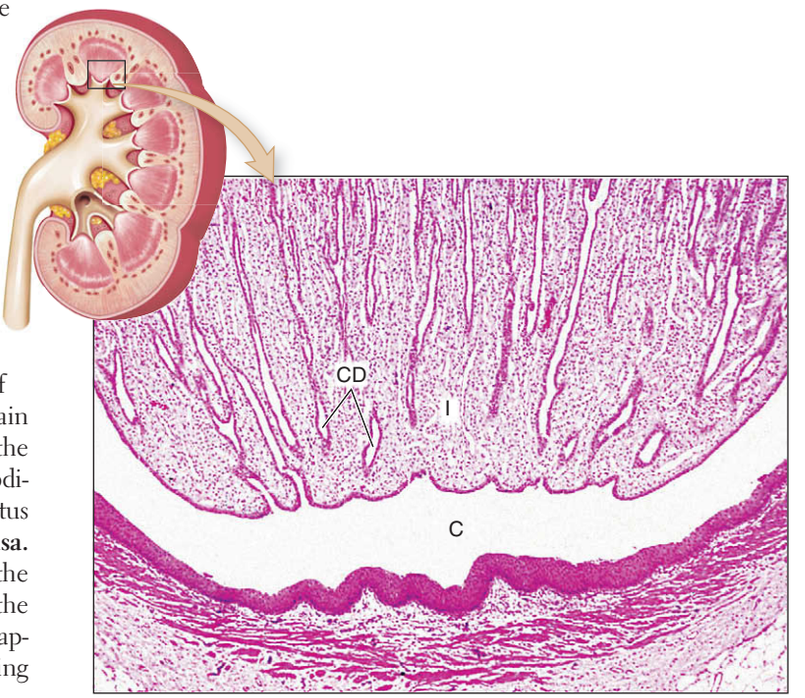


FIGURE 31-16

Renal papilla. Collecting ducts (CD) can be seen opening into a calyx (C) at the papillary tip. The interstitial tissue (I) includes some Henle loops and vasa recta vessels.

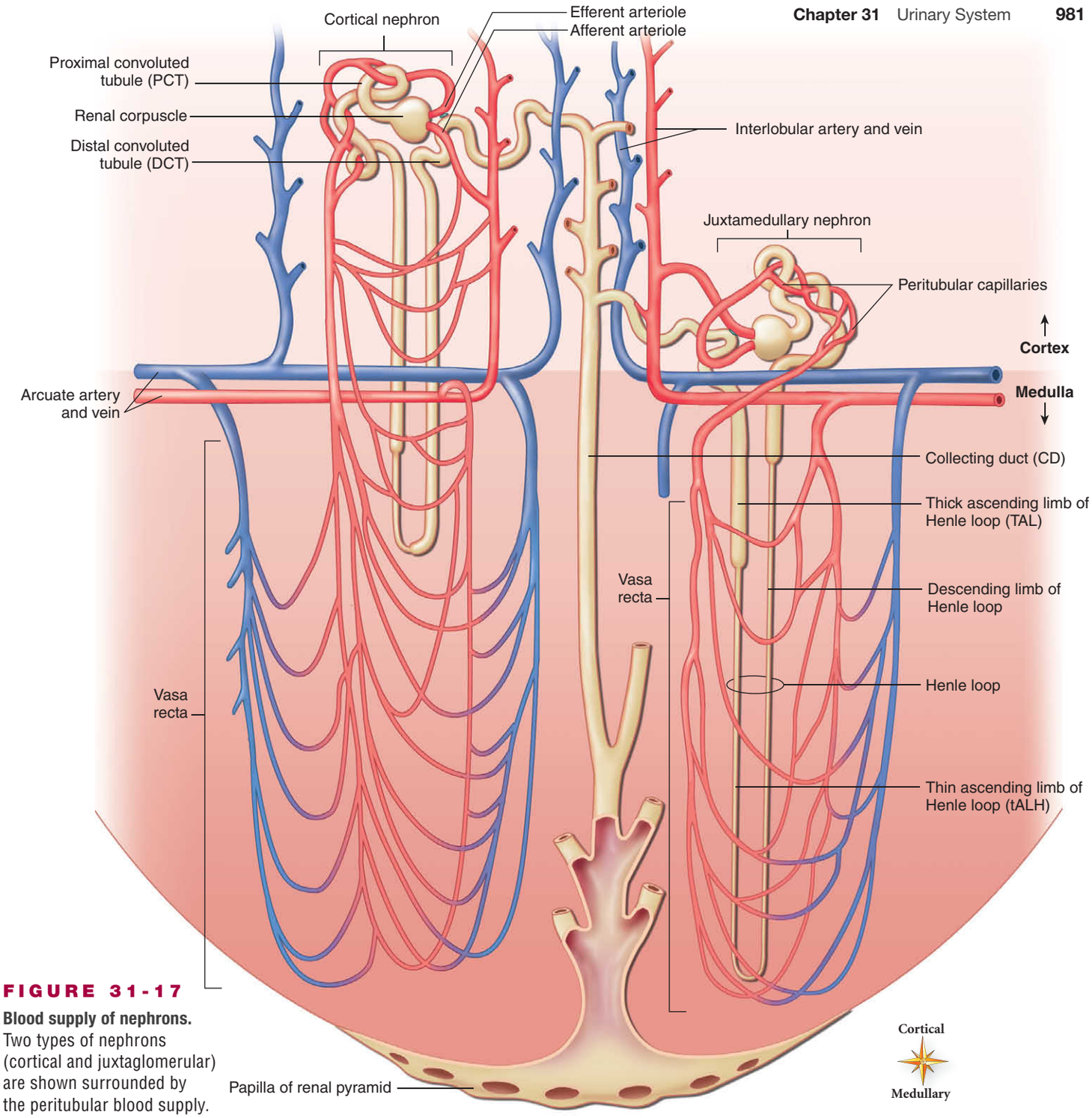


FIGURE 31-17

Blood supply of nephrons. Two types of nephrons (cortical and juxtaglomerular) are shown surrounded by the peritubular blood supply.

TYPES OF NEPHRONS

About 85% of all nephrons are located almost entirely in the renal cortex and are called **cortical nephrons.** The remainder, called **juxtamedullary** (jux-tah-MED-oo-lair-ee) **nephrons,** are found adjoining (*juxta*) the medulla. Juxtamedullary nephrons have long Henle loops that dip far into the medulla (see Figure 31-17). The special role of these long Henle loops of juxtamedullary nephrons in concentrating urine is discussed later.

| QUICK CHECK |

8. Name the segments of the nephron in the order in which fluid flows through them.
9. What characteristics of the glomerular capsular membrane permit filtration?
10. What is the name of the blood supply that surrounds the nephron? The other name for the straight arterioles that follow the nephron loop?

PHYSIOLOGY OF THE URINARY SYSTEM

Overview of Kidney Function

The chief functions of the kidney are to process blood plasma and excrete urine. These functions are vital because they maintain the homeostatic balance of the body. For example, the kidneys are the most important organs in the body for maintaining fluid-electrolyte and acid-base balance. The kidneys do this by varying the amount of water and electrolytes leaving the blood in the urine so that they equal the amounts of these substances entering the blood from various other avenues. Nitrogenous wastes from protein metabolism, notably *urea*, leave the blood by way of the kidneys.

Here are just a few of the blood constituents that cannot be held within their normal concentration ranges if the kidneys fail:

- Sodium
- Potassium
- Chloride
- Nitrogenous wastes (especially urea)

In short, kidney failure means homeostatic failure and, if not relieved, inevitable death.

In addition to processing blood plasma and forming urine, the kidneys also perform other important functions. They influence the rate of secretion of the hormones antidiuretic hormone (ADH) and aldosterone and synthesize the active form of vitamin D, the hormone *erythropoietin*, and certain prostaglandins.

As you already know, the basic functional unit of the kidney is the nephron. It has two main parts—the renal corpuscle and renal tubule—that form urine by means of three processes:

1. **Filtration**—movement of water and protein-free solutes from plasma in the glomerulus, across the glomerular capsular membrane, and into the capsular space of Bowman capsule
2. **Tubular reabsorption**—movement of molecules out of the various segments of the tubule and into the peritubular blood
3. **Tubular secretion**—movement of molecules out of peritubular blood and into the tubule for excretion

These three mechanisms are used in concert to process blood plasma and form urine. First, a hydrostatic pressure gradient drives the filtration of much of the plasma into the nephron (Figure 31-18). Because the filtrate contains materials that the body must conserve (save), the walls of the tubules start reabsorbing these materials back into the blood. As the filtrate (urine) begins to leave the nephron, the kidney may secrete a few "last minute" items into the urine for excretion. In short, the kidney does not selectively filter out only harmful or excess material. It first filters out much of the plasma, then reabsorbs what should not be "thrown out" before the filtrate reaches the end of the tubule and becomes urine. This mechanism allows very fine adjustments to blood homeostasis, as we shall see. Figure 31-19 shows the amounts of some important molecules that are filtered, then reabsorbed, by the nephron.

Filtration

Filtration, the first step in blood processing, is a physical process that occurs in the kidneys' 2.5 million renal corpuscles (see Figures 31-10, 31-12, and 31-15). As blood flows through the glomerular capillaries, water and small solutes filter out of the blood into Bowman capsules. The only blood constituents that do not move out are the blood solids (cells) and most plasma proteins. The result is about 180 liters of glomerular filtrate being formed each day. This filtration takes place through the glomerular capsular membrane.

MECHANISM OF FILTRATION

Filtration from glomeruli into Bowman capsules occurs for the same reason that filtration from other capillaries into interstitial fluid occurs—because of the existence of a pressure gradient. The main factor establishing the pressure gradient between the blood in the glomeruli and the filtrate in the Bowman capsule is the hydrostatic pressure of glomerular blood (Figure 31-20). It tends to cause filtration out of the glomerular blood plasma into Bowman capsules. The intensity of glomerular hydrostatic pressure is influenced by systemic blood pressure and the resistance to blood flow through the glomerular capillaries as described later. However, exerting force in the opposite direction are the osmotic pressure of glomerular blood plasma and the hydrostatic pressure of the capsular filtrate. The net or *effective filtration pressure (EFP)* therefore equals glomerular hydrostatic pressure minus the sum of glomerular osmotic pressure plus capsular hydrostatic pressure (see Figure 31-20). For example, assume the following pressures:

- Glomerular hydrostatic pressure = 60 mmHg
- Glomerular osmotic pressure = 32 mmHg
- Capsular hydrostatic pressure = 18 mmHg
- Capsular osmotic pressure = negligible amount (±0 mmHg)

The EFP (effective filtration pressure), using these particular figures, equals (60 +0) – (32 + 18), or 10 mmHg. An effective filtration

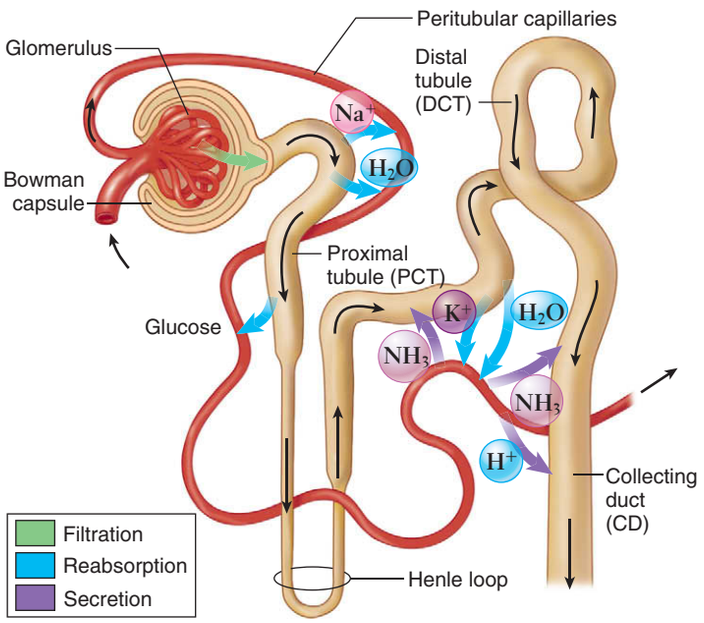


FIGURE 31-18

Overview of urine formation. The diagram shows the basic mechanisms of urine formation—filtration, reabsorption, and secretion—and where they occur in the nephron. Details of these steps are revealed later in this chapter.

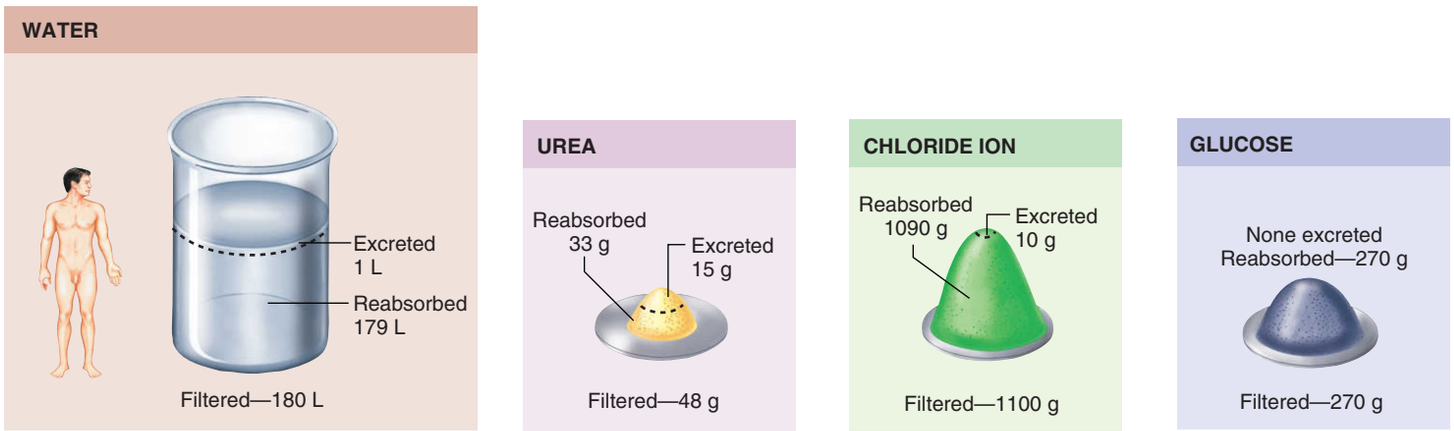


FIGURE 31-19

Filtration and reabsorption volumes. Note the enormous volume of water that is filtered out of glomerular blood per day—180 liters, or many times the total volume of blood in the body. Only a small proportion of this water, however, is excreted into urine. More than 99% of it (179 liters) is reabsorbed into tubular blood.

pressure of 1 mmHg, according to some investigators, produces a glomerular filtration rate of 12.5 ml per minute (including both kidneys). With an EFP of 10 mmHg, the glomerular filtration rate (GFR) would be 125 ml per minute, or about 180 liters in a 24-hour period, a normal rate. (GFR ranges from 150 to 250 liters per day in healthy individuals.) Because only about 1.5 liters of urine is excreted each day, more than 99% of the filtrate must be reabsorbed from the tubular segments of the nephron.

Filtration occurs more rapidly out of glomeruli than out of other tissue capillaries. One reason for this is a structural difference between the endothelium of glomeruli and that of tissue capillaries. Glomerular endothelium has many more pores (fenestrations) in it, so it is more permeable than tissue capillary endothelium. Another reason for more rapid glomerular filtration than tissue capillary filtration is that glomerular hydrostatic pressure is higher than tissue capillary pressure. The reason for this, briefly, is that the efferent arteriole has a smaller diameter than the afferent arteriole does. Therefore, it offers more resistance to blood flow out of the glomerulus than venules offer to blood flow out of tissue capillaries.

GLOMERULAR FILTRATION RATE

The **glomerular filtration rate (GFR)** is the rate of movement of fluid out of the glomerulus and into the capsular space. GFR is directly proportional to the EFP and can be altered by changes in the diameter of the afferent and efferent arterioles or by changes in the systemic blood pressure (Box 31-3). It can also be altered indirectly by changes in the efficiency of cardiac contraction. Stress may lead to intense sympathetic stimulation of the arterioles with greater constriction of the afferent than the efferent arteriole. Consequently, glomerular hydrostatic pressure falls. In severe stress, it may even drop to a level so low that the EFP falls to zero. No glomerular filtration then occurs. The kidneys "shut down," or in technical language, *renal suppression* occurs.

Glomerular hydrostatic pressure and filtration are directly related to systemic blood pressure. That is, a decrease in blood pressure tends to produce a decrease in both glomerular pressure and the GFR. The converse is also true. However, when arterial pressure increases, a smaller increase in glomerular pressure follows because the afferent arterioles constrict. This decreases blood flow into the glomeruli and prevents a marked rise in glomerular pressure or glomerular filtration. For instance, when the mean arterial blood pressure doubles, glomerular filtration reportedly increases only 15% to 20%.

| QUICK CHECK |

11. What are the three basic processes a nephron uses to form urine?
12. What is the GFR? Why is a high GFR important to kidney function?
13. How does blood pressure affect filtration in the kidney?

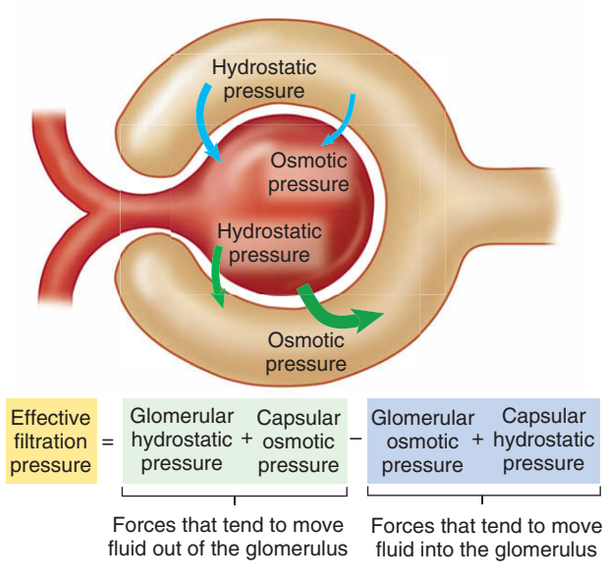


FIGURE 31-20

Forces affecting glomerular filtration. Effective filtration pressure (EFP) is determined by comparing the forces that push fluid into the capillary with those that push it out of the capillary.

Box 31-3 | Changes in Glomerular Filtration Rate

In some types of kidney disease, the permeability of the glomerular endothelium increases sufficiently to allow plasma proteins to filter out into the capsule. Osmotic pressure then develops in the capsular filtrate. To determine how this affects the effective filtration pressure (EFP) in the glomeruli, first calculate the normal EFP by using the Figures that the table lists as "Normal" in the formula given in Figure 31-20. After you have obtained your answer, apply the formula to the Figures given under "Kidney Disease" in the table. You should find an EFP of 10 mmHg with the normal Figures and an EFP of 15 mmHg with the kidney disease figures. A change in the glomerular EFP produces a similar change in the glomerular filtration rate (GFR). Therefore, loss of plasma protein into urine increases not only the EFP but also the GFR.

Intense exercise causes temporary proteinuria in many individuals. Some exercise physiologists believed that intense athletic activities cause kidney damage, but subsequent research has ruled out that explanation. One current hypothesis is that hormonal changes during strenuous exercise increase the permeability of the nephron's filtration membrane, thereby allowing more plasma proteins to enter the filtrate. Some degree of postexercise proteinuria is usually considered normal.

Normal and Abnormal Pressure in the Renal Corpuscle

	HYDROSTATIC PRESSURE	OSMOTIC PRESSURE
Normal		
Glomerular blood	60 mmHg	32 mmHg
Capsular filtrate	18 mmHg	0 mmHg
Kidney Disease		
Glomerular blood	60 mmHg	32 mmHg
Capsular filtrate	18 mmHg	5 mmHg

Reabsorption

Reabsorption, the second step in urine formation, takes place by means of passive and active transport mechanisms from all parts of the renal tubules. A major portion of water and electrolytes and (normally) all nutrients are, however, reabsorbed from the proximal convoluted tubules. The rest of the renal tubule reabsorbs comparatively little of the filtrate. Researchers are still investigating the exact mechanisms of reabsorption in the various segments of the nephron. We have summarized only the essential principles of some of the current concepts in the following paragraphs.

REABSORPTION IN THE PROXIMAL CONVOLUTED TUBULE

As already stated, most of the 180 liters of filtrate that enters the renal tubule from Bowman capsules each day does not get very far. More than two thirds of it is reabsorbed before it reaches the end of the proximal convoluted tubule.

The process of resabsorption begins when sodium ions (Na^+) are actively transported out of the lumen of the tubule and into peritubular blood by the mechanism summarized in Figure 31-21. The microvilli on the luminal surface of each epithelial cell in the tubule wall form a brush border that increases the absorptive surface area of the entire inner face of the tubule. As sodium ions accumulate in the interstitial fluid, the interstitial fluid becomes temporarily positive with respect to the tubule fluid. This electrical gradient (difference in net charge) drives the diffusion of negative ions from the filtrate, into the interstitial fluid, and eventually, into the peritubular blood. In other words, the attraction between negative and positive ions is used to drive the passive transport of chloride (Cl^-), phosphate ($PO_4^{\equiv}$) and other negative ions out of the tubule.

As the concentration of ions in peritubular blood increases, the blood becomes momentarily hypertonic to the tubule fluid. Through the process of osmosis, water diffuses rapidly from the tubule fluid into peritubular blood, thus making the two fluids isotonic. In short, transport of ions out of the proximal convoluted tubules causes osmosis of water out of the tubules as well. This is obligatory water reabsorption—obligatory because it is demanded by the principle of osmosis. Osmosis in the kidney relies on the availability and proper function of a family of water channels called *aquaporins* (see p. 93).

Proximal convoluted tubules reabsorb nutrients from the tubule fluid, notably glucose and amino acids, into peritubular blood by a special type of active transport mechanism called **sodium cotransport.** Recall from Chapter 29 that, in this mechanism, a carrier molecule in the cell membrane first binds to sodium and glucose (see Figure 29-20, p. 921). The carrier then passively transports both substances through the brush border of a proximal convoluted tubule cell into the cell's interior (facilitated diffusion). Sodium moves into the cell because of a concentration gradient maintained by the active transport of sodium out the other side of the cell. Glucose actually moves up its concentration gradient, but no energy is required because it is "riding the coattails" of sodium. Once inside the cell, the substances dissociate from the carrier molecule and diffuse to the far side of the cell. The substances move out of the epithelial cell by different mechanisms. Sodium is transported actively, and glucose is transported passively.

Normally, all the glucose that has filtered out of the glomeruli returns to the blood by this sodium cotransport mechanism. Therefore, very little glucose is lost in urine. If, however, the blood glucose level exceeds a threshold amount (usually between

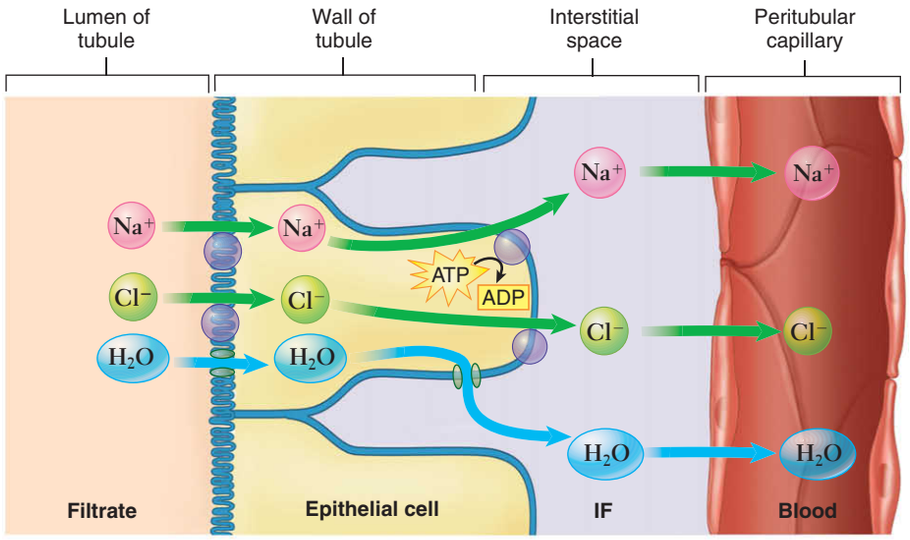


FIGURE 31-21

Mechanisms of tubular reabsorption. Sodium ions (Na^+) are pumped from the tubule cell to interstitial fluid (IF), thereby increasing the interstitial Na^+ concentration to a level that drives diffusion of Na^+ into blood. As Na^+ is pumped out of the cell, more Na^+ passively diffuses in from the filtrate to maintain an equilibrium of concentration. Enough Na^+ moves out of the tubule and into blood that an electrical gradient is established (blood is positive relative to the filtrate). Electrical attraction between oppositely charged particles drives diffusion of negative ions in the filtrate, such as chloride (Cl^-), into blood. As the ion concentration in blood increases, osmosis of water from the tubule occurs. Thus active transport of sodium creates a situation that promotes passive transport of negative ions and water.

130 and 300 mg/100 ml), not all of the glucose can be reabsorbed. The excess glucose remains in urine (Box 31-4). The maximum capacity for moving glucose molecules back into blood is determined by the number of cotransport carriers available. The maximum capacity for moving any substance limited by availability of carriers is called the *transport maximum (Tm* or *Tmax)* of that substance.

Urea is a nitrogen-containing waste formed as a result of protein catabolism (see Chapter 30). Actually, toxic ammonia is formed first, but much of it is quickly transformed into the less toxic urea. Urea in the tubule fluid remains in the proximal convoluted tubule as sodium, chloride, and water are reabsorbed into blood. Once these materials are gone, a tubule fluid high in urea is left. Because the urea concentration in the tubule is then greater than its concentration in peritubular blood, urea passively diffuses into the blood. About half the urea present in the tubule fluid leaves the proximal convoluted tubule this way.

Reabsorption in the proximal convoluted tubules can be summarized in the following manner:

1. Sodium is actively transported out of the tubule fluid and into blood.
2. Glucose and amino acids "hitch a ride" with sodium and passively move out of the tubule fluid by means of the sodium cotransport mechanism.
3. Chloride ions passively move into blood plasma because of an imbalance in electrical charges (positive sodium ions have already moved out, thus making the plasma positive and the tubule fluid negative).
4. Movement of sodium and chloride out of the tubule fluid into plasma creates an osmotic imbalance (the blood is hypertonic to the filtrate), so water is obliged by the principle of osmosis to passively move into blood.
5. About half the urea present in the tubule fluid passively moves out of the tubule, with half the urea thus left to move on to the Henle loop.
6. The total content of the filtrate has been reduced greatly by the time it is ready to leave the proximal convoluted tubule. Most of the water and solutes have been recovered by the blood, and only a small volume of fluid is left to continue to the next portion of the tubule, the Henle loop.

| QUICK CHECK |

14. How are NaCl and water reabsorbed in the proximal convoluted tubule?
15. What is sodium cotransport?
16. What is a transport maximum?

Box 31-4 | HEALTH matters

Glucose in Urine

Occasionally, the maximum cotransport capacity is greatly reduced, and glucose appears in urine *(glycosuria),* even though the blood sugar level may be normal. This condition is known as *renal diabetes* or *renal glycosuria.* It is a congenital defect.

Of course, the most common cause of glycosuria is *diabetes mellitus* (see Chapter 19). In this condition, insulin deficiency or target cell dysfunction causes glucose to accumulate in the blood, causing hyperglycemia. The high glucose content of the filtrate formed in the renal corpuscle exceeds the maximum capacity of the cotransport mechanism. Therefore, glycosuria results.

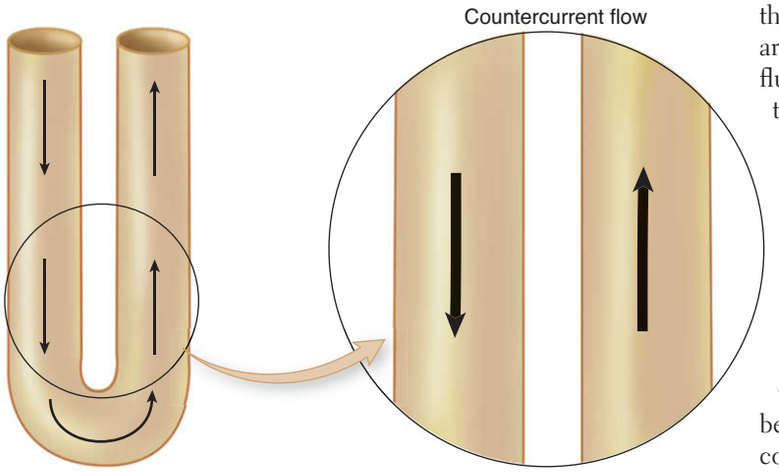


FIGURE 31-22

Concept of countercurrent flow. Countercurrent flow simply refers to flow in opposite directions, as the *inset* shows. Tubule filtrate in the Henle loop flows in a countercurrent manner, as does blood flowing through vasa recta of the peritubular blood supply.

REABSORPTION IN THE HENLE LOOP

In juxtamedullary nephrons—those low in the cortex, near the medulla—the Henle loop and its vasa recta participate in a very unique process called a **countercurrent mechanism.** A countercurrent structure is any set of parallel passages in which the contents flow in opposite directions (Figure 31-22). The Henle loop is a countercurrent structure because the contents of the ascending limb travel in a direction opposite to the flow of urine in the descending limb. The vasa recta also have a countercurrent structure because arterial blood flows down into the medulla and venous blood flows up toward the cortex. The kidney's countercurrent mechanism functions to keep the solute concentration of the medulla extremely high. We will discuss why this is important later on. For now, we will briefly discuss how the countercurrent mechanism achieves this goal.

Before we can understand the kidney's countercurrent mechanisms, we must appreciate the histology of the Henle loop. The descending limb is formed by a much thinner wall than the thick part of the ascending limb (see Figure 31-10). Even more important, the permeability and transport abilities of the two walls are very different. The thin-walled descending limb allows water and urea to diffuse freely into or out of the tubule, depending on their concentration gradients. The thick-walled ascending limb, however, limits the diffusion of most molecules (including water, sodium, chloride, and urea) while actively transporting selected molecules out of the tubule and into the interstitial fluid.

Given the characteristics of each limb, we can see how the system illustrated in Figure 31-23 can develop in the Henle loop. Look at the thick ascending limb. You will see that this limb is actively pumping sodium and chloride out of the tubule fluid and into interstitial fluid. This probably occurs by the same mechanism that operates in the proximal convoluted tubule. Normally, sodium and chloride ions simply diffuse right back into the tubule fluid to achieve equilibrium. The ascending limb prevents the diffusion of these ions, so they are "trapped" in the interstitial area. Under normal circumstances, water moves from the tubule fluid to the interstitial fluid to achieve osmotic balance. However, the wall of the ascending limb is relatively impermeable to water. In short, salt ions are pumped out of the ascending limb, water is prevented from following osmotically, and thus the tubule fluid develops a low solute concentration (low osmotic pressure) and interstitial fluid develops a high solute concentration (high osmotic pressure).

The ion pumps in the ascending limb can maintain an osmotic difference of 200 mOsm across the wall of the tubule. Notice in Figure 31-23 that the movement of salt out of the tubule at any horizontal level creates a difference of 200 mOsm between the tubule fluid and interstitial fluid. Because salt is continually added to the interstitial fluid, the interstitial fluid becomes very concentrated (up to 1200 mOsm in our model). This high solute concentration of the interstitial fluid of the medulla

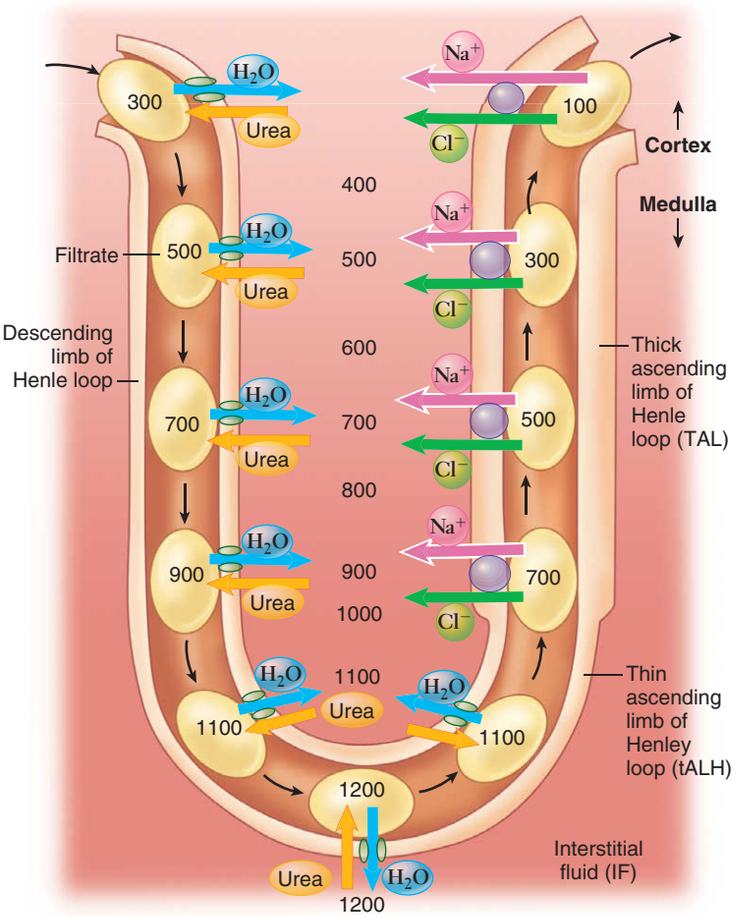


FIGURE 31-23

The countercurrent multiplier system in the Henle loop. Na^+ and Cl^- are pumped from the ascending limb and moved into interstitial fluid (IF) to maintain high osmolality there. Because the salt content of the medullary IF increases, this is called a "multiplier" mechanism. Ion pumping also lowers the tubule fluid's osmolality by 200 mOsm, so fluid leaving the Henle loop is only 100 mOsm (hypotonic), as compared with 300 mOsm (isotonic) when it entered the loop. Numbers in the diagram are expressed in milliosmoles (mOsm).

is created and maintained by the constant pumping of salt by the ascending limb. For this reason, this process is often called a *countercurrent multiplier mechanism*.

You will notice that the tubule fluid in the descending limb equilibrates easily with the interstitial fluid. Because interstitial fluid has a high solute concentration (created by the ion pumps in the ascending limb), the fluid in the descending limb loses water osmotically. Thus the solute concentration of the tubule fluid becomes increasingly higher. Urea, a solute that is also highly concentrated in the renal medulla, diffuses into the tubule fluid in the descending limb—thereby increasing the solute concentration of the tubule fluid even more. However, as the fluid "rounds the bend" and begins moving into the thick portion of the ascending limb, its Na^+ and Cl^- are removed and it becomes increasingly lower in solute concentration.

When tubule fluid enters the Henle loop, it is about 300 mOsm (isotonic to most body fluids). When it leaves the Henle loop, it is about 100 mOsm (hypotonic to most body fluids). Because water is reabsorbed from the fluid in the descending limb, there is a net reduction of tubule fluid volume. And because urea entered the tubule fluid in the descending limb, there is a net increase in urea concentration in the tubule fluid.

You might think that the blood of the vasa recta (a portion of the peritubular blood supply) would remove the excess solute from the medulla's interstitial fluid as it flows through the tissue. Usually it would, but the vasa recta have their own countercurrent mechanism—often called the *countercurrent exchange mechanism*. Figure 31-24 shows how the looping of a vas rectum, down into the medulla, then back up to the cortex, prevents it from accumulating too much solute. Consider also that blood flow through a vas rectum is sluggish; it cannot remove anything very efficiently. Just enough solute is removed to prevent the medulla from crystallizing completely because of a high solute concentration. Thus the tissues of the medulla have the benefits of a blood supply without much loss of its high solute concentration.

The primary functions of the Henle loop are summarized as follows:

- The Henle loop reabsorbs water from the tubule fluid (and picks up urea from the interstitial fluid) in its descending limb. It reabsorbs sodium and chloride from the tubule fluid in the ascending limb.
- By reabsorbing salt from its ascending limb, it makes the tubule fluid dilute (hypotonic).
- Reabsorption of salt in the ascending limb also creates and maintains a high osmotic pressure, or high solute concentration, of the medulla's interstitial fluid.

| QUICK CHECK |

17. What is a countercurrent mechanism?
18. How does the function of the descending limb of the Henle loop differ from the function of the thick ascending limb?
19. What is the purpose of the countercurrent multiplier mechanism of the Henle loop?

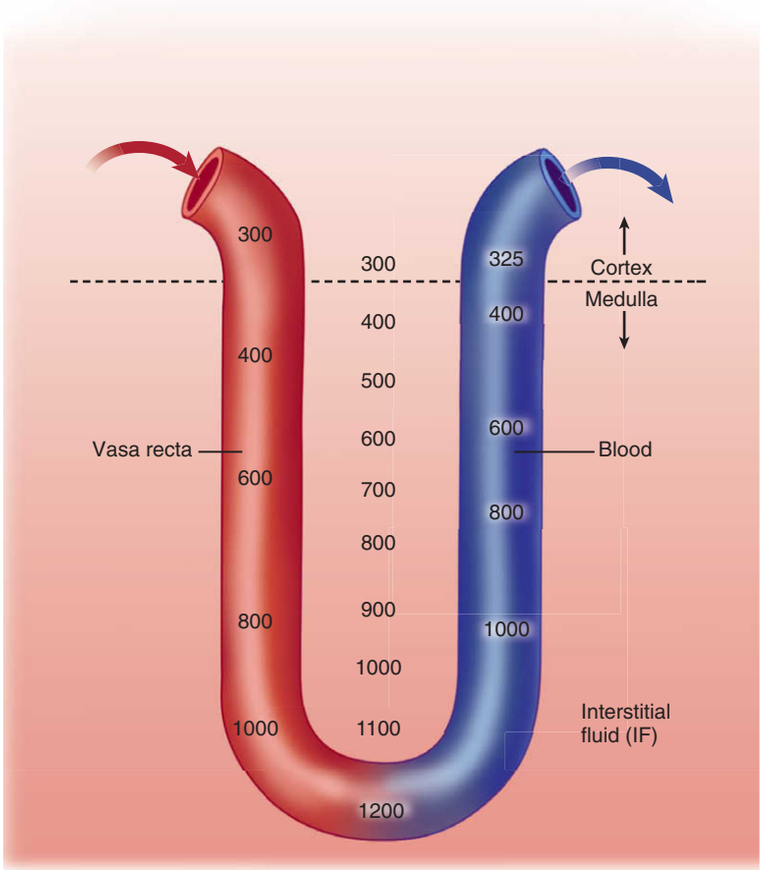


FIGURE 31-24

Countercurrent exchange mechanism in a vas rectum. Because a vas rectum forms a countercurrent loop, blood leaving the capillary bed has only a slightly higher solute content than when it entered. Thus the high osmolality of medullary tissue fluid is maintained. If peritubular blood instead traveled straight through the tissue, all excess solute in the medulla would be removed, and the osmolality of medullary interstitial fluid (IF) would be equivalent to that of the cortex. Numbers in the diagram are expressed in milliosmoles.

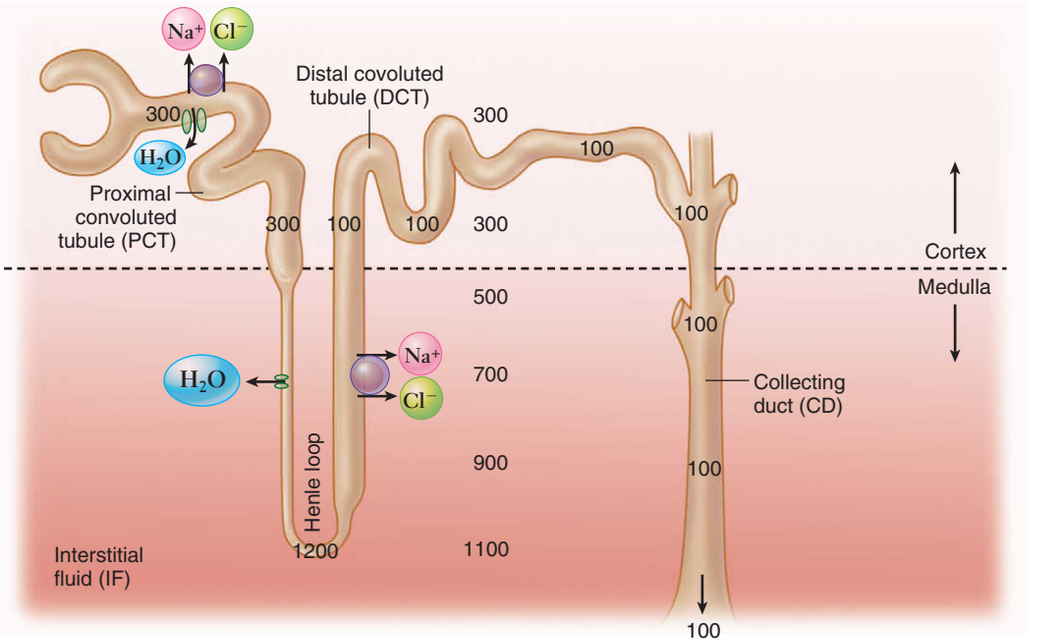
REABSORPTION IN THE DISTAL TUBULES AND COLLECTING DUCTS

The distal convoluted tubule is similar to the proximal convoluted tubule in that it also reabsorbs some sodium by active transport, but in much smaller amounts. Left to themselves, the cells that form the distal tubule's walls are relatively impermeable to water. This means that sodium can be removed, but water cannot follow osmotically, so the solute concentration of the tubule fluid continues to decrease. Recall that the tubule fluid is already hypotonic to most body fluids at this point because of the countercurrent system in the Henle loop.

The cells that form the wall of the collecting duct also prevent water from leaving the filtrate by osmosis. Even though the collecting duct conducts the tubule fluid through the hypertonic medullary region, equilibration does not occur.

FIGURE 31-25

Production of hypotonic urine. Hypotonic urine is produced by the nephron by the mechanism shown here. The isotonic (300 mOsm) tubule fluid that enters the Henle loop becomes hypotonic (100 mOsm) by the time it enters the distal convoluted tubule. The tubule fluid remains hypotonic as it is conducted out of the kidney because the walls of the distal tubule and collecting duct are impermeable to H_2O, Na^+, and Cl^-. Values are expressed in milliosmoles.



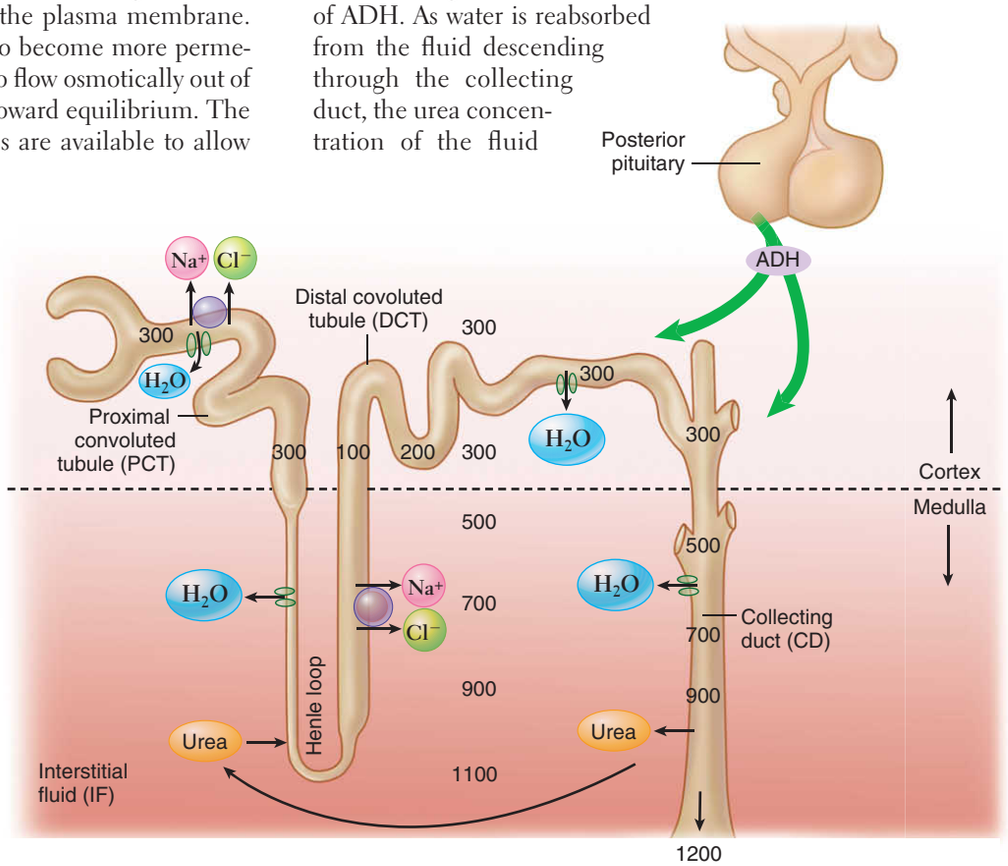
Given no other circumstances, the kidney produces and excretes only very dilute (hypotonic) urine (Figure 31-25). This would be catastrophic because the body would soon dehydrate. A regulatory mechanism centered outside the kidney normally prevents excessive loss of water. This mechanism, illustrated in Figure 31-26, involves *antidiuretic hormone (ADH)*, a hormone secreted by the neurohypophysis (posterior pituitary).

ADH targets cells of the distal tubules and collecting ducts and triggers the cells to move aquaporins to the plasma membrane. These aquaporins allow the tubule wall to become more permeable to water. Water is thereby permitted to flow osmotically out of the tubule and into the interstitial fluid, toward equilibrium. The more ADH present, the more aquaporins are available to allow more water out of the tubule, and the closer the tubule fluid's solute concentration matches that of the surrounding tissue fluid. In this way, the tubule fluid's osmotic pressure could go as high as 1200 mOsm, because the medulla's interstitial fluid can be that high. The solute concentration of the urine excreted depends in large part on the amount of ADH present.

Notice in Figure 31-26 that reabsorption of urea also occurs in the collecting duct when water is reabsorbed under the influence of ADH. As water is reabsorbed from the fluid descending through the collecting duct, the urea concentration of the fluid

FIGURE 31-26

Production of hypertonic urine. Hypertonic urine can be formed when antidiuretic hormone (ADH) is present. ADH, a posterior pituitary hormone, increases the water permeability of the distal tubule and collecting duct. Thus hypotonic (100 mOsm) tubule fluid leaving the Henle loop can equilibrate first with the isotonic (300 mOsm) interstitial fluid (IF) of the cortex, then with the increasingly hypertonic (400 to 1200 mOsm) IF of the medulla. As H_2O leaves the collecting duct by osmosis, the filtrate becomes more concentrated with the solutes left behind. The concentration gradient causes urea to diffuse into the IF, where some of it is eventually picked up by tubule fluid in the descending limb of the Henle loop *(long arrow)*. This countercurrent movement of urea helps maintain a high solute concentration in the medulla. Values are expressed in milliosmoles.



rises. Because the urea concentration is higher inside the lower part of the collecting duct than it is in the surrounding interstitial fluid, urea diffuses out of the lower collecting duct. The addition of urea to the medullary interstitial fluid assists in maintaining a high solute concentration in the medulla. Less than half the urea that leaves the collecting duct is removed by the vasa recta. The dashed line in Figure 31-26 shows that much of the urea in the medullary interstitial fluid diffuses into the descending limb of the Henle loop. Thus urea participates in a sort of countercurrent multiplier mechanism that, together with the countercurrent mechanisms of the Henle loop and vasa recta, maintains the high osmotic pressure needed to form concentrated urine and therefore avoid dehydration.

Tubular Secretion

In addition to reabsorption, tubule cells also secrete certain substances. Tubular secretion means the movement of substances out of the blood and into tubular fluid.

Recall that the descending limb of the Henle loop removes urea by means of diffusion. The distal tubules and collecting ducts secrete potassium, hydrogen, and ammonium ions. They actively transport potassium ions (K^+) or hydrogen ions (H^+) out of the blood into tubule fluid in exchange for sodium ions (Na^+), which diffuse back into the blood (H^+ transport is discussed further in Chapter 33). Potassium secretion increases when the blood aldosterone concentration increases. *Aldosterone*, a hormone of the adrenal cortex, targets distal tubule and collecting duct cells and causes them to increase the activity of the sodium-potassium pumps that move sodium out of the tubule and potassium into the tubule. Hydrogen ion secretion increases when the blood hydrogen ion concentration increases. Ammonium ions are secreted into the tubule fluid by diffusing out of the tubule cells where they are synthesized.

Tubule cells also secrete various organic ions and compounds. Various toxins and many drugs such as penicillin and para-aminohippurate acid (PAH) can be cleared from the blood plasma this way.

Table 31-1 summarizes the functions of the different parts of the nephron in forming urine.

Regulation of Urine Volume

ADH has a central role in the regulation of urine volume. Control of the solute concentration of urine translates into control of urine volume. If no water is reabsorbed by the distal tubule and collecting ducts, urine volume is relatively high—and water loss from the body is high. As water is reabsorbed under the influence of ADH, the total volume of urine is reduced by the amount of water removed from the tubules. Thus ADH reduces water loss by the body.

Another hormone that tends to decrease urine volume—and thus conserves water—is aldosterone, a secretion of the adrenal cortex. It increases distal tubule and collecting duct absorption of sodium, which in turn causes an osmotic imbalance that drives the reabsorption of water from the tubule. Because water reabsorption

TABLE 31-1 Summary of Nephron Function

PART OF NEPHRON	FUNCTION	SUBSTANCE MOVED
Renal corpuscle	Filtration (passive)	Water
		Smaller solute particles (ions, glucose, etc.)
Proximal convoluted tubule (PCT)	Reabsorption (active)	Active transport: Na^+ Cotransport: glucose and amino acids
	Reabsorption (passive)	Diffusion: Cl^-, $PO_4^{\equiv}$, urea, other solutes Osmosis: water
Henle loop		
Descending limb (DLH) and thin ascending limb (tALH)	Reabsorption (passive)	Osmosis: water
	Secretion (passive)	Diffusion: urea
Thick ascending limb (TAL)	Reabsorption (active)	Active transport: Na^+
	Reabsorption (passive)	Diffusion: Cl^-
Distal convoluted tubule (DCT)	Reabsorption (active)	Active transport: Na^+
	Reabsorption (passive)	Diffusion: Cl^-, other anions
		Osmosis: water (only in the presence of ADH)
	Secretion (passive)	Diffusion: ammonia
	Secretion (active)	Active transport: K^+, H^+, some drugs
Collecting duct (CD)	Reabsorption (active)	Active transport: Na^+
	Reabsorption (passive)	Diffusion: urea Osmosis: water (only in the presence of ADH)
	Secretion (passive)	Diffusion: ammonia
	Secretion (active)	Active transport: K^+, H^+, some drugs

ADH, Antidiuretic hormone.

in the distal tubule and collecting duct portions requires ADH, the aldosterone mechanism must work in concert with the ADH mechanism if homeostasis of the fluid content in the body is to be maintained. The cooperative roles of ADH and aldosterone in regulating urine volume—and thus regulating fluid balance in the whole body—are summarized in Figure 31-27.

You may recall from Chapters 19 and 22 that another hormone, specifically, **atrial natriuretic hormone (ANH),** also influences water reabsorption in the kidney. ANH is secreted by specialized muscle fibers in the atrial wall of the heart. Its name implies its function: ANH promotes natriuresis (loss of Na^+ via urine). ANH indirectly acts as an antagonist of aldosterone, by promoting the secretion of sodium into the kidney tubules rather than sodium reabsorption. Thus ANH reduces the plasma and interstitial fluid Na^+ concentration, which in turn, reduces the reabsorption of water by having the effect opposite that of aldosterone. ANH also inhibits the secretion of aldosterone and opposes the aldosterone-ADH mechanism to reabsorb less water and therefore produce more urine. In short, ANH inhibits the ADH mechanism—thus inhibiting water conservation by the internal environment and increasing urine volume.

Urine volume also relates to the total amount of solutes other than sodium excreted in urine. Generally, the more solutes, the more urine. Probably the best known example of this principle occurs in untreated

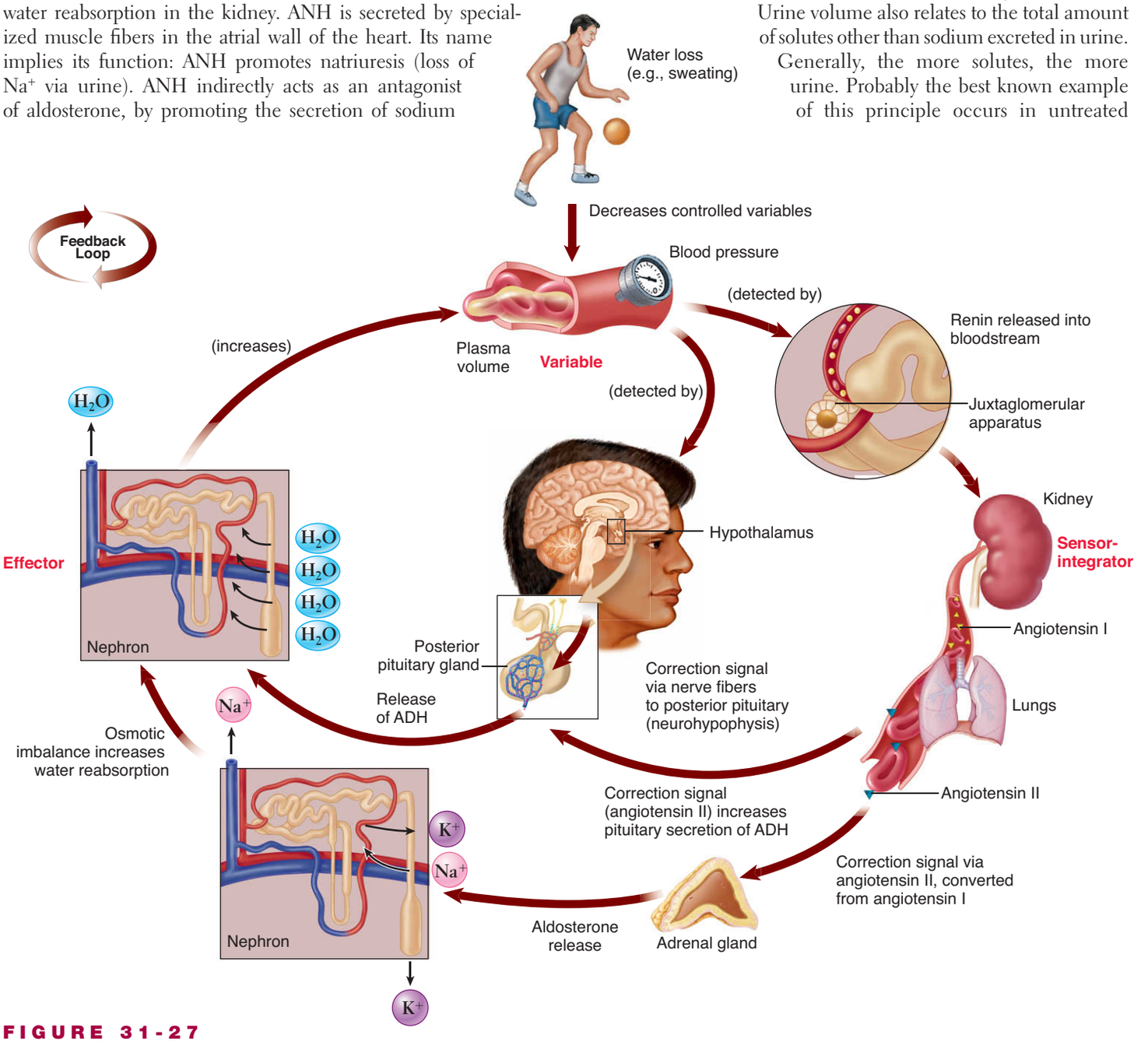


FIGURE 31-27

Cooperative roles of ADH and aldosterone in regulating urine and plasma volume. The drop in blood pressure that accompanies loss of fluid from the internal environment triggers the hypothalamus to rapidly release antidiuretic hormone (ADH) from the posterior pituitary gland. ADH increases water reabsorption by the kidney by increasing the water permeability of the distal tubules and collecting ducts. The drop in blood pressure is also detected by each nephron's juxtaglomerular apparatus, which responds by secreting renin. Recall from Chapter 19 that renin triggers the formation of angiotensin II, which stimulates the release of aldosterone from the adrenal cortex. Aldosterone then slowly boosts water reabsorption by the kidneys by increasing reabsorption of Na^+. Because angiotensin II also stimulates the secretion of ADH, it serves as an additional link between the ADH and aldosterone mechanisms.

diabetes mellitus. The symptom that often brings a person with undiagnosed diabetes to a physician is the voiding of abnormally large amounts of urine. Excess glucose "spills over" into urine, thereby increasing the solute concentration of urine (and decreasing the solute concentration of plasma), which in turn leads to diuresis.

Urine volume is not normally altered by changes in the GFR, which remains remarkably constant in normal individuals over extended periods. A process called *autoregulation* of glomerular filtration by **tubuloglomerular feedback** is dependent on proper functioning of the macula densa cells and the juxtaglomerular apparatus (see p. 980 and Figure 31-12). This regulatory mechanism helps protect the kidney from rapid systemic arterial pressure variations that would otherwise cause large GFR changes. It does so by regulating resistance in both afferent and efferent arterioles. Figure 31-28, *A*, summarizes the major steps of this process. As systemic blood pressure varies, chemoreceptors sensitive to the flow rate and osmolarity of the filtrate can either speed up or slow down the GFR, thus allowing more or less time for chemical processing of tubular filtrate.

In addition, the feedback regulatory response also influences the renin-angiotensin mechanism and systemic blood pressure levels (see Figure 31-27).

The autoregulatory **myogenic mechanism** is yet another rapid and effective way to help maintain a constant GFR during systemic changes in arterial blood pressure (Figure 31-28, *B*). If blood pressure increases, for example, during muscular exertion, the stretched walls of the afferent arterioles automatically contract more strongly to decrease blood flow and return the GFR to resting levels. In circumstances causing a decrease in systemic blood pressure, the smooth muscle in the then relaxed walls of the afferent arterioles will cause dilation, thus increasing blood flow and the GFR to normal "set point" levels.

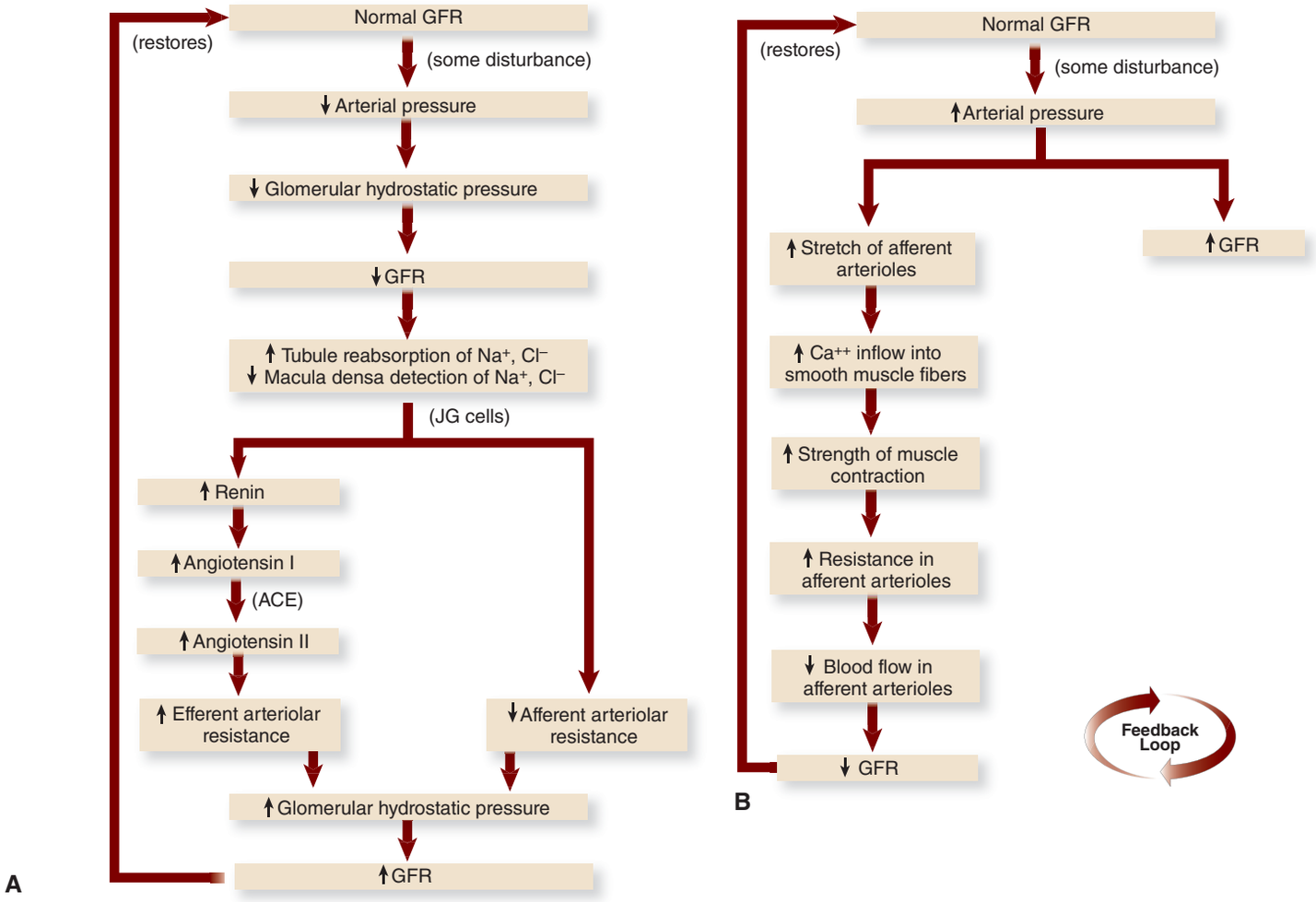


FIGURE 31-28

Autoregulation of renal blood flow and GFR. A, Tubuloglomerular feedback mechanism triggered by a disturbance that decreases renal arterial blood pressure and thus lowers GFR (glomerular filtration rate) below normal. Normal GFR is restored when JG (juxtaglomerular) cells trigger an increase of hydrostatic (blood) pressure in the glomerulus. *ACE,* Angiotensin converting enzyme. **B,** Myogenic mechanism triggered by a disturbance that increases renal arterial blood pressure and thus increases GFR above normal. Afferent arterioles stretch and automatically contract to increase resistance and decrease blood flow, thereby reducing GFR back toward normal.

Urine Composition

The physical characteristics of normal urine are listed in Table 31-2. Notice that normal and abnormal characteristics are listed.

Urine is approximately 95% water, in which are dissolved several kinds of substances; the most important are discussed below:

Nitrogenous wastes—(resulting from protein catabolism) such as urea (the most abundant solute in urine), uric acid, ammonia, and creatinine (Box 31-5).

Electrolytes—mainly the following ions: sodium, potassium, ammonium, chloride, bicarbonate, phosphate, and sulfate. The amounts and kinds of minerals vary with diet and other factors.

Toxins—during disease, bacterial poisons leave the body in urine. One reason for "forcing fluids" on patients suffering with infectious diseases is the need to dilute the toxins that might damage the kidney cells if eliminated in a concentrated form.

TABLE 31-2 Characteristics of Urine

	NORMAL CHARACTERISTICS	ABNORMAL CHARACTERISTICS
Color and Clarity	Normal urine should be clear; color varies with specific gravity Dilute urine: Transparent straw color Concentrated urine: Deep yellow amber (Occasionally, normal urine may be cloudy because of high dietary levels of fat or phosphate)	Abnormally colored urine may result from (1) pathologic conditions; (2) certain foods; and (3) numerous drugs: 1. Pathologic conditions (examples): Kidney cancer (hemorrhage)—red (RBCs) Bile duct obstruction (gallstones)—orange/yellow (bilirubin) Pseudomonas infection—green (bacterial toxins) 2. Foods (examples): Beets—red Rhubarb—brown Carrots—dark yellow 3. Drugs (examples): Pyridium (urinary tract analgesic)—orange Dilantin (anticonvulsant)—pink/red brown Dyrenium (diuretic)—pale blue Cloudy urine may result from (examples): 1. Bacteria—active infection of urinary system organs 2. Blood cells RBCs—hemorrhage from kidney cancer WBCs—pus from urinary tract infection (UTI) 3. Casts—various types of tubelike clumps (blood cell, epithelial, hyaline, waxy, etc.) that form in diseased renal tubes 4. Proteinuria—(protein—usually albumin) in urine 5. Crystals—usually uric acid or phosphate/calcium oxalate in concentrated urine
Compounds	Mineral ions (for example, Na^+, Cl^-, K^+) Nitrogenous wastes: ammonia, creatinine, urea, uric acid Urine pigment: urochrome (product of bilirubin metabolism)	Ketones—generally acetone Protein—generally albumin Glucose Crystals—generally uric acid and phosphate or calcium oxalate Pigments—abnormal levels of bilirubin metabolites
Odor	Slight aromatic Some foods produce a characteristic odor (asparagus) Ammonia-like odor on standing may result from decomposition in stored urine	Strong, sweet, fruity (acetone) odor—uncontrolled diabetes mellitus Foul odor—urinary tract infections (UTIs) Musty odor—phenylketonuria Maple syrup odor—congenital defect in protein metabolism
pH	4.6-8.0 (average 6.0) Toward Low Normal: Some foods (meat & cranberries) and drugs (chlorothiazide diuretics) Toward High Normal: Some foods (citrus fruits, dairy products) and drugs (bicarbonate antacids)	High in alkalosis (kidneys compensate by excreting excess base) Low in acidosis (kidneys compensate by excreting excess H^+)
Specific Gravity	Adult: 1.005-1.030 (usually, 1.010-1.025) Elderly: values decrease with age Newborn: 1.001-1.020	Above normal limits: glycosuria, proteinuria, dehydration, high solute load (may result in precipitation of solutes and kidney stone formation); Below normal limits: chronic renal diseases (inability to concentrate urine), overhydration

Box 31-5 | DIAGNOSTIC study

Blood Indicators of Renal Dysfunction

Renal clearance is the volume of plasma from which a substance is removed from the blood by the kidneys per minute. Elevated urea levels in blood, as measured in a blood urea nitrogen (BUN) test, was one of the earliest clinical measurements of kidney dysfunction. Elevated BUN levels indicate failure of the kidney to clear urea and, therefore, other substances as well (see Mechanisms of Disease, p. 996, for further discussion).

Blood levels of creatinine are also used to test renal function. Creatinine levels in blood seldom change significantly because they are determined by skeletal muscle mass—which seldom changes much. Therefore, an increase in the blood level of plasma creatinine is considered to be a reliable indicator of depressed renal function.

Pigments (especially *urochromes*)—yellowish bile pigments derived from products of the breakdown of old red blood cells in the liver and elsewhere. Various foods and drugs may contain, or be converted to, pigments that are cleared from plasma by the kidneys and are therefore found in the urine.

Hormones—high hormone levels sometimes result in significant amounts of hormone in the filtrate (and therefore in urine).

Abnormal constituents—such as blood, glucose, albumin (a plasma protein), casts (chunks of material, such as mucus, that harden inside the urinary passages and then are washed out in urine), or calculi (small stones).

| QUICK CHECK |

20. Does ADH promote water loss from the internal environment *or* water conservation by the internal environment?
21. How does aldosterone influence secretion in the kidney tubules?
22. How does aldosterone cause the body to conserve water?
23. What gives urine its characteristic yellowish color?

Cycle of LIFE

Urinary System

The kidney plays a critical role in homeostasis by regulating the levels of many substances in blood. Primary renal functions include filtration, reabsorption, and secretion. All are interrelated by complex control systems involving central nervous system activity and hormonal secretions. More than 1 million nephron units in each kidney serve as the structural framework permitting normal function to occur.

Normally, life cycle changes in kidney structure and function occur only within rather narrow limits. Significant structural changes, such as dramatic decreases in the number of nephron units, almost always indicate serious disease or result from trauma such as crush injuries. Functionally, the kidney is able to operate normally throughout life under a wide array of conditions. If, however, the kidneys cannot cope with extreme conditions, such as water deprivation or disease, death will occur from the buildup of toxins in blood.

Initially, kidney function in a newborn is less efficient than in an older child or adult. As a result, the urine is less concentrated because the regulatory mechanisms required to retain water are not fully operative. Incontinence, or an inability to control urination, is normal in very young children. Reflex emptying occurs when the bladder fills, but normal sphincter activity keeps urine in the bladder until filling occurs. In contrast, many older adults have problems with incontinence because of loss of sphincter tone, or control.

Renal clearance is the ability of the kidneys to clear, or cleanse, the blood of a certain substance in a given unit of time, generally 1 minute. This value for certain substances tends to decrease with advanced age, thus indicating deterioration of kidney function. Changes in the porosity of the filtration membrane also occur in the elderly. Loss of functional nephron units is yet another consequence of aging. It contributes to the gradual decline in renal function in this age-group.

the BIG picture

Urinary System and the Whole Body

As our study of the urinary system has shown us, homeostasis of water and electrolytes in body fluids depends largely on proper functioning of the kidneys. Each nephron within the kidney processes blood plasma in a way that adjusts its content to maintain a dynamic constancy of the internal environment of the body. Without renal processing, blood plasma characteristics would soon move out of their set point range. On the other hand, without the blood pressure generated by cardiovascular mechanisms, the kidney could not filter blood plasma and therefore could not process blood plasma. Thus the urinary system and the cardiovascular system are interdependent.

Regulation of urinary function, we have seen, is often centered outside the kidney—mainly in the form of endocrine hormone action. Urinary function is also regulated to some extent by nerve reflexes. Thus both the endocrine system and the nervous system must operate properly to ensure efficient kidney function. The urinary system also interacts with many other body systems and tissues. For example, the kidneys clear the blood plasma of nitrogenous wastes and excess metabolic acids produced by the chemical activity of nearly every cell in the body. The kidneys also can clear some toxins and other compounds that enter the blood via the digestive tract, skin, or respiratory tract.

In the next chapter, we apply some of what we know about urinary function to a broader study of water and ion homeostasis within the human body's internal environment. After that, we discuss the role of the urinary system and other body systems in maintaining a relatively constant pH in the body's internal environment.

MECHANISMS of DISEASE

You may have experienced the discomfort and pain of a bladder infection or know someone who has. Bladder infection is the most common urinary disorder, but it is not usually serious if promptly treated. However, numerous renal and urinary disorders *are* very serious. Any disorder that significantly reduces the effectiveness of the kidneys is immediately life threatening. In this section, we discuss some life-threatening kidney diseases, as well as a few of the less serious, but more common, disorders.

Renal Hypertension

Recall from Chapter 22 (p. 714) that hypertension is abnormally high blood pressure. So-called *renal hypertension* is a common type of secondary hypertension that may be caused by stenosis (narrowing) of the renal artery, often caused by the accumulation of atherosclerotic plaque. In these cases, the elevation is secondary to reduced blood flow, resulting in ischemia of kidney tissues. When this occurs, the cells of the juxtaglomerular apparatus secrete renin, which in turn results in angiotensin production and increased blood pressure (see Figures 22-27 and 31-27 for a review of renin-angiotensin effects). Testing of renal vein blood for increased renin levels is performed to confirm the diagnosis, and insertion of a stent into the lumen of the renal artery to increase blood flow to the kidney may be curative.

Obstructive Disorders

Obstructive urinary disorders are abnormalities that interfere with normal urine flow anywhere in the urinary tract (Box 31-6). The severity of obstructive disorders depends on where the interference occurs and to what degree the flow of urine is impaired. Obstruction of urine flow usually results in "backing up" of the urine, perhaps all the way to the kidney itself. When urine backs up into the kidney, causing swelling of the renal pelvis and calyces, the condition is called **hydronephrosis** (Figure 31-29). A few of the more important obstructive conditions are summarized here.

Renal Calculi

Renal calculi, or *kidney stones*, are crystallized mineral chunks that develop in the renal pelvis or calyces. Many calculi develop as calcium and other minerals crystallize on the renal papillae, then break off into the urine. Blood uric acid levels become elevated in those with *gout*, and deposits of uric acid in the kidneys produce uric acid stones or calculi. *Staghorn calculi* are large, branched stones that form in the pelvis and branched calyces.

If the stones are small enough, they simply pass through the ureters and urethra and are eventually voided with the urine. Larger stones may obstruct the ureters, causing intense pain called *renal colic* as rhythmic muscle contractions of the ureter attempt to dislodge it. Hydronephrosis may occur if the stone does not move from its obstructing position. In the past, only traditional surgical procedures were effective in removing relatively large stones that formed in the calyces and renal pelvis of the kidney. A technique called **lithotripsy,** which uses an ultrasound generator called a **lithotriptor,** is now used quite often to pulverize stones so that they can be flushed out of the urinary tract without surgery.

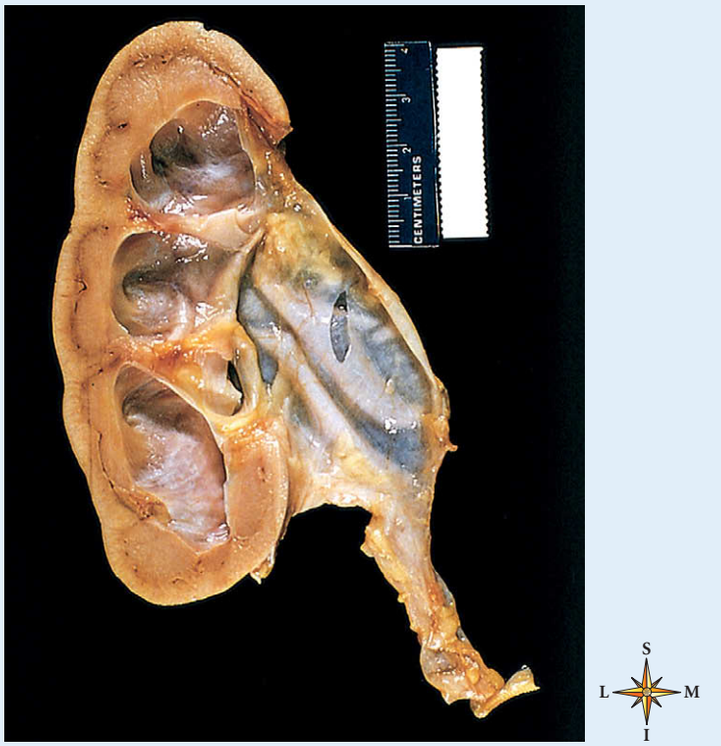


FIGURE 31-29

Hydronephrosis. Note the marked dilation of the renal pelvis and calyces caused by the blockage and "backing up" of urine.

Neurogenic and Overactive Bladder

Disruption of nervous input to the bladder results in loss of normal control of voiding. The condition is called **neurogenic bladder.** Depending on the nature and severity of the lack of nervous control, various signs and symptoms of bladder paralysis or abnormal activity result. Involuntary retention of urine, subsequent distention (bulging) of the bladder, and perhaps a burning sensation or fever with chills are common symptoms. The end result is often *urinary incontinence*—leakage of urine or some degree of involuntary urination. Serious stroke or spinal cord injury often results in a type of neurogenic bladder characterized by total loss of normal control of

Box 31-6 | HEALTH matters

Clinical Terms Associated With Urine Abnormalities

Glycosuria or **glucosuria**—Sugar (glucose) in urine
Hematuria—Blood in urine
Pyuria—Pus in urine
Dysuria—Painful urination
Polyuria—Unusually large amounts of urine
Oliguria—Scant urine
Anuria—Absence of urine

voiding. Called "*reflex incontinence*," this is characterized by periodic but unpredictable and involuntary urination that occurs in the absence of any sensory warning or awareness.

Urinary catheterization is the passage or insertion of a hollow tube or catheter through the urethra into the bladder for the withdrawal of urine. It is a medical procedure commonly performed on many patients who undergo prolonged surgical or diagnostic procedures or who experience problems with urinary retention. Correct catheterization procedures require aseptic techniques to prevent the introduction of infectious bacteria into the urinary system. Clinical studies have proved that improper catheterization techniques cause bladder infections (cystitis) and point out the need for extensive training of health professionals who perform catheterizations. To minimize the risk of infection, some facilities now use ultrasound imaging of the bladder to determine whether urine is being involuntarily retained in the bladder—replacing the former practice of catheterizing a patient.

Overactive bladder refers to the need for frequent urination because of abnormally strong or frequent micturition contractions of the bladder. If you look back to Figure 31-9 on p. 975, you see that these contractions normally do not get strong until there is about 200 to 250 ml of urine in the bladder. With an overactive bladder, the contractions can begin to get stronger with a much lower volume of urine, which is sooner than expected. Therefore the amount voided at any one time is generally small, and feelings of extreme urgency and pain with each voiding are common. Although serious medical outcomes are rare, incontinence associated with overactive bladder is an often embarrassing and frustrating problem for those who are plagued with symptoms. In the past, treatments for this rather common problem were limited to behavioral techniques and in some cases, surgery. Now, medications are available that reduce the involuntary contractions and incontinence associated with overactive bladder. Commonly used drugs include so-called "anticholinergic" medications such as solifenacin (Vesicare) and "alpha-adrenergic blocker" drugs that promote smooth muscle relaxation in the bladder and urethra.

Tumors and Other Obstructions

Tumors of the urinary system typically obstruct urine flow, possibly causing hydronephrosis in one or both kidneys. Most kidney tumors are malignant neoplasms called **renal cell carcinomas.** They usually occur only in one kidney. Bladder cancer occurs about as frequently as renal cancer (each accounts for about 2 in every 100 cancer cases). Renal and bladder cancer have few symptoms early in their development, other than traces of blood in the urine, or **hematuria** (hem-ah-TOO-ree-ah). As the cancer develops, pelvic pain and symptoms of urinary obstruction may occur. Insertion of a **cystoscope** (SIS-toh-skohp) through the urethra and into the bladder permits direct inspection of bladder and other lower urinary tract lesions (Figure 31-30). The hollow tube allows the passage of a light, a viewing lens, and various catheters and operative devices.

Various other conditions can obstruct the normal flow of urine. For example, a person with a low proportion of body fat may lack the pad of fat that normally surrounds the kidneys. One or both kidneys may then drop, a condition called **renal ptosis** (TOH-sis). In renal ptosis, the ureters that drain urine out of the kidney may kink and thus obstruct the normal flow of urine. Urinary passages may also be abnormally narrowed through scarring, inflammation, or external pressure—a condition known as a **stricture.**

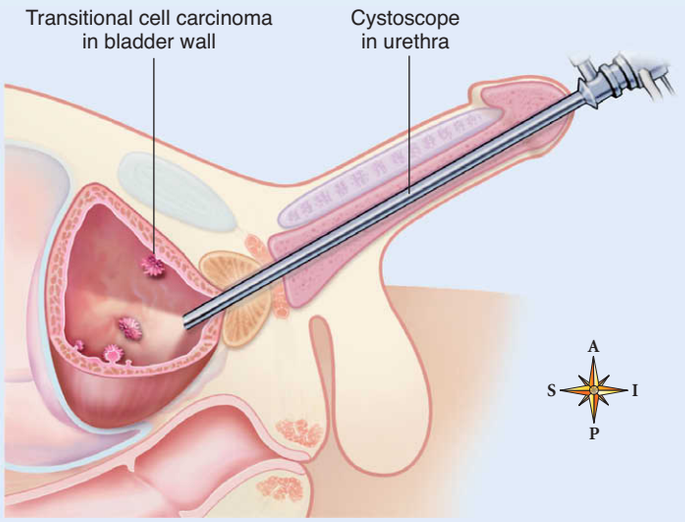


FIGURE 31-30

Cystoscopic view of bladder cancer. The cystoscope inserted through the urethra to view a male bladder.

Urinary Tract Infections

Most *urinary tract infections* (UTIs) are caused by bacteria, usually gram-negative types. UTIs can involve the urethra, bladder, ureter, and/or kidneys. Common types of urinary tract infections are summarized below.

Urethritis is an inflammation of the urethra that commonly results from bacterial infection, often *gonorrhea*. Nongonococcal urethritis is usually caused by a *Chlamydia* infection. Males suffer from urethritis more often than females do.

Cystitis is a term that refers to any inflammation of the bladder. Cystitis commonly occurs as a result of infection but also can accompany calculi, tumors, or other conditions. Bacteria usually enter the bladder through the urethra. Cystitis occurs more frequently in women than in men because the female urethra is shorter and closer to the anus (a source of bacteria) than in males. Bladder infections are characterized by pelvic pain, an urge to urinate frequently, and hematuria. **Interstitial cystitis** is a form of bladder inflammation that occurs without evidence of bacterial infection. It is a persistent and often very painful form of cystitis that is characterized by feelings of urgency, pain on urination, and the appearance of blood in the urine. The bladder wall often shows patches of chronic mucosal ulceration. Antiinflammatory drugs and supportive treatment of symptoms are often coupled with infusion of sterile fluid to distend the bladder and reduce feelings of urgency. Although the cause is unknown, many physicians believe an autoimmune response is involved. Interstitial cystitis is often associated with lupus erythematosus and other autoimmune disease conditions.

Nephritis is a general term referring to kidney disease, especially inflammatory conditions. **Pyelonephritis** is literally "pelvis nephritis" and refers to inflammation of the renal pelvis and connective tissues of the kidney. As with cystitis, pyelonephritis is usually caused by bacterial infection but can also result from viral infection, mycosis (fungal infection), calculi, tumors, pregnancy, and other conditions.

| A&P CONNECT |

Mycotic (fungal) infections most often occur in individuals with a weakened immune system, such as the sick and elderly. To see the effects of fungal growth in the urinary tract, check out the image of an *aspergillosis* infection in ***Visualizing the Urinary Tract*** online at ***A&P Connect.***

Glomerular Disorders

Glomerular disorders, collectively called **glomerulonephritis,** result from damage to the glomerular capsular membrane. This damage can be caused by immune mechanisms, heredity, and other factors. Without successful treatment, glomerular disorders can progress to kidney failure.

Nephrotic syndrome is a collection of signs and symptoms that accompany various glomerular disorders. This syndrome is characterized by the following:

- Proteinuria—presence of proteins (especially *albumin*) in urine. Protein, normally absent from urine, filters through damaged glomerular capsular membranes and is not reabsorbed by the kidney tubules.
- Hypoalbuminemia—low albumin concentration in the blood, resulting from loss of albumin from the blood through holes in the damaged glomeruli. Albumin is the most abundant plasma protein. Because it normally cannot leave the blood vessels, it usually remains as a "permanent" solute in plasma. This keeps the plasma water concentration low and thus prevents the osmosis of large amounts of water out of the blood and into tissue spaces. In hypoalbuminemia, this function is lost and fluid leaks out of the blood vessels and into tissue spaces, thereby causing widespread edema.
- Edema—general tissue swelling caused by the accumulation of fluids in the tissue spaces. The edema associated with nephrotic syndrome is caused by the loss of plasma protein (albumin) and the resulting osmosis of fluid out of the blood.

Acute glomerulonephritis is the most common form of kidney disease. It may be caused by a delayed immune response to streptococcal infection—the same mechanism that causes valve damage in rheumatic heart disease (see Chapter 21). For this reason, it is sometimes called **postinfectious glomerulonephritis.** If antibiotic treatment is not successful, it may progress to a chronic form of glomerulonephritis.

Chronic glomerulonephritis is the general name for various noninfectious glomerular disorders that are characterized by progressive kidney damage leading to renal failure. Immune mechanisms are believed to be the major causes of chronic glomerulonephritis. One immune mechanism involves antigen-antibody complexes that form in the blood when antibodies bind with foreign antigens (or possible self-antigens). These antigen-antibody complexes lodge in the glomerular capsular membrane and trigger an inflammation response. Less commonly, the formation of antibodies that directly attack the glomerular capsular membrane causes chronic glomerulonephritis.

Kidney Failure

Kidney failure, or **renal failure,** is simply failure of the kidney to properly process blood plasma and form urine. Renal failure can be classified as acute or chronic.

Acute renal failure is an abrupt reduction in kidney function that is characterized by oliguria and a sharp rise in nitrogenous compounds in the blood. The concentration of nitrogenous wastes in blood is often assessed by the **blood urea nitrogen (BUN) test**—a high BUN result indicates failure of the kidneys to remove urea from the blood. Acute renal failure can be caused by various factors that alter blood pressure or otherwise affect glomerular filtration. For example, hemorrhage, severe burns, acute glomerulonephritis or pyelonephritis, and obstruction of the lower urinary tract may each progress to kidney failure. If the underlying cause of renal failure is attended to, recovery is usually rapid and complete.

Chronic renal failure is a slow, progressive condition resulting from the gradual loss of nephrons. There are dozens of diseases that may result in the gradual loss of nephron function, including infections, diabetes, glomerulonephritis, tumors, systemic autoimmune disorders, and obstructive disorders.

Polycystic kidney disease (PKD) is a genetic disorder in which large, fluid-filled pockets (cysts) develop in the epithelium of the kidney tubules. In this condition, *primary cilia* in the plasma membrane epithelial cells fail to do their normal job of regulating cell growth—thus allowing cells to overpopulate and obstruct the kidney tubules. The obstructions result in pockets of backed-up urine. Eventually, the kidney fails.

As kidney function is lost as a result of any of these chronic conditions, the glomerular filtration rate (GFR) decreases, causing the BUN levels to climb (Figure 31-31). Chronic renal failure can be described as progressing through three stages:

Stage 1. During the first stage, some nephrons are lost but the remaining healthy nephrons compensate by enlarging and taking over the function of the lost nephrons. As Figure 31-31 shows, BUN is kept within normal limits even though up to 75% of the nephrons are lost (as indicated by a 75% drop in GFR). This stage is often asymptomatic and may last for years, depending on the underlying cause.

Stage 2. The second stage is often called *renal insufficiency.* It is during this stage that the kidney can no longer adapt to the loss of nephrons. The remaining healthy nephrons cannot handle the urea load, and BUN levels climb dramatically (see Figure 31-31). Because the kidney's ability to concentrate urine is impaired, polyuria and dehydration may occur.

Stage 3. The final stage of chronic renal failure is called **uremia,** or **uremic syndrome.** Uremia literally means "high blood urea" and is characterized by a very high BUN value caused by loss of kidney function (see Figure 31-31). During this stage, a low GFR causes low urine production and oliguria. Because fluids are retained by the body rather than eliminated by the kidneys, edema and hypertension often occur. The uremic syndrome includes a long list of other symptoms caused directly or indirectly by the loss of kidney function. Unless an artificial kidney (Box 31-7) is used or a new kidney is transplanted, the progressive loss of kidney function will eventually cause death.

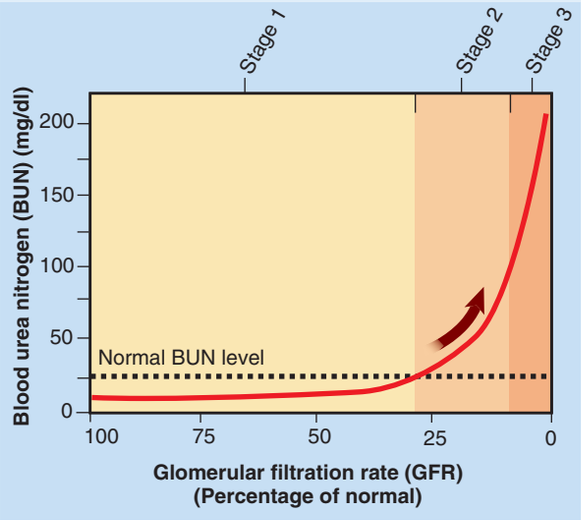


FIGURE 31-31

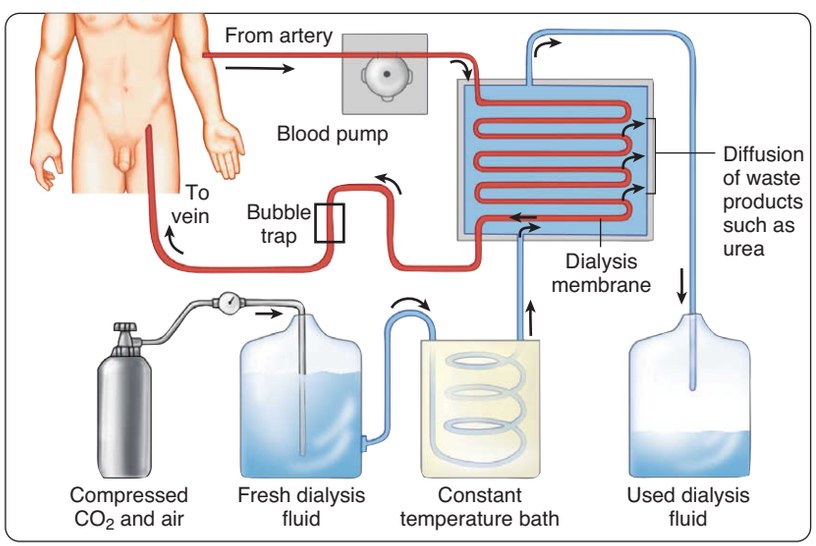
The three stages of chronic renal failure. Stage 1: As nephrons are lost (indicated by decreasing GFR), the remaining healthy nephrons compensate—keeping blood urea nitrogen (BUN) values within the normal range. **Stage 2:** As more than 75% of kidney function is lost, BUN levels begin to climb. **Stage 3:** Uremia (elevated BUN) results from massive loss of kidney function.

Box 31-7 | HEALTH matters

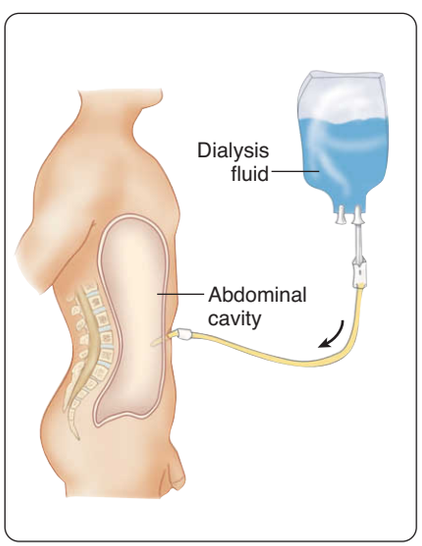
Artificial Kidney

The artificial kidney is a mechanical device that uses the principle of dialysis to remove or separate waste products from the blood. In the event of kidney failure, the process called **hemodialysis** can provide a reprieve from death for the patient. During a hemodialysis treatment, a semipermeable membrane is used to separate large (nondiffusible) particles such as blood cells from small (diffusible) ones such as urea and other wastes. Part *A* of the Figure shows blood from the radial artery passing through a porous (semipermeable) cellophane tube that is housed in a tanklike container. The tube is surrounded by a bath, or dialysis solution, containing varying concentrations of electrolytes and other chemicals. The pores in the membrane are small and allow only very small molecules, such as urea, to escape into the surrounding fluid. Larger molecules and blood cells cannot escape and are returned through the tube to reenter the patient via a wrist or leg vein. By constantly replacing the bath solution in the dialysis tank with freshly mixed solution, levels of waste materials can be kept at low levels. As a result, wastes such as urea in the blood rapidly pass into the surrounding wash solution. For a patient with complete kidney failure, two or three hemodialysis treatments a week are required. New dialysis methods are now being developed, and dramatic advances in treatment are expected in the next few years.

Another technique used in the treatment of renal failure is called **continuous ambulatory peritoneal dialysis (CAPD).** In this procedure, 1 to 3 liters of sterile dialysis fluid is introduced directly into the peritoneal cavity through an opening in the abdominal wall (part *B* of the figure). Peritoneal membranes in the abdominal cavity transfer waste products from blood into the dialysis fluid, which is then drained back into a plastic container after about 2 hours. This technique is less expensive than hemodialysis and does not require the use of complex equipment.



A



B

Hemodialysis.

LANGUAGE OF SCIENCE *(continued from p. 970)*

glomerulus
(gloh-MAIR-yoo-lus)
[*glomer-* **ball**, *-ulus* **little**] *pl.,* glomeruli]

Henle loop
(HEN-lee)
[*Friedrich Gustave Henle* **German anatomist**]

hilum
(HYE-lum)
[*hilum* **least bit**] *pl.,* hila

juxtaglomerular apparatus
(juks-tah-gloh-MER-yoo-lar app-ah-RAT-us)
[*juxta-* **near or adjoining**, *-glomer-* **ball**, *-ul-* **little**, *-ar* **relating to**]

juxtaglomerular cell
(jux-tah-gloh-MAIR-yoo-lar)
[*juxta-* **near or adjoining**, *-glomer-* **ball**, *-ul-* **little**, *-ar* **relating to**, *cell* **storeroom**]

juxtamedullary nephron
(jux-tah-MED-oo-lair-ee NEF-ron)
[*juxta-* **near or adjoining**, *-medulla-* **middle**, *-ary* **relating to**, *nephro-* **kidney**, *-on* **unit**]

kidney

macula densa
(MAK-yoo-lah DEN-sah)
[*macula* **spot**, *densa* **thick**]
pl., maculae densae

mesangial cell
(mess-AN-jee-al)
[*mes-* **middle**, *-angi-* **vessel**, *-al* **relating to**]

myogenic mechanism
(mye-oh-JEN-ik)
[*myo-* **muscle**, *-gen-* **produce**, *-ic* **relating to**]

nephron
(NEF-ron)
[*nephro-* **kidney**, *-on* **unit**]

peritubular capillary
(pair-ee-TOOB-yoo-lar KAP-i-lair-ee)
[*peri-* **around**, *-tub-* **tube**, *-ul-* **little**, *-ar* **relating to**, *capill-* **hair**, *-ary* **relating to**]

proximal convoluted tubule (PCT)
(PROK-si-mal KON-vo-LOO-ted TOO-byool)
[*proxima-* **near**, *-al* **relating to**, *con-* **together**, *-volut-* **roll**, *tub-* **tube**, *-ul-* **little**]

reabsorption
(ree-ab-SORP-shun)
[*re-* **back again**, *-absorp-* **swallow**, *-tion* **process**]

renal clearance
(REE-nal)
[*ren-* **kidney**, *-al* **relating to**]

renal column
(REE-nal)
[*ren-* **kidney**, *-al* **relating to**]

renal corpuscle
(REE-nal KOR-pus-ul)
[*ren-* **kidney**, *-al* **relating to**, *corpus-* **body**, *-cle* **little**]

renal cortex
(REE-nal KOR-teks)
[*ren-* **kidney**, *-al* **relating to**, *cortex* **bark**] *pl.,* cortices

renal medulla
(REE-nal meh-DUL-ah)
[*ren-* **kidney**, *-al* **relating to**, *medulla* **middle**] *pl.,* medullae or medullas

renal pelvis
(REE-nal PEL-vis)
[*ren-* **kidney**, *-al* **relating to**, *pelvis* **basin**]

renal pyramid
(REE-nal PIR-ah-mid)
[*ren-* **kidney**, *-al* **relating to**]

renin
(REE-nin)
[*ren-* **kidney**, *-in* **substance**]

sodium cotransport
(SO-dee-um koh-TRANZ-port)
[*sod-* **soda**, *-ium* **chemical ending**, *co-* **with**, *-trans-* **across**, *-port* **carry**]

trigone
(TRY-gohn)
[*tri-* **three**, *-gon* **corner**]

tubular reabsorption
(TOOB-yoo-lar ree-ab-SORP-shun)
[*tub-* **tube**, *-ul-* **little**, *-ar* **relating to**, *re-* **back again**, *-absorp-* **swallow**, *-tion* **process**]

tubular secretion
(TOOB-yoo-lar seh-KREE-shun)
[*tub-* **tube**, *-ul-* **little**, *-ar* **relating to**, *secret-* **separate**, *-tion* **process**]

tubuloglomerular feedback
(toob-yoo-loh-glow-MER-yoo-lar)
[*tub-* **tube**, *-ul-* **little**, *-glomer-* **ball**, *-ul-* **little**, *-ar* **relating to**]

ureter
(YOOR-eh-ter)
[*ure-* **urine**, *-ter-* **agent or channel**]

urethra
(yoo-REE-thrah)
[*ure-* **urine**, *-thr-* **agent or channel**]

vasa recta
(VAH-sah REK-tah)
[*vas-* **vessel**, *rect-* **straight**] *sing.* vas rectum

LANGUAGE OF MEDICINE

acute glomerulonephritis
(ah-KYOOT gloh-mer-yoo-loh-neh-FRY-tis)
[*acut-* **sharp**, *glomer-* **ball**, *-ul-* **little**, *-nephr-* **kidney**, *-itis* **inflammation**]

anuria
(ah-NOO-ree-ah)
[*a-* **not**, *-ur-* **urine**, *-ia* **condition**]

blood urea nitrogen (BUN) test
(yoo-REE-ah NYE-troh-jen)
[*ure-* **urine**, *nitro-* **soda**, *-gen* **produce**]

chronic glomerulonephritis
(KRON-ik gloh-mer-yoo-loh-neh-FRY-tis)
[*chron-* **time**, *-ic* **relating to**, *glomer-* **ball**, *-ul-* **little**, *-nephr-* **kidney**, *-itis* **inflammation**]

chronic renal failure
(KRON-ik REE-nal FAIL-yoor)
[*chron-* **time**, *-ic* **relating to**, *ren-* **kidney**, *-al* **relating to**]

continuous ambulatory peritoneal dialysis (CAPD)
(AM-byoo-lah-tor-ee pair-i-toh-NEE-al dye-AL-i-sis)
[*ambulat-* **walk**, *-ory* **relating to**, *peritone-* **peritoneum**, *-al* **relating to**, *dia-* **through**, *-lysis* **loosening**]

cystitis
(sis-TYE-tis)
[*cyst-* **bag**, *-itis* **inflammation**]

cystoscope
(SIS-toh-skohp)
[*cyst-* **bag**, *-scop-* **see**]

dysuria
(dis-YOO-ree-ah)
[*dys-* **painful**, *-ur-* **urine**, *-ia* **condition**]

glomerulonephritis
(gloh-mer-yoo-loh-neh-FRY-tis)
[*glomer-* **ball**, *-ul-* **little**, *-nephr-* **kidney**, *-itis* **inflammation**]

glycosuria
(glye-koh-SOO-ree-ah)
[*glyco-* **sweet (glucose)**, *-ur-* **urine**, *-ia* **condition**]

hematuria
(hem-ah-TOO-ree-ah)
[*hema-* **blood**, *-ur-* **urine**, *-ia* **condition**]

hemodialysis
(hee-moh-dye-AL-i-sis)
[*hemo-* **blood**, *-dia-* **through or between**, *-lysis* **loosening**]

hydronephrosis
(hye-droh-neh-FROH-sis)
[*hydro-* **water**, *-nephr-* **kidney**, *-osis* **condition**]

interstitial cystitis
(in-ter-STISH-al sis-TYE-tis)
[*inter-* **between**, *-stit-* **stand**, *-al* **relating to**, *cyst-* **bag**, *-itis* **inflammation**]

lithotripsy
(LITH-oh-trip-see)
[*litho-* **stone**, *-trips-* **pound**, *-y* **action**]

lithotriptor
(LITH-oh-trip-tor)
[*litho-* **stone**, *-trip-* **pound**, *-or* **agent**]

nephritis
(neh-FRY-tis)
[*nephr-* **kidney**, *-itis* **inflammation**]

nephrotic syndrome
(neh-FROT-ik SIN-drohm)
[*nephr-* **kidney**, *-ic* **relating to**]

neurogenic bladder
(noor-oh-JEN-ik BLAD-er)
[*neuro-* **nerves**, *-gen-* **produce**, *-ic* **relating to**]

oliguria
(ohl-i-GOO-ree-ah)
[*olig-* **few or little**, *-ur-* **urine**, *-ia* **condition**]

overactive bladder

polyuria
(pahl-ee-YOO-ree-ah)
[*poly-* **many**, *-ur-* **urine**, *-ia* **condition**]

postinfectious glomerulonephritis
(post-in-FEK-shus gloh-mer-yoo-loh-neh-FRY-tis)
[*post-* **after**, *-infec-* **stain**, *-ous* **relating to**, *glomer-* **ball**, *-ul-* **little**, *-nephr-* **kidney**, *-itis* **inflammation**]

pyelonephritis
(pye-eh-loh-neh-FRY-tis)
[*pyel-* **renal pelvis,** *-nephr-* **kidney,** *-itis* **inflammation**]

pyuria
(pye-YOO-ree-ah)
[*py-* **pus,** *-ur-* **urine,** *-ia* **condition**]

renal calculus
(REE-nal KAL-kyoo-lus)
[*ren-* **kidney,** *-al* **relating to,** *calculi* *little* **stone**] *pl.,* calculi

renal cell carcinoma
(REE-nal cell kar-si-NO-mah)
[*ren-* **kidney,** *-al* **relating to,** *cell* **storeroom,** *carcino-* **cancer,** *-oma* **tumor**]

renal failure
(REE-nal FAIL-yoor)
[*ren-* **kidney,** *-al* **relating to**]

renal ptosis
(REE-nal TOH-sis)
[*ren-* **kidney,** *-al* **relating to,** *ptosis* **falling**]

stricture
(STRIK-chur)
[*stric-* **tighten,** *-ture* **condition**]

uremia
(yoo-REE-mee-ah)
[*ur-* **urine,** *-emia* **blood condition**]

uremic syndrome
(yoo-REE-mik SIN-drohm)
[*ur-* **urine,** *-(h)em-* **blood,** *-ic* **relating to,** *syn-* **together,** *-drome* **running or (race)course**]

urethritis
(yoo-reh-THRY-tis)
[*ure-* **urine,** *-thr-* **agent or channel (urethra),** *-itis* **inflammation**]

CASE study

Nhung felt like he was going to throw up, the pain was so intense. His lower back ached on both sides with a rhythmic, sharp jabbing pain. He took some aspirin, but it didn't help at all. Finally, he gave in and went to his naturopath, someone who uses therapies consisting of natural remedies to treat illnesses. After hearing about Nhung's symptoms, the naturopath suggested a urine check. He had Nhung urinate into a cup, then dip the urine dipstick into the cup. As he expected, the test was positive for red blood cells. Looking at the urine from the cup under a microscope, they could both see very small particles that looked like crystals.

1. Nhung probably has kidney stones. What is most likely causing Nhung's pain?
   a. Failure of his kidneys
   b. Cramping of muscles in the ureter wall
   c. Blockage of the urethra
   d. Irritation of the urinary bladder
2. For a kidney stone to "pass" from the body, it will have to navigate through the following structures in which order?
   a. Ureter, calyces, urethra, renal pelvis, bladder
   b. Urethra, renal pelvis, bladder, ureter, calyces
   c. Bladder, ureter, urethra, calyces, renal pelvis
   d. Calyces, renal pelvis, ureter, bladder, urethra

The naturopath gives Nhung some crampbark (which contains agents that relax smooth muscle) and tells him to increase his water intake.

3. The increase of water intake will likely:
   a. increase Nhung's GFR
   b. increase Nhung's urine volume
   c. cause temporary polyuria
   d. all the above
4. Besides water, all of the following EXCEPT which one should normally be found in Nhung's urine?
   a. Electrolytes
   b. Hormones
   c. Glucose
   d. Pigments

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

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HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

OVERVIEW OF THE URINARY SYSTEM

A. Kidneys—principal organs of the urinary system; accessory organs are the ureters, urinary bladder, and urethra (Figure 31-1)
B. Urinary system—regulates the content of blood plasma to maintain "dynamic constancy" or homeostasis of the internal fluid environment within normal limits

ANATOMY OF THE URINARY SYSTEM

A. Gross structure (Figure 31-2)
   1. Kidney
      a. Shape, size, and location
         (1) Roughly oval with a medial indentation
         (2) Approximately 11 cm by 7 cm by 3 cm
         (3) Left kidney often larger than the right; the right kidney located a little lower
         (4) Both kidneys located in a retroperitoneal position
         (5) Lie on either side of the vertebral column between T12 and L3
         (6) Superior poles of both kidneys extend above the level of the twelfth rib and the lower edge of the thoracic parietal pleura

(7) Renal fasciae anchor the kidneys to surrounding structures
(8) Renal fat pad—heavy cushion of fat that surrounds each kidney
(9) Hilum—concave notch on medial surface where vessels and tubes enter kidney

b. Internal structures of the kidney
(1) Cortex and medulla—outer and inner regions
(2) Renal pyramids—make up much of the medullary tissue; papilla at the tip of each pyramid releases urine through multiple ducts
(3) Renal columns—where cortical tissue dips into the medulla between the pyramids
(4) Calyx—cuplike structure at each renal papilla that collects urine; minor calyces join to form major calyces, which in turn join together to form the renal pelvis
(5) Renal pelvis—narrows as it exits the kidney to become the ureter; acts as a collection basin to drain urine from the kidney

c. Blood vessels of the kidneys—kidneys are highly vascular (Figure 31-3)
(1) Renal artery—large branch of the abdominal aorta; brings blood into each kidney
(2) Interlobular arteries—between the pyramids of the medulla, the renal artery branches; interlobular arteries extend toward the cortex, arch over the bases of the pyramids, and form the arcuate arteries; from the arcuate arteries, the interlobular arteries penetrate the cortex and thus are sometimes called cortical radiate arteries
(3) Afferent arterioles extend to the nephrons (microscopic functional units of kidney tissue)

6. Ureter—tube running from each kidney to the urinary bladder; composed of three layers: mucous lining, muscular middle layer, and fibrous outer layer (Figures 31-4 and 31-7)
7. Urinary bladder (Figures 31-5 and 31-6)
a. Structure—collapsible bag located behind the pubic symphysis
(1) Made mostly of smooth muscle tissue
(2) Lining forms rugae
(3) Bladder can distend considerably

b. Functions
(1) Reservoir for urine before it leaves the body
(2) Aided by the urethra, it expels urine from the body

8. Urethra
a. Small mucous membrane–lined tube extending from the trigone to the exterior of the body
b. In females, lies posterior to the pubic symphysis and anterior to the vagina; approximately 3 cm long (Figure 31-8)
c. In males, after leaving the bladder, passes through the prostate gland where it is joined by two ejaculatory ducts; from the prostate, it extends to the base of the penis, then through the center of the penis, and ends as the urinary meatus; approximately 20 cm long; the male urethra is part of the urinary system, as well as part of the reproductive system

9. Mechanism for voiding bladder (urination or micturition)
a. As bladder volume increases, micturition contractions (of detrusor muscle) increase and the internal urethral sphincter relaxes (Figure 31-9)
b. External urethral sphincter muscle contracts at first, then at appropriate time relaxes to release urine

B. Microscopic structure
1. Nephrons, the microscopic functional units, make up the bulk of the kidney; each nephron is made up of two regions (renal corpuscle and renal tubule) and connects to a shared collecting duct (Figure 31-10)
a. Renal corpuscle—made up of the glomerulus tucked inside a Bowman capsule (Figures 31-11, 31-12, and 31-13); located within the cortex of the kidney
(1) Bowman (glomerular) capsule—cup-shaped mouth of the nephron
(a) Formed by parietal and visceral walls with a space between them
(b) Pedicels in the visceral layer are packed closely together to form filtration slits; a slit diaphragm prevents the filtration slits from enlarging under pressure (Figures 31-14 and 31-15)
(2) Glomerulus—network of fine capillaries surrounded by Bowman capsule
(a) Fenestrations—pores in capillary walls that permit filtration
(a) Mesangial cells—cells located between glomerular capillaries; various structural and functional support functions (Figure 31-13)
(3) Basement membrane lies between the glomerulus and Bowman capsule
(4) Glomerular capsular membrane—formed by glomerular endothelium, basement membrane, and the visceral layer of Bowman capsule; function is filtration (Figure 31-15)

b. Renal tubule
(1) Simple cuboidal and simple squamous epithelium
(a) Epithelial cells each possess a primary cilium
(b) Primary cilia monitor fluid chemistry and rate of flow, thus allowing regulation of tubule growth and other functions
(2) Proximal convoluted tubule (PCT)—first part of the renal tubule nearest to Bowman capsule; follows a winding, convoluted course; also known as the proximal tubule
(3) Henle (nephron) loop (Figure 31-10)
(a) Renal tubule segment just beyond the proximal tubule
(b) Consists of a thin descending limb, a sharp turn, and an ascending limb; ascending limb made up of thin ascending limb (tALH) followed by thick ascending limb (TAL)
(4) Distal convoluted tubule (DCT)—convoluted tubule beyond the Henle loop; also known as the distal tubule
(a) Juxtaglomerular apparatus—located where the afferent arteriole brushes past the distal convoluted tubule

i. Made up of macula densa (wall of distal tubule) and JG (juxtaglomerular) cells surrounding afferent arteriole
ii. Important to maintenance of blood flow homeostasis by reflexively secreting renin when blood pressure in the afferent arteriole drops

(b) Along with other distal tubules, it joins a common collecting duct

c. Collecting duct (CD)
(1) Straight duct joined by the renal tubules of several nephrons
(2) Collecting ducts of one renal pyramid converge to form one tube that opens at a renal papilla into a minor calyx (Figure 31-16)

d. Blood supply of the nephron (Figure 31-17)
(1) Afferent arteriole enters glomerular capillary network
(2) Efferent arteriole leaves glomerulus and extends to the peritubular blood supply
(a) Vasa recta—straight arterioles that run alongside Henle loop
(b) Peritubular capillaries—surround renal tubule

e. Types of nephrons
(1) Juxtamedullary nephron—a nephron with a renal corpuscle near the medulla and a Henle loop that dips far into the medulla
(2) Cortical nephron—a nephron with a Henle loop that does not dip into the medulla but remains almost entirely within the cortex; constitute about 85% of the total nephrons

PHYSIOLOGY OF THE URINARY SYSTEM

A. Overview of kidney function
1. Chief functions of the kidney are to process blood and form urine
2. Basic functional unit of the kidney is the nephron; forms urine through three processes (Figure 31-18)
a. Filtration—movement of water and protein-free solutes from plasma in the glomerulus into the capsular space of Bowman capsule
b. Tubular reabsorption—movement of molecules out of the tubule and into peritubular blood
c. Tubular secretion—movement of molecules out of peritubular blood and into the tubule for excretion

B. Filtration—first step in blood processing; occurs in renal corpuscles
1. Mechanism of filtration
a. Occurs as a result of a pressure gradient (effective filtration pressure, EFP) (Figure 31-20)
b. From blood in the glomerular capillaries, about 180 liters of water and solutes filter into Bowman capsule each day; takes place through the glomerular capsular membrane (Figure 31-19)
c. Glomerular capillary filtration occurs rapidly due to the increased number of fenestrations
2. Glomerular filtration rate (GFR)—rate of movement of fluid out of glomerulus
a. Determined mainly by glomerular hydrostatic pressure and therefore directly related to systemic blood pressure
b. Altered indirectly by changes in efficiency of cardiac contraction

C. Reabsorption—second step in urine formation; occurs as a result of passive and active transport mechanisms from all parts of the renal tubules; major portion of reabsorption occurs in the proximal convoluted tubules (Figure 31-19)
1. Reabsorption in the proximal convoluted tubule—most water and solutes are recovered by the blood, leaving only a small volume of tubule fluid left to move on to the Henle loop
a. Sodium—actively transported out of tubule fluid and into blood (Figure 31-21)
b. Glucose and amino acids—passively transported out of tubule fluid by sodium cotransport mechanisms; transport maximum (Tm or Tmax) is the maximum capacity of reabsorption and depends on carrier availability
c. Chloride, phosphate, and bicarbonate ions passively move into blood because of an imbalance in electrical charge
d. Water—movement of sodium and chloride into blood causes an osmotic imbalance, moving water passively into blood
e. Urea—approximately half of urea passively moves out of the tubule with the remaining urea moving on to the Henle loop
2. Reabsorption in the Henle loop (Figure 31-23)
a. Two countercurrent mechanisms (Figure 31-22)
(1) Countercurrent multiplier mechanism in Henle loop concentrates sodium and chloride in the interstitial fluid (IF) of renal medulla (Figure 31-23)
(2) Countercurrent exchange mechanism in vasa recta maintains high solute concentration in medullary IF (Figure 31-24)
b. Water reabsorbed from the tubule fluid, and urea picked up from the interstitial fluid in the descending limb
c. Sodium and chloride reabsorbed from the filtrate in the ascending limb, where the reabsorption of salt makes the tubule fluid dilute and creates and maintains a high osmotic pressure of the medulla's interstitial fluid

D. Reabsorption in the distal tubules and collecting ducts
1. Distal convoluted tubule reabsorbs sodium by active transport but in smaller amounts than in the proximal convoluted tubule (Figure 31-25)
2. ADH secreted by the posterior pituitary and targets the cells of distal tubules and collecting ducts to make them more permeable to water (Figure 31-26)
3. With reabsorption of water in the collecting duct, the urea concentration of the tubule fluid increases, which causes urea to diffuse out of the collecting duct into the medullary interstitial fluid
4. Urea participates in a countercurrent multiplier mechanism that along with the countercurrent mechanisms of the Henle loop and vasa recta, maintains the high osmotic pressure needed to form concentrated urine and avoid dehydration

E. Tubular secretion
   1. Tubular secretion—the movement of substances out of the blood and into tubular fluid
   2. Descending limb of the Henle loop secretes urea via diffusion
   3. Distal tubule and collecting ducts secrete potassium, hydrogen, and ammonium ions
   4. Aldosterone—hormone that targets the cells of the distal tubule and collecting duct cells; causes increased activity of the sodium-potassium pumps
   5. Secretion of hydrogen ions increases with increased blood hydrogen ion concentration

F. Regulation of urine volume (Figure 31-27)
   1. ADH influences water reabsorption; as water is reabsorbed, the total volume of urine is reduced by the amount of water removed by the tubules; ADH reduces water loss
   2. Aldosterone, secreted by the adrenal cortex, increases distal tubule absorption of sodium, thereby raising the sodium concentration of blood and thus promoting reabsorption of water
   3. Atrial natriuretic hormone (ANH), secreted by atrial muscle fibers, promotes loss of sodium via urine; opposes aldosterone, thus causing the kidneys to reabsorb less water and thereby produce more urine
   4. Tubuloglomerular feedback mechanism maintains a constant GFR by regulating resistance in afferent arterioles. Protects GFR function from rapid blood pressure variations; dependent on macula densa cells and the juxtaglomerular apparatus; may influence reninangiotensin mechanism (Figure 31-28, *A*)
   5. Myogenic mechanism—rapid and effective regulation of GFR via changes in afferent arteriole smooth muscle contraction and relaxation (Figure 31-28, *B*)
   6. Urine volume—also related to the total amount of solutes other than sodium excreted in urine; generally, the more solutes, the more urine

G. Urine composition—approximately 95% water with several substances dissolved in it; the most important are the following
   1. Nitrogenous wastes—result of protein metabolism; include urea, uric acid, ammonia, and creatinine
   2. Electrolytes—mainly the following ions: sodium, potassium, ammonium, chloride, bicarbonate, phosphate, and sulfate; amounts and kinds of minerals vary with diet and other factors
   3. Toxins—during disease, bacterial poisons leave the body in urine
   4. Pigments—especially urochromes
   5. Hormones—high hormone levels may spill into the filtrate
   6. Abnormal constituents—such as blood, bacteria, glucose, albumin, casts, or calculi

THE BIG PICTURE: URINARY SYSTEM AND THE WHOLE BODY

A. Homeostasis of water and electrolytes in body fluids relies on proper functioning of the kidneys; nephrons process blood to adjust its content to maintain a relatively constant internal environment
B. Urinary and cardiovascular systems are interdependent
C. Endocrine and nervous systems must operate properly to ensure efficient kidney function

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. List the principal and accessory organs of the urinary system.
2. Name, locate, and give the main function(s) of each organ of the urinary system.
3. Identify the beginnings of the "plumbing system" of the urinary system.
4. How does the mechanism for voiding urine start?
5. The male urethra is part of two different systems. Identify them.
6. Describe the microscopic structure of the kidney.
7. Diagram the flow of blood through the kidney.
8. Define the terms *filtration*, *tubular reabsorption*, and *tubular secretion*.
9. How is effective filtration pressure calculated?
10. Describe the solute concentration of the interstitial fluid of the medulla.
11. What happens to sodium and chloride in the ascending limb of the Henle loop?
12. What happens to potassium secretion when the blood aldosterone concentration increases?
13. Identify two drugs secreted by tubule cells.
14. What is the normal pH range for freshly voided urine?
15. Identify three body systems in addition to the urinary system that also excrete unneeded substances.
16. Define retention.
17. What is the most common cause of glycosuria?
18. What do elevated BUN levels indicate?
19. Define the term *osmolality*.

CRITICAL THINKING QUESTIONS

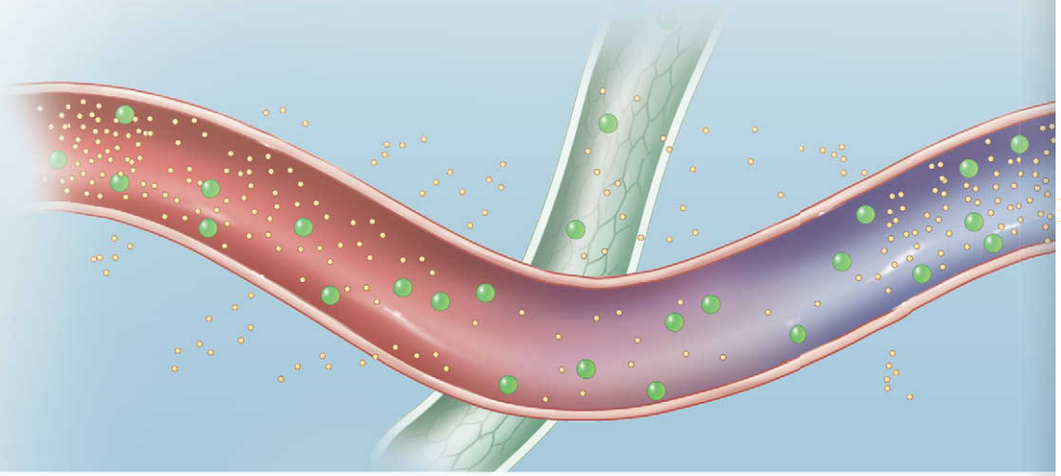


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. What would result if the nerves supplying the bladder and urethra were damaged?
2. Describe the mechanism of urine formation. How is each step related to the part of the nephron that performs it?
3. If the proximal convoluted tubules were unable to transport sodium ions into blood, why would you expect to find high concentrations of both sodium and chloride ions in urine?
4. Why do you think ADH prevents rapid dehydration of the body?
5. How is the function of ANH related to the increase in urine volume?
6. What is the relationship between age and kidney function?

Fluid and Electrolyte Balance

32



CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

Interrelationship of Fluid and Electrolyte Balance, 1004

Total Body Water, 1004

Body Fluid Compartments, 1005

Chemical Content, Distribution, and Measurement of Electrolytes in Body Fluids, 1005
- Extracellular vs. Intracellular Fluids, 1006
- Measuring Electrolyte Reactivity, 1007

Avenues by Which Water Enters and Leaves the Body, 1009

Some General Principles About Fluid Balance, 1009

Mechanisms That Maintain Homeostasis of Total Fluid Volume, 1010
- Regulation of Fluid Intake, 1010
- Regulation of Urine Volume, 1010
- Factors That Alter Fluid Loss Under Abnormal Conditions, 1012

Regulation of Water and Electrolyte Levels in Plasma and Interstitial Fluid, 1012
- Edema, 1015

Regulation of Water and Electrolyte Levels in ICF, 1016

Regulation of Sodium and Potassium Levels in Body Fluids, 1017

Cycle of Life: Fluid and Electrolyte Balance, 1018

The Big Picture: Fluid and Electrolyte Balance, 1019

Mechanisms of Disease, 1019

Case Study, 1021

LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

anion
(AN-eye-on)
[*ana-* **up,** *-ion* **to go (ion)**]

blood colloid osmotic pressure (BCOP)
(KOL-oyd os-MOT-ik)
[*coll-* **glue,** *-oid* **like,** *osmo-* **push,** *-ic* **relating to**]

blood hydrostatic pressure (BHP)
(hye-droh-STAT-ik)
[*hydro-* **water,** *-stat-* **standing,** *-ic* **relating to**]

cation
(KAT-eye-on)
[*cat-* **down,** *-ion* **to go (ion)**]

colloid osmotic pressure
(KOL-oyd os-MOT-ik)
[*coll-* **glue,** *-oid* **like,** *osmo-* **push,** *-ic* **relating to**]

dehydration
(dee-hye-DRAY-shun)
[*de-* **remove,** *-hydro* **water,** *-ation* **process**]

dissociate
(di-SOH-see-ayt)
[*dis-* **apart,** *-socia* **-unite,** *-ate* **action**]

electrolyte
(eh-LEK-troh-lyte)
[*electro-* **electricity,** *-lyt-* **loosening**]

extracellular fluid compartment
(ek-strah-SELL-yoo-lar)
[*extra-* **outside,** *-cell-* **storeroom,** *-ular* **relating to**]

extracellular fluid (ECF)
(eks-trah-SELL-yoo-lar)
[*extra-* **outside,** *-cell-* **storeroom,** *-ular* **relating to**]

fluid and electrolyte balance
(eh-LEK-troh-lyte)
[*electro-* **electricity,** *-lyt-* **loosening**]

continued on p. 1020

*The phrase **fluid and electrolyte balance** implies homeostasis, or constancy, of body fluid and electrolyte levels. It means that both the amount and distribution of body fluids and electrolytes are normal and constant. For homeostasis to be maintained, body "input" of water and electrolytes must be balanced by "output." If water and electrolytes enter the body in excess of requirements, they must be selectively eliminated, and if excess losses occur, prompt replacement is critical. The volume of fluid and the electrolyte concentrations inside the cells, in the interstitial spaces, and in the blood vessels all remain relatively constant when a condition of homeostasis exists. Fluid and electrolyte imbalance, then, means that both the total volume of water and the level of electrolytes in the body or the amounts in one or more of its fluid compartments have increased or decreased beyond normal limits.*

INTERRELATIONSHIP OF FLUID AND ELECTROLYTE BALANCE

Several of the basic physical properties of matter discussed in Chapter 2 help explain the mechanisms of fluid and electrolyte balance. The concept of chemical bonding is a good example. The type of chemical bonds between molecules of certain chemical compounds, such as sodium chloride (NaCl), permits breakup, or dissociation, into separate particles (Na^+ and Cl^-). Recall that such compounds are known as **electrolytes.** The dissociated particles of an electrolyte are called **ions** and carry an electrical charge. Organic substances such as glucose, however, have a type of bond that does not permit the compound to break up, or **dissociate,** in solution. Such compounds are known as **nonelectrolytes.**

Many electrolytes and their dissociated ions are of critical importance in fluid balance. Fluid balance and electrolyte balance are so interdependent that if one deviates from normal, so does the other. A discussion of one therefore necessitates a discussion of the other.

TOTAL BODY WATER

Normal values for total body water expressed as a percentage of total body weight will vary between 45% and 75%. Differences occur because of age, fat content of the body, and gender. In newborn infants, total body water represents about 75% of body weight. This percentage then decreases rapidly during the first 10 years of life. At adolescence, adult values are reached and gender differences, which account for about a 10% variation in body fluid volumes between the sexes, appear. In young, nonobese adults, males weighing 70 kg (154 pounds) will have on average about 60% of their body weight as water (nearly 40 liters) and females about 50% (Table 32-1). Adipose, or fat, tissue contains the least amount of water of any tissue (including bone) in the body. Therefore, regardless of age, obese individuals, with their high body fat content, have less body water per kilogram of weight than slender people do. In aged individuals of either sex, body water content may decrease to 45% of total body weight. One reason for this is that old age is often accompanied by a decrease in muscle mass (65% water) and an increase in fat (20% water). In addition, with advancing age the kidneys are less able to produce concentrated urine, and sodium-conserving responses become less effective.

TABLE 32-1 Volumes of Body Fluid Compartments*

BODY FLUID	INFANT	ADULT MALE	ADULT FEMALE
Extracellular fluid			
Plasma	4	4	4
Interstitial fluid	26	16	11
Intracellular fluid	45	40	35
TOTAL	75	60	50

*Percentage of body weight.

TABLE 32-2 Commonly Used Acronyms for Body Fluids and Fluid Pressures

ACRONYM	TERM	MEANING
BCOP	Blood colloid osmotic pressure	Force that draws water into the plasma (from the presence of colloid particles in plasma)
BHP	Blood hydrostatic pressure	Force of the blood pushing outward on blood vessel walls; blood pressure
ECF	Extracellular fluid	Any fluid outside cells, such as interstitial fluid (IF) or blood plasma
ICF	Intracellular fluid	Fluid inside the cell (cytosol)
IF	Interstitial fluid	Fluid between tissue cells
IFCOP	Interstitial fluid colloid osmotic pressure	Force that draws water out of the blood and into tissue spaces (from the presence of colloid particles in IF)
IFHP	Interstitial fluid hydrostatic pressure	Force (pressure) of the fluid between tissue cells

BODY FLUID COMPARTMENTS

Functionally, the total body water can be subdivided into two major **fluid compartments** called the **extracellular** and the **intracellular fluid compartments. Extracellular fluid (ECF)** consists mainly of the *plasma* found in the blood vessels and the *interstitial fluid* that surrounds the cells (Table 32-2). In addition, the lymph and so-called *transcellular fluid*—such as cerebrospinal fluid, joint fluids, and humors of the eye—are also considered extracellular fluid. The distribution of body water by compartment is shown in Figure 32-1. **Intracellular fluid (ICF)** refers to the water inside the cells.

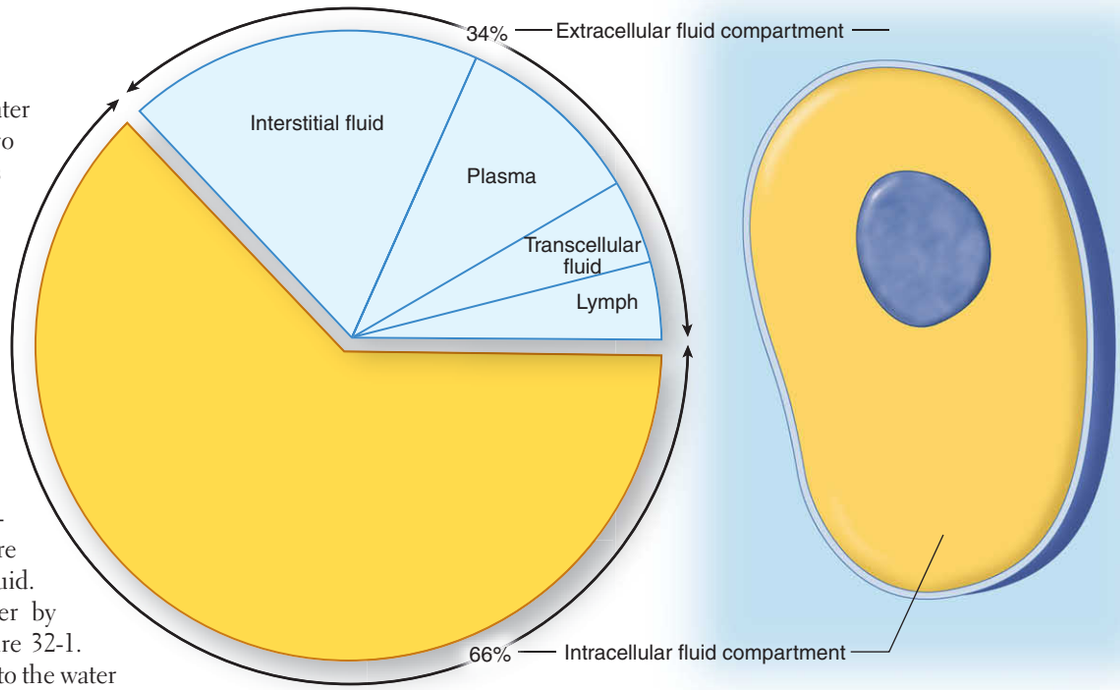


FIGURE 32-1
Distribution of total body water.

Extracellular fluid makes up the internal environment of the body. It therefore serves the dual vital functions of providing a relatively constant environment for cells and transporting substances to and from them. Intracellular fluid, on the other hand, because it is a solvent, functions to facilitate intracellular chemical reactions that maintain life. When compared according to volume, intracellular fluid is the largest (25 L), plasma the smallest (3 L), and interstitial fluid in between (12 L). Figure 32-2 illustrates the typical normal fluid volumes in a young adult male, and Table 32-1 lists volumes of the body fluid compartments for both sexes as a percentage of body weight.

CHEMICAL CONTENT, DISTRIBUTION, AND MEASUREMENT OF ELECTROLYTES IN BODY FLUIDS

We have defined an electrolyte as a compound that will break up or dissociate into charged particles called *ions* when placed in solution. Sodium chloride, when dissolved in water, provides a positively charged sodium ion (Na^+) and a negatively charged chloride ion (Cl^-).

If two electrodes charged with a weak current are placed in an electrolyte solution, the ions will move, or migrate, in opposite directions according to their charge. Positive ions such as Na^+ will be attracted to the negative electrode (cathode) and are called **cations.** Negative ions such as Cl^- will migrate to the positive electrode (anode) and are called **anions.** Various anions and cations serve critical nutrient or regulatory roles in the body. Important cations include sodium (Na^+), calcium (Ca^{++}), potassium (K^+), and magnesium (Mg^{++}). Important anions include chloride (Cl^-), bicarbonate (HCO_3^-), phosphate ($HPO_4^=$), and many proteins.

The importance of electrolytes in controlling the movement of water between the body fluid compartments is discussed in this chapter. Their role in maintaining acid-base balance is examined in Chapter 33.

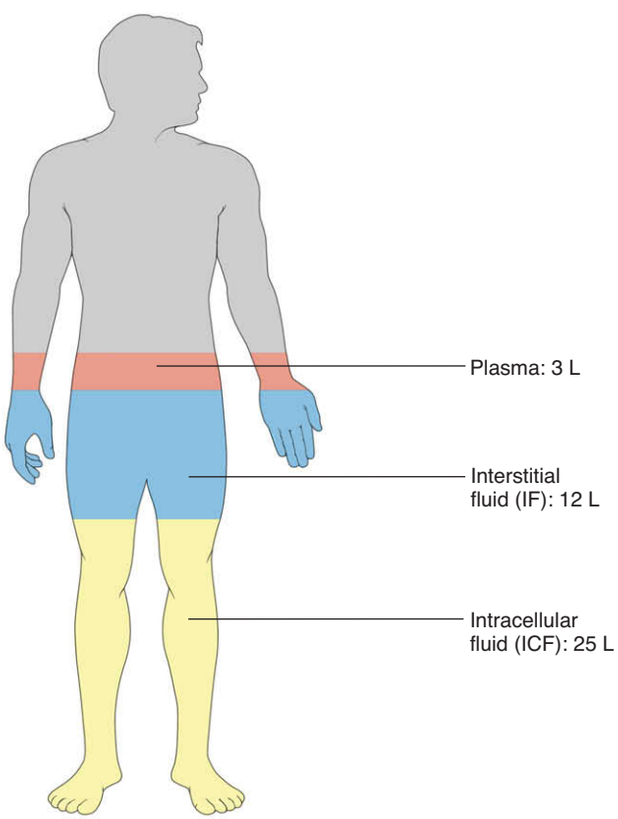


FIGURE 32-2
Relative volumes of three body fluids. Values represent fluid distribution in a young adult male.

Extracellular vs. Intracellular Fluids

Compared chemically, plasma and **interstitial** fluid (the two extracellular fluids) are almost identical. Intracellular fluid, on the other hand, shows striking differences as compared with either of the two extracellular fluids. Let us examine first the chemical structure of plasma and interstitial fluid as shown in Figure 32-3 and Table 32-3.

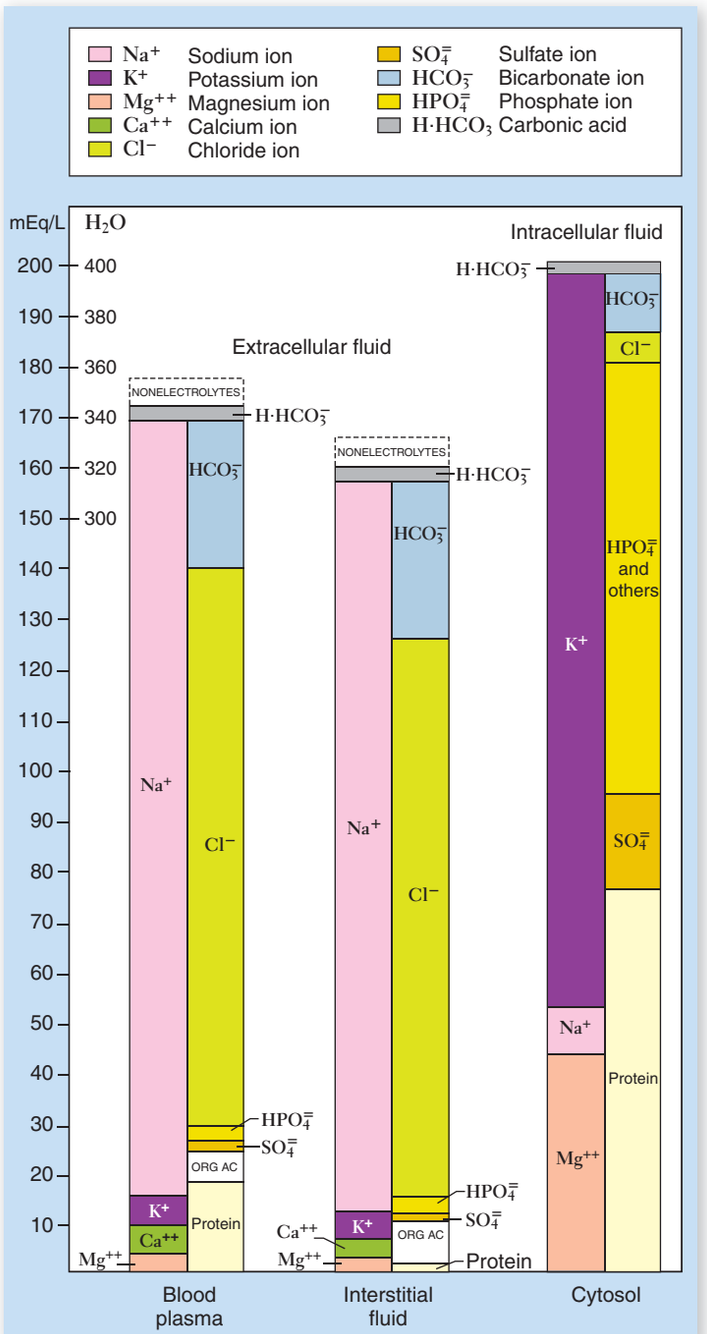


FIGURE 32-3

Chief chemical constituents of three fluid compartments. The column of figures at the left (200, 190, 180, etc.) indicates the amount of cation or anion, whereas the figures on the right (400, 380, 360, etc.) indicate the sum of the cations and anions. *ORG AC,* Organic acid.

TABLE 32-3 Electrolyte Composition of Blood Plasma

	CATIONS	ANIONS
	142 mEq Na^+	102 mEq Cl^-
	4 mEq K^+	26 HCO_3^-
	5 mEq Ca^{++}	17 protein
	2 mEq Mg^{++}	6 other
		2 $HPO_4^=$
TOTAL	153 mEq/L plasma	153 mEq/L plasma

Perhaps the first difference between the two extracellular fluids that you notice (see Figures 32-3 and 32-4) is that blood plasma contains a slightly larger total of electrolytes (ions) than interstitial fluids do. If you compare the two fluids, ion for ion, you will discover the most important difference between blood plasma and interstitial fluid. Look at the anions (negative ions) in these two extracellular fluids. Note that blood contains an appreciable amount of protein anions. *Interstitial fluid, in contrast, contains hardly any protein anions.* This is the only functionally important difference between blood and interstitial fluid. It exists because the normal capillary membrane is practically impermeable to proteins. Hence, almost all protein anions remain behind in the blood instead of filtering out into the interstitial fluid. Because proteins remain in the blood, certain other differences also exist between blood and interstitial fluid—notably, blood contains more sodium ions and fewer chloride ions than interstitial fluid does.

Extracellular fluids and intracellular fluid are more unlike than alike chemically. Chemical difference predominates between the extracellular and intracellular fluids. Chemical similarity predominates between the two extracellular fluids. Study Figures 32-3 and 32-4 and make some generalizations about the main chemical differences between the extracellular and intracellular fluids. For example: What is the most abundant cation in extracellular

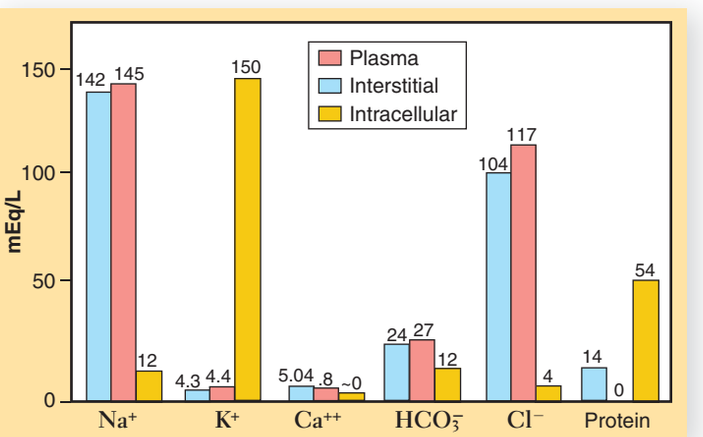


FIGURE 32-4

Electrolyte and protein concentrations in body fluid compartments. This illustration compares individual electrolyte and protein concentration in the three fluid compartments.

fluids? In intracellular fluid? What is the most abundant anion in extracellular fluids? In intracellular fluid? What about the relative concentrations of protein anions in extracellular fluids and intracellular fluid?

The reason we call attention to the chemical structure of the three body fluids is that here, as elsewhere, structure determines function. In this instance the chemical structure of the three fluids helps control water and electrolyte movement between them. Or, phrased differently, the chemical structure of body fluids, if normal, functions to maintain homeostasis of fluid distribution and, if abnormal, results in fluid imbalance. **Hypervolemia** (excess blood volume) is a case in point. **Edema** (discussed in detail on p. 1015), too, frequently stems from changes in the chemical structure of body fluids. Box 32-1 discusses therapies involving administration of fluids and electrolytes.

Before discussing mechanisms that control water and electrolyte movement between blood, interstitial fluid, and intracellular fluid, it is important to understand the units used for measuring electrolytes.

Measuring Electrolyte Reactivity

After the important electrolytes and their constituent ions in the body fluid compartments had been established, physiologists needed to measure changes in their levels to understand the mechanisms of fluid balance. To have meaning, measurement units used to report electrolyte levels must be related to actual physiological activity. In the past, only the weight of an electrolyte in a given amount of solution—its *concentration*—was measured. The number of milligrams per 100 ml of solution (mg%) was one of the most frequently used units of measurement. However, simply reporting the concentration of an important electrolyte such as sodium or calcium in milligrams per 100 ml of blood (mg%) gives no direct information about its chemical combining power or physiological activity in body fluids. The importance of valence and electrovalent or ionic bonding in chemical reactions was discussed in Chapter 2. The reactivity or combining power of an electrolyte depends not just on the number of molecular particles present but also on the total number of ionic charges (valence).

Box 32-1 | Fluid and Electrolyte Therapy

The term **parenteral therapy** is used to describe the administration of nutrients, special fluids, and/or electrolytes by injection. The term implies that whatever is administered enters the body by injection and not through the alimentary canal. Examples of **parenteral** routes include **intravenous injection** (into veins) and **subcutaneous injection** (under the skin). Significant quantities of nutrient or electrolyte solutions that are injected subcutaneously must be isotonic with plasma or cellular damage will occur. Such solutions may be administered intravenously, however, regardless of tonicity, if correct rates of administration are used. The intravenous route is generally the preferred route for all fluid and electrolyte solutions. It permits the body to adjust its fluid compartments in the same way that it does after the ordinary intake of water and food. The ideal route for the absorption of nutrients and fluids is, of course, the digestive tract. However, if for any reason the digestive tract route cannot be used, parenteral administration of these substances is required to sustain life.

Parenteral solutions are generally given to accomplish one or more of three primary objectives:

1. To meet current maintenance needs for nutrients, fluids, and electrolytes
2. To replace past losses
3. To replace concurrent losses (additional losses that are in excess of maintenance needs)

Although many different types and combinations of nutrients and electrolytes in solution are available to meet almost every medical need, 85% to 95% of all individuals needing fluid therapy are treated with one or more of the seven basic solutions listed below:

1. Carbohydrate in water
2. Carbohydrate in various strengths of saline
3. Normal saline (0.9% NaCl)
4. Potassium solutions
5. Ringer's solution
6. Lactate solutions
7. Ammonium chloride solutions

Carbohydrate and water solutions not only supply water for body needs but also provide calories required for energy. Dextrose (glucose) and fructose (levulose) are the common parenteral carbohydrates. Perhaps the most frequently used parenteral solution is 5% dextrose in water (D_5W).

Various carbohydrate and saline solutions are also available for parenteral use. Such solutions are of primary value in individuals who have a chloride deficit and ongoing fluid and caloric needs. Patients who are vomiting or undergoing gastric suction that results in the loss of chloride in hydrochloric acid need these solutions. Prolonged and heavy sweating and diarrhea also produce chloride deficits.

Current trends in parenteral therapy have reduced the frequency of normal saline use administered independently of other electrolytes or carbohydrates. In recent decades, normal saline as a general purpose electrolyte has been replaced by the use of Ringer's solution, which provides more of the essential electrolytes in physiological proportions. Ringer's solution is often described as normal saline modified by the addition of calcium and potassium in amounts approximating those found in plasma. Normal saline is still useful and widely used in cases where chloride loss is equal to or greater than the loss of sodium, however.

Potassium, lactate, and ammonium chloride solutions are specialty fluids used in the treatment of such conditions as acid-base imbalance or, in the case of potassium, administered during the healing phase of severe burns or in patients with actual potassium deficiency. In acidosis, lactate is rapidly converted by the liver to bicarbonate ions, and administration of ammonium chloride is useful in treating alkalosis. Acid-base imbalances and their treatment are discussed in Chapter 33.

Univalent ions such as sodium (Na^+) carry only a single charge, but the divalent calcium ion (Ca^{++}) carries two units of electrical charge.

The need for a unit of measurement more related to activity has resulted in increasing use of a more meaningful measurement yardstick—the **milliequivalent (mEq).** Milliequivalents measure the number of ionic charges or electrovalent bonds in a solution and therefore serve as an accurate measure of the chemical (physiological) combining power, or *reactivity*, of a particular electrolyte solution. The number of milliequivalents of an ion in a liter of solution (mEq/L) can be calculated from its weight in 100 ml (mg%) by using a convenient conversion formula.

Conversion of milligrams per 100 ml (mg%) to milliequivalents per liter (mEq/L):

$$\text{mEq/L} = \frac{\text{mg/100 ml} \times 10 \times \text{Valence}}{\text{Atomic weight}}$$

Example: Convert 15.6 mg% K^+ to mEq/L

Atomic weight of $K^+ = 39$

Valence of $K^+ = 1$

$$\text{mEq/L} = \frac{15.6 \times 10 \times 1}{39} = \frac{156}{39} = 4$$

Therefore, 15.6 mg/100 ml K^+ = 4 mEq/L.

| QUICK CHECK |

1. List three important cations and anions that serve critical nutrient or regulatory roles in the body.
2. Name the most abundant chemical constituent in blood plasma, interstitial fluid, and intracellular fluid.
3. Identify the units used to describe electrolyte concentration and electrolyte reactivity.

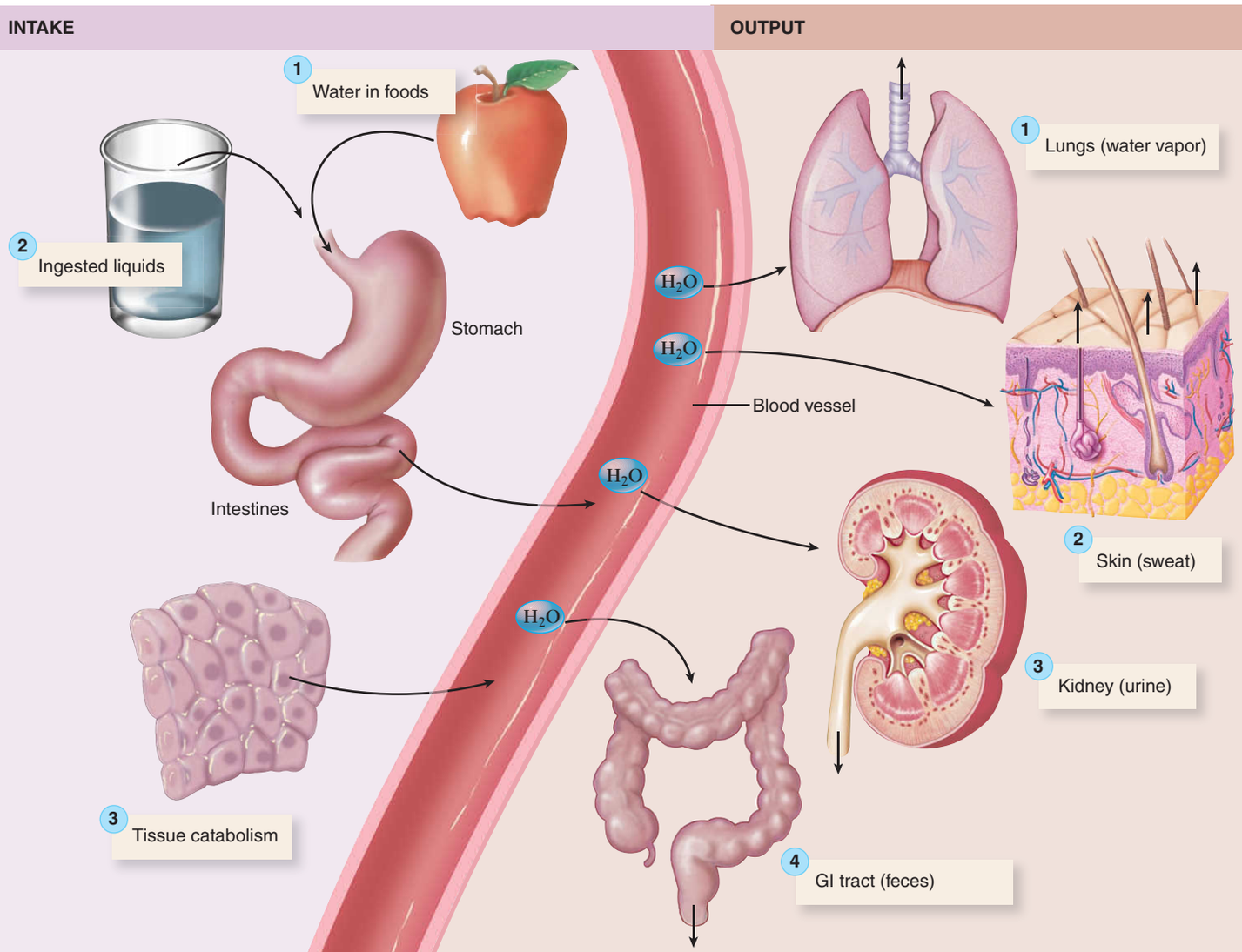


FIGURE 32-5
Sources of fluid intake and output.

AVENUES BY WHICH WATER ENTERS AND LEAVES THE BODY

Water enters the body, as everyone knows, by way of the digestive tract—in the liquids one drinks and in the foods one eats (Figure 32-5). But, in addition, and less universally known, water enters the body—that is, is added to its total fluid volume—by way of its billions of cells. Each cell produces water as it catabolizes foods, and this water enters the bloodstream. Water normally leaves the body by four exits: kidneys (urine), lungs (water in expired air), skin (by diffusion and by sweat), and intestines (feces). In accord with the cardinal principle of fluid balance, the total volume of water entering the body normally equals the total volume leaving. In short, fluid intake normally equals fluid output. Figure 32-5 illustrates the portals of water entry and exit, and Table 32-4 gives their normal volumes. These volumes, however, can vary considerably and still be considered normal.

| QUICK CHECK |

4. Name the type of chemical compound that breaks up, or dissociates, in solution to form ions.
5. Plasma and interstitial fluid are subdivisions of what major body fluid compartment?
6. List the volumes of body fluid compartments in a young adult female as a percentage of body weight.
7. List the major "portals" of water entry and exit from the body.

SOME GENERAL PRINCIPLES ABOUT FLUID BALANCE

The cardinal principle about fluid balance is this: fluid balance can be maintained only if intake equals output. Obviously, if more water or less leaves the body than enters it, imbalance will result. Total fluid volume will increase or decrease but cannot remain constant under these conditions.

TABLE 32-4 Typical Normal Values (24 Hours) for Each Portal of Water Entry and Exit (With Wide Variations)

INTAKE		OUTPUT	
Water in foods	700 ml	Lungs	350 ml
Ingested liquids	1500 ml	Skin	
Water formed by catabolism	200 ml	By diffusion	350 ml
		By sweat	100 ml
		Kidneys (urine)	1400 ml
		Intestines (in feces)	200 ml
TOTAL	2400 ml		2400 ml

Mechanisms for varying output so that it equals intake are the most crucial means of maintaining fluid balance, but mechanisms for adjusting intake to output also operate. Figure 32-6 summarizes the role that the *renin-angiotensin-aldosterone system (RAAS)* has in decreasing fluid output (urine volume) to compensate for decreased intake.

Recall from Chapter 31 that cells in the outer zone of the adrenal cortex that secrete aldosterone are also influenced by *juxtaglomerular (JG) cells* in the kidney. If blood pressure decreases or if increased levels of plasma K^+ occur, additional aldosterone will be secreted. When stimulated, juxtaglomerular cells in the kidney secrete renin, which, in turn, acts on angiotensinogen in the bloodstream to form angiotensin I, which

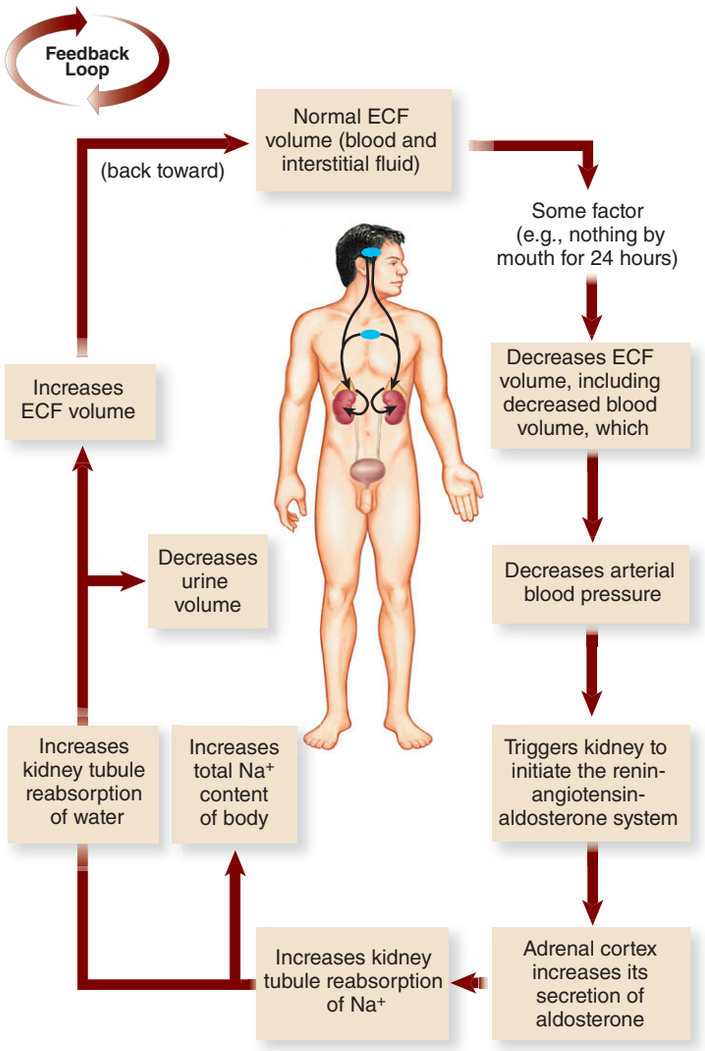


FIGURE 32-6

Role of aldosterone in ECF homeostasis. Aldosterone tends to restore normal extracellular fluid *(ECF)* volume when it decreases below normal. Excess aldosterone, however, leads to excess ECF volume, that is, excess blood volume (hypervolemia) and excess interstitial fluid volume (edema), as well as an excess of the total Na^+ content of the body. Details of the reninangiotensin-aldosterone system (RAAS) are shown in Figure 19-19.

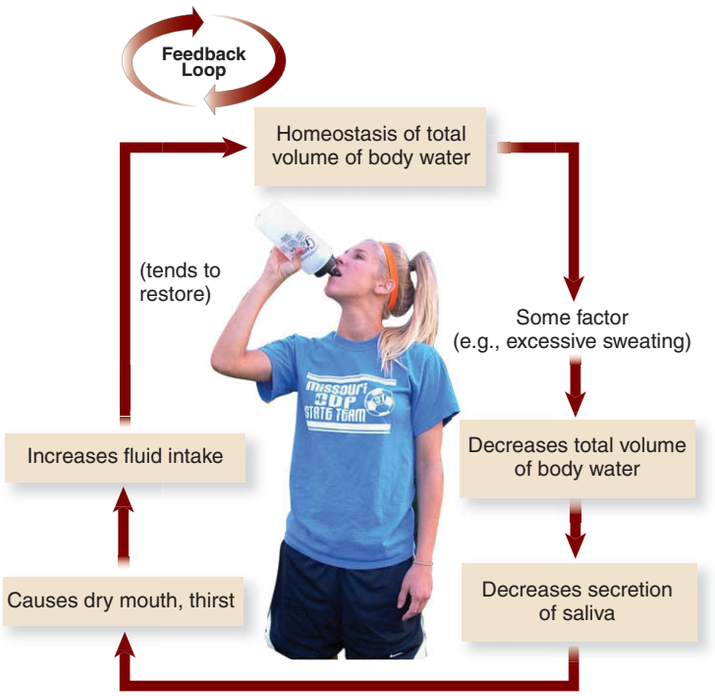


FIGURE 32-7

Homeostasis of the total volume of body water. A basic mechanism for adjusting intake to compensate for excess output of body fluid is diagrammed.

is eventually converted in lung tissue to angiotensin II (see Figure 19-19, p. 579). Angiotensin I and II increase aldosterone secretion and also act on the brain to stimulate the sensation of thirst. Thirst is associated with any factor that decreases the total volume of body water, such as blood loss or hemorrhage. Simple dehydration caused by sweating also results in reduced saliva secretion and thirst. Additional details of the *renin-angiotensin-aldosterone system* are discussed in Chapter 19. Figure 32-7 diagrams a mechanism for adjusting intake to compensate for excess output.

Mechanisms for controlling water movement between the fluid compartments of the body are the most rapid-acting fluid balance processes. They serve first of all to maintain normal blood volume at the expense of interstitial fluid volume.

MECHANISMS THAT MAINTAIN HOMEOSTASIS OF TOTAL FLUID VOLUME

Under normal conditions, homeostasis of the total volume of water in the body is maintained or restored primarily by mechanisms that adjust output (urine volume) to intake and secondarily by mechanisms that adjust fluid intake.

Regulation of Fluid Intake

A detailed explanation of the mechanism for controlling fluid intake so that it increases when output increases and decreases when output decreases is not yet available. However, research has shown that nerve cells located in the roof of the third ventricle of the brain, in a structure called the **subfornical organ,** or **SFO,** act as critical regulators of fluid homeostasis. Nervous connections exist between SFO cells and other areas of the brain, including the cerebrum and the supraoptic and paraventricular nuclei of the hypothalamus. These nuclei are involved in antidiuretic hormone (ADH) production, which is important in conservation of body water when fluid intake is restricted (see Chapter 19, p. 570, and Figure 32-16).

Physiologists now identify both SFO and ADH-secreting cells in the hypothalamus as important **osmoreceptors,** which together make up the functional **thirst center** of the brain. Osmoreceptors are cells able to detect an increase in solute concentration (osmolality) in extracellular fluid caused by water loss. Signals generated by osmoreceptors in the SFO and hypothalamus stimulate ADH secretion and also affect a number of other body functions, including a decrease in the secretion of saliva.

Signals from the SFO are also sent directly to the cerebrum, where they trigger a conscious sense of dry mouth and thirst and initiate complex behaviors and thought processes, which in many individuals include a perceived need to increase the consumption of water, especially. Have you ever heard someone say "soda pop tastes good but nothing satisfies my thirst like a glass of water"? The end result is an overall increase in fluid intake to offset increased loss, regardless of cause, and this tends to restore fluid balance (see Figure 32-7). If, however, an individual takes nothing by mouth for several days, fluid balance cannot be maintained despite every effort of homeostatic mechanisms to compensate for the zero intake. Obviously, under this condition, the only way balance could be maintained would be for fluid output to also decrease to zero. But this cannot occur. Some output is obligatory. Why? Because as long as respirations continue, some water leaves the body by way of expired air. Also, as long as life continues, an irreducible minimum of water diffuses through the skin.

Regulation of Urine Volume

Two factors together determine urine volume: the glomerular filtration rate and the rate of water reabsorption by the renal tubules. The glomerular filtration rate, except under abnormal conditions, remains fairly constant—hence it does not normally cause urine volume to fluctuate. The rate of tubular reabsorption of water, on the other hand, fluctuates considerably. The rate of tubular reabsorption, therefore, rather than the glomerular filtration rate, normally adjusts urine volume to fluid intake. The amount of antidiuretic hormone (ADH) and aldosterone secreted regulates the amount of water reabsorbed by the kidney tubules (discussed on

p. 1017; see also Figure 32-6). In other words, urine volume is regulated chiefly by hormones secreted by the posterior pituitary (ADH) and by the adrenal cortex (aldosterone) and by atrial natriuretic hormone (ANH). Regulation of aldosterone secretion by the renin-angiotensin mechanism has also been discussed.

Although changes in the volume of fluid loss via the skin, the lungs, and the intestines also affect the fluid intake-output ratio, these volumes are not automatically adjusted to intake volume, as is the volume of urine. Figure 32-8 summarizes the fluid and electrolyte regulation mechanisms that involve ADH, aldosterone, and ANH.

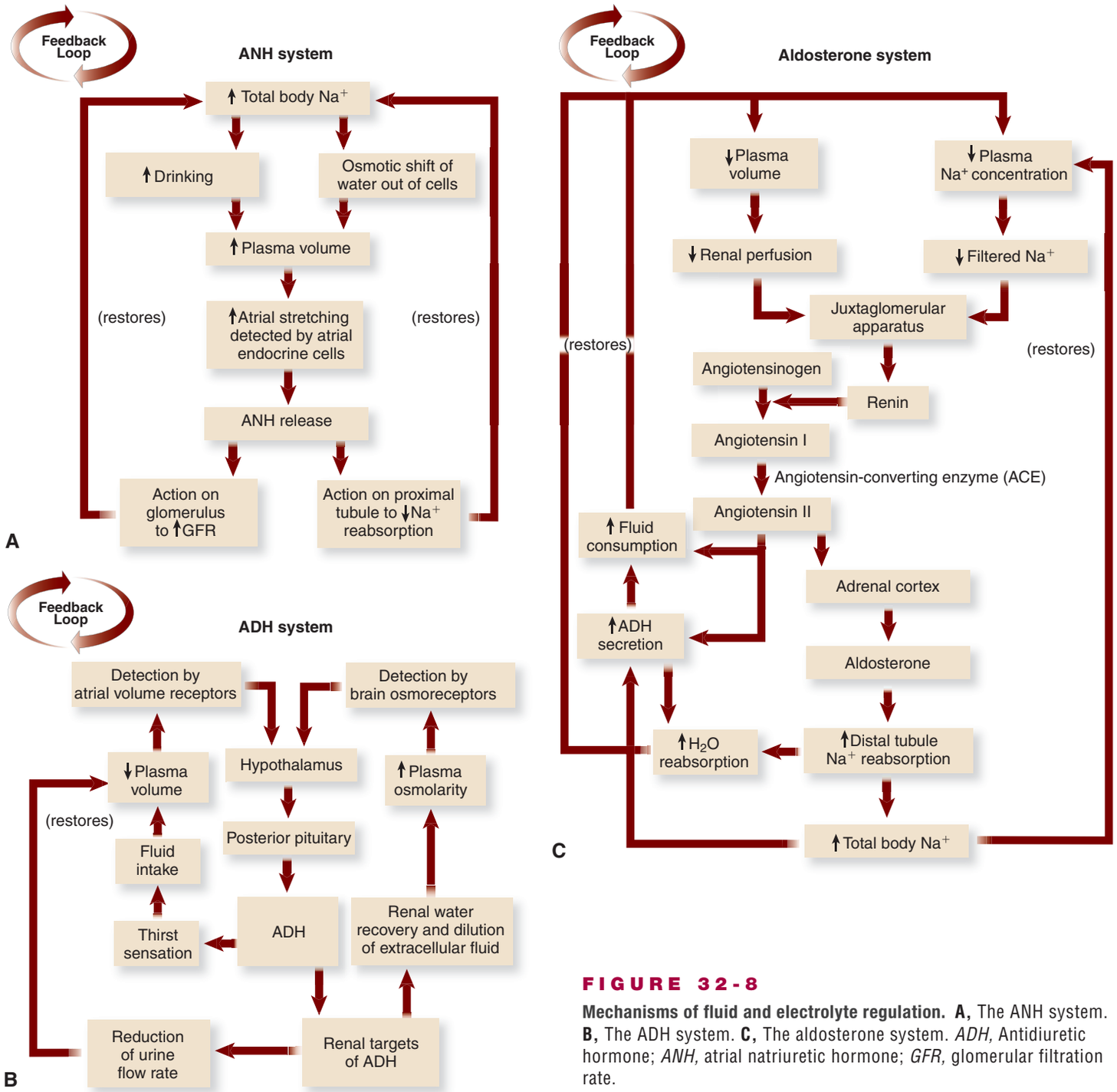


FIGURE 32-8

Mechanisms of fluid and electrolyte regulation. A, The ANH system. **B,** The ADH system. **C,** The aldosterone system. *ADH,* Antidiuretic hormone; *ANH,* atrial natriuretic hormone; *GFR,* glomerular filtration rate.

Factors That Alter Fluid Loss Under Abnormal Conditions

The rate of respiration and the volume of sweat secreted may greatly alter fluid output under certain abnormal conditions. For example, a patient who hyperventilates for an extended time loses an excessive amount of water via the expired air. If, as frequently happens, the individual also takes in less water by mouth than normal, the fluid output then exceeds intake and a fluid imbalance develops, namely, **dehydration** (that is, a decrease in total body water). The severity of dehydration can be measured by weight loss as a percentage of the normal (hydrated) body weight (Figure 32-9). Symptoms range from simple thirst to muscle weakness and kidney failure. Clinically, dehydration is often detected by loss of skin elasticity or *turgor*. If a fold of skin, when pinched, returns to its original shape slowly—a condition called "tenting"—dehydration is suspected. Dehydration is more fully discussed in Box 32-2. Other abnormal conditions such as vomiting, diarrhea, or intestinal drainage also cause fluid and electrolyte output to exceed intake and thus produce fluid and electrolyte imbalances.

| QUICK CHECK |

8. How does aldosterone secretion restore normal extracellular fluid (ECF) volume when it decreases below normal?
9. Identify the two substances that are most important in regulating the amount of water reabsorbed by the kidney tubules.
10. Name the two most important factors that alter fluid loss under abnormal conditions.

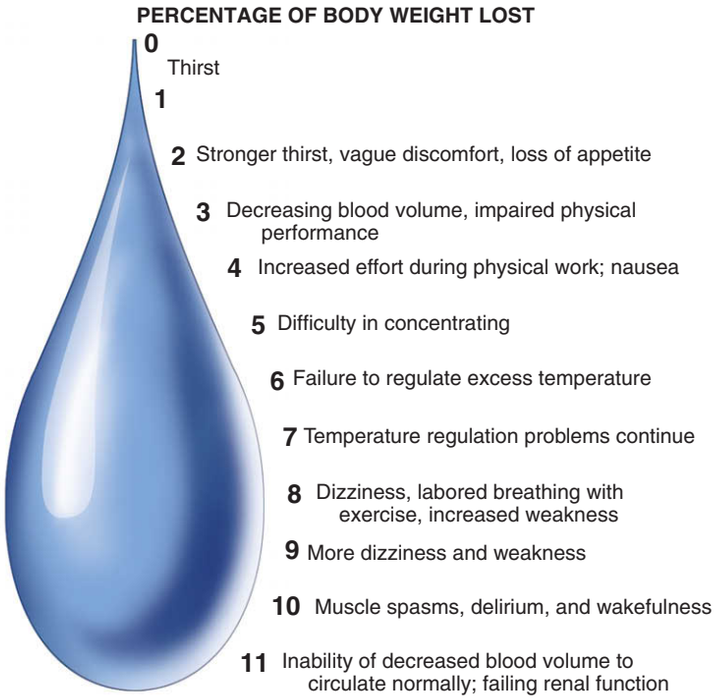


FIGURE 32-9

The effects of dehydration.

Box 32-2 | Dehydration

The term **dehydration** is used to describe the condition that results from excessive loss of body water. Loss of skin resiliency or pressure—often described as a loss of **turgor**—is a sign of dehydration (Figure *A*). Water deprivation or loss triggers a complex series of protective responses designed to maintain homeostasis of water and electrolyte levels. Unfortunately, the term *dehydration* is incomplete. It does not, by definition, include the loss of electrolytes. To understand the control mechanisms that ensure fluid and electrolyte balance or properly interpret the clinical signs and symptoms of dehydration in disease states, it is important to realize that in any process of dehydration, water loss is always accompanied by loss of electrolytes. If water intake is reduced to the point of dehydration, a corresponding quantity of electrolytes must be removed to maintain the normal ionic content of body fluids. The same is true in the case of electrolyte loss when an accompanying loss of water must occur to maintain homeostasis of both fluid and electrolyte levels. Understanding the close interrelationships of water and electrolyte loss in dehydration provides the rationale for effective treatment. Water alone is inadequate; treatment of dehydration also requires appropriate electrolyte replacement therapy.

As discussed in Chapter 7, maintaining a constant core body temperature in a hot environment is an important function of the skin. As sweat evaporates, excess body heat can be eliminated. In hot weather or during extended periods of strenuous physical activity, the volume of water lost because of sweat production can reach 15 L per day (Figure *B*). If water intake is inadequate, signs of dehydration will appear very rapidly. As body water levels decrease, the initial defense mechanisms are directed toward maintaining an adequate blood volume.

In addition to water, sweat contains significant quantities of sodium and chloride. However, the relative loss of water in sweat is greater than the loss of electrolytes. Therefore, as water is shifted from the interstitial fluid compartment to the plasma to compensate for fluid loss, the kidneys excrete the excess electrolytes to preserve normal ionic concentrations in the two compartments.

REGULATION OF WATER AND ELECTROLYTE LEVELS IN PLASMA AND INTERSTITIAL FLUID

More than 70 years ago, the English physiologist Ernest Starling advanced a hypothesis about the nature of the mechanism that controls water movement between plasma and interstitial fluid (extracellular fluid [ECF])—that is, across the capillary membrane. This hypothesis has since become one of the major premises of physiology and is often spoken of as *Starling's law of the capillaries*, illustrated in Figure 22-26 on p. 703. According to this law, the control mechanism for water exchange between

The chemical composition and actual volume of fluids lost from the body will also affect the type and effectiveness of defense mechanisms that occur. For example, fluids lost through vomiting or diarrhea will have differing ratios of fluid to electrolytes than sweat has, and the actual electrolyte composition and concentration will also be different. As a result, the type of electrolyte excretion or retention by the kidneys that will be needed to maintain ionic balance in the fluid compartments will also change.

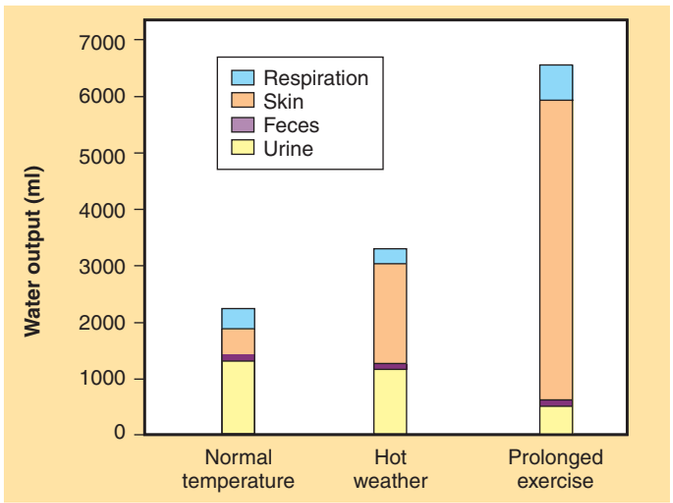
There is a lag in the volume-electrolyte adjustment mechanism triggered by dehydration. Shifts in fluid occur more quickly between compartments than does the adjustment in electrolyte levels. However, if water and electrolyte losses are limited and the interval between loss and replacement is short, the symptoms of dehydration will be mild and transitory.

In severe and prolonged water deprivation or loss, the initial shift of interstitial fluid to plasma will be followed by movement of water from the intracellular compartment as well. Over time, the extracellular and intracellular fluid losses are about equal.

Extracellular (interstitial) water is more "expendable" and quickly accessible as a fluid source to maintain blood volume in the early stages of body fluid loss. It is said to serve as the "first line of defense" against dehydration. As extracellular fluid is depleted, intracellular water must be used to prolong survival time. Ultimately, the volume of extracellular fluid can be reduced by almost 60% and intracellular fluid by 30% before death occurs.



A



B

A, Testing for dehydration. Loss of skin elasticity or turgor is a sign of dehydration. Skin that does not return quickly to its normal shape after being pinched indicates interstitial water loss. **B, Water loss during varying conditions.** During hot weather or prolonged exercise, there is a dramatic increase in water output—mostly from the skin in the form of sweat. Water intake must also dramatically increase to offset the difference, otherwise dehydration will occur.

plasma and interstitial fluid consists of four types of pressure: *blood hydrostatic* and *colloid osmotic pressure* on one side of the capillary membrane and *interstitial fluid hydrostatic* and *colloid osmotic pressure* on the other side.

We are ready now to try to answer the following question: How does the chemical structure of body fluids control water movement between them and thereby control fluid distribution in the body?

According to the physical laws governing filtration and osmosis, **blood hydrostatic pressure** (**BHP**) tends to force fluid out of capillaries into interstitial fluid (IF), but **blood colloid osmotic pressure** (**BCOP**) tends to draw it back into them. **Interstitial fluid hydrostatic pressure** (**IFHP**), in contrast, tends to force fluid out of the interstitial fluid into the capillaries, and **interstitial fluid colloid osmotic pressure** (**IFCOP**) tends to draw it back out of capillaries. In short, two of these forces push fluids in one direction and two in the opposite direction.

The process described here is similar in many ways to the mechanism responsible for the formation of glomerular filtrate studied in the last chapter. Either example is an application of *Starling's law of the capillaries.*

The movement of fluids and electrolytes between plasma and interstitial fluid caused by hydrostatic and colloid osmotic pressure

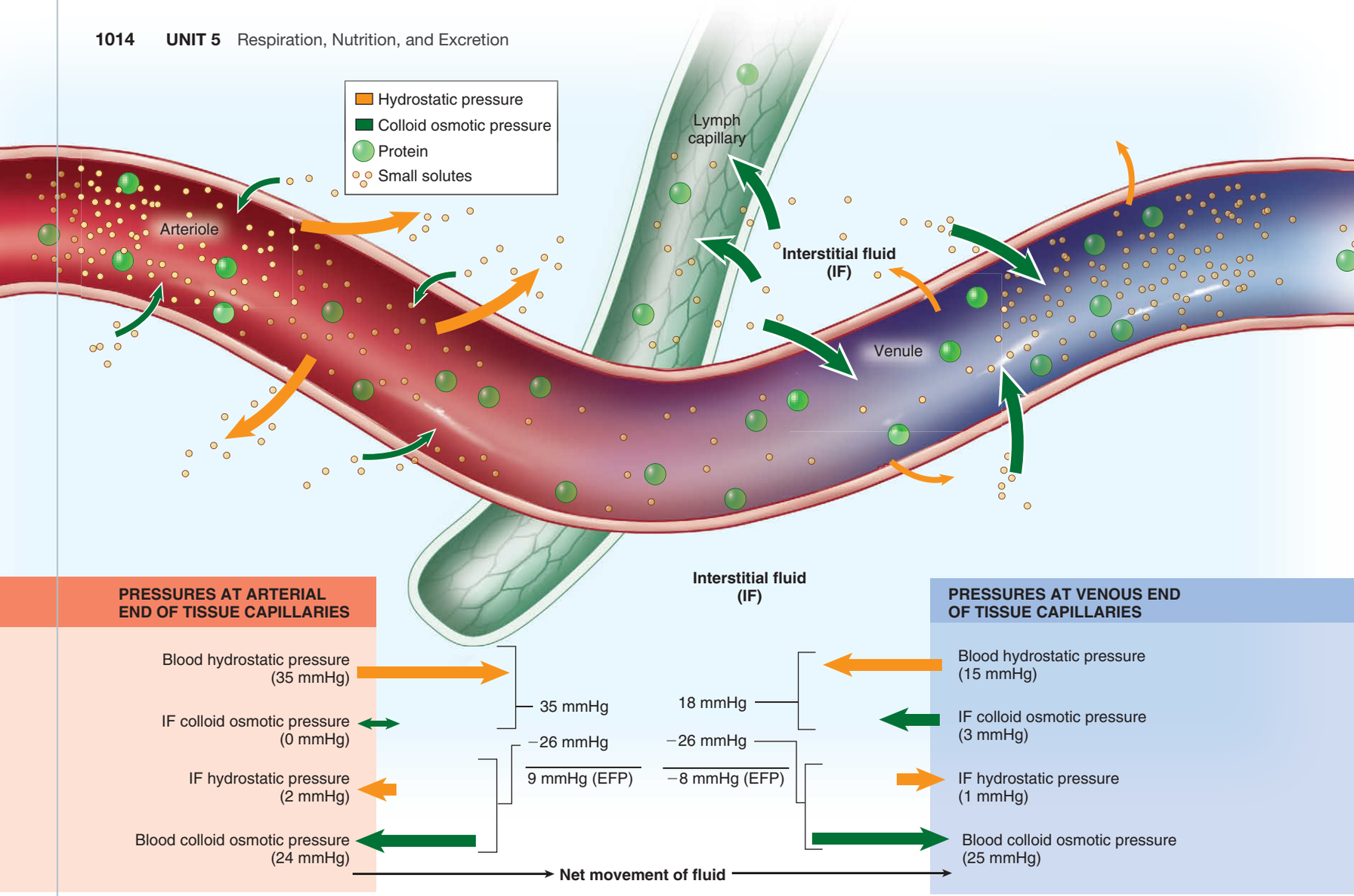


FIGURE 32-10

Movement of fluids and electrolytes between plasma and interstitial fluid caused by hydrostatic and colloid osmotic pressure. *EFP,* Effective filtration pressure. See text for discussion.

is illustrated in Figure 32-10. Note also in Figure 32-10 that the presence of blind-ended lymphatic vessels in the tissue spaces also serves as a mechanism for drainage of excess interstitial fluid. Osmotic and diffusion forces result in the movement of interstitial fluid and small proteins into the lymphatic system. Eventually, the lymph formed in this way will enter the circulatory system and become part of the circulating blood volume.

The difference between the two sets of opposing forces obviously represents the net or effective filtration pressure—in other words, the effective force tending to produce the net fluid movement between blood and interstitial fluid. In general terms, therefore, we may state Starling's law of the capillaries this way: the rate and direction of fluid exchange between capillaries and interstitial fluid are determined by the hydrostatic and colloid osmotic pressures of the two fluids. Or, we may state it more specifically as a formula:

$$(BHP + IFCOP) - (IFHP + BCOP) = EFP^{*}$$

To illustrate operation of Starling's law (see Figure 32-10), let us consider how it controls water exchange at the arterial ends of tissue capillaries. The lower left-hand portion of Figure 32-10 gives normal pressures. Using these figures in Starling's law of the capillaries we get (35 + 0) − (2 + 24) = 9 mmHg net pressure *(effective filtration pressure [EFP])*, which causes water to filter out of blood at the arterial ends of capillaries into interstitial fluid.

*Note that the factors enclosed in the first set of parentheses tend to move fluid out of capillaries and that those in the second set oppose this movement—they tend to move fluid into the capillaries.



FIGURE 32-11

Pitting edema. Note the finger-shaped depressions that do not rapidly refill after an examiner has exerted pressure.

The same law operates at the venous end of capillaries (see the lower right-hand portion of Figure 32-10). Again, apply Starling's law of the capillaries. What is the net effective pressure at the venous ends of capillaries? In which direction does it cause water to move? Assuming that the figures given are normal, do you agree that theoretically "the same amount of water returns to the blood at the venous ends of the capillaries as left it from the arterial ends"?

On the basis of our discussion thus far, we can formulate some principles about the transfer of water between blood and interstitial fluid.

1. No net transfer of water occurs between blood and interstitial fluid as long as the effective filtration pressure (EFP) equals 0, that is, when

(BHP + IFCOP) = (IFHP + BCOP)

2. A net transfer of water, a "fluid shift," occurs between blood and interstitial fluid whenever the EFP does not equal 0, that is, when

(BHP + IFCOP)
does not equal
(IFHP + BCOP)

3. Because (BHP + IFCOP) is a force that tends to move water out of capillary blood, fluid shifts out of blood into interstitial fluid whenever

(BHP + IFCOP)
is greater than
(IFHP + BCOP)

4. Because (IFHP + BCOP) is a force that tends to move water out of interstitial fluid into capillary blood, fluid shifts out of interstitial fluid into blood whenever

(IFHP + BCOP)
is greater than
(BHP + IFCOP)

Or, stated the other way around, fluid shifts out of interstitial fluid into blood whenever

(BHP + IFCOP)
is less than
(IFHP + BCOP)

Edema

Edema is a classic example of fluid imbalance and may be defined as the presence of abnormally large amounts of fluid in the intercellular tissue spaces of the body. Edema may occur in any organ or tissue of the body. However, the lungs, brain, and dependent body areas such as the legs and lower part of the back are affected most often. One of the most common areas for swelling to occur is in the subcutaneous tissues of the ankle and foot. The term **pitting edema** is used to describe depressions in swollen subcutaneous tissue in this area that do not rapidly refill after an examiner has exerted finger pressure (Figure 32-11). The condition may be caused by disturbances in any of the factors that govern the interchange between blood plasma and the interstitial fluid compartments. Examples include the following:

- Retention of electrolytes (especially Na^+) in the extracellular fluid as a result of increased aldosterone secretion or after serious renal disease such as acute glomerulonephritis.
- An increase in capillary blood pressure. Normally, fluid is drawn from the tissue spaces into the venous end of a tissue capillary because of the low venous hydrostatic pressure and the high water-pulling force of plasma proteins (Figure 32-12). This balance is upset by anything that increases the capillary hydrostatic pressure. The generalized venous congestion of heart failure is the most common cause of widespread edema. In patients with this condition, blood cannot flow freely through the capillary beds, and therefore the pressure will increase until venous return of blood improves.

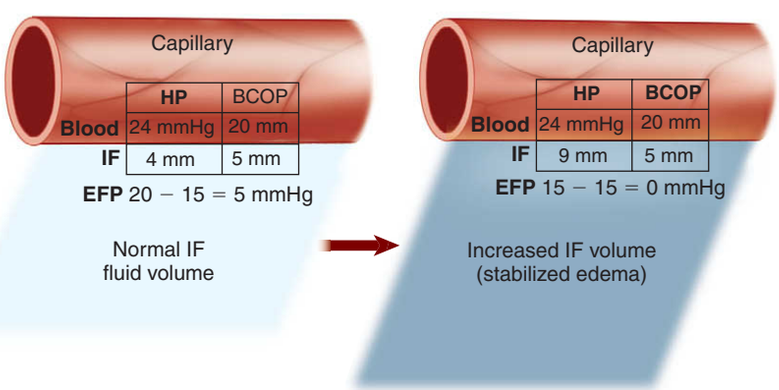


FIGURE 32-12

Edema formation. The mechanism of edema formation can be initiated by a decrease in blood protein concentration and, therefore, a decrease in blood colloid osmotic pressure *(BCOP)*. In the diagram on the left, blood osmotic pressure has just decreased to 20 from the normal 25 mmHg. This increases the effective filtration pressure *(EFP)* to 5 mmHg from a normal of 0 (see Starling's formula, p. 1014). The EFP of 5 mmHg causes fluid to shift out of blood into interstitial fluid *(IF)* until the EFP again equals 0—in this case, when the interstitial fluid volume has increased enough to raise interstitial fluid hydrostatic pressure *(HP)* to 9 mmHg, as shown in the diagram on the right. At this point a new equilibrium is established, and equal amounts of water once more are exchanged between blood and interstitial fluid. Thus the increased interstitial fluid volume—that is, the edema—becomes stabilized.

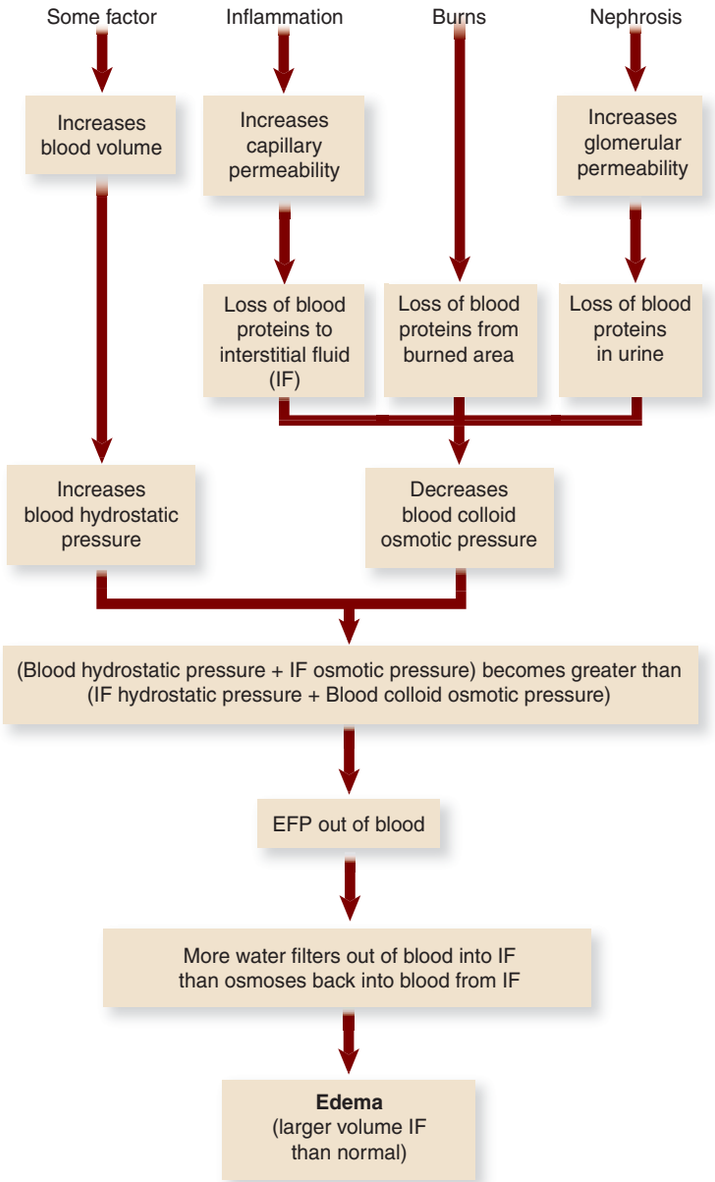


FIGURE 32-13

Mechanisms of edema formation in some common conditions. *EFP,* Effective, or net, filtration pressure; *IF,* interstitial fluid (see also Figure 32-6).

- A decrease in the concentration of plasma proteins normally retained in the blood (Figures 32-12 and 32-13). This may occur as a result of increased capillary permeability caused by infection, burns, or shock.

| QUICK CHECK |

11. Name the four pressures that control water exchange between plasma and interstitial fluid.
12. Define the term *edema.* How can tissue inflammation or burns cause edema?
13. List the mechanisms that regulate movement of solutes and water between the ECF and ICF spaces.
14. Why does fluid balance depend on electrolyte balance?

REGULATION OF WATER AND ELECTROLYTE LEVELS IN ICF

It is the plasma membrane that separates the intracellular and extracellular fluid compartments. We know that a chemical difference predominates between these two fluids, and it is the plasma membrane that plays a critical role in the regulation of intracellular fluid composition.

The mechanism that regulates water movement through cell membranes is similar to the one that regulates water movement through capillary membranes. In other words, interstitial fluid and intracellular fluid hydrostatic and colloid osmotic pressure regulate water transfer between these two fluids. But because the colloid osmotic pressure of interstitial and intracellular fluids varies more than their hydrostatic pressure, their colloid osmotic pressure serves as the chief regulator of water transfer across cell membranes. Their colloid osmotic pressure, in turn, is directly related to the electrolyte concentration gradients—notably sodium and potassium—maintained across cell membranes. As Figures 32-3 and 32-4 show, most of the body sodium is outside the cells. A concentration of 138 to 143 mEq/L makes sodium the chief electrolyte by far in interstitial fluid. The main electrolyte of intracellular fluid is potassium. Therefore, a change in the sodium or the potassium concentration of either of these fluids causes the exchange of fluid between them to become unbalanced.

Pores in the selectively permeable cell membrane retain large molecules, such as proteins, inside the cell but permit many smaller ions such as sodium and potassium to either diffuse through or be selectively transported across the membrane. The electrical charge difference that is created by the unequal concentration of electrolytes on either side of the cell membrane also influences the composition of intracellular fluid. Mechanisms that regulate the movement of solutes and water between extracellular and intracellular fluid spaces are summarized in Figure 32-14.

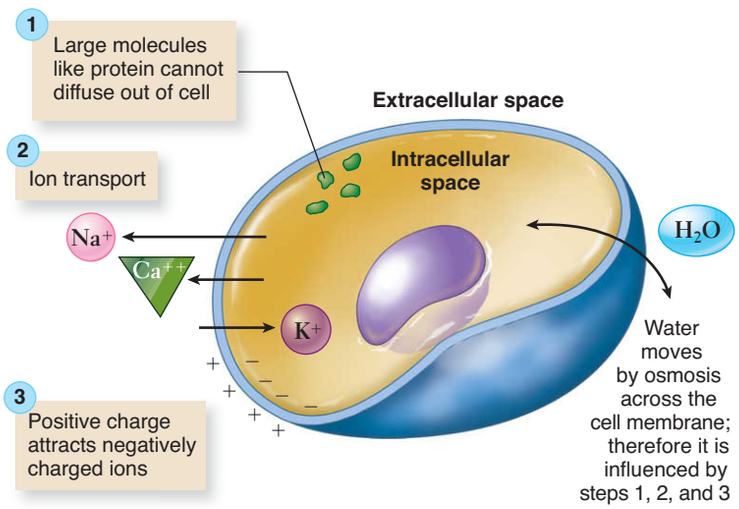


FIGURE 32-14

Mechanisms regulating movement of water and solutes between ECF and ICF spaces. Osmotic pressure is influenced by large protein molecules in the ICF, which cannot diffuse through the small pores of the cell membrane. In addition, electrolyte transport and diffusion and the charge difference across the cell membrane also influence water movement by osmosis. *ECF,* Extracellular fluid; *ICF,* intracellular fluid.

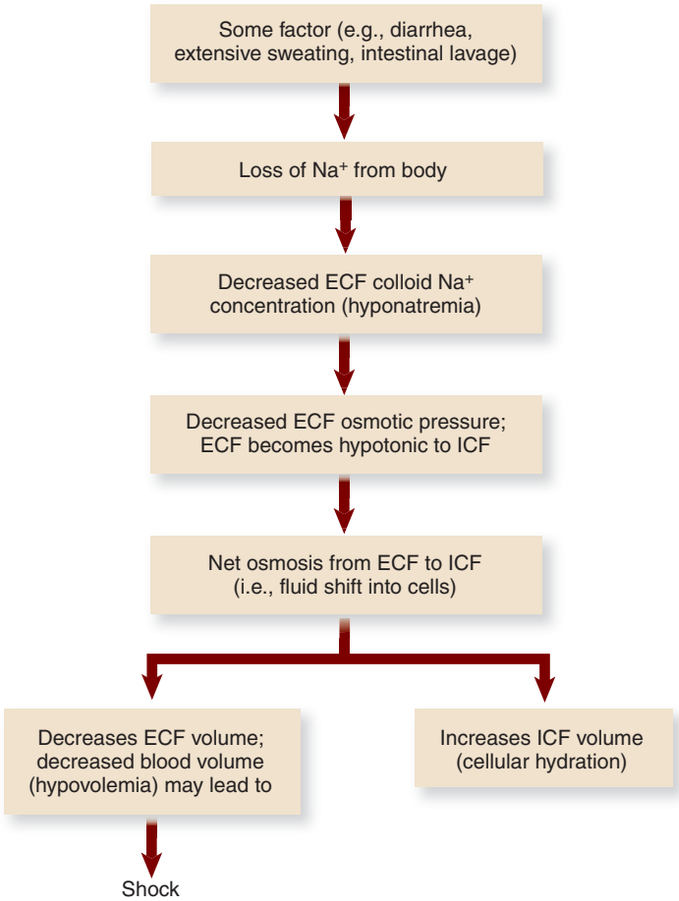


FIGURE 32-15

How electrolyte imbalance leads to fluid imbalances. The schematic uses the example of sodium deficit (hyponatremia) and resulting hypovolemia (cellular hydration). *ECF,* Extracellular fluid; *ICF,* intracellular fluid.

Any change in the solute concentration of extracellular fluid will have a direct effect on water movement across the cell membrane in one direction or another. If for any reason dehydration occurs, the concentration of solutes in the extracellular fluid will increase, and osmosis will cause water to move from the intracellular space into the extracellular space (see Box 32-2). In severe dehydration, the increasing concentration of intracellular fluid caused by water loss to the extracellular space results in abnormal metabolism or cellular death. Increased movement of water into the cell is caused by a decreased concentration of solutes in the extracellular fluids.

A decrease in interstitial fluid sodium concentration immediately decreases interstitial fluid colloid osmotic pressure, thus making it hypotonic to intracellular fluid colloid osmotic pressure. In other words, a decrease in interstitial fluid sodium concentration establishes a colloid osmotic pressure gradient between interstitial and intracellular fluid. This gradient causes net osmosis of fluid to occur, that is, fluid moves out of interstitial fluid into cells. In short, interstitial fluid and intracellular fluid electrolyte concentrations are the main determinants of their colloid osmotic pressure; their colloid osmotic pressure regulates the amount and direction of water transfer between the two fluids, and this regulates their volumes. Hence, fluid balance depends on electrolyte balance. Conversely, electrolyte balance depends on fluid balance. An imbalance in one produces an imbalance in the other (Figure 32-15).

REGULATION OF SODIUM AND POTASSIUM LEVELS IN BODY FLUIDS

A normal sodium concentration in interstitial fluid and potassium concentration in intracellular fluid depend on many factors, especially on the amount of ADH and aldosterone secreted. As shown in Figure 32-16, ADH regulates extracellular fluid electrolyte concentration and colloid osmotic pressure by regulating the amount of water reabsorbed into blood by renal tubules. Aldosterone, on the other hand, regulates extracellular fluid volume by regulating the amount of sodium reabsorbed into blood by renal tubules (see Figure 32-6).

If for any reason conservation of body sodium is required, the normal kidney is capable of excreting an essentially sodium-free urine and is therefore considered the chief regulator of sodium levels in body fluids. Sodium lost in sweat can become appreciable with elevated environmental temperatures or fever. However, the thirst that results may lead to replacement of water but not the lost sodium, and because of the increased fluid intake, the remaining sodium pool may be diluted even more. Sodium loss in sweat is not therefore considered a normal means of regulation.

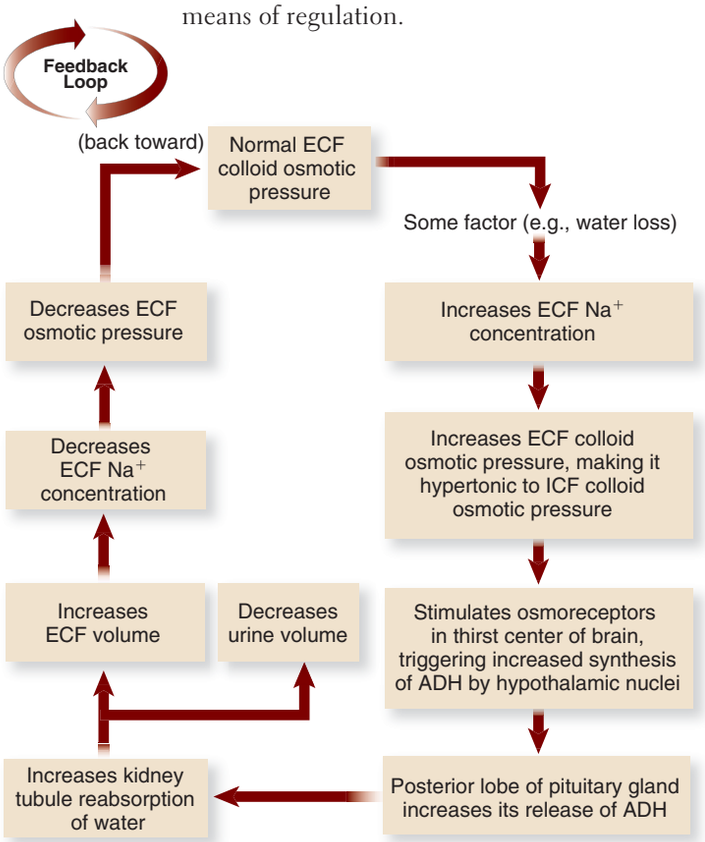


FIGURE 32-16

Antidiuretic hormone (ADH) mechanism for ECF homeostasis. The ADH mechanism helps maintain homeostasis of extracellular fluid (*ECF*) colloid osmotic pressure by regulating its volume and thereby its electrolyte concentration, that is, mainly ECF Na^+ concentration. *ICF,* Intracellular fluid.

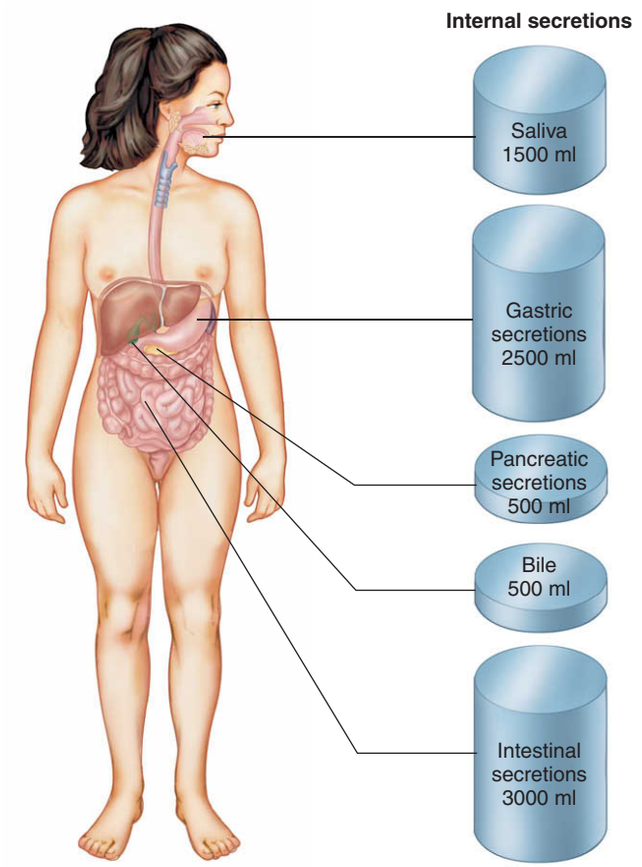


FIGURE 32-17

Sodium-containing internal secretions. Average volumes are shown. Depending on circumstances, the actual total volume of these secretions may reach 8000 or more milliliters in a 24-hour period.

In addition to the well-regulated movement of sodium into and out of the body and between the three primary fluid compartments, there is a continuous movement or circulation of this important electrolyte between a number of internal secretions. More than 8 *L* of various internal secretions such as saliva, gastric and intestinal secretions, bile, and pancreatic fluid is produced every day (Figure 32-17). The total daily secretion of sodium into these alimentary tract fluids alone will average between 1200 and 1400 mEq. A 70-kg (154-lb) adult has a total body sodium pool of only 2800 to 3000 mEq. Precise regulatory and conservation mechanisms for sodium are required for survival.

Chloride is the most important extracellular anion and is almost always linked to sodium. Generally ingested together, they provide in large part for the isotonicity of extracellular fluid. Chloride ions are usually excreted in the urine as a potassium salt, and therefore chloride deficiency—**hypochloremia**—is often found in cases of potassium loss.

The total body potassium content in the average-sized adult is approximately 4000 mEq. Because the majority of body potassium is intracellular, plasma (serum) determinations, which normally fall between 4.0 and 5.0 mEq/L, may not be the best index to reflect imbalances. The body may lose a third to a half of its intracellular potassium reserves before the loss is reflected in lowered plasma potassium levels.

Potassium deficit, or **hypokalemia,** occurs whenever there is cell breakdown, as in starvation, burns, trauma, or dehydration. As individual cells disintegrate, potassium enters the extracellular fluid and is rapidly excreted because it is not reabsorbed efficiently by the kidney.

Cycle of LIFE

Fluid and Electrolyte Balance

Although the amount of total water in the body does not vary much from day to day, the proportions of water to fat and dry solids in the body changes noticeably over the life span. Figure 32-18 shows the shift in water percentages (of body mass) over the lifespan. As the diagram clearly shows, we start life with over two thirds of our body mass being water and progress to about half of body mass being water in adulthood. Because muscles and other metabolically active cells are high in water content, active adults have more water content than nonactive adults. Often, we become less active during late adulthood—a factor that contributes to less water in our bodies as we age. Advanced age can also bring on some of the kidney problems mentioned earlier in this chapter that can affect our ion balance as well.

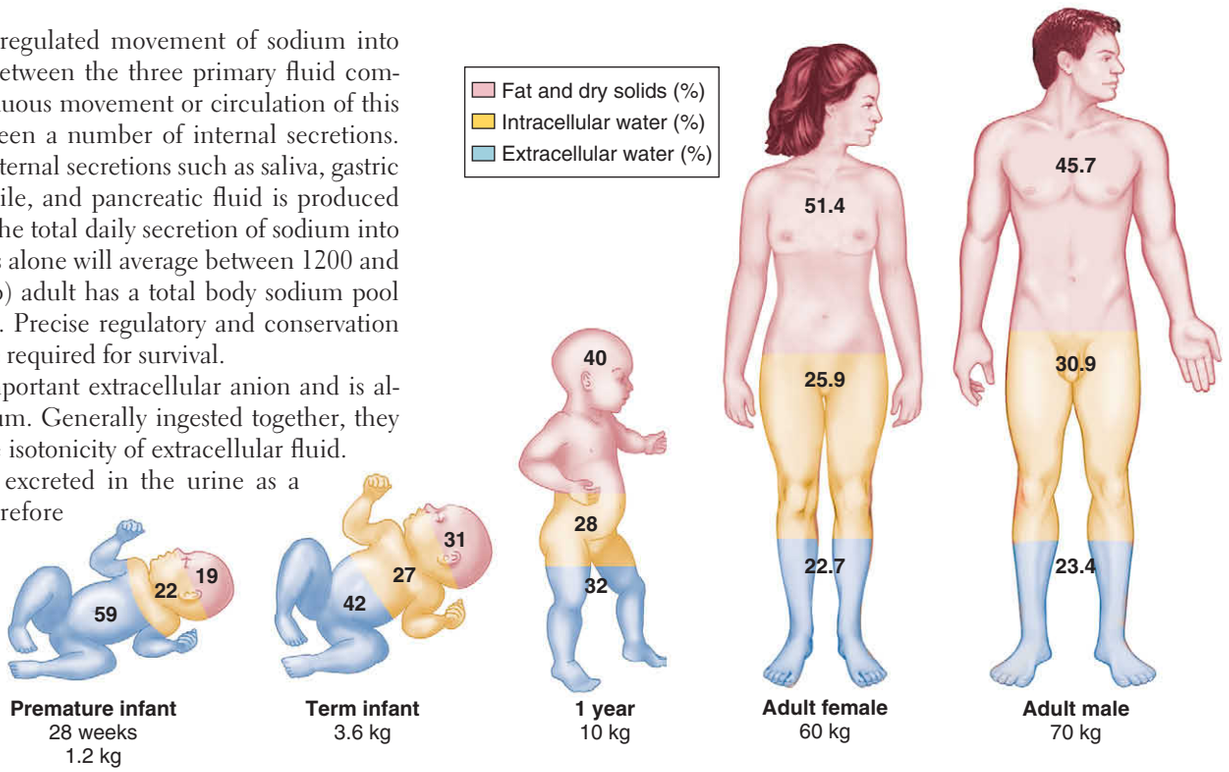


FIGURE 32-18

Body water over the life span. Fluid and nonfluid components of the body expressed as percentage of body weight.

the BIG picture

Fluid and Electrolyte Balance

In discussing the chemical basis for life in Chapter 2, water was described as the "cradle of life." Each of the more than 100 trillion cells that make up the human body must be bathed in a precisely controlled and homeostatically regulated fluid medium. That medium, ever-changing and yet remarkably constant when a condition of homeostasis exists, fills the cells, interstitial spaces, and blood vessels of the body.

Although unique differences in many variables, such as specific fluid volumes, buffers, electrolyte levels, nutrients, circulating wastes, and protein concentrations, exist in each of the body's fluid compartments at any point in time, these changing concentrations and volumes remain within amazingly narrow ranges of their set point normal values in a healthy individual.

Recall from previous chapters that many ions must exist in precise balances within various fluid compartments of the body for normal operation of many vital functions. For example, proper calcium ion balance is required in bone formation or reabsorption, contraction of all three muscle types, synaptic transmission, some types of endocrine signal transduction, and other potentially vital functions. Sodium and potassium concentrations directly affect impulses in nerves and muscles. Chloride balance can affect sodium balance and thus also affect nerve and muscle function. And also recall that acids and bases are ions, and thus pH homeostasis is related to ion homeostasis.

Disease states, atypical circumstances such as fluid deprivation or specific electrolyte losses, as well as normal day-to-day variation in our fluid and nutrient intake, cause the body to initiate "compensatory activities" that help restore or maintain homeostasis. These activities often involve complex neuroendocrine responses that affect multiple body organ systems, including the muscular, digestive, cardiovascular, respiratory, and urinary systems. Homeostasis of fluid and electrolyte levels are one of the most crucial "big picture" requirements for the maintenance of life itself. Every cell and organ system in the body—every physiological response—depends on maintenance of homeostasis in these critical areas.

MECHANISMS of DISEASE

FLUID AND ELECTROLYTE DISORDERS

Fluid Imbalances

Total body water makes up 40% to 60% of body weight in adults and is regulated by homeostatic mechanisms of the neuroendocrine system, heart, kidneys, and blood vessels. Normal water losses, known as insensible water losses, occur through expired air from the lungs and from the skin, making up about 0.4 to 0.5 ml/hr/kg body weight. Abnormally excessive water losses produce a decline in the volume of body fluid and can lead to a state of dehydration, or **hypovolemia,** in which there is inadequate fluid volume in the extracellular compartment (see Box 32-2). If left untreated, it can result in hypovolemic shock. Many causes of dehydration exist. The most common cause of dehydration is fluid loss from the gastrointestinal tract as a result of vomiting or diarrhea. Dehydration also occurs when an individual fails to take in sufficient oral fluid because of depression, nausea, or oral trauma. *Diaphoresis,* or excessive perspiration, may also cause dehydration, with rapid respirations leading to water vapor losses. Any disorder of the kidneys that increases urine excretion, such as nephritis, can lead to dehydration. Fluid can also shift into a space outside the normal fluid compartments during certain disease states, including ascites, burns, pancreatitis, and traumatic injuries. Regardless of the cause, fluid volume deficits cause low blood pressure and cardiac output, electrolyte disturbances, or acid-base abnormalities. Symptoms include dizziness, lightheadedness, weakness, poor skin turgor, and tachycardia. Restoration of the fluid losses is the main goal of therapy. If the deficit is mild, volume can be replaced orally. If the dehydration is severe, fluid volume is replaced intravenously. Examining the person's weight, skin turgor, blood pressure, and urine output will provide important data on fluid volume stability.

Fluid volume excess, or **hypervolemia,** is an expansion of fluid volume in the body. This can occur if the kidneys retain a large amount of sodium and water, as in congestive heart failure, nephrotic syndrome, renal failure, and liver failure. Manifestations include weight gain (the most consistent sign), edema, dyspnea, tachycardia, and pulmonary congestion. Approaches to this disorder are to treat the original pathological process (i.e., renal failure), monitor the person's weight closely, and use diuretics cautiously to remove the excess fluid (Box 32-3).

Water intoxication may result from rapidly drinking large volumes of water or giving hypotonic solutions to persons unable to dilute and excrete urine normally. This may occur in patients with kidney insufficiency or abnormal "thirst" mechanisms resulting from neurological disorders. Water content is elevated, and plasma sodium levels are diluted. Development of subtle mental changes such as confusion and lethargy occur. If intoxication is severe, stupor, seizures, and coma may result. Correction of the neurological impairment along with water restriction can reverse the symptoms.

Water intoxication can happen in normal individuals if water intake is rapid enough that the urinary mechanisms of water loss cannot keep up. Although this is unusual, it can happen—as witnessed by millions a few years ago when a radio station held a "water drinking race" on the air and a contestant died from the effects of severe water intoxication.

Box 32-3 | HEALTH matters

Diuretics

The word **diuretic** is from the Greek word *diouretikos,* meaning "causing urine." By definition, a diuretic drug is a substance that promotes or stimulates the production of urine.

As a group, diuretics are among the most commonly used drugs in medicine. They are used because of their role in influencing water and electrolyte balance, especially sodium, in the body. Diuretics have their effect on tubular function in the nephron, and the differing types of diuretics are often classified according to their major site of action. Examples include (1) *proximal tubule diuretics* such as acetazolamide (Diamox), (2) *Henle loop diuretics* such as ethacrynic acid (Edecrin) or furosemide (Lasix), and (3) *distal tubule diuretics* such as chlorothiazide (Diuril).

Diuretics can also be classified according to the effect the drug has on the level or concentration of sodium (Na^+), chloride (Cl^-), potassium (K^+), and bicarbonate (HCO_3^-) ions in the tubular fluid.

Implications for caregivers monitoring patients receiving diuretics both in hospitals and in home health care environments include keeping a careful record of fluid intake and output and assessing the patient for signs and symptoms of electrolyte and water imbalance. For example, diuretic-induced dehydration resulting in a loss of only 6% of initial body weight will cause tingling in the extremities, stumbling gait, headache, fever, and an increase in both pulse and respiratory rates.

Electrolyte Imbalances

Disturbances in electrolytes can occur in fluid volume abnormalities and many different disease states. **Hyponatremia** is a condition of decreased plasma sodium concentration below the normal range (less than 136 mEq/L) and is usually the result of an excess of water relative to solute. It may also result from excessive losses of sodium. Causes of hyponatremia include skin losses via profuse perspiration, overzealous use of salt-wasting diuretics, adrenal insufficiency, renal or liver failure, low salt intake, or excessive water intake (diluting sodium content). Signs and symptoms include muscle cramps, nausea and vomiting, postural blood pressure changes, poor skin turgor, fatigue, and difficulty breathing. Cerebral swelling can occur in severe cases, causing confusion, hemiparesis (motor weakness on one side of the body), seizures, and coma. Management includes neurological assessment and the administration of sodium orally or intravenously. Water restriction may also suffice.

Hypernatremia is elevation of the plasma sodium concentration higher than 145 mEq/L. It is usually indicative of a body water deficit relative to sodium, but can also result from grossly elevated sodium intake. Causes include lack of fluid intake, diarrhea, diabetes insipidus, loss of water via the respiratory tract, heart disease or congestive heart failure, renal failure, or ingestion of salt in abnormal amounts. Signs and symptoms are similar to those of dehydration and include thirst, disorientation, lethargy, and seizures. The neurological symptoms are thought to be due to cellular dehydration. Replacement with a hypotonic solution will help lower the sodium level slowly, thereby reducing the risk for cerebral edema.

A common type of electrolyte imbalance is **hypokalemia,** a condition in which potassium is lost from the body, resulting in a plasma potassium level below 3.5 mEq/L. Causes include potassium-wasting diuretics, increased urine output with loss of potassium, and vomiting or gastric suctioning without potassium replacement. Hypokalemia can be life threatening and includes manifestations of anorexia, muscle weakness, decreased reflexes, low blood pressure, and cardiac dysrhythmias. Potassium can be replaced through the diet, with potassium-rich foods, or intravenously with caution.

The opposite of hypokalemia is **hyperkalemia,** or a plasma potassium level above 5.5 mEq/L. This can be even more dangerous than hypokalemia because myocardial muscle can be profoundly affected. The common cause of hyperkalemia is kidney disease, but other factors such as vomiting, diarrhea, potassium-conserving diuretics, extensive tissue damage as in burn or trauma victims, severe infections, and Cushing syndrome are also cited. Notable changes can be seen on the electrocardiogram, such as peaked T waves. Hyperkalemia can induce ventricular dysrhythmias, thereby leading to possible cardiac arrest. Because potassium is a part of neuromuscular functions, the person may experience extremity muscle weakness or failure of the respiratory muscles. Intermittent diarrhea, nausea, and intestinal colic are also manifested. Dietary restriction of potassium is sufficient in mild cases, but emergency intravenous administration of calcium gluconate may be required to correct cardiac symptoms. Also, correction of the underlying condition (i.e., trauma) and dialysis to remove the excess potassium can be instituted to correct severe hyperkalemia.

LANGUAGE OF SCIENCE (continued from p. 1003)

fluid compartment interstitial
(in-ter-STISH-al)
[*inter-* **between**, *-stit-* **stand**, *-al* **relating to**]

interstitial fluid colloid osmotic pressure (IFCOP)
(in-ter-STISH-al KOL-oyd os-MAH-tik)
[*inter-* **between**, *-stit-* **stand**, *-al* **relating to**, *coll-* **glue**, *-oid* **like**, *osmo-* **push**, *-ic* **relating to**]

interstitial fluid hydrostatic pressure (IFHP)
(inter-STISH-al hye-droh-STAT-ik)
[*inter-* **between**, *-stit-* **stand**, *-al* **relating to**, *hydro-* **water**, *-stat-* **stand**, *-ic* **relating to**]

intracellular fluid compartment
(in-trah-SELL-yoo-lar)
[*intra-* **occurring within**, *-cell-* **storeroom**, *-ular* **relating to**]

intracellular fluid (ICF)
(in-trah-SELL-yoo-lar FLOO-id)
[*intra-* **occurring within**, *-cell-* **storeroom**, *-ular* **relating to**]

ion
(EYE-on)
[*ion* **to go**]

milliequivalent (mEq)
(mil-i-ee-KWIV-ah-lent)
[*milli-* 1/1000 **part**, *-equi-* **equal**, *-val-* **strength**, *-ent* **state**]

nonelectrolyte
(non-eh-LEK-troh-lyte)
[*non-* **not**, *-electro-* **electricity**, *-lyt-* **loosening**]

osmoreceptor
(os-moh-ree-SEP-tor)
[*osmo-* **push**, *-recept-* **receive**, *-or* **agent**]

parenteral
(pah-REN-ter-al)
[*par-* **beside**, *-enter-* **intestine**, *-al* **relating to**]

subfornical organ (SFO)
(sub-FOR-nih-kal)
[*sub-* **under**, *-fornic-* **arch**, *-al* **relating to**]

thirst center

LANGUAGE OF MEDICINE

diuretic
(dye-yoo-RET-ik)
[*dia-* **through**, *-ure-* **urine**, *-ic* **relating to**]

edema
(eh-DEE-mah)
[*edema* **swelling**]

hyperkalemia
(hye-per-kah-LEE-mee-ah)
[*hyper-* **excessive**, *-kali-* **potassium**, *-emia* **blood condition**]

hypernatremia
(hye-per-nah-TREE-mee-ah)
[*hyper-* **excessive**, *-natri-* **sodium**, *-emia* **blood condition**]

hypervolemia
(hye-per-voh-LEE-mee-ah)
[*hyper-* **excessive**, *-vol-* **volume**, *-emia* **blood condition**]

hypochloremia
(hye-poh-kloh-REE-mee-ah)
[*hypo-* **under or below**, *-chlor-* **green (chlorine)**, *-emia* **blood condition**]

hypokalemia
(hye-poh-kah-LEE-mee-ah)
[*hypo-* **under or below**, *-kal-* **potassium**, *-emia* **blood condition**]

hyponatremia
(hye-poh-nah-TREE-mee-ah)
[*hypo-* **under or below**, *-natri-* **sodium**, *-emia* **blood condition**]

hypovolemia
(hye-poh-voh-LEE-mee-ah)
[*hypo-* **under or below**, *-vol-* **volume**, *-emia* **blood condition**]

intravenous injection
(in-trah-VEE-nus in-JEK-shun)
[*intra-* **within**, *-ven-* **vein**, *-ous* **relating to**, *in-* **in**, *-ject* **throw**, *-tion* **process**]

parenteral therapy
(pah-REN-ter-al)
[*par-* **beside**, *-enter-* **intestine**, *-al* **relating to**]

pitting edema
(eh-DEE-mah)

subcutaneous injection
(sub-kyoo-TAY-nee-us in-JEK-shun)
[*sub-* **under**, *cut-* **skin**, *-aneous* **relating to**, *in-* **in**, *-ject-* **throw**, *-tion* **process**]

turgor
(TUR-ger)
[*turg-* **swollen**, *-or* **condition**]

CASE study

The Louisiana sun beat down on Whitney's head as she and her classmates cleared rubble around what used to be their college's courtyard before the hurricane. Her shirt was soaked with sweat, and she kept having to wipe her forehead as sweat dripped into her eyes. Whitney knew she should be drinking more water, but the cooler was on the bus—two blocks away. She just didn't have the energy to face that walk. "We'll be finished in just another hour," she thought. As she bent down to pick up a cement block, she suddenly felt dizzy and sat down quickly.



Whitney's teacher rushed over, felt her skin and pulse and said, "You haven't been drinking any water today, have you?"

1. What is your best diagnosis for Whitney's condition?
   a. Hypervolemia
   b. Ascites
   c. Hypovolemia
   d. Hypokalemia

2. What would be the best fluid to give Whitney now?
   a. Distilled water
   b. Cold beer
   c. Cold soda
   d. A sports drink

3. What two hormones will be released to compensate for Whitney's condition?
   a. ADH and aldosterone
   b. Estrogen and renin
   c. Aldosterone and TSH
   d. Renin and angina

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

INTERRELATIONSHIP OF FLUID AND ELECTROLYTE BALANCE

A. Fluid and electrolyte balance—implies homeostasis
B. Electrolytes have chemical bonds that allow dissociation into ions, which carry an electrical charge; of critical importance in fluid balance
C. Fluid balance and electrolyte balance are interdependent

TOTAL BODY WATER

A. Fluid content of the human body ranges from 45% to 75% of its total weight
B. Fluid content varies according to age, gender, weight, and fat content of the body

BODY FLUID COMPARTMENTS

A. Two major fluid compartments (Figure 32-1)
B. Extracellular fluid (ECF) makes up the internal environment of the body
   1. Consists mainly of plasma and interstitial fluid
   2. Lymph, cerebrospinal fluid, and joint fluids are considered extracellular
   3. ECF provides a relatively constant environment for cells and transports substances to and from the cells
C. Intracellular fluid (ICF)—water inside the cells
   1. ICF facilitates intracellular chemical reactions that maintain life
   2. By volume, ICF is the largest body fluid compartment

CHEMICAL CONTENT, DISTRIBUTION, AND MEASUREMENT OF ELECTROLYTES IN BODY FLUID

A. Extracellular vs. intracellular fluids
   1. Plasma and interstitial fluid (ECFs) are almost identical in chemical make-up; intracellular fluid quite different in comparison (Figure 32-3)
   2. Differences between extracellular fluids (blood and interstitial fluid)
      a. Blood contains a slightly larger total of ions than interstitial fluid does
      b. Functionally important difference between blood and interstitial fluid
         (1) Blood has appreciable amount of protein anions, whereas interstitial fluid has hardly any
         (2) Because the capillary membrane is practically impermeable to proteins, almost all protein anions remain in the blood
   3. Chemical structure of plasma, interstitial fluid, and intracellular fluid helps control water and electrolyte movement between them
B. Measuring electrolyte reactivity
   1. Concentration or weight of an electrolyte can be expressed as the number of milligrams per 100 ml of solution (mg %); conversion of mg% to milliequivalents per liter (mEq/L) provides information on actual physiological activity
   2. Milliequivalent—measures the number of ionic charges or electrocovalent bonds in a solution; accurately measures the physiological combining power of an electrolyte solution

AVENUES BY WHICH WATER ENTERS AND LEAVES THE BODY

A. Water enters the body via the digestive tract; water is also added to the total fluid volume from each cell as it catabolizes food, and the resulting water enters the bloodstream (Figure 32-5)
B. Water leaves the body via four exits (Figure 32-5)
   1. As urine through the kidney
   2. As water in expired air through the lungs
   3. As sweat through the skin
   4. As feces from the intestine

SOME GENERAL PRINCIPLES ABOUT FLUID BALANCE

A. Cardinal principle of fluid balance: fluid balance can be maintained only if intake equals output
B. Mechanisms are available to adjust output and intake to maintain fluid balance, e.g., renin-angiotensin-aldosterone system (RAAS) (Figures 32-6 and 32-8)
C. Most rapid fluid balance mechanisms are those for controlling water movement between fluid compartments of the body; will maintain normal blood volume at the expense of interstitial fluid volume

MECHANISMS THAT MAINTAIN HOMEOSTASIS OF TOTAL FLUID VOLUME

A. Under normal conditions, homeostasis of total volume of water is maintained or restored primarily by adjusting urine volume and secondarily by fluid intake (Figure 32-7)
B. Regulation of fluid intake—decrease in fluid intake causes osmoreceptors in "thirst center"—wall of third ventricle (subfornical organ) and in supraoptic and paraventricular nuclei of hypothalamus—to increase secretion of ADH (Figure 32-16)
C. Regulation of urine volume—determined by two factors
   1. Glomerular filtration rate, except under abnormal conditions, remains fairly constant
   2. Rate of tubular reabsorption of water fluctuates considerably; normally adjusts urine volume to fluid intake; influenced by amount of antidiuretic hormone and aldosterone

D. Factors that alter fluid loss under abnormal conditions
   1. Rate of respiration and volume of sweat secreted may alter fluid output under certain abnormal conditions
   2. Vomiting, diarrhea, or intestinal drainage can produce fluid and electrolyte imbalances; symptoms range from simple thirst to muscle weakness and kidney failure

REGULATION OF WATER AND ELECTROLYTE LEVELS IN PLASMA AND INTERSTITIAL FLUID

A. Law of capillaries—the control mechanism for water exchange between plasma and interstitial fluid consists of four types of pressure: blood hydrostatic and colloid osmotic pressure on one side of the capillary membrane and interstitial fluid hydrostatic and colloid osmotic pressure on the other side; two of the pressures produce a vector in one direction and the other two in the opposite direction
   1. Blood hydrostatic pressure (BHP) forces fluid out of capillaries into interstitial fluid (IF)
   2. Blood colloid osmotic pressure (BCOP) draws fluid from IF into capillaries
   3. Interstitial fluid hydrostatic pressure (IFHP) forces fluid out of IF into capillaries
   4. Interstitial fluid colloid osmotic pressure (IFCOP) draws fluid from capillaries to IF

B. The rate and direction of fluid exchange between capillaries and interstitial fluid are determined by the hydrostatic and colloid osmotic pressure of the two fluids (Figure 32-10)

C. Some principles about transfer of water between blood and interstitial fluid
   1. No net transfer of water occurs as long as (BHP + IFCOP) = (IFHP + BCOP)
   2. A net transfer of fluid occurs when (BHP + IFCOP) ≠ (IFHP + BCOP)
   3. Fluid shifts out of blood into interstitial fluid whenever (BHP + IFCOP) > (IFHP + BCOP)
   4. Fluid shifts out of interstitial fluid into blood whenever (BHP + IFCOP) < (IFHP + BCOP)

D. Edema—classic example of fluid imbalance
   1. Defined as presence of abnormally large amounts of fluid in the intercellular tissue spaces of the body (Figure 32-11)
   2. Can be caused by disturbances in any factors that govern interchange between blood plasma and interstitial fluid compartments
      a. Retention of electrolytes in the extracellular fluid
      b. Increase in capillary blood pressure
      c. Decrease in the concentration of plasma proteins normally retained in the blood (Figure 32-12)

REGULATION OF WATER AND ELECTROLYTE LEVELS IN INTRACELLULAR FLUID

A. Plasma membrane plays critical role in regulating ICF composition

B. IF and ICF hydrostatic and colloid pressure regulates water transfer between ECF and ICF
   1. Colloid osmotic pressure is the chief regulator of water transfer across cell membranes
   2. Colloid osmotic pressure is directly related to the electrolyte concentration gradients maintained across cell membranes (Figure 32-14)

REGULATION OF SODIUM AND POTASSIUM LEVELS IN BODY FLUIDS

A. Normal sodium concentration in IF and potassium concentration in ICF depend on various factors, especially the amount of ADH and aldosterone secreted
   1. ADH regulates ECF electrolyte concentration and colloid osmotic pressure by regulating amount of water reabsorbed into blood by renal tubules
   2. Aldosterone regulates ECF volume by regulating the amount of sodium reabsorbed into blood by renal tubules

B. Kidneys are considered the chief regulator of sodium levels; when conservation of body sodium is required, the kidneys excrete an essentially sodium-free urine

C. Chloride—most important extracellular anion and almost always linked to sodium
   1. Chloride ions generally excreted in urine in association with potassium
   2. Thus hypochloremia is often associated with cases of potassium loss

D. Hypokalemia (potassium deficit) occurs where there is cell breakdown
   1. Examples: starvation, burns, trauma, dehydration
   2. As cells disintegrate, potassium enters the ECF and is rapidly excreted because it is not reabsorbed efficiently by the kidney

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Discuss the changes in total body water content from infancy to adulthood.
2. How does total body water content differ in men and women?
3. List the compartments of extracellular fluid.
4. What are the four exits by which water normally leaves the body?
5. What are the objectives for giving parenteral solutions?
6. What is the cardinal principle regarding fluid balance?
7. How is urine volume regulated?
8. Define the terms *cation* and *anion*.
9. Are plasma and interstitial fluid chemically similar or different? Explain.
10. Describe the electrolyte composition of blood plasma.
11. Define the term *milliequivalent*. How is it used to measure electrolyte reactivity?
12. What are the four pressures involved in Starling's law?

13. When effective filtration pressure equals 0, what is the net transfer of water between blood and interstitial fluid?
14. When does a "fluid shift" occur between blood and interstitial fluid?
15. Identify various mechanisms that may lead to edema.
16. What role does the plasma membrane play in the regulation of intracellular fluid composition?
17. How does the antidiuretic hormone mechanism maintain homeostasis of extracellular fluid colloid osmotic pressure?
18. In your own words, define dehydration.

CRITICAL THINKING QUESTIONS

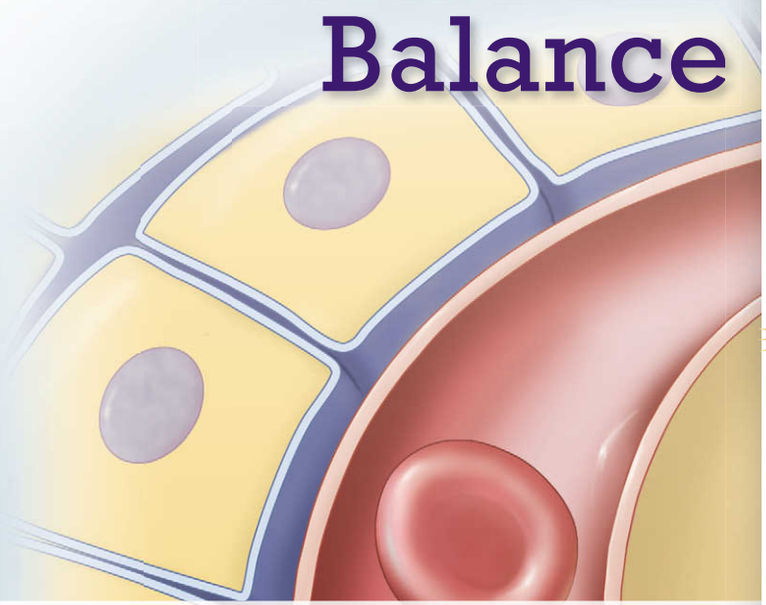


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. How would you define fluid and electrolyte balance? Based on what you know, what would be the impact of glucose deficiency on the electrolyte balance of the body?
2. How would you summarize the role of aldosterone in thirst?
3. Can you make a distinction between anions in the two extracellular fluids? What causes this difference?
4. How would you explain Starling's law of the capillaries?
5. How does hyponatremia lead to fluid imbalance? Can you identify the possible causes?
6. Where are osmoreceptors located, and how are they related to the maintenance of fluid balance?
7. What information would you use to support the view that the homeostasis of fluid and electrolyte levels is one of the most crucial requirements for the maintenance of life itself?

Acid-Base Balance

33



CHAPTER OUTLINE

HINT *Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.*

Mechanisms That Control pH of Body Fluids, 1026
- Review of the pH Concept, 1026
- Sources of pH-Influencing Chemicals, 1027
- Types of pH Control Mechanisms, 1027
- Effectiveness of pH Control Mechanisms—Range of pH, 1028

Buffer Mechanisms for Controlling pH of Body Fluids, 1028
- Buffers Defined, 1028
- Buffer Pairs Present in Body Fluids, 1028
- Buffer Actions That Prevent Marked Changes in pH of Body Fluids, 1028
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Respiratory Mechanisms of pH Control, 1032
- Explanation of Respiratory Mechanisms, 1032
- Respiratiory Adjustment to Counter pH Imbalance of Arterial Blood, 1032
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Urinary Mechanisms That Control pH, 1033
- General Principles Concerning Urinary Mechanisms, 1033
- Mechanisms That Control Urine pH, 1034

The Big Picture: Acid-Base Balance, 1036

Mechanisms of Disease, 1036

Case Study, 1039

LANGUAGE OF SCIENCE

HINT *Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.*

acid
(ASS-id)
[*acid* **sour**]

acidity
(ah-SID-ih-tee)
[*acid-* **sour,** *-ity* **state**]

acidosis
(ass-i-DOH-sis)
[*acid-* **sour,** *-osis* **condition**]

alkaline
(AL-kah-lin)
[*alkal-* **ashes,** *-ine* **relating to**]

alkalinity
(al-kah-LIN-ih-tee)
[*alkal-* **ashes,** *-in-* **relating to,** *-ity* **state**]

alkalosis
(al-kah-LOH-sis)
[*alkal-* **ashes,** *-osis* **condition**]

base
[*bas-* **foundation**]

buffer
(BUFF-er)
[*buffe-* **cushion,** *-er* **agent**]

buffer pair
(BUFF-er)
[*buffe-* **cushion,** *-er* **agent**]

carbonic anhydrase
(kar-BON-ik an-HYE-drays)
[*carbon-* **coal (carbon),** *-ic* **relating to,** *an-* **not,** *-hydr-* **water,** *-ase* **enzyme**]

chemical buffer
(KEM-ih-kal BUFF-er)
[*buffe-* **cushion,** *-er* **agent**]

chloride shift
(KLOR-ide shift)
[*chlor-* **green,** *-ide* **chemical**]

compensation
(kom-pen-SAY-shun)

continued on p. 1039

Acid-base balance is one of the most important of the body's homeostatic mechanisms. The term refers to regulation of hydrogen ion concentration in the body fluid. Therefore the study of acid-base physiology is, in a very real sense, the study of the hydrogen ion (H^+).

Many of the body's most biologically important molecules contain chemical groups that can either "donate" or "accept" a hydrogen ion (H^+) and thus behave as a weak acid or base. As a molecule's pH changes so does its shape and biological activity. The shape and functional ability of ion channels, membrane receptors, hemoglobin, and a variety of enzymes and other important body proteins closely depends on the maintenance of precise regulation of hydrogen ion concentration. Thus, even slight deviations from the normal pH range in body cells and fluids result in pronounced, systemic, and potentially fatal changes in metabolic activity. For example, activity of the Na-K pump, arguably the most important active transport mechanism in the cell membrane, falls by 50% when pH decreases by approximately 1 pH unit. An even more dramatic effect is seen in the activity of a key enzyme (phosphofructokinase) involved in the breakdown of glucose in the absence of O_2 during anaerobic catabolism (glycolysis). The biological activity of this key enzyme falls by approximately 90% when the pH decreases by only 0.1 unit!

Maintaining acid-base balance within narrow and precise ranges is necessary for survival.

MECHANISMS THAT CONTROL pH OF BODY FLUIDS

Review of the pH Concept

Recall from Chapter 2 that water and all water solutions contain hydrogen ions (H^+) and hydroxide ions (OH^-). pH is a symbol used to represent the negative logarithm (exponent of 10) of the number of hydrogen ions (H+) present in 1 liter of a solution. It is expressed as a number between 0 and 14. In Figure 33-1 the pH value is shown on the right side of the scale and the corresponding logarithmic value is on the left. Take a moment to review the pH unit. **pH** indicates the degree of **acidity** or **alkalinity** of a solution. As the concentration of hydrogen ions increases, the pH goes down and the solution becomes more acid; a decrease in hydrogen ion concentration makes the solution more **alkaline** and the pH goes up. A pH of 7 indicates neutrality (equal amounts of H^+ and OH^-), a pH of less than 7 indicates acidity (more H^+ than OH^- and a pH greater than 7 indicates alkalinity (more OH^- than H^+). With a pH of about 1, gastric juice is the most acid substance in the body.

With a pH of 7.0, intracellular fluid is essentially neutral. Arterial and venous blood are slightly alkaline because both have a pH slightly higher than 7.0. The slight increase in acidity of venous blood (pH 7.36) compared with arterial blood (pH 7.40) results primarily from carbon dioxide entering venous blood as a waste product of cellular metabolism. Although any pH value above 7.0 is considered chemically basic, in clinical medicine the term **acidosis** is used to describe an arterial blood pH of less than 7.35 and **alkalosis** is used to describe an arterial blood pH greater than 7.45. The lungs remove the equivalent of more than 30 liters of carbonic acid each day from the venous blood by elimination of carbon dioxide, and yet 1 liter of venous blood contains only about 1/100,000,000 grams more hydrogen ions than does 1 liter of arterial blood. What incredible constancy! The pH homeostatic mechanism does indeed control effectively—astonishingly so.

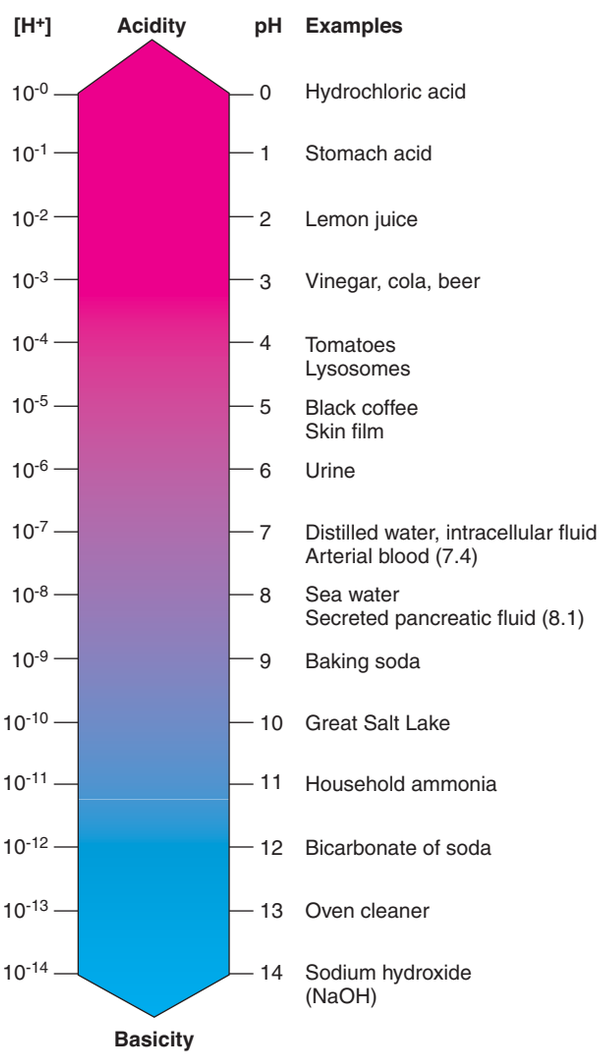


FIGURE 33-1

The pH range. See text for discussion.

Sources of pH-Influencing Chemicals

Acids and **bases** continually enter the blood as a result of absorbed foods and the metabolism of nutrients at the cellular level. Therefore, some kind of mechanism for neutralizing or eliminating these substances is necessary if blood pH is to remain constant. Although both acidic and basic components are important, the homeostasis of body pH depends largely on the control of hydrogen ion concentration in the extracellular fluid. Hydrogen ions are continually entering the body fluids from (1) carbonic acid, (2) lactic acid, (3) sulfuric acid, (4) phosphoric acid, and (5) acidic ketone bodies.

Carbonic and lactic acids are produced by the aerobic and anaerobic metabolism of glucose, respectively. Sulfuric acid is produced when sulfur-containing amino acids are oxidized, and phosphoric acid accumulates when certain phosphoproteins and ribonucleotides are broken down for energy purposes. Acidic ketone bodies, which include *acetone*, *acetoacetic acid*, and *beta-hydroxybutyric acid*, accumulate during the incomplete breakdown of fats. Each of these acids contributes hydrogen ions in varying amounts to the extracellular fluid and influences acid-base balance. Toxic accumulation of acidic ketone bodies is a common complication of untreated diabetes mellitus.

Minerals that remain after food has been metabolized are said to be either acid-forming minerals or base-forming minerals, depending on whether they contribute to formation of an acidic or basic medium when in solution. Acid-forming elements include chlorine, sulfur, and phosphorus—all are abundant in high-protein foods such as meat, fish, poultry, and eggs. They are also present in some grains such as wheat, corn, and oats. These foods are often designated as acid-forming foods.

After metabolism is complete, most mixed diets contain a surplus of acid-forming mineral elements that must be continually buffered to maintain acid-base balance. Extremely high-protein diets that produce a predominantly *acid mineral residue* when metabolized may tax the body's ability to remain in acid-base balance if consumed over prolonged periods.

Mineral elements that are alkaline, or basic, in solution include *potassium*, *calcium*, *sodium*, and *magnesium*. All these elements are found in fruits and vegetables, which nutritionists often label as *base-forming foods*. The predominantly *basic residue* that results after metabolism of a strict vegetarian diet may also tax the ability of the body to maintain acid-base balance because of a high influx of alkaline components into the extracellular fluid.

Foods containing acids that cannot be metabolized, such as rhubarb (oxalic acid) and cranberries (benzoic acid), are said to be direct acid-forming foods, whereas antacids such as sodium bicarbonate and calcium carbonate are examples of direct base-forming substances. Box 33-1 gives some examples of acid-forming and base-forming foods.

| QUICK CHECK |

1. Define the term *pH*.
2. Is a solution with a pH above 7 acid or alkaline?
3. Identify three acid-forming and three base-forming elements.
4. Does CO_2 entering venous blood increase or decrease the pH level?

Box 33-1 | FYI

Acid-Forming and Base-Forming Potential of Foods

Examples of foods that have acid-forming characteristics include corn and corn oil, olives and olive oil, blueberries (see figure), cranberries, oats, wheat, rice, peanuts, red beans, black beans, butter, cheese, beef, fish, pork, turkey, canola oil, and sugar. On the other hand, many of the foods we eat may have base-forming characteristics, such as peppers, sea salt, tofu, almonds, mineral water, citrus fruits, grapes, blackberries, bananas, tomatoes, apples, green beans, lettuce, garlic, broccoli, carrots, and avocado.



Blueberries. Blueberries have an acid-forming effect.

Types of pH Control Mechanisms

The two major types of control systems listed in Table 33-1—chemical and physiological—operate to maintain the constancy of body pH.

In the discussion that follows, buffer action is defined and the specific types of *chemical* and *physiological buffer systems* are discussed. The rapid-acting **chemical buffers** immediately combine with any added acid or alkali that enters the body fluids and thus prevent drastic changes in hydrogen ion concentration and pH. As explained later, all **buffers** act to prevent swings in pH even if hydrogen ion concentrations change. If the immediate action of chemical buffers cannot stabilize pH, the **physiological buffers**

TABLE 33-1 pH Control Systems

TYPE	RESPONSE TIME	EXAMPLE
Chemical buffer systems	Immediate	Bicarbonate buffer system Phosphate buffer system Protein buffer system
Physiological buffer systems	Minutes Hours	Respiratory response system Renal response system

serve as a secondary defense against harmful shifts in pH of body fluids. pH shifts that are not halted by the immediate effects of chemical buffering cause the respiratory system to respond in 1 to 2 minutes, and changes in the rate and depth of breathing occur. For reasons explained later, such changes in carbon dioxide levels alter hydrogen ion concentration and help stabilize pH. If respiratory mechanisms are unable to stop the pH shift, a more powerful, but slower-acting, renal physiological buffer system involving the excretion of either an acid or alkaline urine will be initiated within 24 hours. Collectively, these mechanisms—buffers, respirations, and kidney excretion of acids and bases—might be said to make up the *pH homeostatic mechanism*. One example of the relationship between these three mechanisms is shown in Figure 33-2. The equilibrium between hydrogen ions, carbonic acid, bicarbonate, and carbon dioxide within red blood cells illustrates the interrelated nature of the pH control mechanisms. Note that an increase in body carbon dioxide levels results in excess acid formation in red blood cells, which is counteracted by a corresponding increase in elimination of both carbon dioxide by the lungs and excess hydrogen ion in the urine.

Effectiveness of pH Control Mechanisms—Range of pH

The most convincing evidence of the effectiveness of the pH control mechanism is the extremely narrow range of blood pH—normally 7.36 to 7.41. Maintaining the body's pH within this narrow range is essential to sustain healthy life. Moving outside this pH range causes disruption of many of the body's essential chemical processes.

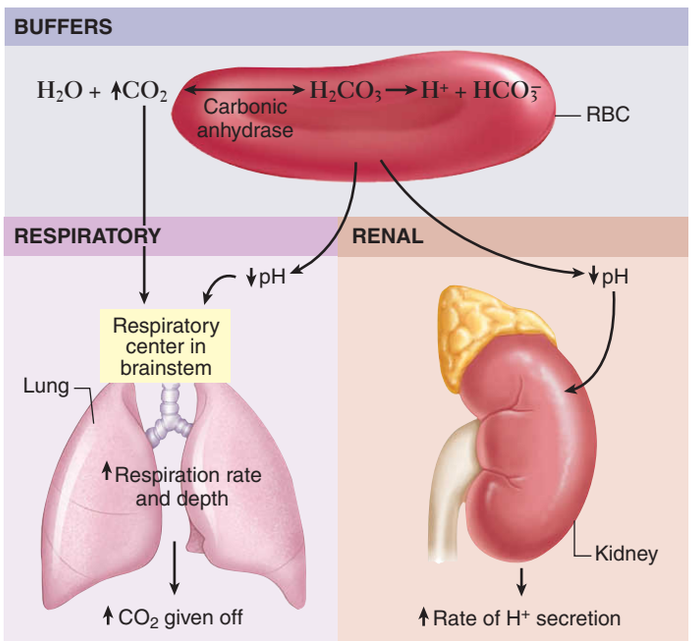


FIGURE 33-2

Integration of pH control mechanisms. Elevated carbon dioxide (CO_2) levels result in increased formation of carbonic acid in red blood cells. The resulting increase in hydrogen ions, coupled with elevated CO_2 levels, results in an increase in respiratory rate and secretion of hydrogen ions (H^+) by the kidneys, thus helping regulate the pH of body fluids.

BUFFER MECHANISMS FOR CONTROLLING pH OF BODY FLUIDS

Buffers Defined

In terms of action, a **buffer** is a substance that prevents marked changes in the pH of a solution when an acid or a base is added to it. Let us suppose that a small amount of a strong acid, hydrochloric acid, is added to a solution that contains a buffer (e.g., blood) and that its pH decreases from 7.41 to 7.27. If the same amount of hydrochloric acid were added to pure water containing no buffers, its pH would decrease much more markedly, from 7 to perhaps 3.4. In both instances, pH decreased after addition of the acid, but much less so with buffers present than without them. Stated another way, buffers do not prevent pH changes, but they do help to minimize them.

In terms of chemical composition, buffers consist of two kinds of substances and are therefore often referred to as **buffer pairs**.

Buffer Pairs Present in Body Fluids

Most of the body fluid buffer pairs consist of a weak acid and a salt of that acid. The main buffer pairs in body fluids are the following:

$$\text{Bicarbonate pairs: } \frac{NaHCO_3}{H_2CO_3}, \frac{KHCO_3}{H_2CO_3}, \text{ etc.}$$

$$\text{Plasma • protein pair: } \frac{\text{Na • Proteinate}}{\text{Proteins (weak acids)}}$$

$$\text{Hemoglobin pairs: } \frac{K \bullet Hb}{Hb} \text{ and } \frac{K \bullet HbHO_2}{HbO_2}$$

(Hb and HbO_2 are weak acids)

$$\text{Phosphate buffer pair: } \frac{Na_2HPO_4}{NaH_2PO_4} \frac{\text{(basic phosphate)}}{\text{(acid phosphate)}}$$

Buffer Actions That Prevent Marked Changes in pH of Body Fluids

Buffers react with a relatively strong acid (or base) to transform it into a relatively weak acid (or base). That is, an acid that highly dissociates to yield many hydrogen ions is changed into a weaker acid that dissociates less highly to yield fewer hydrogen ions. Thus by way of the buffer reaction, instead of the strong acid remaining in the solution and contributing many hydrogen ions that would drastically lower the pH of the solution, the newly formed weaker acid takes its place, contributes fewer additional hydrogen ions to the solution, and thereby lowers its pH only slightly. Because blood contains buffer pairs, its pH fluctuates much less widely than it would without them. In other words, blood buffers act as one of the mechanisms for preventing marked changes in blood pH.

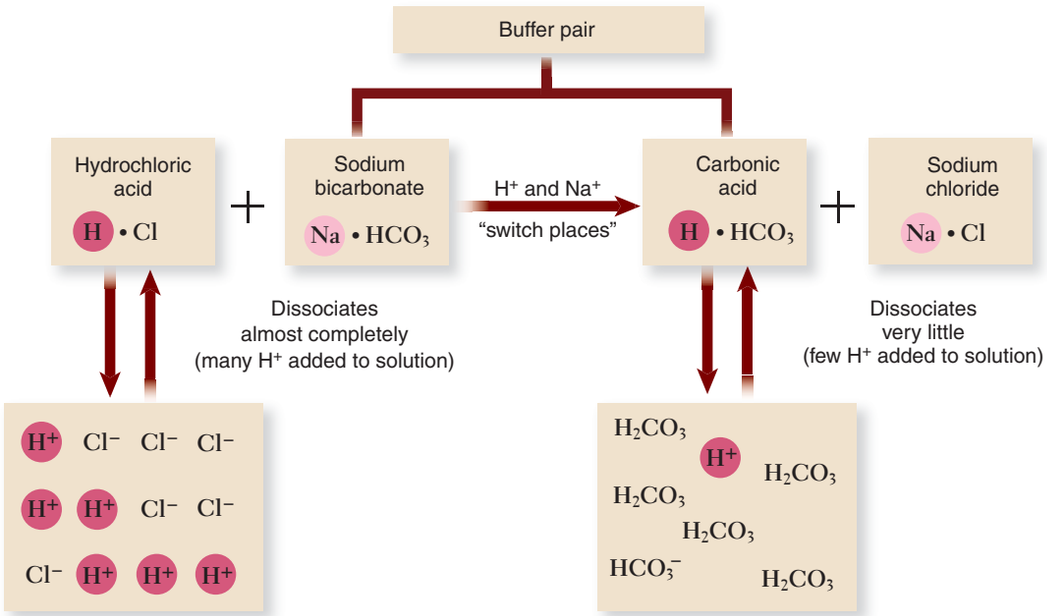


FIGURE 33-3

Buffering action of sodium bicarbonate. Buffering of acid HCl by $NaHCO_3$. As a result of the buffer action, the strong acid (HCl) is replaced by a weaker acid ($H \cdot HCO_3$). Note that HCl, as a strong acid, "dissociates" almost completely and releases more H^+ than does H_2CO_3. Buffering decreases the number of H^+ in the system.

Let us consider, as a specific example of buffer action, how the sodium bicarbonate ($NaHCO_3$)–carbonic acid (H_2CO_3) system works in the presence of a strong acid or base.

The addition of a strong acid, such as hydrochloric acid (HCl), to the sodium bicarbonate–carbonic acid buffer system would initiate the reaction shown in Figure 33-3. Note how this reaction between HCl and the base bicarbonate ($NaHCO_3$) applies the principle of buffering. As a result of the buffering action of $NaHCO_3$, the weak acid, $H \cdot HCO_3$, replaces the very strong acid HCl, and therefore the hydrogen ion concentration of the blood increases much less than it would have if HCl were not buffered.

If, on the other hand, a strong base such as sodium hydroxide (NaOH) is added to the same buffer system, the reaction shown in Figure 33-4 would take place. The hydrogen ion of $H \cdot HCO_3$, the weak acid of the buffer pair, combines with hydroxide ion (OH^-) of the strong base NaOH to form water. Note what this accomplishes. It decreases the number of hydroxide ions added to the solution, and this in turn prevents the drastic rise in pH that would occur in the absence of buffering.

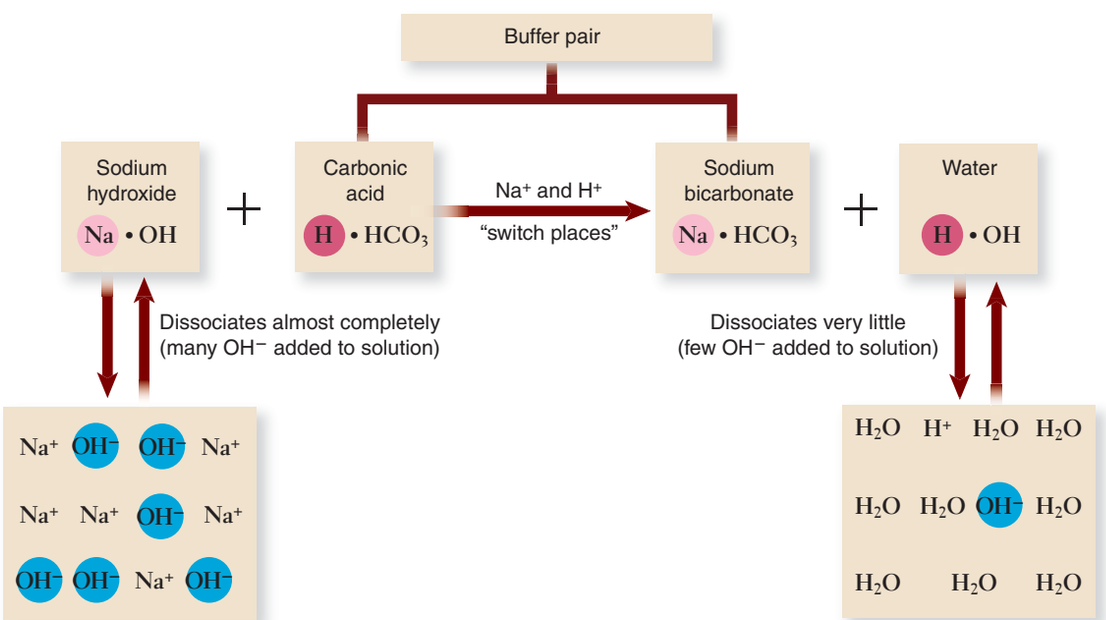


FIGURE 33-4

Buffering action of carbonic acid. Buffering of the base NaOH by H_2CO_3. As a result of buffer action, the strong base (NaOH) is replaced by $NaHCO_3$ and H_2O. As a strong base, NaOH "dissociates" almost completely and releases large quantities of OH^-. Dissociation of H_2O is minimal. Buffering decreases the number of OH^- ions in the system.

Box 33-2 discusses how loss of chloride during severe vomiting could affect the balance of buffers in the body and thus increase the body's pH above normal levels.

The principles of buffer action illustrated by the reaction of HCl and NaOH with the sodium bicarbonate buffer pair can be applied equally to the plasma protein, hemoglobin, and phosphate buffer systems.

Carbon dioxide and other acid waste products are being formed continuously as a result of cellular metabolism. The formation of carbonic acid from carbon dioxide and water requires the enzyme **carbonic anhydrase** (see Figure 33-2), which is found in the red blood cells (RBCs). Although there are numerous types of zinc-containing carbonic anhydrases in the body, it is carbonic anhydrase 1, or CA1, that is present in the cytoplasm of erythrocytes and is primarily responsible for the formation of carbonic acid from CO_2 and water in the RBC. Carbonic acid is buffered primarily by the potassium salt of hemoglobin inside the RBC, as shown in Figure 33-5.

It is interesting to note that the $KHCO_3$ formed by the buffering of carbonic acid dissociates in the RBC, and the bicarbonate ion diffuses down its concentration gradient into the blood plasma. Because of the movement of these negatively charged ions out of the RBC, chloride ions move into the cell from the plasma to maintain the electrical balance on both sides of the RBC membrane. The process of exchanging a bicarbonate ion formed in the red blood cell with a chloride ion from the plasma is called the **chloride shift.** This process makes it possible for carbon dioxide to be buffered in the RBC and then carried as bicarbonate in the plasma. Figure 33-6 summarizes the reactions of the chloride shift.

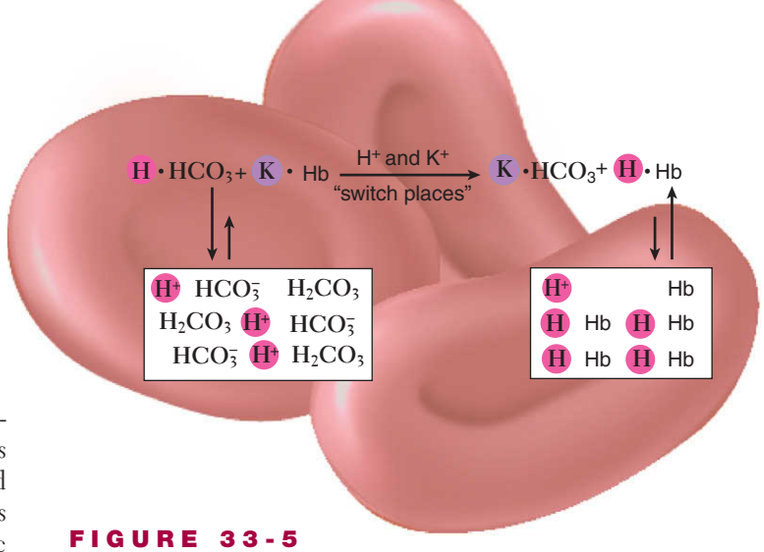
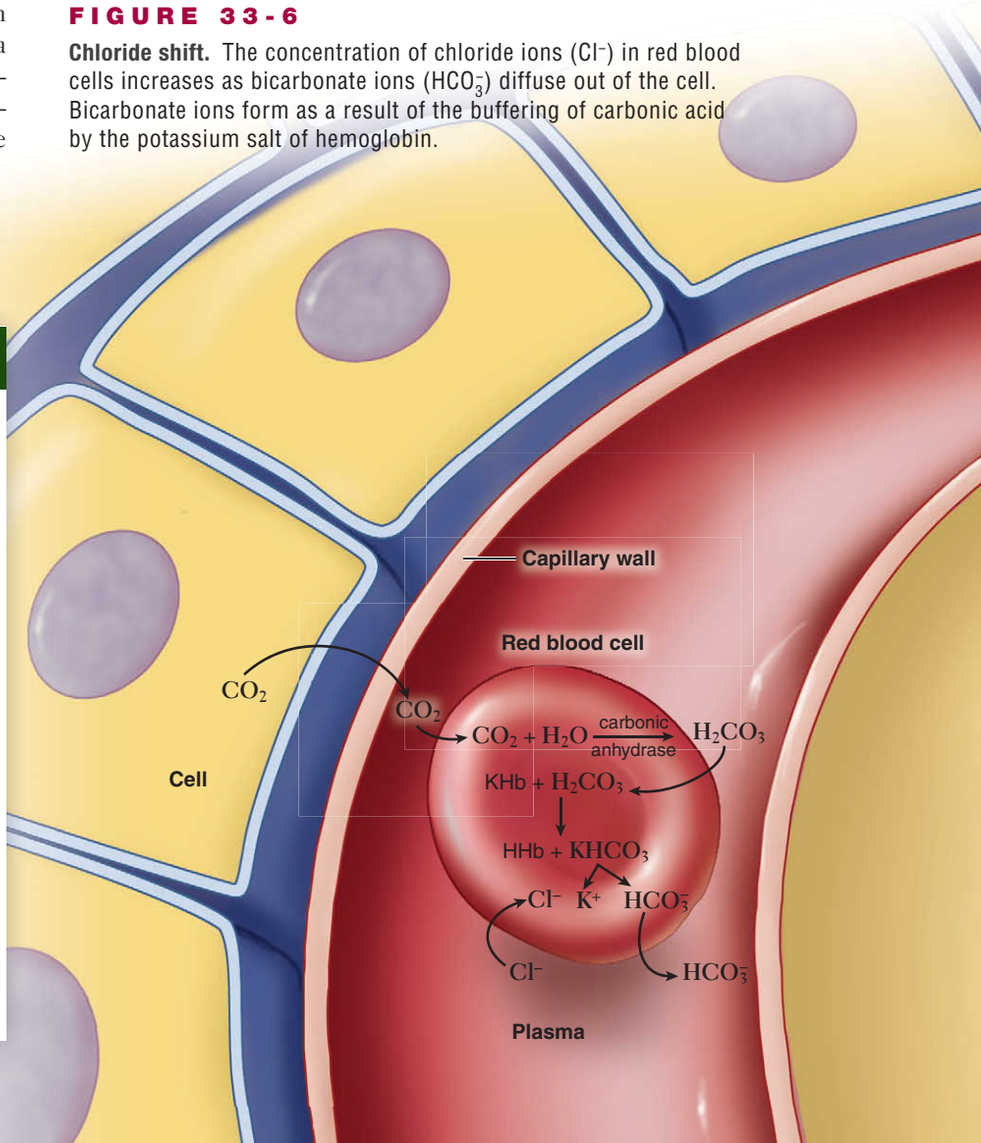


FIGURE 33-5

Buffering of the volatile carbonic acid (H • HCO_3) inside red blood cell by potassium salt of hemoglobin. Note that each molecule of carbonic acid is replaced by a molecule of acid hemoglobin. Because hemoglobin is a weaker acid than carbonic acid, fewer of these hemoglobin molecules dissociate to form hydrogen ions (H^+). Hence, fewer hydrogen ions are added to red blood cell intracellular fluid than would be added by unbuffered carbonic acid. Also, because some of the carbonic acid in the red blood cell has come from plasma, fewer hydrogen ions remain in blood than would have if there were no buffering of carbonic acid.

FIGURE 33-6

Chloride shift. The concentration of chloride ions (Cl^-) in red blood cells increases as bicarbonate ions (HCO_3^-) diffuse out of the cell. Bicarbonate ions form as a result of the buffering of carbonic acid by the potassium salt of hemoglobin.



Box 33-2 | HEALTH matters

Metabolic Alkalosis Caused by Vomiting

Vomiting, sometimes referred to as **emesis,** is the forcible emptying or expulsion of gastric and occasionally intestinal contents through the mouth. It occurs as a result of many stimuli, including foul odors or tastes, irritation of the stomach or intestinal mucosa, and some vomitive or *emetic* drugs such as ipecac. A "vomiting center" in the brain regulates the many coordinated (but primarily involuntary) steps involved (see Figure 29-18, p. 919). Severe vomiting such as the **pernicious vomiting** of pregnancy or the repeated vomiting associated with pyloric obstruction in infants can be life threatening. One of the most frequent and serious complications of vomiting is **metabolic alkalosis.** The bicarbonate excess of metabolic alkalosis results because of the massive loss of chloride from the stomach as hydrochloric acid. It is the loss of chloride that causes a compensatory increase of bicarbonate in the extracellular fluid. The result is *metabolic alkalosis.* Therapy includes intravenous administration of chloride-containing solutions such as **normal saline** (0.9% NaCl in water). The chloride ions of the solution replace bicarbonate ions and thus help relieve the bicarbonate excess responsible for the imbalance.

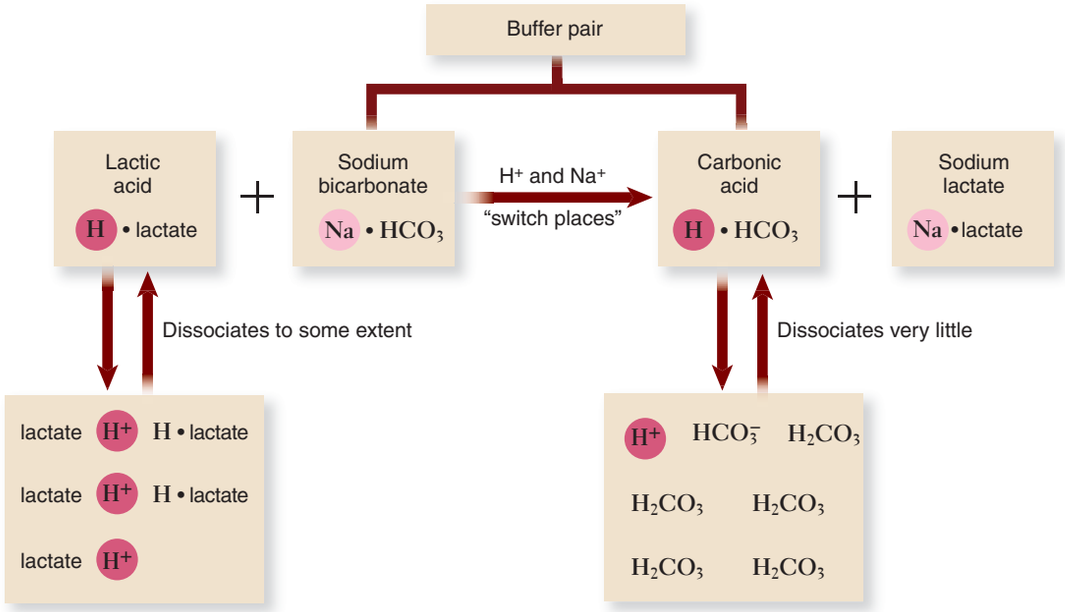


FIGURE 33-7

Lactic acid buffered by sodium bicarbonate. Lactic acid and other "fixed" acids are buffered by $NaHCO_3$ in the blood. Carbonic acid ($H \cdot HCO_3$ or H_2CO_3, a weaker acid than lactic acid) replaces lactic acid. As a result, fewer hydrogen ions (H^+) are added to blood than would be if lactic acid were not buffered.

Nonvolatile, or fixed, acids, such as hydrochloric acid, lactic acid, and ketone bodies, are buffered mainly by sodium bicarbonate (Figure 33-7). Box 33-3 discusses why some athletes consume bicarbonate to counteract the effects of lactic acid produced by exercise. Box 33-4 discusses how an excess of lactic acid can result from the use of a popular diabetes drug.

Normal blood pH and acid-base balance depend on a base bicarbonate–to–carbonic acid buffer pair ratio of 20:1 in the extracellular fluid. Actually, in a state of acid-base balance (pH 7.4), a liter of plasma contains 27 mEq of $NaHCO_3$ as base bicarbonate (BB)—ordinary baking soda—and 1.3 mEq of carbonic acid (CA):

$$\frac{27 \text{ mEq } NaHCO_3}{1.3 \text{ mEq } H_2CO_3} = \frac{BB}{CA} = \frac{20}{1} = \text{pH } 7.4$$

The **ratio** of base to acid is critical. If the ratio is maintained, acid-base balance (pH) remains near normal despite changes in the

Box 33-3 | SPORTS and FITNESS

Bicarbonate Loading

The buildup of lactic acid in the blood, released as a waste product from working muscles, has been blamed for the soreness and fatigue that sometimes accompanies strenuous exercise. Some athletes adopt a technique called **bicarbonate loading,** in which large amounts of sodium bicarbonate ($NaHCO_3$) are ingested to counteract the effects of lactic acid buildup. Their theory is that fatigue is avoided because the $NaHCO_3$, a base, buffers the lactic acid. Unfortunately, the excess bicarbonate intake and diarrhea that often result can trigger fluid and electrolyte imbalances. Long-term $NaHCO_3$ abuse can lead to metabolic alkalosis and its disastrous effects.

Box 33-4 | Lactic Acidosis and Metformin

Metformin hydrochloride (Glucophage) is one of the most widely used and effective of the oral antidiabetic drugs. It is used with diet and exercise to lower blood glucose levels in type 2 diabetes mellitus. A rare but very serious complication of metformin therapy is **lactic acidosis.** It is characterized by elevated blood lactate levels, electrolyte disturbances, and decreased blood pH. It is reported in only about 1 in 33,000 patients taking metformin over the course of a year. However, when it does occur, it can be fatal in nearly 50% of cases. Symptoms include a variety of gastrointestinal and respiratory complaints and feelings of weakness and muscle pain. Patients with kidney and liver disease are known to be at higher risk for lactic acidosis while taking the drug.

absolute amounts of either component of the buffer pair. This type of adjustment is called **compensation.** For example, a BB/CA ratio of 40:2 or 10:0.5 would result in a compensated state of acid-base balance. However, an increase in the ratio causes an increase in pH **(uncompensated alkalosis),** and a decrease in the ratio causes a decrease in pH **(uncompensated acidosis).** The ability of the body to regulate the amount of either component of the bicarbonate buffer pair—to maintain the correct ratio for acid-base balance—makes this system one of the most important for controlling pH of body fluids. **Correction** of acid-base balance is said to occur when components of the buffer pair return to a normal 20:1 ratio.

Evaluation of the Role of Buffers in pH Control

Buffering alone cannot maintain homeostasis of pH. As we have seen, hydrogen ions are added continually to capillary blood despite buffering. If even a few hydrogen ions were added every time blood circulated and no way was provided for eliminating them, blood hydrogen ion concentration would necessarily increase and thereby decrease blood pH. "Acid blood," in other words, would soon develop. Respiratory and urinary mechanisms must therefore function concurrently with buffers to remove from the blood and from the body the hydrogen ions continually being added to blood. Only then can the body maintain constancy of pH over time.

| QUICK CHECK |

5. Define the term *buffer.*
6. Identify the two major types of buffer systems in the body. Which buffer system is the most rapid acting?
7. Using equations, explain the buffering of HCl by sodium bicarbonate and NaOH by carbonic acid.
8. Define the term *chloride shift.*

RESPIRATORY MECHANISMS OF pH CONTROL

Explanation of Respiratory Mechanisms

Respirations play a vital role in controlling pH. With every expiration, carbon dioxide and water leave the body in the expired air. The carbon dioxide comes from the venous blood—diffuses out of it as it moves through the lung capillaries. Therefore, less carbon dioxide remains in the arterial blood leaving the lung capillaries. The lower P_{CO_2} in arterial blood reduces the amount of carbonic acid and the number of hydrogen ions that can be formed in red blood cells by the following reactions:

$$CO_2 + H_2O \xrightarrow{\text{(carbonic anhydrase)}} H_2CO_3$$

$$H_2CO_3 \longrightarrow H^+ + HCO_3^-$$

Arterial blood therefore has a lower hydrogen ion concentration and a higher pH than does venous blood. A typical average pH for venous blood is 7.36, and 7.41 is a typical average pH for arterial blood.

Respiratory Adjustment to Counter pH Imbalance of Arterial Blood

For respirations to serve as a mechanism of pH control, there must be some mechanism for changing the rate and/or depth of respirations as needed to maintain or restore normal pH. Suppose that blood pH has decreased; that is, the hydrogen ion concentration has increased. Respirations then need to increase in rate and/or depth to eliminate more carbon dioxide from the body and thereby leave less carbonic acid and fewer hydrogen ions in the blood.

One mechanism for adjusting respirations to counter arterial blood carbon dioxide content or pH operates in the following way: neurons of the respiratory center are sensitive to changes in arterial blood carbon dioxide content and to changes in its pH. If the amount of carbon dioxide in arterial blood increases beyond a certain level, or if arterial blood pH decreases below about 7.38, the respiratory center is stimulated and respirations accordingly increase in rate and depth. This, in turn, eliminates more carbon dioxide, reduces carbonic acid and hydrogen ions, and increases pH back toward the normal level (Figure 33-8). The carotid chemoreflexes are also mechanisms by which respirations adjust to blood pH and, in turn, adjust pH.

Principles That Relate Respirations to pH Value

A few basic principles, summarized briefly here, help us understand the relationship of respiratory function to the pH of the body's internal environment.

- A decrease in blood pH below normal (acidosis) tends to stimulate increased respirations (hyperventilation), which tends to increase pH back toward normal. In other words, acidosis causes hyperventilation, which in turn acts as a compensating mechanism for the acidosis.
- Prolonged hyperventilation—beyond that needed to restore normal pH—may increase blood pH enough to produce alkalosis.
- An increase in blood pH above normal (or alkalosis) triggers hypoventilation, which serves as a compensating mechanism for the alkalosis by decreasing blood pH back toward normal.
- Prolonged hypoventilation—beyond that needed to restore normal pH—may decrease blood pH enough to produce acidosis.

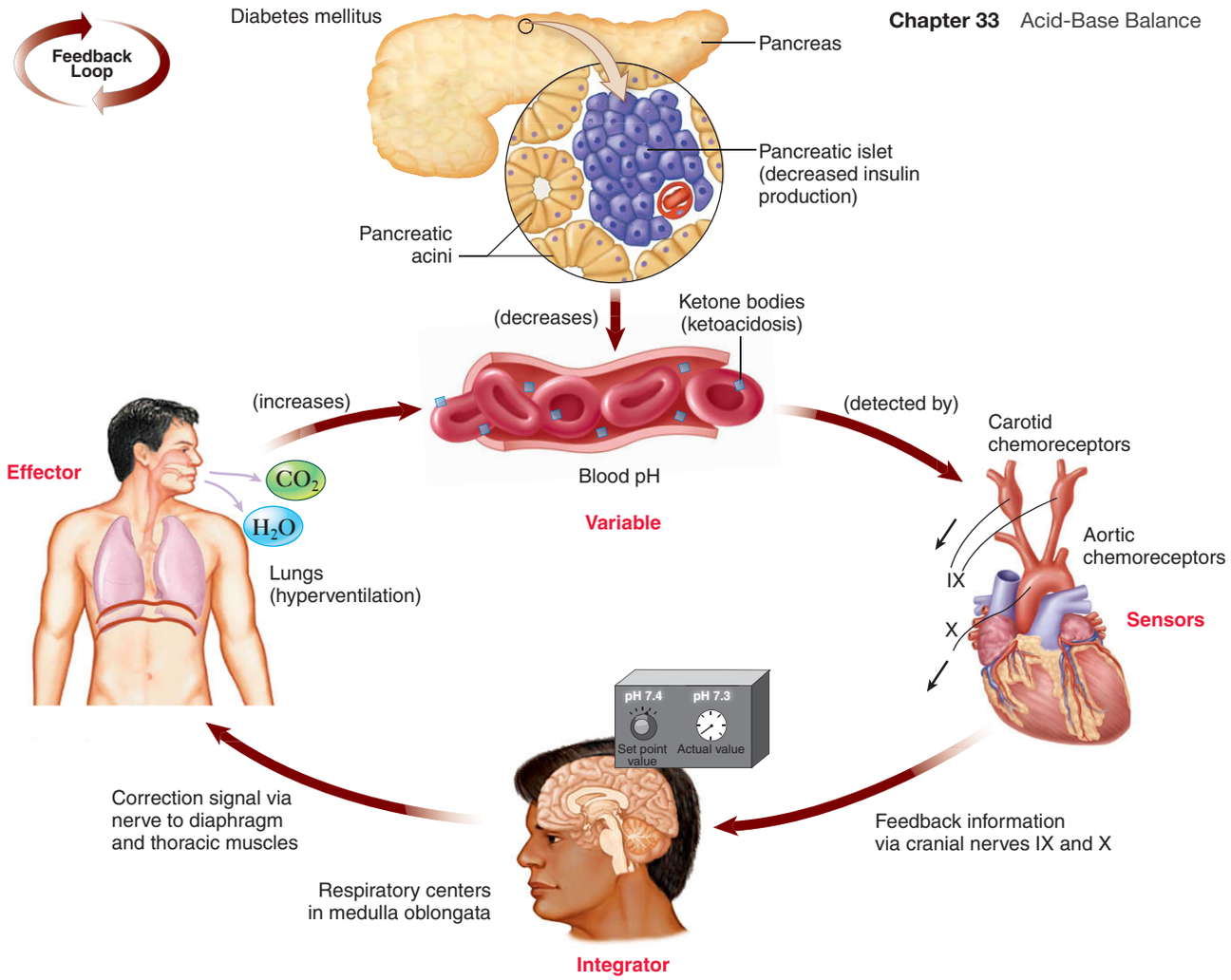


FIGURE 33-8

Respiratory mechanism of pH control. A rise in arterial blood carbon dioxide (CO_2) content or a drop in its pH (below about 7.38) stimulates respiratory center neurons. Hyperventilation results. Less CO_2 and therefore less carbonic acid and fewer hydrogen ions remain in the blood so that blood pH increases, often reaching the normal level.

URINARY MECHANISMS THAT CONTROL pH

General Principles Concerning Urinary Mechanisms

Because the kidneys can excrete varying amounts of acid and base, they, like the lungs, play a vital role in pH control. Kidney tubules, by excreting many or few hydrogen ions in exchange for reabsorbing many or few sodium ions, control urine pH and thereby help control blood pH. If, for example, blood pH decreases below normal, the kidney tubules secrete more hydrogen ions from blood to urine and, in exchange for each hydrogen ion, reabsorb a sodium ion from the urine back into the blood. This, of course, decreases urine pH. But simultaneously—and of far more importance—it increases blood pH back toward normal. This urinary mechanism of pH control is a process for excreting varying amounts of hydrogen ions from the body to match the amounts entering the blood.

The urinary mechanism is a much more effective process for adjusting hydrogen output to hydrogen input than does the body's only other mechanism for expelling hydrogen ions, namely, the respiratory mechanisms previously described. But abnormalities of any one of the three pH control mechanisms soon throw the body into a state of acid-base imbalance. Only when all three parts of this complex mechanism—buffering, respirations, and urine secretion—function adequately can acid-base balance be maintained.

Let us turn now to mechanisms that adjust urine pH to counteract changes in blood pH.

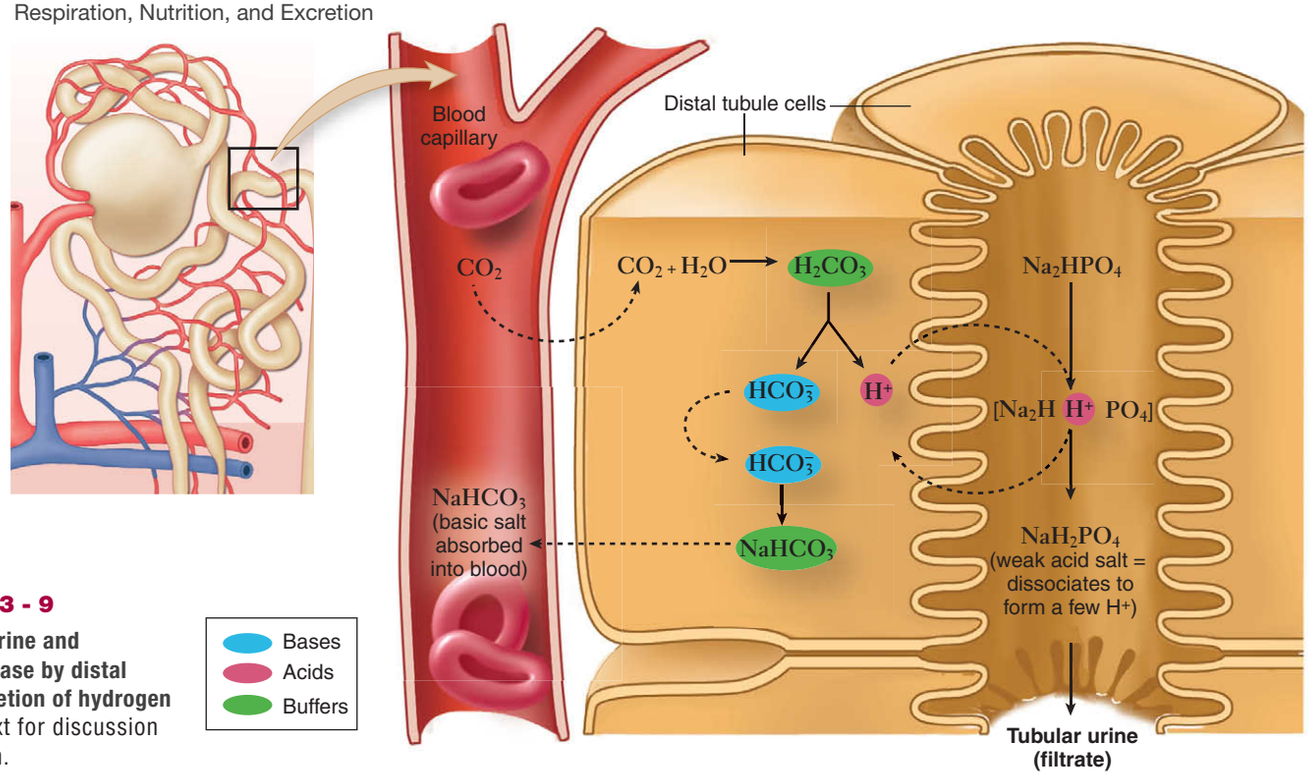


FIGURE 33-9

Acidification of urine and conservation of base by distal renal tubule excretion of hydrogen ions (H^+). See text for discussion of the mechanism.

Mechanisms That Control Urine pH

A decrease in blood pH accelerates the renal tubule ion exchange mechanisms that acidify urine and conserve blood's base, thereby tending to increase blood pH back to normal. Several different such mechanisms work together to remove acid from the body's internal environment.

In one urinary acidification mechanism, the distal tubules and collecting ducts secrete hydrogen ions into the urine in exchange for basic ions, which they reabsorb. Refer to Figure 33-9 as you read the rest of this paragraph. Note that carbon dioxide diffuses from tubule capillaries into distal tubule cells, where the enzyme carbonic anhydrase accelerates the combining of carbon dioxide with water to form carbonic acid. The carbonic acid dissociates into hydrogen ions and bicarbonate ions. The hydrogen ions then move into the tubular urine, where they displace basic ions (most often sodium) from a basic salt of a weak acid and thereby change

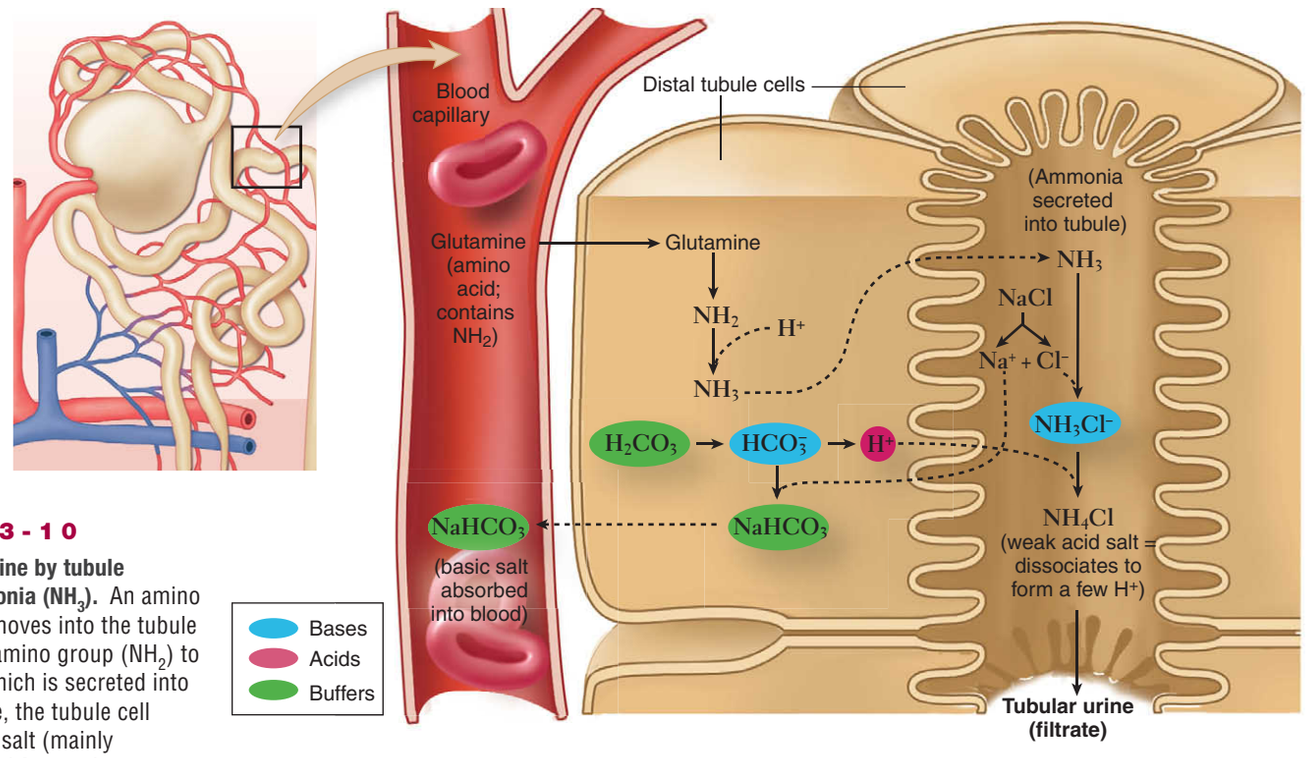


FIGURE 33-10

Acidification of urine by tubule excretion of ammonia (NH_3). An amino acid (glutamine) moves into the tubule cell and loses an amino group (NH_2) to form ammonia, which is secreted into urine. In exchange, the tubule cell reabsorbs a basic salt (mainly $NaHCO_3$) into blood from urine.

the basic salt to an acid salt or to a weak acid that is eliminated in the urine. While this is happening, the displaced sodium or other basic ion diffuses into a tubule cell. There it combines with the bicarbonate ion left over from the carbonic acid dissociation to form sodium bicarbonate. The sodium bicarbonate then diffuses—is reabsorbed—into the blood.

Consider the various results of this mechanism. Sodium bicarbonate (or other base bicarbonate) is conserved for the body. Instead of all the basic salts that filter out of glomerular blood leaving the body in the urine, considerable amounts are recovered into peritubular capillary blood. In addition, extra hydrogen ions are added to the urine and thereby eliminated from the body. Both the reabsorption of base bicarbonate into blood and the excretion of hydrogen ions into urine tend to increase the ratio of the bicarbonate buffer pair $B \cdot HCO_3/H \cdot HCO_3$ (BB/CA) present in blood. This automatically increases blood pH. In short, kidney tubule base bicarbonate reabsorption and hydrogen ion excretion both tend to alkalinize blood by acidifying urine.

In another urinary mechanism, the renal tubules can excrete hydrogen or potassium in exchange for the sodium they reabsorb. Therefore, in general, the more hydrogen ions they excrete, the fewer potassium ions they can excrete. In acidosis, tubule excretion of hydrogen ions increases markedly and potassium ion excretion decreases—an important factor because it may lead to **hyperkalemia** (excessive blood potassium), a condition that can cause heart block and death.

In yet another urinary mechanism, the distal tubule and collecting duct cells excrete ammonia into the tubular urine. As Figure 33-10 shows, the ammonia combines with hydrogen to form an ammonium ion. The ammonium ion displaces sodium or some other basic ion from a salt of a fixed (nonvolatile) acid to form an ammonium salt. The basic ion then diffuses back into a tubule cell and combines with a bicarbonate ion to form a basic salt, which in turn diffuses into tubular blood. Thus, like the renal tubules' excretion of hydrogen ions, their excretion of ammonia and its combining with hydrogen to form ammonium ions also tend to increase the blood bicarbonate buffer pair ratio and therefore tend to increase blood pH. Quantitatively, however, ammonium ion excretion is more important than hydrogen ion excretion.

Renal tubule excretion of hydrogen and ammonia is controlled at least in part by the blood pH level. As indicated in Figure 33-11, a decrease in blood pH accelerates tubule excretion of both hydrogen and ammonia. An increase in blood pH produces the opposite effects.

| QUICK CHECK |

9. What is the function of carbonic anhydrase in buffer action?
10. How does respiratory rate affect blood pH levels?
11. List two ways in which acidification of urine occurs.

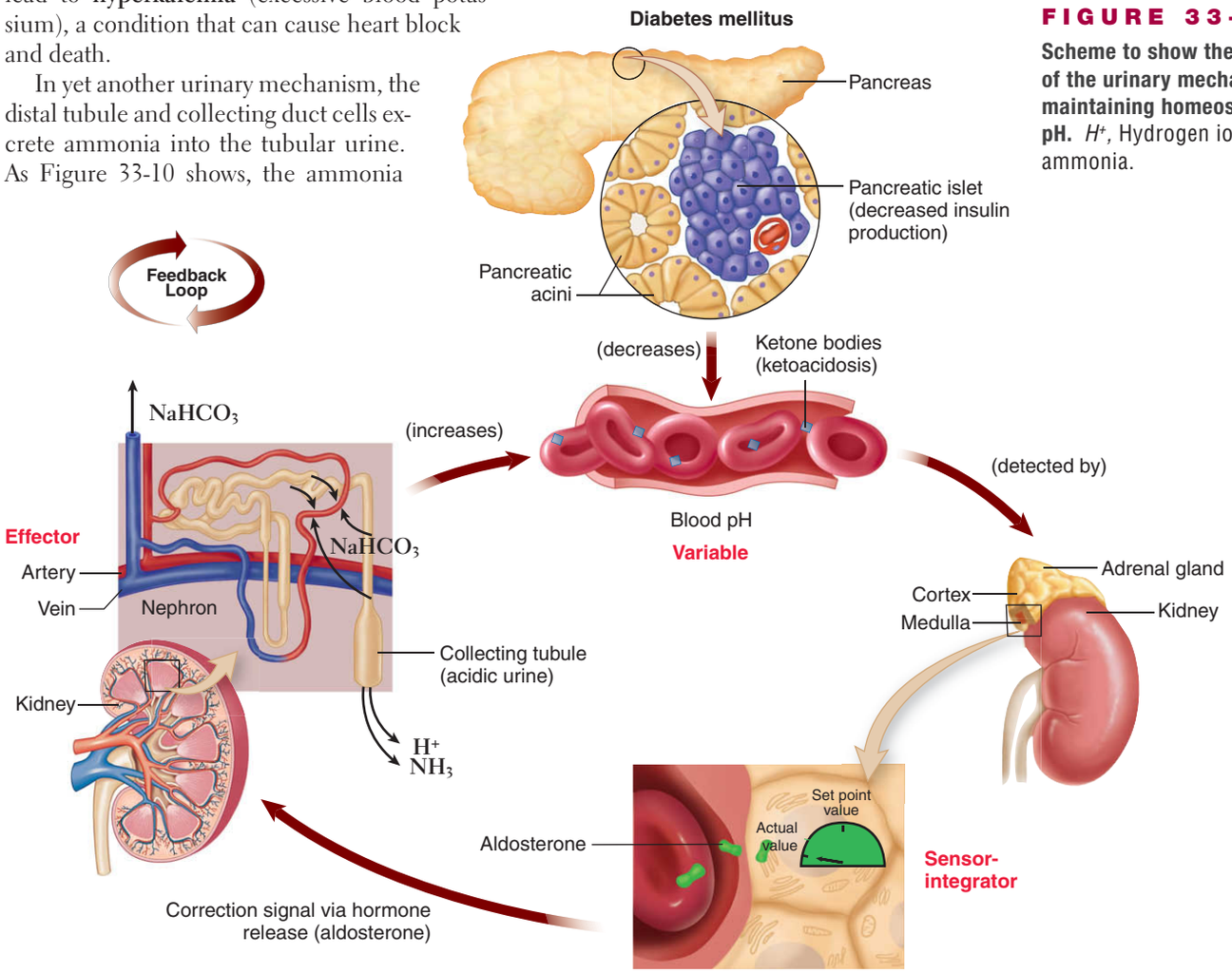


FIGURE 33-11

Scheme to show the main elements of the urinary mechanism for maintaining homeostasis of blood pH. H^+, Hydrogen ion; NH_3, ammonia.

the BIG picture

Acid-Base Balance

Ultimately, all functions occur at the cellular level and, without exception, each vital physiological function depends on the maintenance of an appropriate, stable, and tightly regulated acid-base environment. Regulating chemical reactions at the cellular level permits us to control the flow of energy in the body. We need to control energy flow to accomplish cellular work and to store and transfer energy so that we can meet our immediate and long-term needs. Enzymes are the biological catalysts that permit or assist our cells in the regulation of all energy-based metabolic reactions required for the maintenance of life. Enzymes involved in metabolic reactions have both optimal pH ranges for maximal activity and limited pH ranges in which activity is maintained. Therefore, anything that disrupts the homeostasis of acid-base balance by disrupting enzyme activity is immediately life threatening because it affects our ability to initiate and regulate the metabolic activity required to sustain life.

The elaborate and highly sensitive pH control mechanisms intended to provide homeostasis of our acid-base environment are critical for the enzymatic action necessary for healthy metabolism and for life itself.

MECHANISMS of DISEASE

ACID-BASE IMBALANCES

All of the buffer pairs in body fluids play an important role in acid-base balance. However, only in the bicarbonate system can the body regulate quickly and precisely the levels of both chemical components in the buffer pair. Carbonic acid levels can be regulated by the respiratory system and bicarbonate ion by the kidneys. Recall that a 20:1 ratio of base bicarbonate to carbonic acid (BB/CA) maintains acid-base balance and normal blood pH. Therefore, from a clinical standpoint, disturbances in acid-base balance depend on the relative quantities of carbonic acid and base bicarbonate in the extracellular fluid. Two types of disturbances, metabolic and respiratory, can alter the proper ratio of these components. Metabolic disturbances affect the bicarbonate element, and respiratory disturbances affect the carbonic acid element of the buffer pair.

Metabolic acidosis and *respiratory acidosis*, for example, are separate and very different types of acid-base imbalances. Both are treated by the intravenous infusion of solutions containing **sodium lactate.** The infused lactate ions are metabolized by liver cells and converted to bicarbonate ions. This therapy helps replace the depleted bicarbonate reserves required to restore acid-base balance in metabolic acidosis. In respiratory acidosis, the additional bicarbonate ions function to offset elevated carbonic acid levels.

Metabolic Disturbances

Metabolic Acidosis (Bicarbonate Deficit)

During the course of certain diseases such as untreated diabetes mellitus or during starvation, abnormally large amounts of acids enter the blood. The ratio of BB/CA is altered as the base bicarbonate component of the buffer pair reacts with the acids. The result may be a new ratio near 10:1. The decreasing ratio lowers the blood pH, and the respiratory center is stimulated (Figure 33-12). The resulting hyperventilation results in a "blow-off" of carbon dioxide, with a decrease in carbonic acid. This compensatory action of the respiratory system, coupled with excretion of H^+ and NH_3 in exchange for Na^+ reabsorbed by the kidneys, may be sufficient to adjust the ratio of BB/CA, and therefore blood pH, to normal. (The compensated BB/CA ratio may approach 10:0.5.) If, despite these compensating homeostatic processes, the ratio and pH cannot be corrected, uncompensated **metabolic acidosis** develops. Drug use (see Box 33-4) or metabolic conditions that increase lactic acid can also cause acidosis.

An increased blood hydrogen ion concentration, that is, decreased blood pH, as we have noted, stimulates the respiratory center. For this reason, hyperventilation is an outstanding clinical sign of acidosis. Increases in hydrogen ion concentration above a certain level depress the central nervous system and therefore produce such symptoms as disorientation and coma. In a terminal illness, death from acidosis is likely to follow coma, whereas death from alkalosis generally follows tetany and convulsions.

Metabolic Alkalosis (Bicarbonate Excess)

Patients suffering from chronic stomach problems such as hyperacidity sometimes ingest large quantities of alkali—often plain baking soda, or sodium bicarbonate—for extended periods. Such improper use of antacids or excessive vomiting (see Box 33-2) can produce **metabolic alkalosis**. Initially, the condition results in an increase in the BB/CA ratio to perhaps 40:1 (Figure 33-13).

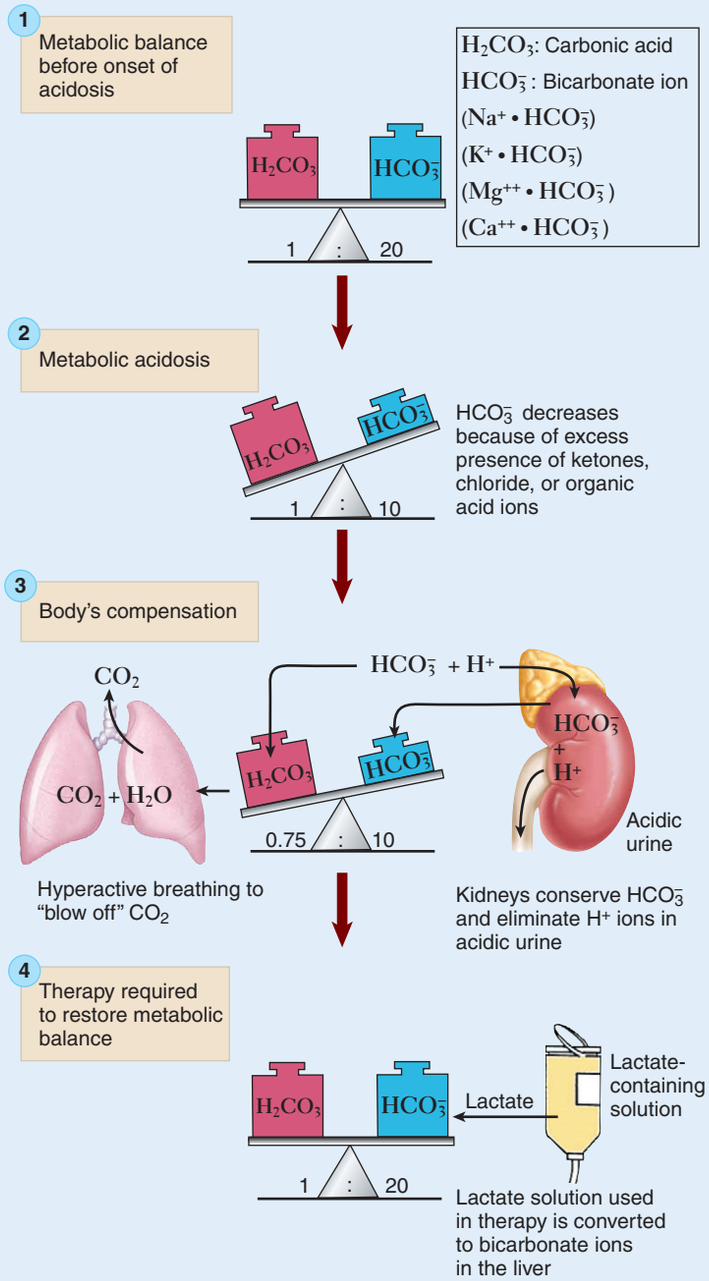


FIGURE 33-12
Metabolic acidosis.

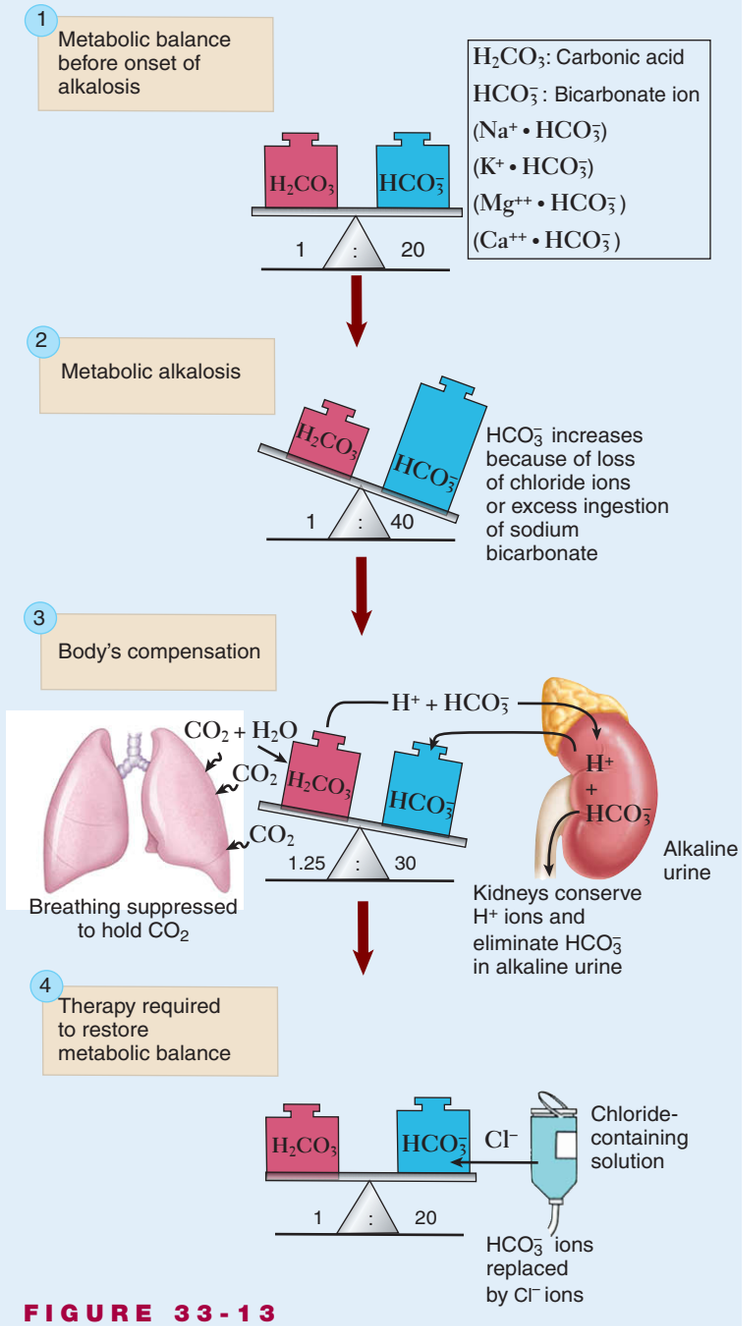


FIGURE 33-13
Metabolic alkalosis.

Compensatory mechanisms are aimed at increasing carbonic acid and decreasing the bicarbonate load. With breathing suppressed and the kidneys excreting bicarbonate ions, a compensated ratio of 30:1.25 might result. Such a ratio would restore acid-base balance and blood pH to normal. In uncompensated metabolic alkalosis the ratio, and therefore the pH, remain increased.

Respiratory Disturbances

Respiratory Acidosis (Carbonic Acid Excess)

Clinical conditions such as pneumonia or emphysema tend to cause retention of carbon dioxide in the blood. Also, drug abuse or overdose, such as barbiturate poisoning, suppresses breathing

and results in **respiratory acidosis** (Figure 33-14). The carbonic acid component of the bicarbonate buffer pair increases above normal in respiratory acidosis. Body compensation, if successful, increases the bicarbonate fraction so that a new BB/CA ratio (perhaps 23:0) will return blood pH to normal or near-normal levels.

Respiratory Alkalosis (Carbonic Acid Deficit)

Hyperventilation caused by fever or mental disease (hysteria) can result in excessive loss of carbonic acid and lead to **respiratory alkalosis** (Figure 33-15) with a bicarbonate buffer pair ratio of 20:0.5. Compensatory mechanisms may adjust the ratio to 10:0.5 and return blood pH to near normal.

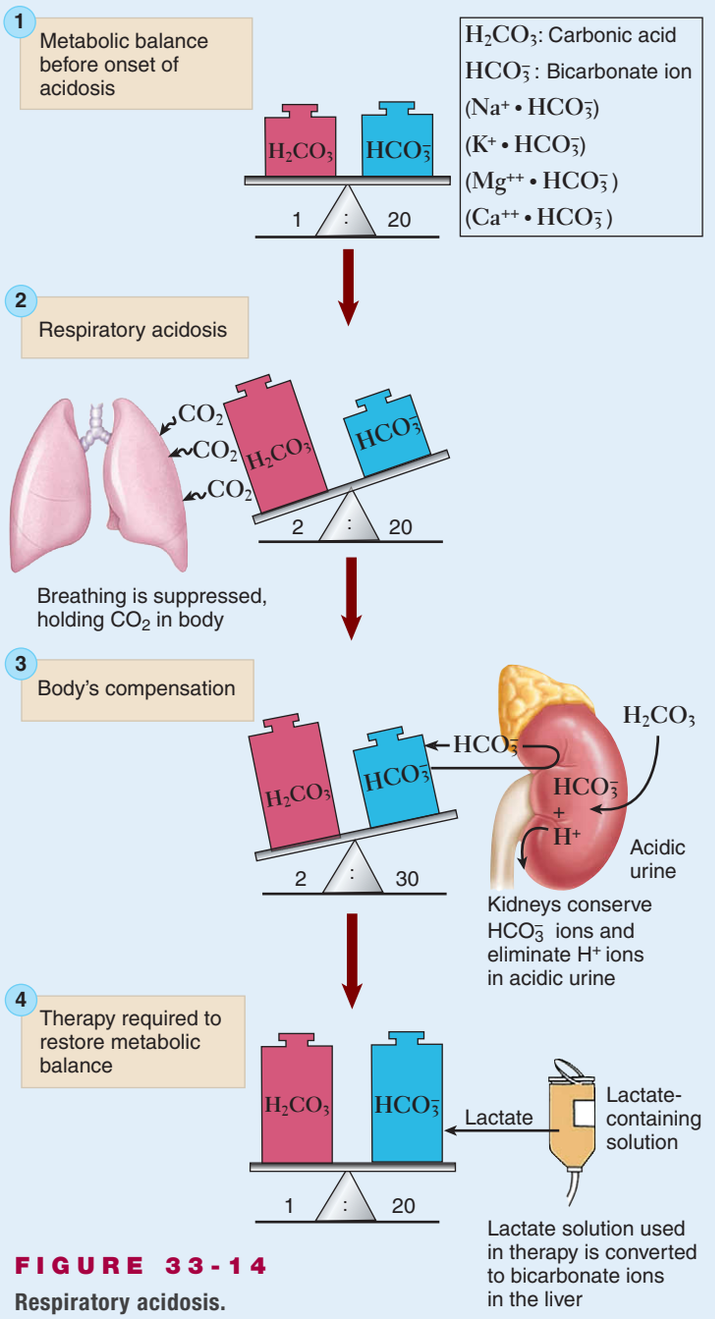


FIGURE 33-14
Respiratory acidosis.

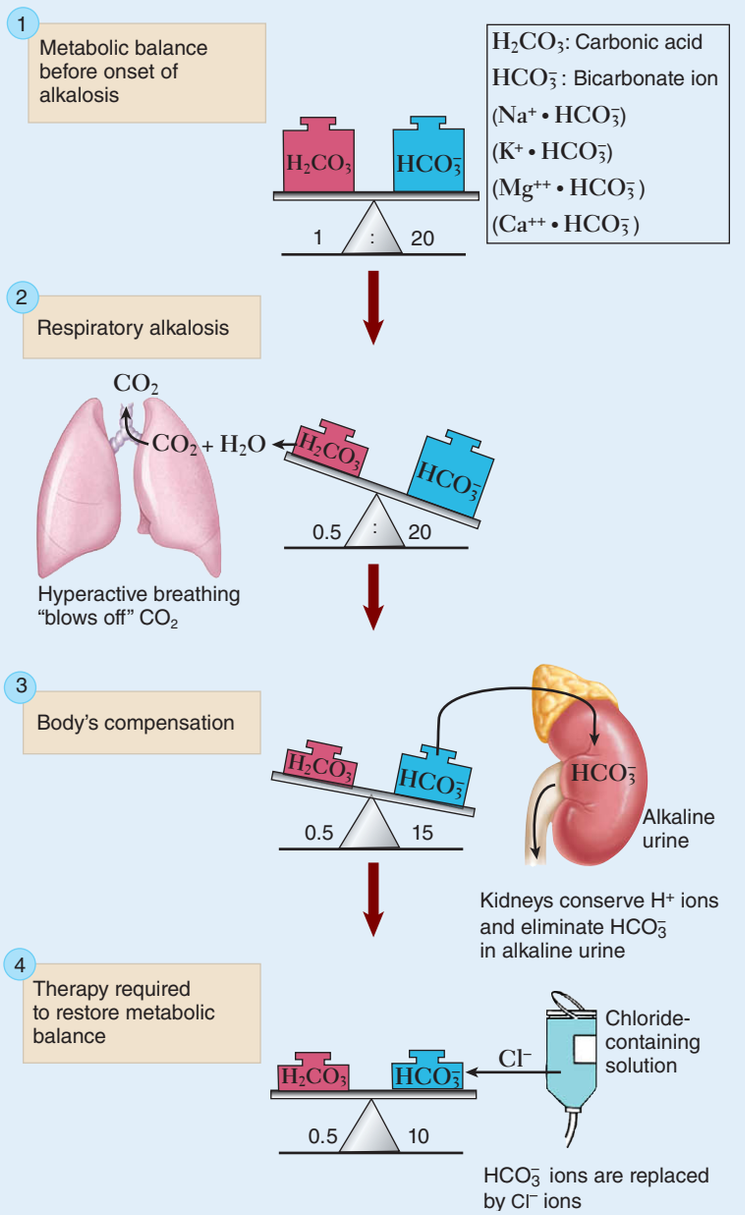


FIGURE 33-15
Respiratory alkalosis.

LANGUAGE OF SCIENCE *(continued from p. 1025)*

correction
normal saline
[*sal-* **salt**, *-ine* **relating to**]

pH
(pee-AYCH)
[**abbreviation for** *potenz* **power**, *hydrogen* **hydrogen**]

physiological buffer
(fiz-ee-o-LOJ-i-kal BUFF-er)
[*physio-* **nature (function)**, *-o-* **combining form**, *-log-* **words (study of)**, *-ical* **relating to**, *buffe-* **cushion**, *-er* **agent**]

ratio
(RAY-shee-oh)
[*ratio* **a reckoning**]

uncompensated acidosis
(un-KOM-pen-say-ted ass-ih-DOH-sis)
[*acid-* **sour**, *-osis* **condition**]

uncompensated alkalosis
(un-KOM-pen-say-ted al-kah-LOH-sis)
[*alkal-* **ashes**, *-osis* **condition**]

LANGUAGE OF MEDICINE

bicarbonate loading
(bye-KAR-boh-net)
[*bi-* **two**, *-carbon-* **coal (carbon)**, *-ate* **oxygen**]

emesis
(EM-eh-sis)
[*emesis* **to vomit**]

hyperkalemia
(hye-per-kah-LEE-mee-ah)
[*hyper-* **excessive**, *-kal-* **potassium**, *-emia* **blood condition**]

lactic acidosis
(LAK-tik ass-ih-DOH-sis)
[*lac-* **milk**, *-ic* **relating to**, *acid-* **sour**, *-osis* **condition**]

metabolic acidosis
(met-ah-BOL-ik ass-ih-DOH-sis)
[*metabol-* **change**, *-ic* **relating to**, *acid-* **sour**, *-osis* **condition**]

metabolic alkalosis
(met-ah-BOL-ik al-kah-LOH-sis)
[*metabol-* **change**, *-ic* **relating to**, *alkal-* **ashes**, *-osis* **condition**]

pernicious vomiting
(per-NISH-us)
[*pernici-* **destruction**, *-ous* **relating to**]

respiratory acidosis
(RES-pih-rah-tor-ee ass-ih-DOH-sis)
[*re-* **again**, *-spir-* **breathe**, *-tory* **relating to**, *acid-* **sour**, *-osis* **condition**]

respiratory alkalosis
(RES-pih-rah-tor-ee al-kah-LOH-sis)
[*re-* **again**, *-spir-* **breathe**, *-tory* **relating to**, *alkal-* **ashes**; *-osis* **condition**]

sodium lactate
(SO-dee-um LAK-tayt)
[*sod-* **soda**, *-um* **thing or substance**, *lact-* **milk**, *-ate* **chemical**]

CASE study

"Come on—take a deep breath for me." Coming out of the anesthetic, Dorie heard the nurse talking, trying to get her to take some deep breaths. But she just couldn't. The pain was so much more than she had expected. Having had a hip replacement in the past, Dorie knew her hip would hurt after the surgery, but why did everything else ache so much? It hurt to take even a shallow breath. She continued breathing in short, shallow gasps; she was hypoventilating.

1. As Dorie continued her breathing pattern, her body began developing what condition as a result?
   a. Respiratory acidosis
   b. Metabolic acidosis
   c. Respiratory alkalosis
   d. Metabolic alkalosis
2. If this situation continues, which body system will make adjustments to bring her pH back towards normal?
   a. Respiratory
   b. Digestive
   c. Urinary
   d. Cardiovascular
3. Which is the most likely chemical trade-off to occur because of Dorie's breathing abnormality?
   a. Secretion of hydrogen ions and absorption of sodium ions
   b. Excretion of hydrogen ions and reabsorption of sodium ions
   c. Absorption of hydrogen ions and excretion of chloride ions
   d. Excretion of bicarbonate and reabsorption of hydrogen ions
4. What is the normal pH range for Dorie's blood?
   a. 7.0-10.0
   b. 6.0-7.0
   c. 7.1-7.5
   d. 7.35-7.45

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook, **A&P Connect**, and other resources.*

CAREER choices



Craig Huard, MSN, CRNA

Certified Registered Nurse Anesthetist

I practice anesthesiology as a Certified Registered Nurse Anesthetist (CRNA) at Beaumont Hospital in Royal Oak, Michigan. I also have an independent practice in office-based settings for ear, nose, and throat doctors and plastic surgeons. Having researched what a CRNA's job entails, I felt drawn to the career because of the level of independence possible and the wide variety of patients and surgical cases I would encounter.

A trend of major importance in my field is the decentralization of surgical care of low-acuity patients to outpatient/same-day surgical centers. Estimates put the total number of surgical cases performed on an outpatient basis in the United States at 60% to 64%. CRNAs, by virtue of their training and education, are able to serve this population well. An understanding of new medications and their pharmacodynamics and pharmacokinetics is just one part of the requisite body of knowledge that CRNAs use to ensure safe, effective anesthesia care for all of their patients.

The most rewarding aspect of my career is the knowledge that I make a real difference in patients' lives. Often a person facing surgery isn't doing so by choice; there is a very high level of stress there. Earning that person's trust in a very short amount of time, seeing him or her safely through the anesthesia and surgery, and speaking to the person afterward brings a sense of completion to my day.

A thorough understanding of A&P is essential to knowing how and where medications work. It is also essential in knowing where to administer (e.g., intradermally or intravenously) the medications to achieve the desired results. I recall studying A&P long into the night, at times wondering if the systems' interplay would ever make sense to me. At the same time, I recall marveling at how it did make sense when the "light" finally came on. I used mnemonics frequently to learn associations, orders, processes, and structures during my study. This is still a useful technique for me.

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

INTRODUCTION

A. Acid-base balance is one of the most important of the body's homeostatic mechanisms
B. Acid-base balance refers to regulation of hydrogen ion concentration in body fluids
C. Precise regulation of pH at the cellular level is necessary for survival
D. Slight pH changes have dramatic effects on cellular metabolism

MECHANISMS THAT CONTROL pH OF BODY FLUIDS

A. Review of pH concept—negative logarithm of hydrogen ion concentration of a solution (Figure 33-1)
   1. pH indicates degree of acidity or alkalinity of a solution
   2. Acidosis describes arterial blood pH of less than 7.35
   3. Alkalosis describes arterial blood pH greater than 7.45
B. Sources of pH-influencing chemicals
   1. Carbonic acid—formed by aerobic glucose metabolism
   2. Lactic acid—formed by anaerobic glucose metabolism
   3. Sulfuric acid—formed by oxidation of sulfur-containing amino acids
   4. Phosphoric acid—formed in the breakdown of phosphoproteins and ribonucleotides
   5. Acidic ketone bodies—formed in the breakdown of fats
      a. Acetone
      b. Acetoacetic acid
      c. Beta-hydroxybutyric acid
   6. Acid-forming potential of foods—determined by chloride, sulfur, and phosphorus content
C. Types of pH control mechanisms
   1. Chemical—rapid-action buffers
      a. Bicarbonate buffer system
      b. Phosphate buffer system
      c. Protein buffer system
   2. Physiological—delayed-action buffers
      a. Respiratory response
      b. Renal response
   3. Summary of pH control mechanisms
      a. Buffers
      b. Respiration
      c. Kidney excretion of acids and bases
D. Effectiveness of pH control mechanisms—range of pH—extremely effective, normally maintain pH within a very narrow range of 7.36 to 7.40

BUFFER MECHANISMS FOR CONTROLLING pH OF BODY FLUIDS

A. Buffers defined
   1. Substances that prevent a marked change in pH of a solution when an acid or base is added to it
   2. Consist of a weak acid (or its acid salt) and a basic salt of that acid

B. Buffer pairs present in body fluids—mainly carbonic acid, proteins, hemoglobin, acid phosphate, and sodium and potassium salts of these weak acids

C. Buffer actions that prevent marked changes in pH of body fluids
   1. The chloride shift makes it possible for carbonic acid to be buffered in the red blood cell and then carried as bicarbonate in the plasma (Figure 33-6)
   2. Nonvolatile acids, such as hydrochloric acid, lactic acid, and ketone bodies, buffered mainly by sodium bicarbonate
   3. Volatile acids, chiefly carbonic acid, buffered mainly by potassium salts of hemoglobin and oxyhemoglobin (Figure 33-5)
   4. Bases buffered mainly by carbonic acid (when homeostasis of pH at 7.4 exists)

$$\text{Ratio} \quad \frac{B \bullet HCO_3}{H_2CO_3} = \frac{20}{1}$$

   5. Base-to-acid ratio of 20:1 is critical
      a. Compensation—process of adjustment of pH balance to maintain ratio, such as 40:2 or 10:0.5
      b. Uncompensated alkalosis or acidosis—occurs when base-to-acid ratio is abnormal (unbalanced at a proper ratio)
      c. Correction—occurs when components of buffer pair return to normal 20:1 ratio

D. Evaluation of the role of buffers in pH control—cannot maintain normal pH without adequate functioning of the respiratory and urinary pH control mechanisms

RESPIRATORY MECHANISMS OF pH CONTROL

A. Explanation of respiratory mechanisms
   1. Amount of blood carbon dioxide directly relates to the amount of carbonic acid and therefore to the concentration of H^+
   2. With increased respirations, less carbon dioxide remains in blood, hence less carbonic acid and fewer H^+ ions; with decreased respirations, more carbon dioxide remains in blood, hence more carbonic acid and more H^+ ions

B. Respiratory adjustment to counter pH imbalance of arterial blood
   1. If CO_2 in arterial blood increases or decreases beyond set level, respiratory center is stimulated and respiration increases in rate and/or depth
   2. Carotid chemoreflexes also cause respiration adjustments

C. Principles that relate respirations to pH value
   1. Acidosis triggers hyperventilation, which increases rate of CO_2/H_2CO_3 loss from the body and thus reduces blood H^+ and restores homeostasis
   2. Prolonged hyperventilation, by decreasing blood H^+ excessively, may produce alkalosis
   3. Alkalosis triggers hypoventilation, which tends to correct alkalosis by increasing blood CO_2 and therefore blood H_2CO_3 and H^+
   4. Prolonged hypoventilation, by eliminating too little CO_2, causes an increase in blood H_2CO_3 and consequently in blood H^+, thereby producing acidosis

URINARY MECHANISMS THAT CONTROL pH

A. General principles concerning urinary mechanisms—plays vital role in acid-base balance because kidneys can eliminate more H^+ from the body while reabsorbing more base when pH tends toward the acid side and eliminates fewer H^+ while reabsorbing less base when pH tends toward the alkaline side

B. Mechanisms that control urine pH
   1. Secretion of H^+ into urine—when blood CO_2, H_2CO_3, and H^+ increase above normal, distal tubules secrete more H^+ into urine to displace basic ion (mainly sodium) from a urine salt and then reabsorb sodium into blood in exchange for the H^+ excreted
   2. Secretion of NH_3—when blood hydrogen ion concentration increases, distal tubules secrete more NH_3, which combines with the H^+ of urine to form ammonium ion, which displaces a basic ion (mainly sodium) from a salt; the basic ion is then reabsorbed back into blood in exchange for the ammonium ion excreted

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. How are carbonic acid and lactic acid produced?
2. Are fruits and vegetables acid-forming or base-forming foods?
3. Identify several acid-forming elements.
4. What is a physiological buffer?
5. What is the normal range of blood pH?
6. Describe the buffering action of sodium bicarbonate.
7. Identify the main buffer pairs in body fluids.
8. How is the distal renal tubule involved in the acidification of urine and the conservation of base?
9. How can sodium lactate be useful in the treatment of both metabolic acidosis and respiratory acidosis?
10. Discuss hyperventilation in relation to the development of an acid-base imbalance.

CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. How would you explain pH in terms of the ions involved? What would be the hydrogen ion concentration of a solution with a pH of 4? With a pH of 6?
2. Define and summarize the purpose of the chloride shift.
3. What do you predict might happen to the pH if a drug is administered that lowers the $NaHCO_3$ concentration to 23.8 mEq but maintains the H_2CO_3 concentration at 1.3 mEq?
4. Explain the role of the respiratory system in maintaining proper blood pH.
5. How would you describe the causes and a possible treatment of the acid-base imbalance that occurs with prolonged vomiting?

Unit Six

Reproduction and Development

The chapters of Unit Six deal with human reproduction, growth, development, genetics, and heredity. The anatomical structures and complex control mechanisms characteristic of the male and the female reproductive systems are intended to ensure survival of our genes. These systems in men and women are adapted structurally and functionally for the specific sequence of events that permit development of sperm or ova, followed by fertilization, normal development, and birth of a baby. Chapter 36 details the developmental changes that occur from fertilization to death. Chapter 37 discusses the scientific study of genetics and heredity along with medical applications.

SEEING THE BIG PICTURE



34 **Male Reproductive System, 1044**



35 **Female Reproductive System, 1063**

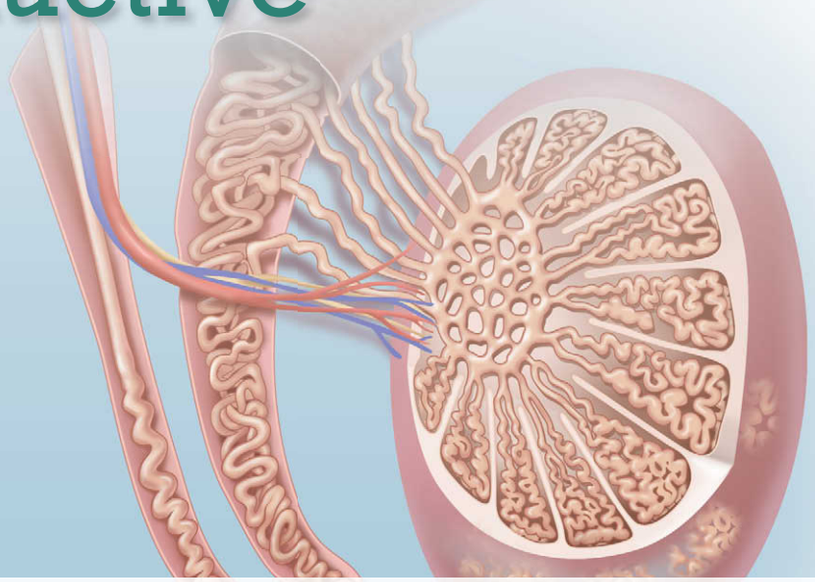


36 **Growth and Development, 1096**



37 **Genetics and Heredity, 1131**

34 Male Reproductive System



LANGUAGE OF SCIENCE

HINT *Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.*

androgen
(AN-droh-jen)
[*andro-* **male,** *-gen* **produce**]

androgen-binding protein (ABP)
(AN-droh-jen-BYND-ing)
[*andro-* **male,** *-gen* **produce,** *prote-* **first rank,** *-in* **substance**]

blood-testis barrier (BTB)
(blud TES-teez)

bulbourethral gland
(BUL-boh-yoo-REE-thral)
[*bulb-* **swollen root,** *-ure-* **urine,** *-thr-* **agent or channel (urethra),** *-al* **relating to**]

capacitation
(kah-pas-i-TAY-shun)

corpus cavernosum
(KOHR-pus kav-er-NO-sum)
[*corpus* **body,** *cavern-* **large hollow,** *-os-* **relating to,** *-um* **thing**] *pl.,* corpora cavernosa

corpus spongiosum
(KOHR-pus spun-jee-OH-sum)
[*corpus* **body,** *spong-* **sponge,** *-os-* **relating to,** *-um* **thing**] *pl.,* corpora spongiosa

ejaculation
(ee-jak-yoo-LAY-shun)
[*e-* **out or away,** *-jacula-* **throw,** *-ation* **process**]

emission
(ee-MISH-un)
[*e-* **out or away,** *-mis-* **send,** *-sion* **process**]

epididymis
(ep-i-DID-i-mis)
[*epi-* **upon,** *-didymis* **pair**]
pl., epididymes

erection
(ee-REK-shun)

continued on p. 1058

CHAPTER OUTLINE

HINT *Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.*

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The importance of reproductive system function is notably different from that of any other organ system of the body. Ordinarily, systems function to maintain the relative stability and survival of the individual organism. The reproductive system, on the other hand, ensures survival not of the individual but of the genes that characterize the human species. In both sexes, organs of the reproductive system are adapted for the specific sequence of functions that are concerned primarily with transferring genes to a new generation of offspring. A male reproductive system in one parent and a female reproductive system in another parent are needed to reproduce. This chapter begins with a brief description of the male reproductive system. Chapter 35 then follows with the story of the female reproductive system.

SEXUAL REPRODUCTION

Sexual reproduction requires two parent organisms, a male and female, each of which contributes half of the nuclear chromosomes needed to form the first cell of an offspring organism. *Asexual reproduction*, on the other hand, requires only one parent who produces an offspring genetically identical to itself. An advantage of sexual reproduction is that a new mixture of genes in each offspring increases the variety of genetic characteristics in the population. This variety of characteristics makes it more likely that in the case of infectious disease or environmental changes such as natural disaster or shifting climatic conditions, there will be at least some individuals likely to survive and carry on the reproductive line.

Besides producing the cells needed to form the offspring, each reproductive system produces hormones that regulate development of the secondary sex characteristics that promote successful reproduction. For example, hormones create structural and behavioral differences in the sexes that permit adults to recognize and form sexual attractions with the opposite sex. Reproductive hormones and other regulatory mechanisms give us the urge to have sex, which is often reinforced with the pleasant sensations that sexual activity can produce. This sex drive is essential to success in producing offspring.

Sexual maturity and the ability to reproduce occur at puberty. The male reproductive system consists of organs whose functions are to produce, transfer, and ultimately introduce mature sperm into the female reproductive tract, where the nuclear chromosomes from each parent can unite to form a new offspring.

MALE REPRODUCTIVE ORGANS

Organs of the reproductive system (Figure 34-1) may be classified as *essential organs* for the production of **gametes** (sex cells) or as *accessory organs* that play some type of supportive role in the reproductive process.

In both sexes the essential organs of reproduction that produce the gametes, or sex cells (sperm or ova), are called **gonads.** In Chapter 36, we will explore the development of male and female reproductive organs more thoroughly. The gonads of the male are the **testes.**

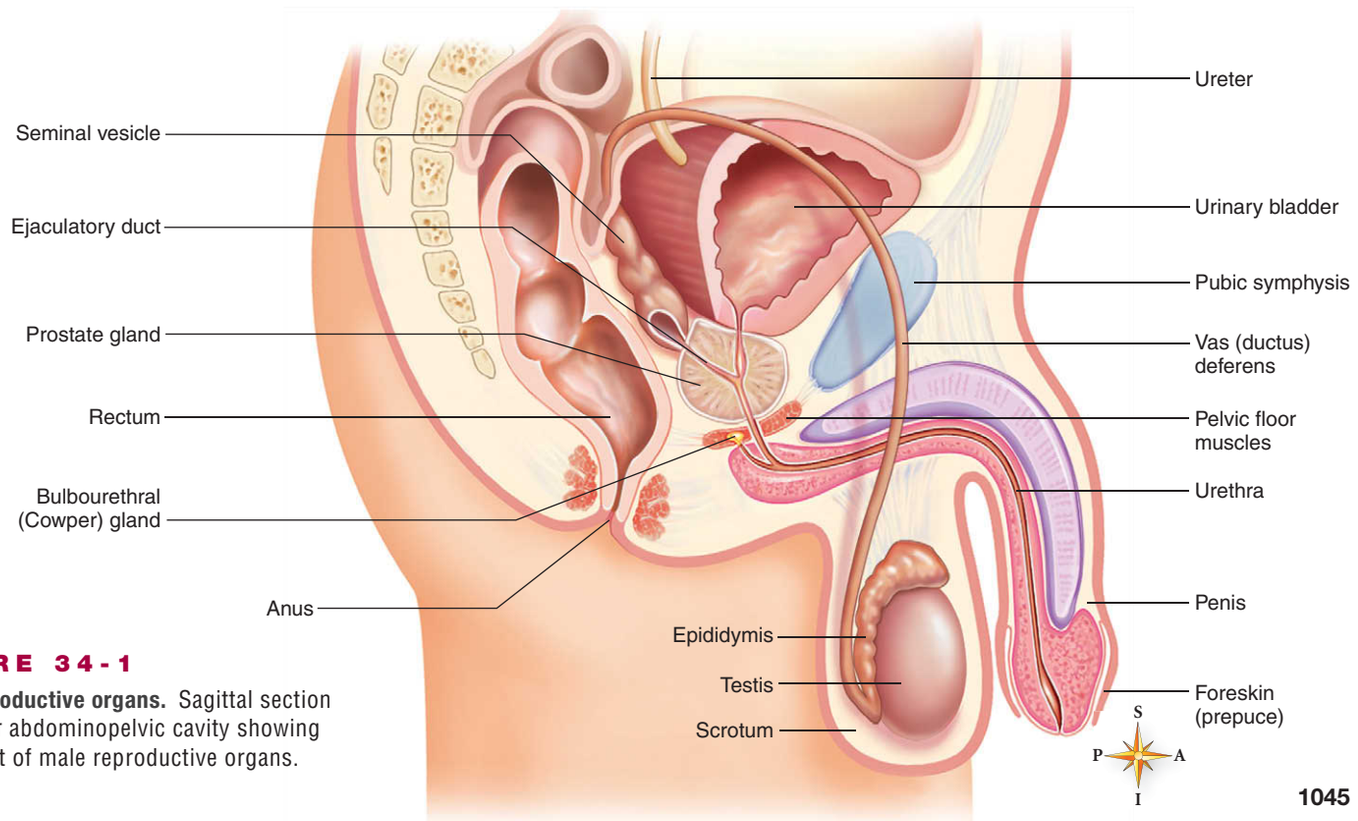


FIGURE 34-1

Male reproductive organs. Sagittal section of inferior abdominopelvic cavity showing placement of male reproductive organs.

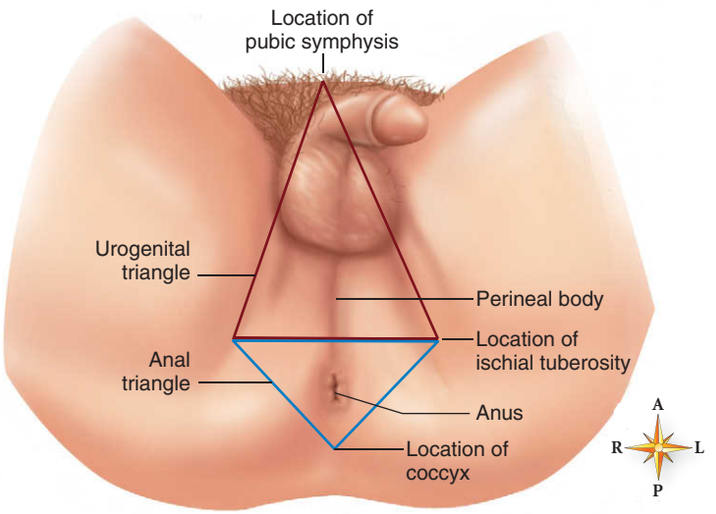


FIGURE 34-2

Male perineum. Sketch showing outline of the urogenital triangle *(red)* and anal triangle *(blue)*.

The accessory organs of reproduction in the male include genital ducts, glands, and supporting structures.

Reproductive ducts convey sperm to the outside of the body. They are also called *genital ducts*. The ducts are a pair of *epididymides* (*singular*, epididymis), the paired *vasa deferentia* (*singular*, vas deferens), a pair of *ejaculatory ducts*, and the *urethra*. *Accessory glands* in the reproductive system produce secretions that serve to nourish, transport, and mature sperm. The glands are a pair of *seminal vesicles*, one *prostate*, and a pair of *bulbourethral glands*.

Supporting structures include the *scrotum*, the *penis*, and a pair of *spermatic cords*.

Perineum

The **perineum** in the male is an area between the thighs shaped roughly like a diamond (Figure 34-2). It extends from the pubic symphysis anteriorly to the coccyx posteriorly. Its most lateral boundary on either side is the ischial tuberosity. A line drawn between the two ischial tuberosities divides the area into a larger *urogenital triangle*, which contains the external genitals (penis and scrotum), and the *anal triangle*, which surrounds the anus.

| QUICK CHECK |

1. How is the normal function of the reproductive system different from the end result of "normal function" in other organ systems?
2. Identify the essential and accessory organs of reproduction.
3. Describe the location, shape, and subdivisions of the perineum.

TESTES

Structure and Location

The **testes** are small, ovoid glands that are somewhat flattened from side to side, measure about 4 or 5 cm in length, and weigh 10 to 15 grams each. They are both located in a supporting sac called the *scrotum*. The left testis is generally located about 1 cm lower in the scrotal sac than the right. Both testes are

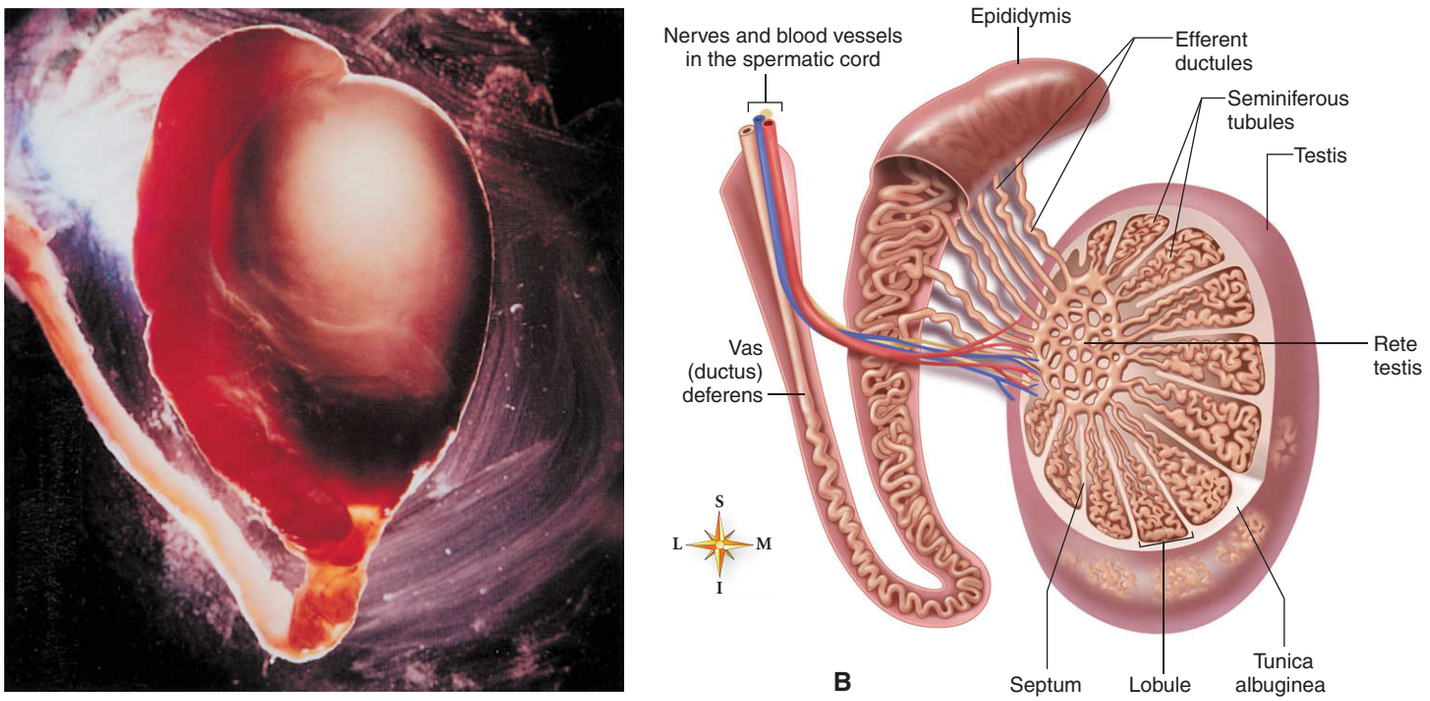


FIGURE 34-3

Tubules of the testis and epididymis. A, Transilluminated photograph; the testis is the darker sphere in the center. **B,** Illustration showing epididymis lifted free of testis. The ducts and tubules are exaggerated in size.

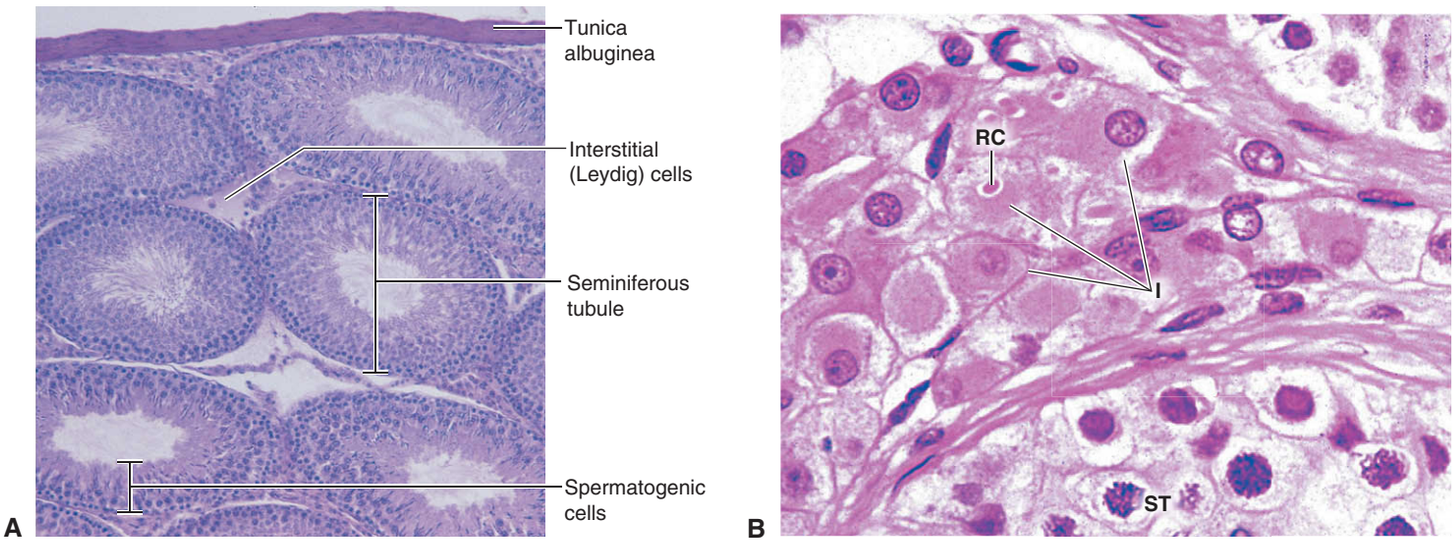


FIGURE 34-4

Testis. A, Low-power view micrograph showing several seminiferous tubules surrounded by septa containing interstitial (Leydig) cells. **B,** High-power micrograph showing a cluster of interstitial cells (I) between seminiferous tubules (ST). Spermatogenic cells can be identified in the wall of a seminiferous tubule. Note the presence of a Reinke crystalloid (RC) in an interstitial cell.

suspended in the pouch by attachment to scrotal tissue and by the spermatic cords (Figure 34-3). Note in Figure 34-3, *B*, that testicular blood vessels reach the testes by passing through the spermatic cord.

A dense, white, fibrous capsule called the **tunica albuginea** encases each testis and then enters the gland, sending out partitions (septa) that radiate through its interior, dividing it into 200 or more cone-shaped *lobules*.

Each lobule of the testis contains scattered *interstitial cells* and one to three tiny, coiled **seminiferous tubules,** which, if unraveled, would measure about 75 cm (more than 2 feet) in length. The tubules from each lobule come together to form a plexus called the *rete testis*. A series of sperm ducts called *efferent ductules* then drain the rete testis and pierce the tunica albuginea to enter the head of the epididymis (see Figure 34-3).

Microscopic Anatomy of the Testis

Figure 34-4, *A* is a low-power (×70) micrograph of testicular tissue showing a number of cut seminiferous tubules and numerous **interstitial cells,** or *Leydig cells*, in the surrounding connective tissue septa. In this figure, maturing sperm appear as dense nuclei with their tails projecting into the lumen of the tubule. The wall of each seminiferous tubule may contain five or more layers of cells. At puberty, when sexual maturity begins, spermatogenic cells in diverse stages of development appear, and the hormone-producing interstitial cells become more prominent in the surrounding septa. Figure 34-4, *B*, is a high-power micrograph showing a group of typically round interstitial cells clustered between seminiferous tubules. A unique cellular feature often visible in interstitial cells is an elongated rectangular-shaped mass called a *crystalloid*. Also called *Reinke crystalloids*, these masses are absent before puberty and then increase in number during the reproductive years into old age. The functional significance of these structures remains uncertain.

Irregular elongated **sustentacular cells** have a supportive and regulatory function important for the developing germ cells. Sustentacular cells of the testis are also called *nurse cells* or *Sertoli cells*. These cells provide mechanical support and protection for spermatids attached to their luminal surface and are visible in Figure 34-5 within a section of seminiferous epithelium.

Sustentacular cells also secrete the hormone *inhibin*, which inhibits gonadotropin-releasing hormone (GnRH) in the hypothalamus and follicle-stimulating hormone (FSH) production in the anterior pituitary. A drop in FSH lowers the rate of sperm production. This sets up a negative feedback mechanism in which the supportive sustentacular cells can slow down sperm production to manageable levels if needed.

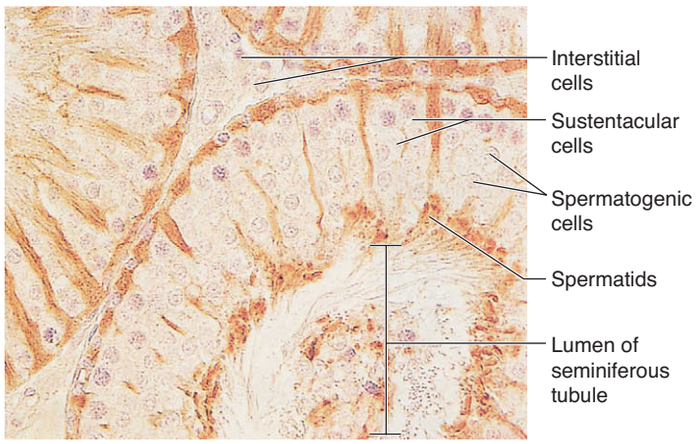


FIGURE 34-5

Sustentacular cells within seminiferous epithelium. Sustentacular cells are columnar in shape, extending from basement membrane to lumen of the tubule. Spermatids can be seen attached to the luminal surface of the sustentacular cells. Sustentacular cells are also called *nurse cells* or *Sertoli cells.*

At sexual maturity, sustentacular cells begin to secrete **androgen-binding protein,** or **ABP,** that binds to testosterone, a steroid lipid hormone, to make it more water soluble. This increases the testosterone concentration within the seminiferous tubules. High concentrations of testosterone are required for normal germ cell maturation. Thus sustentacular cells play an important role in spermatogenesis (sperm production).

Sustentacular cells are columnar in shape and extend from the basement membrane to the luminal surface of the seminiferous tubule (Figures 34-5 and 34-6). *Tight junctions* exist between adjacent sustentacular cells and divide the wall of the tubule into two compartments that house either meiotically active cells near the luminal surface or spermatogonia near the basement membrane.

Tight junctions between sustentacular cells form the **blood-testis barrier (BTB).** This structure isolates the developing sperm cells, which have active surface antigens different from somatic body cells, from the body immune system. If these antigens were to escape from the tubule epithelium and enter the bloodstream by breaking through the basement membrane, an autoimmune reaction could occur.

Testes Functions

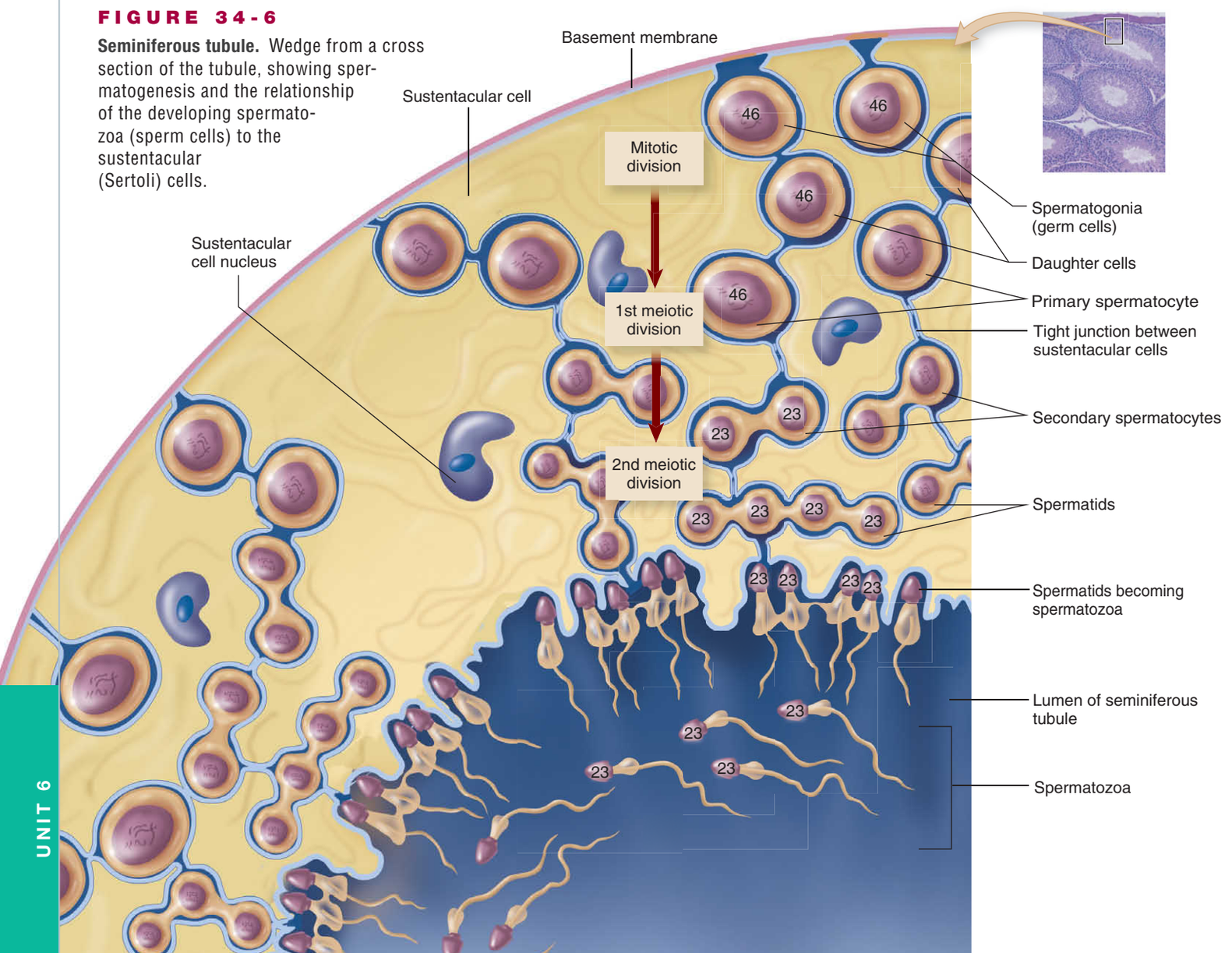
The testes perform two primary functions: spermatogenesis and secretion of hormones.

Spermatogenesis is the production of spermatozoa (sperm), the male gametes, or reproductive cells. The seminiferous tubules produce the sperm. Figure 34-6 shows a cross section of a seminiferous tubule in which two meiotic divisions result in a reduction of chromosomes from 46 in the spermatogonia to 23 in the spermatids and mature sperm. Details of spermatogenesis are discussed in Chapter 36.

Testosterone is the major **androgen** (masculinizing hormone) produced in humans. Testosterone is a steroid hormone produced by interstitial cells. Another hormone, inhibin, is produced by sustentacular cells of the testis.

FIGURE 34-6

Seminiferous tubule. Wedge from a cross section of the tubule, showing spermatogenesis and the relationship of the developing spermatozoa (sperm cells) to the sustentacular (Sertoli) cells.



Testosterone has several functions. One important group of functions is that it promotes "maleness," or development and maintenance of male secondary sex characteristics, accessory organs such as the prostate, seminal vesicles, and adult male sexual behavior.

Testosterone also helps regulate metabolism. It is usually classified as an anabolic hormone because it stimulates the protein anabolism. By stimulating protein anabolism, testosterone promotes growth of skeletal muscles (responsible for greater male muscular development and strength). This effect has tempted some athletes to take various synthetic versions of testosterone or testosterone promoters to enhance muscular strength. Testosterone also stimulates bone growth and promotes closure of the epiphyses (see Chapter 8, p. 202). Early sexual maturation leads to early epiphyseal closure. The converse also holds true: late sexual maturation, delayed epiphyseal closure, and tallness tend to go together.

Testosterone also plays a part in fluid and electrolyte balance. Testosterone has a mild stimulating effect on kidney tubule reabsorption of sodium and water; it also promotes kidney tubule excretion of potassium.

The anterior pituitary gland controls the testes by means of its gonadotropic hormones—specifically, FSH and luteinizing hormone (LH). FSH stimulates the seminiferous tubules to produce sperm more rapidly. In the male, LH stimulates interstitial cells to increase their secretion of testosterone.

If the blood concentration of testosterone reaches a high level, it will inhibit hypothalamic secretion of gonadotropin-releasing hormone (GnRH). As a result, anterior pituitary secretion of LH will decrease and testosterone levels will return to the normal set point value (Figure 34-7). Increasing blood levels of *inhibin* will selectively decrease GnRH secretion by the hypothalamus and FSH secretion by the anterior pituitary—thus decreasing the rate of sperm production. However, if sperm counts decrease below the normal set point, inhibin secretion will drop, FSH secretion will increase, and sperm numbers will increase to normal levels. Thus a negative feedback mechanism operates between the hypothalamus, the anterior pituitary gland, and the hormone-producing cells of the testes—interstitial cells producing testosterone and sustentacular cells producing inhibin. The end result is homeostatic control of the full range of effects influenced by testosterone levels—including a direct influence on sperm numbers.

Small but measurable amounts of *estrogen* are present in healthy adult males. More research is needed to explore its role in normal male physiology. Some of the estrogen, a steroid hormone derived from testosterone, is made in interstitial cells (see Figure 18-5 on p. 549). However, most of the estrogen in males is probably made in the liver and other tissues. Possible roles for estrogen in men includes regulation of spermatogenesis, feedback inhibition of FSH and LH, and promoting normal male sexual behavior and partner preference.

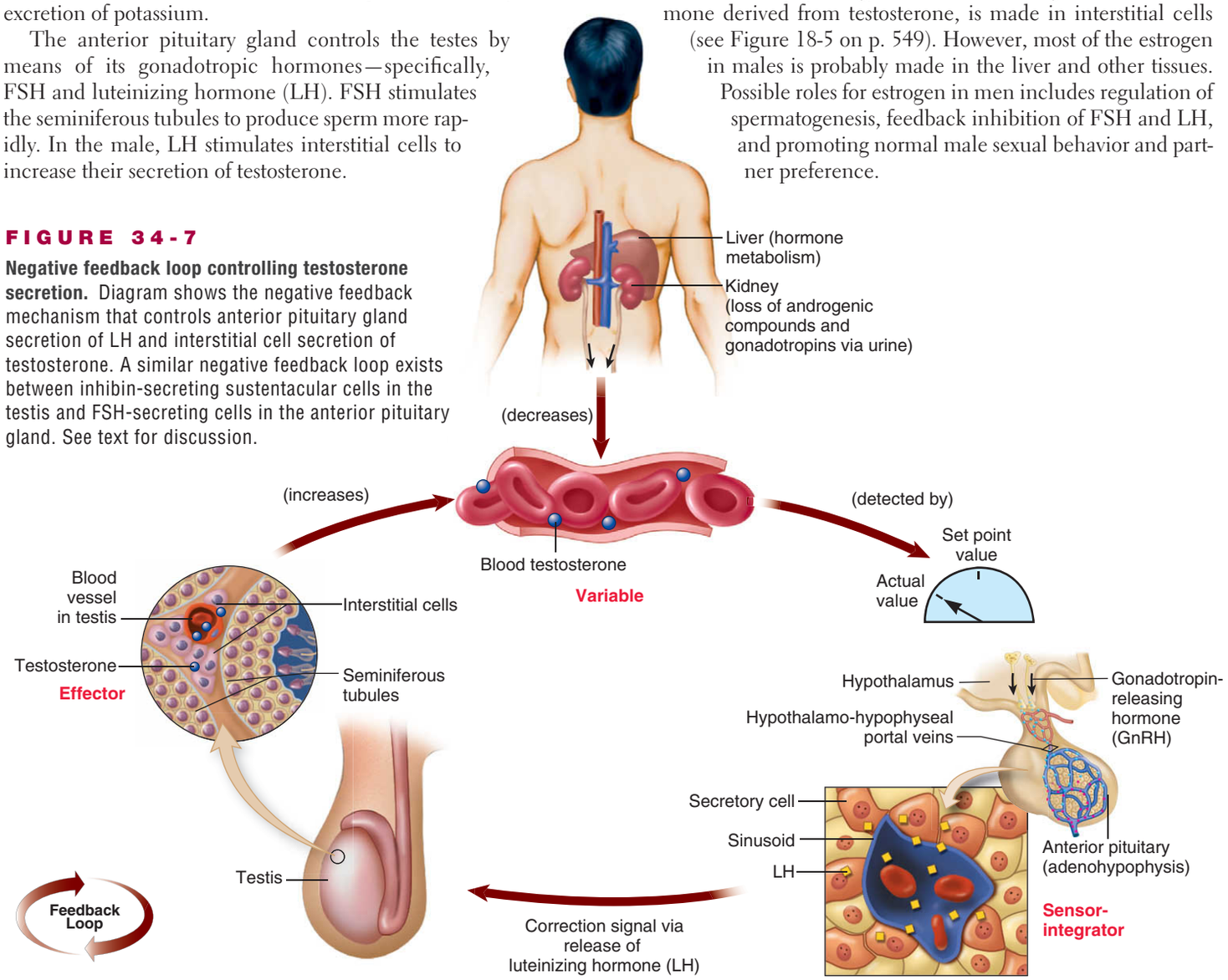


FIGURE 34-7

Negative feedback loop controlling testosterone secretion. Diagram shows the negative feedback mechanism that controls anterior pituitary gland secretion of LH and interstitial cell secretion of testosterone. A similar negative feedback loop exists between inhibin-secreting sustentacular cells in the testis and FSH-secreting cells in the anterior pituitary gland. See text for discussion.

TABLE 34-1 Male Reproductive Hormones

HORMONE	SOURCE	TARGET	ACTION
Dehydroepiandrosterone (DHEA)	Adrenal gland, testis, other tissues	Converted to other hormones	Eventually converted to estrogens, testosterone, or both (see Figure 18-5 on p. 549)
Estrogen	Testis (interstitial cells), liver, other tissues	Testis (spermatogenic tissue), other tissues	Role of estrogen in men is still uncertain; may play role in spermatogenesis, inhibition of gonadotropins, male sexual behavior and partner preference
Follicle-stimulating hormone (FSH)	Anterior pituitary (gonadotroph cells)	Testis (spermatogenic tissue)	Gonadotropin; promotes development of testes and stimulates spermatogenesis
Gonadotropin-releasing hormone (GnRH)	Hypothalamus (neuroendocrine cells)	Anterior pituitary (gonadotroph cells)	Stimulates production and release of gonadotropins (FSH and LH) from anterior pituitary
Inhibin	Testis (sustentacular cells)	Hypothalamus Anterior pituitary (gonadotroph cells)	Inhibits GnRH secretion by the hypothalamus and FSH production in the anterior pituitary
Luteinizing hormone (LH)	Anterior pituitary (gonadotroph cells)	Testis (interstitial cells)	Gonadotropin; stimulates production of testosterone by interstitial cells of testis
Testosterone	Testis (interstitial cells)	Spermatogenic cells, skeletal muscle, bone, other tissues	Stimulates spermatogenesis, stimulates development of primary and secondary sexual characteristics, promotes growth of muscle and bone (anabolic effect)

Table 34-1 summarizes some of the reproductive hormones in males.

Spermatozoa

The elongated tail-bearing **spermatozoa** seen in the seminiferous tubules (Figure 34-8, *B*) appear fully formed. We know, however, that they undergo a process of "ripening," or maturation, as they pass through the genital ducts before ejaculation. Although anatomically complete and highly motile when ejaculated, sperm must still undergo a complex process called **capacitation** before they are actually capable of fertilizing an egg cell or ovum (female gamete). Normally, capacitation occurs in sperm only after they have been introduced into the vagina of the female.

Figure 34-8, *C*, shows the characteristic parts of a spermatozoon: head, middle piece, and elongated, lashlike tail.

The head of a spermatozoon is, in essence, a highly compact package of genetic chromatin material, about 5 µm long, covered by an *acrosome* and *acrosomal (head) cap*. The acrosome contains hydrolytic (splitting) enzymes, which are released during capacitation. During the process of capacitation, the acrosomal enzymes first break down cervical mucus, allowing sperm to pass into the uterus and uterine tubes. If an ovum is present in the female reproductive tract when **semen** is introduced, continued release of acrosomal enzymes assists the sperm cells to digest and penetrate the outer covering of the egg and initiate fertilization. This is the primary reason a high sperm count is essential for male fertility. The process of fertilization is explored further in Chapter 36.

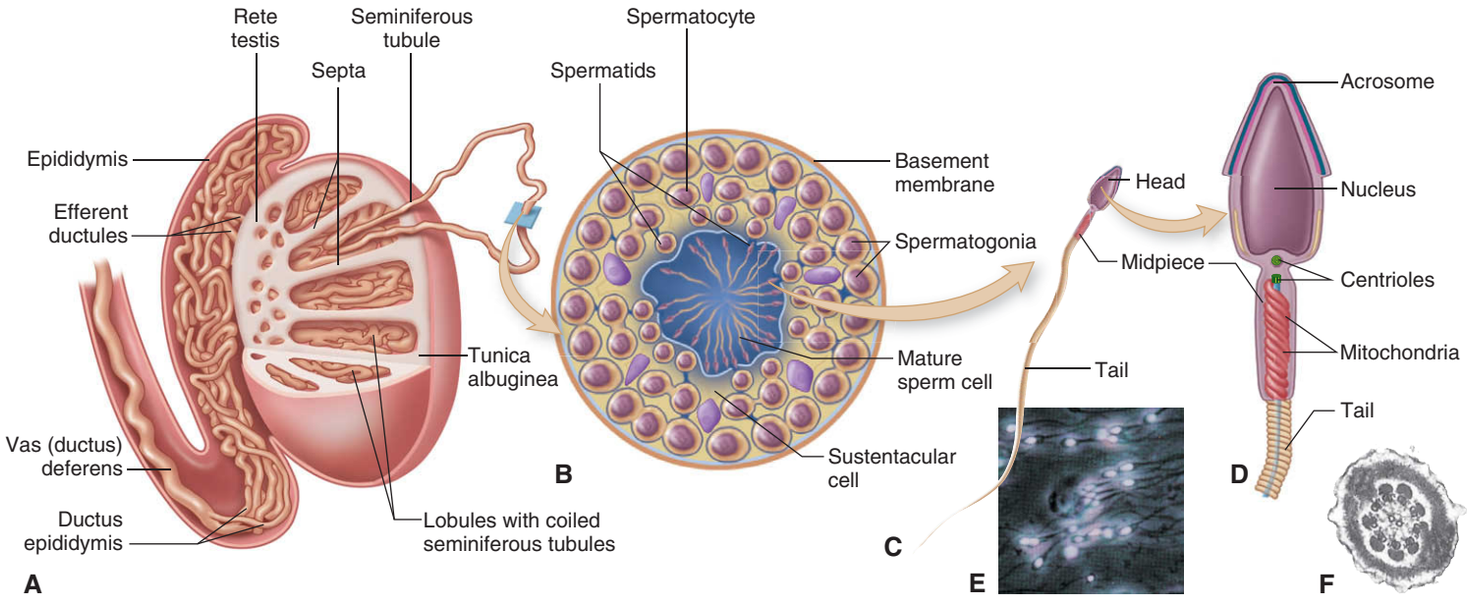


FIGURE 34-8
Development and structure of sperm. A, View of testis and seminiferous tubules. **B,** Spermatid cells in a seminiferous tubule. **C,** Mature sperm. **D,** Enlarged view of head and midpiece. **E,** Micrograph of sperm that shows taken up nuclear material that glows with a fluorescent dye. **F,** Electron micrograph (EM) of a cross section of sperm tail showing nine double microtubules arranged around two single central microtubules.

The sperm nucleus, which takes up most of the room inside the sperm head, is released into the ovum during the process of fertilization. When the genetic material of the sperm nucleus and egg nucleus unite, they form the nucleus of a new offspring cell.

The cylindrical middle piece or *midpiece* of the sperm is connected to the sperm head by a narrow *neck*. The midpiece is about 7 µm long, is characterized by a helical arrangement of mitochondria arranged end to end around a central core. It is this mitochondrial sheath that provides energy for sperm locomotion. Within the core are the ends of the microtubules that extend all the way through the sperm tail. Motor molecules within the core of the midpiece cause the microtubules to move in their typical, propellerlike fashion.

The tail is divided into a principal piece, about 40 µm long, and a short end piece, 5 to 10 mm in length. If the tail portion of a spermatozoon is cut in cross section and viewed with an electron microscope (Figure 34-8, *F*), its microstructure looks like other flagella capable of motility (see Chapter 3, p. 82). Note in Figure 34-8, *F* that the central portion of the sectioned sperm tail is a cylinder composed of nine double microtubules arranged around two single microtubules in the center.

Progesterone and other molecules released by cells that surround the ovum trigger increased sperm motility and attract sperm toward the ovum.

| QUICK CHECK |

4. Describe the location, the size, and the shape of the testes.
5. List the two primary functions of the testes and identify the cell type or structure involved in each function.
6. List the general functions of testosterone.
7. Identify the structural components of a spermatozoon and give the function of each.

REPRODUCTIVE DUCTS

Epididymis

STRUCTURE AND LOCATION

Each **epididymis** consists of a single, tightly coiled tube enclosed in a fibrous casing. The tube has a very small diameter (just barely macroscopic) but measures approximately 6 meters (20 feet) in length. It lies along the top and behind the testis (see Figure 34-3). The comma-shaped epididymis is divided into a blunt superior *head* (which is connected to the testis by the efferent ductules), a central *body*, and a tapered inferior portion that is continuous with the vas deferens, called the *tail*. If the epididymis is cut or sectioned and a slide prepared as in Figure 34-9, the compact and highly coiled nature of the tubule is apparent.

FUNCTIONS

The epididymis serves as one of the ducts through which sperm pass in their journey from the testis to the exterior. Each epididymis stores sperm, which spend from 1 to 3 weeks in this segment of the duct system. While there, the sperm continue to mature with the support of nutrients from the epididymis. The epididymal secretions also eventually become a small part of the seminal fluid (semen) that is eventually ejaculated with the sperm during the male sexual response. After about 3 weeks, any unused sperm break down and are reabsorbed by the body.

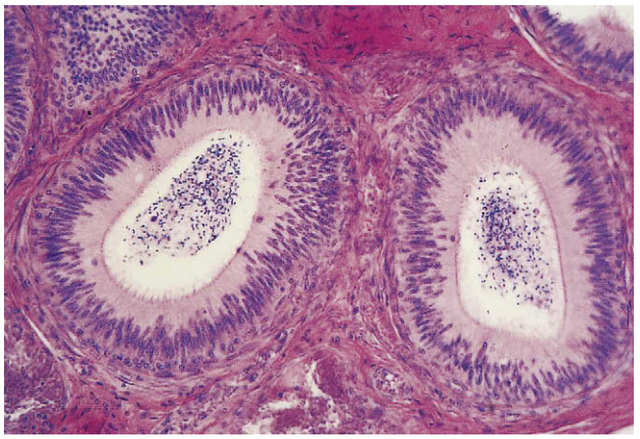


FIGURE 34-9

Epididymis section. Two cross sections of this extensively coiled tubule are visible. Note the presence of spermatozoa within the lumina of the tubules.

Vas Deferens

STRUCTURE AND LOCATION

The **vas deferens,** like the epididymis, is a tube. Also called the *ductus deferens*, the vas deferens is a duct that extends from the tail of the epididymis. The vas deferens has thick, muscular walls (Figure 34-10) and can be palpated in the scrotal sac as a smooth, movable cord. Note in Figure 34-10 that the muscular layer of the vas deferens has three layers: a thick intermediate circular layer of muscle fibers and inner and outer longitudinal layers. The muscular layers of the vas deferens help in propelling sperm through the duct system.

The vas deferens from each testis ascends from the scrotum and passes through the inguinal canal as part of the spermatic cord—enclosed by fibrous connective tissue with blood vessels, nerves, and lymphatics—into the abdominal cavity. Here it extends over the top and down the posterior surface of the bladder where an enlarged and tortuous portion called the *ampulla* joins

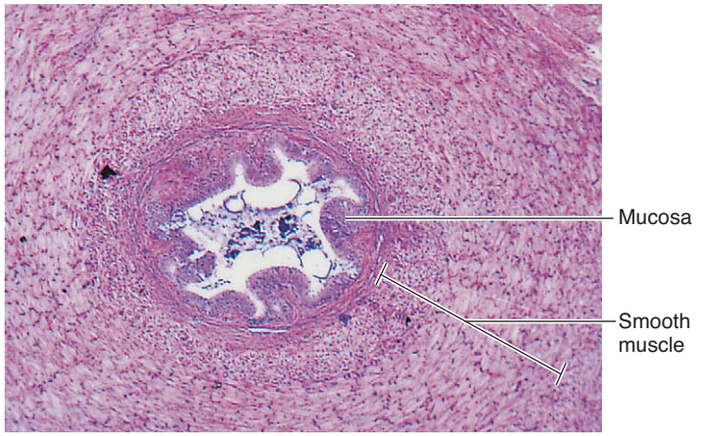
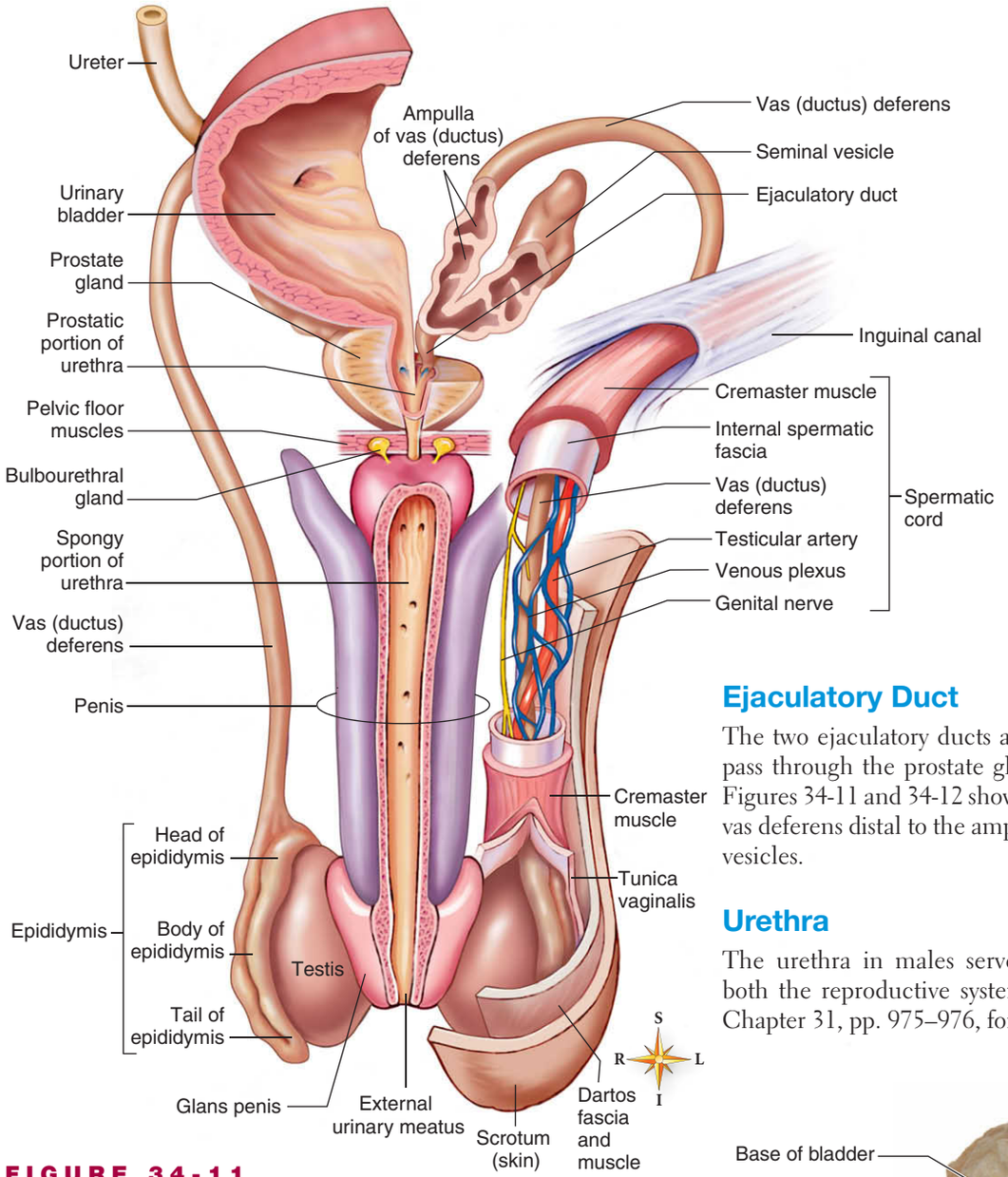


FIGURE 34-10

Transverse section of vas deferens. Mucosa protrudes into the lumen in several low folds. Note the thick muscular coat surrounding the mucosa.



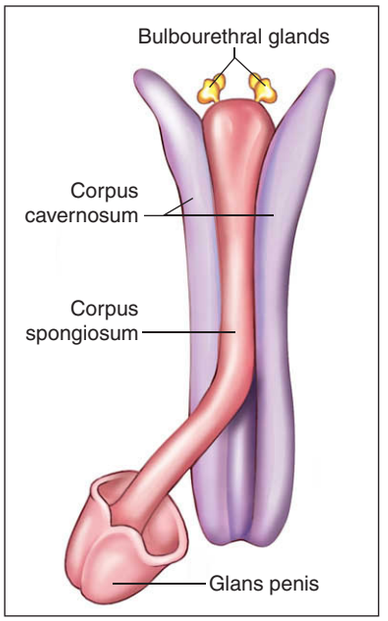


FIGURE 34-11

The male reproductive system. Illustration shows the testes, epididymis, vas (ductus) deferens, and glands of the male reproductive system in an isolation/dissection format.

the duct from the seminal vesicle to form the ejaculatory duct (Figures 34-1, 34-11, and 34-12).

FUNCTION

The vas deferens serves as one of the male genital ducts connecting the epididymis with the ejaculatory duct. Sperm remain in the vas deferens for varying periods of time depending on the degree of sexual activity and frequency of ejaculation. Storage time may exceed 1 month with no loss of fertility.

Severing or clamping off the vas deferens—that is, performing a **vasectomy,** usually done through an incision in the scrotum—makes a man sterile. Why? Because it interrupts the route to the exterior from the epididymis. To leave the body, sperm must journey in succession through the epididymis, vas deferens, ejaculatory duct, and urethra.

Ejaculatory Duct

The two ejaculatory ducts are short tubes about 1 cm long that pass through the prostate gland to terminate in the urethra. As Figures 34-11 and 34-12 show, they are formed by the union of the vas deferens distal to the ampulla with the ducts from the seminal vesicles.

Urethra

The urethra in males serves a dual function, which involves both the reproductive system and the urinary system. Refer to Chapter 31, pp. 975–976, for a discussion of this duct.

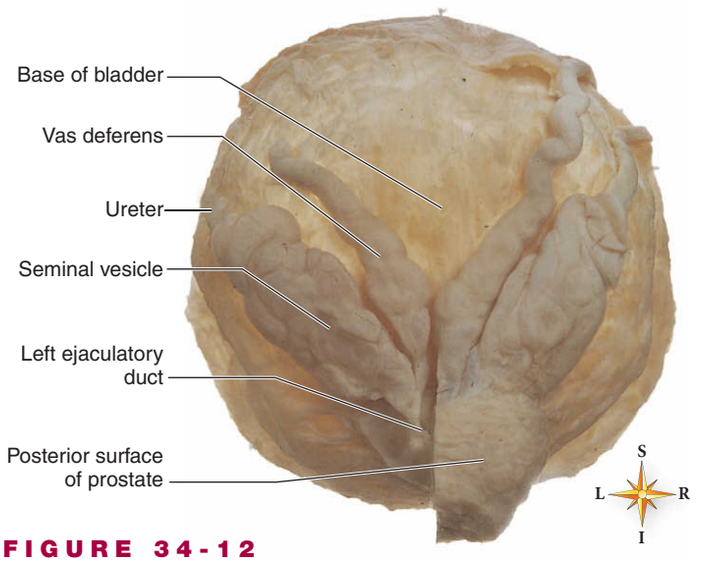


FIGURE 34-12

Prostate and related structures. Cadaver dissection showing the prostate gland and other male reproductive structures viewed from behind. The prostate has been sectioned on the left side to reveal the ejaculatory duct.

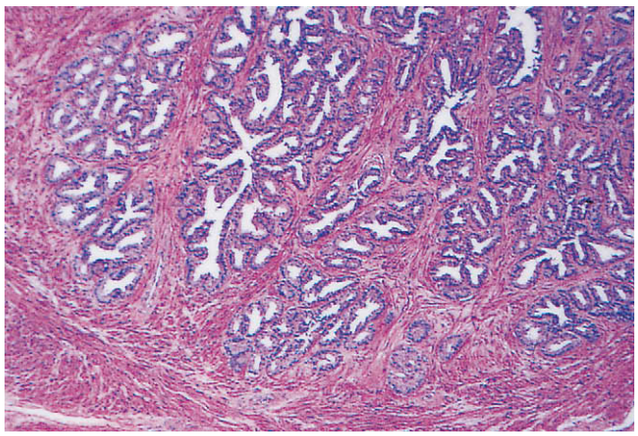


FIGURE 34-13

Seminal vesicle. Note the highly branched and convoluted nature of the secretory epithelium.

ACCESSORY REPRODUCTIVE GLANDS

Seminal Vesicles

STRUCTURE AND LOCATION

The **seminal vesicles** are highly convoluted pouches that, when fully extended, are about 15 cm in length. Each is a tubular diverticulum of the vas deferens on one side and is coiled on itself so that it forms a body about 5 to 7 cm in length. The two vasa deferentia lie along the lower part of the posterior surface of the bladder, directly in front of the rectum (see Figures 34-1, 34-11, and 34-12). Figure 34-12 is an isolated cadaver specimen showing the relationships of a number of the male reproductive structures, including the seminal vesicles, when viewed from behind. The highly branched and convoluted nature of the secretory epithelium filling the lumen of the seminal vesicles is apparent in Figure 34-13.

FUNCTION

The seminal vesicles secrete an alkaline, viscous, creamy-yellow liquid that constitutes about 60% of semen volume. The alkalinity helps neutralize the acid pH environment of the terminal urethra and in the vagina. Fructose found in this component of the semen serves as an energy source for sperm motility after ejaculation. Other components include prostaglandins, which are involved in cyclic AMP formation, and a non–blood type coagulating enzyme called *vesiculase*.

Prostate Gland

STRUCTURE AND LOCATION

The **prostate** is a compound tubuloalveolar gland that lies just below the bladder and is shaped like a doughnut. The fact that the urethra passes through the small hole in the center of the prostate is a matter of considerable clinical significance. Many older men suffer from a noncancerous enlargement of this gland called **benign prostatic hypertrophy** (see p. 1058). As the prostate enlarges, it squeezes the urethra, frequently closing it so completely that urination becomes impossible. Urinary retention results. Surgical removal of the gland (prostatectomy) is required as a cure for this condition when other less radical methods of treatment fail.

FUNCTION

The prostate secretes a watery, milky-looking, and slightly acidic fluid that constitutes about 30% of the seminal fluid volume. Citrate, found in prostatic fluid, serves as a nutrient for sperm. Other constituents include enzymes such as hyaluronidase and *prostate-specific antigen* (PSA) (Box 34-1). Prostatic fluid plays an important role in sperm activation, viability, and motility.

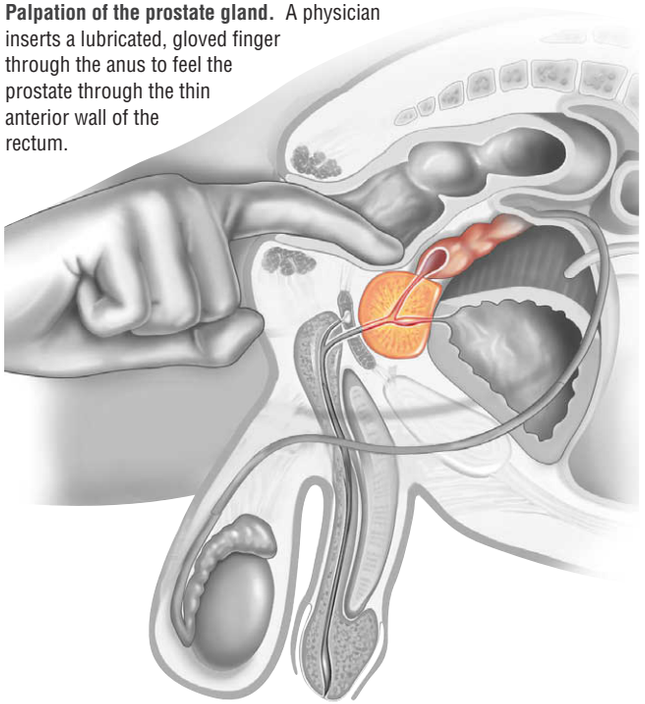
Box 34-1 | DIAGNOSTIC study

Prostate Cancer Screening

Many of the 32,000 men who die each year from prostate cancer—the most common nonskin type of cancer in American men—could be saved if the cancer was detected early enough for effective treatment. Several screening tests are available for the detection of prostate cancer once it develops. Cancerous growths in the gland can often be palpated through the wall of the rectum (figure).

Sometimes, rectal examinations are performed in conjunction with a screening test called the *PSA test.* This test is a type of blood analysis that screens for *prostate-specific antigen (PSA),* a substance sometimes found to be elevated in the blood of men with prostate cancer. Unfortunately, PSA levels may not be elevated with prostate cancer and may be high in some men without prostate cancer. Thus the PSA test is most useful when used with other screening methods.

A nuclear medicine *bone scan* is often used either to exclude metastatic spread of prostate cancer or to locate areas of the body where secondary prostate cancer tumors have already developed. An image of a bone scan showing the metastasis of prostate cancer can be viewed in ***Bone Scans*** online at ***A&P Connect.***



Palpation of the prostate gland. A physician inserts a lubricated, gloved finger through the anus to feel the prostate through the thin anterior wall of the rectum.

Bulbourethral Glands

STRUCTURE AND LOCATION

The two **bulbourethral glands** *(Cowper glands)* resemble peas in size and shape. You can see the location of these compound tubuloalveolar glands in Figure 34-11. A duct approximately 2.5 cm (1 inch) long connects them with the penile portion of the urethra.

FUNCTION

Like the seminal vesicles, the bulbourethral glands secrete an alkaline fluid that is important for counteracting the acid present in the male urethra and the female vagina. Mucus produced in these glands serves to lubricate the urethra and helps protect sperm from friction damage during ejaculation.

| QUICK CHECK |

8. List, in sequence, the reproductive ducts sperm pass through from formation to ejaculation.
9. What is the structural relationship between the prostate gland and the urethra?
10. Compare the volume, viscosity, pH, and composition of the secretions produced by the accessory reproductive glands.

SUPPORTING STRUCTURES

Scrotum

The **scrotum** is a skin-covered pouch suspended from the perineal region. Internally, it is divided into two sacs by a septum, each sac containing a testis, epididymis, and lower part of a spermatic cord.

The *dartos* fascia and muscle are located just below the skin of the scrotum (see Figure 34-11). Contraction of the dartos muscle fibers causes slight elevation of the testes and wrinkling of the scrotal pouch. In addition, contraction of the *cremaster muscle*, also seen in Figure 34-11, causes significant elevation of the testes. The cremaster muscle forms an elongated pouch for each testis within the scrotum. Each pouch containing one testis is lined with a doubled serous membrane called the *tunica vaginalis*, which permits the testis within to slide around. This testicular sliding protects against possible injury by allowing the testes to move out of harm's way when the scrotum is pressed or pinched. When the cremaster muscle contracts, the testes are pulled upward against the perineum. Sexual arousal, cold temperature, and threat of injury provide the stimulus for contraction of both the dartos and cremaster muscles.

The temperature required for optimum sperm formation is about 3° C below normal body temperature. This is the "functional" reason that justifies placement of the testes outside the body cavity where they are exposed and subject to traumatic injury. In a warm environment the scrotum becomes elongated and its skin appears loose and wrinkle free, permitting the testes to descend away from the body. In the cold, the scrotum elevates and becomes heavily wrinkled, effectively pulling the testes upward toward the body wall. Both actions help maintain the temperature of the testes at a more constant level. Factors other than temperature, including blood flow dynamics and tissue oxygen levels, are also suggested as "reasons" for scrotal placement of the testes.

Penis

STRUCTURE

Three cylindrical masses of erectile, or cavernous, tissue, enclosed in separate fibrous coverings and held together by a covering of skin, compose the **penis** (Figure 34-14). The two larger and uppermost of these cylinders are named the **corpora cavernosa,**

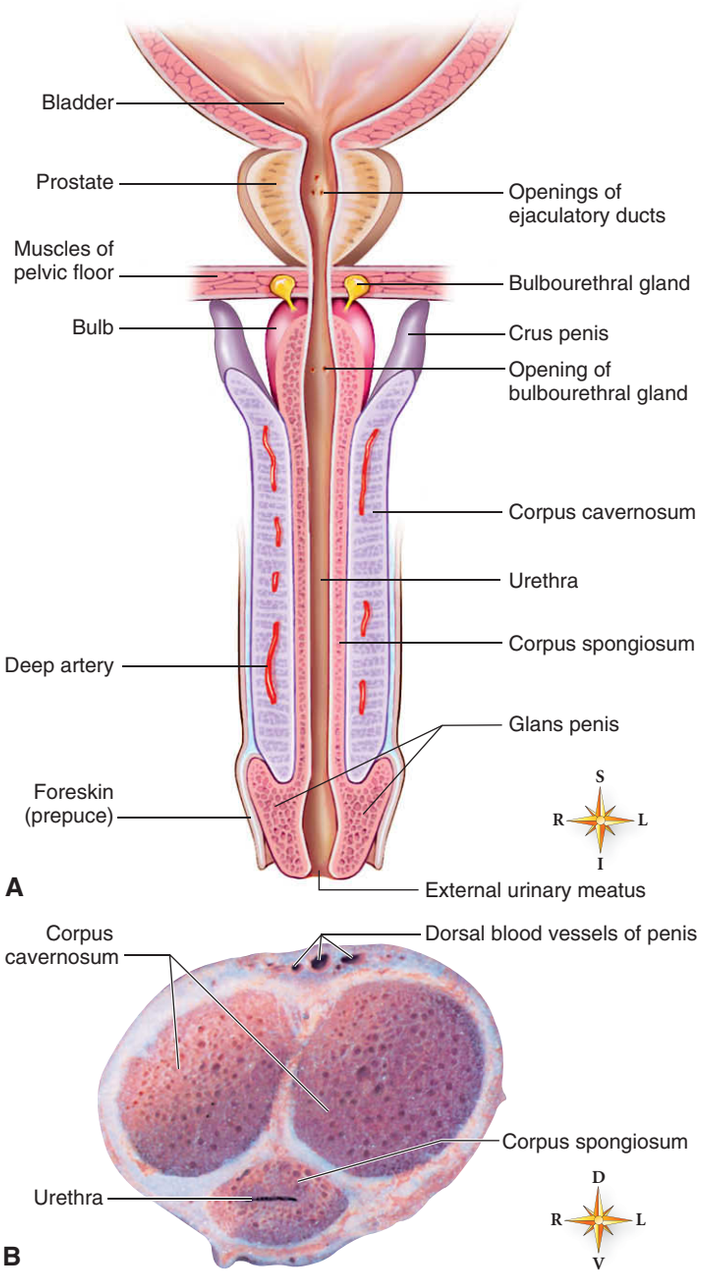


FIGURE 34-14

The penis. A, In this sagittal section of the penis viewed from above, the urethra is exposed throughout its length and can be seen exiting from the bladder and passing through the prostate gland before entering the penis to end at the external urinary meatus (urethral orifice). **B,** Photograph of a cross section of the shaft of the penis showing the three columns of erectile, or cavernous, tissue. Note the urethra within the substance of the corpus spongiosum.

whereas the smaller, lower one, which contains the urethra, is called the **corpus spongiosum.**

The distal part of the corpus spongiosum overlaps the terminal end of the two corpora cavernosa to form a slightly bulging structure, the **glans penis,** over which the skin is folded doubly to form a more or less loose-fitting, retractable casing known as the **prepuce,** or foreskin. The opening of the urethra at the tip of the glans is called the *external urinary meatus.*

| A&P CONNECT |

Removal of the foreskin is called circumcision. Learn more about how and why this procedure is done in ***Male Circumcision*** online at ***A&P Connect.***

evolve

FUNCTIONS

The penis contains the urethra, the terminal duct for both urinary and reproductive tracts. During sexual arousal, the erectile tissue of the penis fills with blood, causing the organ to become rigid and enlarge in both diameter and length. The result, called an **erection,** permits the penis to serve as a penetrating copulatory organ during sexual intercourse. The scrotum and penis constitute the external **genitals**, or *genitalia*, of the male.

Spermatic Cords

The **spermatic cords** are cylindrical casings of white, fibrous tissue located in the inguinal canals between the scrotum and the abdominal cavity. They enclose the vasa deferentia, blood vessels, lymphatics, and nerves (see Figure 34-11).

COMPOSITION AND COURSE OF SEMINAL FLUID

The following structures secrete the substances that, together, make up the *seminal fluid*, or **semen:**

- Testes and epididymis—secretions constitute less than 5% of the seminal fluid volume.
- Seminal vesicles—combined secretions are reported to contribute about 60% of the seminal fluid volume.
- Prostate gland—secretions constitute about 30% of the seminal fluid volume.
- Bulbourethral glands—secretions are said to constitute less than 5% of the seminal fluid volume.

Besides contributing slightly to the seminal fluid, the testes also add hundreds of millions of sperm. In traversing the distance from their place of origin to the exterior, the sperm must pass from the testis through the epididymis, vas deferens, ejaculatory duct, and urethra. Note that sperm originate in the testes, glands located outside the body (that is, not within a body cavity), travel to the inside of the body, and finally are expelled to the outside (external environment) by way of ejaculation.

Box 34-2 summarizes important elements of the male sexual response.

MALE FERTILITY

Male fertility relates to many factors—most of all to the number of sperm ejaculated but also to their size, shape, and motility. Fertile sperm have a uniform size and shape. They are highly motile. Although only one sperm fertilizes an ovum, millions of sperm seem to be necessary for fertilization to occur. According to one estimate, when the sperm count falls below about 25 million/ml of semen, functional sterility results.

One hypothesis suggested to explain this puzzling fact is this: semen that contains an adequate number of sperm also contains enough hyaluronidase and other hydrolytic enzymes to liquefy the intercellular substance between the cells that encase each ovum. Without this, a single sperm cannot penetrate the layers of cells around the ovum and hence cannot fertilize it. Infertility may also be caused by production of antibodies some men make against their own sperm. This type of sperm destruction or inactivation, called "immune infertility," is caused by an antigen-antibody reaction. A sperm surface protein called *fertilization antigen (FA-1)* triggers antibody production, which results in infertility.

Box 34-2 | FYI

Neural Control of the Male Sexual Response

Recall that all body functions but one have the ultimate goal of survival of the individual. Only the function of reproduction serves a different, a longer-range, and no doubt in nature's scheme, a more important purpose—survival of the human species. Male functions in reproduction consist of the production of male sex cells (spermatogenesis) and introduction of these cells into the female body *(coitus, copulation,* or *sexual intercourse).* For coitus to take place, erection of the penis must first occur, and for sperm to enter the female body, both the sex cells and secretions from the accessory glands must be introduced into the urethra (emission) and semen must be ejaculated from the penis.

Erection is a parasympathetic reflex initiated mainly by certain tactile, visual, and mental stimuli. It consists of dilation of the arteries and arterioles of the penis, which in turn floods and distends spaces in its erectile tissue and compresses its veins. Therefore more blood enters the penis through the dilated arteries than leaves it through the constricted veins. Hence it becomes larger and rigid, or in other words, erection occurs.

Emission is the reflex movement of sex cells, or spermatozoa, and secretions from the genital ducts and accessory glands into the prostatic urethra. Once emission has occurred, ejaculation will follow.

Ejaculation of semen is also a reflex response. It is the usual outcome of the same stimuli that initiate erection. Ejaculation and various other responses—notably accelerated heart rate, increased blood pressure, hyperventilation, dilated skin blood vessels, and intense sexual excitement—characterize the male **orgasm,** or sexual climax.

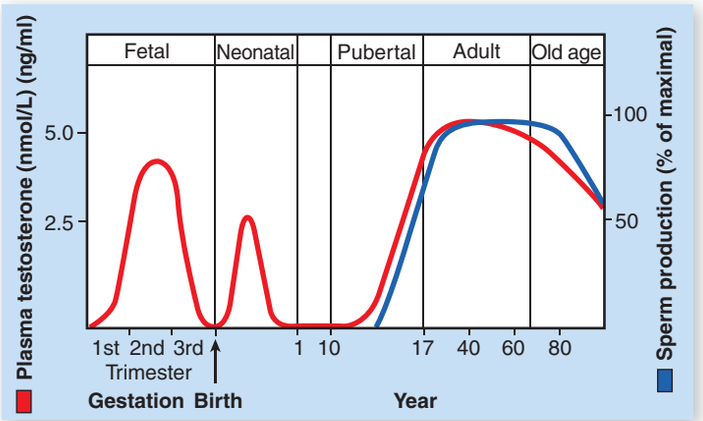


FIGURE 34-15

Testosterone levels and sperm production. Plasma testosterone levels (red line) rise during fetal development, when it stimulates early development of male sexual organs. Testosterone rises again briefly around the time of birth, which facilitates descent of the testes into the scrotum. Then at puberty, testosterone rises enough to support sperm production (blue line) and later tapers off in advanced old age.

Figure 34-15 shows that as average plasma testosterone levels increase during puberty, sperm production begins. Testosterone levels—and thus sperm production—reach a peak in early adulthood and remain high into old age. In advanced old age, testosterone production tapers off—and thus so does fertility, as seen in the dropping sperm count.

| QUICK CHECK |

11. What two structures constitute the external genitals of the male?
12. What is the function of the dartos and cremaster muscles? How does this function influence fertility?
13. Identify by name the three cylindrical masses of erectile tissue in the penis.
14. What factors influence male fertility?

Cycle of LIFE

Male Reproductive System

The reproductive system is unlike all other systems of the male body with regard to normal changes that occur throughout the life span. All other systems perform their functions from the time they develop in utero until advanced old age, when degeneration may cause loss of function and, perhaps, death. The male reproductive system, however, does not begin to perform its functions until puberty—usually during the early teenage years. Of course, the biological advantage of this "late start" is that a person does not have the biological, psychological, or social maturity to become a parent before that time.

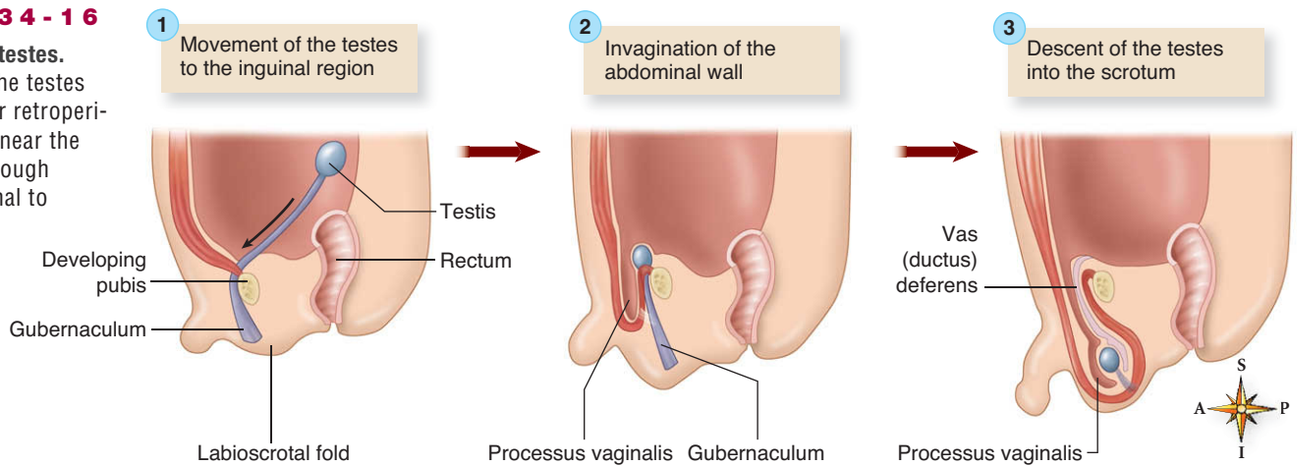
Initial development of the male reproductive organs begins before birth, when the reproductive tract differentiates into the male form rather than the female form (see Figures 36-17 and 36-18 on p. 1112). At about the seventh week of embryonic development, genes in the Y chromosome in males trigger the production of enough testosterone to stimulate the development of male reproductive organs. Without this early spurt of testosterone (see Figure 34-15), the organs would instead develop into the female form.

A couple of months before birth, the immature testes descend behind the parietal peritoneum into the scrotum (Figure 34-16). The testes are guided in their descent by a threadlike, fibrous gubernaculum. It is not uncommon for them to be late in completing the descent, perhaps not arriving in the scrotum until several weeks after birth. Figure 34-15 shows a spurt in testosterone levels around the time of birth that can then stimulate descent of the testes.

The testes and other reproductive organs remain in an immature form—and thus remain incapable of providing reproductive function—until puberty, when high levels of reproductive hormones stimulate the final stages of their development (see Figure 34-15). From puberty until advanced old age the male reproductive system continues to operate efficiently enough to permit successful reproduction. A gradual decline in hormone production during late adulthood may decrease sexual desire and fertility to some degree, but a man may be able to father a child until the time of death.

FIGURE 34-16

Descent of the testes. Prior to birth, the testes move from their retroperitoneal location near the kidneys and through the inguinal canal to the scrotum.



the BIG picture

Male Reproductive System

Propagation of the genes of a species is truly a "big picture" outcome related to functioning of the reproductive system in both sexes.

In males, the reproductive and urinary tracts are partly shared—causing some to group them together as the *genitourinary tract*. Such structural sharing also means functional sharing. For example, the urethra conducts urine during micturition but instead conducts semen during ejaculation. Changes to muscular control of the bladder, urethra, and ejaculatory duct prevent flow of urine—and backflow of semen into the bladder—during the sexual response.

Both the primary and secondary sexual functions in males depend on complex interrelationships involving nervous, endocrine, muscular, urinary, and circulatory system structures. Even the skin is a sexual organ, receiving some of the stimuli needed to produce the sexual response.

MECHANISMS of DISEASE

DISORDERS OF THE MALE REPRODUCTIVE SYSTEM

Several disorders of the male reproductive system cause **infertility**. Infertility is an abnormally low ability to reproduce. If there is a complete inability to reproduce, the condition is called **sterility.** Infertility or sterility involves an abnormally reduced capacity to deliver healthy sperm to the female reproductive tract. Reduced reproductive capacity may result from factors such as a decrease in the testes' production of sperm, structural abnormalities in the sperm, or obstruction of the reproductive ducts.

| A&P CONNECT |

Infections of the reproductive tract, often acquired through sexual contact with infected individuals, can progress into conditions that may cause sterility—or even death. These *sexually transmitted diseases (STDs)* are discussed in ***Sexually Transmitted Diseases*** online at ***A&P Connect.***

evolve

Disorders of the Testes

Disruption of the sperm-producing function of the seminiferous tubules can result in decreased sperm production, a condition called **oligospermia** (ol-i-go-SPER-mee-ah). If the *sperm count* is too low, infertility may result. A large number of sperm is needed to ensure that many sperm will reach the ovum and dissolve its coating—allowing a single sperm to unite with the ovum. Oligospermia can result from factors such as infection, fever, radiation, malnutrition, and high temperature in the testes. In some cases, oligospermia is temporary—as in some acute infections. Oligospermia is a leading cause of infertility. Of course, total absence of sperm production results in sterility.

Early in fetal life the testes are located in the abdominal cavity near the kidneys but normally descend into the scrotum about 2 months before birth (see Figure 34-16). Occasionally a baby is born with undescended testes, a condition called **cryptorchidism** (krip-TOR-ki-diz-em), which is readily observed by palpation of the scrotum at delivery (Figure 34-17). The word *cryptorchidism* is from the Greek words *kryptikos* ("hidden") and *orchis* ("testis"). Failure of the testes to descend may be caused by hormonal imbalances in the developing fetus or by a physical deficiency or obstruction. Regardless of cause, in the cryptorchid infant the testes remain "hidden" in the abdominal cavity. Because the higher temperature inside the body cavity inhibits spermatogenesis, measures must be taken to bring the testes down into the scrotum to prevent permanent sterility. Early treatment of this condition by surgery or by injection of testosterone, which stimulates the testes to descend (see Figure 34-15), may result in normal testicular and sexual development.

Most testicular cancers arise from the sperm-producing cells of the seminiferous tubules. Malignancies of the testes are most common among men 20 to 35 years old. Besides age, this type of cancer is associated with genetic predisposition, trauma or infection of the testis, and cryptorchidism. Treatment of testicular cancer is most effective when the diagnosis is made early in the development of the tumor.



FIGURE 34-17

Screening for cryptorchidism in a newborn infant. Properly descended testes can be palpated easily in the scrotal sac at birth.

| A&P CONNECT |

Many physicians encourage male patients to perform regular self-examination of their testes, especially if they are in a high-risk group. Check out ***Male Genital Self-Examination*** online at ***A&P Connect.***

Disorders of the Prostate

A noncancerous condition called **benign prostatic hypertrophy (BPH)** occurs in 75% of men older than 50 years. As the name suggests, the condition is characterized by an enlargement, or hypertrophy, of the prostate gland. As discussed earlier in the chapter, the fact that the urethra passes through the center of the prostate after exiting from the bladder is a matter of considerable clinical significance. As the prostate enlarges, it squeezes and may distort the normal passage of the urethra, frequently closing it so completely that urination becomes very difficult or even impossible. Often the first area of the prostate to enlarge in BPH involves the so-called *periurethral glandular tissue* surrounding the urethra. Tissue near the periphery of the prostate, called *peripheral zone glandular tissue*, may remain normal even though the gland as a whole increases in size.

Surgical removal of some of the swollen tissue surrounding the urethra in a **transurethral resection (TUR)** will often be effective in reducing symptoms and improving urine flow rates. In this procedure, a tubelike instrument called a *cystoscope*—which contains operative devices, a lighting system, and viewing lenses, is inserted through the penis and into the prostatic urethra to surgically remove (resect) prostatic tissue surrounding the lumen. Alternative procedures using laser therapy, focused ultrasound, or the insertion of urethral stents may also be employed. The use of robotic devices to assist in TURs has helped improve accuracy and thus reduce surgical complications. In severe cases total removal of the gland, a procedure called **prostatectomy** (pros-ta-TEK-toh-mee), may become necessary.

Disorders of the Penis and Scrotum

The penis is subject to numerous sexually transmitted infections, as well as structural abnormalities. One such structural abnormality is **phimosis** (fi-MOH-sis), a condition in which the foreskin fits so tightly over the glans that it cannot retract. The usual treatment for this condition is **circumcision**—a procedure in which the foreskin is cut along the base of the glans and removed. Severe phimosis can obstruct the flow of urine, possibly causing the death of an infant born with this condition. Milder phimosis can result in accumulation of dirt and organic matter under the foreskin, possibly causing severe infections.

Failure to achieve an erection of the penis adequate enough to permit sexual intercourse is called *impotence* or **erectile dysfunction (ED).** ED affects men of all ages but is experienced most often after age 65 years. ED does not affect sperm production, but infertility often results because normal intercourse may not be possible. In the past, psychological problems such as anxiety, depression, and stress were often cited as the most important causes of impotence in sexually active men. There is no doubt that such conditions contribute to ED. However, current research suggests that purely psychological problems account for far fewer cases of impotence than previously thought. We now know that ED is frequently caused by medical problems related to abnormal vascular or neural control of penile blood flow. Arteriosclerosis, diabetes, alcohol abuse, numerous medications, radiation therapy, tumors, spinal cord trauma, and surgery, especially if pelvic organs such as the prostate are involved, may all cause ED.

The most common treatment option is the use of drugs that increase blood flow to the spongy cavernous tissue of the penis, causing it to stiffen and become erect. Most of the ED drugs affect the levels of nitric oxide, a local regulator and neurotransmitter that controls tension of the smooth muscles in the vessels of the penis. Other possible treatments involve vacuum pumps, internal penile supports, and other methods.

Swelling of the scrotum can be caused by various conditions. One of the most common causes of scrotal swelling is an accumulation of fluid called **hydrocele** (HYE-dro-seel). Hydroceles may be congenital, resulting from structural abnormalities present at birth. In adults, hydrocele often occurs when fluid produced by the serous membrane lining the scrotum is not absorbed properly. The cause of adult hydrocele is not always known but, in some cases, it can be linked to trauma or infection.

Swelling of the scrotum may also occur when the intestines push through the weak area of the abdominal wall that separates the abdominopelvic cavity from the scrotum. This condition is a form of **inguinal** (IN-gwi-nal) **hernia** (see ***Hernias*** online at ***A&P Connect***). If the intestines protrude into the scrotum, the digestive tract may become obstructed—resulting in death. Inguinal hernia often occurs while lifting heavy objects because of the high internal pressure generated by the contraction of abdominal muscles. Inguinal hernia may also be congenital. Small inguinal hernias may be treated with external supports that prevent organs from protruding into the scrotum; more serious hernias must be repaired surgically.

LANGUAGE OF SCIENCE (continued from p. 1044)

gamete
(GAM-eet)
[*gamete* **marriage partner**]

genital
(JEN-i-tall)
[*gen-* **produce**, *-al* **relating to**]
pl., genitals or genitalia

glans penis
(glans PEE-nis)
[*glans* **acorn**, *penis* **male sex organ**]
pl., glandes penes

gonad
(GO-nad)
[*gon-* **offspring**, *-ad* **relating to**]

interstitial cell
(in-ter-STISH-al sell)
[*inter-* **between**, *-stit-* **stand**, *-al* **relating to**, *cell* **storeroom**]

orgasm
(OR-gaz-um)
[*orgasm* **excitement**]

penis
(PEE-nis)
[*penis* **male sex organ**] *pl.,* penes or penises

perineum
(pair-i-NEE-um)
[*peri-* **around**, *-ine-* **excrete**, *-um* **thing**] *pl.,* perinea

prepuce
(PREE-pus)
[*pre-* **before,** *-puc-* **penis**]

prostate
(PROSS-tayt)
[*pro-* **before,** *-stat-* **set or place**]

scrotum
(SKROH-tum)
[*scrotum* **bag**] *pl.,* scrota or scrotums

semen
(SEE-men)
[*semen* **seed**]

seminal vesicle
(SEM-i-nal VES-i-kul)
[*semen-* **seed,** *-al* **relating to,** *vesic-* **blister,** *-cle* **little**]

seminiferous tubule
(seh-mih-NIF-er-us TOOB-yool)
[*semin-* **seed,** *-fer-* **bear or carry,** *-ous* **relating to,** *tub-* **tube,** *-ul-* **little**]

spermatic cord
(sper-MAT-ik kord)
[*sperma-* **seed,** *-ic* **relating to**]

spermatogenesis
(sper-mah-toh-JEN-eh-sis)
[*sperma-* **seed,** *-gen-* **produce,** *-esis* **process**]

spermatozoon
(sper-mah-tah-ZOH-on)
[*sperma-* **seed,** *-zoon* **animal**]
pl., spermatozoa

sustentacular cell
(sus-ten-TAK-yoo-lar)
[*sustent-* **support,** *-acular* **relating to**]

testis
(TES-tis)
[*testis* **witness (male gonad)**]
pl., testes

testosterone
(tes-TOS-teh-rohn)
[*test-* **witness (testis),** *-stero-* **solid or steroid derivative,** *-one* **chemical**]

tunica albuginea
(TOO-nih-kah al-byoo-JIN-ee-ah)
[*tunica* **tunic or coat,** *albuginea* **white**] *pl.,* tunicae albuginea

vas deferens
(vas DEF-er-enz)
[*vas* **duct or vessel,** *deferens* **carrying away**] *pl.,* vasa deferentia

LANGUAGE OF MEDICINE

benign prostatic hypertrophy (BPH)
(be-NYNE pro-STAT-ik hye-PER-troh-fee)
[*benign* **kind,** *pro-* **before,** *-stat-* **set or place,** *-ic* **relating to,** *hyper-* **excessive or above,** *-troph-* **nourishment,** *-y* **state**]

circumcision
(ser-kum-SIH-zhun)
[*circum-* **around,** *-cision* **cutting**]

cryptorchidism
(krip-TOR-ki-diz-em)
[*crypt-* **hidden,** *-orchid-* **testis,** *-ism* **condition**]

erectile dysfunction (ED)
(ee-REK-tyle dis-FUNGK-shun)
[*erect* **make upright,** *-ile* **relating to,** *dys-* **bad or painful,** *-function* **performance**]

hydrocele
(HYE-dro-seel)
[*hydro-* **water,** *-cele* **tumor**

infertility
(in-fer-TIL-i-tee)
[*in-* **not,** *-fertil-* **fruitful,** *-ity* **state**]

inguinal hernia
(IN-gwi-nal HER-nee-ah)
[*inguin-* **groin,** *-al* **relating to,** *hernia* **rupture**] *pl.,* herniae or hernias

oligospermia
(ol-i-go-SPER-mee-ah)
[*oligo-* **few or little,** *-sperm-* **seed,** *-ia* **condition**]

phimosis
(fi-MOH-sis)
[*phimosis* **muzzle**]

prostatectomy
(pros-ta-TEK-toh-mee)
[*pro-* **before,** *-stat-* **set or place (prostate gland),** *-ec-* **out,** *-tom-* **cut,** *-y* **action**]

sterility
(steh-RIL-i-tee)
[*steril-* **barren,** *-ity* **state**]

transurethral resection (TUR)
(tranz-yoor-REE-thral rih-SEK-shun)
[*trans-* **across or through,** *-ure-* **urine,** *-thr-* **agent or channel (urethra),** *-al* **relating to,** *re-* **again,** *-sect-* **cut,** *-tion* **process**]

vasectomy
(va-SEK-toh-mee)
[*vas-* **duct or vessel (vas deferens),** *-ec-* **out,** *-tom-* **cut,** *-y* **action**]

CASE study

Carlos and his wife had been trying for years to have a baby with no success. Carlos had always assumed they just had bad timing. But recently they had started tracking Maria's cycle and found everything seemed to be on schedule. Finally, at Maria's request, they made an appointment with an infertility specialist. Carlos was expecting them to order expensive tests. But after the introductions, one of the first things the doctor asked about was what kind of underwear Carlos wore. "What business is that of yours?" Carlos thought. Then the specialist added, "because that may affect the average temperature of the testes."

1. Sperm production occurs optimally at what temperature?
   a. 3° C above body temperature
   b. At body temperature
   c. 3° C below body temperature
   d. Optimal temperature changes with the seasons

Next, Carlos was asked to provide a sperm sample. "We're going to analyze the sperm count and morphology," said the doctor.

2. What number should Carlos' sperm count be above for that factor to be ruled out as a cause of the couple's infertility?
   a. 250 million/ml
   b. 25 million/ml
   c. 2500/ml
   d. 250/ml
3. Which is the correct pathway the sperm would take during ejaculation?
   a. Seminiferous tubules, rete testis, efferent ductules, epididymis, vas deferens, ejaculatory duct, urethra
   b. Rete testis, seminiferous tubules, efferent ductules, epididymis, vas deferens, urethra, ejaculatory duct
   c. Epididymis, vas deferens, seminiferous tubules, rete testis, ejaculatory duct, urethra
   d. Seminiferous tubules, rete testis, epididymis, vas deferens, efferent ductules, urethra, ejaculatory duct
4. What hormone directly stimulates sperm production?
   a. Estrogen
   b. Progesterone
   c. LH
   d. Testosterone

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

SEXUAL REPRODUCTION

A. Functioning of the reproductive system ensures the survival of the genetic characteristics of a species
B. Male reproductive system consists of organs whose functions are to produce, transfer, and introduce mature sperm into the female reproductive tract where fertilization can occur

MALE REPRODUCTIVE ORGANS

A. Classified as essential organs for production of gametes or accessory organs that support the reproductive process (Figure 34-1)
   1. Essential organs—gonads of the male; testes
   2. Accessory organs of reproduction
      a. Reproductive (genital) ducts convey sperm to outside of body; include pair of epididymides, paired vasa deferentia, pair of ejaculatory ducts, and the urethra
      b. Accessory glands produce secretions that nourish, transport, and mature sperm; include pair of seminal vesicles, the prostate, and pair of bulbourethral glands
      c. Supporting structures—scrotum, penis, and pair of spermatic cords
B. Perineum—in males, roughly diamond-shaped area between thighs
   1. Extends anteriorly from pubic symphysis to coccyx posteriorly
   2. Lateral boundary is the ischial tuberosity on either side
   3. Divided into the urogenital triangle and the anal triangle (Figure 34-2)

TESTES

A. Structure and location
   1. Several lobules composed of seminiferous tubules and interstitial cells (Leydig cells), separated by septa, encased in fibrous capsule called the *tunica albuginea* (Figure 34-3)
   2. Seminiferous tubules in testis open into a plexus called *rete testis*, which is drained by a series of efferent ductules that emerge from the top of the organ and enter the head of epididymis
   3. Located in scrotum, one testis in each of two scrotal compartments
B. Microscopic anatomy (Figures 34-4, 34-5, 34-6)
   1. Interstitial (Leydig) cells—endocrine cells between the seminiferous tubules
   2. Seminiferous tubules
      a. Spermatogenic cells produce sperm
      b. Sustentacular cells—also called *nurse* or *Sertoli cells*
         (1) Support and regulate sperm-producing functions of the testis
         (2) Produce androgen-binding protein (ABP) that binds to testosterone to make it more soluble and thus increase its concentration, supporting sperm production
         (3) Inhibin—inhibits release of GnRH by the hypothalamus and FSH by anterior pituitary, thus allowing the testis to have some control over spermatogenesis
         (4) Tight junctions between sustentacular cells form the blood-testis barrier (BTB) that protects developing sperm from the immune system
C. Functions
   1. Spermatogenesis—formation of mature male gametes (spermatozoa) by seminiferous tubules; stimulated by FSH (follicle-stimulating hormone) from the anterior pituitary (and also GnRH from hypothalamus)
   2. Secretion of hormones by interstitial cells (Figure 34-7)
      a. Testosterone
         (1) Type of androgen—maleness hormone
         (2) Multiple functions, including promoting primary and secondary male sexual characteristics, promoting anabolism, affecting fluid and electrolyte balance
         (3) Regulated by LH (luteinizing hormone) from anterior pituitary
      b. Estrogen—small amounts secreted by interstitial cells, liver, and other organs; role in males uncertain but may influence spermatogenesis and other functions
D. Spermatozoa (Figure 34-8)
   1. Structure—consist of a head (covered by acrosome), neck, midpiece, and tail; tail is divided into a principal piece and a short end piece
   2. Function—capacition in the female tract releases acrosomal enzymes that digest barrier around ovum and promotes sperm motility; sperm nucleus unites with egg nucleus to form first cell of new offspring

REPRODUCTIVE DUCTS

A. Epididymis
   1. Structure and location
      a. Single tightly coiled tube enclosed in fibrous casing (Figure 34-9)
      b. Lies along top and side of each testis
      c. Anatomical divisions include head, body, and tail
   2. Functions
      a. Duct for seminal fluid
      b. Also secretes part of seminal fluid
      c. Sperm become capable of motility while they are passing through the epididymis
B. Vas deferens (ductus deferens) (Figures 34-10 and 34-11)
   1. Structure and location
      a. Tube, extension of epididymis
      b. Extends through inguinal canal, into abdominal cavity, over top and down posterior surface of bladder
      c. Enlarged terminal portion called *ampulla*—joins duct of seminal vesicle

2. Function
   a. One of excretory ducts for seminal fluid
   b. Connects epididymis with ejaculatory duct

C. Ejaculatory duct (Figure 34-12)
1. Formed by union of vas deferens with duct from seminal vesicle
2. Passes through prostate gland, terminating in urethra

D. Urethra—serves a dual function (see Chapter 31, pp. 975–976)

ACCESSORY REPRODUCTIVE GLANDS

A. Seminal vesicles (Figure 34-13)
1. Structure and location—convoluted pouches about 5 to 7 cm long on posterior surface of bladder
2. Function—secrete the viscous, nutrient-rich part of seminal fluid (60% of semen volume)

B. Prostate gland (Figure 34-14)
1. Structure and location
   a. Doughnut shaped
   b. Encircles urethra just below bladder
2. Function—adds slightly acidic, watery, milky-looking secretion to seminal fluid (30% of semen volume)

C. Bulbourethral glands
1. Structure and location
   a. Small, pea-shaped structures with about 2.5-cm (1 inch) long ducts leading into urethra
   b. Lie below prostate gland
2. Function—secrete alkaline fluid that is part of semen (5% of semen volume)

SUPPORTING STRUCTURES

A. Scrotum
1. Skin-covered pouch suspended from perineal region into which the testes descend near the time of birth (Figure 34-11)
2. Divided into two compartments
3. Contains testis, epididymis, and lower part of a spermatic cord
4. Dartos and cremaster muscles elevate the scrotal pouch

B. Penis (Figure 34-14)
1. Structure—composed of three cylindrical masses of erectile tissue, one of which contains urethra
2. Functions—penis contains the urethra, the terminal duct for both urinary and reproductive tracts; during sexual arousal, penis becomes erect, serving as a penetrating copulatory organ during sexual intercourse

C. Spermatic cords (internal)
1. Fibrous cylinders located in inguinal canals
2. Enclose seminal ducts, blood vessels, lymphatics, and nerves

COMPOSITION AND COURSE OF SEMINAL FLUID

A. Consists of secretions from testes, epididymides, seminal vesicles, prostate, and bulbourethral glands
B. Each milliliter contains millions of sperm
C. Passes from testes through epididymis, vas deferens, ejaculatory duct, and urethra

MALE FERTILITY

A. Relates to many factors—number of sperm; size, shape, and motility
B. Infertility may be caused by antibodies some men make against their own sperm
C. Male fertility begins at puberty and extends into old age (Figure 34-15)

CYCLE OF LIFE: MALE REPRODUCTIVE SYSTEM

A. Reproductive functions begin at time of puberty
B. Development of organs begins before birth; immature testes descend into scrotum before or shortly after birth (Figure 34-16)
C. Puberty—high levels of hormones stimulate final stages of development
D. System operates to permit reproduction until advanced old age
E. Late adulthood—gradual decline in hormone production may decrease sexual appetite and fertility

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Name the accessory glands of the male reproductive system.
2. List the genital ducts in the male.
3. List the supporting structures of the male reproductive system.
4. What is the tunica albuginea? How does it aid in dividing the testis into lobules?
5. What are the two primary functions of the testes?
6. What are the general functions of testosterone?
7. Discuss the structure of a mature spermatozoon.
8. What is meant by the term *capacitation*?
9. List the three functions of the epididymis.
10. List the anatomical divisions of the epididymis.
11. Discuss the formation of the ejaculatory ducts.
12. Discuss the type of secretion typical of the prostate gland and seminal vesicles.
13. What and where are the bulbourethral glands?
14. Describe the structure, location, and function or functions of the scrotum.
15. Name the three cylindrical masses of erectile, or cavernous, tissue in the penis.
16. What and where is the glans penis? The prepuce, or foreskin?
17. What is the spermatic cord? From what does it extend, and what does it contain?
18. Identify and define the male functions in reproduction.

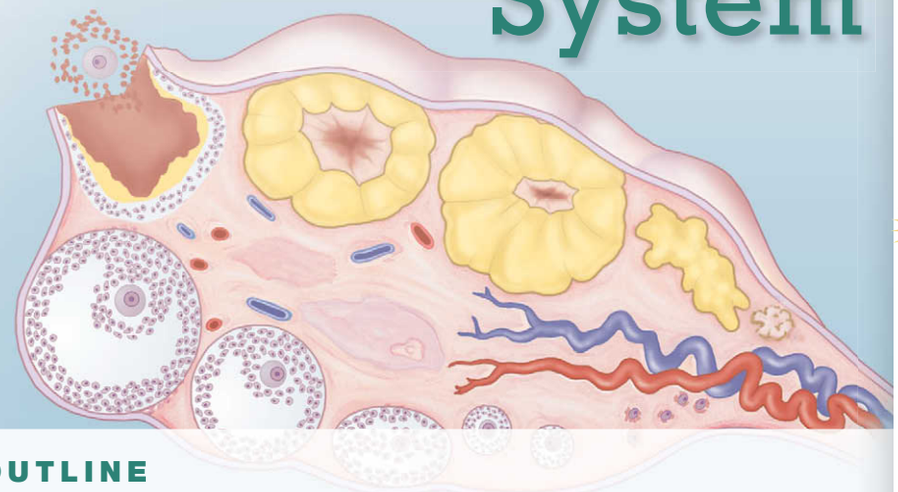
CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. How does the function of reproduction differ from all other body functions?
2. Can you identify the functions of the male reproductive system?
3. What is the relationship between the rete testis, seminiferous tubules, and efferent ductules?
4. How is the prostate gland related to the urethra? What problems can result from this relationship?
5. List the structures in the reproductive system that contribute to the formation of seminal fluid.
6. Trace the course of seminal fluid from its formation to ejaculation.
7. What is the chemical in seminal fluid that is important to fertility? What is its function?
8. How is the structure of the spermatozoa related to its function?

35 Female Reproductive System



CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

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- Function of the Female Reproductive System, 1064
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Mechanisms of Disease, 1086

Case Study, 1092

LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

accessory organ
(ak-SES-oh-ree OR-gan)
[*access-* **extra,** *-ory* **relating to,** *organ* **instrument**]

ampulla
(am-PUL-ah)
[*ampu-* **flask,** *-ulla* **little**] *pl.,* ampullae

anal triangle
[*an-* **ring (anus),** *-al* **relating to**]

anterior fornix
(an-TEER-ee-or FOR-niks)
[*ante-* **front,** *-er-* **more,** *-or* **quality,** *fornix* **arch**] *pl.,* fornices

anterior ligament
(an-TEER-ee-or LIG-ah-ment)
[*ante-* **front,** *-er-* **more,** *-or* **quality,** *liga-* **bind,** *-ment* **condition**]

areola
(ah-REE-oh-lah)
[*are-* **area or space,** *-ola* **little**]
pl., areolae, areoles, or areolas

body of uterus
(YOO-ter-us)
[*uterus* **womb**]

broad ligament
(LIG-ah-ment)
[*liga-* **bind,** *-ment* **condition**]

cervical canal
(SER-vi-kal kah-NAL)
[*cervic-* **neck,** *-al* **relating to**]

cervix
(SER-viks)
[*cervix* **neck**] *pl.,* cervices or cervixes

climacteric
(klye-MAK-ter-ik)
[*climacter-* **critical point in life,** *-ic* **relating to**]

clitoris
(KLIT-oh-ris)
pl., clitorides

continued on p. 1091

In the previous chapter, we discussed the structure and function of the male reproductive system. In this chapter, we discuss the structure and function of the female reproductive system. As you study this chapter, keep in mind that both systems must function properly if successful reproduction and survival of offspring are to occur. The next chapter explores the processes of development of offspring.

OVERVIEW OF THE FEMALE REPRODUCTIVE SYSTEM

Function of the Female Reproductive System

The physiological importance of the female reproductive system is best understood in terms of its final outcome: production of offspring and continued existence of the genetic code. The female reproductive system produces gametes that may unite with a male gamete to form the first cell of the offspring. The function of conception emphasizes the similarity between the male and female reproductive systems. Unlike the male system, however, the female reproductive system also provides protection and nutrition to the developing offspring for up to several years after conception, as we shall see.

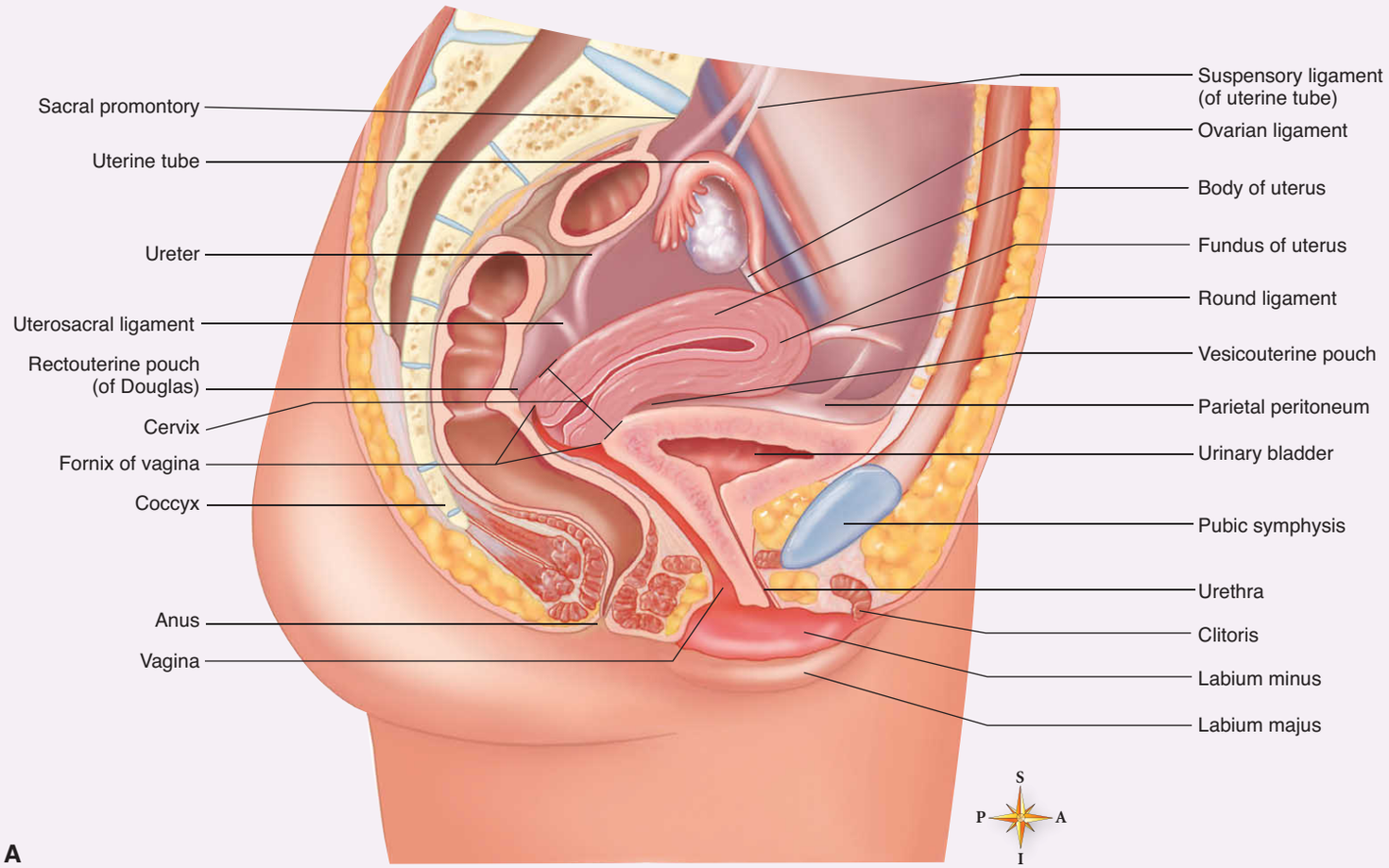
Structural Plan of the Female Reproductive System

So many organs make up the female reproductive system that we need to look first at the structural plan of the system as a whole (Figure 35-1). As we stated in the previous chapter, reproductive organs can be classified as **essential organs** or **accessory organs,** depending on how directly they are involved in producing offspring. The essential organs of reproduction in women, the *gonads*, are the paired **ovaries.** The female gametes, or **ova,** are produced by the ovaries. The accessory organs of reproduction in women consist of the following structures:

- A series of ducts or modified duct structures that extend from near the ovaries to the exterior. This group of organs includes the *uterine tubes*, *uterus*, and *vagina*. Along with the

FIGURE 35-1

Female reproductive organs. A, Diagram (sagittal section) of pelvis showing location of female reproductive organs. **B,** (on following page) Magnetic resonance imaging (MRI) scan (sagittal view) of female pelvic viscera.



A

ovaries, these organs are sometimes collectively called the "internal genitals."

- The *vulva*, or external reproductive organs. These organs are often called the "external genitals" of the female.
- Additional glands, including the *mammary glands*, which secrete milk to provide nourishment for developing offspring.

Most of the essential and accessory organs of the female reproductive system can be seen in Figures 35-1, 35-2, and 35-3. Refer to these illustrations often as you read about each structure in the pages that follow.

Perineum

The perineum is the skin-covered muscular region between the vaginal orifice and the anus (see Figure 35-2). It is a roughly diamond-shaped area between the thighs. The perineum extends from the pubic symphysis anteriorly to the coccyx posteriorly. Its most lateral boundary on either side is the ischial tuberosity. A line drawn between the two ischial tuberosities divides the area into a larger **urogenital triangle,** which contains the external genitals (labia, vaginal orifice, clitoris) and urinary opening, and the **anal triangle,** which surrounds the anus.

The perineum has great clinical importance because of the danger of its being torn during childbirth. Such tears are often deep, have irregular edges, and extend all the way through the perineum, the muscular **perineal body,** and even through the anal sphincter, resulting in involuntary seepage from the rectum until the laceration is repaired. In addition, injuries to the perineal body can result

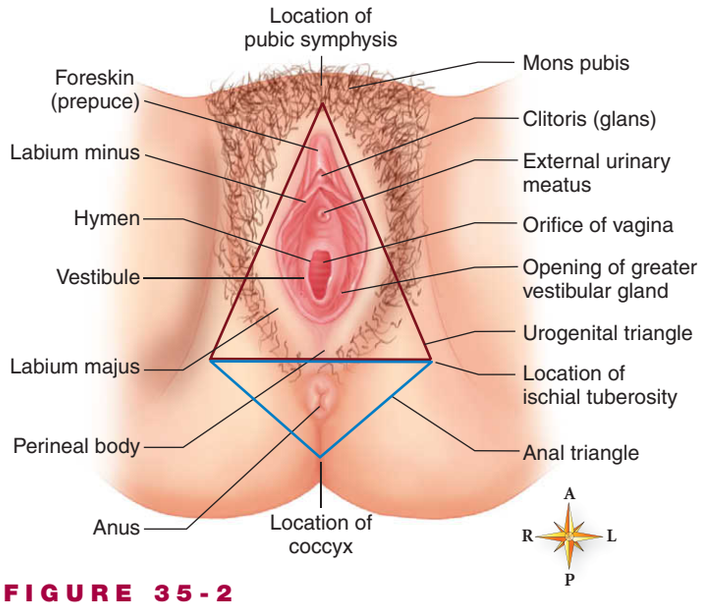
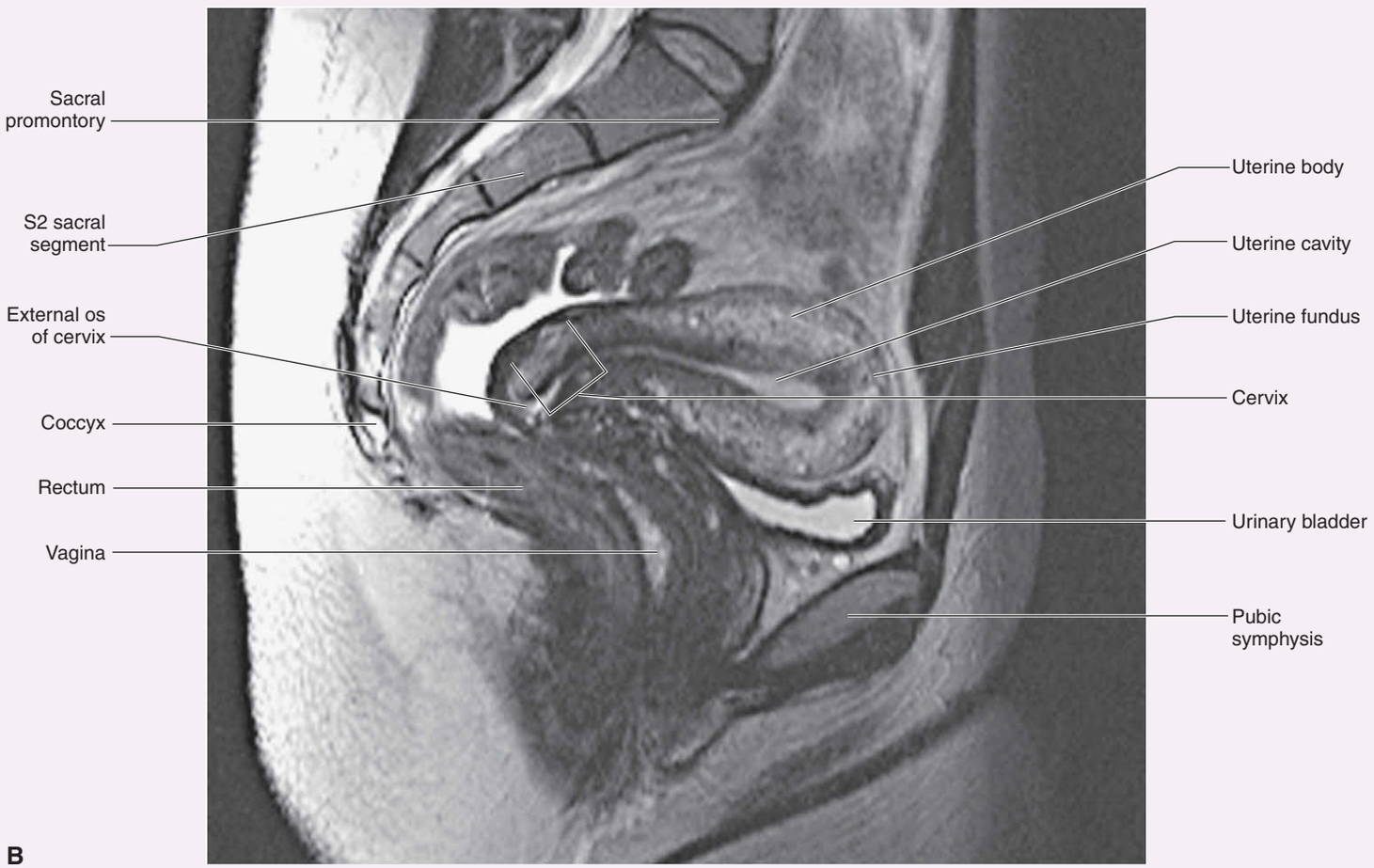


FIGURE 35-2

Female perineum. Inferior view. Sketch showing outline of the urogenital triangle (red) and anal triangle (blue).



in partial uterine or vaginal prolapse if this important support structure is weakened. To avoid these possibilities in a woman prone to such injuries, a surgical incision known as an **episiotomy** may be made in the perineum, particularly at the birth of a first baby. In current medical practice, episiotomy procedures are decreasing in frequency and are no longer performed on a routine basis preceding vaginal delivery of a baby.

| QUICK CHECK |

1. What are the *essential organs* of the female reproductive system?
2. List the *major accessory organs* of the female reproductive system.

OVARIES

Location of the Ovaries

The female gonads, or ovaries, are homologous (similar in origin) to the testes in the male. They are nodular glands that after puberty present a puckered, uneven surface, resemble large almonds in size and shape, and are located one on each side of the uterus, below and behind the uterine tubes. Each ovary weighs about 3 grams and is attached to the posterior surface of the broad ligament by a structure called the *mesovarium*, which contains blood vessels and nerves. The *ovarian ligament* anchors it to the uterus. The distal portion of the uterine tube curves about the ovary in such a way that the fingerlike fimbriae at the end of the uterine tube cup over the ovary, with only one fimbria actually being attached to the ovary (see Figure 35-3, A). This loose configuration makes it possible for a pregnancy to begin in the pelvic cavity instead of in the uterus as is normal. Development of the fetus in a location other than the uterus is referred to as an **ectopic pregnancy** (from the Greek *ektopos*, "displaced"). In the cadaver dissection specimen of the internal female reproductive organs shown in Figure 35-3, *B*, removal of parts of the posterior wall of the body of the uterus and cervix exposes a triangular uterine cavity communicating by way of the internal os with the cervical canal.

Microscopic Structure of the Ovaries

The ovary, like a number of other organs in the body, consists of two major layers of tissue—an outer **cortex** and inner **medulla.** Covering the outer cortex is a surface layer of slightly raised squamous-shaped epithelial cells called the *germinal epithelium.* The term *germinal* is misleading because the epithelial cells of this layer do not give rise to ova. Deep to the surface layer of epithelial cells is a tough gray-white connective tissue layer called the *tunica albuginea* that covers the **ovarian cortex.** Scattered throughout and embedded in the connective tissue matrix of the cortex are

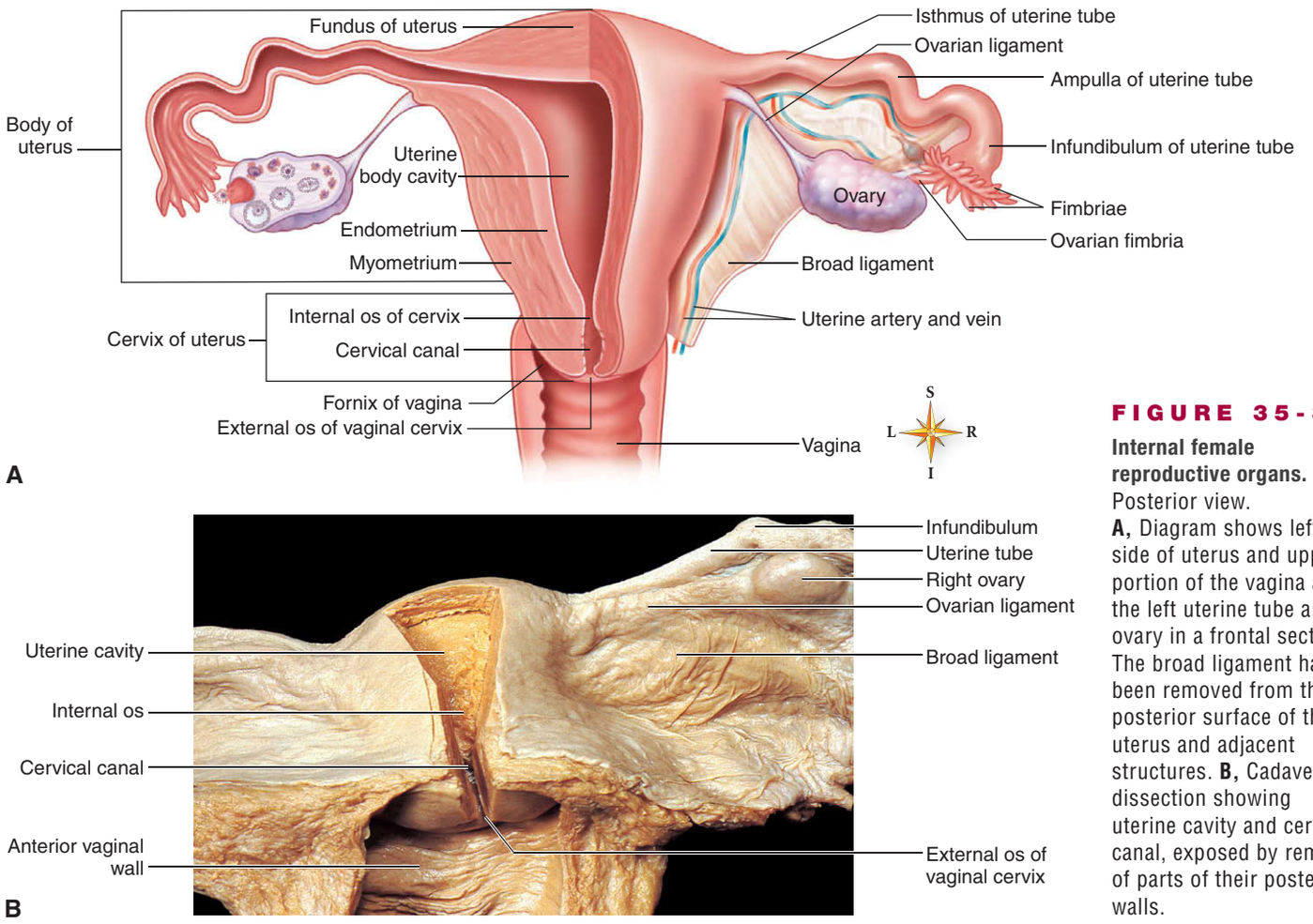


FIGURE 35-3

Internal female reproductive organs. Posterior view. **A,** Diagram shows left side of uterus and upper portion of the vagina and the left uterine tube and ovary in a frontal section. The broad ligament has been removed from the posterior surface of the uterus and adjacent structures. **B,** Cadaver dissection showing uterine cavity and cervical canal, exposed by removal of parts of their posterior walls.

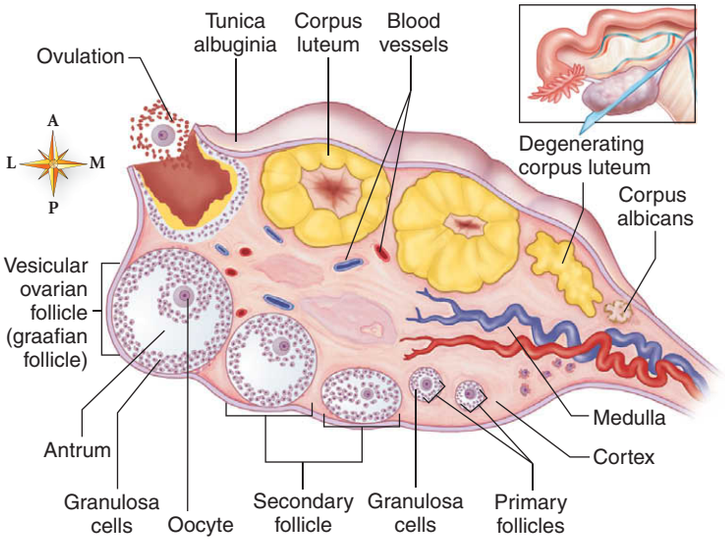


FIGURE 35-4

Stages of ovarian follicle development. Artist's rendition shows the successive stages of ovarian follicle and oocyte development. Begin with the first stage (primary follicle) and follow around clockwise to the final stage that is labeled *degenerating corpus luteum.* Remember, however, that all the stages shown occur over time to a *single* follicle, and the presence of all these stages at a single point in time is an artificial construct for learning purposes only.

thousands of microscopic structures called **ovarian follicles.** Ovarian follicles contain the immature female sex cells, or *oocytes*, and their surrounding cells. After puberty, the oocytes and the specialized cells that surround them are present in varying stages of development. The **ovarian medulla** contains supportive connective tissue cells, blood vessels, nerves, and lymphatics.

Refer to Figure 35-4, and trace the development of a female sex cell from its most primitive state through ovulation. Figure 35-5 shows more detail of the structural differences that appear during follicle maturation. Throughout the process the oocyte grows in size. So, too, does the number of cell layers surrounding it.

Initially, the primary follicle is surrounded by a single layer of *granulosa cells.* As maturation proceeds, the number of granulosa cell layers increases and the cells begin secreting increasing amounts of an estrogen-rich fluid that pools around the oocyte in a space called an *antrum.* The outer layer of granulosa cells in a developing follicle condenses into a layer of *theca cells* (Figure 35-5, A). The theca cell layer soon separates into an outer layer, or *theca externa*, which transforms into a fibrous capsule surrounding the follicle and a *theca interna* layer of cells, which secrete a precursor androgen hormone that granulosa cells ultimately convert into additional estrogen. As the primary follicle matures into a secondary, then eventually into a mature *vesicular ovarian follicle* or **graafian follicle,** a clump of granulosa cells called *cumulus cells* attaches the oocyte to the follicle wall when it is surrounded by fluid in the antrum. This mass of cells continues to cover the mature *ovum*, as it is called, after its release from the follicle. Cumulus cells secrete progesterone, which helps attract sperm cells toward the ovum and promotes sperm motility.

The developing oocyte also secretes the *zona pellucida* (ZP) (see Figure 35-5), a clear gel-like matrix that coats the ovum (underneath the cumulus cells).

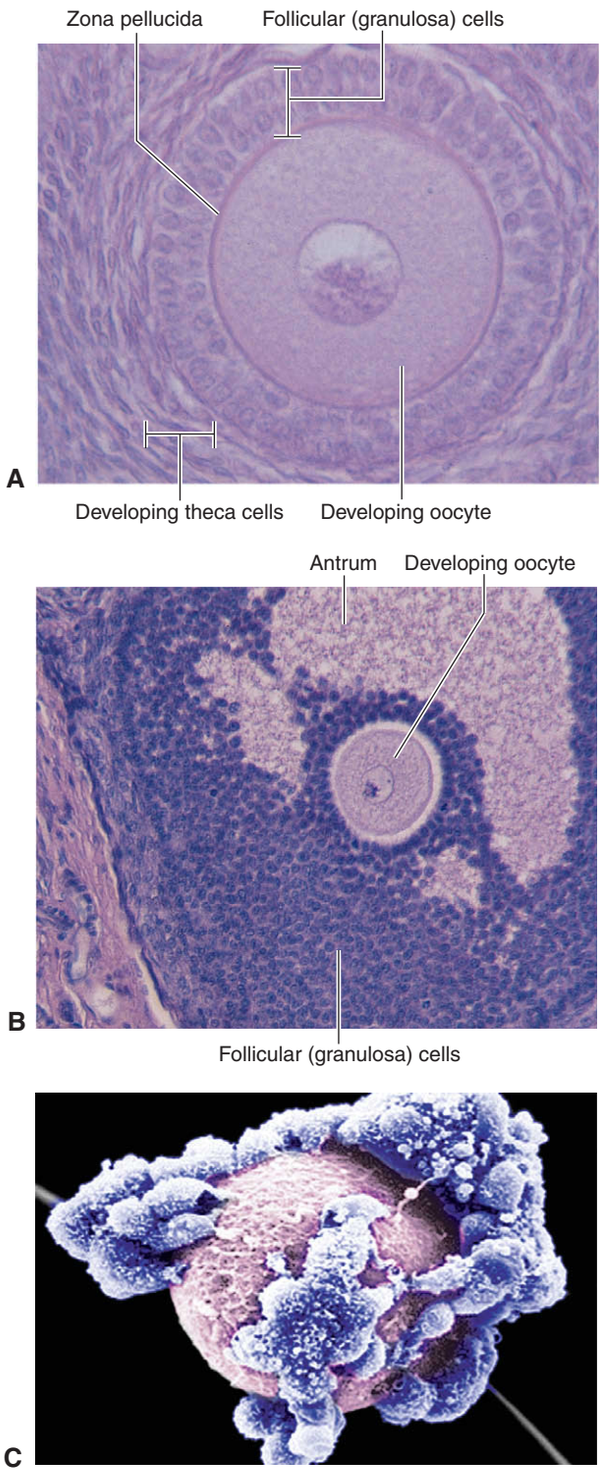


FIGURE 35-5

Developing ova. Female gametes mature within follicles in the outer region of an ovary. Follicles in early stages of development, **A,** and late stages of development, **B,** exhibit a developing oocyte (immature ovum) surrounded by hormone-secreting follicular (granulosa) cells. Notice that the more mature ovarian follicle in **B** has a fluid-filled cavity called the *antrum.* At ovulation, a mature ovum, **C,** is released. The fibers of the gel-like zona pellucida (ZP) can be seen coating the ovum, which also has many cumulus cells clinging to it. At ovulation, the ovum typically has a mass of about 20,000 cumulus cells that slowly slough away.

Box 35-1 | FYI

Mittelschmerz

A few women experience pain within a few hours after ovulation. This is referred to as **mittelschmerz**—German for "middle pain" and generally occurs during days 14 to 16 in a 28-day cycle. It has been ascribed to irritation of the peritoneum by hemorrhage from the ruptured follicle.

The release of an ovum at the end of oogenesis is an event called **ovulation.** When ovulation occurs, blood hemorrhages from the highly vascular theca interna cell layer and fills the antrum. A small quantity of blood may also enter the peritoneal cavity and irritate its pain-sensitive surface, causing the transient lower abdominal pain many women experience at the time of ovulation (Box 35-1). The blood clot filling the antrum, sometimes called the *corpus hemorrhagicum*, is soon replaced by proliferating granulosa and theca interna cells to form a yellow body called the **corpus luteum.** The corpus luteum secretes the hormones progesterone, inhibin, relaxin, and limited amounts of estrogen. Progesterone and inhibin, a peptide hormone, suppress follicle-stimulating hormone (FSH) secretion and prevent the continued development of new follicles during the functional life of the corpus luteum. The small amounts of relaxin secreted by the corpus luteum each month help "quiet" or "calm" uterine contractions, thus improving the chances for successful implantation if fertilization should occur. If pregnancy does occur, larger amounts of these hormones continue to be produced by the placenta.

Functions of the Ovaries

Recall that the ovaries are considered to be the essential organs of the female reproductive system. This means that it is the ovaries that produce female gametes, or ova. The process that culminates in the release of an ovum is called *oogenesis*, a term that literally means "egg production." As Figure 35-4 shows, ovulation involves the rupture of an ovarian follicle and the subsequent release of fluid and an ovum. The ovum, surrounded by a coat of follicular cells, moves into the uterine tube, where it may draw a sperm cell into it and thus become the first cell of an offspring.

The ovaries are also endocrine organs, secreting the female sex hormones. **Estrogens** (chiefly estradiol and estrone) and **progesterone** are secreted by cells of ovarian tissues. These hormones help regulate reproductive function in the female—making the ovaries even more essential to female reproductive function.

More details of oogenesis and fertilization are discussed in Chapter 36. Further discussion of hormonal regulation of reproductive functions, as well as associated changes within the ovaries, appears later in this chapter.

| QUICK CHECK |

3. Briefly describe the location of the ovaries.
4. What are ovarian follicles?
5. List the two major functions of the ovaries.

UTERUS

Structure of the Uterus

SIZE AND SHAPE OF THE UTERUS

In a woman who has never been pregnant, the **uterus** is pear shaped and measures approximately 7.5 cm (3 inches) in length, 5 cm (2 inches) in width at its widest part, and 3 cm (1 inch) in thickness. Note in Figure 35-3 that the uterus has two main parts: a wide, upper portion, the **body,** and a lower, narrow "neck," the **cervix.** Did you notice that the body of the uterus rounds into a bulging prominence above the level at which the uterine tubes enter? This bulging upper component of the body is called the **fundus.**

LOCATION OF THE UTERUS

The uterus is located in the pelvic cavity between the urinary bladder in front and the rectum behind. Age, pregnancy, and distention of related pelvic viscera such as the bladder alter the position of the uterus (see Figure 35-1).

Between birth and puberty the uterus descends gradually from the lower abdomen into the true pelvis. At **menopause** the uterus begins a process of involution that results in a decrease in size and a position deep in the pelvis. Some variation among women in uterine placement within the pelvis is common.

POSITION OF THE UTERUS

Normally the uterus is said to be *anteflexed* between the body and cervix, with the body lying over the superior surface of the bladder, pointing forward and slightly upward (see Figure 35-1). The cervix points downward and backward from the point of flexion, joining the vagina at approximately a right angle (Figure 35-6). Protrusion of the cervix into the lumen of the vagina creates corner spaces called the **anterior fornix** and **posterior fornix** (see Figure 35-6). These corners help increase the probability of reproductive success (fertilization) by retaining and pooling seminal fluid for a brief period following intercourse near the external os—especially if the female remains in a supine position with knees flexed. This in turn helps increase the numbers of spermatozoa that enter the uterus and, ultimately, the uterine tubes where fertilization occurs. Several ligaments hold the uterus in place but allow its body considerable movement, a characteristic that often leads to malpositions of the organ. Fibers from several muscles that form the pelvic floor (see Figure 11-15, p. 321) converge to form a node called the **perineal body** (see Figure 35-2), which also serves an important role in support of the uterus.

The uterus may lie in any one of several abnormal positions. A common one is *retroflexion*, or backward tilting, of the entire organ. Retroflexion may allow the uterus to prolapse, or descend, into the vaginal canal.

Eight *uterine ligaments* (three pairs, two single ones) hold the uterus in its normal position by anchoring it in the pelvic cavity. These ligaments include the broad (paired), uterosacral (paired), posterior (single), anterior (single), and round (paired) ligaments. Six of these so-called ligaments are actually extensions of the parietal peritoneum in different directions. The round ligaments are fibromuscular cords. Many of the structures listed on the next page can be identified in Figures 35-1 and 35-3.

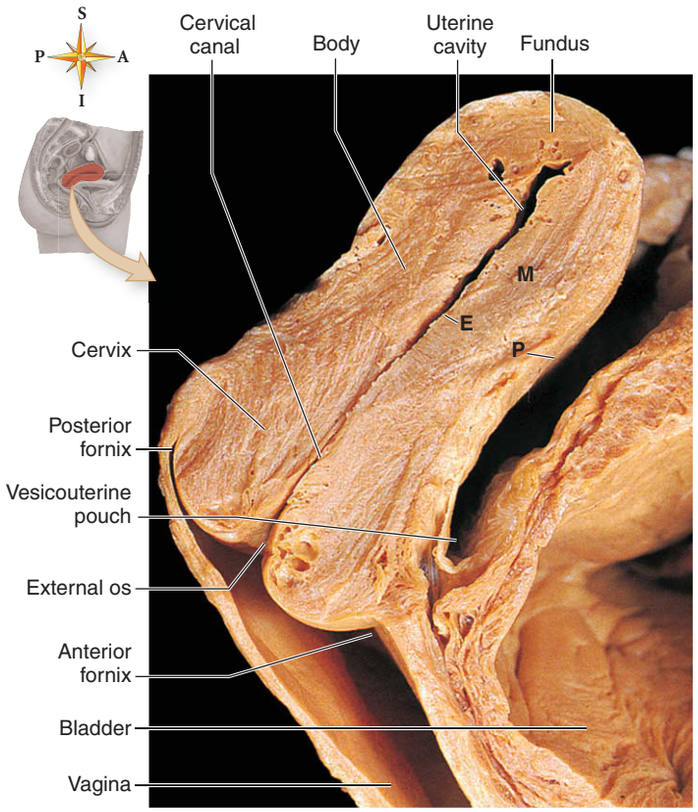


FIGURE 35-6

Uterus and vagina in sagittal section. Note that (1) the body of the uterus is "anteflexed" over the superior surface of the bladder pointing forward and slightly upward, and (2) the cervix protrudes into the vagina at approximately a right angle. *E,* Endometrium; *M,* myometrium; *P,* perimetrium.

- The *two* **broad ligaments** are double folds of parietal peritoneum that form a kind of partition across the pelvic cavity. The uterus is suspended between these two folds.
- The *two* **uterosacral ligaments** are foldlike extensions of the peritoneum from the posterior surface of the uterus to the sacrum, one on each side of the rectum.
- The **posterior ligament** is a fold of peritoneum extending from the posterior surface of the uterus to the rectum. This ligament forms a deep pouch posteriorly known as the **rectouterine pouch (of Douglas),** between the uterus and rectum. Because this is the lowest point in the pelvic cavity, pus collects here when pelvic inflammations develop. To secure drainage, an incision may be made at the top of the posterior wall of the vagina. The procedure is called a *posterior colpotomy.*
- The **anterior ligament** is the fold of peritoneum formed by the extension of the peritoneum on the anterior surface of the uterus to the posterior surface of the bladder. This fold is located anteriorly and forms the **vesicouterine pouch,** which is less deep than the rectouterine pouch (see Figures 35-1 and 35-6).
- The *two* **round ligaments** are fibromuscular cords extending from the upper, outer angles of the uterus through the inguinal canals and terminating in the labia majora.

WALL OF THE UTERUS

Three layers compose the walls of the uterus: the inner endometrium, a middle myometrium, and an outer incomplete layer of parietal peritoneum.

Endometrium

The lining of mucous membrane, called the **endometrium,** is composed of three layers of tissues:

1. *Compact layer*—a compact surface layer of partially ciliated, simple columnar epithelium
2. *Spongy layer*—a spongy middle, or intermediate, layer of loose fibrous connective tissue; also called *functional layer*
3. *Basal layer*—a dense inner layer that attaches the endometrium to the underlying myometrium.

During menstruation and after delivery of a baby, the compact and spongy layers slough off. The endometrium varies in thickness from 0.5 mm just after the menstrual flow to about 5 mm near the end of the endometrial cycle.

The endometrium has a rich supply of blood capillaries, as well as numerous exocrine *uterine glands* that secrete mucus and other substances onto the endometrial surface. The mucous glands in the lining of the cervix produce mucus that changes in consistency during the female reproductive cycle. Most of the time, cervical mucus acts as a barrier to sperm. Around the time of ovulation, however, cervical mucus becomes more slippery and actually facilitates the movement of sperm through the cervix and into the body of the uterus.

Myometrium

The **myometrium** is the thick, middle layer of the uterine wall. It consists of three layers of smooth muscle fibers that extend in all directions, longitudinally, transversely, and obliquely, and give the uterus great strength. The bundles of smooth muscle fibers interlace with elastic and connective tissue components and generally blend into the endometrial lining with no sharp line of demarcation between the two layers. The myometrium is thickest in the fundus and thinnest in the cervix—a good example of the principle of structural adaptation to function. To expel a fetus, that is, move it down and out of the uterus, the fundus must contract more forcibly than the lower part of the uterine wall, and the cervix must be stretched or dilated.

Perimetrium

The **perimetrium** is an external layer of serous membrane. The uterus is *retroperitoneal*; therefore this membrane is part of the *parietal peritoneum.* It is incomplete because it covers none of the cervix and only part of the body (all except the lower one fourth of its anterior surface). The fact that the entire uterus is not covered with peritoneum has clinical significance because it makes it possible to perform operations on this organ without the same risk of infection that occurs in procedures that cut through the peritoneum.

CAVITIES OF THE UTERUS

The cavities of the uterus are small because of the thickness of its walls (see Figure 35-3). The cavity of the body is flat and

triangular. Its apex is directed downward and constitutes the **internal os,** which opens into the **cervical canal.** The cervical canal is constricted on its lower end also, forming the **external os,** which opens into the vagina. The uterine tubes open into the cavity of the uterine body at its upper, outer angles.

BLOOD SUPPLY OF THE UTERUS

The uterus receives a generous supply of blood from uterine arteries, branches of the internal iliac arteries (see Figure 35-3). In addition, blood from the ovarian and vaginal arteries reaches the uterus by anastomosis with the uterine vessels. Tortuous arterial vessels enter the layers of the uterine wall as arterioles and then break up into capillaries between the endometrial glands.

Uterine, ovarian, and vaginal veins return venous blood from the uterus to the internal iliac veins.

Functions of the Uterus

The uterus, or womb, has many functions important to successful reproductive function. The uterus serves as part of the female reproductive tract, permitting sperm from the male to ascend toward the uterine tubes. If fusion of gametes (*fertilization*, or *conception*) occurs, the developing offspring implants in the endometrial lining of the uterus and continues its development during the term of pregnancy (*gestation*). The tiny endometrial glands produce nutrient secretions—sometimes called "uterine milk"—to sustain the developing offspring until a *placenta* can be produced. The placenta is a unique organ that permits the exchange of materials between the offspring's blood and the maternal blood. The rich network of endometrial capillaries promotes efficiency of this exchange function. Rhythmic contractions of the myometrium are inhibited during gestation but are allowed to occur as the time of delivery approaches. Myometrial contractions are the "labor contractions" that help push the offspring out of the mother's body.

If conception or the implantation of the offspring does not occur successfully, the outer layers of the endometrium are shed during *menstruation*. **Menstruation** is a regular event of the female reproductive cycle that permits the endometrium to renew itself in anticipation of conception and implantation during the next cycle. The myometrial contractions seem to aid menstruation by promoting the complete sloughing of the outer endometrial layers. Fatigue of the myometrial muscle tissues may contribute to the abdominal cramping sometimes associated with menstruation.

UTERINE TUBES

The uterine tubes are also sometimes called *fallopian tubes*, or *oviducts*.

Location of the Uterine Tubes

The uterine tubes are about 10 cm (4 inches) long and are attached to the uterus at its upper outer angles (see Figures 35-1 and 35-3). They lie in the upper free margin of the broad ligaments and extend upward and outward toward the sides of the pelvis and then curve downward and backward.

Structure of the Uterine Tubes

WALL OF THE UTERINE TUBES

The same three layers (mucous, smooth muscle, and serous) of the uterus compose the tubes (Figure 35-7). The mucosal lining of the tubes, however, is directly continuous with the peritoneum lining the pelvic cavity. This has great clinical significance because the tubal mucosa is also continuous with that of the uterus and vagina and therefore often becomes infected by gonococci or other organisms introduced into the vagina. Inflammation of the tubes **(salpingitis)** may readily spread to become inflammation of the peritoneum **(peritonitis),** a serious condition. Inflammation of the uterine tubes may also lead to scarring and partial or complete closure of the lumen, even if the original infection is cured with antibiotics (see Mechanisms of Disease, p. 1086). In the male, there is no such direct route by which microorganisms can reach the peritoneum from the exterior.

DIVISIONS OF THE UTERINE TUBES

Each uterine tube consists of three divisions (see Figure 35-3):

1. A medial third that extends from the upper outer angle of the uterus called the **isthmus.**
2. An intermediate dilated portion called the **ampulla** that follows a winding path over the ovary.
3. A funnel-shaped terminal component called the **infundibulum** that lies just above and extends laterally over the ovary and opens directly into the peritoneal cavity. The open outer margin of the infundibulum resembles a fringe in its irregular outline. The fringelike projections are known as **fimbriae** (see Figure 35-3). The *ovarian fimbria* is the only one of the fimbriae of each uterine tube that actually attaches directly to the ovary, helping anchor the distal end of the tube in place.

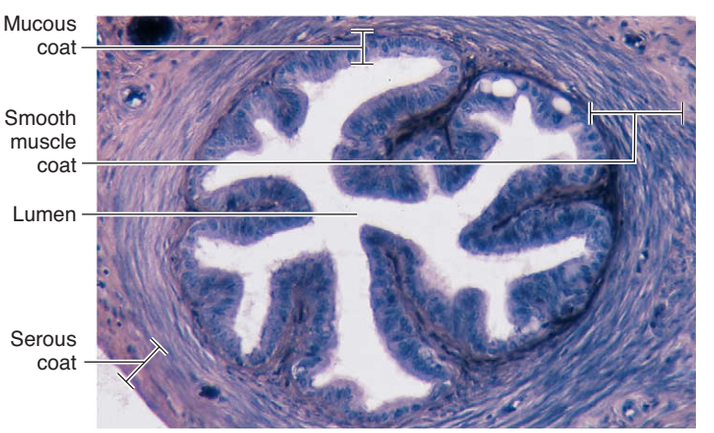


FIGURE 35-7

Transverse section of uterine tube. This micrograph shows a section of the uterine (fallopian) tube in the isthmus region. Notice the highly folded nature of the epithelial, mucous lining of the tube. The folding is even more exaggerated in the ampulla region.

HISTOLOGY OF THE UTERINE TUBES

Figure 35-7 is a low-power micrograph that illustrates the mucosal lining of the oviduct cut in cross section. These shapes are typical of the appearance of the mucosal lining throughout most of the duct. Note the extensive folds of mucosa that project as shelves into the lumen of the tube. An area of smooth muscle (muscularis layer) can be seen surrounding the mucosa in this section. Cilia, which are important in maintaining currents within the tube that move the ovum toward the uterus, can be seen projecting from the luminal surface in Figure 35-8.

Function of the Uterine Tubes

The uterine tubes are extensions of the uterus that communicate loosely with the ovaries. This arrangement allows an ovum released from the surface of the ovary to be collected by the fimbriae and swept along the uterine tube toward the body of the uterus by ciliary action. The uterine tubes serve as more than mere transport channels, however. The uterine tube is also the site of fertilization. Sperm and ova most often meet, and fertilization occurs, in the ampulla of the uterine tube. A relatively small number of the sperm deposited in the vagina during sexual intercourse move up the uterine tube, where they meet the ovum traveling toward them. It is generally there, within the ampulla of the uterine tube, that the primary function of human sexual reproduction occurs: recombination of the genetic information from both parents in the first cell of the offspring. Totally blocking the openings into either the distal (abdominal) or proximal (uterine) ends of both uterine tubes, for any reason, results in sterility (Box 35-2).

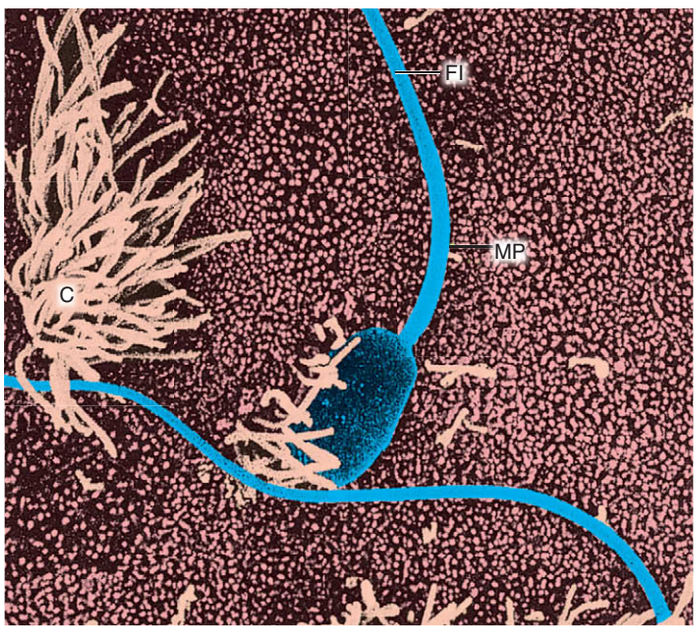


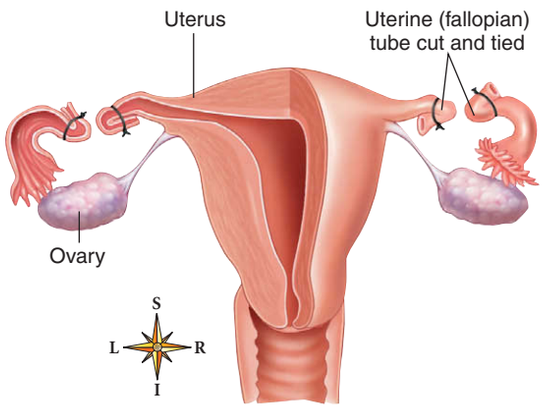
FIGURE 35-8

Luminal surface of the uterine tube. This scanning electron micrograph shows the surface of the uterine tube wall that faces the lumen, as well as some spermatozoa that are present (Fl, flagellum; MP, midpiece). The smaller, raised projections are microvilli, and the larger projections, found in clumps, are cilia (C).

Box 35-2 | FYI

Tubal Ligation

Tubal ligation literally means "tying a tube," and thus this surgical procedure is often referred to as "having one's tubes tied." Tubal ligation involve tying a piece of suture material around each uterine tube in two places, then cutting each tube between these two points (see the figure). Other methods using clips or bands instead of cutting and tying the tubes are also used. Because sperm and eggs are thus blocked from meeting, fertilization and subsequent pregnancy are prevented. For this reason, tubal ligation is also called *surgical sterilization* and is functionally comparable to vasectomy in the male. However, vasectomy can be done under local anesthetic in a medical office and therefore is a minor procedure when compared to tubal ligation.



Tubal Ligation

| QUICK CHECK |

6. Name the three principal layers of the uterine wall.
7. Describe the anatomical position of the uterus. How is it held in place?
8. List the chief functions of the uterus.
9. What are the functions of the uterine (fallopian) tubes?

VAGINA

Location of the Vagina

The vagina is a tubular organ situated between the rectum, which lies posterior to it, and the urethra and bladder, which lie anterior to it (see Figure 35-6). It extends upward and backward from its external orifice in the vestibule between the labia minora of the vulva to the cervix (see Figures 35-1, 35-2, and 35-3).

The right and left *levator ani* muscles (Figure 11-15, p. 307, and Figure 31-8, p. 975) unite at the midline to form a

hammock-shaped muscular sheet often referred to as the "floor of the pelvis." In the female, the anatomical relationships between the various parts of this supportive muscular sheet and the perineal body, vagina, rectum, and urethra have clinical significance. Fibers of the levator ani insert into and become a part of all these structures.

It is not an uncommon occurrence for at least some fibers of the levator ani to become stretched or damaged in women who have experienced vaginal delivery of a full-term infant. The unfortunate result is often the appearance of a number of troublesome and often chronic symptoms. For example, damage to muscle fibers of the levator ani that constitute a part of the urethral or anal sphincters may result in urinary or fecal *incontinence*. If leakage of urine or fecal material following damage to the sphincter is associated with—or precipitated by—an increase in abdominal pressure caused by events such as coughing, laughing, or lifting weight, the condition is called *stress incontinence*.

When muscle fibers in the vagina or perineal body are significantly weakened, the vaginal walls will lose tone and the important role of the perineal body in providing support of pelvic viscera will be affected. The result may involve prolapse of the uterus into the vagina or some degree of rectal prolapse through the anus. In severe cases surgery or other treatments may be required to raise or support the pelvic floor or to repair structural damage. However, in less severe cases where symptoms are limited to occasional leakage of urine, many women benefit from a noninvasive treatment option called *Kegel exercise*. Designed primarily to reduce urinary stress incontinence, Kegel exercises consist of an ongoing exercise program that involves a repetitive series of voluntary contractions of the muscles of the pelvic floor and perineum, similar to that required to stop the flow of urine when voiding. In time, the exercise program will strengthen the external urethral sphincter and improve retention of urine.

Structure of the Vagina

The vagina is a collapsible tube about 7 or 8 cm (about 3 inches) long that is capable of great distention. It is composed mainly of smooth muscle and is lined with mucous membrane arranged in rugae. The vaginal mucosa contains numerous tiny exocrine mucous glands that secrete lubricating fluid during the female sexual response. Box 35-3 discusses the "G spot" on the anterior wall of the vagina.

Note that the anterior wall of the vagina is shorter than the posterior wall because of the way the cervix protrudes into the uppermost portion of the tube (see Figures 35-1 and 35-6). In some cases—especially in young girls—a fold of mucous membrane, the **hymen,** forms a border around the external opening of the vagina, partially closing the orifice. Occasionally, this structure completely covers the vaginal outlet, a condition referred to as **imperforate hymen.** Perforation must be performed at puberty before the menstrual flow can escape.

Functions of the Vagina

The **vagina** is a portion of the female reproductive tract that has several important functions. During sexual intercourse, the lining of the vagina lubricates and stimulates the glans penis, which in turn triggers the ejaculation of semen. Thus the vagina also serves as a receptacle for semen, which often pools in the anterior or posterior fornix of the vagina where it meets the cervix of the uterus (see Figure 35-6). Sperm within the semen may move further into the female reproductive tract by "climbing" along fibrous strands of mucus in the cervical canal.

The vagina also serves as the lower portion of the birth canal. At the time of delivery, the offspring is pushed from the body of the uterus, through the cervical canal, and finally through the vagina and out of the mother's body. The placenta, or "afterbirth," is also expelled through the vagina.

Another important function of the vagina is transport of blood and tissue shed from the lining of the uterus during menstruation.

VULVA

Structure of the Vulva

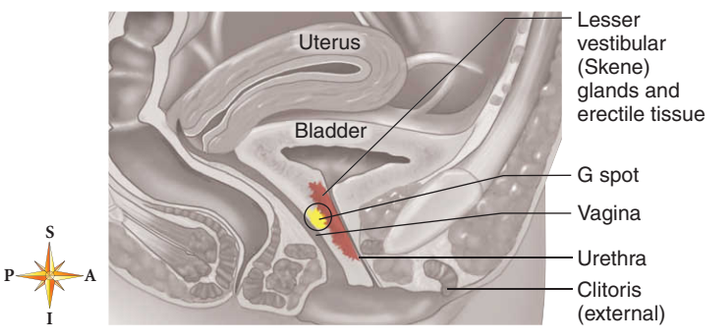
Figure 35-9, *A*, shows the structures that, together, constitute the female external genitals (reproductive organs). Collectively, these structures are called the **vulva** or *pudendum*. They are described in the following paragraphs.

Box 35-3 | FYI

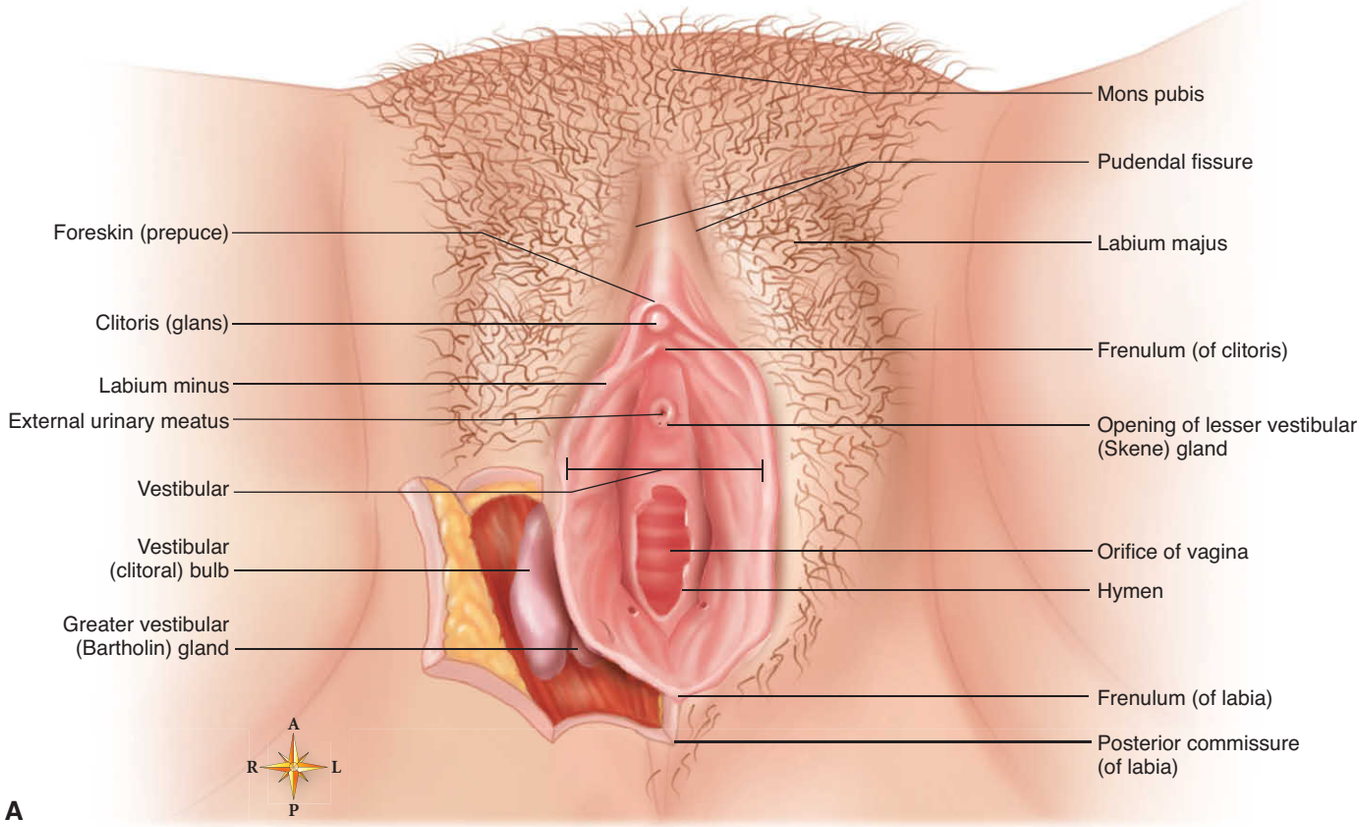
The "G Spot"

In 1950, Dr. Ernest Gräfenberg described what he called an "erotic zone" about the size of a dime on the anterior wall of the vagina midway between the pubic symphysis and cervix (see figure). The area was later named the "Gräfenberg spot," or "G spot." In fact, this was a rediscovery of the "prostatae" in female anatomy originally described by Dutch anatomist Regnier de Graaf in 1672.

The G spot is located at the site of the spongy lesser vestibular (Skene) glands and nearby erectile tissue between the wall of the vagina and the urethra. This set of structures is now often called the *female prostate*. Not all women seem to have the same amount of glandular tissue and not all are equally sensitive in this area of the vaginal wall, so the concept of a G spot continues to be controversial among scientists.



G spot (female prostate).



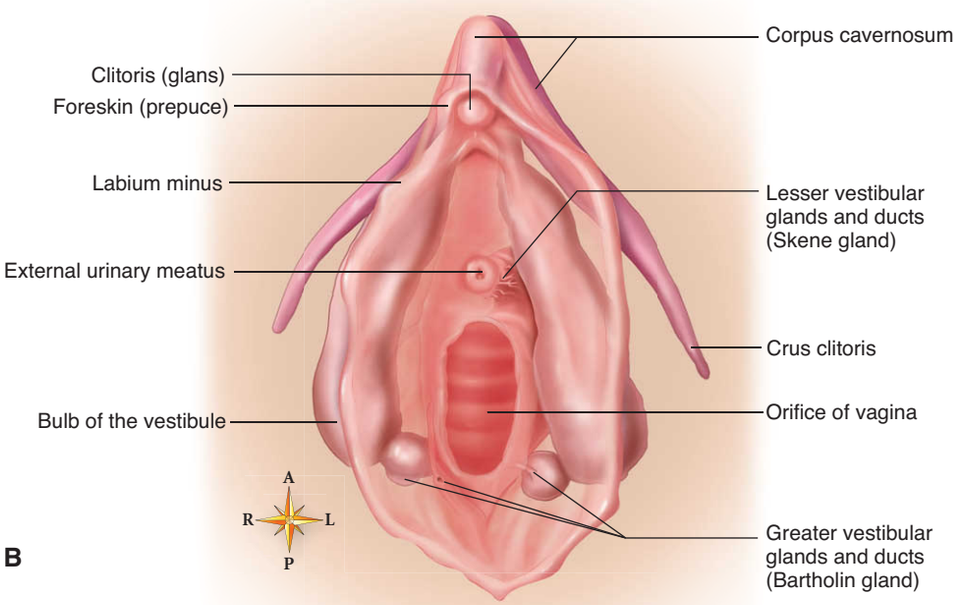


FIGURE 35-9

Vulva (pudendum). A, Sketch showing major features of the external female genitals (genitalia). Compare to Figure 35-2 on p. 1065). **B,** Sketch showing the full structure of the clitoris, which in life is mostly hidden by overlying external tissue.

The **mons pubis** is a skin-covered pad of fat over the pubic symphysis. Coarse pubic hairs appear on this structure at puberty and persist throughout life.

The **labia majora** (Latin, "large lips") are covered with pigmented skin and hair on the outer surface and are smooth and free from hair on the inner surface. Each labium majus is composed mainly of fat and connective tissue with numerous sweat and sebaceous glands on the inner surface. The labia majora are homologous to the scrotum in the male.

The **labia minora** (Latin, "small lips") are located medial to the labia majora. Each labium minus is covered with hairless skin. The two labia minora come together anteriorly in the midline. The area between the labia minora is the **vestibule.**

The **clitoris** is composed of erectile tissue, just a portion of which is visible just behind the junction of the labia minora. The structure of this organ is homologous to penile structure in the male. Look again at Figure 34-11 on p. 1052, and compare the erectile tissues of the penis in that illustration with the sketch

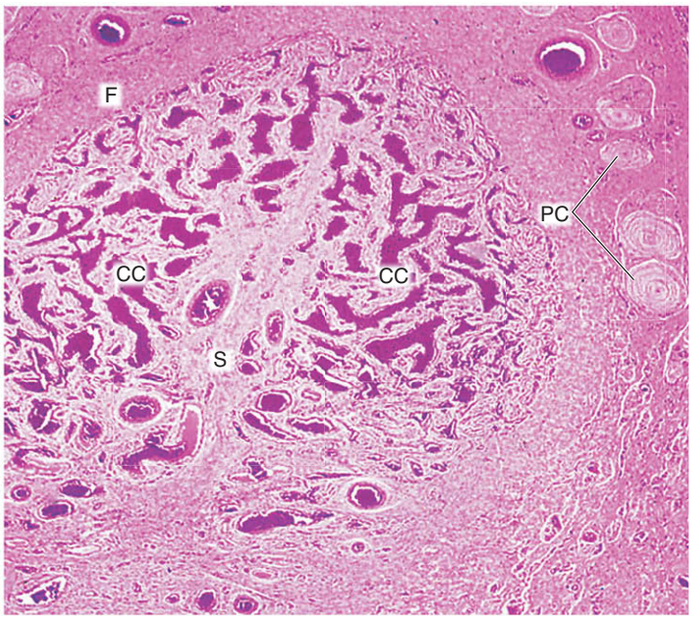


FIGURE 35-10

Micrograph of clitoris. Note the two corpora cavernosa *(CC)* separated by an incomplete central septum *(S)*. Sectioned lamellar (Pacini) corpuscles *(PC)* are visible just outside the surrounding fibrocollagenous sheath *(F)*. (Compare with Figure 34-14, B, on p. 1054.)

of the clitoris shown in Figure 35-9, *B*. The micrograph of the clitoris in Figure 35-10 shows a similar "spongy" structure seen in the erectile tissues of the penis. Like the erectile tissue of the male, the clitoris becomes engorged with blood during the sexual response.

The *glans clitoris* is the only visible part of the erectile structures of the clitoris. The glans clitoris is equivalent to the *glans penis* in the male. The glans clitoris is covered with highly sensitive skin involved in sexual stimulation that produces the female sexual response. In the female, the corpora cavernosa are separated into an inverted Y shape. Underneath each labium majus is a *bulb (of vestibule)* that corresponds to the male corpus spongiosum.

A clitoral *foreskin* or *prepuce* forms a hood over the superior surface of the glans clitoris. On the inferior surface of the glans clitoris there is a thin midline *frenulum* that is the female equivalent of the frenulum visible on the undersurface of the glans of the penis.

The *external urinary meatus* (urethral orifice) is the small opening of the urethra, situated between the clitoris and the vaginal orifice.

The **vaginal orifice** is an opening that is larger than the urinary meatus. It is located posterior to the meatus.

The **greater vestibular glands** are two bean-shaped glands, one on each side of the vaginal orifice. Each gland opens by means of a single, long duct into the space between the hymen and the labium minus. These glands, which are also called *Bartholin glands*, are of clinical importance because they can be infected (bartholinitis or Bartholin abscess), particularly by gonococci. They are homologous to the bulbourethral glands in the male.

Opening into the vestibule near the urinary meatus by way of two small ducts is a group of tiny mucous glands, the **lesser vestibular glands.** Also called *Skene glands*, they have clinical interest because gonococci that lodge there are difficult to eradicate.

Functions of the Vulva

The various components of the external genitals of the female operate alone or separately to accomplish several functions important to successful reproduction. The protective features of the mons pubis and labia help prevent injury to the delicate tissues of the clitoris and vestibule. The clitoris becomes erect during sexual stimulation and, like the male glans, possesses a large number of sensory receptors that feed back information to the sexual response areas of the brain. In Figure 35-10, a number of sectioned lamellar (Pacini) corpuscles, encapsulated touch and pressure receptors (see Chapter 17), can be seen just outside the fibrocollagenous sheath surrounding the clitoris. Of course, the vaginal orifice serves as the boundary between the internal and external female genitals.

| QUICK CHECK |

10. List three functions of the vagina.
11. What is another name for the external genitals of the female?
12. How are the clitoris of the female and the glans penis of the male similar in structure and function?

FEMALE REPRODUCTIVE CYCLES

Recurring Cycles

Many changes recur periodically in the female during the years between the onset of the menses **(menarche)** and their cessation **(menopause,** or **climacteric).** Most obvious, of course, is menstruation—the outward sign of changes in the endometrium. Most women also note periodic changes in their breasts. But these are only two of many changes that occur over and over again at fairly uniform intervals during the approximately 3 decades of female reproductive maturity.

First we shall describe the major cyclical changes, and then we shall discuss the mechanisms that produce them.

OVARIAN CYCLE

Before a female child is born, precursor cells in her ovarian tissue, called **oogonia,** begin a type of cell division characterized as *meiosis*. Meiotic cell division differs from mitotic cell division in that it reduces the number of chromosomes in the daughter cells by half (recall Chapter 5, p. 125). By the time the child is born, her ovaries contain many primary follicles, each containing an oocyte that has temporarily suspended the meiotic process before it is complete. Once each month, on about the first day of menstruation, the oocytes within several primary follicles resume meiosis. At the same time, the follicular cells surrounding them proliferate and start to secrete estrogens (and tiny amounts of progesterone). Usually, only one of these developing follicles matures

and migrates to the surface of the ovary. Just before **ovulation,** the meiosis within the oocyte of the mature follicle halts again. It is this cell, which has not quite completed meiosis, that is expelled from the ruptured wall of the mature follicle during ovulation. Meiosis is completed only when, and if, the head of a sperm cell is later drawn into the ovum during the process of fertilization.

When does ovulation occur? This is a question of great practical importance and one that in the past was given many answers. Today it is known that ovulation usually occurs 14 days before the next menstrual period begins. (Only in a 28-day menstrual cycle is this also 14 days after the beginning of the preceding menstrual cycle, as explained subsequently.)

Immediately after ovulation, cells of the ruptured follicle enlarge and, because of the appearance of lipoid substances in them, become transformed into a golden-colored body, the **corpus luteum.** The corpus luteum grows for 7 or 8 days. During this time, it secretes progesterone in increasing amounts. Then, provided fertilization of the ovum has not taken place, the size of the corpus luteum and the amount of its secretions gradually diminish. In time, the last components of each nonfunctional corpus luteum are reduced to a white scar called the **corpus albicans,** which moves into the central portion of the ovary and eventually disappears (see Figure 35-4).

ENDOMETRIAL, OR MENSTRUAL, CYCLE

During menstruation, bits of the compact and spongy layers of the endometrium slough off, leaving denuded bleeding areas. The dark menstrual discharge generally does not clot and may vary from about 30 to 100 ml, with a majority lost during the first 3 days of the menses. As with the length of the cycle, considerable variation is considered normal. After menstruation, the cells of these layers proliferate, causing the endometrium to reach a thickness of 2 or 3 mm by the time of ovulation. During this period, endometrial glands and arterioles grow longer and more coiled—two factors that also contribute to the thickening of the endometrium. After ovulation, the endometrium grows still thicker, reaching a maximum of about 4 to 6 mm. Most of this increase, however, is believed to be caused by swelling produced by fluid retention rather than by further proliferation of endometrial cells. The increasingly coiled endometrial glands start to secrete their nutrient fluid during the time between ovulation and the next menses. Then, the day before menstruation starts again, a drop in progesterone causes muscle in the walls of the tightly coiled arterioles to constrict, producing endometrial ischemia. This leads to death of the tissue, sloughing, and once again, menstrual bleeding.

The menstrual cycle is customarily divided into phases, named for major events occurring in each: menses, postmenstrual phase, ovulation, and premenstrual phase.

1. The **menses,** or **menstrual period,** occurs on days 1 to 5 of a new cycle. There is some individual variation, however.
2. The **postmenstrual phase** occurs between the end of the menses and ovulation. Therefore it is the **preovulatory phase,** as well as the postmenstrual phase. In a 28-day cycle, it usually includes cycle days 6 to 13 or 14. However, the length of this phase varies more than the others. It lasts longer in long cycles and ends sooner in short cycles. This phase is also called the **estrogenic phase,** or **follicular phase,** because of the high blood estrogen level resulting from secretion by the developing follicle. Increases in estrogen levels cause predictable changes in the appearance, amount, and consistency of cervical mucus. Collectively, these changes can be used as a fertility sign to predict ovulation (Box 35-4). Increasing estrogen levels cause cervical mucus to become elastic, a property that can be observed by placing the mucus between and then separating two glass microscope slides. The clear, watery cervical mucus found at the time of ovulation will stretch 8 cm or more before the resulting thread will break. This phenomenon is called *spinnbarkeit* (SPIN-bahr-kit). Further, if left to dry on a clean glass slide, cervical mucus produced at or near the time of ovulation will dry in a characteristic featherlike or "fern" pattern. **Proliferative phase** is still another name for this phase because proliferation of endometrial cells occurs at this time.

Box 35-4 | FYI

Fertility Signs Used in Predicting the Time of Ovulation

Many rhythmic and recurring events that a woman may recognize on almost a monthly schedule during her reproductive years are called "fertility signs" and are manifestations of the body changes required for successful reproductive function. They include cyclical changes in the ovaries, in the amount and consistency of the cervical mucus produced during each cycle, in the myometrium, in the vagina, in gonadotropin secretion, in body temperature, and even in mood or "emotional tone." Accurately predicting the time of ovulation in any given menstrual cycle by recognizing one or more of these recurring fertility signs would obviously be of help in either avoiding or achieving conception. However, knowing the length of a previous cycle or even a series of cycles cannot ensure with any degree of accuracy the time of appearance of other fertility signs in a current cycle or how many days the preovulatory phase will last in the next or some future cycle.

Simply put, prior cycle length is not an accurate fertility sign. This fact accounts for most of the unreliability of the *calendar rhythm method* of fertility planning. Other more sophisticated *natural family planning (NFP)* methods are available that are not based on a knowledge of previous cycle lengths to predict the day of ovulation. Instead, such natural methods base their judgments about fertility at any point in a woman's cycle on other changes. For example, measurement of basal body temperature and recognition of cyclical changes in the amount and consistency of cervical mucus, both of which occur in response to changes in circulating hormones that control ovulation. Typically, use of NFP for 1 year to avoid pregnancy will result in approximately 25 of every 100 women becoming pregnant.

The time of ovulation also can be approximated by over-the-counter urine tests that detect the high levels of luteinizing hormone (LH) associated with ovulation (LH surge).



FIGURE 35-11

Ovulation. The rupture of a mature follicle on the surface of an ovary results in the release of an ovum into the pelvic cavity. This process of *ovulation* often occurs on day 14 in a 28-day menstrual cycle, but its exact timing depends on the length of the postmenstrual (preovulatory) phase. Notice in this photograph that the ovum released during ovulation is surrounded by a mass of cells.

3. **Ovulation,** that is, rupture of the mature follicle with expulsion of its ovum into the pelvic cavity (Figure 35-11), occurs most often on cycle day 14 in a 28-day cycle. However, it occurs on different days in different-length cycles, depending on the length of the preovulatory phase. For example, in a 32-day cycle the preovulatory phase probably lasts until cycle day 18, and ovulation would then occur on cycle day 19 instead of 14. In short, because the majority of women show some month-to-month variation in the length of their cycles, the day of ovulation in a current or future cycle cannot be predicted with accuracy based on the length of previous cycles (see Box 35-4). Typically, there is a decrease in basal body temperature just before ovulation and a rise in temperature at the time of ovulation. This constitutes yet another "fertility sign" (see Figure 35-14).
4. The **premenstrual phase,** or **postovulatory phase,** occurs between ovulation and the onset of the menses. This phase is also called the **luteal phase,** or more simply, the **secretory phase,** because the corpus luteum secretes only during this time. It is also called the **progesterone phase** because the corpus luteum secretes mainly this hormone. The length of the premenstrual phase is fairly constant, lasting usually 14 days—or cycle days 15 to 28 in a 28-day cycle. Differences in length of the total menstrual cycle therefore exist mainly because of differences in duration of the postmenstrual rather than of the premenstrual phase.

MYOMETRIAL CYCLE

The myometrium contracts mildly but with increasing frequency during the 2 weeks preceding ovulation. Contractions decrease or disappear between ovulation and the next menses, thereby lessening the probability of expulsion of a fertilized ovum that may have implanted in the endometrium.

GONADOTROPIC CYCLE

The adenohypophysis (anterior pituitary gland) secretes two hormones called *gonadotropins* that influence female reproductive cycles. Their names are **follicle-stimulating hormone (FSH)** and **luteinizing hormone (LH).** The amount of each gonadotropin secreted varies with a rhythmic regularity that can be related, as we shall see, to the rhythmic ovarian and uterine changes just described.

| QUICK CHECK |

13. What is the function of the corpus luteum?
14. How is the corpus luteum formed?
15. What is the difference between the ovarian cycle and the menstrual (endometrial) cycle?
16. Why is the postmenstrual phase of the menstrual cycle sometimes called the *proliferative phase?*

Control of Female Reproductive Cycles

Physiologists agree that hormones play a major role in producing the cyclical changes characteristic in women during the reproductive years. The development of a method called *radioimmunoassay* has made it possible to measure blood levels of gonadotropins. By correlating these with the monthly ovarian and uterine changes, investigators have worked out the main features of the control mechanism.

A brief description follows of the mechanisms that produce cyclical changes in the ovaries and uterus and in the amounts of gonadotropins secreted.

CONTROL OF CYCLICAL CHANGES IN THE OVARIES

Cyclical changes in the ovaries result from cyclical changes in the amounts of gonadotropins secreted by the anterior pituitary gland. An increasing FSH blood level has two effects: it stimulates one or more primary follicles and their oocytes to start growing, and it stimulates the follicular cells to secrete **estrogens.** (Developing follicles also secrete very small amounts of progesterone.) Because of the influence of FSH on follicle secretion, the level of estrogens in blood increases gradually for a few days during the postmenstrual phase. Then suddenly, on about the twelfth cycle day, it leaps upward to a maximum peak. Scarcely 12 hours after this "estrogen surge," an "LH surge" occurs and presumably triggers ovulation a day or two later. This hormone surge is the basis of the over-the-counter "ovulation test" (see Box 35-4, p. 1075). The control of cyclical ovarian changes by the gonadotropins FSH and LH is summarized in Figure 35-12. As Figure 35-12 shows, LH brings about the following changes:

1. Completion of growth of the follicle and oocyte maturation with increasing secretion of estrogens before ovulation. LH and FSH act as synergists to produce these effects.

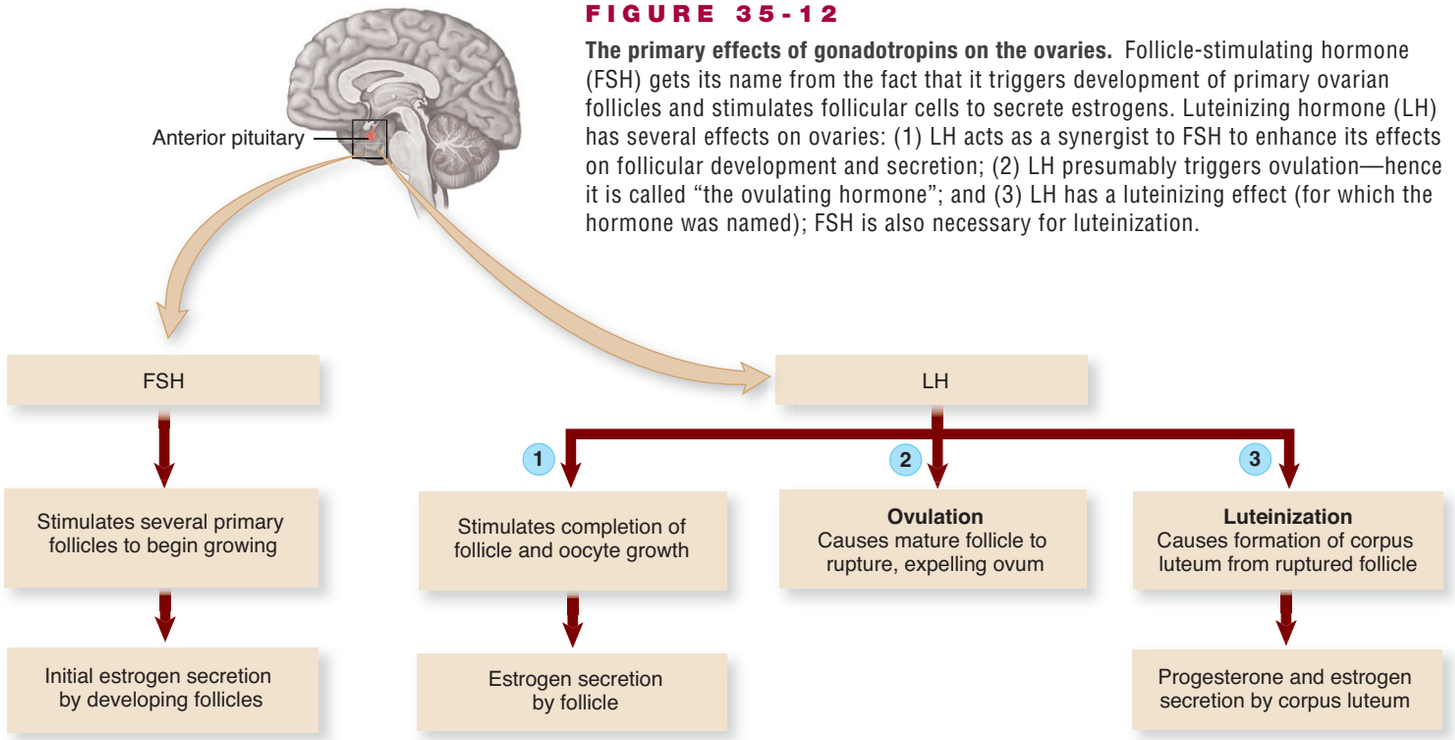


FIGURE 35-12

The primary effects of gonadotropins on the ovaries. Follicle-stimulating hormone (FSH) gets its name from the fact that it triggers development of primary ovarian follicles and stimulates follicular cells to secrete estrogens. Luteinizing hormone (LH) has several effects on ovaries: (1) LH acts as a synergist to FSH to enhance its effects on follicular development and secretion; (2) LH presumably triggers ovulation—hence it is called "the ovulating hormone"; and (3) LH has a luteinizing effect (for which the hormone was named); FSH is also necessary for luteinization.

2. Rupturing of the mature follicle with expulsion of its ovum (ovulation). Because of this function, LH is sometimes also called "the ovulating hormone."
3. Formation of a golden body, the corpus luteum, in the ruptured follicle (process called **luteinization**). The name *luteinizing hormone* refers, obviously, to this LH function—a function to which, experiments have shown, FSH also contributes.

The corpus luteum functions as a temporary endocrine gland. It secretes only during the luteal (postovulatory, or premenstrual) phase of the menstrual cycle. Its hormones are progestins (the important one of which is progesterone) and also estrogens. The blood level of progesterone rises rapidly after the "LH surge" described earlier. It remains at a high level for about a week, then decreases to a very low level approximately 3 days before menstruation begins again. This low blood level of progesterone persists during both the menstrual and the postmenstrual phases. What are its sources? Not the corpus luteum, which secretes only during the luteal phase, but the developing follicles and the adrenal cortex. Blood's estrogen content increases during the luteal phase but to a lower level than develops before ovulation.

If pregnancy does not occur, lack of sufficient LH and FSH causes the corpus luteum to regress in about 14 days. The corpus luteum is then replaced by the corpus albicans. Review Figure 35-4, which shows the cyclical changes in the ovarian follicles.

CONTROL OF CYCLICAL CHANGES IN THE UTERUS

Cyclical changes in the uterus are brought about by changing blood concentrations of estrogens and progesterone. As blood estrogens increase during the postmenstrual phase of the menstrual cycle, they produce the following main changes in the uterus:

- Proliferation of endometrial cells, producing a thickening of the endometrium
- Growth of endometrial glands and of the spiral arteries of the endometrium
- Increase in the water content of the endometrium
- Increased myometrial contractions

Increasing blood progesterone concentration during the premenstrual phase of the menstrual cycle produces progestational changes in the uterus—that is, changes favorable for pregnancy—specifically the following:

- Secretion by endometrial glands, thereby preparing the endometrium for implantation of a fertilized ovum
- Increase in the water content of the endometrium
- Decreased myometrial contractions

As mentioned earlier, low levels of FSH and LH cause regression of the corpus luteum if pregnancy does not occur. This in turn causes a drop in estrogen and progesterone levels, with the result that their maintenance of a thick, vascular endometrium ceases. Thus a drop in estrogen and progesterone levels at the end of the premenstrual phase triggers the endometrial sloughing that characterizes the menstrual phase.

CONTROL OF CYCLICAL CHANGES IN GONADOTROPIN SECRETION

Both negative and positive feedback mechanisms help control anterior pituitary secretion of the gonadotropins FSH and LH. These mechanisms involve the ovaries' secretion of inhibin,

estrogens, and progesterone and secretion of releasing hormones by the hypothalamus. Figure 35-13 describes a negative feedback mechanism that controls gonadotropin secretion. Examine it carefully. Note particularly the effects of a sustained high blood concentration of estrogens and progesterone on anterior pituitary gland secretion and the effect of a low blood concentration of FSH on follicular development: essentially, follicles do not mature and ovulation does not occur.

Several observations and animal experiments strongly suggest that sustained high blood levels of estrogens, progesterone, and inhibin decrease pituitary secretion of FSH and LH. These ovarian hormones appear to inhibit certain neurons of the hypothalamus (part of the central nervous system) from secreting gonadotropin-releasing hormone (GnRH) into the hypophyseal portal vessels (see Figure 35-13). Without the stimulating effects of these releasing hormones, the pituitary's secretion of FSH and LH decreases.

A positive feedback mechanism has also been postulated to control LH secretion. The sudden and marked increase in blood's estrogen content that occurs late in the follicular phase of the menstrual cycle is thought to stimulate the hypothalamus to secrete GnRH into the hypophyseal portal vessels. GnRH stimulates the release of LH by the anterior pituitary, which in turn accounts for the "LH surge" that triggers ovulation. The fact that a part of the brain—the hypothalamus—secretes gonadotropin-releasing hormones has interesting implications. This may be part of the pathway by which changes in a woman's environment or in her emotional state can alter her menstrual cycle. That this occurs is a matter of common observation. Stress, for example—such as intense fear of either becoming or not becoming pregnant—often delays menstruation.

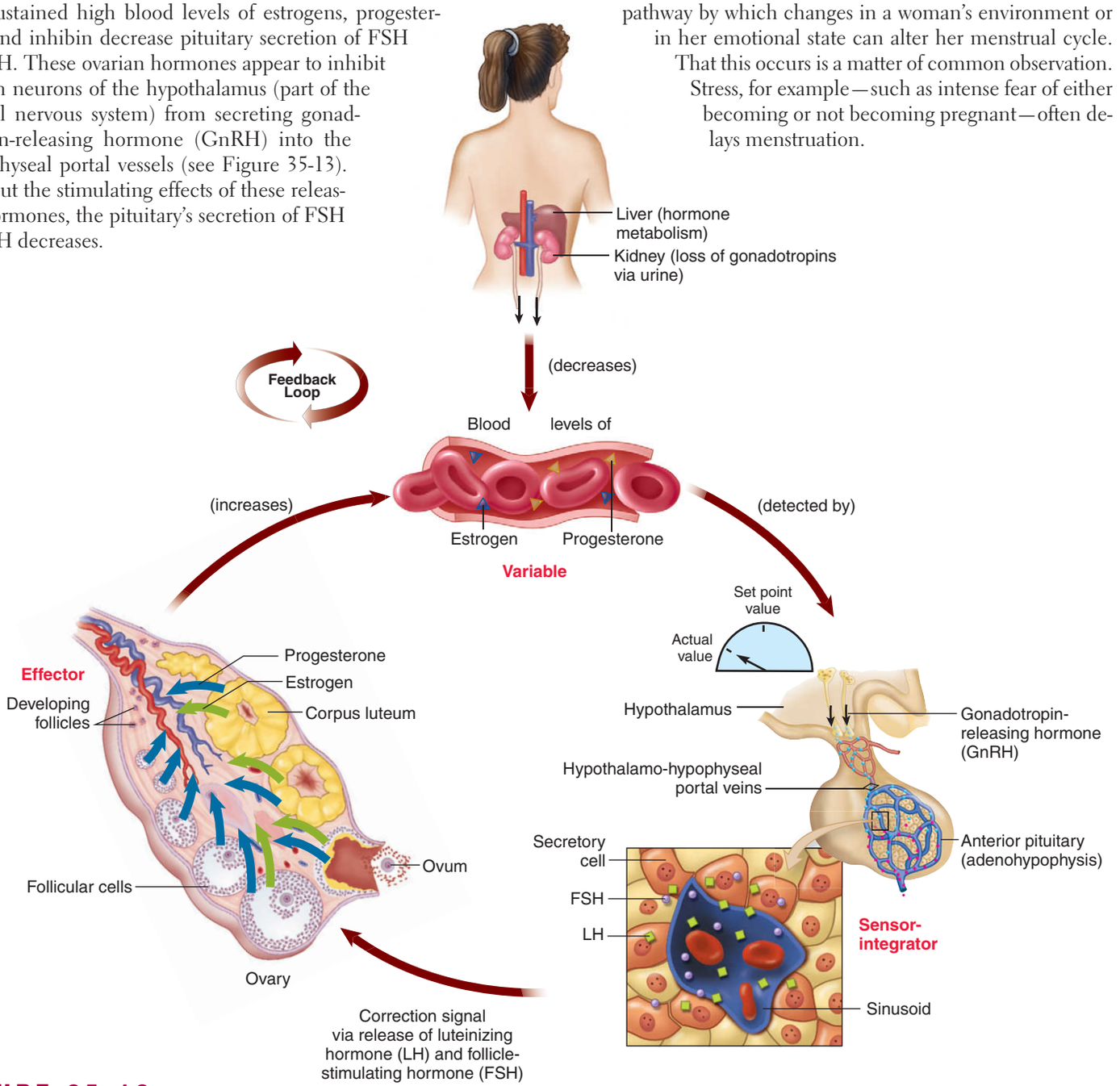


FIGURE 35-13

Control of FSH and estrogen secretion. A negative feedback mechanism controls anterior pituitary secretion of follicle-stimulating hormone (FSH) and ovarian secretion of estrogens. A high blood level of FSH stimulates estrogen secretion, whereas the resulting high estrogen level inhibits FSH secretion. How does this compare with the LH testosterone feedback mechanism in the male? (See Figure 34-7, p. 1049, if you want to check your answer.) According to the diagram, what effect does a high blood concentration of estrogens have on anterior pituitary secretion of FSH? of LH?

Importance of Female Reproductive Cycles

Several important functional roles are played by the female reproductive cycles. As Figure 35-14 shows, the changes associated with the different cycles are all closely interrelated. The primary role of the ovarian cycle, for example, is to produce an ovum at regular enough intervals to make reproductive success likely. The ovarian cycle's secondary role is to regulate the endometrial (menstrual) cycle by means of the sex hormones estrogen and progesterone. The role of the endometrial cycle, in turn, is to ensure that the lining of the uterus is suitable for the implantation of an embryo if fertilization of the ovum occurs. The constant renewal of the endometrium makes successful implantation more likely. The cyclical mechanisms of female reproductive function, and the fact that an ovum must unite with a sperm during the first 24 hours or so after ovulation to reach the uterus at the proper stage of development to implant, result in the fact that a woman is fertile

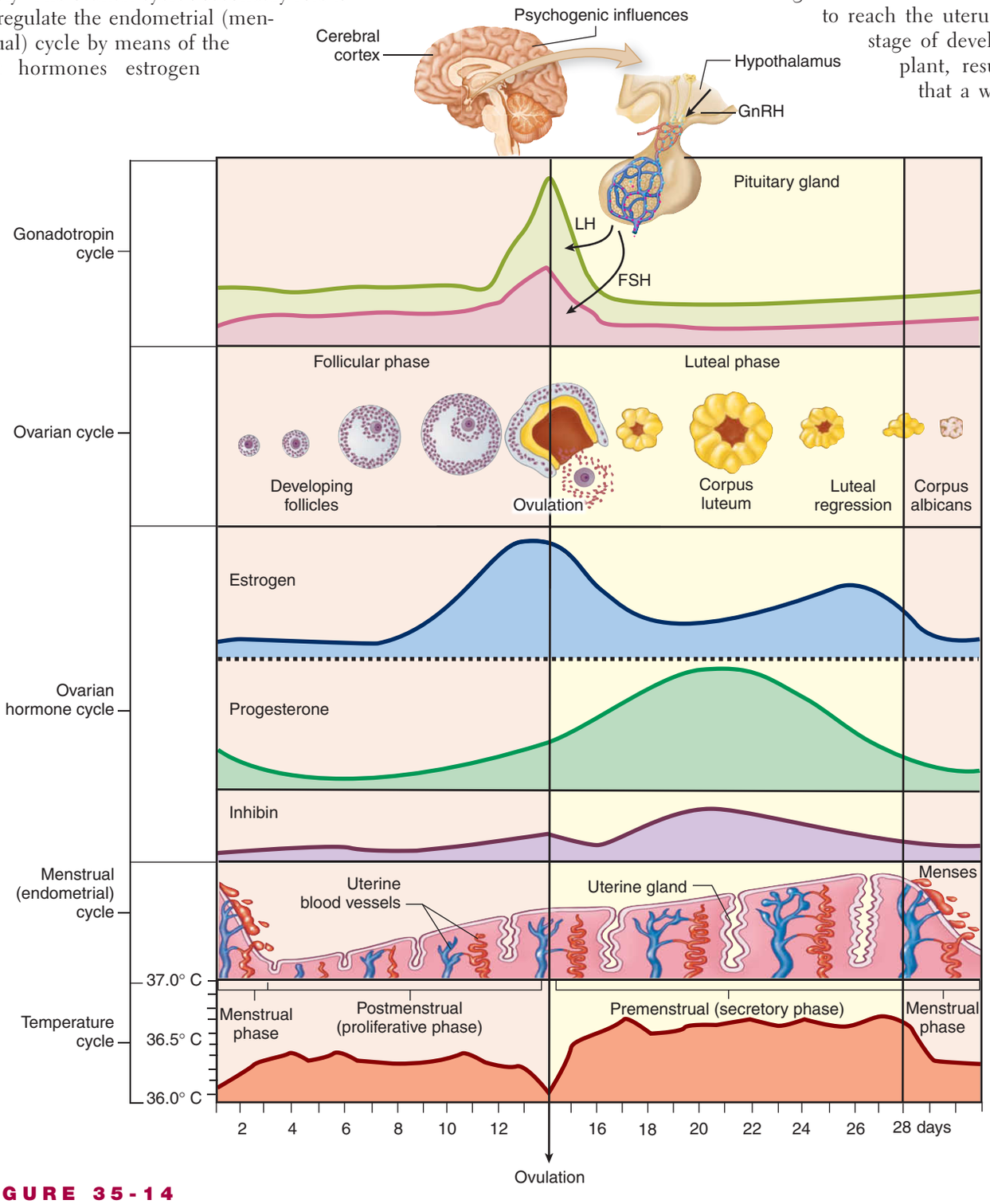


FIGURE 35-14

Female reproductive cycles. This diagram illustrates the interrelationships among the cerebral, hypothalamic, pituitary, ovarian, and uterine functions throughout a standard 28-day menstrual cycle. The variations in basal body temperature are also illustrated.

only a few days out of each monthly cycle. Human fertility is further limited by the fact that sperm usually cannot survive in the female reproductive tract for more than a few days. Such limited fertility increases the likelihood that conception will occur only when the woman's body is at its reproductive peak.

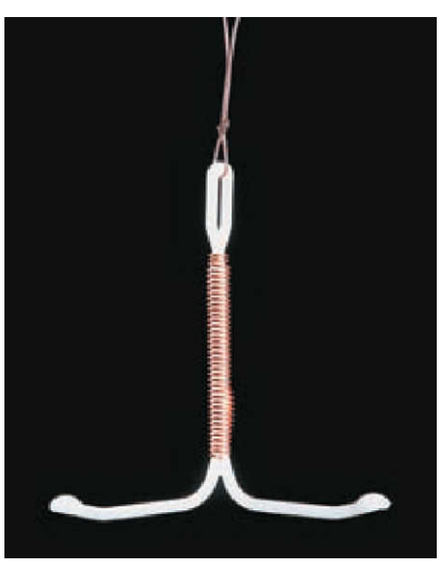
Box 35-5 discusses some common methods for managing fertility.

Box 35-5 | HEALTH matters

Methods of Contraception

Hormonal methods of contraception began with establishment of the relationship between sex hormone levels and ovulation. Continuing research in this area led to the development of **oral contraceptives**—often collectively called "the Pill." Numerous oral contraceptive products are now available that contain different types, combinations, and dosages of estrogen and progesterone. The so-called "minipill" contains only synthetic progesterone. Most hormonal contraceptives were developed to prevent pregnancy by initiating negative feedback inhibition of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretion. As a result, mature follicles do not develop, and LH levels required to initiate ovulation do not occur. The next menses, however, does take place if the progesterone and estrogen dosage is stopped in time to allow their blood levels to decrease as they normally do near the end of the cycle to bring on menstruation. For this reason, the Pill can be used to regulate the menstrual cycle, as well as prevent pregnancy. If used correctly and consistently, the pill is an extremely effective contraceptive with an unintended pregnancy rate estimated at between 0.1% and 3%. The higher percentage reflects "typical" rather than "ideal" use, and underscores the impact of human error in using any form of birth control.

In addition to oral contraceptives taken in pill form, other types of hormonal birth control "delivery mechanisms" are available in some parts of the world. They include hormone-impregnated vaginal inserts, hormone injections, transcutaneous administration using skin "patches," and surgical insertion of hormone-containing implants under the skin.



Intrauterine device (IUD)

The effects of hormonal contraceptives—indeed, of estrogens and progesterone—are much more complex than our explanation here indicates. They have widespread effects on the body quite independent of their action on the reproductive and endocrine systems and are still not completely understood. Possible side effects—some extremely serious—including stroke and heart attack, may limit or prohibit use of these birth control methods by some women. Side effects of hormonal contraceptives are especially troublesome if these products are used for extended periods, by older women, by women who smoke, and in women with blood clotting problems or cardiovascular disease. On the other hand, long-term use has also been shown to have some beneficial health effects such as protection against uterine and **ovarian cancer.**

In addition to hormonal methods of contraception, many other methods, each with differing rates of effectiveness and unique advantages and disadvantages, are available. For example, *spermicidal methods* involve use of preparations (foams, jellies, and creams) that act to kill sperm, and *mechanical barrier methods* use devices such as condoms, diaphragms, and cervical caps to block sperm from entering the uterus. So-called *surgical methods* such as tubal ligation (see Box 35-1) and male vasectomy result in permanent sterility.

An **intrauterine device** or IUD is usually a small, copper-wrapped object (pictured) inserted into the lumen of the uterine body, where it remains for months or years. IUDs trigger an inflammatory response called the *foreign body reaction,* which is toxic to sperm and probably also ova. By thus inhibiting gametes, the IUD works by preventing fertilization. Some IUDs also release progesterone and thus have an action similar to other hormonal contraceptives. A common misconception not supported by research is that IUDs work by triggering abortions.

Decision making concerning the use of contraceptive methods to regulate reproductive function involves many complex interactions that are uniquely human—and very personal. The decision to use or avoid contraception—or employ any particular contraceptive method—at any point in time is often influenced by differing medical, social, cultural, ethical, and religious factors as well as by the cost, reliability, safety, or ease of use of a particular method. Informed and thoughtful decision making regarding this human behavior is critically important. It will often be necessary for some individuals to seek out a variety of information—from different but credible and knowledgeable sources—in order to make an informed decision that is "right" for those individuals. Regardless, seeking counsel and advice from a trusted health care provider early in the process is always recommended.

Infertility and Use of Fertility Drugs

Infertility is often defined as failure to conceive after 1 year of regular unprotected intercourse. Infertility may be caused by a wide variety of medical, environmental, and even lifestyle factors, such as smoking or alcohol abuse. Causal factors may be traced to various problems in either the male or female partner, each accounting for about 40% of cases. Of the remaining 20% of affected couples, infertility in about 10% is due to problems shared by both partners and in about 10% the reason is never determined. If testing identifies the female member of the couple as infertile, she joins a subset of about 25% of women in the overall population who will experience some period of infertility during their reproductive years. In many cases, infertility results from a failure to ovulate—often caused by a medical condition such as *polycystic ovary syndrome* or *PCOS* (see Mechanisms of Disease). Significant numbers of infertile women experiencing ovulatory dysfunction desire to become pregnant and, after a sometimes long and complex medical "workup" and selection process, become candidates to receive so-called *fertility drugs*—either alone or in combination with other "assisted reproductive procedures" such as artificial insemination.

An orally administered fertility drug called *clomiphene* (Clomid, Serophene) may be used to treat women who have anovulatory cycles. It is an antiestrogen agent that competes with estrogen for estrogen-receptor binding sites. By blocking estrogen it acts as an ovulatory stimulant. How? By effectively "tricking" the pituitary gland into producing FSH and LH. The gonadotropin surge causes normal follicle growth and subsequent ovulation. Clomiphene is given in daily doses of 50 or 100 mg for 5 days, generally starting on day 5 of the menstrual cycle. In a successful treatment program, ovulation most often occurs from 5 to 10 days after a course of the drug. The incidence of multiple births is about 5% to 7% (mostly twins), a percentage much lower than what is observed following direct administration (injection) of FSH and LH, where the intent is to produce multiple follicles before inducing ovulation.

Supraovulation, or simultaneous rupture of multiple mature follicles, is an infertility treatment option that may be employed if clomiphene use proves ineffective or if multiple ova are deemed desirable in assisted reproductive procedures such as **in vitro fertilization (IVF).** It most frequently involves self-administered injections of either (1) drugs called **menotropins** or (2) genetically developed (recombinant) gonadotropins. Menotropins contain high concentrations of FSH and LH that are extracted from the urine of pregnant women or from postmenopausal women. Recombinant gonadotropins include human menopausal gonadotropins (hMGs) and FSH.

Menarche and Menopause

The menstrual flow first occurs **(menarche)** at puberty, at about the age of 13 years, although there is individual variation according to race, nutrition, health, and heredity. Normally, it recurs about every 28 days for about 3 decades, except during pregnancy, and then ceases **(menopause,** or **climacteric).** The average age at which menstruation ceases is reported to have increased markedly—from about age 40 years a few decades ago to between ages 45 and 50 years more recently.

Recall that gonadotropins extracted from the urine of menopausal women (menotropins) are used as fertility drugs. Figure 35-15 shows how the changes just described relate to changes in hormone levels over the life span. Relatively low concentrations of gonadotropins (FSH and LH) sustain a peak of estrogen secretion from menarche to menopause. After menopause, estrogen concentration decreases dramatically—which causes a negative feedback response that increases the gonadotropin levels. Because the follicular cells are no longer sensitive to gonadotropins after menopause, the increased gonadotropin level has no effect on estrogen secretion.

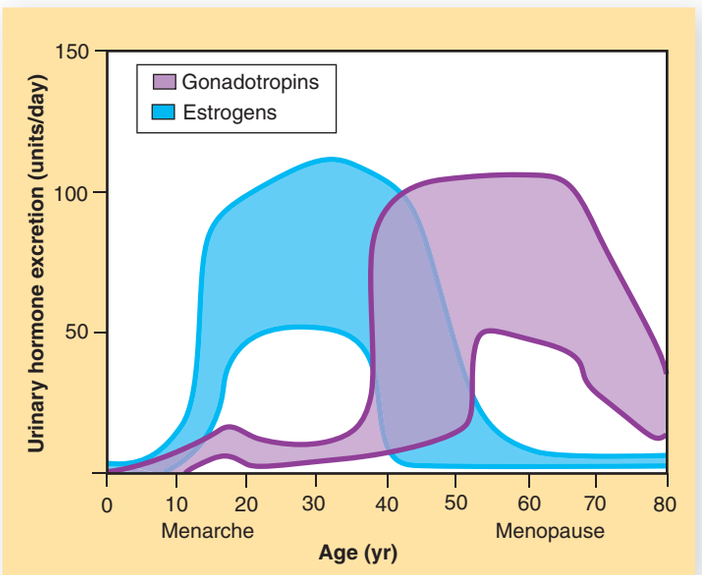


FIGURE 35-15

Gonadotropin and estrogen levels over the life span. This graph shows changes in hormone levels as reflected in urinary excretion rates from birth to advanced old age. Note that an increase in the gonadotropin level at the time of menarche sustains a high but variable level of estrogens until the time of menopause, when ovarian follicular cells cease to respond to gonadotropins. A negative feedback mechanism tries to increase estrogen levels to their former high levels by increasing the gonadotropin levels—a strategy that always fails.

TABLE 35-1 Some Female Reproductive Hormones*

HORMONE	SOURCE	TARGET	ACTION
Dehydroepiandrosterone (DHEA)	Adrenal gland, ovary, other tissues	Converted to other hormones	Eventually converted to estrogens, testosterone, or both (see Figure 18-5 on p. 548)
Estrogens (including estradiol [E_2] and estrone)	Ovary and placenta (small amounts in other tissues)	Uterus, breast, other tissues	Stimulates development of female sexual characteristics, breast development, bone and nervous system maintenance
Follicle-stimulating hormone (FSH)	Anterior pituitary (gonadotroph cells)	Ovary	Gonadotropin; promotes development of ovarian follicle; stimulates estrogen secretion
Gonadotropin-releasing hormone (GnRH)	Hypothalamus (neuroendocrine cells)	Anterior pituitary (gonadotroph cells)	Stimulates production and release of gonadotropins (FSH and LH) from anterior pituitary
Human chorionic gonadotropin (hCG)	Placenta	Ovary	Stimulates secretion of estrogen and progesterone during pregnancy
Inhibin	Ovary	Hypothalamus Anterior pituitary (gonadotroph cells)	Inhibits GnRH production in the hypothalamus and FSH production in the anterior pituitary
Luteinizing hormone (LH)	Anterior pituitary (gonadotroph cells)	Ovary	Gonadotropin; triggers ovulation; promotes development of corpus luteum
Oxytocin (OT)	Posterior pituitary	Uterus and mammary glands	Stimulates uterine contractions; stimulates ejection of milk into ducts of mammary glands; involved in social bonding
Progesterone	Ovary and placenta	Uterus, mammary glands, other tissues	Helps maintain proper conditions for pregnancy
Prolactin (PRL) (lactogenic hormone)	Anterior pituitary (lactotroph cells)	Mammary glands (alveolar secretory cells)	Promotes milk secretion
Relaxin	Placenta	Uterus and joints	Inhibits uterine contractions during pregnancy and softens pelvic joints to facilitate childbirth
Testosterone	Adrenal glands, ovaries	Nervous tissue, bone tissue, other tissues	May affect mood, sex drive, learning, sleep, protein anabolism, other functions

*The role of some hormones related to pregnancy, labor, and delivery are discussed in more detail in the next chapter (Chapter 36, Growth and Development).

Table 35-1 summarizes some of the hormones important in female reproductive function.

| QUICK CHECK |

17. A surge in FSH and LH is associated with what major event of the ovarian cycle?
18. How does an increase in estrogen level affect the uterine lining?
19. What is *menopause?* What causes menopause to occur?

BREASTS

Location and Size of the Breasts

Two breasts lie over the pectoral muscles and are attached to them by a layer of connective tissue (fascia) (Figure 35-16). Breasts are made up of milk-producing **mammary glands,** which are present in all mammals, along with extensive supporting tissues. Breasts are present in both males and females—but only infrequently develop or produce milk in males.

Estrogens and progesterone, two types of ovarian hormones, control breast development during puberty. Estrogens stimulate growth of the ducts of the mammary glands, whereas progesterone stimulates development of the actual secreting cells. Breast size is determined more by the amount of fat around the glandular tissue than by the amount of glandular tissue itself. Hence the size of the breast is not related to its ability to produce milk.

Structure of the Breasts

Each breast consists of several lobes separated by septa (walls) of connective tissue. Each lobe consists of several *lobules*, which, in turn, are composed of connective tissues in which are embedded the pouches of milk-secreting cells. These pouches, or *alveoli*, are arranged in grapelike clusters around the tiny ductule. Figure 35-17 shows one of the mammary alveoli and the milk-producing cells that form its walls. Notice that a special type of epithelial cell called a *myoepithelial cell* is present around the outside of the alveolus. This type of cell contracts slightly, as if it were a muscle cell, thus squeezing milk out into the secretory duct.

The ductules from the various lobules unite, forming a single *lactiferous duct* for each lobe, or between 15 and 20 in each breast. The term lactiferous simply means "milk carrying." These main lactiferous ducts converge toward the nipple, like the spokes of a wheel. They enlarge slightly into small *lactiferous sinuses* before reaching the **nipple** (see Figure 35-16, A). The lactiferous sinuses are positioned to be squeezed by the suckling motion of a baby's jaws during breastfeeding—thus allowing the sinuses to act as little pumping chambers that help move milk out of the breast (Figure 35-18). Each of the main ducts terminates in a tiny opening on the surface of the nipple.

A comparatively large amount of adipose tissue is deposited around the surface of the gland, just under the skin, and between the lobes. *Suspensory ligaments (of Cooper)* throughout the connective tissue of the breast help support the glandular and

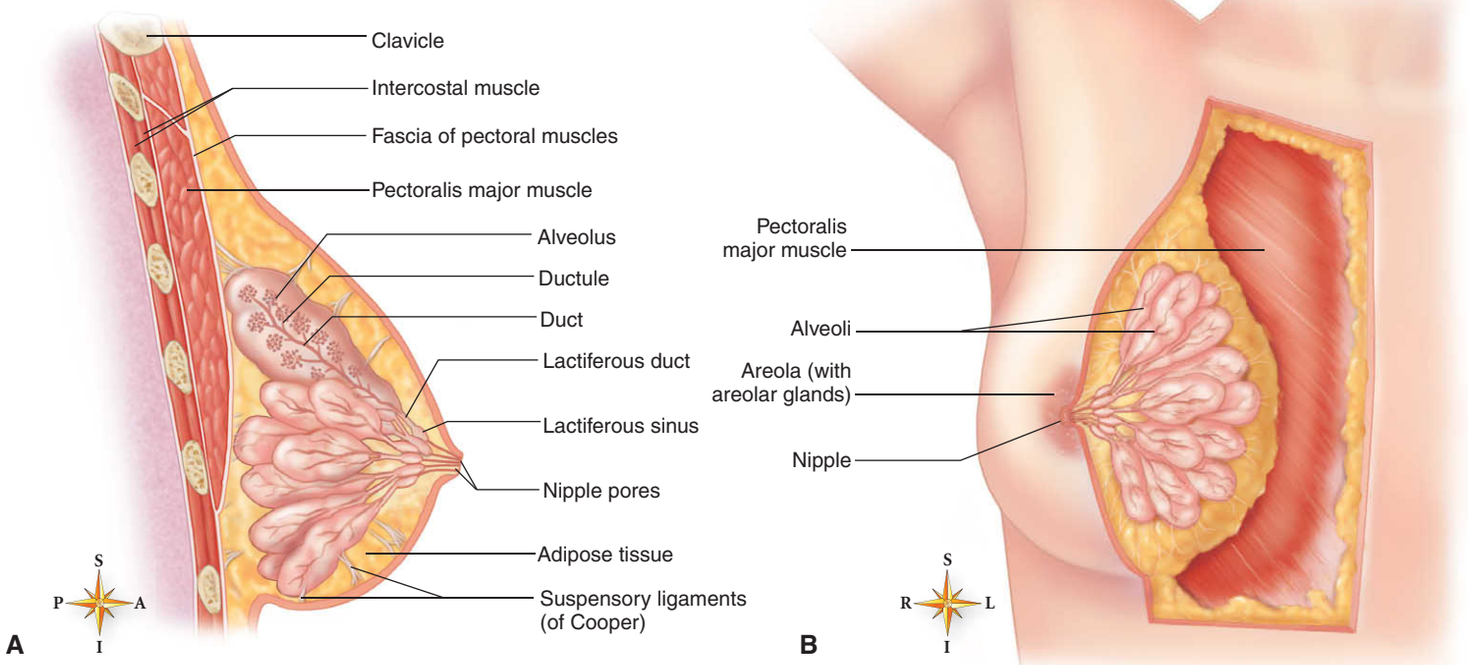


FIGURE 35-16

The female breast. A, Sagittal section of a lactating breast. Notice how the glandular structures are anchored to the overlying skin and to the pectoral muscles by the suspensory ligaments of Cooper. Each lobule of glandular tissue is drained by a lactiferous duct that eventually opens through the nipple. **B,** Anterior view of a lactating breast. Overlying skin and connective tissue have been removed from the medial side to show the internal structure of the breast and underlying skeletal muscle. In nonlactating breasts, the glandular tissue is much less prominent, with adipose tissue making up most of each breast.

connective tissues of the entire structure, anchoring them to the coverings of the underlying pectoral muscles.

The nipples are bordered by a circular pigmented area, the **areola** (see Figure 35-16, *B*). It contains numerous sebaceous glands that appear as small nodules under the skin. Sebum produced by these *areolar glands* helps reduce irritating dryness of the areolar skin associated with nursing. Areolar secretions also contain pheromones that enhance the mother-infant social bond. In some lighter-skinned women, the areola and nipple change color from pink to brown early in pregnancy—a fact of value in diagnosing a first pregnancy. The color decreases

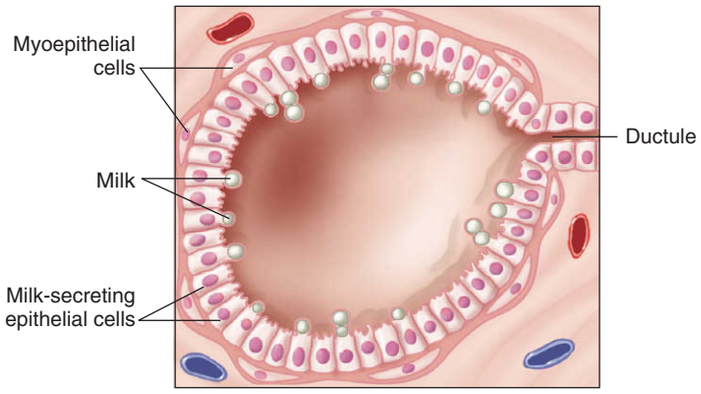


FIGURE 35-17

Alveolus of the mammary gland. Notice the contractile myoepithelial cells that surround the milk-producing cells. Milk is released by apocrine secretion, in which vesicles of fluid pinch off the cell (see Figure 6-12 on p. 142).

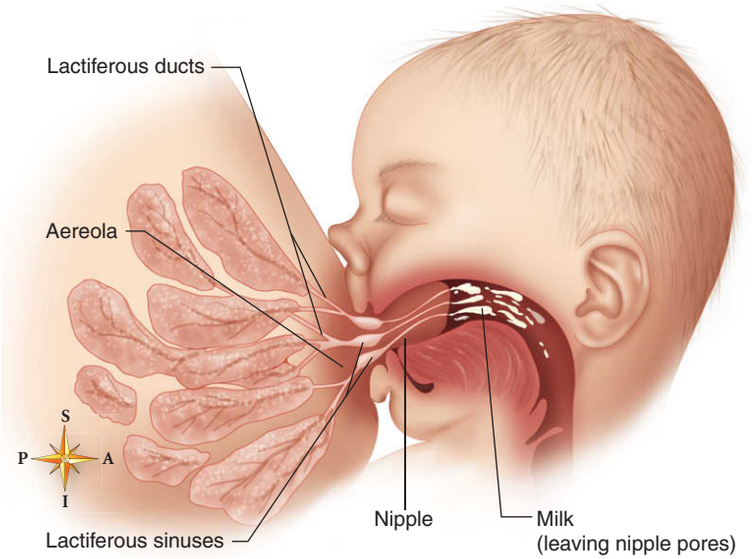


FIGURE 35-18

Function of lactiferous sinuses. When an infant is properly latched on to the breast, its jaws squeeze the lactiferous sinuses rhythmically, thus pumping milk out of the breast and into the back of the infant's mouth.

after lactation has ceased but never entirely returns to the original hue. In some darker-skinned women, no noticeable color change in the areola or nipple heralds the first pregnancy.

Knowledge of the lymphatic drainage of the breast is important in clinical medicine because cancerous cells from malignant breast tumors often spread to other areas of the body through the lymphatics. Lymphatic drainage of the breast is presented in Chapter 23.

Function of the Breasts

The function of the mammary glands is lactation, that is, the secretion of milk for the nourishment of newborn infants.

MECHANISM CONTROLLING LACTATION

Very briefly, **lactation** is controlled as follows and as shown in Figure 35-19:

- The ovarian hormones, estrogens and progesterone, act on the breasts to make them structurally ready to secrete milk. Estrogens promote development of the ducts of the breasts. Progesterone acts on the estrogen-primed breasts to promote completion of the development of the ducts and development of the alveoli, the secreting cells of the breasts. This is an example of hormonal *permissiveness*; estrogen permits progesterone to have its full effect. A high blood concentration of estrogens during pregnancy also inhibits anterior pituitary secretion of prolactin.
- Shedding of the placenta after delivery of the baby cuts off a major source of estrogens. The resulting rapid drop in the blood concentration of estrogens stimulates anterior pituitary secretion of prolactin. Also, the suckling movements of a nursing baby stimulate anterior pituitary secretion of prolactin and posterior pituitary secretion of oxytocin.
- Prolactin stimulates lactation, that is, stimulates alveoli of the mammary glands to secrete milk. Milk secretion starts about the third or fourth day after delivery of a baby, supplanting a thin, yellowish secretion called *colostrum*. With repeated stimulation by the suckling infant, plus various favorable mental and physical conditions, lactation may continue for extended periods.
- Oxytocin stimulates myoepithelial cells in the alveoli of the breasts to eject milk into the ducts, thereby making it accessible for the infant to remove by suckling.

This summary highlights only the major hormonal mechanisms that regulate lactation. Table 35-2 shows that there are *many* hormones that support the processes needed for successful lactation

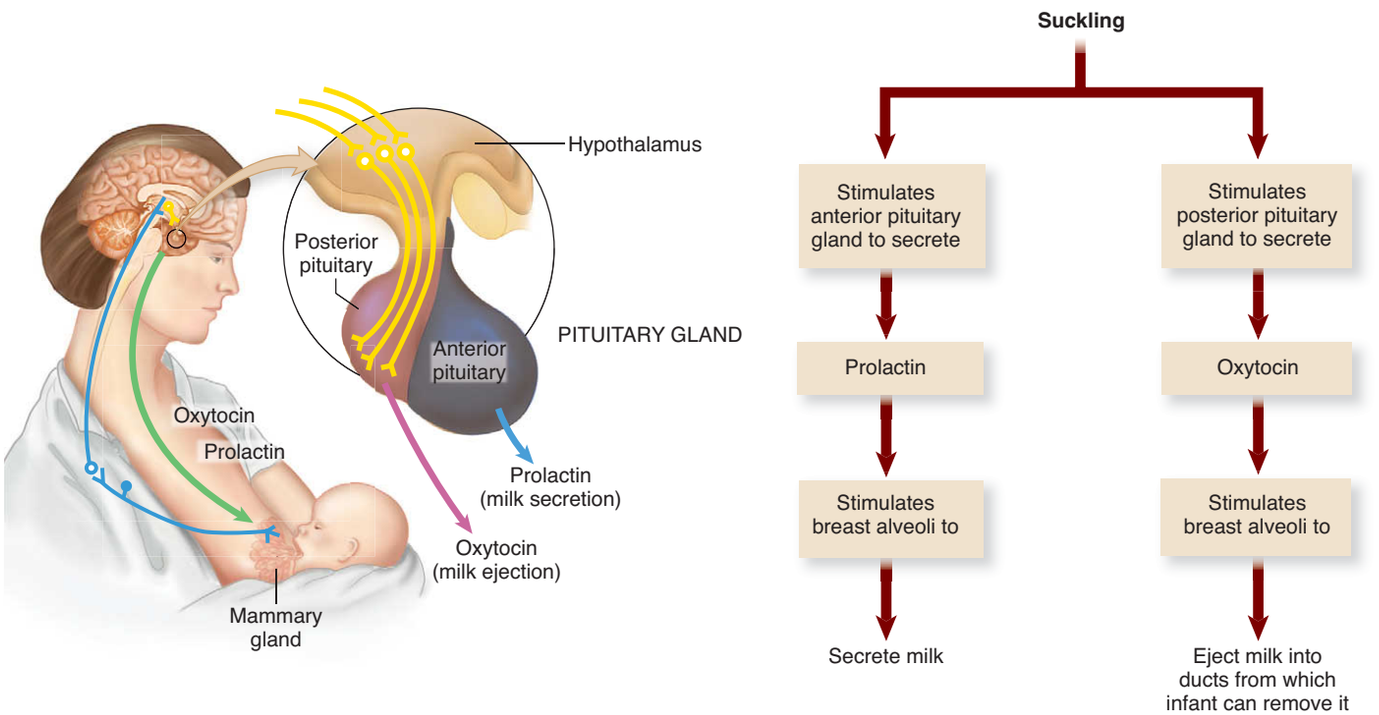


FIGURE 35-19

Lactation. The illustration and accompanying flowchart summarize the mechanisms that control the secretion and ejection of milk.

TABLE 35-2 Hormones That Support Milk Production

CATEGORY	ROLE IN LACTATION	HORMONES
Mammogenic hormones	Promote tissue growth and development	↑ Estrogens ↑ Growth hormone (GH) ↑ Insulin-like growth factor (IGF-1) ↑ Insulin ↑ Cortisol ↑ Prolactin (PRL) ↑ Relaxin ↑ Epidermal growth factor (EGF)
Lactogenic hormones	Initiate milk production by secretory cells of alveolus	↑ Prolactin (PRL) ↑ Placental lactogen (hPL) ↑ Cortisol ↑ Insulin ↑ Insulin-like growth factor (IGF-I) ↑ Thyroid hormones (T_3, T_4) ↑ Growth hormone (GH) ↓ Estrogens ↓ Progesterone
Galactokinetic hormones	Promote milk ejection by stimulating myoepithelial cells surrounding alveoli	↑ Oxytocin (OT) ↑ Antidiuretic hormone (ADH) (vasopressin [AVP])
Galactopoietic hormones	Maintain milk production (after it has already started)	↑ PRL ↑ Cortisol ↑ Insulin ↑ IGF-1 ↑ T_3, T_4

and defines the major roles that these hormones play. Many of these mechanisms are adaptations of hormonal processes discussed earlier, such as insulin's ability to get glucose into cells—a function clearly needed in cells that produce sugar-rich milk.

THE IMPORTANCE OF LACTATION

The process of **lactation** plays an important role in the ultimate success of the reproductive system. The biological goal of human reproduction does not lie solely in delivering a healthy infant—the infant must also survive until reproductive age. If a child does not survive to reproduce, then the genetic code cannot be passed on to successive generations and the ultimate goal of reproduction has not been met. Humans and other mammals help ensure the survival of offspring for up to several years by producing nutrient-rich milk. Nursing from the mother's breast provides several advantages for human offspring, including:

- Milk is a rich source of proteins, fat, calcium, vitamins, and other nutrients in proportions needed by a young, developing body.
- Human milk provides passive immunity to the offspring in the form of maternal antibodies present in both colostrum and the milk.
- Nursing enhances the emotional bond between mother and child. Such bonding fosters healthy psychological development in the child and strengthens family relationships that contribute to successful human development.

| QUICK CHECK |

20. Briefly describe the network of ducts and secreting cells that form the mammary glands.
21. List the hormones that prepare the breast structurally for lactation.
22. Which hormone causes milk to be ejected into the lactiferous ducts?

Cycle of LIFE

Female Reproductive System

As mentioned in Chapter 34, the reproductive system is unlike any other body system with regard to the normal changes that occur during the life span. Unlike other systems, the female reproductive system does not begin to perform its functions until the teenage years (puberty), and unlike the male reproductive system, the female reproductive system ceases its principal functions in middle adulthood.

The female organs begin their initial stages of development in the womb. As a matter of fact, the first stage of meiotic development of all the ova that will ever be produced by a woman is completed by the time she is born. However, full development of the reproductive organs—and the gametes within the ovaries—does not resume until puberty. At puberty, reproductive hormones stimulate the organs of the reproductive tract to become functional and produce a mature ovum one at a time. Reproductive function then continues in a cyclical fashion until menopause. Menopause is an event that is usually marked by the passage of at least 1 full year without menstruation. After that time, a woman may continue to enjoy normal sexual activity, but she cannot produce more offspring.

the BIG picture

Female Reproductive System and the Whole Body

As stated several times in this chapter, the importance of reproductive function lies in the fact that it imparts virtual immortality to our genes. This is important not only to the survival of the human species but also to the survival of life itself. After all, life as we know it could not exist without a genetic code. The "big picture" of human reproduction requires two systems, one reproductive system in each parent. The combined roles of the male and female reproductive systems will be explored as a single topic in the early part of the next chapter.

For now, we will take a closer look at the female reproductive system and its relationships with other systems within a woman's body. As with any system, the female reproductive system cannot function without the maintenance functions of the circulatory, immune, respiratory, digestive, and urinary systems. The female reproductive system shares a special anatomical relationship with the urinary system. These two systems develop in close proximity to each other and thus share a common structure: the vulva. A special anatomical relationship with the skeletal muscular system is evident in the structure known as the *perineum*. Of course the skeletal and muscular systems both support and protect the internal organs of the female reproductive system. An even more special relationship with the integumentary system should be noted. The breasts, containing the milk-producing mammary glands, are actually modifications of the skin. Although structurally the breasts can be thought of as belonging to the integumentary system, functionally they are best considered as a part of the reproductive system. Nervous and endocrine regulation of female reproductive function has been outlined in this chapter and is explored further in the next chapter.

MECHANISMS of DISEASE

DISORDERS OF THE FEMALE REPRODUCTIVE SYSTEM

Hormonal and Menstrual Disorders

Dysmenorrhea (dis-men-oh-REE-ah), meaning "painful menstruation," is the term used to describe *menstrual cramps*, the painful periods that affect 75% to 80% of women at some time during their reproductive years. For significant numbers of those affected, severe lower abdominal cramping and back pain accompanied by headache, nausea, and vomiting will disrupt their school, work, athletic, or other activities. *Primary dysmenorrhea* is the most common type, occurring primarily in adolescents and young women. Symptoms, which can last from hours to days and vary in severity from cycle to cycle, are caused by an abnormally increased concentration of certain prostaglandins produced by the uterine lining. High concentrations of prostaglandin E_2 (PGE_2) and prostaglandin F_2 (PGF_2) cause painful spasms by decreasing blood flow and oxygen delivery to uterine muscle. Fortunately, primary dysmenorrhea is not associated with pelvic disease, such as an infection or tumor, and can generally be treated effectively with over-the-counter antiinflammatory and prostaglandin-inhibiting drugs such as ibuprofen and naproxen. In more severe cases a physician may prescribe more powerful antiinflammatory drugs or certain hormones, including oral contraceptives, to alter menstrual cycle activity or reduce the level or frequency of cyclical uterine contractions.

Secondary dysmenorrhea refers to menstrual-related pain caused by some type of pelvic pathological condition, including inflammatory conditions and cervical stenosis. Treatment of secondary dysmenorrhea conditions and cervical stenosis involves treating the underlying disorder.

Amenorrhea (ah-men-oh-REE-ah) is the absence of normal menstruation. *Primary amenorrhea* is the failure of menstrual cycles to begin and may be caused by various factors, such as hormone imbalances, genetic disorders, brain lesions, or structural deformities of the reproductive organs. *Secondary amenorrhea* occurs when a woman who has previously menstruated slows to three or fewer cycles per year. Secondary amenorrhea may be a symptom of weight loss, pregnancy, lactation, menopause, or disease of the reproductive organs. Treatment of amenorrhea involves treating the underlying disorder or condition. If amenorrhea occurs as a component of the "sports triad" (Box 35-6), treatment may become part of extensive and long-term therapy needed to address a number of complex nutritional, hormonal, and self-image issues.

Dysfunctional uterine bleeding (DUB) is irregular or excessive uterine bleeding that most often results from either a structural problem or some type of hormonal imbalance that causes a disruption of blood supply rather than from an infection or other disease condition. Excessive uterine bleeding from any cause can result in life-threatening anemia. Therefore, DUB is a significant medical problem—one that affects nearly 2 million women in the United States each year. To diagnose the cause, a physician may employ ultrasound or x-ray studies, look directly inside the uterus using a scope inserted through the vagina and cervix, or examine tissue obtained by biopsy to exclude cancer.

Transabdominal pelvic ultrasound is perhaps the most widely used and useful imaging technique to look at the uterus and adjacent reproductive structures. During this procedure a transducer is placed on the lower anterior abdominal wall and high-frequency sound waves are transmitted into the pelvic viscera. The returning echoes are then viewed on a screen similar to that of a sonar receiver or "fish-finder." The resulting image, a "slice picture," may be enhanced by filling the uterus with saline solution (Figure 35-20). Structural problems, such as growth of a uterine malignancy or benign tumor, may cause DUB by injuring

Box 35-6 | SPORTS and FITNESS

The "Sports Triad" in Elite Female Athletes

A disturbing trend among some elite female athletes involves development of a so-called "triad" of undesirable outcomes. In an attempt to improve performance, these athletes couple severe caloric restriction with overtraining. The result is often a flawed sense of body image that equates thinness with athletic potential. The triad involves (1) low energy availability, (2) menstrual disorders, and (3) low bone mineral density.

Low energy availability often results from disordered eating and weight loss. *Amenorrhea* (failure to have a menstrual period) and other menstrual problems are caused by a drastic decrease in estrogen secretion as the body attempts to conserve energy by closing down the reproductive function. It is the decrease in estrogen levels that trigger early loss of bone density—perhaps even *osteoporosis* and permanent skeletal damage. As it progresses, the *sports triad* may also be accompanied by development of other serious and potentially fatal outcomes.



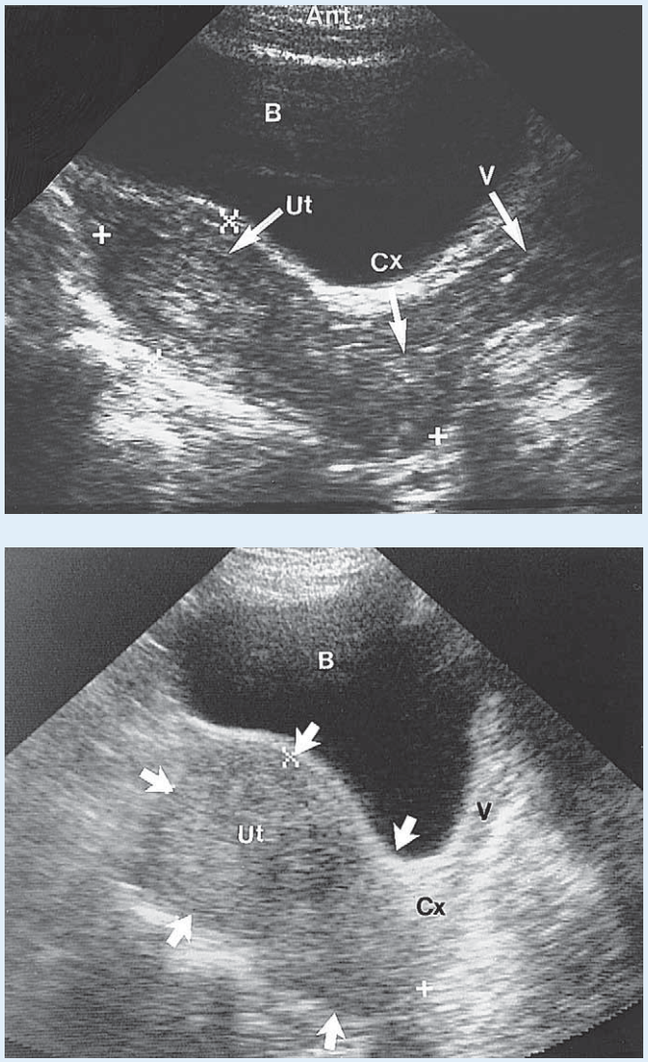


FIGURE 35-20

Female pelvic transabdominal ultrasound. A, Normal longitudinal ultrasound image. The bladder *(B),* uterus *(Ut),* cervix *(Cx),* and vagina *(V),* are visible. **B,** Longitudinal ultrasound image of uterine fibroids causing dysfunctional uterine bleeding *(DUB).* Echo pattern shows an enlarged and "lumpy" appearing (arrows) uterus *(Ut)* protruding into the bladder *(B).* The cervix *(Cx)* and vagina *(V)* are visible.

the blood vessels of the uterine wall or lining as the tissue mass grows in size and the normal contours of the organ are distorted. Figure 35-20, A, shows a normal longitudinal pelvic ultrasound image. It was taken "looking down" through the anterior abdominal wall in the mid portion of the pelvis. Note how the bladder was used as a "window" to view the uterus and adjacent reproductive structures below. The bladder, uterus, contours of the uterine cavity, cervix, and vagina are all visible. Figure 35-20, *B*, shows the appearance of a similar ultrasound image in a patient suffering from DUB caused by a structural problem—abnormal muscular growths called **uterine fibroids** (discussed on pp. 1088–1089). The uterus is enlarged and pushing into the bladder, it appears "lumpy," and the cavity contours are obviously distorted. Surgical removal or treatment to shrink the fibroid growths is usually curative.

If hormonal imbalance is the cause of DUB, it is the excessive growth (hyperplasia) and breakdown of delicate endometrial tissue that results in heavy bleeding. In these cases, treatment generally begins with administration of nonsteroidal antiinflammatory drugs and hormonal manipulation using low-dose birth control pills. If conservative treatment fails to stop the endometrial lining from hemorrhaging, hysterectomy remains one of the most effective curative options. However, less invasive procedures, including *endometrial ablation* techniques, are now being used more frequently to destroy the endometrial lining and halt or permanently reduce excessive menstrual blood loss in many women suffering from DUB. In *thermal ablation*, a balloon is inserted into the uterus and filled with fluid. A heat probe is then inserted into the balloon and the fluid is heated to a temperature that will destroy the endometrium. In *radiofrequency ablation*, a gold-plated mesh fabric is used to fill the uterine cavity and is then charged with radiofrequency energy that destroys the friable and bleeding

endometrial cells. Both procedures carry less risk and have shorter recovery periods than does a hysterectomy.

Premenstrual syndrome (PMS) is a condition that involves a collection of symptoms that regularly occur in many women during the premenstrual phase of their reproductive cycles. Symptoms include headache, irritability, fatigue, nervousness, weight gain, sleep changes, depression, and other problems that are often distressing enough to limit activity and affect personal relationships. Because the cause of PMS is still unclear, current treatments focus on relieving the symptoms.

Infection and Inflammation

Infections of the female reproductive tract are often classified as *exogenous* or *endogenous*. Exogenous infections result from pathogenic organisms transmitted from another person, such as *sexually transmitted diseases (STDs)*. Endogenous infections result from pathogens that normally inhabit the intestines, vulva, or vagina. You may recall from Chapter 1 that many areas of the body are normally inhabited by pathogenic microorganisms but that they cause infection only when there is a change in conditions or they are moved to a new area.

| A&P CONNECT |

Review examples of important STDs in ***Sexually Transmitted Diseases*** online at ***A&P Connect.***

evolve

Pelvic inflammatory disease (PID) occurs as either an acute or chronic inflammatory condition that can be caused by several different pathogens, which usually spread upward from the vagina. PID is a major cause of infertility and sterility and affects more than 800,000 women each year in the United States. It is a common complication following infection by chlamydial and gonococcal STD organisms. Infection involving the uterus, uterine tubes, ovaries, and other pelvic organs often results in development of scar tissue and adhesions. Direct laparoscopic examination is often used to determine the severity of the PID infection and the reproductive organs involved (Figure 35-21).

PID that results in uterine tube inflammation, a condition called **salpingitis** (sal-pin-JYE-tis) is often characterized by obstruction of the lumen and marked dilation at the end of the tube caused by accumulation of fluid that cannot escape—a condition physicians refer to as **hydrosalpinx** (hye-droh-SAL-pinks) (see Figure 35-21, *B*). Because ultrasound images cannot show whether the lumen of the uterine tube is open or obstructed, other imaging techniques are required to make a definitive diagnosis of infertility caused by tubal obstruction. Figure 35-22 shows two x-ray images of the uterus and uterine tubes called **hysterosalpingograms** (his-ter-oh-sal-PING-go-grams). In the x-ray technique used to produce these images, a cannula is inserted into the cervical canal and contrast material is injected into the uterine cavity and allowed to fill the uterine tubes. In the normal image shown in Figure 35-22, *A*, the contrast material has filled the uterine tubes and flowed out into the peritoneal cavity, demonstrating that the tubes are not obstructed.

Figure 35-22, *B*, is an abnormal hysterosalpingogram of a woman who was treated for salpingitis at an earlier date and later

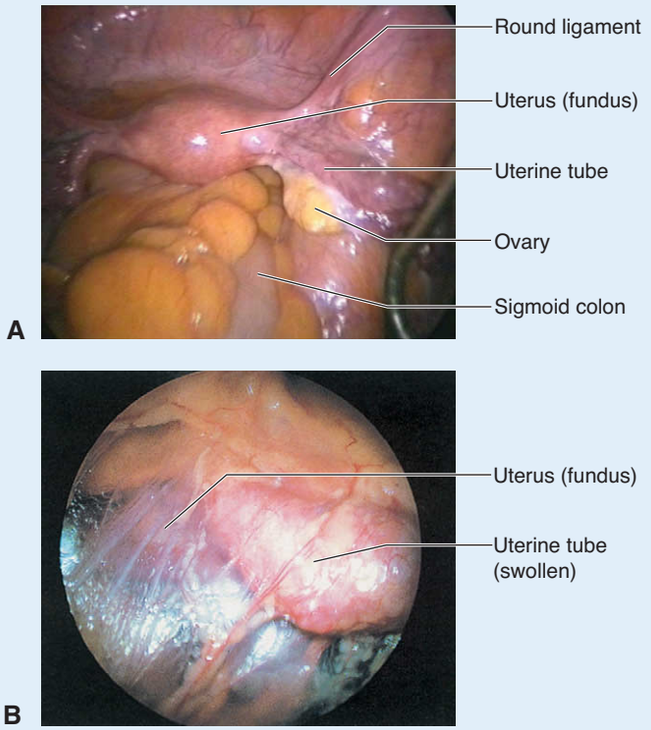


FIGURE 35-21

Laparoscopic views of the female pelvis. A, Laparoscopic image shows normal female pelvic reproductive organs. **B,** Laparoscopic view of pelvic inflammatory disease (PID). Note the clear reddish inflammatory membrane that covers and fixes the ovary, uterine tube, and uterus to the surrounding structures. The inflamed and dilated end of the fluid-filled uterine tube (hydrosalpinx) is clearly visible.

experienced infertility. Note how the contrast material fills and then collects in the dilated portion of the uterine tube (hydrosalpinx) but does not spill into the pelvis. In this case the radiograph allows the physician to make a definitive diagnosis—infertility caused by uterine tube obstruction—and treat it appropriately.

Although some chlamydial infections may not cause symptoms, most cases of PID are accompanied by fever, pelvic tenderness, and pain. Unfortunately, because of scarring and adhesions, pain may continue even after antibiotic therapy has eliminated the active infection. If left untreated, PID infections may spread to other tissues, including the blood, resulting in septic shock and death.

Vaginitis (vaj-i-NYE-tis) is inflammation or infection of the vaginal lining. Vaginitis most often results from STDs or from a "yeast infection." So-called yeast infections are usually opportunistic infections of the fungus *Candida albicans*, producing **candidiasis** (kan-dih-DYE-eh-sis). Candidiasis infections are characterized by a whitish discharge—a symptom known as **leukorrhea** (loo-koh-REE-ah).

Tumors and Related Conditions

Fibroid, myoma (my-OH-mah), and **fibromyoma** (fye-broh-my-OH-mah) are all terms used to describe benign (noncancerous) tumors of uterine fibrous or smooth muscle tissue. Individual fibroids may occur, but multiple growths are not unusual. Fibroids are common in women during their reproductive years and

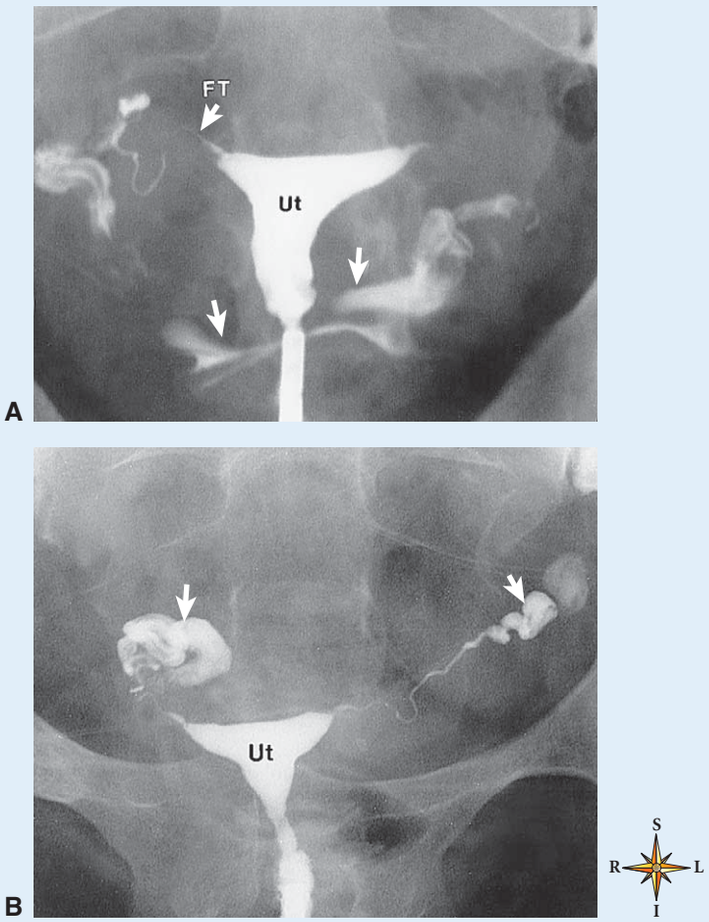


FIGURE 35-22

Hysterosalpingogram. A, Normal image. A tube is inserted in the uterine cervix, and contrast material has filled the uterus *(Ut)* and uterine (fallopian) tubes *(FT). Arrows* indicate contrast material that has flowed out into the peritoneal cavity, indicating that the tubes are not obstructed. **B,** Abnormal image. Contrast material fills the uterine cavity and tubes with no spill into the pelvis. *Arrows* point to the dilated ends of the uterine tubes (hydrosalpinx). Image confirms distal obstruction of the uterine tubes.

develop most often in the myometrium of the uterine body and rarely in the cervix. The fact that they are seldom seen before puberty, increase in size during pregnancy, and tend to shrink in postmenopausal women suggests that age and estrogen levels may play a role in their development. Fibroids range in size from small asymptomatic nodules to massive tumors that may be painful and exert pressure on other pelvic organs. Growth during pregnancy may result in placental hemorrhage or malpresentation of the fetus, complicating labor and delivery. In addition to pain, symptoms will vary depending on the size and location of the tumor. Even small tumors developing beneath the endometrium can cause severe hemorrhage (dysfunctional uterine bleeding, DUB). Tumor size, location, and severity of symptoms will determine treatment options. A technique similar to a heart catheterization, called *uterine artery embolization*, involves snaking a small catheter through an artery in the groin into the arterial vessel supplying blood to the fibroid. Tiny inert pellets are then injected into the artery, blocking the flow of blood. The procedure results in dramatic shrinkage of the treated fibroid and a reduction in symptoms, including hemorrhage. Surgical removal of individual fibroids or, in more severe cases, hysterectomy may be indicated.

Polycystic ovary syndrome (PCOS) is a condition that affects 10% of reproductive-age women but can also affect girls as young as 11 years old. It is characterized by enlarged ovaries that usually are studded with fluid-filled cysts about 0.5 to 1.5 cm in diameter (Figure 35-23). The cysts are found on both ovaries and develop from mature follicles that fail to rupture completely. Corpora lutea are generally absent. Women with PCOS frequently have numerous endocrine abnormalities, including high levels of androgens, infrequent menstrual cycles, and persistent anovulation. PCOS is the most common cause of female infertility.

Ovarian cysts are very common fluid-filled cysts that develop either from follicles that fail to rupture completely *(follicular cysts)* or from corpora lutea that fail to degenerate *(luteal cysts)*. Most women develop a number of these cysts during their reproductive years and their presence does not constitute a diagnosis of polycystic ovary syndrome. Although ovarian cysts are often multiple, they rarely become dangerous. However, on occasion they may become quite large and painful and be diagnosed by palpation or ultrasonography. Luteal cysts are less common than follicular cysts but tend to cause more symptoms, such as pelvic pain, and menstrual irregularities. Rarely, rupture of a large luteal cyst will result in internal bleeding that requires surgical intervention. The vast majority of all ovarian cysts will disappear within a few months of their appearance, most within 60 days.

Endometriosis (en-doh-mee-tree-OH-sis) is a benign but often painful condition that commonly affects the female reproductive tract. It is characterized by the presence of functioning endometrial tissue outside the uterus. The displaced endometrial tissue is most often found attached to an ovary or to the pelvic or abdominal organs and is occasionally found in other places throughout the body. Just how endometrial tissue spreads from the uterine cavity into the peritoneal cavity has not yet been determined. One theory suggests "retrograde menstruation" or backward movement of some endometrial tissue through the uterine tubes into the peritoneal cavity during the menstrual period. Although rare, the almost bizarre appearance of endometrial tissue in the lungs and lymph nodes has led some researchers to speculate that endometrial tissue "seeds"



FIGURE 35-23

Polycystic ovary syndrome (PCOS). The ovary is studded with fluid-filled cysts developed from follicles that have failed to rupture.

pass through vascular or lymphatic channels. Regardless of how the movement occurs, the development of endometriosis is a significant clinical condition that often causes infertility, dysmenorrhea, and severe pain. Symptoms reflect the fact that displaced endometrial tissue reacts to ovarian hormones in the same way as the normal endometrium—exhibiting a cycle of growth and sloughing off. The disorder afflicts approximately 10% of women, a majority between 30 and 45 years of age.

Breast cancer, often a form of adenocarcinoma, is the most common nonskin malignancy in American women. Although heart disease kills more women than any other cause, breast cancer remains the leading cause of death in women ages 40 to 44 years and of all malignancies, only lung cancer kills more women of all ages. The risk of developing breast cancer increases with increasing age, posing a lifetime risk of one in eight for women who reach advanced old age. Fortunately, treatment of breast cancer is often successful if the cancerous tumor is detected early. Because such tumors are often painless, most physicians recommend monthly breast self-examinations and annual mammograms.

| A&P CONNECT |

Self-examination of breasts is a recommended routine to monitor breast health. Learn more in ***Breast Self-Examination*** online at ***A&P Connect.***

Treatments for breast cancer often involve surgery, chemotherapy, and radiation therapy. Surgeries can be very conservative, as with a simple lump removal or **lumpectomy.** If metastasis to surrounding tissue is suspected, a **radical mastectomy** (mas-TEK-toh-mee) may be performed. In this procedure the entire breast, with nearby muscle tissues and lymph nodes, is removed. Just as lumpectomy results in less trauma than radical mastectomy, so-called *limited-field radiation* can provide effective treatment for clearly defined early-stage cancers that have not spread. It does so with shorter treatment cycles and fewer side effects than whole-breast radiation.

In the past, after women had completed their initial treatment for breast cancer they had few options available to lessen the possibility of recurrence. For a number of years the drug *tamoxifen* has been used extensively to prevent the recurrence of breast cancers fueled by estrogen. It does so by blocking the estrogen receptor sites on the cancer cell membrane. Unfortunately, tamoxifen's effectiveness is limited to about 5 years. A relatively new class of drugs called "aromatase inhibitors" (letrozole and others) are now being given to breast cancer patients to prevent recurrence of the disease. Instead of blocking estrogen receptor sites, these drugs block estrogen production. They may replace tamoxifen or be prescribed for use after 5 years of tamoxifen therapy. Other "rational" drugs such as trastuzumab (Herceptin) are now being used to successfully manage recurring forms of breast cancer that in the past were very difficult to treat.

Cancer of the uterus can affect the body of the uterus or the cervix. Cancers of the uterine body most often involve the endometrium (**endometrial cancer**) and mostly affect women beyond childbearing years; a common symptom is postmenopausal uterine bleeding. Risk factors for this type of cancer include obesity, prolonged estrogen therapy, and infertility. **Cervical cancer** occurs most often in women between the ages of 30 and 50 years. *Human papilloma virus (HPV)* infections, for which a vaccine is available, can cause cervical cancer. Cervical cancer is often diagnosed early, through screening tests such as the **Papanicolaou** (pah-peh-nik-oh-LAH-oo) **test (Pap smear)** (Figure 35-24). In this test, cells swabbed from the cervix are smeared on a glass slide, stained, and examined microscopically to determine whether any abnormalities exist. Because screening tests and other early detection methods have been so successful, the death rates for uterine cancers have dropped dramatically over the last few decades.

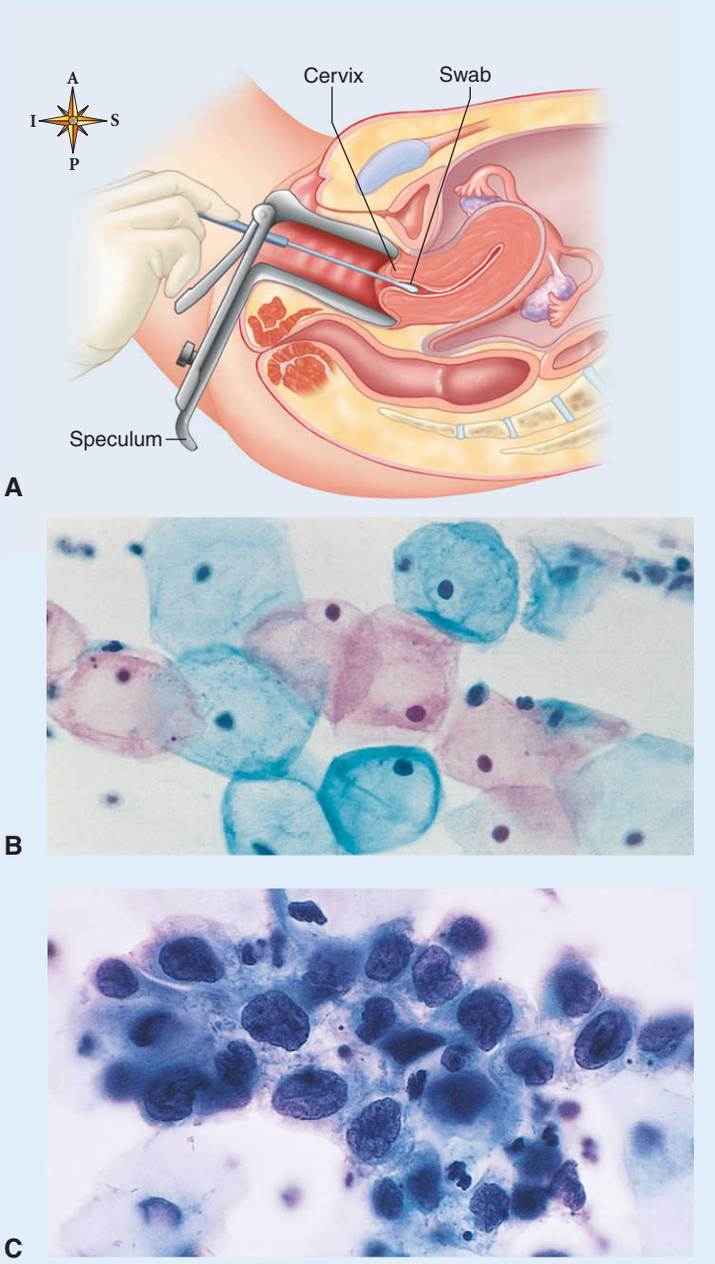


FIGURE 35-24

Papanicolaou (Pap) smear. A, Obtaining a Pap smear. **B,** Appearance of normal cervical epithelial cells in Pap smear. **C,** Appearance of cervical cancer cells in Pap smear. Note the reduction in cytoplasm and increased prominence of the nuclei compared with normal epithelial cells.

 (continued from p. 1063)

corpus albicans
(KOHR-pus AL-bi-kanz)
[*corpus* **body,** *albicans* **whitening**]
pl., corpora albicantia

corpus luteum
(KOHR-pus LOO-tee-um)
[*corpus* **body,** *lute-* **yellow,** *-um* **thing**] *pl.,* corpora lutea

cortex
(KOHR-teks)
[*cortex* **bark**] *pl.,* cortices

endometrium
(en-doh-MEE-tree-um)
[*endo-* **within,** *-metr-* **womb,** *-um* **thing**] *pl.,* endometria

essential organ
[*organ* **instrument**]

estrogen
(ES-troh-jen)
[*estr-* **frenzy,** *-gen* **produce**]

estrogenic phase
(es-troh-JEN-ik fayz)
[*estr-* **frenzy,** *-gen-* **produce,** *-ic* **relating to**]

external os
[*extern-* **outside,** *-al* **relating to,** *os* **mouth or opening**] *pl.,* ora

fimbria
(FIM-bree-ah)
[*fimbria* **fringe**] *pl.,* fimbriae

follicle-stimulating hormone (FSH)
(FOL-lik-ul-STIM-yoo-lay-ting HOR-mohn)
[*foll-* **bag,** *-icle* **little,** *hormon-* **excite**]

follicular phase
(foh-LIK-yoo-lar fayz)
[*foll-* **bag,** *-icul-* **little,** *-ar* **relating to**]

fundus
(FUN-duss)
[*fundus* **bottom**] *pl.,* fundi

graafian follicle
(GRAH-fee-en FOL-li-kul)
[*Reijnier de Graaf* **Dutch physician,** *-an* **relating to,** *foll-* **bag,** *-icle* **little**]

greater vestibular gland
(ves-TIB-yoo-lar)
[*vestibul-* **entrance hall,** *-ar* **relating to,** *gland* **acorn**]

hymen
(HYE-men)
[*hymen* **Greek god of marriage**]

imperforate hymen
(im-PER-fah-rayt HYE-men)
[*im-* **not,** *-perfor-* **pierce,** *-ate* **state,** *hymen* **Greek god of marriage**]

infundibulum
(in-fun-DIB-yoo-lum)
[*infundibulum* **funnel**]

internal os
[*intern-* **inside,** *-al* **relating to,** *os* **mouth or opening**] *pl.,* ora

isthmus
(ISS-muss)
[*ithmus* **narrow connection or passage**]

labia majora
(LAY-bee-ah mah-JOH-rah)
[*labia* **lips,** *majora* **large**] *sing.,* labium majus

labia minora
(LAY-bee-ah mih-NO-rah)
[*labia* **lips,** *minora* **small**] *sing.,* labium minor

lactation
(lak-TAY-shun)
[*lact-* **milk,** *-ation* **process**]

lesser vestibular gland
(ves-TIB-yoo-lar)
[*vestibul-* **entrance hall,** *-ar* **relating to,** *gland* **acorn**]

luteal phase
(LOO-tee-al fayz)
[*lute-* **yellow,** *-al* **relating to**]

luteinization
(loo-tee-in-i-ZAY-shun)
[*lute-* **yellow,** *-ization* **process**]

luteinizing hormone (LH)
(loo-tee-in-EYE-zing HOR-mohn)
[*lute-* **yellow,** *-izing* **process,** *hormon-* **excite**]

mammary gland
(MAM-mah-ree)
[*mamma-* **breast,** *-ry* **relating to,** *gland* **acorn**]

medulla
(meh-DUL-ah)
[*medulla* **middle**] *pl.,* medullae or medullas

menarche
(meh-NAR-kee)
[*men-* **month,** *-arche* **beginning**]

menopause
(MEN-oh-pawz)
[*men-* **month,** *-paus-* **cease**]

menses
(MEN-seez)
[*menses* **months**] *pl.,* menses

menstrual period
(MEN-stroo-al)
[*mens-* **month,** *-al* **relating to**]

menstruation
(men-stroo-AY-shun)
[*mens-* **month,** *-ation* **process**]

mons pubis
(monz PYOO-bis)
[*mons* **mountain,** *pubis* **groin**] *pl.,* montes pubis

myometrium
(my-oh-MEE-tree-um)
[*myo-* **muscle,** *-metr-* **womb,** *-um* **thing**]

nipple
(NIP-el)
[*nip-* **beak,** *-le* **small**]

oogonium
(oh-oh-GO-nee-um)
[*oo-* **egg,** *-gon-* **offspring,** *-um* **thing**] *pl.,* oogonia

ovarian cortex
(oh-VAIR-ee-an KOHR-teks)
[*ov-* **egg,** *-arian* **relating to,** *cortex* **bark**] *pl.,* cortices

ovarian follicle
(oh-VAIR-ee-an FOL-i-kul)
[*ov-* **egg,** *-arian* **relating to,** *foll-* **bag,** *-icle* **little**]

ovarian medulla
(oh-VAIR-ee-an meh-DUL-ah)
[*ov-* **egg,** *-arian* **relating to,** *medulla* **middle**] *pl.,* medullae or medullas

ovary
(OH-var-ee)
[*ov-* **egg,** *-ar-* **relating to,** *-y* **location of process**]

ovulation
(ov-yoo-LAY-shun)
[*ov-* **egg,** *-ation* **process**]

ovum
(OH-vum)
[*ovum* **egg**] *pl.,* ova

perimetrium
(pair-i-MEE-tree-um)
[*peri-* **around,** *-metr-* **womb,** *-um* **thing**]

perineal body
(pair-i-NEE-al)
[*peri-* **around,** *-ine-* **excrete (perineum),** *-al* **relating to**]

posterior fornix
(pohs-teer-ee-or FOR-niks)
[*poster-* **behind,** *-or* **quality,** *fornix* **arch**]

posterior ligament
(pohs-TEER-ee-or LIG-ah-ment)
[*poster-* **behind,** *-or* **quality,** *liga-* **bind,** *-ment* **condition**]

postmenstrual phase
(post-MEN-stroo-al fayz)
[*post-* **after,** *-mens-* **month,** *-al* **relating to**]

postovulatory phase
(post-ov-yoo-lah-TOR-ee fayz)
[*post-* **after,** *-ov-* **egg,** *-ory* **relating to**]

premenstrual phase
(pree-MEN-stroo-al fayz)
[*pre-* **before,** *-mens-* **month,** *-al* **relating to**]

preovulatory phase
(pree-ov-yoo-lah-TOR-ee fayz)
[*pre-* **before,** *-ov-* **egg,** *-ory* **relating to**]

progesterone
(pro-JES-ter-ohn)
[*pro-* **provide for,** *-gester-* **bearing (pregnancy),** *-stero-* **solid or steroid derivative,** *-one* **chemical**]

progesterone phase
(proh-JES-ter-ohn fayz)
[*pro-* **provide for,** *-gester-* **bearing (pregnancy),** *-stero-* **solid or steroid derivative,** *-one* **chemical**]

proliferative phase
(PROH-lif-er-eh-tiv fayz)
[*proli-* **offspring,** *-fer-* **bear or carry,** *-at-* **process,** *-ive* **relating to**]

rectouterine pouch (of Douglas)
(rek-toh-YOO-ter-in)
[*recto-* **straight,** *-uter-* **womb,** *-ine* **relating to,** *James Douglas Scots* **anatomist**]

round ligament
(LIG-ah-ment)
[*liga-* **bind,** *-ment* **condition**]

secretory phase
(SEEK-reh-toh-ree fayz)
[*secret-* **separate,** *-ory* **relating to**]

urogenital triangle
(yoor-oh-GEN-i-tal)
[*uro-* **urine,** *-gen-* **produce,** *-al* **relating to**]

uterine tube
(YOO-ter-in toob)
[*uter-* **womb,** *-ine* **relating to**]

uterosacral ligament
(yoo-ter-oh-SAK-ral LIG-ah-ment)
[*uter-* **womb,** *sacr-* **sacred (sacrum),** *-al* **relating to,** *liga-* **bind,** *-ment* **condition**]

uterus
(YOO-ter-us)
[*uterus* **womb**]

vagina
(vah-JYE-nah)
[*vagina* **sheath**]

vaginal orifice
(VAH-ji-nal OR-i-fis)
[*vagina-* **sheath,** *-al* **relating to,** *ori-* **mouth,** *-fice-* **something made**]

vesicouterine pouch
(ves-i-koh-YOO-ter-in)
[*vesic-* **blister,** *-uter-* **womb,** *-ine* **relating to**]

vestibule
(VES-ti-byool)
[*vestibul-* **entrance hall**]

vulva
(VUL-vah)
[*vulva* **wrapper**]

LANGUAGE OF MEDICINE (continued from p. 1091)

amenorrhea
(ah-men-oh-REE-ah)
[*a-* **without,** *-men-* **month,** *-rrhea* **flow**]

breast cancer
[*cancer* **crab or malignant tumor**]

cancer of the uterus
[*cancer* **crab or malignant tumor**]

candidiasis
(kan-dih-DYE-eh-sis)
[*candid-* **white,** *-asis* **condition**]

cervical cancer
(SER-vi-kal)
[*cervic-* **neck,** *-al* **relating to,** *cancer* **crab or malignant tumor**]

dysfunctional uterine bleeding (DUB)
(dis-FUNK-shun-al YOO-ter-in)
[*dys-* **difficult,** *-function-* **performance,** *-al* **relating to,** *uter-* **womb,** *-ine* **relating to**]

dysmenorrhea
(dis-men-oh-REE-ah)
[*dys-* **painful,** *-men-* **month,** *-rhea* **flow**]

ectopic pregnancy
(ek-TOP-ik)
[*ec-* **out of,** *-top-* **place,** *-ic* **relating to**]

endometrial cancer
(en-doh-MEE-tree-al KAN-ser)
[*endo-* **within,** *-metr-* **womb,** *-al* **relating to,** *cancer* **crab or malignant tumor**]

endometriosis
(en-doh-mee-tree-OH-sis)
[*endo-* **within,** *-metr-* **womb,** *-osis* **condition**]

episiotomy
(eh-piz-ee-OT-oh-mee)
[*episi-* **vulva,** *-tom-* **cut,** *-y* **action**]

fibroid
(FYE-broyd)
[*fibr-* **fiber,** *-oid* **of or like**]

fibromyoma
(fye-broh-my-OH-mah)
[*fibr-* **fiber,** *-my-* **muscle,** *-oma* **tumor**]

hydrosalpinx
(hye-droh-SAL-pinks)
[*hydro-* **water,** *-salpinx* **tube**]
pl., hydrosalpinges

hysterosalpingogram
(his-ter-oh-sal-PING-go-gram)
[*hyster-* **uterus,** *-salping-* **tube,** *-gram* **drawing**]

intrauterine device (IUD)
(in-trah-YOU-ter-in)
[*intra-* **inside** or **within,** *-uter-* **womb,** *-ine* **relating to**]

in vitro fertilization (IVF)
(in VEE-troh FER-ti-li-ZAY-shun)
[*in* **within,** *vitro* **glass,** *fertil-* **fruitful,** *-iz-* **action,** *-ation* **process**]

infertility
(in-fer-TIL-i-tee)
[*in-* **not,** *-fertil-* **fruitful,** *-ity* **state**]

leukorrhea
(loo-koh-REE-ah)
[*leuko-* **white,** *-rrhea* **flow**]

lumpectomy
(lump-EK-toh-mee)
[*lump-* **mass,** *-ec-* **out,** *-tom-* **cut,** *-y* **action**]

menotropin
(men-oh-TROHP-in)
[*men-* **month,** *-trop-* **nourish,** *-in* **substance**]

mittelschmerz
(MIT-el-schmertz)
[*mittel-* **middle,** *-schmerz* **pain**]

myoma
(my-OH-mah)
[*my-* **muscle,** *-oma* **tumor**]

oral contraceptive
(kon-tra-SEP-tiv)
[*contra-* **against,** *-cept-* **take or receive (conception),** *-ive* **agent**]

ovarian cancer
(oh-VAIR-ee-an)
[*ovum* **egg,** *cancer* **crab or malignant tumor**]

ovarian cyst
(oh-VAIR-ee-an SIST)
[*ov-* **egg,** *-arian* **relating to,** *cyst-* **bag**]

Papanicolaou test (Pap smear)
(pah-peh-ni-koh-LAH-oo)
[*George N. Papanicolaou* **Greek physician**]

pelvic inflammatory disease (PID)
(PEL-vik in-FLAM-ah-tor-ee)
[*pelv-* **basin,** *-ic* **relating to,** *inflam-* **set afire,** *-ory* **relating to**]

peritonitis
(pair-i-toh-NYE-tis)
[*peri-* **around,** *-ton-* **stretch (peritoneum),** *-itis* **inflammation**]

polycystic ovary syndrome (PCOS)
(pahl-ee-SIS-tik OH-var-ee)
[*poly-* **many,** *-cyst-* **bag,** *-ic* **relating to,** *ov-* **egg,** *-ar-* **relating to,** *-y* **location of process**]

premenstrual syndrome (PMS)
(pree-MEN-stroo-all SIN-drohm)
[*pre-* **before,** *-mens-* **month,** *-al* **relating to,** *syn-* **together,** *-drome* **running or (race)course**]

radical mastectomy
(RAD-i-kal mas-TEK-toh-mee)
[*radic-* **root,** *-al* **relating to,** *mast-* **breast,** *-ec-* **out,** *-tom-* **cut,** *-y* **action**]

salpingitis
(sal-pin-JYE-tis)
[*salping-* **tube,** *-itis* **inflammation**]

supraovulation
(soo-prah-o-vyoo-LAY-shun)
[*supra-* **above or over,** *-ov-* **egg,** *-ation* **process**]

transabdominal pelvic ultrasound
(tranz-ab-DOM-i-nal PEL-vik UL-trah-sound)
[*trans-* **across,** *-abdomin-* **belly,** *-al* **relating to,** *pelv-* **basin (pelvis),** *-ic* **relating to,** *ultra-* **beyond, sound**]

uterine fibroid
(YOO-ter-in FYE-broyd)
[*uter-* **womb,** *-ine* **relating to,** *fibr-* **fiber,** *-oid* **of or like**]

vaginitis
(vaj-i-NYE-tis)
[*vagin-* **sheath (vagina),** *-itis* **inflammation**]

CASE study

Carlos and his wife had been trying for years to have a baby with no success. After a visit to an infertility specialist, they found that Carlos had a low sperm count. Before suggesting a solution, the physicians will also check Maria's reproductive system. One of the tests they order is a hysterosalpingogram, which will confirm an open pathway for the egg.

1. Assuming no obstruction, which areas should the dye used for the hysterosalpingogram enter?
   a. Cervix, uterus, uterine tube, ovaries
   b. Cervix, uterine tube, uterus, vulva
   c. Cervix, uterine tube, ovaries, peritoneal cavity
   d. Cervix, uterus, uterine tube, peritoneal cavity

Finding no blockage in Maria's reproductive tract, the physicians recommended an intrauterine insemination (IUI). To increase the chances of a sperm encountering an egg, a medication called Clomid (*clomiphene*) was prescribed for Maria. Clomid works as an antiestrogen agent, causing the body to perceive low estrogen levels. It is given on about days 5 to 10 of the menstrual cycle.

2. What effect will Clomid have on FSH production?
   a. Increase FSH production
   b. Decrease FSH production
   c. No change in FSH production
   d. Slight decrease in FSH production followed by a sharp increase

3. After ovulation, the follicular cells first transform into what?
   a. Corpus lucidum
   b. Corpus luteum
   c. Corpus rubrum
   d. Corpus albicans

CASE study (continued)

4. Where in the female reproductive tract should the sperm and the oocyte meet (hopefully completing the process of fertilization)?
   a. In the cervix
   b. In the uterus
   c. In the uterine tubes
   d. In the ovaries

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook, **A&P Connect**, and other resources.*

CHAPTER SUMMARY

*To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the **Audio Chapter Summaries** online at evolve.elsevier.com.*

HINT *Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.*

OVERVIEW OF THE FEMALE REPRODUCTIVE SYSTEM

A. Function of the female reproductive system
   1. To produce offspring and thereby ensure continuity of the genetic code
   2. To produce eggs, or female gametes, each of which has the potential to unite with a male gamete to form the first cell of an offspring
   3. To provide nutrition and protection to the offspring for up to several years after conception

B. Structural plan of the female reproduction system
   1. Reproductive organs are classified as essential or accessory (Figure 35-1)
      a. Essential organs—gonads are the paired ovaries; gametes are ova produced by the ovaries—the ovaries are also internal genitals
      b. Accessory organs
         (1) Internal genitals—uterine tubes, uterus, and vagina—ducts or duct structures that extend from the ovaries to the exterior
         (2) External genitals—the vulva
         (3) Additional sex glands such as the mammary glands

C. Perineum (Figure 35-2)
   1. Skin-covered region between the vaginal orifice and the rectum
   2. Area that may be torn during childbirth

OVARIES

A. Location of the ovaries
   1. Nodular glands located on each side of the uterus, below and behind the uterine tubes (Figure 35-3)
   2. Ectopic pregnancy—development of the fetus in a place other than the uterus

B. Microscopic structure of the ovaries (Figure 35-4)
   1. Surface of the ovaries is covered by the germinal epithelium
   2. Ovarian follicles contain the developing female sex cells
   3. Ovum—an oocyte released from the ovary

C. Functions of the ovaries
   1. Ovaries produce ova—the female gametes
   2. Oogenesis—process that results in formation of a mature egg (Figure 35-5)
   3. Ovaries are endocrine organs that secrete the female sex hormones (estrogens and progesterone)

UTERUS

A. Structure of the uterus (Figure 35-3)
   1. Size and shape of the uterus
      a. Pear-shaped structure with two main parts—the cervix and the body
      b. Bulging upper part of the body called the fundus
   2. Location of the uterus
      a. Located in the pelvic cavity between the urinary bladder and the rectum (Figure 35-1)
      b. Uterus position (Figure 35-6) is altered by age, pregnancy, and distention of related pelvic viscera
      c. Uterus descends, between birth and puberty, from the lower abdomen to the true pelvis
      d. Uterus begins to decrease in size at menopause
   3. Position of the uterus
      a. Body lies flexed over the bladder
      b. Cervix points downward and backward, joining the vagina at a right angle
      c. Several ligaments hold the uterus in place but allow some movement
   4. Wall of the uterus—composed of three layers—the inner endometrium (mucous membrane), the middle myometrium (smooth muscle), and the perimetrium (outer incomplete layer of parietal peritoneum)
   5. Cavities of the uterus—small because of the thickness of the uterine walls
      a. The body cavity's apex constitutes the internal os and opens into the cervical canal
      b. Cervical canal is constricted at its lower end and forms the external os that opens into the vagina
   6. Blood supply of the uterus—supplied by uterine arteries

D. Functions of the uterus
   1. Uterus is part of the reproductive tract and permits sperm to ascend toward the uterine tubes
   2. If conception occurs, an offspring develops in the uterus
      a. Embryo is supplied with nutrients by endometrial glands until the production of the placenta

b. Placenta is an organ that permits the exchange of materials between the mother's blood and the fetal blood but keeps the two circulations separate
c. Myometrial contractions occur during labor and help push the offspring out of the mother's body

3. If conception does not occur, outer layers of endometrium are shed during menstruation—a cyclical event that allows the endometrium to renew itself

UTERINE TUBES

A. Uterine tubes also called fallopian tubes, or oviducts
B. Location of uterine tubes
   1. Attached to the uterus at its upper outer angles
   2. Extend upward and outward toward the sides of the pelvis and then curve downward and backward
C. Structure of the uterine tubes
   1. Uterine tubes consist of mucous, smooth muscle, and serous lining (Figure 35-7)
   2. Mucosal lining is directly continuous with the peritoneum lining the pelvic cavity
      a. Tubal mucosa is continuous with that of the vagina and uterus, which means it may become infected with organisms introduced into the vagina and thereby cause salpingitis or peritonitis
      b. Inflammation of uterine tubes may lead to scarring and partial or complete closure of the lumen
   3. Each uterine tube has three divisions: isthmus, ampulla, and infundibulum
D. Function of the uterine tubes—serve as transport channels for ova and as the site of fertilization (Figure 35-8)

VAGINA

A. Location of the vagina—a tubular organ located between the rectum, urethra, and bladder
B. Structure of the vagina
   1. A collapsible tube capable of distention, composed of smooth muscle, and lined with mucous membrane arranged in rugae
   2. Anterior wall shorter than the posterior wall because the cervix protrudes into its uppermost portion
   3. Hymen—a mucous membrane that typically forms a border around the vagina in young premenstrual girls
C. Functions of the vagina
   1. Lining of the vagina lubricates and stimulates the penis during sexual intercourse and acts as a receptacle for semen
   2. Vagina is the lower portion of the birth canal
   3. Vagina transports tissue and blood shed during menstruation to the exterior

VULVA

A. Structure of the vulva (pudendum; the female external genitals)—mons pubis, labia majora, labia minora, clitoris, urinary meatus, vaginal orifice, and greater vestibular glands (Figure 35-9)
B. Functions of the vulva
   1. Mons pubis and labia protect the clitoris and vestibule
   2. Clitoris contains sensory receptors that send information to the sexual response area of the brain (Figure 35-10)
   3. Vaginal orifice is the boundary between the internal and external genitals

FEMALE REPRODUCTIVE CYCLES

A. Female reproductive system has many cyclical, recurring changes that start with the beginning of menses
   1. Ovarian cycle
      a. Ovaries at time of birth contain oocytes in primary follicles in which the meiotic process has been suspended
      b. At the beginning of menstruation each month, several of the oocytes resume meiosis
      c. Meiosis will stop again just before the cell is released during ovulation (Figure 35-11)
   2. Menstrual cycle (endometrial cycle) is divided into four phases
      a. Menses
      b. Postmenstrual phase
      c. Ovulation
      d. Premenstrual phase
   3. Myometrial cycle
   4. Gonadotropic cycle
B. Control of female reproductive cycles
   1. Hormones control cyclical changes
   2. Cyclical changes in the ovaries result from changes in the gonadotropins secreted by the pituitary gland (Figures 35-12 and 35-13)
   3. Cyclical changes in the uterus are caused by changes in estrogens and progesterone (Figure 35-14)
   4. Low levels of FSH and LH cause regression of the corpus luteum if pregnancy does not occur; this causes a decrease in estrogen and progesterone, which triggers endometrial sloughing of the menstrual phase
   5. Control of cyclical changes in gonadotropin secretion is caused by positive and negative feedback mechanisms and involves estrogens, progesterone, and secretion of releasing hormones by the hypothalamus
C. Importance of the female reproductive cycles
   1. Ovarian cycle
      a. Primary function is to produce ova at regular intervals
      b. Secondary function is to regulate the endometrial cycle through estrogen and progesterone
   2. Endometrial cycle—functions to make the uterus suitable for implantation of a new offspring
   3. Cyclical nature of the reproductive system and the fact that fertilization will occur within 24 hours after ovulation mean that a woman is fertile only a few days of each month
D. Infertility—failure to conceive after 1 year of regular unprotected intercourse
   1. Causes are varied and can involve either or both partners
   2. Fertility drugs and other assisted reproductive procedures such as IVF (in vitro fertilization) are available
E. Menstrual flow begins at puberty, and the menstrual cycle continues for about 3 decades (Figure 35-15)

BREASTS

A. Location and size
   1. Breasts lie over the pectoral muscles
   2. Estrogens and progesterone control breast development
   3. Breast size is determined by the amount of fat around glandular tissue (Figure 35-16)
   4. Alveoli of the mammary gland produce milk (Figure 35-17), and a system of lactiferous ducts carries it to the nipple (Figure 35-18), surrounded by an areola

B. Structure of the breasts
   1. Each consists of several lobes separated by septa of connective tissue
   2. Lobes consist of several lobules, composed of connective tissue embedded with pouches of milk-secreting cells (alveoli)
   3. Lactiferous duct from each lobe converges toward nipple
   4. Suspensory ligaments help support the breast

B. Function of the breasts
   1. Function of mammary glands is lactation
   2. Mechanism of lactation (Figure 35-19)
      a. Ovarian hormones make the breasts structurally ready to produce milk
      b. Shedding of the placenta results in a decrease of estrogens and thus stimulates prolactin
      c. Prolactin stimulates lactation
      d. Additional hormones (e.g., oxytocin) also support lactation (Table 35-2)
   3. Importance of lactation
      a. Can provide nutrient-rich milk to offspring for up to several years from birth
      b. Some advantages of breast milk
         (1) Nutrients
         (2) Passive immunity from antibodies present in the colostrum and milk
         (3) Emotional bonding between mother and child

THE BIG PICTURE: THE FEMALE REPRODUCTIVE SYSTEM AND THE WHOLE BODY

A. Reproductive system imparts immortality to genes and ensures survival of the species

B. Relationship of the female reproductive system with other body systems
   1. Close proximity to the urinary system; share a common structure: the vulva
   2. Anatomical relationship with the skeletal muscles in the perineum
   3. Breasts are actually modifications of the skin in the integumentary system

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Identify the essential and accessory organs in the female reproductive system.
2. Describe the three layers that compose the wall of the uterus.
3. Identify the vessels that supply blood to the uterus.
4. List the eight ligaments that hold the uterus in a normal position.
5. How does the uterus serve as part of the female reproductive tract?
6. What and where are the uterine tubes? Approximately how long are they? What lines the uterine tubes? Their lining is continuous on their distal ends with what? With what on their proximal ends?
7. Trace the development of a female sex cell from its most primitive state through ovulation.
8. What hormones are secreted by the cells in ovarian tissue?
9. Identify all vaginal functions.
10. List all the structures that make up the female external genitals.
11. Define the term *episiotomy*.
12. Identify the advantages that nursing from the mother's breast provides offspring.
13. What method makes it possible to measure blood levels of gonadotropins?
14. Describe the hormonal changes during menopause.
15. Define the term *mittelschmerz*.

CRITICAL THINKING QUESTIONS

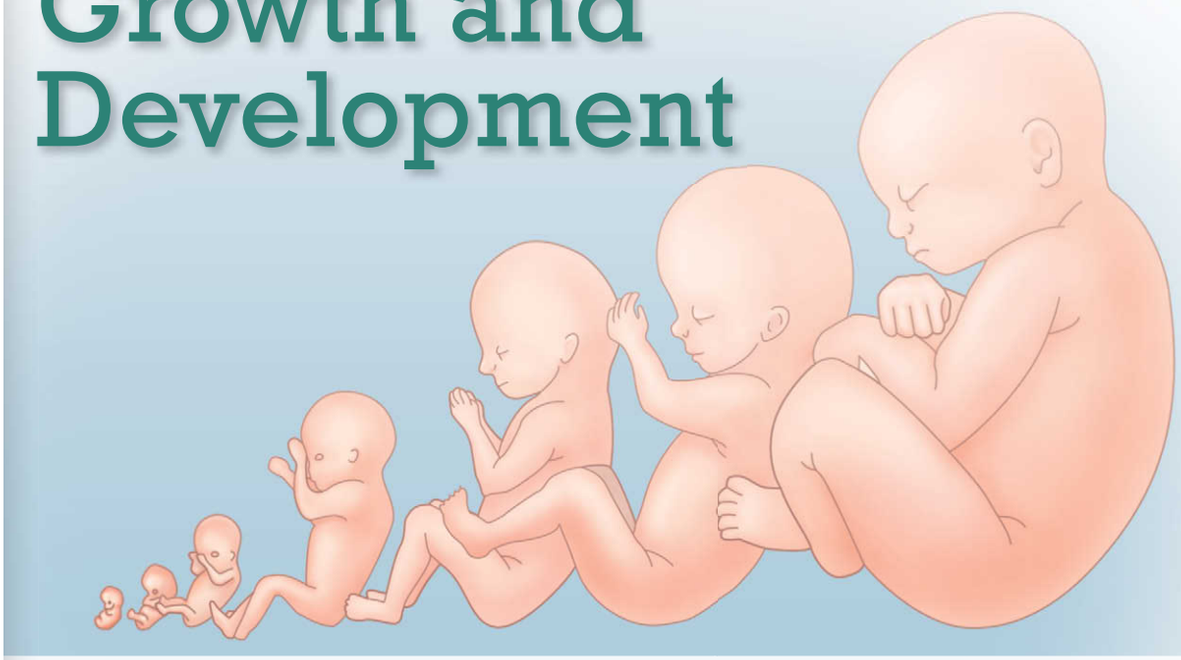


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Name and explain the function of the various hormones that regulate lactation. Where are they produced, and how would you summarize their function and their influence on lactation?
2. List the phases of the menstrual cycle. Which of these phases shows the most variance in length of time? How do the events in each phase contribute to the overall function of the reproductive system?
3. How would you explain the interaction of the hormones that result in ovulation? From what is the name "luteinizing" hormone derived?
4. State in your own words the control of cyclical ovarian changes brought on by FSH and LH.
5. Explain, in your own words, the control of cyclical uterine changes brought on by the ovarian hormones. The drop in the level of these hormones triggers what event?
6. Regarding hormone functions, what is the reason contraceptive pills and implants are effective in preventing pregnancy?
7. How would you correlate the events of the ovarian cycle with the events of the uterine cycle?
8. It is not uncommon for women with eating disorders, such as anorexia, to develop amenorrhea. Explain the link between these two conditions.
9. Female athletes may experience an undesirable condition called *amenorrhea*. What evidence can you find to support this statement?

36

Growth and Development



LANGUAGE OF SCIENCE

HINT

Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.

acrosome reaction
(AK-roh-sohm)
[*acro-* **top or tip,** *-some* **body**]

adolescence
(ad-oh-LESS-ens)
[*adolesc-* **grow up,** *-ence* **state**]

adulthood

amniotic cavity
(am-nee-OT-ik KAV-i-tee)
[*amnio-* **fetal membrane,** *-ic* **relating to,** *cav-* **hollow,** *-ity* **state**]

blastocyst
(BLASS-toh-sist)
[*blasto-* **bud,** *-cyst* **pouch**]

childhood

chorion
(KOH-ree-on)
[*chorion* **skin**]

corona radiata
(ko-ROHN-ah ray-dee-AH-tah)
[*corona* **crown,** *radiata* **radiant (with rays)**]

developmental biology
[*bio-* **life,** *-log-* **words (study of),** *-y* **activity**]

diploid
(DIP-loyd)
[*diplo-* **twofold,** *-oid* **of or like**]

ectoderm
(EK-toh-derm)
[*ecto-* **outside,** *-derm* **skin**]

endoderm
(EN-doh-derm)
[*endo-* **within,** *-derm* **skin**]

fertilization
(FER-ti-li-ZAY-shun)
[*fertil-* **fruitful,** *-ation* **process**]

first polar body
[*pol-* **pole,** *-ar* **relating to**]

fraternal twin

continued on p. 1125

CHAPTER OUTLINE

HINT

Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.

A New Human Life, 1097
- Production of Sex Cells, 1097
  - Meiosis, 1097
  - Spermatogenesis, 1098
  - Oogenesis, 1101
- Ovulation and Insemination, 1101
- Fertilization, 1101

Prenatal Period, 1103
- Cleavage and Implantation, 1103
- Placenta, 1105
- Periods of Development, 1107
- Stem Cells, 1110
- Formation of the Primary Germ Layers, 1111
  - Endoderm, 1111
  - Ectoderm, 1111
  - Mesoderm, 1111
- Histogenesis and Organogenesis, 1111

Birth, or Parturition, 1114
- Stages of Labor, 1115
- Multiple Births, 1115

Postnatal Period, 1116
- Infancy, 1116
- Childhood, 1117
- Adolescence and Adulthood, 1118
- Older Adulthood and Senescence, 1118

Effects of Aging, 1120
- Skeletal System, 1120
- Muscular System, 1120
- Integumentary System (Skin), 1120
- Urinary System, 1121
- Respiratory System, 1121
- Cardiovascular System, 1122
- Special Senses, 1122
- Reproductive Systems, 1122
- Benefits of Aging, 1122

Causes of Death, 1122

The Big Picture: Growth, Development, and the Whole Body, 1123

Mechanisms of Disease, 1124

Case Study, 1126

Many of your fondest and most vivid memories are probably associated with your birthdays. The day of birth is an important milestone of life. Most people continue to remember their birthday in some special way each year; birthdays are pleasant and convenient reference points to mark periods of transition or change in our lives. The actual day of birth marks the end of one phase of development called the ***prenatal period*** *and the beginning of a second called the* ***postnatal period.*** *The prenatal period begins at conception and ends at birth; the postnatal period begins at birth and continues until death. Although important periods in our lives such as childhood and adolescence often are remembered as a series of individual and isolated events, they are in reality part of an ongoing and continuous process. In reviewing the field of human developmental biology—study of the many changes that occur during the cycle of life from conception to death—it is often convenient to isolate certain periods such as infancy or old age for study. However, the life cycle is not a series of stop-and-start events or individual and isolated periods of time. Instead, it is a biological process that is characterized by continuous modification and change.*

This chapter discusses some of the basic concepts of important events and changes that occur in the ongoing development of the individual from conception to death. Study of development during the prenatal period is followed by a review of changes occurring during infancy and adulthood, and finally, by some of the more important changes that occur in the individual organ systems of the body as a result of aging.

A NEW HUMAN LIFE

Production of Sex Cells

Before a new human life can begin, some preliminary processes must occur. Of utmost importance is the production of mature *gametes*, or sex cells, by each parent. Spermatozoa, gametes of the male parent, are produced by a process called **spermatogenesis.** Ova, gametes of the female parent, are produced by a process called **oogenesis.**

MEIOSIS

Both types of gamete production require a special form of cell division characterized by **meiosis.** Recall from Chapter 5 that meiosis is the orderly arrangement and distribution of chromosomes that, unlike *mitosis*, reduces the number of chromosomes in each daughter cell to half the number present in the parent cell.

The necessity for chromosome reduction as a preliminary step to union of the sex cells is explained by the fact that the cells of each species of living organisms contain a specific number of chromosomes. Human cells, for example, contain 23 pairs, or a total of 46 chromosomes. This total of 46 chromosomes per body cell is known as the **diploid** number of chromosomes. Diploid comes from the Greek *diploos*, meaning "twofold." If the male and female cells united without first halving their respective chromosomes, the resulting cell would contain twice as many chromosomes as is normal for human beings. Mature ova and sperm therefore contain only 23 chromosomes, or half as many, as other human cells. This total of 23 chromosomes per sex cell is known as the **haploid** number of chromosomes (from the Greek *haploos*, meaning "single").

Meiotic division consists of two cell divisions that take place one after the other in succession. They are referred to as meiotic division I and meiotic division II, and in both, prophase, metaphase, anaphase, and telophase occur (Figure 36-1).

In the interphase that precedes prophase I (of meiotic division I) the same events occur as take place in the interphase preceding mitotic division. Specifically, each DNA molecule replicates and thereby becomes a pair of chromatids, attached to each other only at the centromere. The term *chromosome* applies to any condensed chromatin with its own centromere. For simplicity's sake, in both Figures 36-1 and 36-2, only 4 of the 46 chromosomes are shown. Notice that early in meiosis I, homologous pairs of chromosomes are moved together to form groupings called *tetrads.* During anaphase I the tetrads split (recall that in mitosis it is the chromosomes that split during anaphase).

In meiosis I the phenomenon of "*crossing over*" occurs. During crossing over a chromatid segment of each chromosome crosses over and becomes part of the adjacent chromosome in the pair (see Figure 37-4). This is a highly significant event and is discussed in some detail in the next chapter. Because each chromatid segment consists of specific genes, the crossing over of chromatids reshuffles the genes—that is, it transfers some of them from one chromosome to another. This exchange of genetic material can add almost infinite variety to the ultimate genetic makeup of an individual.

Metaphase I follows the last stage of prophase I, and as in mitosis, the chromosomes align themselves along the equator of the spindle fibers, as Figure 36-1 shows. But in anaphase I the two chromatids that make up each chromosome do not separate from each other as they do in mitosis to form two new chromosomes out of each original one. In anaphase I, only one of each pair of chromosomes moves to each pole of the parent cell.

As you can see in Figures 36-1 and 36-2, when the parent cell divides to form two cells in meiotic division I, each daughter cell contains two chromosomes or half as many as the parent cell had. Remember that each chromosome still consists of two sister chromatids joined at the centromere. Thus the daughter cells formed by meiotic division I contain a haploid number of chromosomes, or half as many as the diploid number in the parent cell.

As you can see in Figure 36-1, meiotic division II is essentially the same as mitotic division. In both spermatogenesis and

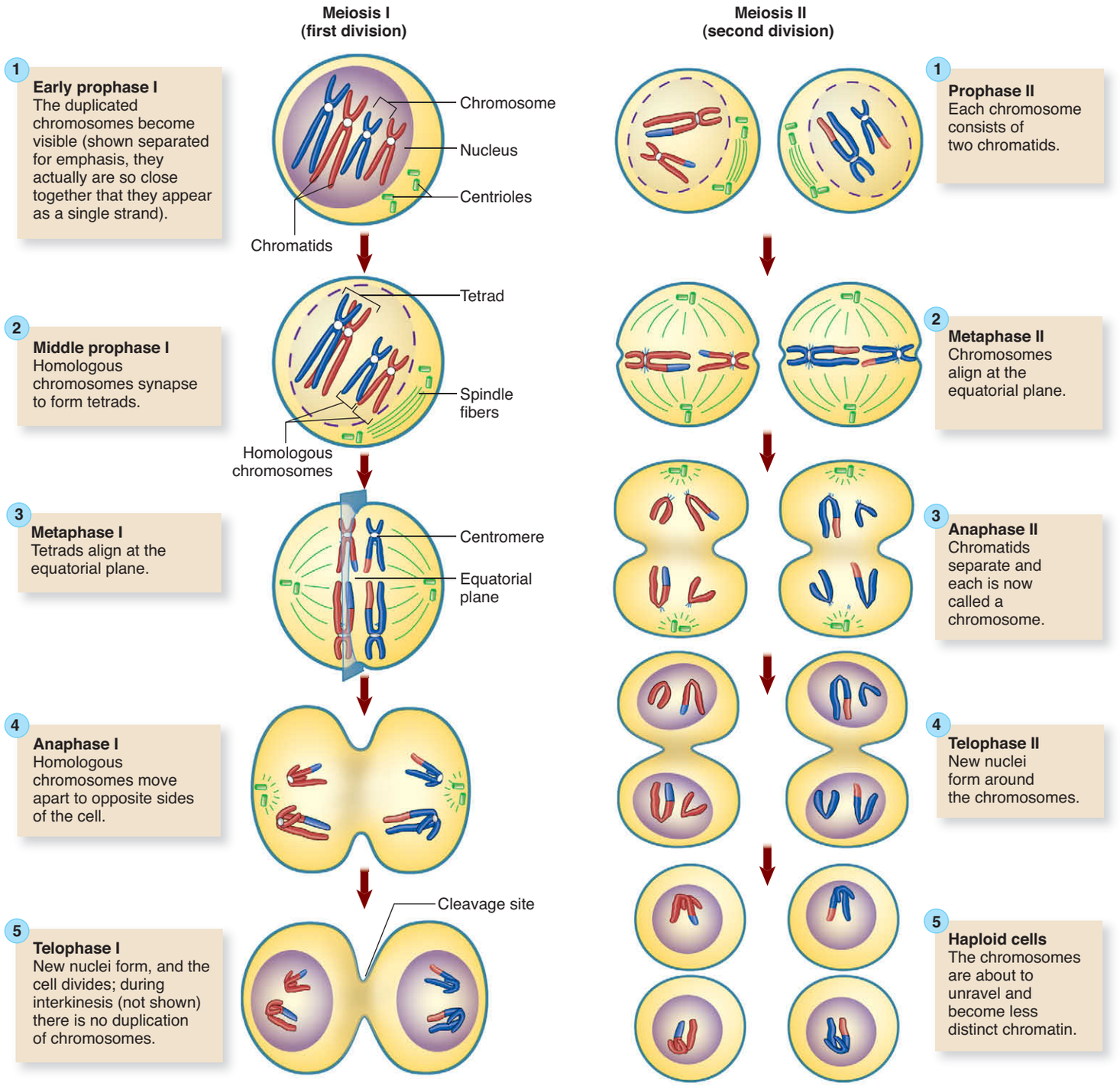


FIGURE 36-1

Meiotic cell division. Meiosis is a series of events that involves two separate division processes called *meiosis I* and *meiosis II*. Notice that four daughter cells, each with the haploid number of chromosomes, are produced from each parent cell that enters meiotic cell division. For simplicity's sake, only four chromosomes are shown in the parent cell instead of the usual 46.

oogenesis, the second meiotic division reproduces each of the two cells formed by meiotic division I and so forms four cells, each with the haploid number of chromosomes.

SPERMATOGENESIS

Spermatogenesis is the process by which the primitive sex cells, or **spermatogonia,** already formed in the seminiferous tubules of a newborn baby boy can later become transformed into mature sperm, or *spermatozoa*. Spermatogenesis begins at about the time of puberty and usually continues throughout a man's life. Figure 36-3 shows some of the major steps of spermatogenesis. Trace each step in this diagram with your finger as you read the following paragraph.

Each primary spermatocyte undergoes meiotic division I to form two secondary spermatocytes, each with a haploid number

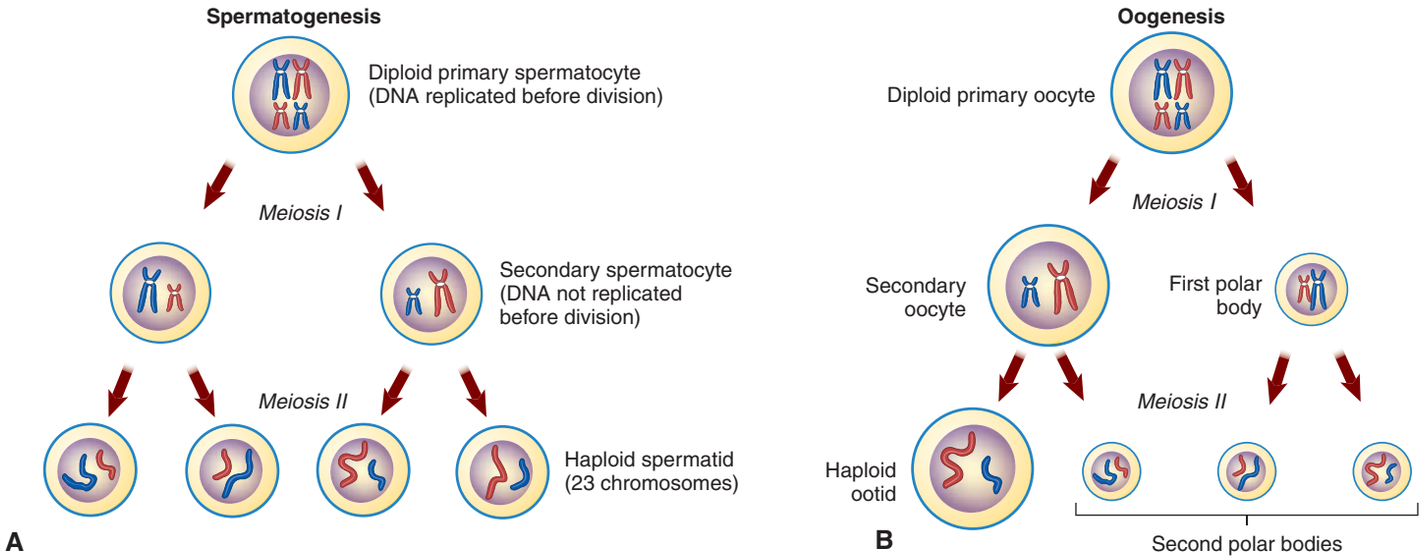


FIGURE 36-2

Overview of gamete production. A, Spermatogenesis. A primary spermatocyte (diploid) undergoes meiotic division to produce four haploid daughter spermatids. **B,** Oogenesis. A primary oocyte undergoes meiotic division to produce a single ovum and three small polar bodies.

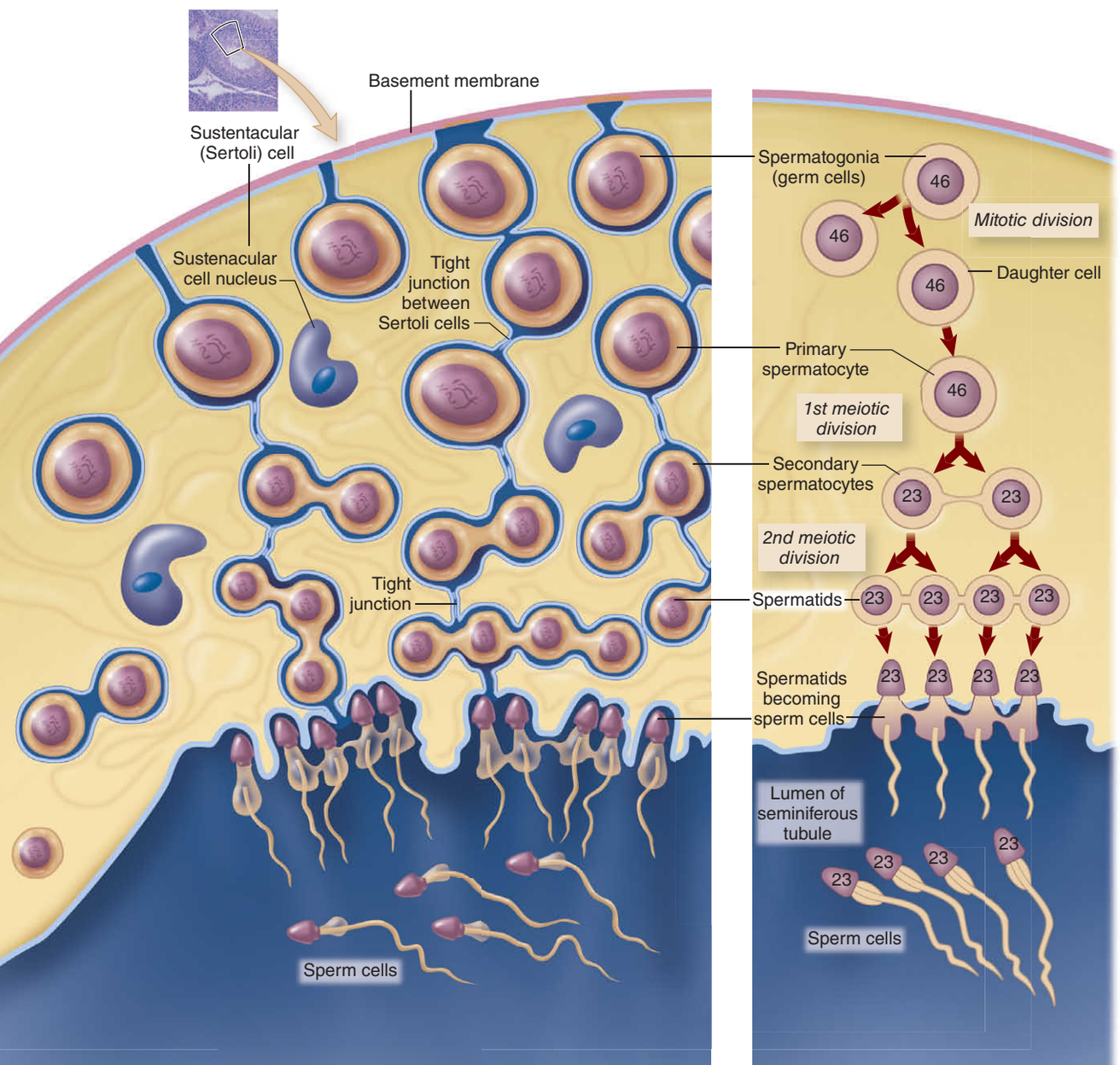


FIGURE 36-3

Spermatogenesis. First, spermatogonia in the outer rim of the seminiferous tubule produce daughter cells by mitotic division. These daughter cells, each with 46 chromosomes, become primary spermatocytes. A primary spermatocyte then undergoes meiotic division I to form two secondary spermatocytes, each with a haploid number of chromosomes (23). Each of the two secondary spermatocytes undergoes meiotic division II to form a total of four spermatids. Spermatids then differentiate to form heads and tails, eventually becoming mature spermatozoa—all with 23 chromosomes. Recall the role of the sustentacular, or Sertoli, cells, which support the developing male gametes structurally (by physically supporting them) and functionally (by releasing nutrients to them and by secretion of the hormone inhibin).

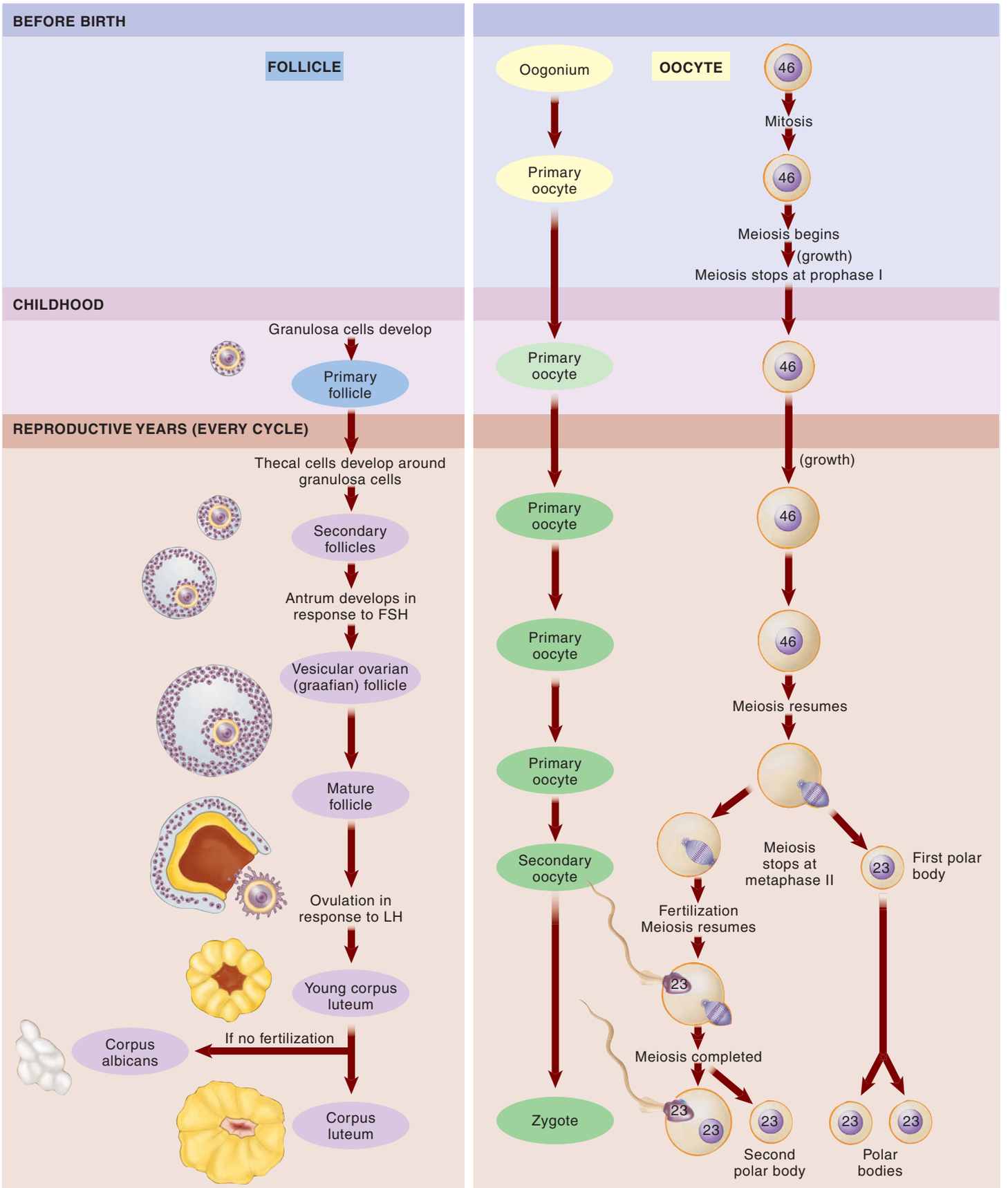


FIGURE 36-4

Oogenesis. Production of a mature ovum (oocyte) and subsequent fertilization are shown on the right as a series of cell divisions and on the left as a series of changes in the ovarian follicle. *FSH,* Follicle-stimulating hormone; *LH,* luteinizing hormone.

of chromosomes (23). Each secondary spermatocyte undergoes meiotic division II to form a total of four spermatids. Spermatids then differentiate to form heads and tails, eventually becoming mature *spermatozoa*. Thus spermatogenesis forms four spermatozoa (singular, *spermatozoon*)—each with only 23 chromosomes—from one primary spermatocyte that had 23 pairs, or 46 total chromosomes.

OOGENESIS

Oogenesis is the process by which primitive female sex cells, or **oogonia,** become mature ova. As you read through the following paragraphs, trace the steps of oogenesis in Figure 36-4.

During the fetal period, oogonia in the ovaries undergo mitotic division to form **primary oocytes**—about a half million of them by the time a baby girl is born. Most of the primary oocytes develop to prophase I of meiosis before birth. There they stay until puberty.

| A&P CONNECT |

What physiological advantage is gained by postponing the completion of meiotic division as an ovum matures? The surprising answer is found in ***Arrest of Oocyte Development*** online at ***A&P Connect.***

evolve

During childhood, **granulosa cells** develop around each primary oocyte, forming a **primary follicle.** Although several thousand primary oocytes do not survive into puberty, by the time a female child reaches sexual maturity, about 400,000 primary oocytes remain.

Beginning at puberty, during each cycle, about a thousand primary oocytes resume meiosis. Their surrounding follicles begin to mature and some of the outer granulosa cells differentiate to become **theca cells.** Theca cells produce *androgen*, a steroid that is converted by granulosa cells into estrogen. At this point, the follicles are known as **secondary follicles.** As the secondary follicles mature, they migrate toward the surface of the ovary—sometimes in several waves during one cycle. Usually only one follicle per cycle survives and matures enough to reach the surface of the ovary, where it can be seen as a fluid-filled bump. The fluid-filled space within each mature follicle is called the *antrum*. A mature *vesicular ovarian follicle* ready to burst open from the ovary's surface is also called a *graafian follicle*.

By that time, meiosis has resumed inside the primary oocyte within the mature follicle. Meiosis I produces a **secondary oocyte** and the **first polar body** (see Figure 36-2, *B*). Just before ovulation, meiosis again halts—this time at metaphase II. Under the influence of LH (luteinizing hormone), ovulation occurs. Ovulation, you may recall, is the release of an oocyte from a burst follicle.

Meiosis II in the released oocyte resumes only when, and if, the head of a sperm cell enters the secondary oocyte (ovum). If fertilization does not occur, then the ovum simply degenerates. If fertilization does occur, however, then meiotic division of the secondary oocyte produces a second polar body and a mature, fertilized ovum called the **zygote** (ZYE-goht).

Note that during oogenesis, the cytoplasm is *not* equally divided among the daughter cells. Of the four daughter cells produced, only one is large enough to survive. Thus each primary oocyte produces only one mature ovum, plus three tiny *polar bodies*. These polar bodies quickly break down and are reabsorbed into nearby cells. A total of four mature sperm cells are formed from each primary spermatocyte in spermatogenesis. This difference may be accounted for by the fact that for reproductive success, an ovum must have a huge store of cytoplasm with all of its organelles, nutrients, and regulatory molecules. In other words, nearly all the cytoplasm is conserved by the one daughter oocyte that survives.

Ovulation and Insemination

After gamete formation, the second preliminary step necessary for conception of a new individual consists of bringing the sperm and ovum into proximity with each other so that the union of the two can take place. Two processes are involved in the accomplishment of this step:

1. Ovulation or expulsion of the mature ovum from the mature ovarian follicle into the abdominopelvic cavity, from which it enters one of the uterine (fallopian) tubes.
2. Insemination or expulsion of the seminal fluid from the male urethra into the female vagina. Recall from Chapter 34 that a process called *capacitation* occurs after ejaculation, and this enables the sperm to eventually unite with an egg. Several million sperm enter the female reproductive tract with each ejaculation of semen. By lashing movements of their flagella-like tails, assisted by various processes in the female reproductive tract, the sperm make their way into the external os of the cervix, through the cervical canal and uterine cavity, and into the uterine (fallopian) tubes.

Fertilization

After ovulation the discharged ovum first enters the abdominopelvic cavity and then soon finds its way into the uterine (fallopian) tubes, where conception, or **fertilization,** may take place (Figure 36-5).

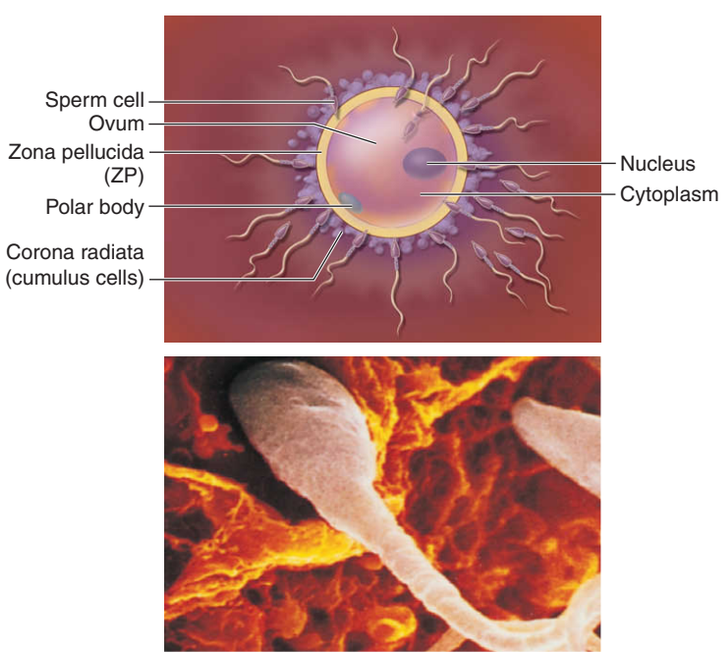


FIGURE 36-5

Fertilization. Fertilization is a specific biological event. It occurs when the male and female sex cells fuse. After union between a sperm cell and the ovum has occurred, the cycle of life begins. The scanning electron micrograph shows spermatozoa beginning to burrow into the surface of the zona pellucida (ZP) layer surrounding the ovum. Only one sperm may enter the ovum.

Sperm cells "swim" up the uterine tubes toward the ovum. Look at the relationship of the ovary, the uterine tube, and the uterus in Figure 36-6. Recall from Chapter 35 that each uterine tube extends outward from the uterus for about 10 cm (4 inches). It then ends in the abdominal cavity near the ovary, as you can see in Figure 36-6, in an opening surrounded by fringelike processes, the fimbriae. Sperm cells that are deposited in the vagina must enter and "swim" through the uterus and then move out of the uterine cavity and through the uterine tube to meet the ovum. Fertilization most often occurs in the outer one third of the oviduct, as shown in Figure 36-6.

| A&P CONNECT |

Artificial fertilization outside the body is sometimes used to enhance reproductive success. Read a brief description of this strategy and other *assisted reproductive technologies (ARTs)* in ***In Vitro Fertilization*** online at ***A&P Connect.***

The process of sperm movement is assisted by mechanisms within the female reproductive tract. For example, mucous strands in the cervical canal guide the sperm on their way into the uterus. Peristaltic contractions of the female reproductive tract and ciliary movement along the lining of the uterine tubes also assist the movement of sperm. Sperm are attracted to the warmer temperatures of the uterine tubes—a process of attraction called **thermotaxis.** Despite all this, however, only a small fraction of the sperm deposited in the vagina ever reach the ovum. Only 50 to 100 sperm out of 250 million to 500 million sperm actually reach their target.

The ovum also takes an active role in the process of fertilization. Experiments show that the ovum and its surrounding layers actually attract nearby sperm with various regulatory molecules. Recall that such movement toward a chemical attractant is called *chemotaxis.* These layers around the ovum include a thick jellylike film called the **zona pellucida (ZP)** with an outer envelope of *cumulus cells* called the **corona radiata.** Receptor molecules on these ovum-surrounding layers bind sperm attracted to the area. Once bound to a receptor, an **acrosome reaction** occurs at the head of the sperm. This acrosome reaction allows the release of enzymes from the acrosome that break down the outer layers surrounding the ovum. The cumulus cells also release progesterone and other molecules that promote increased sperm motility, which aids sperm movement through the outer layers and toward the ovum.

Once the sperm reaches the surface of the ovum, the two plasma membranes fuse and the nucleus of the sperm moves inside the ovum. In addition to the sperm nucleus, RNA and protein molecules from the sperm cell also enter the egg. The RNA molecules apparently code for proteins needed early in development—thus adding to the ovum's cellular resources. RNA molecules involved in "gene silencing" may also be released into the ovum during fertilization (see Box 5-2 on p. 120).

As soon as the head and neck of one spermatozoon fuse with the ovum (the tail degenerates), complex mechanisms in the egg are activated by sperm proteins to ensure that no more sperm enter. Specifically, sperm proteins trigger an increase in calcium concentration that causes vesicles just inside the ovum's plasma membrane to release enzymes that inactivate the sperm receptors on the ZP. This thick film, then, becomes an impenetrable barrier

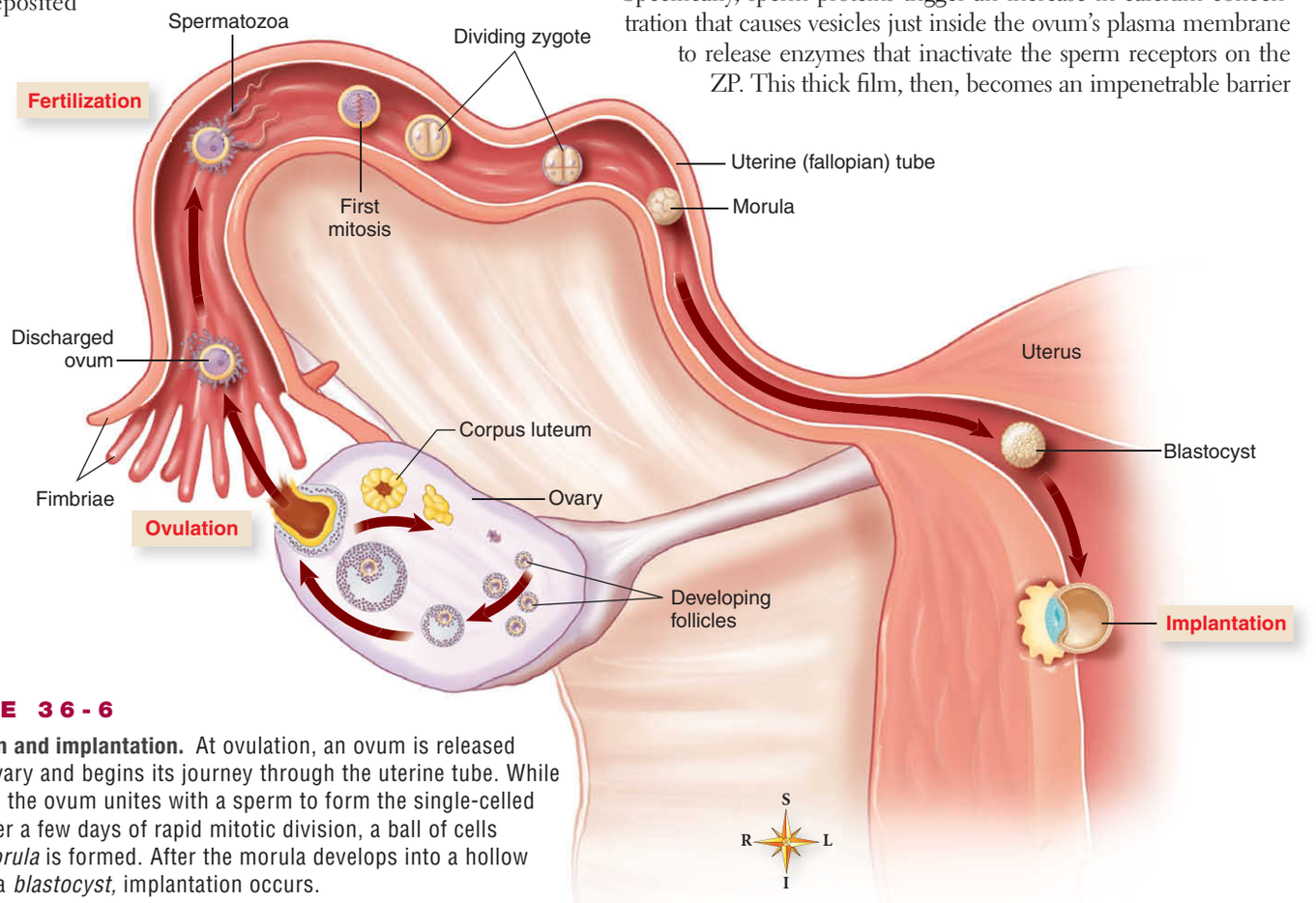


FIGURE 36-6

Fertilization and implantation. At ovulation, an ovum is released from the ovary and begins its journey through the uterine tube. While in the tube, the ovum unites with a sperm to form the single-celled zygote. After a few days of rapid mitotic division, a ball of cells called a *morula* is formed. After the morula develops into a hollow ball called a *blastocyst,* implantation occurs.

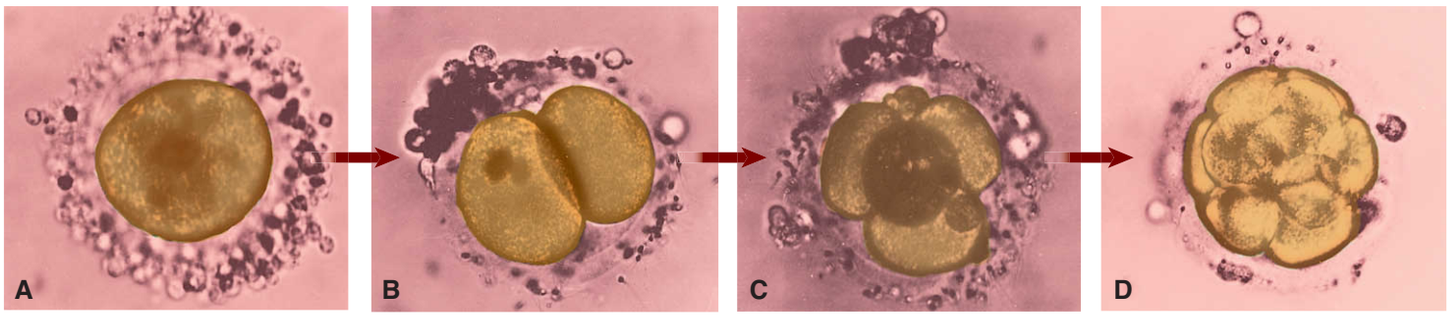


FIGURE 36-7

Initial rapid cell division in human development. **A,** Fertilized ovum, or zygote. **B** to **D,** Early cell divisions produce more and more cells. The solid mass of cells shown in **D** forms the morula—an early stage in embryonic development.

sometimes called the *fertilization membrane.* The 23 chromosomes from the sperm nucleus combine with the 23 chromosomes already in the ovum to restore the diploid number of 46 chromosomes.

In as much as the ovum lives only a short time (probably only a day or so) after leaving the ruptured follicle, the fertilization "window" occurs around the time of ovulation. Because sperm may live up to a few days after entering the female tract, sexual intercourse any time from about 3 days before ovulation to a day or so after ovulation may result in fertilization.

The fertilized ovum, or zygote, is genetically complete; it represents the first cell of a genetically new individual. Time, nourishment, and a proper prenatal environment are all that are needed for expression of characteristics such as sex, hair, and skin color that were determined at the time of fertilization.

| QUICK CHECK |

1. What is the function of meiotic division?
2. How does meiosis differ from mitosis?
3. Where in the female reproductive tract does fertilization usually occur?
4. What is the technical name for the fertilized ovum?

PRENATAL PERIOD

The **prenatal period** of development begins at the time of conception, or fertilization (i.e., at the moment the female ovum and the male sperm cell unite). The period of prenatal development continues until the birth of the child about 39 weeks later. The science of the development of the individual before birth is called **embryology** (em-bree-OL-oh-gee). It is a story of biological marvels, describing the means by which a new human life is begun and the steps by which a single microscopic cell is transformed into a complex human being.

Cleavage and Implantation

As you can see in Figure 36-6, once the zygote is formed, it immediately begins to cleave, or divide, and in about 3 days a solid mass of cells called a **morula** (MOR-yoo-lah) is formed. The cells of the morula begin to form an inner cavity as they continue to divide, and by the time the developing embryo reaches the uterus, it is a hollow ball of cells called a **blastocyst** (BLASS-toh-sist). At about 1 week after fertilization, the process of **implantation** begins. In about 10 days from the time of fertilization, the blastocyst is completely implanted in the uterine lining—before nutrients from the mother are available to nourish it. Of course, problems in development or implantation may occur at any stage—resulting in loss of the offspring and termination of the developmental process.

The rapid cell division taking place up to the blastocyst stage occurs with no significant increase in total mass compared with the zygote (Figure 36-7). One of the specializations of the ovum (and its surrounding layers) is its incredible store of nutrients that support this embryonic development until implantation has occurred.

Note in Figure 36-8 that the blastocyst consists of an outer layer of cells and an **inner cell mass.** The outer wall of the blastocyst is called the **trophoblast** (see Figure 36-8). As the blastocyst develops further, the inner cell mass forms a structure with two cavities called the **yolk sac** and **amniotic** (am-nee-OT-ik) **cavity**

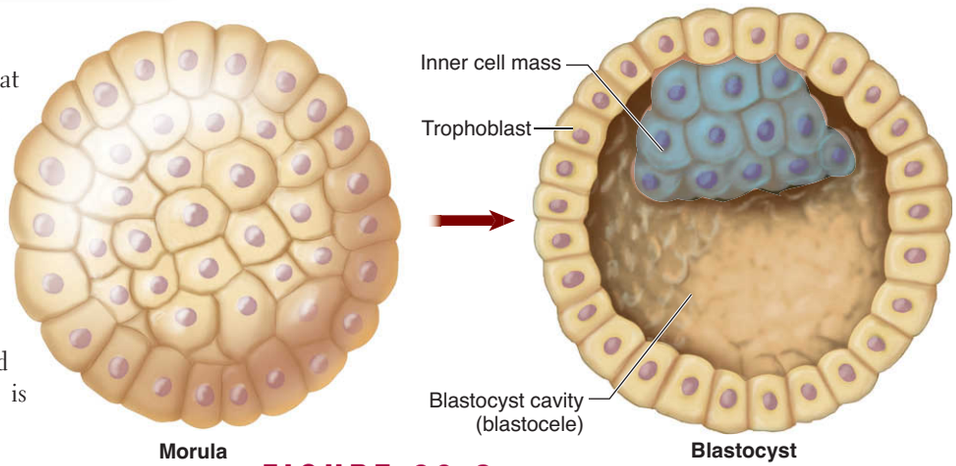


FIGURE 36-8

Early stages in the development of the human embryo. The morula consists of an almost solid spherical mass of cells. The embryo reaches this stage about 3 days after fertilization. The blastocyst (hollowing) stage develops next, before implantation in the uterine lining.

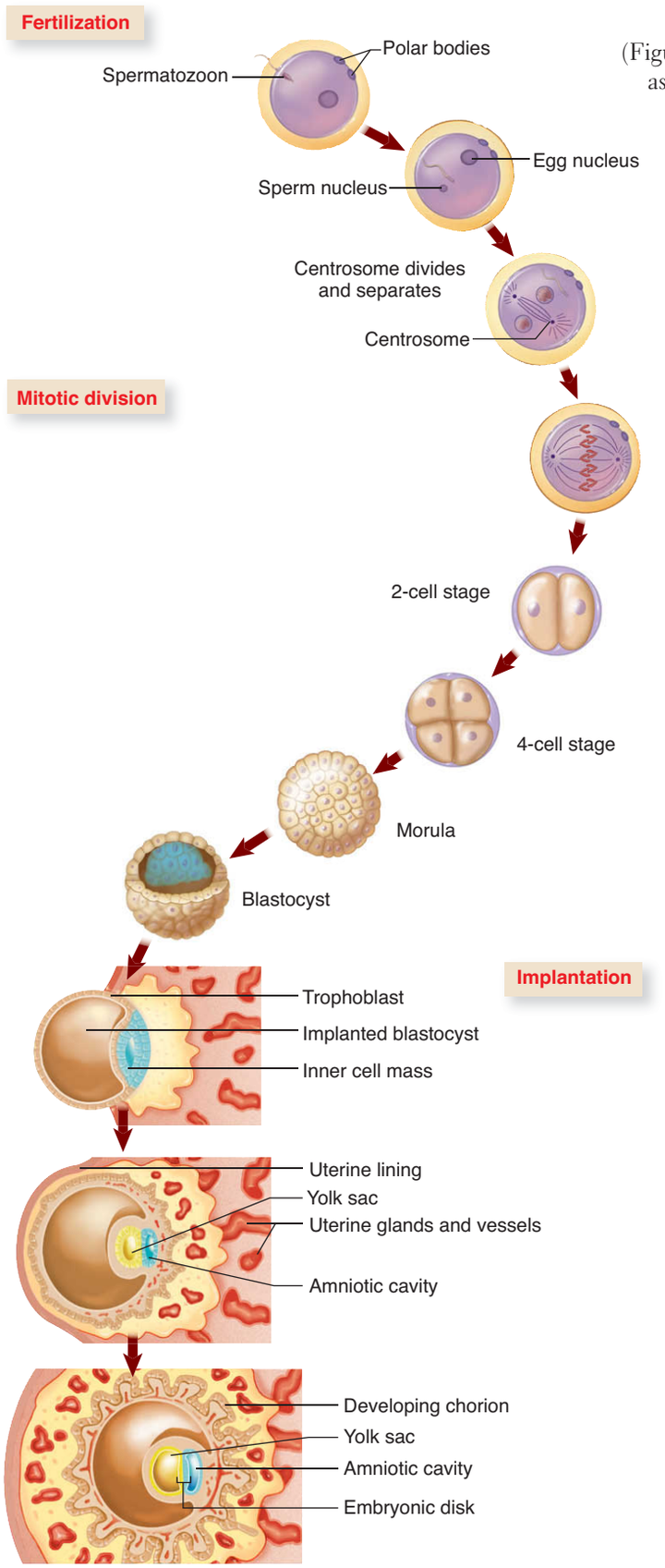


FIGURE 36-9

From fertilization to implantation and development of the yolk sac. Rapid growth of uterine glands and vessels covers the developing blastocyst at the time of implantation.

(Figures 36-9 and 36-10). The yolk sac is most important in animals such as birds that depend heavily on yolk as a nutrient for the developing embryo. In these animals the yolk sac digests the yolk and provides the resulting nutrients to the embryo. Because the uterine lining provides nutrients to the developing embryo in humans, the function of the yolk sac is not a nutritive one. Instead, it has other functions, including production of blood cells. It is the inner cell mass that eventually forms the tissues of the offspring's body. The trophoblast, on the other hand, forms the support

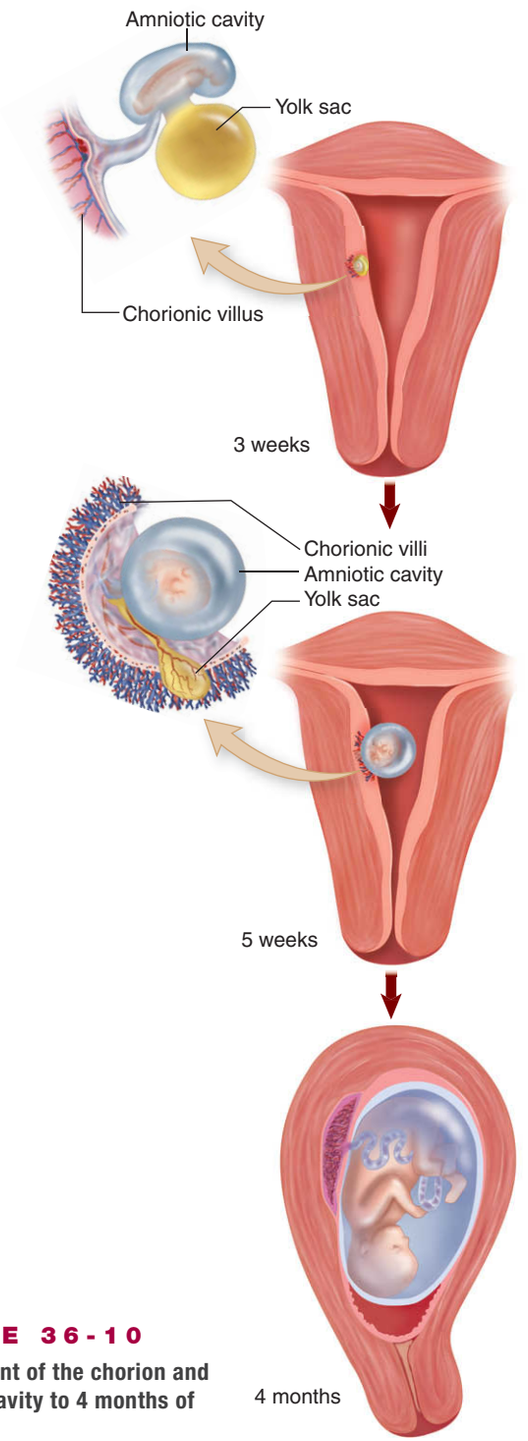


FIGURE 36-10

Development of the chorion and amniotic cavity to 4 months of gestation.

Box 36-1 | FYI

Developmental Biology

Developmental biology is the name given to the branch of life science that studies the process of change over the life cycle. This process of change is called *development.* It is important to realize that in developmental biology, the terms *growth* and *development* do not mean the same thing. Growth is simply an increase in body mass. Development, on the other hand, refers to the complex series of changes that occur at various times of life. Early stages of development—particularly the prenatal stages—are characterized by rapid growth, whereas later stages of development are characterized by little, if any, growth of body tissues.

In this chapter, we briefly discuss various subtopics within the field of human developmental biology. For example, prenatal development is studied by a branch of developmental biology called **embryology.** The biological changes observed during late adulthood are studied by a branch of developmental biology called **gerontology.**

Basic concepts of embryology, gerontology, and other subdisciplines of developmental biology seem to have taken on a greater practical importance during the past few decades than ever before. One reason is the explosion in knowledge of developmental processes and our ability to treat the abnormalities that we can now find. Procedures such as fetal surgery, electrocardiography, and ultrasound permit physicians to diagnose and treat the fetus much like any other patient. Recent discoveries about the processes of aging—as well as the rapidly growing population of aged individuals—have spawned new methods of recognizing and treating physical and psychological problems in the elderly. Another reason developmental biology has taken on great practical importance is that it is a field that serves to unify human biology into a framework that integrates anatomy, physiology, cell biology, molecular biology, medicine, and other disciplines. Thus developmental biology gives us an excellent view of the "big picture" of the human body.

structures described in the following paragraphs. (Box 36-1 discusses the field of *developmental biology.*)

The amniotic cavity becomes a fluid-filled, shock-absorbing sac, sometimes called the "bag of waters," in which the embryo floats during development. The **chorion** (KOH-ree-on), shown in Figures 36-9 to 36-11, develops from the trophoblast to become an important fetal membrane in the **placenta** (plah-SEN-tah). The *chorionic villi* shown in Figures 36-10 and 36-11 are extensions of the blood vessels of the chorion that bring the embryonic circulation to the placenta. The placenta (see Figure 36-11) anchors the developing offspring to the uterus and provides a "bridge" for the exchange of nutrients and waste products between mother and baby.

Placenta

The placenta is a unique structure that has a temporary but very important set of functions during pregnancy. It is composed of tissues from mother and offspring and functions not only as a structural "anchor" and nutritive bridge but also as an excretory, respiratory, and endocrine organ.

Placental tissue normally separates the maternal and fetal blood supplies so that no intermixing occurs. The very thin layer of placental tissue that separates maternal and fetal blood also serves as an effective "barrier" that can protect the developing baby from many harmful substances that may enter the mother's bloodstream. Unfortunately, toxic substances such as alcohol and

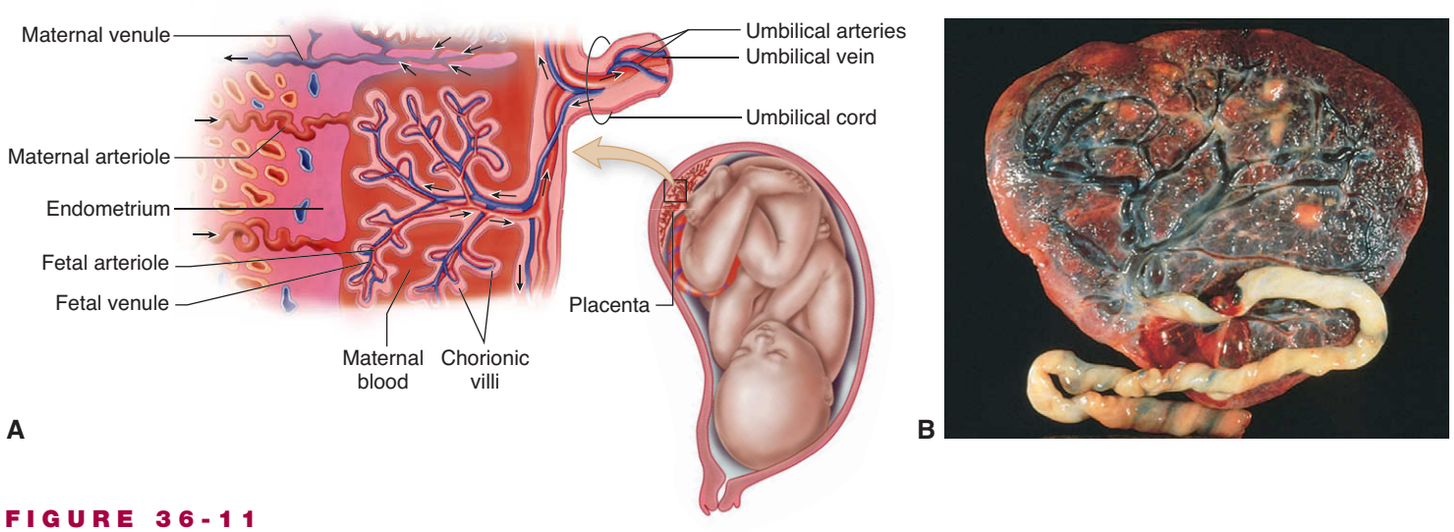


FIGURE 36-11

Structural features of the placenta. The close proximity of the fetal blood supply and the maternal blood supply permits diffusion of nutrients and other substances. The placenta also forms a thin barrier that prevents diffusion of most harmful substances. No mixing of fetal and maternal blood occurs. **A,** Diagram showing a cross section of the placental structure. **B,** Photograph of a normal, full-term placenta (fetal side) showing the branching of the placental blood vessels and umbilical cord.

some infectious organisms may penetrate this protective placental barrier and injure the developing baby (see Box 21-3 on p. 666). The virus responsible for German measles (rubella), for example, can easily pass through the placenta and cause tragic developmental defects in the fetus.

Placental tissue also has important endocrine functions. As Figure 36-12, A, shows, placental tissue secretes large amounts of **human chorionic gonadotropin (hCG)** early in pregnancy. hCG secretion peaks about 8 or 9 weeks after fertilization, then drops to a continuous low level by about week 16. The function of hCG, as its name implies, is to act as a gonadotropin and stimulate the corpus luteum to continue its secretion of estrogen and progesterone. Recall from Chapter 35 (see Figure 35-14 on p. 1079) that reduced levels of the anterior pituitary gonadotropins (FSH and LH) after ovulation normally cause a corresponding reduction in luteal secretion of the estrogen and progesterone needed to sustain the uterine lining. The drop in estrogen and progesterone secretion results from the fact that the FSH and LH needed to maintain the corpus luteum are now in short supply. To prevent menstruation and to allow successful implantation and development of the offspring, the cells of the trophoblast and, later, the placenta secrete enough hCG to maintain the corpus luteum and thus keep luteal estrogen and progesterone levels high.

As the placenta develops, it begins to secrete its own estrogen and progesterone. As Figure 36-12, A, shows, as more estrogen and progesterone are secreted from the placenta, a corresponding decrease in hCG secretion produces a drop in luteal secretion of these hormones. After about 3 months, the corpus luteum has degenerated and the placenta has completely taken over the job of secreting the estrogen and progesterone needed to sustain the pregnancy.

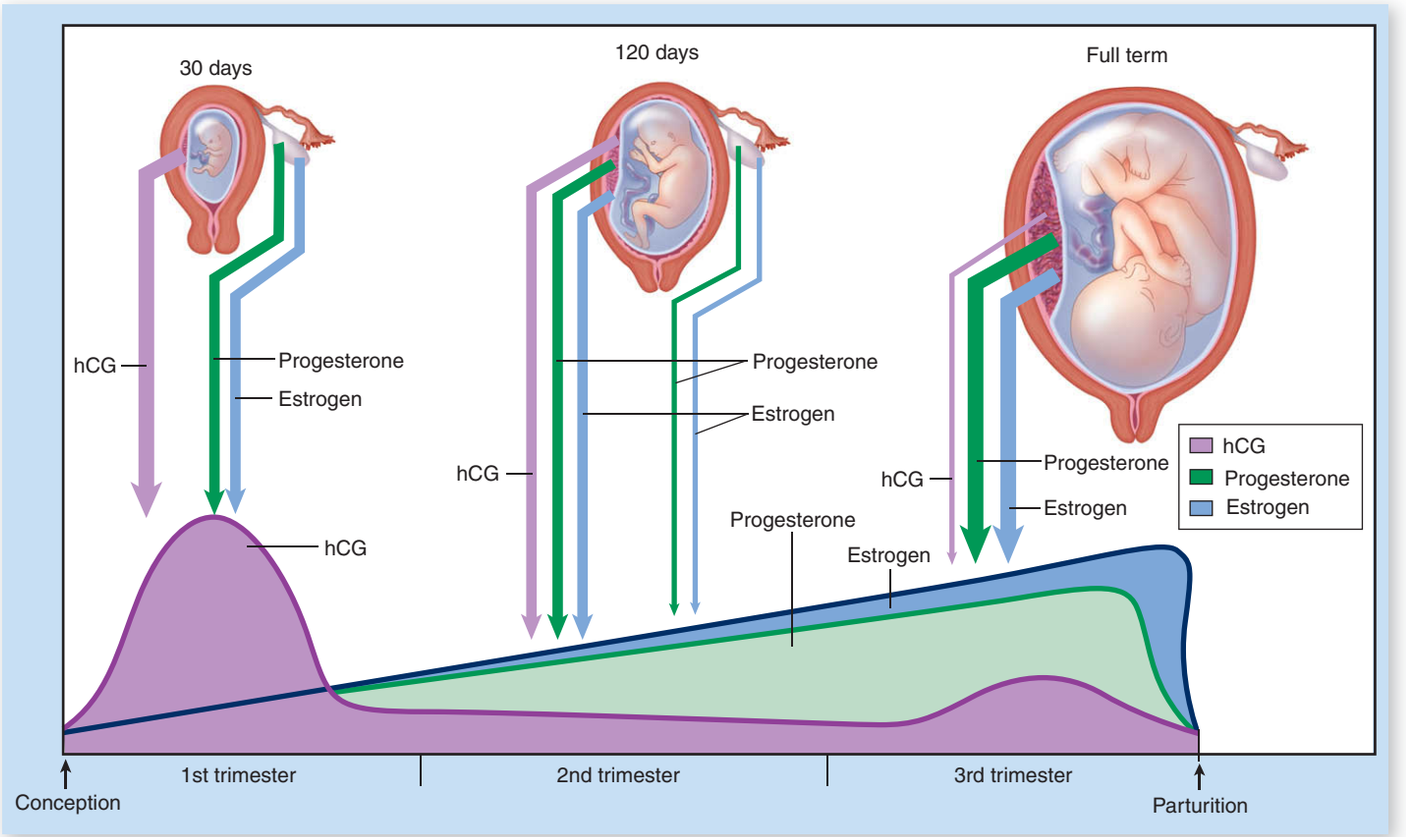


FIGURE 36-12

Hormone levels during pregnancy. A, Diagram showing the changes that occur in the blood concentration of human chorionic gonadotropin (hCG), estrogen, and progesterone during gestation. Note that high hCG levels produced by placental tissue early in pregnancy maintain estrogen and progesterone secretion by the corpus luteum. This prevents menstruation and promotes maintenance of the uterine lining. As the placenta takes over the job of secreting estrogen and progesterone, hCG levels drop, and the corpus luteum subsequently ceases secreting these hormones. **B,** Graph showing other hormones important in supporting pregnancy and lactation. Growth hormone remains stable, as does free T_4 (although total T_4 rises).

Over-the-counter "early pregnancy" tests detect the presence of the hCG that is excreted in the urine during the first couple of months of a pregnancy. Such tests can detect hCG in the urine as early as 1 or 2 days after implantation occurs.

Figure 36-12, *B*, shows some other hormones that help support pregnancy. The functions of these hormones were discussed in previous chapters. During pregnancy some hormones, such as growth hormone (GH), remain stable, but others *increase* during pregnancy. All of these hormones directly or indirectly promote the physiological processes of fetal development and lactation. Cortisol, for example, also helps trigger important events during pregnancy—including the onset of labor.

| QUICK CHECK |

5. What is a morula? What is a blastocyst?
6. What structures are derived from the trophoblast (outer wall) of the blastocyst?
7. What placental hormone maintains the corpus luteum during the early weeks of pregnancy?

Periods of Development

The length of pregnancy (about 39 weeks)—called the **gestation period**—is divided into three approximately 3-month segments called *trimesters*. The first trimester extends from the first day of the last menstrual period to the end of the twelfth week. The second trimester extends from the twelfth to the twenty-eighth week of pregnancy. The third trimester extends from the twenty-eighth week of pregnancy until the baby is delivered. Several terms such as *embryo* and *fetus* are used to describe stages of development during the three trimesters of pregnancy.

During the first trimester, or 3 months, of pregnancy, numerous terms are used. Zygote is used to describe the ovum just after fertilization by a sperm cell. After about 3 days of constant cell division, the solid mass of cells, identified earlier as the morula, enters the uterus. Continued development transforms the morula into the hollow blastocyst, which then implants into the uterine wall (see Figure 36-9).

The embryonic phase of development extends from fertilization until the end of week 8 of gestation. During this period in the first trimester, the term *embryo* is used to describe the developing individual. The fetal phase is used to indicate the development extending from week 8 to 39. During this period, the term *embryo* is replaced by the term *fetus*.

By day 35 of gestation (Figure 36-13, *A*), the heart is beating and, although the embryo is only 8 mm (about 3.8 inch) long, the eyes and so-called *limb buds*, which ultimately form the arms and legs, are clearly visible. Figure 36-13, *C*, shows the stage of development at the end of the first trimester of gestation, when the offspring becomes known as a fetus. Body size is about 7 to 8 cm (3 inches) long (Figure 36-14). The facial features of the fetus

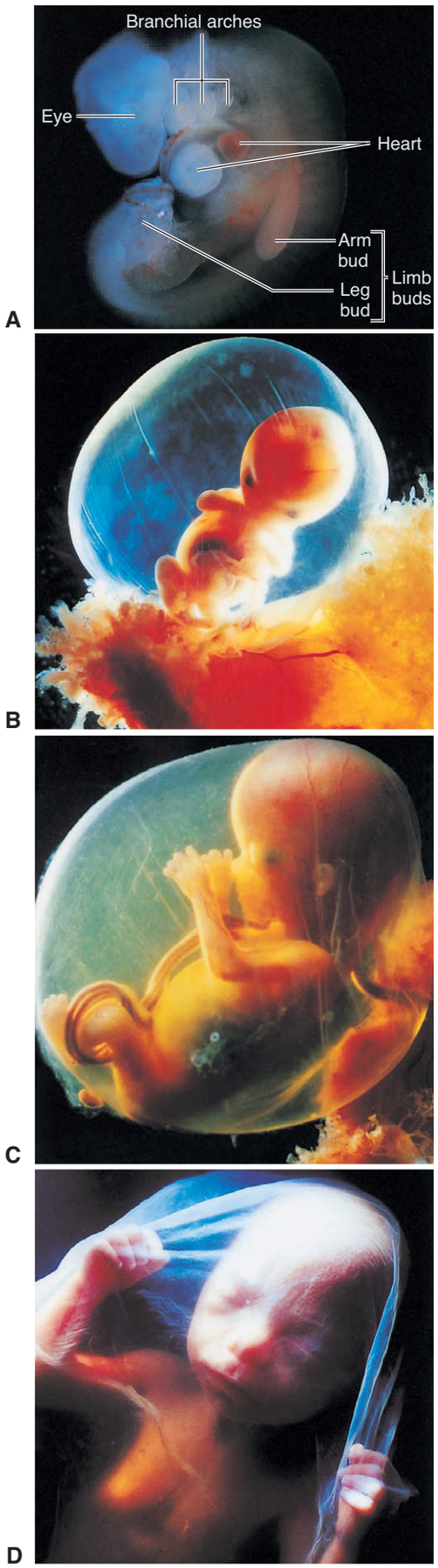


FIGURE 36-13

Human embryos and fetuses. A, At 35 days. **B,** At 49 days. **C,** At the end of the first trimester. **D,** At 4 months.

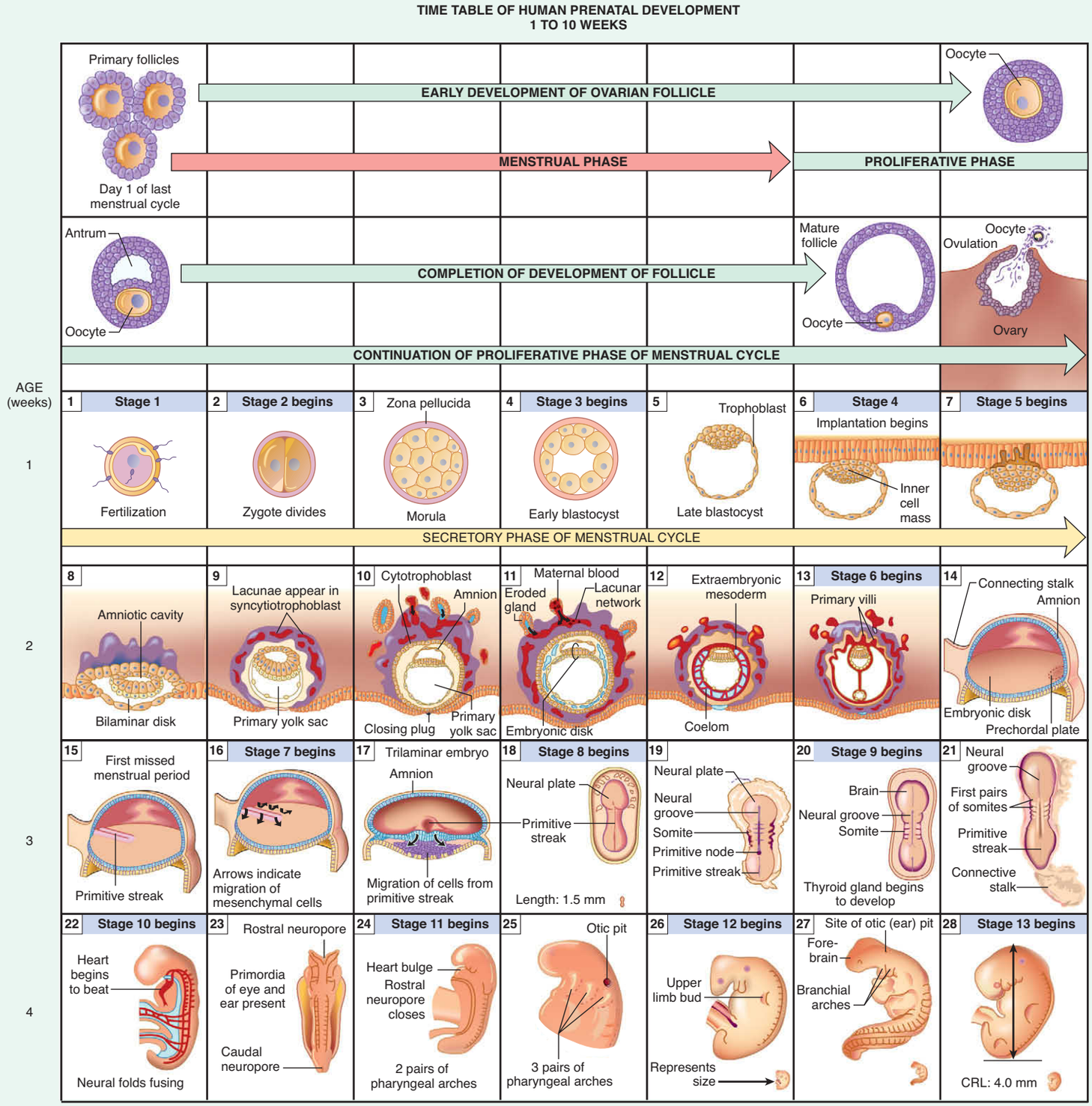
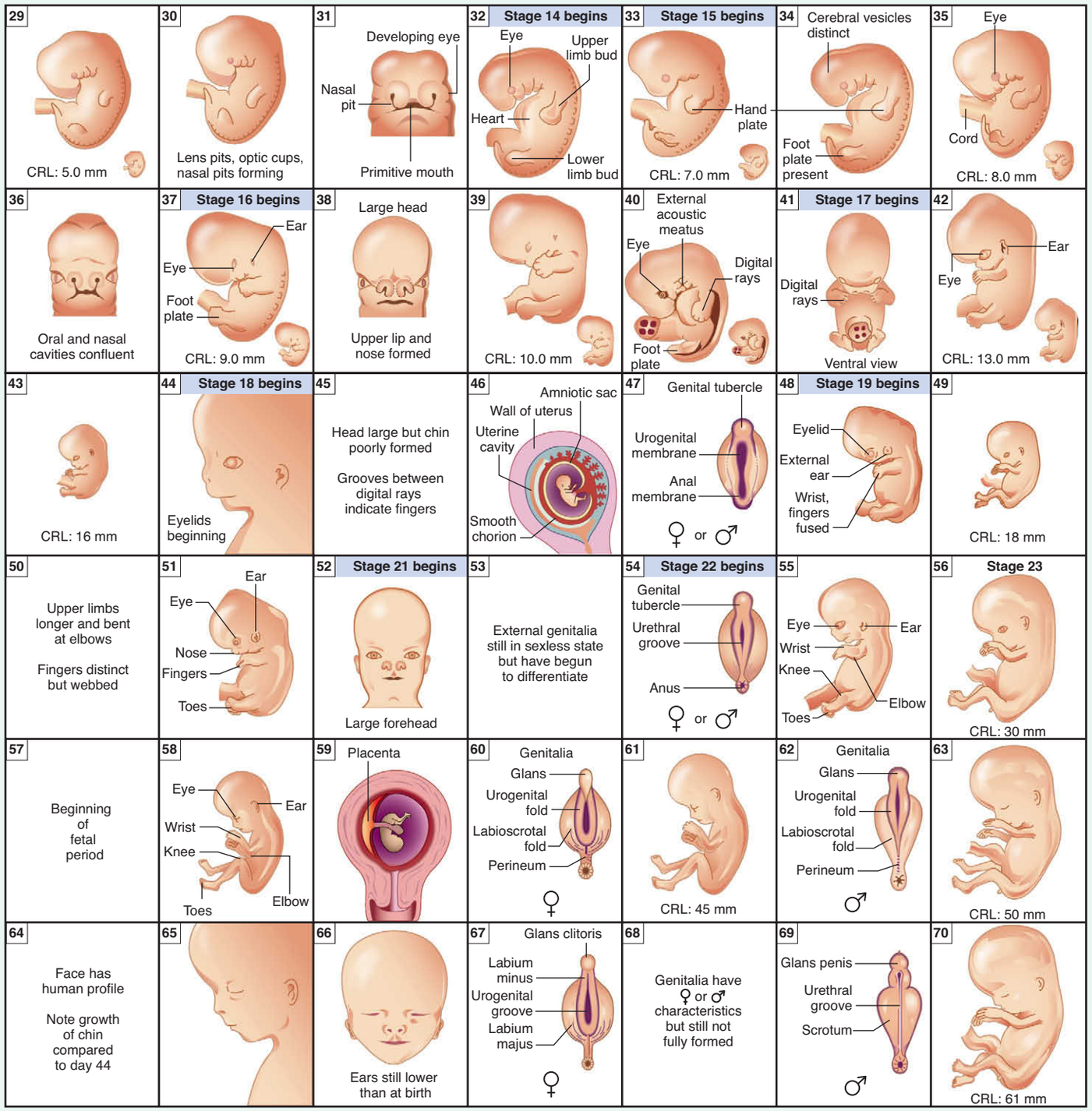


FIGURE 36-14

Developmental events during the first trimester of pregnancy. Each box represents a day, and each row represents a week. Compare this timetable with the preceding figures of this chapter. *CRL,* Crown-to-rump length.


29
CRL: 5.0 mm
30
Lens pits, optic cups, nasal pits forming
31
Developing eye
Nasal pit
Primitive mouth
32 Stage 14 begins
Eye
Upper limb bud
Heart
Lower limb bud
33 Stage 15 begins
Hand plate
CRL: 7.0 mm
34
Cerebral vesicles distinct
Foot plate present
35
Eye
Cord
CRL: 8.0 mm
36
Oral and nasal cavities confluent
37 Stage 16 begins
Ear
Eye
Foot plate
CRL: 9.0 mm
38
Large head
Upper lip and nose formed
39
CRL: 10.0 mm
40
External acoustic meatus
Eye
Digital rays
Foot plate
41 Stage 17 begins
Digital rays
Ventral view
42
Ear
Eye
CRL: 13.0 mm
43
CRL: 16 mm
44 Stage 18 begins
Eyelids beginning
45
Head large but chin poorly formed
Grooves between digital rays indicate fingers
46
Amniotic sac
Wall of uterus
Uterine cavity
Smooth chorion
47
Genital tubercle
Urogenital membrane
Anal membrane
♀ or ♂
48 Stage 19 begins
Eyelid
External ear
Wrist, fingers fused
49
CRL: 18 mm
50
Upper limbs longer and bent at elbows
Fingers distinct but webbed
51
Ear
Eye
Nose
Fingers
Toes
52 Stage 21 begins
Large forehead
53
External genitalia still in sexless state but have begun to differentiate
54 Stage 22 begins
Genital tubercle
Urethral groove
Anus
♀ or ♂
55
Eye
Ear
Wrist
Knee
Elbow
Toes
56 Stage 23
CRL: 30 mm
57
Beginning of fetal period
58
Eye
Ear
Wrist
Knee
Toes
Elbow
59
Placenta
60
Genitalia
Glans
Urogenital fold
Labioscrotal fold
Perineum
♀
61
CRL: 45 mm
62
Genitalia
Glans
Urogenital fold
Labioscrotal fold
Perineum
♂
63
CRL: 50 mm
64
Face has human profile
Note growth of chin compared to day 44
65
66
Ears still lower than at birth
67
Glans clitoris
Labium minus
Urogenital groove
Labium majus
♀
68
Genitalia have ♀ or ♂ characteristics but still not fully formed
69
Glans penis
Urethral groove
Scrotum
♂
70
CRL: 61 mm

are apparent, the limbs are complete, and sex can be identified. By month 4 (Figure 36-13, *D*), all organ systems are formed and functioning to some extent. Growth of the embryo to 4 months is summarized in the photographs in Figures 36-13 and 36-14; growth to full term is summarized in the graph in Figure 36-15. Box 36-2 discusses methods of diagnosis and treatment in these early developmental stages.

Stem Cells

Stem cells are unspecialized cells that reproduce to form specific lines of specialized cells. At the very beginning of the embryonic stage, all the cells are stem cells. At this stage, they have their highest "stemness" or potency—that is, they are capable of producing many different kinds of cells in the body.

Scientists call the single cell of the zygote *totipotent*, meaning "totally potent," because it is the ancestor to all the body's cell types. After the zygote cell divides, many *pluripotent* cells are formed—cells that can produce many (but not all) kinds of cells. It is these early pluripotent cells that are commonly referred to as *embryonic stem cells*. It is the embryonic stem cells that form the germ layers described in the next section.

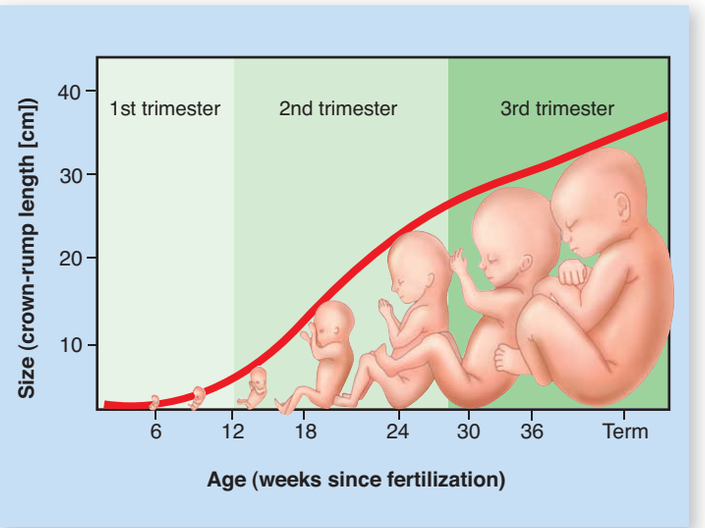


FIGURE 36-15

Increase in size during prenatal development. This graph shows the usual progression in size and body shape during the three trimesters of fetal development.

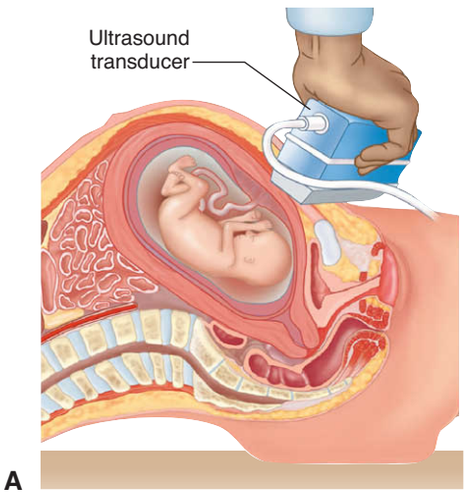
Box 36-2 | DIAGNOSTIC study

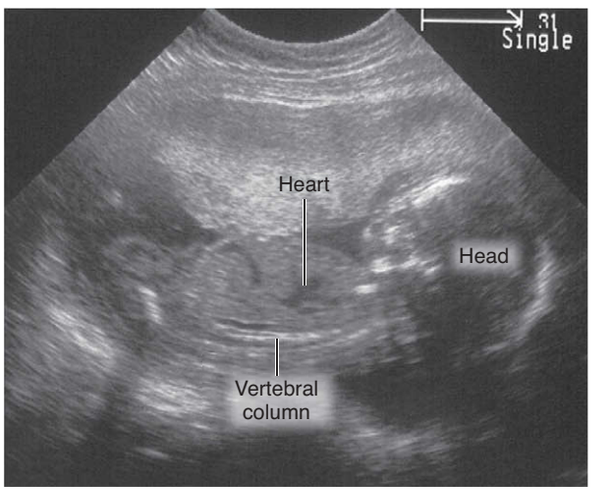
Antenatal Diagnosis and Treatment

Advances in **antenatal** (from the Latin *ante-*, "before" and *-natus,* "birth") **medicine** now permit extensive diagnosis and treatment of disease in the fetus much like any other patient. This new dimension in medicine began with techniques by which Rh+ babies could be given transfusions before birth.

Current procedures using images provided by **ultrasonography** equipment (see the figure) allow physicians to prepare for and perform, before the birth of a baby, corrective surgical procedures such as bladder repair. These procedures also allow physicians to monitor the progress of other types of treatment on a developing fetus. Part A of the figure shows placement of the ultrasound transducer on the abdominal wall. The resulting image (see part B of the figure), called an *ultrasonogram,* shows a 20-week-old fetus.

Ultrasonography. A, Placement of the ultrasound transducer on the abdominal wall. **B,** Ultrasonogram showing a midsagittal view of a 20-week-old fetus.





Some stem cells remain throughout development and maturity. These *multipotent* stem cells, such as the hematopoietic stem cells found in adult bone marrow, can only produce a few types of cells. *Adult stem cells*, as these multipotent cells are usually called, are found in many tissues of the body. For example, adult stem cells are found in the skin, many glands, muscles, nerve tissue, bone, and the gastrointestinal (GI) tract. Adult stem cells replace the specialized cells in a tissue and thus ensure stable, functional populations of the cell types needed for survival.

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Formation of the Primary Germ Layers

Early in the first trimester of pregnancy, three layers of unique cells develop that embryologists call the **primary germ layers.** Cells of the *embryonic disk* seen in Figure 36-9 differentiate into distinct types that form each of these three primary germ layers. Pluripotent stem cells in each layer continue to differentiate and thus give rise to the various specific organs and systems of the body, such as the skin, nervous tissue, muscles, or digestive organs (Figure 36-16). As new tissues and organs develop, older cells often die through the process of apoptosis (see Chapter 5) and thus make room for newer, more specialized cells. Each primary germ layer is called, respectively, **endoderm** (EN-dohderm), or inside layer; **ectoderm** (EK-toh-derm), or outside layer; and **mesoderm** (MEZ-oh-derm), or middle layer.

ENDODERM

The inner germ layer, or *endoderm*, forms the linings of various tracts, as well as several glands. For example, the lining of the respiratory tract and GI tract, including some of the accessory structures such as tonsils, is derived from the endoderm. The linings of the pancreatic ducts, hepatic ducts, and urinary tract also have an endodermal origin. The glandular epithelium of the thymus, thyroid, and parathyroid glands is also derived from the endoderm.

ECTODERM

The outer germ layer, or *ectoderm*, forms many of the structures around the periphery of the body. For example, the epidermis of the skin, enamel of the teeth, and cornea and lens of the eye are derived from the ectoderm. Besides these peripheral structures, various components of the nervous system—including the brain and the spinal cord—also have an ectodermal origin.

MESODERM

The middle germ layer, or *mesoderm*, forms most of the organs and other structures between those formed by the endoderm and ectoderm. For example, the dermis of the skin, the skeletal muscles and bones, many of the glands of the body, kidneys, gonads, and components of the circulatory system are derived from the mesoderm. Look carefully at Figure 36-16 to discern the logical pattern exhibited by germ layer development and differentiation.

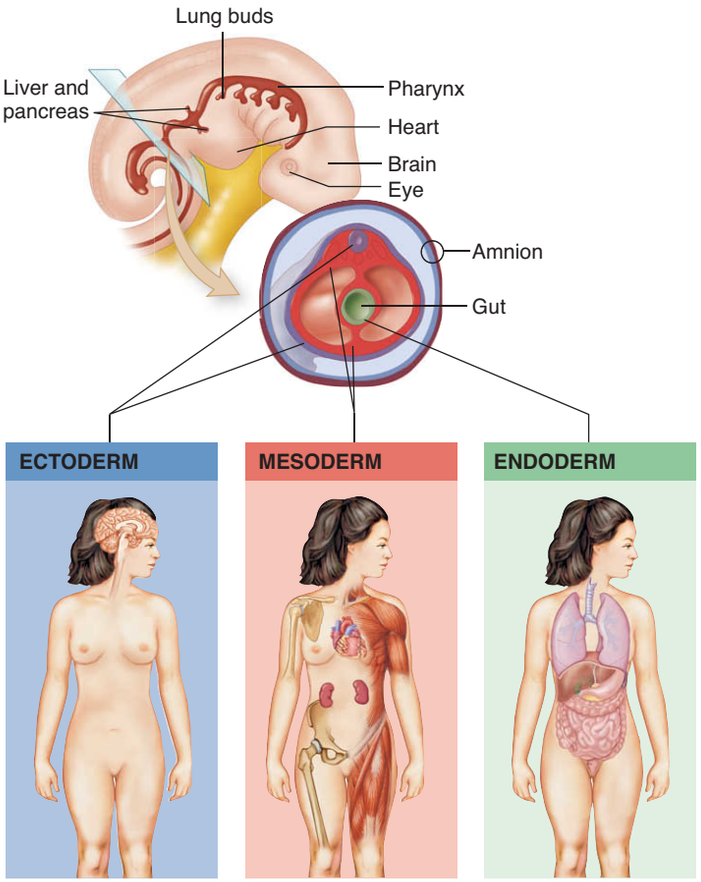


FIGURE 36-16

The primary germ layers. Illustration shows the primary germ layers and the body systems into which they develop.

Histogenesis and Organogenesis

The process by which the primary germ layers develop into many different kinds of tissues is called **histogenesis** (hiss-toh-JEN-eh-sis). The way these tissues arrange themselves into organs is called **organogenesis** (or-gah-no-JEN-eh-sis).

The fascinating story of histogenesis and organogenesis in human development is long and complicated; its telling belongs to the science of embryology. However, a brief example of organogenesis that is particularly useful in our current discussion of reproduction and development is the differentiation and development of the sex organs.

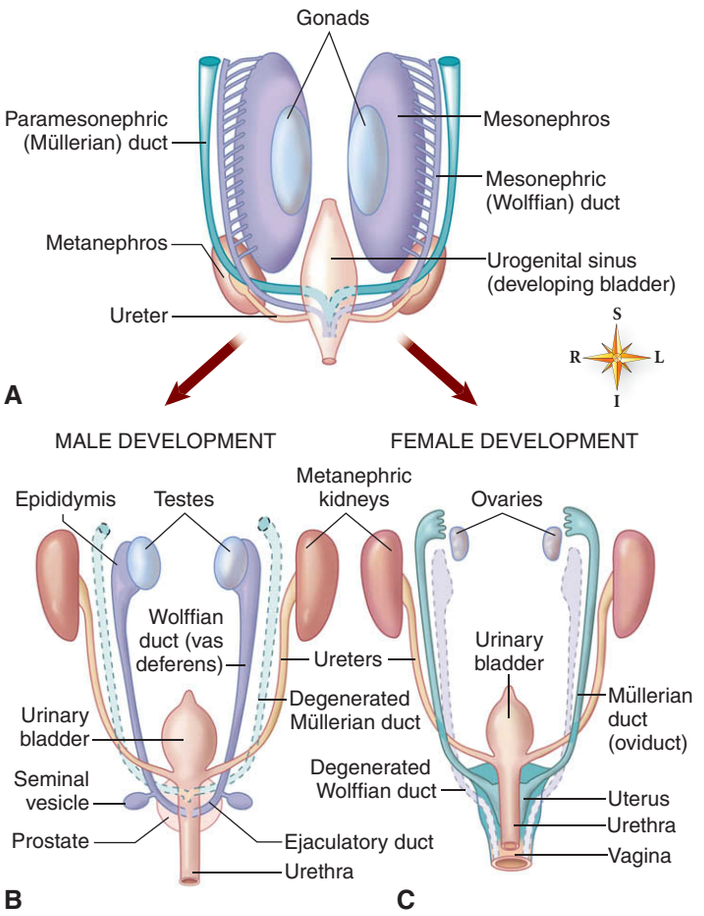


FIGURE 36-17

Development of the reproductive tracts. Both the male and female adult reproductive tracts are similar in their basic outline because they have a shared early development. **A,** Early in embryonic development, an undifferentiated set of gonads and ducts develops in both males and females. **B,** In males, the gonads (now testes) attach to the mesonephric (wolffian) ducts, which develop into the main part of the male reproductive tract. The paramesonephric ducts degenerate in males. **C,** In females, the gonads do not attach directly to a duct. It is the paramesonephric (müllerian) ducts that develop into the female reproductive tract and the mesonephric ducts that degenerate.

As Figure 36-17 shows, the reproductive tracts of both the male and the female begin their development as sets of undifferentiated ducts and gonads. But as embryonic development continues in the male, the gonads attach to the *mesonephric (wolffian) duct*—which along with the urethra develops into the male reproductive tract (Figure 36-17, B). In the female, by contrast, it is the nearby *paramesonephric (müllerian) duct* that instead develops into a female reproductive tract separate from the urinary tract (Figure 36-17, C). Note that the female gonads (ovaries) do not attach to their ducts during development. Figure 36-18 outlines the development of the male and female genitals. Notice how they develop along slightly different paths to eventually become distinct types of structures.

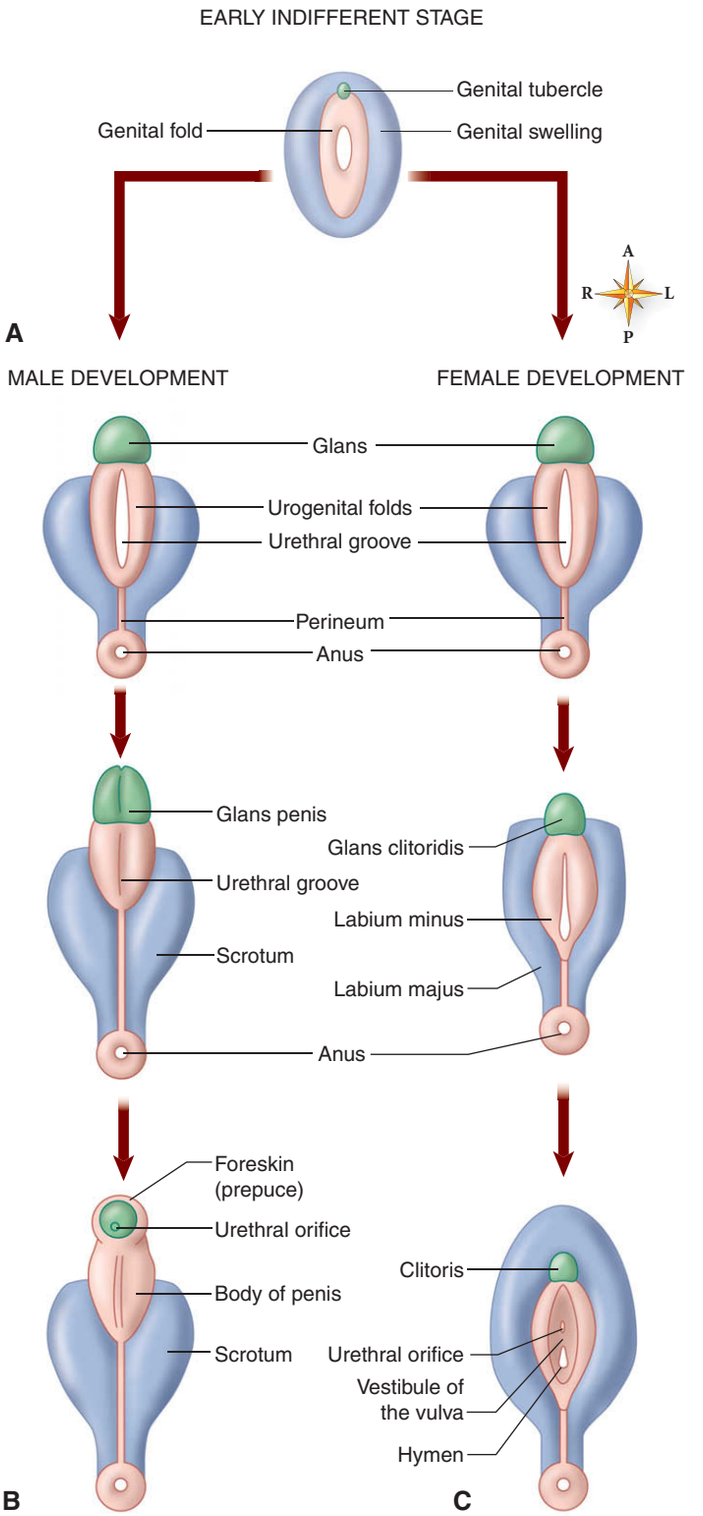


FIGURE 36-18

Development of the genitals. **A,** In early stages of development, the genitals are indifferent (not yet distinguishable). **B,** In the male, the genital tubercle eventually becomes the glans of the penis and the folds become the penis shaft and scrotum. **C,** In the female, the genital tubercle becomes the clitoris and the folds become the labia.

A complete outline of the embryonic development of each organ and system is beyond the scope of this book. For the beginning student of anatomy and physiology, it seems sufficient to appreciate that human development begins when two sex cells unite to form a single-celled zygote and that the new offspring's body evolves by a series of processes consisting of cell differentiation, multiplication, growth, apoptosis, and rearrangement, all of which take place in a definite, orderly sequence. Development of structure and function go hand in hand, and from 4 months of gestation, when every organ system is in place and functioning to some extent, until term (about 280 days), development of the fetus is mainly a matter of growth.

Figure 36-19 shows the normal intrauterine position of a fetus just before birth in a full-term pregnancy. The large size of the pregnant uterus toward the end of pregnancy affects the normal function of the mother's body greatly. For example, you might be able to tell from Figure 36-19 that a woman's center of gravity is shifted forward. This can make walking and other movements of the body difficult—or even hazardous—because the sensory and motor control systems often do not compensate completely for this shift. The pregnant uterus presses on the rectum, sometimes adversely affecting intestinal motility and thus may cause constipation and/or hemorrhoids. Pressure on the bladder reduces its urine-storing capacity, which results in frequent urination. Upward pressure pushes the abdominal organs against the diaphragm, making deep breathing difficult and sometimes causing the stomach to protrude into the thoracic cavity—a condition called *hiatal hernia*.

| QUICK CHECK |

8. What is a *trimester?*
9. What is the difference between an *embryo* and a *fetus?*
10. Name the three primary germ layers.
11. What is *histogenesis?*

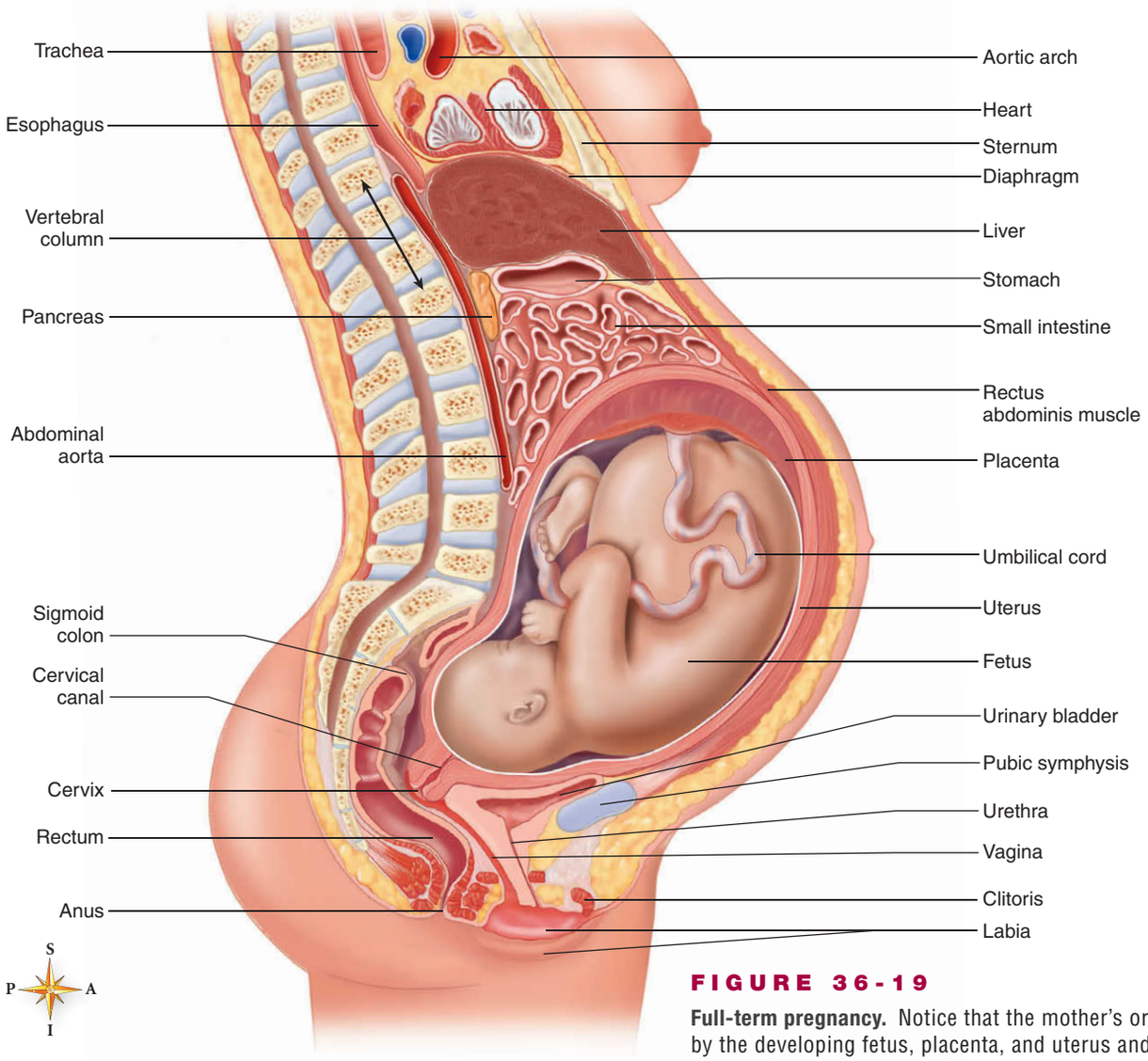


FIGURE 36-19

Full-term pregnancy. Notice that the mother's organs are being pushed by the developing fetus, placenta, and uterus and that the woman's center of gravity is now shifted forward.

BIRTH, OR PARTURITION

Birth, or **parturition,** is the point of transition between the prenatal and postnatal periods of life. As the fetus signals the end of pregnancy, the uterus becomes "irritable" and, ultimately, muscular contractions begin and cause the cervix to dilate (open), thus permitting the fetus to move from the uterus through the vagina or "birth canal" to the exterior. The process normally begins with the fetus taking a head-down position fully against the cervix (Figure 36-20, A). When contractions occur, the amniotic sac, or "bag of waters," usually ruptures, and labor begins.

Several hormones help to signal the time of labor and promote the processes needed for successful delivery. High levels of cortisol at the end of pregnancy trigger a drop in hCG, which in turn causes a drop in progesterone levels (see Figure 36-12). Progesterone inhibits the release of oxytocin (OT) earlier in the pregnancy—but at this point, the "brake" on the uterine muscle is

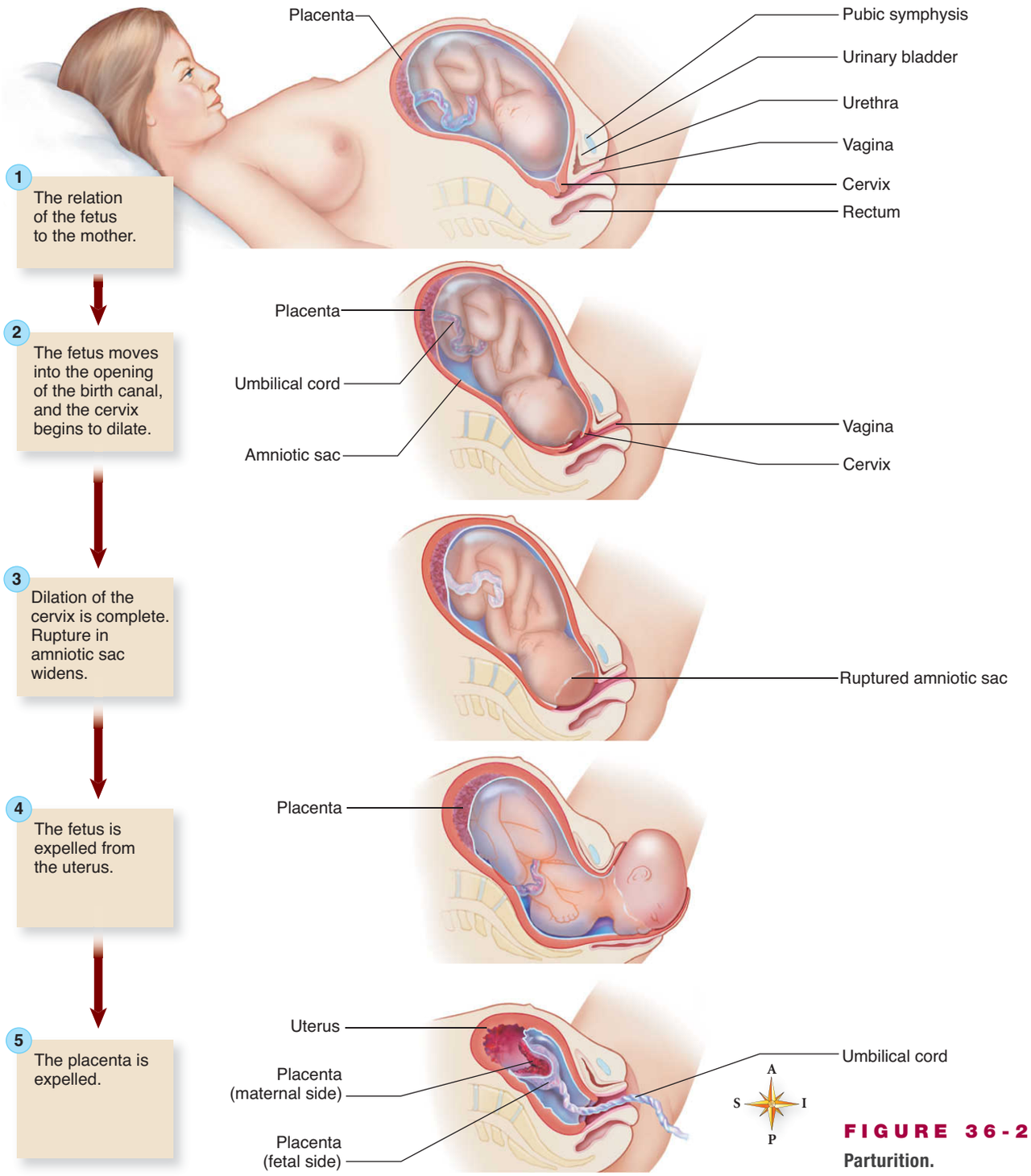


FIGURE 36-20
Parturition.

released. Recall from Chapter 1 that OT is released in a positive feedback mechanism that amplifies the rate and strength of labor contractions (see illustration in Box 1-3 on p. 7). An injection of an OT preparation (Pitocin) can stimulate labor contractions in a difficult or delayed delivery. Prostaglandins E_2 and F_2 (PGE_2, PGF_2) released by the placenta also play a role in the onset of labor by further sensitizing the myometrium of the uterus to OT.

Stages of Labor

Labor is the term used to describe the process that results in the birth of the baby. It is divided into three stages (see Figure 36-20, *B* to *E*):

1. Stage one—period from onset of uterine contractions until dilation of the cervix is complete
2. Stage two—period from the time of maximal cervical dilation until the baby exits through the vagina
3. Stage three—process of expulsion of the placenta through the vagina

The time required for normal vaginal birth varies widely and may be influenced by many variables, including whether the woman has previously had a child. In most cases, stage one of labor lasts from 6 to 24 hours, and stage two lasts from a few minutes to an hour. Delivery of the placenta (stage three) is normally within 15 minutes after the birth of the baby. If abnormal conditions of the mother or fetus (or both) make normal vaginal delivery hazardous or impossible, physicians may suggest a **cesarean** (seh-SAIR-ee-an) **section.** Often called simply a *C-section*, it is a surgical procedure in which the newborn is delivered through an incision in the abdomen and uterine wall.

Immediately after birth, the umbilical cord is cut and clamped. Recall from Chapter 21 that at birth, the circulatory route of the infant changes as the placenta is lost and the lungs begin to function (see Figure 21-37 on p. 668). Eventually, the remainder of the cord sloughs off—leaving the umbilicus or navel as an abdominal landmark.

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Multiple Births

The term *multiple birth* refers to the birth of two or more infants from the same pregnancy. The birth of twins is more common than the birth of triplets, quadruplets, or quintuplets. Multiple-birth babies are often born prematurely, so they are at a greater than normal risk of complications in infancy. However, premature infants that have modern medical care available have a much lower risk of complications than those without such care.

Twinning, or double births, can result from either of two different processes:

1. **Identical twins** result from the splitting of embryonic tissue from the same zygote early in development. One way this happens is that, during the blastocyst stage of development, the inner cell mass divides into two masses. Each inner cell mass thus formed develops into a separate individual. As Figure 36-21, *A*, shows, identical twins usually share the same placenta but have separate umbilical cords. This is not surprising because in this type of twinning there is a single, shared trophoblast. Because they develop from the same fertilized egg, identical twins have the same genetic code. Despite this, identical twins are not absolutely identical in terms of structure and function. Different environmental factors and personal experiences lead to individuality even in genetically identical twins.
2. **Fraternal twins** result from the fertilization of two different ova by two different spermatozoa (Figure 36-21, *B*). Fraternal twinning requires the production of more than one mature ovum during a single menstrual cycle, a trait that is often inherited. Multiple ovulation may also occur in response to certain fertility drugs, especially the gonadotropin preparations. Fraternal twins are no more closely related genetically than any other brother-sister relationship. Because two separate fertilizations must occur, it is even possible for fraternal twins to have different biological fathers. Triplets, quadruplets, and other multiple births may be identical, fraternal, or any combination.

| QUICK CHECK |

12. Briefly describe the three stages of labor.
13. How does identical twinning differ from fraternal twinning?

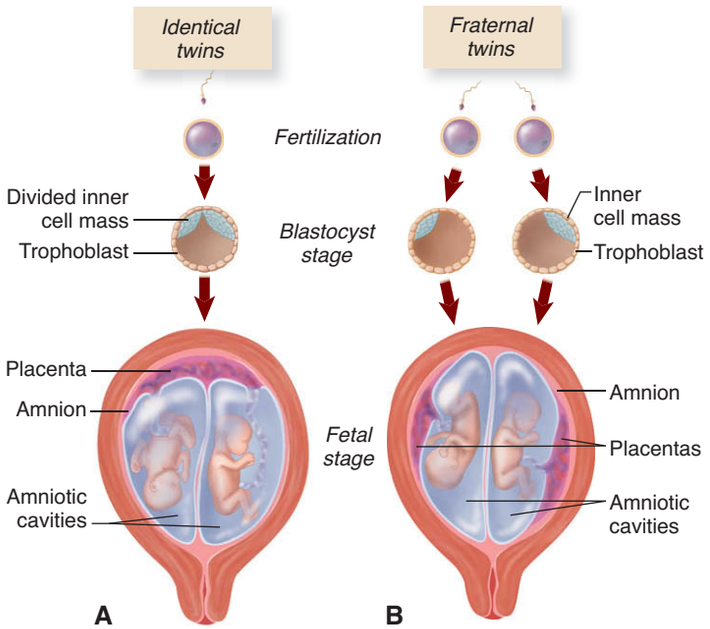


FIGURE 36-21

Multiple births. A, Identical twins develop when embryonic tissue from a single zygote splits to form two individuals. Notice that, because the trophoblast is shared, the placenta and the part of the amnion separating the amniotic cavities are shared by the twins. **B,** Fraternal twins develop when two ova are fertilized at the same time, producing two separate zygotes. Notice that each fraternal twin has its own placenta and amnion.

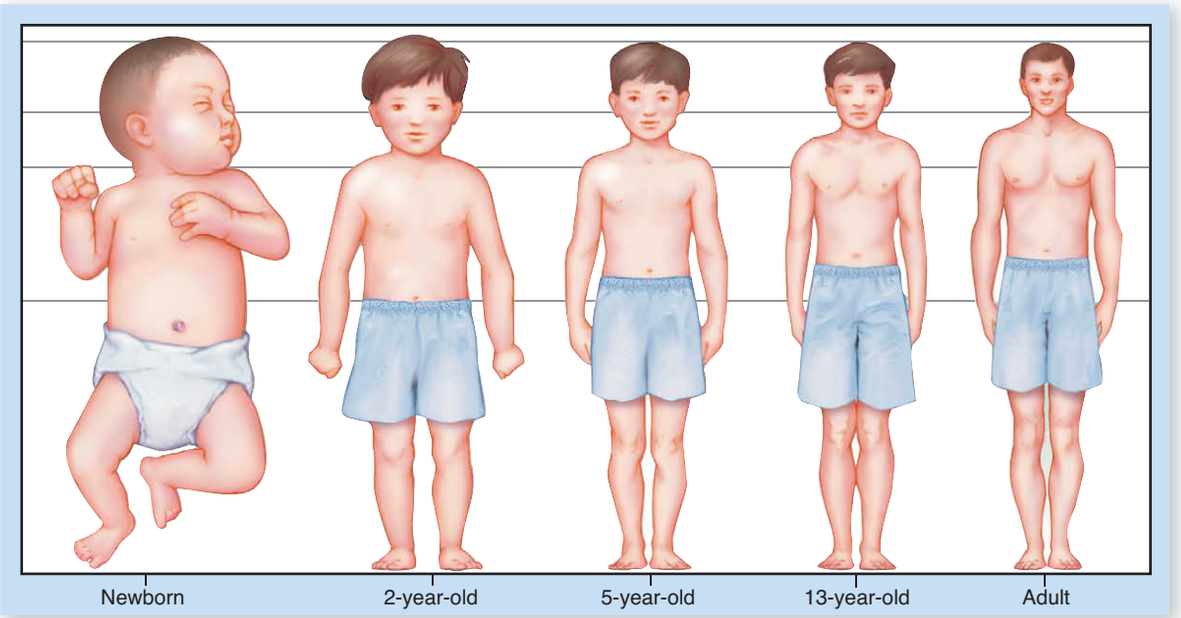


FIGURE 36-22

Changes in the proportions of body parts from birth to maturity. Note the dramatic differences in relative head size.

POSTNATAL PERIOD

The **postnatal period** begins at birth and lasts until death. It is often divided into major periods for study, but people need to understand and appreciate the fact that growth and development are continuous processes that occur throughout the life cycle. Gradual changes in the physical appearance of the body as a whole and in the relative proportions of the head, trunk, and limbs are quite noticeable between birth and adolescence. Note in Figure 36-22 the obvious changes in the size of bones and in the proportionate sizes between different bones and body areas. The head, for example, becomes proportionately smaller. Whereas the infant head is approximately one fourth the total height of the body, the adult head is only about one eighth the total height. The facial bones also show several changes between infancy and adulthood. In an infant the face is one eighth of the skull surface, but in an adult the face is half of the skull surface. Another change in proportion involves the trunk and lower extremities. The legs become proportionately longer and the trunk proportionately shorter. In addition, the thoracic and abdominal contours change from round to elliptical.

Such changes are good examples of the ever-changing and ongoing nature of growth and development. It is unfortunate that many of the changes that occur in the later years of life do not result in an increased function. These degenerative changes are certainly important, however, and will be discussed later in this chapter (see pp. 1118–1122).

The following are the most common postnatal periods: (1) **infancy,** (2) **childhood,** (3) **adolescence** and **adulthood,** and (4) **older adulthood.** Table 36-1 summarizes the projected changes in U.S. population numbers in selected age-groups from 2010 through the year 2050. Notice the proportionally higher rise in older age-groups, particularly those over age 85 years.

Infancy

The period of infancy begins abruptly at birth and lasts about 18 months. The first 4 weeks of infancy are often referred to as the **neonatal period.** Dramatic changes occur at a rapid rate during this short but critical period. **Neonatology** (nee-oh-nay-TOL-oh-jee) is the medical and nursing specialty concerned with the diagnosis and treatment of disorders of the

TABLE 36-1 U.S. Population—Selected Census Bureau Projections 2020–2050*

	2010	2020	2030	2040	2050	PERCENT CHANGE
Total Population	310,233	341,387	373,504	405,655	439,010	42%
Under 20 years	84,150	90,703	97,682	104,616	112,940	34%
20-64 years	185,854	195,880	203,729	219,801	237,523	28%
65-84 years	34,478	48,208	63,348	67,041	69,506	102%
85+ years	5,571	6,597	8,745	14,198	19,041	242%

*Numbers in thousands.

newborn. Advances in this area have resulted in dramatically reduced infant mortality.

Many of the changes that occur in the cardiovascular and respiratory systems at birth are necessary for survival (see Figures 21-36, p. 667, and Figure 21-37, p. 668). Whereas the fetus totally depended on the mother for life support, the newborn infant, to survive, must become totally self-supporting in terms of blood circulation and respiration immediately after birth. A baby's first breath is deep and forceful. The stimulus to breathe results primarily from the increasing amounts of carbon dioxide (CO_2) that accumulate in the blood after the umbilical cord is cut shortly after delivery.

To assess the general condition of a newborn, a system that scores five health criteria is often used. The criteria are heart rate (HR), respiration, muscle tone, skin color, and response to stimuli. Each aspect is scored as 0, 1, or 2—depending on the condition of the infant. The resulting total score is called the **Apgar score.** The Apgar score in a completely healthy newborn is 10.

Many developmental changes occur between the end of the neonatal period and 18 months of age. Birth weight generally doubles during the first 4 to 6 months and then triples by 1 year. The baby also increases in length by 50% by the twelfth month. The "baby fat" that accumulated under the skin during the first year begins to decrease, and the plump infant becomes leaner.

Early in infancy the baby has only one spinal curvature (Figure 36-23). The cervical curve appears as the infant begins holding up her head. The lumbar curvature appears between 12 and 18 months, as the once-helpless infant becomes a toddler who can stand (Figure 36-24). One of the most striking changes to occur during infancy is the rapid development of the nervous and muscular systems. This permits the infant to follow a moving object with the eyes (2 months); lift the head and raise the chest (3 months); sit when well supported (4 months); crawl (10 months); stand alone (12 months); and run, although a bit stiffly (18 months).

Childhood

Childhood extends from the end of infancy to sexual maturity, or puberty—12 to 14 years in girls and 14 to 16 years in boys. Overall, growth during early childhood continues at a rather rapid pace, but month-to-month gains become less consistent. By the age of 6 years the child appears more like a preadolescent than an infant or toddler. The child becomes less chubby, the potbelly becomes flatter, and the face loses its babyish look. The nervous and muscular systems continue to develop rapidly during the middle years of childhood; by 10 years of age the child has developed numerous motor and coordination skills.

The *deciduous teeth*, which began to appear at about 6 months of age, are lost during childhood, beginning at about 6 years of age. The *permanent teeth*, with the possible exception of the third molars (wisdom teeth), have all erupted by age 14 years.

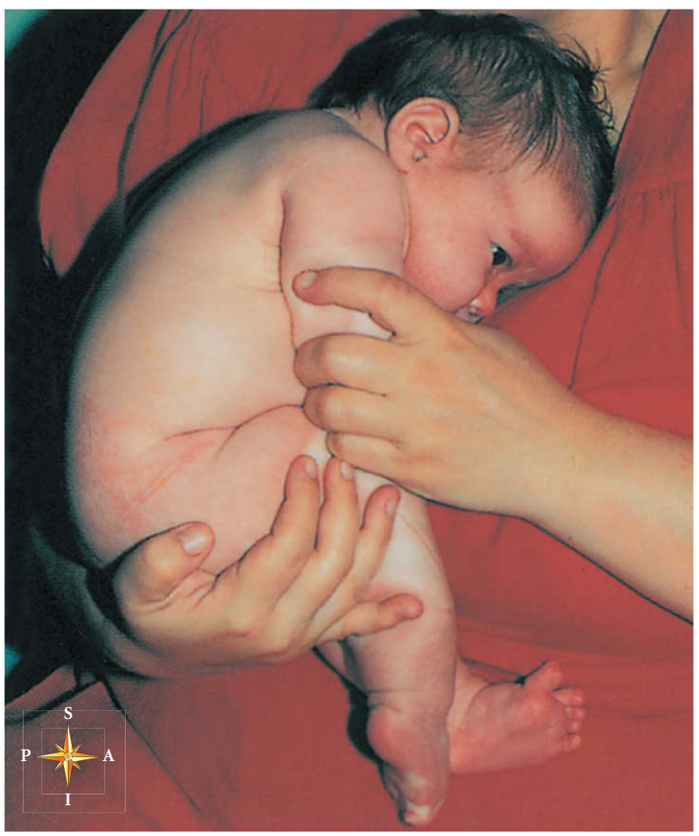


FIGURE 36-23

The infant spine. Photograph showing the normal rounded curvature of the vertebral column in an infant.



FIGURE 36-24

The toddler spine. Photograph showing the normal curvature of the vertebral column in a toddler. The dark shadow emphasizes the distinct lumbar curvature that develops with the ability to walk (compare with Figure 36-23).

Adolescence and Adulthood

The average age range of **adolescence** varies but generally the teenage years (13 to 19) are used as the standard age range. The period is marked by rapid and intense physical growth, which ultimately results in sexual maturity.

The stage of adolescence in which a person becomes sexually mature is called **puberty.** Many of the developmental changes that occur during this period are controlled by the secretion of gonadotropins (FSH and LH) and sex hormones such as testosterone and estrogen (Figure 36-25). Some of these changes involve development of the gonads themselves and are called **primary sex characteristics.** However, most of the more visible changes involve development of the **secondary sex characteristics** such as skeletal changes, fat distribution patterns, growth of pubic and body hair, and growth of the larynx.

Breast development is often the first sign of approaching puberty in girls, beginning about age 9 or 10 years. Most girls begin to menstruate at 12 to 14 years of age. In boys the first sign of puberty is often enlargement of the testes, which begins between 10 and 14 years of age. Both sexes show a spurt in height during adolescence (Figure 36-26). In girls the spurt in height begins between the ages of 10 and 12 years and is nearly complete by 14 or 15 years. In boys the period of rapid growth begins between 12 and 13 years and is generally complete by 16 or 17 years.

Many developmental changes that begin early in childhood are not completed until the early or middle years of **adulthood.** Examples include the maturation of bone, resulting in the full closure of the growth plates, and changes in the size and placement of other body components such as the sinuses. Many body traits do not become apparent for years after birth. Normal balding patterns, for example, are determined at the time of fertilization by heredity but do not appear until maturity. As a rule, adulthood is characterized by the maintenance of existing body tissues. With the passage of years the ongoing effort of maintenance and repair of body tissues becomes more and more difficult. As a result, degeneration begins. This is part of the process of aging, and it culminates in death.

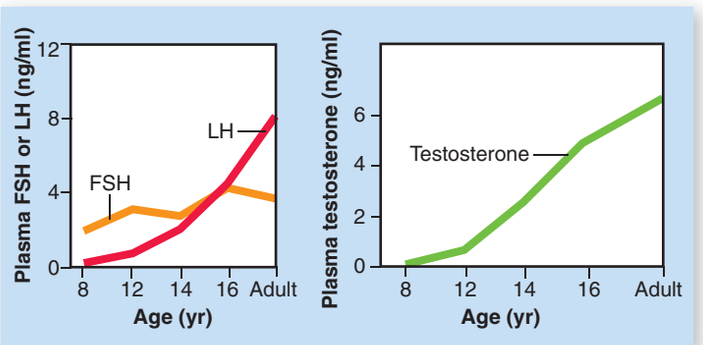


FIGURE 36-25

Hormone changes during puberty. The left graph shows the increase in gonadotropin (LH and FSH) secretion during puberty. The right graph shows changes in testosterone levels (in males) during puberty that result from increased gonadotropin levels. Female hormones show a similar change within a monthly cycle of dramatic highs and lows (see Figures 35-14 and 35-15). *FSH,* Follicle-stimulating hormone; *LH,* luteinizing hormone.

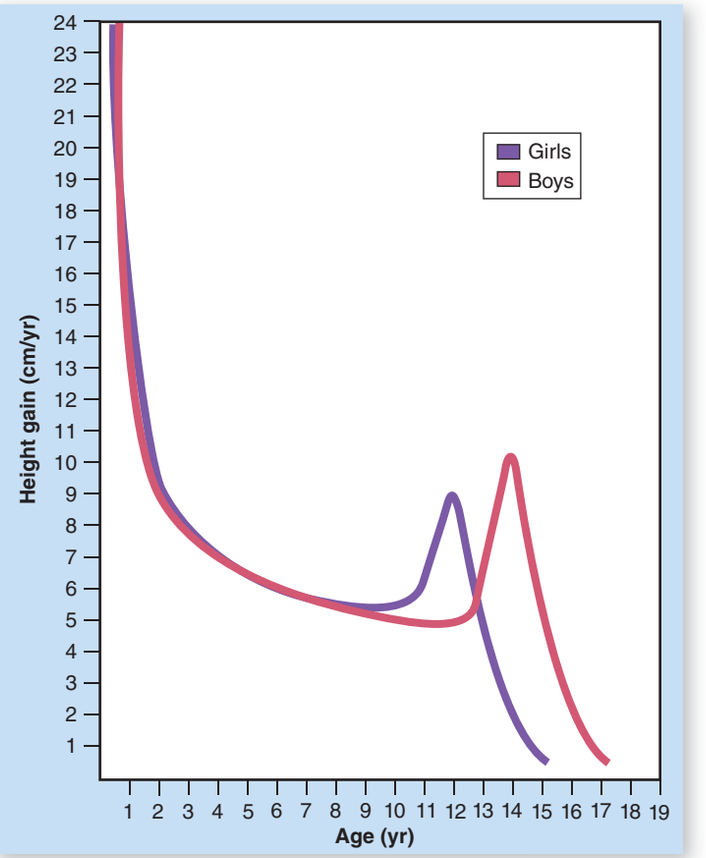


FIGURE 36-26

Growth in height. The graph shows typical patterns of gain in height from birth to adulthood for girls and boys. Notice the rapid gain in height during the first few years, a period of slower growth, then another burst of growth during adolescence—finally ending at the beginning of adulthood.

Older Adulthood and Senescence

Most body systems are in peak condition and function at a high level of efficiency during early adulthood. As a person grows older, a gradual but certain decline takes place in the functioning of every major organ system in the body. The study of aging is called **gerontology.** Unfortunately, the mechanisms and causes of aging are not well understood.

Some gerontologists believe that an important aging mechanism is the limit on cell reproduction. Laboratory experiments show that many types of human cells cannot reproduce more than 50 times—thus limiting the maximum life span. Cells die continually in a process called *apoptosis*, no matter what a person's age, but in older adulthood, many dead cells are not replaced—causing degeneration of tissues. Perhaps the cells are not replaced because the surrounding cells have reached their limit of reproduction. Perhaps differences in each adult's aging process result from differences in the reproductive capacity of cells. This mechanism seems to operate in individuals with **progeria** (pro-JEE-ree-ah), a rare, inherited condition in which a person appears to age rapidly (Box 36-3).

Various factors that affect the rates of cell death and cell reproduction have been cited as causes of aging. Some gerontologists believe that nutrition, injury, disease, and other environmental factors affect the aging process. A few have even proposed that aging

Box 36-3 | DIAGNOSTIC study

Progeria



Progeria, also called *Hutchinson-Gilford disease,* is a rare, inherited condition in which a young child appears to age rapidly. In progeria (*pro-,* "before"; *-ger-,* "old age";*-ia,* "condition") the reproductive capacity of cells seems to be diminished. Thus the tissues of the body fail to maintain or repair themselves normally and many of the degenerative conditions more commonly seen in elderly individuals appear. Many of these conditions can be seen in this photograph of a young boy with progeria: thin, wrinkled skin; hair loss; loss of subcutaneous fat; and arthritis (causing stiff, partially flexed, and swollen joints). Most victims of progeria die of cardiovascular disease within the first or second decade of life.

results from cellular changes caused by slow-acting "aging" viruses found in all living cells. Other gerontologists have proposed that aging is caused by "aging" genes that regulate apoptosis or other cell functions—genes in which aging is "preprogrammed."

Another proposed cause of aging is autoimmunity. You may recall from Chapter 24 that autoimmunity occurs when the immune system attacks a person's own tissues. Yet another theory of aging suggests that as a person ages, mitochondria become less able to shuttle adenosine triphosphate (ATP) out to the cytosol. Decreasing ATP availability renders cells less able to perform their functions and even causes them to degenerate—hallmarks of the aging process. One popular theory of aging states that oxygen *free radicals* play a major role in cellular aging (see Figure 30-24, p. 952). Free radicals are highly reactive forms of oxygen that normally result from mitochondrial activity, but may damage the cell. As a person's cells produce more and more free radicals during the later years, more damage happens to cellular structures and functions. In addition, as free-radical production increases, mitochondrial function decreases and therefore availability of ATP decreases (Figure 36-27)

Many different genes have been put forth as having direct or indirect effects on aging and longevity. Most of them operate in

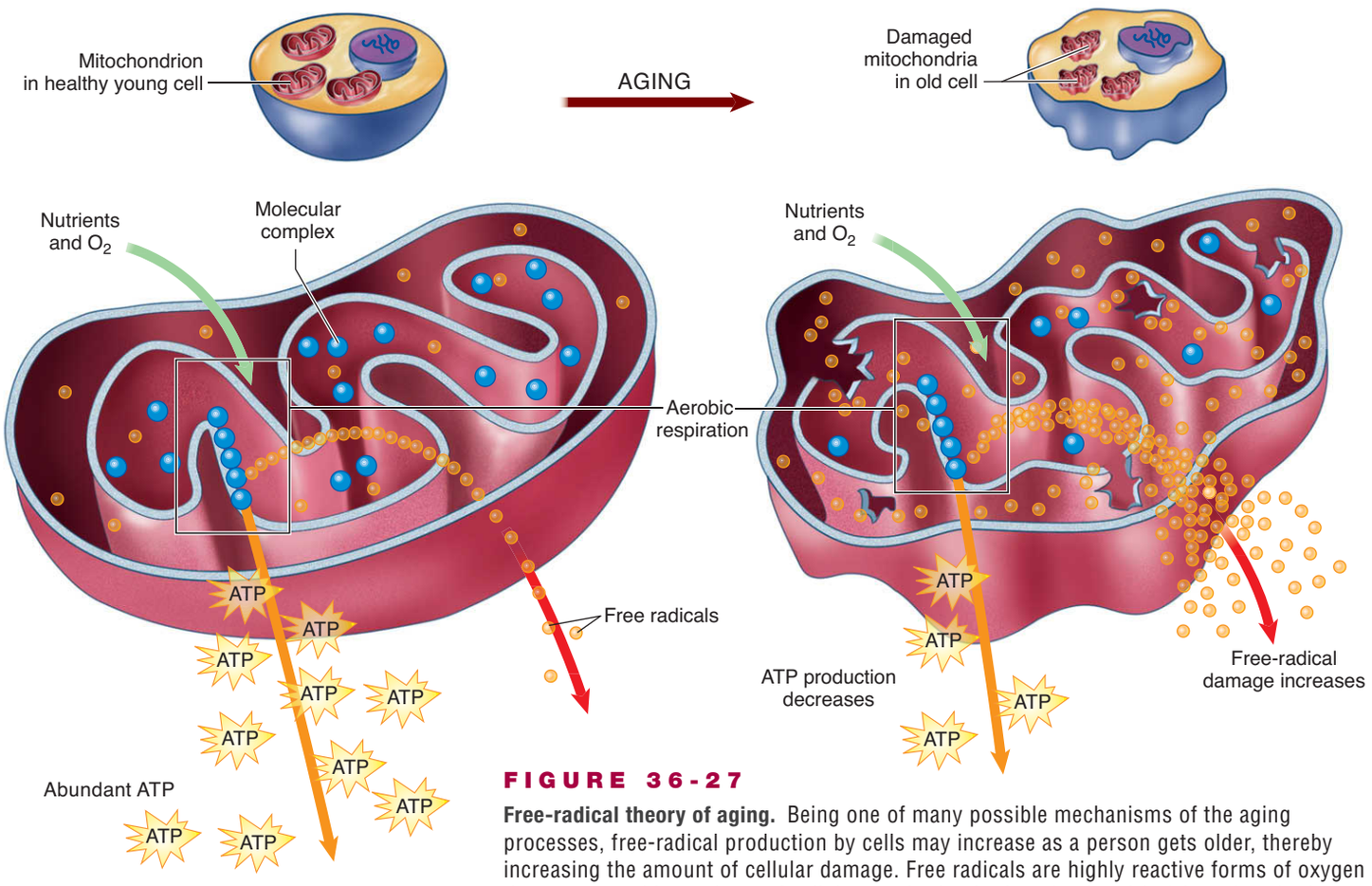


FIGURE 36-27

Free-radical theory of aging. Being one of many possible mechanisms of the aging processes, free-radical production by cells may increase as a person gets older, thereby increasing the amount of cellular damage. Free radicals are highly reactive forms of oxygen that are normal byproducts of cellular respiration in the mitochondria (shown) and other cell processes. As one ages, the number of free radicals increases as cellular efficiency decreases. Thus more cellular damage occurs, especially damage to cellular membranes, causing degeneration of the cell.

one or more of the aging mechanisms already discussed. It is clear that there is a genetic component to how we age and how long we live. However, the mechanisms by which these genes influence aging still remain unclear.

Although the causes and basic mechanisms of aging are yet to be understood, at least many of the signs of aging are obvious. The remainder of this chapter deals with some of the more common degenerative changes that frequently characterize **senescence** (seh-NES-enz), or older adulthood.

| QUICK CHECK |

14. Name the four major phases of the postnatal period.
15. When does the *neonatal period* of human development occur?
16. What signs characterize the *adolescent period* of human development?
17. Briefly describe one of the proposed mechanisms of the aging process.

EFFECTS OF AGING

Aging affects each individual in different ways. Environment, genetics, and perhaps even attitude may affect the degree to which the structure and function of a person's body change through older adulthood. Despite advances in understanding how some of the effects of aging can be minimized or even avoided, one cannot completely avoid the fact that body structures degenerate and functions decrease as we get older. Figure 36-28 summarizes a few of the many biological changes that occur by the time we reach late adulthood.

Skeletal System

In older adulthood, bones undergo changes in texture, degree of calcification, and shape. Instead of clean-cut margins, older bones develop indistinct and shaggy-appearing margins with spurs—a process called *lipping*. This type of degenerative change restricts movement because of the piling up of bone tissue around the joints.

With advancing age, changes in calcification of bones reduce the *bone mineral density (BMD)* as you can see in Figure 36-29, A. This may result in reduction of bone size and in bones that are porous and subject to fracture. The lower cervical and thoracic vertebrae are the site of frequent fractures. The result is curvature of the spine and the shortened stature so typical of late adulthood (Figure 36-29, *B*). The onset of *osteoporosis* and other types of bone loss associated with aging may be avoided—at least to some extent—by maintaining a high BMD through exercise and sufficient calcium in the diet.

Degenerative joint diseases such as **osteoarthritis** (os-tee-oh-ar-THRY-tis) are also common in elderly adults.

| A&P CONNECT |

Bone loss during aging is an important health concern, especially as our life expectancy increases and more people hope to live healthy lives into late adulthood. Explore these issues further in ***Measuring Bone Mineral Density*** and ***Skeletal Variations*** online at ***A&P Connect.***

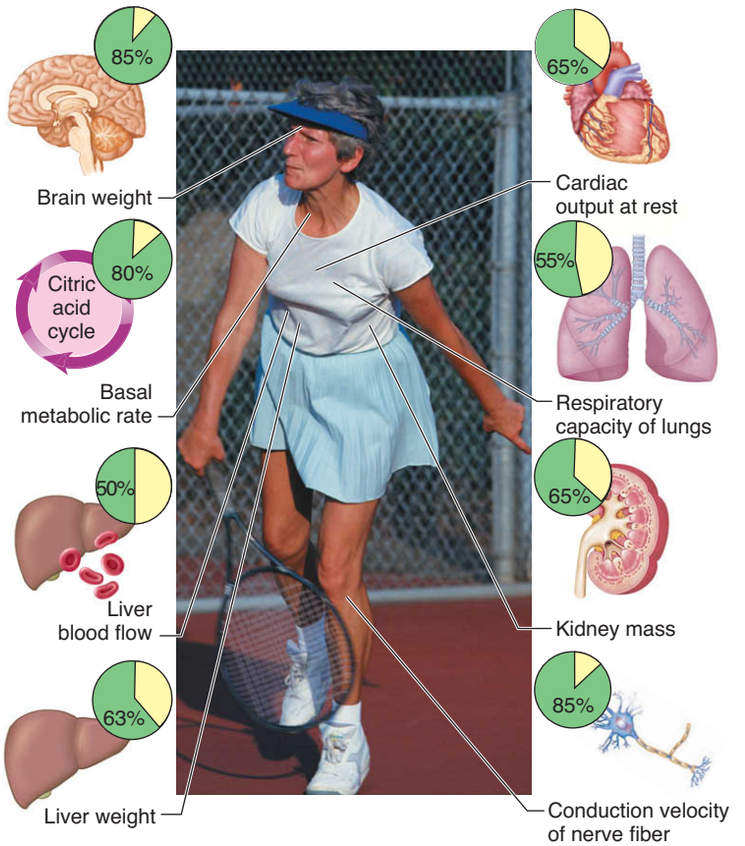


FIGURE 36-28

Some biological changes associated with maturity and aging. Insets show proportion of remaining function in the organs of a person in late adulthood compared with a 20-year-old person.

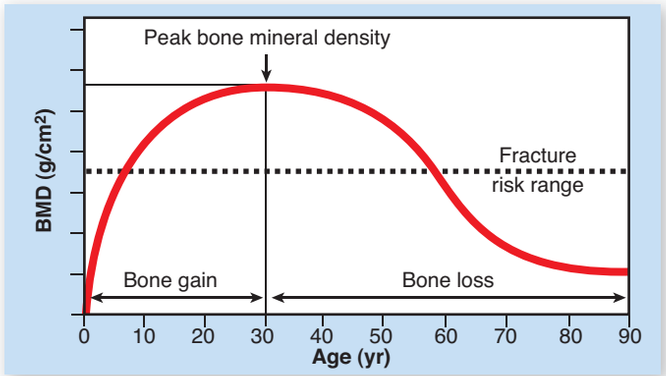
Muscular System

Getting older usually involves losing muscle mass. This can begin as early as age 25 years but does not usually reach 10% loss in muscle mass until 50 years of age or so. By age 80 years, many people have lost about 50% of their skeletal muscle mass. Most of the age-related loss of muscle mass is due to a loss of muscle fibers. However, weight training before and during one's later years can increase the mass of the remaining fibers and thus counteract at least some of the reduction in the number of muscle fibers (Box 36-4).

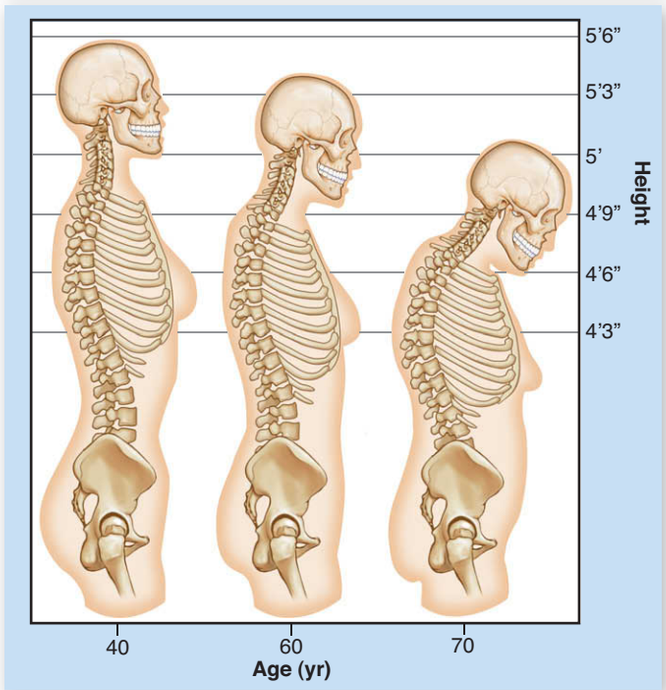
Another change in our muscles as we age is that many muscle fibers develop into slower type fibers or into an intermediate form between the "fast type" and "slow type" of muscle fiber. This usually means that the overall ratio of "fast" to "slow" function decreases—that is, our muscle function becomes relatively "slower." As Figure 36-30 shows, the different fiber types also begin to group together in bunches and change their shape slightly. These effects seem unavoidable—even with exercise.

Integumentary System (Skin)

With advancing age the skin becomes dry, thin, and inelastic. It "sags" on the body because of increased wrinkling and



A



B

FIGURE 36-29

Loss of bone mineral density (BMD) in late adulthood. A, Graph showing changes in BMD over the life span in females. BMD peaks in young adulthood and decreases in late adulthood to a point at which there is an increased risk of bone fracture. Males also have a decrease in BMD beginning around age 50 years, but the decline is more gradual than in women. **B,** The normal spinal curvatures of young adulthood give way to possible changes later in life because of a decrease in BMD.

skinfolds—as well as a loss of body fat under the skin. Pigmentation changes and the thinning or loss of hair are also common conditions associated with aging.

Urinary System

The number of functioning nephron units in the kidney decreases by almost 50% between the ages of 30 and 75 years. Also, because less blood flows through the kidneys as an individual ages, there is a reduction in overall function and excretory capacity or the ability to produce urine. In the bladder, significant age-related problems often occur because of diminished muscle tone. Muscle atrophy (wasting) in the bladder wall results in decreased capacity and inability to empty, or void, completely.

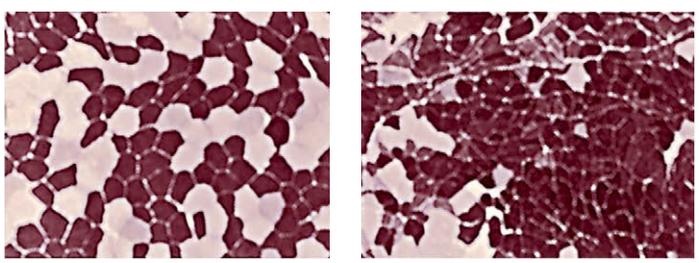
Box 36-4 | SPORTS and FITNESS

Exercise and Aging

A sound exercise program throughout life can reduce some of the common effects of aging. The improved cardiovascular condition associated with aerobic training can prevent or reduce the effects of several age-related circulatory problems. The loss of bone mass that occurs in older adulthood is less troublesome if one enters this period with a higher than average bone density developed through exercising. Finally, the relatively high ratio of body fat to muscle often seen in the elderly can be reduced or avoided entirely by a lifelong fitness program.

Respiratory System

In older adulthood the costal cartilages that connect the ribs to the sternum become hardened or calcified. This makes it difficult for the rib cage to expand and contract as it normally does during inspiration and expiration. In time the ribs gradually become "fixed" to the sternum, and chest movements become difficult. When this occurs the rib cage remains in a more expanded position, respiratory efficiency decreases, and a condition called "barrel chest" results. With advancing years a generalized atrophy, or wasting, of muscle tissue takes place as the contractile muscle cells are replaced by connective tissue. This loss of muscle cells decreases the strength of the muscles associated with inspiration and expiration.



A B

FIGURE 36-30

Muscle changes in late adulthood. Skeletal muscle tissue changes as we age. **A,** Younger muscle shows a typical "checkerboard" pattern of fast and slow fibers (distinguished by stains here). **B,** However, in the elderly the fast and slow fibers tend to group together rather than remain distributed evenly throughout the muscle organ. Note the overall increase in the slower fibers, which appear darker than the other fibers here. Also, the more angular appearance of each muscle fiber cross section in the young changes to a more rounded cross section in the elderly.

Cardiovascular System

Degenerative heart and blood vessel disease is one of the most common and serious effects of aging. Fatty deposits build up in blood vessel walls and narrow the passageway for the movement of blood, much as the buildup of scale in a water pipe decreases flow and pressure. The resulting condition, called **atherosclerosis** (ath-er-oh-skleh-ROH-sis), often leads to eventual blockage of the coronary arteries and a "heart attack" (myocardial infarction [MI]). If fatty accumulations or other substances in blood vessels calcify, actual hardening of the arteries, or **arteriosclerosis** (ar-tee-ree-oh-skleh-ROH-sis), occurs. Rupture of a hardened vessel in the brain (stroke) is a frequent cause of serious disability or death in the older adult. **Hypertension (HTN),** or high blood pressure, is also more common.

Special Senses

The sense organs, as a group, all show a gradual decline in performance and capacity as a person ages.

Most people are farsighted by age 65 years because eye lenses become hardened and lose elasticity; the lenses cannot become curved to accommodate for near vision. This hardening of the lens is called **presbyopia** (pres-bee-OH-pee-ah), which means "old eye." Many individuals first notice the change at about 40 or 45 years of age, when it becomes difficult to do close-up work or read without holding printed material at arm's length. This explains the increased need, with advancing age, for bifocals (glasses that incorporate two lenses) to automatically accommodate for near and distant vision.

Loss of transparency of the lens or its covering capsule is another common age-related eye change. If the lens actually becomes cloudy and significantly impairs vision, it is called a **cataract** and must be removed surgically. The incidence of **glaucoma** (glaw-KOH-mah), the most serious age-related eye disorder, increases with age. Glaucoma causes an increase in the pressure within the eyeball and, unless treated, often results in blindness.

In many elderly people a very significant loss of hair cells in the organ of Corti (spiral organ of the inner ear) causes a serious decline in the ability to hear certain frequencies. In addition, the eardrum and attached ossicles become more fixed and less able to transmit mechanical sound waves. Some degree of hearing impairment is universally present in the older adult.

The sense of taste is also decreased. Loss of appetite may be caused, at least in part, by the replacement of taste buds with connective tissue cells. Only about 40% of the taste buds present at age 30 years remain fully functional in an individual at age 75 years.

Interestingly, not everything in the sensory system diminishes with age. Evidence shows that older people are much better than younger people at spotting small movements in a visual scene. This is more a matter of interpreting sensory information in the brain than it is a matter of sensory reception. This should not be surprising, as a growing body of evidence supports our longstanding cultural notion that older adults have a sort of "wisdom" or improved thinking abilities that develop over time.

Reproductive Systems

Although most men and women remain sexually active throughout their later years, mechanisms of sexual response may change, and fertility declines. In men, erection may be more difficult to achieve and maintain, and urgency for sex may decline. In women, lubrication of the vagina may decrease. Although men can continue to produce gametes as they age, women experience a cessation of reproductive cycling between the ages of 45 and 60 years—**menopause.** Menopause results from a decrease in the cyclical production of the primary sex hormones, especially estrogen, with advancing age. The decrease in estrogen accounts for the common symptoms of menopause: cessation of menstrual cycles, hot flashes, and thinning of the vaginal wall. The exact mechanism of hot flashes is not clearly understood, but it is related to the hormonal changes that occur during menopause. Rarely serious, hot flashes usually subside over time. Estrogen therapy may be used to relieve menopause symptoms in some cases.

The decrease in estrogen levels associated with menopause may also contribute to *osteoporosis.* This condition is characterized by loss of bone mass (see Chapter 8). Osteoporosis is often treated with short-term, low-dose estrogen replacement therapy (ERT) and nonhormonal bone building drugs. Therapy to restore or maintain bone mineral density may also include high doses of vitamin D, calcium supplements, and weight-bearing exercise.

Benefits of Aging

It is easy to see the "down side" of aging—degradation of structures and loss of functions—but there is an "up side" to aging. For example, studies show that as one ages, anxiety and hostility lessen, control over fear increases, and resistance to happiness decreases. And even though the image quality of vision may decrease as we age, we actually improve in our ability to interpret what we see—such as the ability to detect and track motion in our visual field. Of course, there is the accumulation of learning over time and problem-solving ability often improves. Historically, we have attributed wisdom mainly to our elders—a concept that has been supported by neurological research of the traits that characterize wisdom.

There may be a few social advantages to aging if we live in a culture and a social network that values and provides for the aged.

CAUSES OF DEATH

No matter what your age, death of the individual is also part of the human life cycle. Figure 36-31 shows the leading causes of death in the United States. These figures are consistent with causes of death in other economically developed countries. Notice that some of these causes of death have been diminishing over the years (such as heart diseases and stroke), some have remained roughly stable (such as cancer), and some have increased (such as Alzheimer disease, Parkinson disease, and kidney disease).

| A&P CONNECT |

The human life span has been increasing over time—even more so in developed areas of the world. Read about the role of genetics in this phenomenon in ***Genes and Longevity*** online at ***A&P Connect.***

1. Diseases of heart
2. Malignant neoplasms (cancer)
3. Chronic lower respiratory disease (including COPD)
4. Cerebrovascular diseases (including stroke)
5. Accidents (unintentional injuries)
6. Alzheimer disease (AD)
7. Diabetes mellitus (DM)
8. Influenza and pneumonia
9. Nephritis, nephrotic syndrome, and nephrosis
10. Intentional self-harm (suicide)
11. Septicemia
12. Chronic liver disease and cirrhosis
13. Essential (primary) hypertension (HT) and hypertensive renal disease
14. Parkinson disease (PD)
15. Assault (homicide)

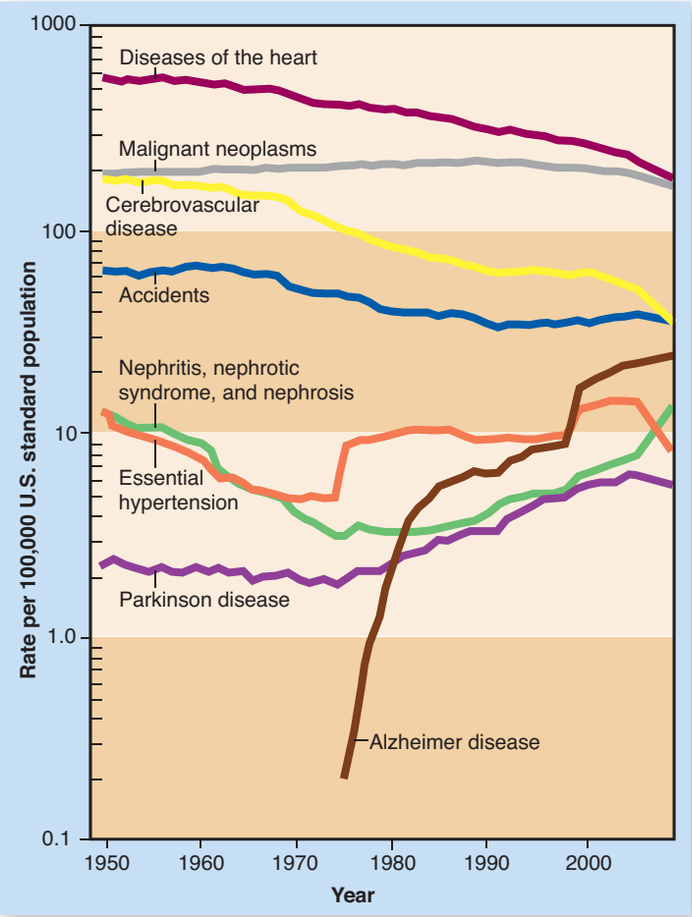


FIGURE 36-31

Leading causes of death. The 15 leading causes of death in the United States are listed in the inset. The trends in some of these causes of death are graphed out on a logarithmic (powers of 10) scale.

Although heart disease, cancer, stroke, and so on are the leading killers in developed nations, it is a somewhat different story among the developing nations. In developing nations around the world, infectious diseases such as HIV/AIDS, diarrheal diseases, malaria, and measles are among the top killers. But even so, in developing areas heart disease and stroke are also near the very top of the list.

| QUICK CHECK |

18. What kinds of changes occur in the skeleton as one ages?
19. List some age-related changes in the cardiovascular system.
20. How can age affect a person's vision?
21. What are some of the leading causes of death in the United States?

the BIG picture

Growth, Development, and the Whole Body

Understanding basic concepts of human growth and development is essential for understanding the dynamic, ever-changing nature of the human body. It is important to remember that life is a biological process characterized by continuous change in the structure and function of our body.

As we discussed in this and earlier chapters, production of offspring is vital to the survival of the genetic code. Many biologists believe that this gives an important biological meaning to life in general—continued flow of genetic information from one generation to the next. Production of offspring in humans is not successful unless and until a person grows and develops for many years—more than a decade—to the point where viable gametes can be produced. Gametogenesis, then, is the first process necessary to ready the genetic material of the parent to be passed along to the offspring.

Once gametes are available, the sexual union of a male and female may result in fusion of the gametes of the two adults to form the first cell of the offspring. Thus genetic information from two different individuals is now united in a new and unique way in the zygote.

The first cell of the offspring—the zygote—quickly divides again and again to eventually produce a mass of cells that will hopefully implant in the wall of the mother's uterus. Then a process unlike any other we have discussed takes over. The offspring and mother biologically connect to each other so that the mother's physiological mechanisms can sustain the offspring until its own systems are developed sufficiently. All the mother's systems alter their function to some degree to maintain the homeostatic balance of both the mother and the offspring.

After many weeks of growth and development—including histogenesis and organogenesis of a full complement of human structures—delivery of the offspring occurs. This event marks the beginning of a continuing series of changes: infancy, childhood, puberty, adolescence, adulthood, senescence, and death.

At some point in adolescence or adulthood many of us have the opportunity to complete the "circle of life" by passing some of the genetic code we received from our parents on to yet another human generation.

MECHANISMS of DISEASE

DISORDERS OF PREGNANCY AND EARLY DEVELOPMENT

Implantation Disorders

A pregnancy has the best chance of a successful outcome, the birth of a healthy baby, if the blastocyst is implanted properly in the uterine wall. However, proper implantation does not always occur. Many offspring are lost before implantation occurs, often for unknown reasons. As mentioned in this chapter and the previous chapter, implantation outside the uterus results in an ectopic pregnancy. If the blastocyst implants in a region of endometriosis or normal peritoneal membrane, the pregnancy may be successful if there is room for the developing fetus to grow. Ectopic pregnancies that do succeed must be delivered by C-section rather than by normal vaginal birth. If an ectopic pregnancy occurs in a uterine tube, which cannot stretch to accommodate the developing offspring, the tube may rupture and cause life-threatening hemorrhaging. So-called **tubal pregnancies** are the most common type of ectopic pregnancy.

Occasionally, the blastocyst implants in the uterine wall near the cervix. This in itself may present no problem, but if the placenta grows too close to the cervical opening a condition called **placenta previa** (PREE-vee-ah) results. The normal dilation and softening of the cervix that occur in the third trimester often cause painless bleeding as the placenta near the cervix separates from the uterine wall. The massive blood loss that may result can be life-threatening for both mother and offspring (Figure 36-32, *A*).

Separation of the placenta from the uterine wall can occur even when implantation takes place in the upper part of the uterus. When this occurs in a pregnancy of 20 weeks or more, the condition is called **abruptio placentae** (ab-RUP-shee-oh plah-SEN-tay). Complete separation of the placenta causes the immediate death of the fetus. The severe hemorrhaging that often results, sometimes hidden in the uterus, may cause circulatory shock and death of the mother within minutes. A cesarean section and perhaps also a hysterectomy must be performed immediately to prevent blood loss and death (Figure 36-32, *B*).

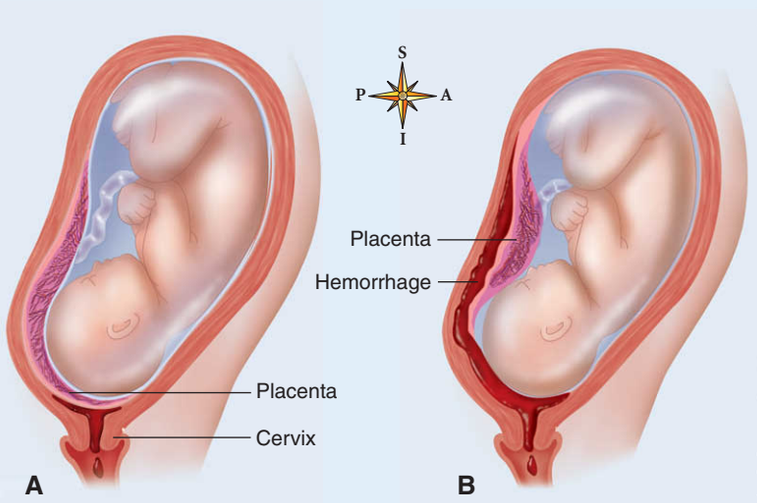


FIGURE 36-32

Implantation disorders. A, Placenta previa. **B,** Abruptio placentae.

PIH and Preeclampsia

It is not uncommon for a woman's blood pressure to rise during pregnancy and remain elevated until the end of pregnancy—a condition often called **pregnancy-induced hypertension (PIH).** In about 6% to 8% of all pregnancies, PIH may progress to a condition called **preeclampsia** (pree-eh-KLAMP-see-ah). Formerly known as *toxemia of pregnancy*, preeclampsia is a serious disorder characterized by the onset of acute hypertension after the twenty-fourth week, accompanied by proteinuria and edema. The causes of PIH and preeclampsia are largely unknown, but intense research efforts have led to the discovery of a gene that regulates how the kidney handles salt and that may also be involved in raising blood pressure during pregnancy. Preeclampsia can result in complications such as abruptio placentae, stroke, hemorrhage, fetal malnutrition, and low birth weight. This condition can progress to **eclampsia,** a life-threatening form of toxemia that causes severe convulsions, coma, kidney failure, and perhaps death of the fetus and mother.

Fetal Death

A **miscarriage** is the loss of an embryo or fetus before the twentieth week (or a fetus weighing less than 500 grams, or 1.1 pounds). Technically known as a **spontaneous abortion,** the most common cause of such a loss is a structural or functional defect in the developing offspring. Abnormalities of the mother, such as hypertension, uterine abnormalities, and hormonal imbalances, can also cause spontaneous abortions. After 20 weeks, delivery of a lifeless infant is termed a **stillbirth.**

Birth Defects

Birth defects, also called **congenital abnormalities,** include any structural or functional abnormality present at birth. Congenital defects may be inherited or may be acquired during gestation or delivery. Inherited defects are discussed in the next chapter. Acquired defects result from agents called **teratogens** (TER-ah-toh-jenz) that disrupt normal histogenesis and organogenesis. Some teratogens are chemicals such as alcohol, antibiotics, and other drugs. Microorganisms, such as those that cause rubella (a viral infection), can also cross the placental barrier and disrupt normal embryonic development. Radiation and other physical factors can also cause birth defects. Some teratogens are mutagens because they do their damage by changing the genetic code in cells of the developing embryo.

Postpartum Disorders

Puerperal (pyoo-ER-per-al) **fever,** or *child-bed fever,* is a syndrome of postpartum mothers characterized by bacterial infection that progresses to septicemia (blood infection) and possibly death. Until the

1930s, puerperal fever was the leading cause of maternal death—claiming the lives of more than 20% of postpartum women. Modern antiseptic techniques prevent most postpartum infections now. Puerperal infections that do occur are usually treated successfully by an immediate and intensive program of antibiotic therapy.

After a child is born, it needs the nourishment of milk to survive. However, several disorders of lactation (milk production) may occur to prevent a mother from nursing her infant. For example, anemia, malnutrition, emotional stress, and structural abnormalities of the breast can all interfere with normal lactation. **Mastitis** (mas-TYE-tis), or breast inflammation, often caused by infection, can result in lactation problems or production of milk contaminated with pathogenic organisms. In many cultures, the availability of other nursing mothers or breast milk substitutes allows proper nourishment of the infant, even when lactation problems develop. Most breast milk substitutes are formulations of milk from another mammal such as the cow. Infants who lack the enzyme *lactase* may not be able to digest the lactose present in human or animal milk, resulting in a condition called **lactose intolerance.** Infants with lactose intolerance are sometimes given a lactose-free milk substitute made from soy or other plant products.

LANGUAGE OF SCIENCE *(continued from p. 1096)*

gestation period
(jes-TAY-shun)
[*gesta-* **bear,** *-tion* **process**]

granulosa cell
(gran-yoo-LOH-sah)
[*gran-* **grain,** *-ul-* **little,** *-osa* **relating to,** *cell* **storeroom**]

haploid
(HAP-loyd)
[*haplo-* **single,** *-oid* **of or like**]

histogenesis
(hiss-toh-JEN-eh-sis)
[*histo-* **tissue,** *-gen-* **produce,** *-esis* **process**]

human chorionic gonadotropin (hCG)
(koh-ree-ON-ik go-nah-doh-TROH-pin)
[*chorion-* **skin,** *-ic* **relating to,** *gon-* **offspring,** *-ad-* **relating to,** *-trop-* **nourishment,** *-in* **substance**]

identical twin

implantation
(im-plan-TAY-shun)
[*im-* **in,** *-planta-* **set or place,** *-ation* **process**]

infancy
[*infan-* **unable to speak,** *-y* **state**]

inner cell mass

labor
(LAY-bor)

meiosis
(my-OH-sis)
[*meiosis* **becoming smaller**]

mesoderm
(MEZ-oh-derm)
[*meso-* **middle,** *-derm* **skin**]

morula
(MOR-yoo-lah)
[*mor-* **mulberry,** *-ula* **little**]
pl., morulae

neonatal period
(nee-oh-NAY-tal)
[*neo-* **new,** *-nat-* **birth,** *-al* **relating to**]

older adulthood

oogenesis
(oh-oh-JEN-eh-sis)
[*oo-* **egg,** *-gen-* **produce,** *-esis* **process**]

oogonium
(oh-oh-GO-nee-um)
[*oo-* **egg,** *-gonium* **offspring**]
pl., oogonia

organogenesis
(or-gah-no-JEN-eh-sis)
[*organ-* **instrument (organ),** *-gen-* **produce,** *-esis* **process**]

parturition
(pahr-too-RIH-shun)
[*parturi-* **give birth,** *-tion* **process**]

placenta
(plah-SEN-tah)
[*placenta* **flat cake**] *pl.,* placentae or placentas

postnatal period
(POST-nay-tal)
[*post-* **after,** *-nat-* **birth,** *-al* **relating to**]

prenatal period
(PREE-nay-tal)
[*pre-* **before,** *-nat-* **birth,** *-al* **relating to**]

primary follicle
(FOL-i-kul)
[*prim-* **first,** *-ary* **state, folli-** *bag, -cle* **small**]

primary germ layer
[*prim-* **first,** *-ary* **state,** *germ* **sprout**]

primary oocyte
(OH-oh-syte)
[*prim-* **first,** *-ary* **state,** *oo-* **egg,** *-cyte* **cell**]

primary sex characteristic
[*prim-* **first,** *-ary* **state,** *charassein* **to engrave**]

puberty
(PYOO-ber-tee)
[*pubert-* **age of maturity,** *-y* **state**]

secondary follicle
(FOL-i-kul)
[*second-* **second,** *-ary* **relating to,** *folli-* **bag,** *-cle* **small**]

secondary oocyte
(OH-oh-site)
[*second-* **second,** *-ary* **relating to,** *oo-* **egg,** *-cyte* **cell**]

secondary sex characteristics

senescence
(seh-NES-enz)
[*senesc-* **grow old,** *-ence* **state**]

spermatogenesis
(sper-mah-toh-JEN-eh-sis)
[*sperm-* **seed,** *-gen-* **produce,** *-esis* **process**]

spermatogonium
(sper-mah-toh-GO-nee-um)
[*sperm-* **seed,** *-gonia* **offspring**]
pl., spermatogonia

theca cell
(THEE-kah)
[*theca* **sheath,** *cell* **storeroom**]

thermotaxis
(ther-moh-TAK-sis)
[*therm-* **heat ,***-taxis* **movement or reaction**]

trophoblast
(TROH-foh-blast)
[*tropho-* **nourishment,** *-blast* **sprout**]

yolk sac

zona pellucida (ZP)
(ZOH-nah pah-LOO-sih-dah)
[*zona* **belt or girdle,** *pellucida* **transparent**] *pl.,* zonae pellucidae

zygote
(ZYE-goht)
[*zygot-* **union or yoke**]

LANGUAGE OF MEDICINE

abruptio placentae
(ab-RUP-shee-oh plah-SEN-tay)
[*ab-* **away from,** *-ruptio* **rupture,** *placentae* **of flat cake (placenta)**]

antenatal medicine
(an-tee-NAY-tal)
[*ante-* **before,** *-nat-* **birth,** *-al* **relating to**]

Apgar score
(AP-gar)
[*Virginia Apgar* **American physician**]

arteriosclerosis
(ar-tee-ree-oh-skleh-ROH-sis)
[*arteri-* **vessel (artery),** *-sclero-* **harden,** *-osis* **condition**]

LANGUAGE OF MEDICINE *(continued from p. 1125)*

atherosclerosis
(ath-er-oh-skleh-ROH-sis)
[*ather-* **meal**, *-sclero-* **harden**, *-osis* **condition**]

cataract
(KAT-ah-rakt)
[*cataract* **waterfall**]

cesarean section
(seh-SAIR-ee-an SEK-shun)
[*Julius Caesar* **Roman emperor**, *-ean* **of**]

congenital abnormality
(kon-JEN-i-tall ab-nor-MAL-i-tee)
[*con-* **with**, *-genit-* **born**, *-al* **relating to**]

eclampsia
(eh-KLAMP-see-ah)
[*ec-* **out**, *-lamp-* **shine forth**, *-sia* **condition**]

embryology
(em-bree-OL-oh-gee)
[*em-* **in**, *-bryo-* **fill to bursting**, *-log-* **words (study of)**, *-y* **activity**]

gerontology
(jair-on-TAHL-oh-jee)
[*geronto-* **old age**, *-log-* **words (study of)**, *-y* **activity**]

glaucoma
(glaw-KOH-mah)
[*glauco-* **gray**, *-oma* **growth**]

hypertension (HTN)
(hye-per-TEN-shun)
[*hyper-* **excessive**, *-tens-* **stretch or pull tight**, *-sion* **state**]

lactose intolerance
(LAK-tohs in-TOL-er-ans)
[*lact-* **milk**, *-ose* **carbohydrate (sugar)**, *in-* **not**, *-toler-* **bear**, *-ance* **state**]

mastitis
(mas-TYE-tis)
[*mast-* **breast**, *-itis* **inflammation**]

menopause
(MEN-oh-pawz)
[*men-* **month**, *-pause* **cease**]

miscarriage

neonatology
(nee-oh-nay-TOL-oh-jee)
[*neo-* **new**, *-nat-* **born**, *-log-* **words (study of)**, *-y* **activity**]

osteoarthritis
(os-tee-oh-ar-THRY-tis)
[*osteo-* **bone**, *-arthr-* **joint**, *-itis* **inflammation**]

placenta previa
(plah-SEN-tah PREE-vee-ah)
[*placenta* **flat cake**, *previa* **gone before**]

preeclampsia
(pree-ee-KLAMP-see-ah)
[*pre-* **before**, *-lamp-* **shine forth**, *-sia* **condition**]

pregnancy-induced hypertension (PIH)
(PREG-nan-see-in-DOOST hye-per-TEN-shun)
[*hyper-* **excessive**, *-tens-* **stretch or pull tight**, *-sion* **state**]

presbyopia
(pres-bee-OH-pee-ah)
[*presby-* **aging**, *-op-* **vision**, *-ia* **condition**]

progeria
(proh-JEER-ee-ah)
[*pro-* **early**, *-ger-* **old age**, *-ia* **condition**]

puerperal fever
(pyoo-ER-per-al FEE-ver)
[*puerp-* **childbirth**, *-al* **relating to**]

spontaneous abortion
(spon-TAY-nee-us ah-BOR-shun)
[*ab-* **away from**, *-or-* **be born**, *-tion* **process**]

stem cell

stillbirth

teratogen
(TER-ah-toh-jen)
[*terato-* **monster**, *-gen* **produce**]

tubal pregnancy
(TOO-bal)
[*tub-* **tube**, *-al* **relating to**]

ultrasonography
(ul-trah-son-OG-rah-fee)
[*ultra-* **beyond**, *-sono-* **sound**, *-graph-* **draw**, *-y* **process**]

CASE study



Carlos and his wife had been trying for years to have a baby with no success. After a visit to an infertility specialist, they found that Carlos had a low sperm count. After looking at all of their options, they decided to try an intrauterine insemination (IUI). A day or so after the procedure, although they didn't know it yet, Carlos' sperm had indeed found Maria's ova and had fused together, that is, the ova had been fertilized.

1. What is a newly fertilized ovum called?
   a. Zygote
   b. Embryo
   c. Fetus
   d. Blastocyst

2. How much time will elapse from fertilization to full implantation?
   a. 2 days
   b. 4 days
   c. 24 hours
   d. 10 days

At 13 weeks, an ultrasound is performed to make sure everything is going smoothly. Maria is looking at the screen and sees what appears to be two separate images. "Is that what I think it is?" she asks the technician. "Officially, the doctor has to tell you—but I can just let you watch the screen as I measure two heartbeats and make two sets of measurements," says the technician. "One boy and one girl."

3. What type of twins is Maria expecting?
   a. Maternal
   b. Fraternal
   c. Identical
   d. Sibling

At week 37, Maria starts feeling some slight contractions, but she passes them off as indigestion. Later that night though, she notices a thin, watery fluid leaking from her vagina, and the contractions are getting stronger. She wakes up Carlos, and they head to the birthing center.

4. What was the watery fluid Maria noted?
   a. Placental fluid
   b. Chorionic fluid
   c. Amniotic fluid
   d. Urine

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

INTRODUCTION

A. Prenatal period—period beginning with conception and ending at birth
B. Postnatal period—period beginning with birth and continuing until death
C. Human developmental biology—study of changes occurring during the cycles of life from conception to death

A NEW HUMAN LIFE

A. Production of sex cells—spermatozoa are produced by spermatogenesis; ova are produced by oogenesis
   1. Meiosis (Figures 36-1 and 36-2)
      a. Special form of cell division that reduces the number of chromosomes in each daughter cell to one half of those in the parent cell
      b. Mature ova and sperm contain only 23 chromosomes, half as many as other human cells
      c. Meiotic division—two cell divisions that occur one after another in succession
         (1) Meiotic division I and meiotic division II
         (2) Both divisions made up of an interphase, prophase, metaphase, anaphase, and telophase
      d. During prophase I of meiosis, "crossover" occurs in which genetic material is "shuffled"
      e. Daughter cells formed by meiotic division I contain a haploid number of chromosomes
      f. Meiotic division II—essentially the same as mitotic division; reproduces each of the two cells formed by meiotic division I and forms four cells, each with the haploid number of chromosomes
   2. Spermatogenesis (Figure 36-3)—process by which primitive male sex cells become transformed into mature sperm; begins at approximately puberty and continues throughout a man's life
      a. Meiotic division I—one primary spermatocyte forms two secondary spermatocytes, each with 23 chromosomes
      b. Meiotic division II—each of the two secondary spermatocytes forms a total of four spermatids
   3. Oogenesis (Figure 36-4)—process by which primitive female sex cells become transformed into mature ova
      a. Mitosis—oogonia reproduce to form primary oocytes; most primary oocytes begin meiosis and develop to prophase I before birth; there they stay until puberty
      b. Once during each menstrual cycle, a few primary oocytes resume meiosis and migrate toward the surface of the ovary; usually only one oocyte matures enough for ovulation, and meiosis again halts at metaphase II
      c. Meiosis resumes only if the head of a sperm cell enters the ovum
B. Ovulation and insemination
   1. Ovulation—expulsion of the mature ovum from the mature ovarian follicle, into the abdominopelvic cavity, and then into the uterine (fallopian) tube
   2. Insemination—expulsion of seminal fluid from the male into the female vagina; capacitation renders sperm able to fertilize; sperm travel through the cervix and uterus and into the uterine (fallopian) tubes
C. Fertilization—also known as *conception* (Figure 36-5)
   1. Most often occurs in the outer one third of the uterine tube
   2. Thermotaxis—sperm are attracted to warmth of uterine tubes
   3. Chemotaxis—ovum attracts and "traps" sperm with special molecules
   4. Acrosome reaction permits the release of enzymes that burrow through the outer layers of ovum (zona pellucida and corona radiata)
   5. When one spermatozoon enters the ovum, the ovum stops collecting sperm on its surface
   6. The sperm releases its nuclear chromosomes into the ovum; proteins and RNA from the sperm enter the ovum to assist with early development
   7. 23 chromosomes from the sperm head and 23 chromosomes in the ovum make up a total of 46 chromosomes
   8. Zygote—fertilized ovum; genetically complete

PRENATAL PERIOD

A. Begins with conception and continues until the birth of a child
B. Cleavage and implantation (Figure 36-6)—once zygote is formed, it immediately begins to divide
   1. Morula—solid mass of cells formed from zygote; takes approximately 3 days; continues to divide (Figure 36-7)
   2. Blastocyst—a hollow ball of cells that develops by the time the embryo reaches the uterus, where it implants into the uterine lining (Figure 36-8)
   3. A store of nutrients in the ovum supports embryonic development until implantation has occurred (approximately 10 days from fertilization to implantation)
   4. Blastocyst has an outer layer of cells and an inner cell mass
      a. Trophoblast—outer wall of the blastocyst
      b. Inner cell mass—as blastocyst develops, yolk sac and amniotic cavity are formed (Figure 36-9)
         (1) In humans, yolk sac's functions are largely non-nutritive
         (2) Amniotic cavity becomes a fluid-filled, shock-absorbing sac (bag of waters) in which the embryo floats during development (Figure 36-10)
      c. Chorion develops from trophoblast to become an important fetal membrane in the placenta
   5. Placenta (Figure 36-11)
      a. Anchors fetus to the uterus and provides a "bridge" for the exchange of nutrients and waste products between mother and baby

b. Also serves as an excretory, respiratory, and endocrine organ
c. Placental tissue normally separates maternal and fetal blood supplies
d. Has important endocrine functions—secretes large amounts of hCG, which stimulate the corpus luteum to continue its secretion of estrogen and progesterone (Figure 36-12)

C. Periods of development (Figures 36-13 to 36-15)
1. Gestation period—approximately 39 weeks; divided into three 3-month segments called trimesters
2. Embryonic phase extends from fertilization until the end of week 8 of gestation
3. Fetal phase—weeks 8 to 39

D. Stem cells
1. Stem cell—unspecialized cell that produces lines of specialized cells; has a certain level of potency (range of types it can produce)
2. Totipotent stem cell—can produce any type of cell; found in zygote
3. Pluripotent stem cell—embryonic stem cell that can produce a broad range of cell types; found in embryonic germ layers
4. Multipotent stem cell—adult stem cell found in some tissues can produce a few cell types and thus maintain functional populations of specialized cells

E. Formation of the primary germ layers
1. Three layers of developmental cells arise early in the first trimester of pregnancy
2. Cells of embryonic disk differentiate and form each of the three primary germ layers
3. Each of the three primary germ layers gives rise to specific organs and systems of the body (Figure 36-16)
a. Endoderm—inside layer
b. Ectoderm—outside layer
c. Mesoderm—middle layer

F. Histogenesis and organogenesis (Figure 36-16)
1. Histogenesis—process by which primary germ layers develop into different kinds of tissues
2. Organogenesis—how tissues arrange themselves into organs
3. Differentiation and development of the reproductive systems are an example
a. Reproductive tract (Figure 36-17)
(1) Gonads attach to mesonephric (wolffian) ducts, which become the male reproductive tract
(2) Gonads (unattached) and paramesonephric (müllerian) ducts develop into the female reproductive tract
b. External genitals (Figure 36-18)
(1) In the male, the genital tubercle eventually becomes the glans of the penis and the folds become the penis shaft and scrotum
(2) In the female, the genital tubercle becomes the clitoris and the folds become the labia

BIRTH, OR PARTURITION

A. Transition between prenatal and postnatal periods of life
B. Cortisol triggers labor by reducing hCG and thus also progesterone, removing the "brake" on OT, which stimulates the uterine muscles to produce labor contractions (amplified by a positive feedback effect); PGs enhance OT's effects
C. Stages of labor (Figure 36-20)
1. Stage one—period from onset of uterine contractions until cervical dilation is complete
2. Stage two—period from maximal cervical dilation until the baby exits through the vagina
3. Stage three—process of expulsion of the placenta through the vagina
D. Multiple births—birth of two or more infants from the same pregnancy; twins are most common (Figure 36-21)
1. Identical twins result from the splitting of embryonic tissue from the same zygote early in development
2. Fraternal twins result from the fertilization of two different ova by two different spermatozoa

POSTNATAL PERIOD

A. Begins at birth and continues until death; commonly divided into a number of periods (Figure 36-22)
B. Infancy begins at birth and lasts until approximately 18 months
1. Neonatal period—first 4 weeks of infancy; dramatic changes occur at a rapid rate (Figure 36-23)
2. Changes allow the infant to become totally self-supporting, especially the respiratory and cardiovascular systems (Figure 36-24)
3. Apgar score assesses general condition of a newborn infant
C. Childhood extends from end of infancy to sexual maturity, or puberty
1. Early childhood—growth continues at a rapid pace but month-to-month gains are less consistent
2. By age 6 years, child looks more like a preadolescent than an infant or toddler
3. Nervous and muscular systems develop rapidly during the middle years of childhood
4. Deciduous teeth are lost during childhood, beginning at approximately 6 years of age
5. Permanent teeth have erupted by age 14 years, except for the third molars (wisdom teeth)
D. Adolescence and adulthood
1. Adolescence is considered to be the teenage years (from 13 to 19); marked by rapid and intense physical growth, resulting in sexual maturity
a. Puberty—stage of adolescence during which a person becomes sexually mature
b. Changes triggered by increases in reproductive hormones (Figure 36-25)
c. Primary sexual characteristics—maturation of gonads and reproductive tract
d. Secondary sexual characteristics—fat and hair distribution, skeletal changes, etc. (Figure 36-26)

2. Adulthood—characterized by maintenance of existing body tissues

E. Older adulthood and senescence
1. As a person grows older, a gradual decline occurs in every major organ system in the body
2. Gerontologists theorize a number of different aging mechanisms, all of which may be involved in the processes of aging
   a. Limit on cell reproduction
   b. Environmental factors
   c. Viruses
   d. Aging genes
   e. Degeneration of mitochondria—perhaps associated with progressive damage by oxygen free radicals (Figure 36-27)

EFFECTS OF AGING

A. Common degenerative changes frequently characterize senescence (Figure 36-28)
B. Skeletal system (Figure 36-29)
1. Bones decrease in BMD (bone mineral density) and thus change in texture, degree of calcification, and shape
2. Lipping occurs, which can limit range of motion
3. Decreased bone size and density lead to increased risk of fracture
4. Decreased BMD can be avoided (at least partly) by exercise and adequate calcium intake

C. Muscular system (Figure 36-30)
1. Muscle mass decreases to about 90% by age 50 years and around 50% by age 80 years
2. The number of muscle fibers decreases as we age but can be offset by an increase in muscle fiber size through exercise
3. Ratio of "fast" to "slow" functioning in muscle fibers decreases, slowing the function of muscle organs

D. Integumentary system (skin)
1. Skin becomes dry, thin, and inelastic
2. Pigmentation changes and thinning hair are common problems associated with aging

E. Urinary system
1. Number of nephron units in the kidney decreases by almost 50% between the ages of 30 and 75 years
2. Decreased blood flow through kidneys reduces overall function and excretory capacity
3. Diminished muscle tone in bladder results in decreased capacity and inability to empty, or void, completely

F. Respiratory system
1. Costal cartilages become calcified
2. Respiratory efficiency decreases
3. Decreased strength of respiratory muscles

G. Cardiovascular system
1. Degenerative heart and blood vessel disease—one of the most common and serious effects of aging
2. Atherosclerosis—buildup of fatty deposits on blood vessel walls narrows the passageway for blood
3. Arteriosclerosis—"hardening" of the arteries
4. Hypertension—high blood pressure

H. Special senses
1. Sense organs—gradual decline in performance and capacity with aging
2. Presbyopia—farsightedness caused by hardening of lens
3. Cataract—cloudy lens, which impairs vision
4. Glaucoma—increased pressure within the eyeball; if left untreated, often results in blindness
5. Decreased hearing
6. Decreased taste

I. Reproductive systems
1. Mechanism of sexual response may change
2. Fertility decreases
3. In females, menopause occurs between ages 45 and 60 years

J. Benefits of aging—mostly improved brain functions: less anxious or fearful, less resistant to happiness, better interpretation of visual information, improved problem solving and wisdom

CAUSES OF DEATH

A. In developed countries such as the United States, heart disease, cancer, and stroke (cerebrovascular accident [CVA]) are among the leading causes of death (Figure 36-31)
B. In developing countries, heart disease and stroke are also leading causes of death, along with infectious diseases such as HIV/AIDS, diarrheal disorders, and malaria

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Define the terms *developmental biology*, *growth*, and *development*.
2. Outline the major steps in spermatogenesis. Do the same for oogenesis.
3. Identify the two processes necessary to bring the sperm and ovum into proximity with each other.
4. During fertilization, how does the ovum attract sperm?
5. At what developmental stage does implantation occur?
6. Describe the structural differences between a morula and a blastocyst.
7. How does the placenta develop?
8. What functions does the placenta provide?
9. Outline the hormonal levels of human chorionic gonadotropin (hCG), estrogen, and progesterone at various stages during gestation.
10. During what period of growth is the term *embryo* replaced by the term *fetus*?
11. List the various structures derived from each of the three primary germ layers.
12. Explain the three stages of labor.
13. What is the difference between identical and fraternal twins?

14. From birth to maturity, how does the size of the head compare with the rest of the body?
15. What are the time spans of the following postnatal periods: infancy, childhood, adolescence?
16. During what postnatal period do the secondary sex characteristics develop? What initiates this development?
17. What structural changes may result from the changes in bone calcification because of aging?
18. Define the terms *atherosclerosis*, *arteriosclerosis*, and *hypertension*.
19. Identify and describe the most serious age-related eye disorder.

CRITICAL THINKING QUESTIONS

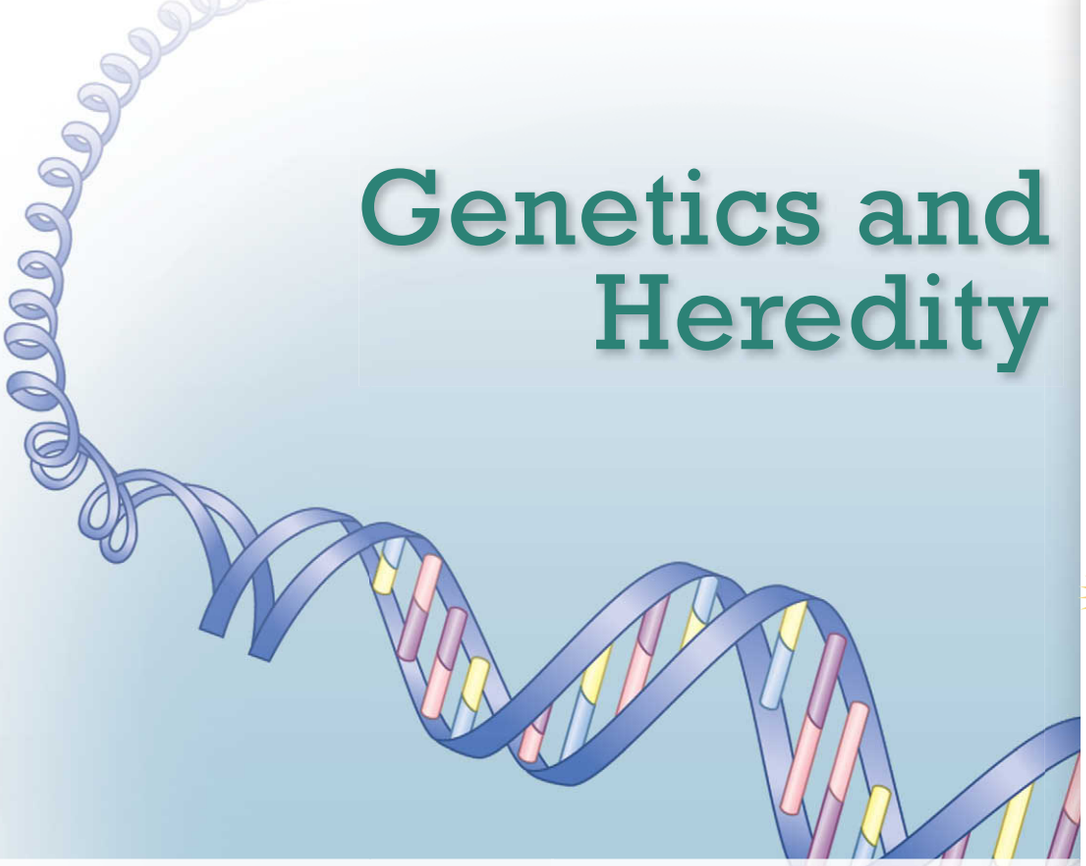


After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. How is the process of meiosis different from mitosis?
2. If a diploid cell rather than a haploid cell were used for human reproduction, what would the number of chromosomes per cell be after three generations?
3. How do histogenesis and organogenesis differ? Which of these occurs first in development?
4. Explain the procedure a physician might use if a normal vaginal delivery would be dangerous for the mother or baby.
5. What are the symptoms of the drop in estrogen that occurs during menopause? To what skeletal disorder might this drop be related?
6. Explain the process of in vitro fertilization. What is the probability of the success of this procedure, that is, resulting in a full-term birth?
7. Using physiological principles, explain how a sound exercise program can reduce some of the common effects of aging.

Genetics and Heredity

37



CHAPTER OUTLINE

HINT *Scan this outline before you begin to read the chapter, as a preview of how the concepts are organized.*

The Science of Genetics, 1132

Chromosomes and Genes, 1132
- Mechanism of Gene Function, 1132
- The Human Genome, 1133
- Distribution of Chromosomes to Offspring, 1135
  - Meiosis, 1135
  - Principle of Independent Assortment, 1135

Gene Expression, 1136
- Hereditary Traits, 1136
  - Dominant and Recessive Traits, 1136
  - Polygenic Traits, 1137
  - Codominant Traits, 1137
- Sex-Linked Traits, 1138
- Genetic Mutations, 1140

Medical Genetics, 1141
- Mechanisms of Genetic Diseases, 1141
  - Nuclear Inheritance, 1141
  - Mitochondrial Inheritance, 1142
- Single-Gene Diseases, 1142
- Chromosomal Diseases, 1144
- Genetic Basis of Cancer, 1145

Prevention and Treatment of Genetic Diseases, 1146
- Genetic Counseling, 1146
  - Pedigree, 1146
  - Punnett Square, 1146
  - Karyotype, 1147
- Treating Genetic Diseases, 1148

The Big Picture: Genetics, Heredity, and the Whole Body, 1149

Case Study, 1151

LANGUAGE OF SCIENCE

HINT *Before reading the chapter, say each of these terms out loud. This will help you avoid stumbling over them as you read.*

autosome
(AW-toh-sohm)
[*auto-* **self,** *-som-* **body**]

carrier

chromatin
(KROH-mah-tin)
[*chrom-* **color,** *-in* **substance**]

chromosome
(KROH-meh-sohm)
[*chrom-* **color,** *-som-* **body**]

chromosome territory (CT)
(KROH-meh-sohm TAIR-it-or-ee)
[*chrom-* **color,** *-som-* **body,** *terri-* **land,** *-ory* **place**]

codominance
(koh-DOM-i-nans)
[*co-* **together,** *-domina-* **rule,** *-ance* **state**]

crossing over

deletion

diploid
(DIP-loyd)
[*diplo-* **twofold,** *-oid* **form of**]

dominant gene

epigenetics
(ep-i-jeh-NET-iks)
[*epi-* **upon,** *gen-* **produce,** *-ic* **relating to**]

gametes
(GAM-eets)
[*gamete* **marriage partner**]

gene
[*gen-* **produce or generate**]

gene linkage
[*gen-* **produce or generate**]

genetic mutation
(jeh-NET-ik myoo-TAY-shun)
[*gene-* **produce,** *-ic* **relating to,** *muta-* **change,** *-ation* **process**]

continued on p. 1149

*It seems that today we are hearing more and more about the importance of **genetics,** the scientific study of inheritance, to all fields of human biology—especially anatomy, physiology, and medicine. Popular news magazines are running story after story on the revolution in treating fatal inherited disorders by using something called gene therapy. Health and science columns in newspapers keep us informed of the latest discoveries of genes involved with disease, human behavior, and even longevity. Television programs outline the progress of the largest coordinated biological quest that anyone can remember: mapping the entire human genetic code and listing all the proteins encoded there. Even commercial ads call attention to genetic health risks. Clearly, one cannot be informed about human biology today without some knowledge of basic genetics and heredity. In this chapter, we briefly review the essential concepts of genetics and explain how heredity affects every structure and function in the body.*

THE SCIENCE OF GENETICS

History shows that humans have been aware of patterns of inheritance—or *heredity*—for thousands of years, but it was not until the 1860s that the scientific study of these patterns—genetics—was born. At that time, a monk living in Brno, Moravia (now the Czech Republic) became the first to discover the basic mechanism by which traits are transmitted from parents to offspring. That man, Gregor Mendel, proved that independent units (which we now call **genes**) are responsible for the inheritance of biological traits.

The science of genetics developed from Mendel's quest to explain how normal biological characteristics are inherited. As time went by and more genetic studies were done, it became clear that certain diseases also have a genetic basis. As you may recall from Chapter 1, some diseases are inherited directly. For example, the group of blood-clotting disorders called *hemophilia* can be inherited by children from parents who have the genetic code for hemophilia. Directly inherited diseases are often called "hereditary diseases." Other diseases are only partly determined by genetics—that is, they involve genetic risk factors (Chapter 1, pp. 25–27). For example, certain forms of skin cancer are thought to have a genetic basis. A person who inherits the genetic code associated with skin cancer will develop the disease only if the skin is also heavily exposed to the ultraviolet radiation in sunlight.

CHROMOSOMES AND GENES

Mechanism of Gene Function

Mendel proposed that the genetic code is transmitted to offspring in discrete, independent units that we now call genes. Recall from Chapters 2 and 4 that each gene is a sequence of nucleotide bases in the deoxyribonucleic acid (DNA) molecule.

Figure 37-1 shows a detailed view of human DNA. Beginning at the left of the diagram, you can see a fully condensed **chromosome** unfold toward the right, where a single double-helix strand of DNA is visible. As the genetic codes of a DNA molecule's genes are being actively transcribed in a cell's nucleus, the DNA is in the threadlike form called **chromatin.** Chromatin, as you can see in Figure 37-1, is actually a thread of DNA wound around little spools made of proteins called **histones.** The chromatin is thus organized into little "thread on spool" subunits called **nucleosomes.**

During cell division, each replicated strand of chromatin coils on itself to form a compact chromosome (see Figure 37-1). Each DNA molecule can be called either a chromatin strand or a chromosome, depending on what form it is in. Throughout this chapter we will use the term *chromosome* for DNA, regardless of its actual form, and the term *gene* for each distinct encoding segment within a DNA molecule.

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In nondividing cells, chromosomes are found in the form of chromatin strands that occupy specific **chromosome territories (CTs)** within the nucleus. See an example of a CT map in ***Chromosome Territories*** online at ***A&P Connect.***

evolve

Each gene in a chromosome contains a genetic code that the cell transcribes to a ribonucleic acid (RNA) molecule (see Box 5-2 on p. 120). Some RNA molecules do not code for polypeptides but have a functional role—for example, ribosomal RNA (rRNA) and transfer RNA (tRNA). A transcribed messenger RNA (mRNA) molecule, however, associates with a ribosome in which the code is translated to form a specific polypeptide molecule. By way of slight differences in editing of mRNA, one mRNA may perhaps actually produce several specific polypeptides. And the polypeptides may be complete tertiary proteins by themselves—or they may combine with any of several other polypeptides to form several different specific large quaternary proteins (see Figure 2-28 on p. 54).

Many of the protein molecules formed from the polypeptides encoded by genes are *enzymes*, functional proteins that help regulate the various metabolic pathways of the body by catalyzing specific chemical reactions. Because enzymes and other functional proteins such as hemoglobin regulate the biochemistry of the body, they regulate the entire structure and function of the body. Some proteins, such as collagen and keratin, are important structural components of the body—and thus determine important structural characteristics of various body parts.

As you can see, genes determine the structure and function of the human body by producing a set of specific structural proteins, along with many functional proteins and RNA molecules.

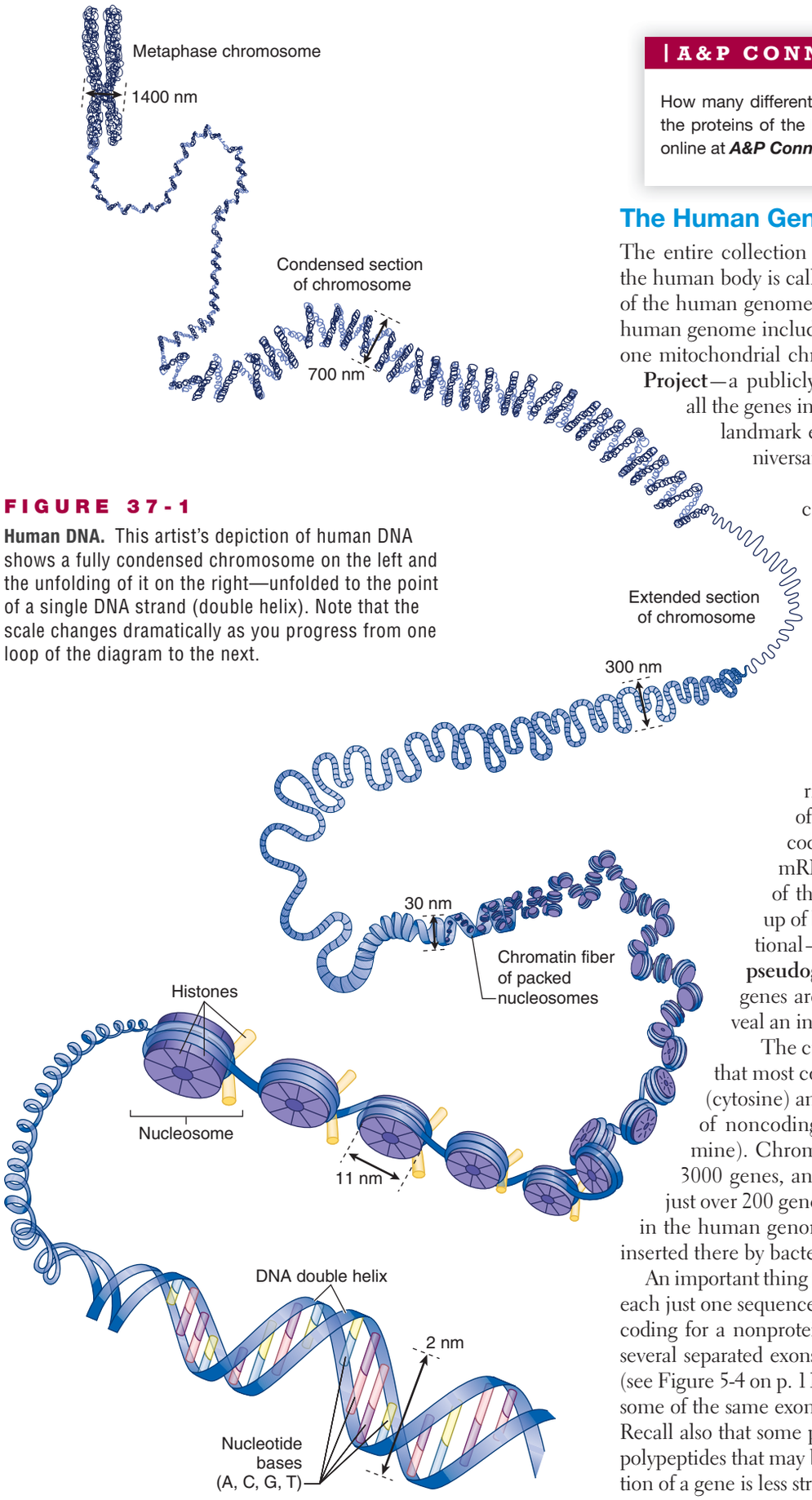


FIGURE 37-1

Human DNA. This artist's depiction of human DNA shows a fully condensed chromosome on the left and the unfolding of it on the right—unfolded to the point of a single DNA strand (double helix). Note that the scale changes dramatically as you progress from one loop of the diagram to the next.

| A&P CONNECT |

How many different kinds of amino acids are needed to form the proteins of the body? Find out in ***Amazing Amino Acids*** online at ***A&P Connect.***

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The Human Genome

The entire collection of genetic material in each typical cell of the human body is called the **genome** (JEE-nome). The structure of the human genome is summarized in Figure 37-2. The typical human genome includes 46 individual nuclear chromosomes and one mitochondrial chromosome. In 2003, the **Human Genome Project**—a publicly funded, worldwide collaboration to map all the genes in the human genome—was completed. This landmark event coincided exactly with the fiftieth anniversary of the discovery of DNA.

We now know that the human genome contains only about 20,000 to 25,000 genes. This is about one fifth to one quarter of the number originally estimated. Amazingly, it is roughly the same number of genes as in a rat or mouse—and only about one and one-half times as many genes as in a fruit fly!

We also know that less than 2% of the DNA carries protein-coding genes. A bit more of the DNA carries code for functional RNAs, such as rRNA, tRNA, and ribozymes (see Figure 5-2 on p. 115). Most of the rest of the DNA is often called "junk" code that is either not used or is edited out of mRNA before it is used to make proteins. Some of this noncoding DNA may actually be made up of broken bits of genes that are no longer functional—remnants of our evolutionary past. Termed **pseudogenes,** these bits of formerly functional genes are like genetic fossils that have begun to reveal an interesting history of our genetic past.

The current draft of the human genome shows us that most coding genes tend to lie in clusters rich in C (cytosine) and G (guanine), separated by long stretches of noncoding DNA rich in A (adenine) and T (thymine). Chromosome 1 has the most genes, with nearly 3000 genes, and the Y chromosome has the fewest, with just over 200 genes. Hundreds of the newly discovered genes in the human genome seem to be bacterial in origin, perhaps inserted there by bacteria in our distant ancestors.

An important thing to remember about genes is that they are not each just one sequence that codes for one protein. Besides possibly coding for a nonprotein such as RNA, each gene is made up of several separated exons that join together before protein synthesis (see Figure 5-4 on p. 116). In some cases, different combinations of some of the same exons can make up genes for different products. Recall also that some proteins are quaternary proteins made up of polypeptides that may be made from different genes. So the definition of a gene is less straightforward than it first appears!

Although we now have the essential picture of the details of the human genome, much work still lies ahead in the field of **genomics** (jeh-NOM-iks), the analysis of the genome's code. Besides filling in the remaining details of the rough draft, we have much work to do in discovering all the possible mutations that might exist (see the discussion later in this chapter) and all the proteins encoded by the genes that make up the human genome (Box 37-1).

In fact, this quest has generated several other fields related to the genetic code. For example, **transcriptomics** (transkript-OHM-iks) is the analysis of all the mRNA codes actually transcribed from the human genome—the **transcriptome** (tran-SKRIPT-ome). This field may eventually shed light on which genes are expressed and under what conditions.

A field called **proteomics** (pro-tee-OH-miks) is the analysis of the proteins encoded by the genome. The entire group of proteins encoded by the human genome is called the human **proteome** (PRO-tee-ohm). The ultimate goal of proteomics is to understand the role of each protein in the body. Understanding the roles of every single protein in the body will certainly go a long way toward improving our knowledge of the normal function of the body as well as mechanisms for many diseases.

The analysis of the human genome, transcriptome, and proteome has surged forward recently with the widespread use of *RNA interference (RNAi)* techniques that silence particular genes in the laboratory setting as a means to find out what they do in the body—what proteins are transcribed from them.

Another proven technique that "knocks out" individual genes has been used for some time to demonstrate the effects of specific genes. Using embryonic stem cells from laboratory mice in which specific genes are targeted and disabled, a generation of genetically altered "knockout mice" can be produced. The mice are then studied to find out the effects of the gene(s) missing from the mouse genome.

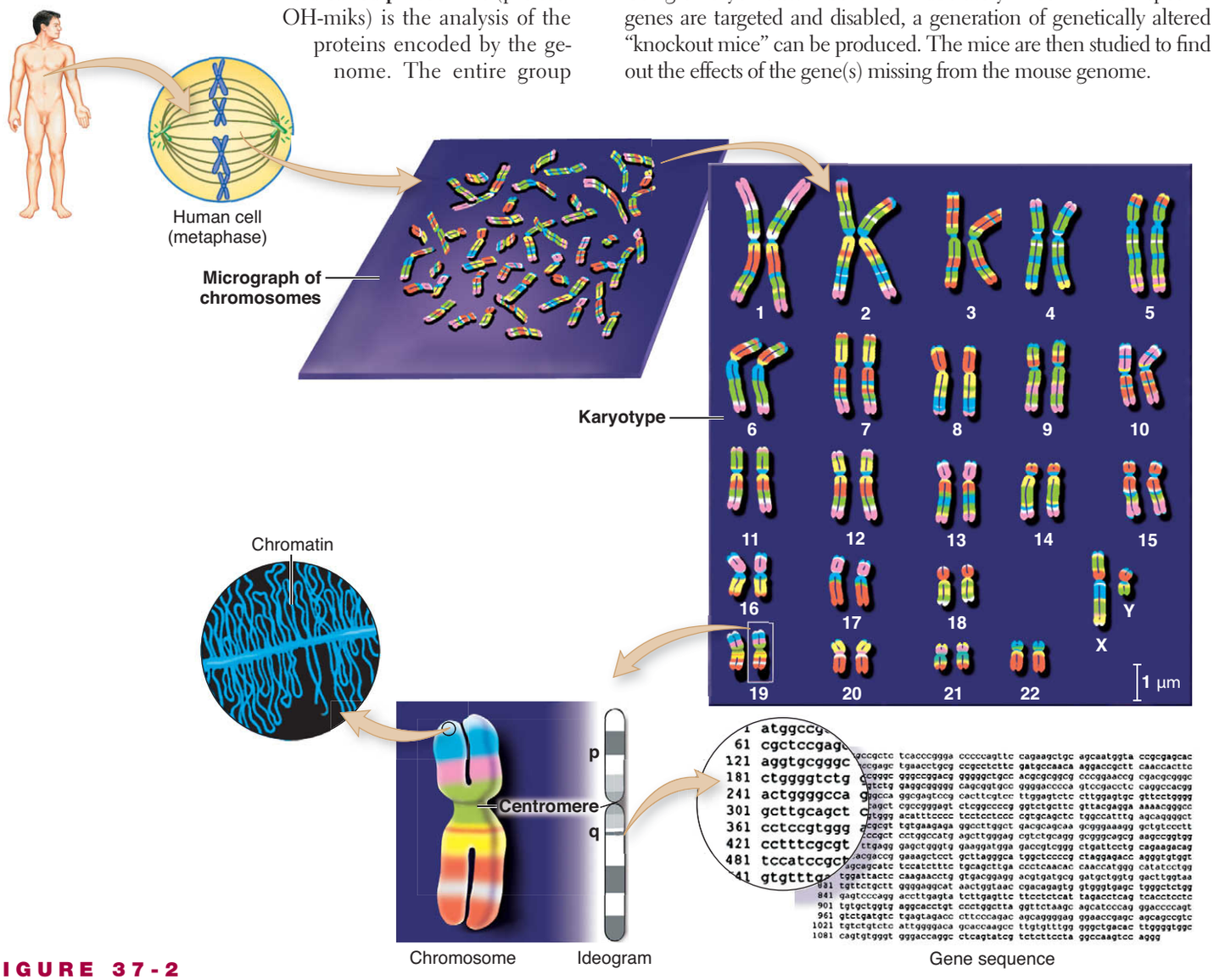


FIGURE 37-2

Human genome. A cell taken from the body is stained and photographed. A photograph of nuclear chromosomes is then cut and pasted, arranging each of the 46 chromosomes into numbered pairs of decreasing size to form a chart called the karyotype. Each chromosome is a coiled mass of chromatin (DNA). In this figure, differentially stained bands in each chromosome appear as different, bright colors. Such bands are useful as reference points when identifying the locations of specific genes within a chromosome. The staining bands are also represented on an ideogram, or simple graph, of the chromosome as reference points to locate specific genes. The genes themselves are usually represented as the actual sequence of nucleotide bases, abbreviated as *a, c, g,* and *t.* In this figure, the sequence of one exon (segment) of a gene called *GPI* from chromosome 19 is shown. Each of the different images in this figure can be thought of as a different type of "genetic map."

Box 37-1 | FYI

1000 Genomes Project

An international research partnership sponsored in part by the United States government is currently building a catalog of at least 1000 individual human genomes. This effort, called the *1000 Genomes Project,* promises to reveal the many variant forms of genes present in the whole human genome. Although over a thousand complete individual genomes have already been cataloged—most notably the genomes of gene pioneers Craig Venter and James Watson—much more information is needed. The initial goal to is study about 2500 individual genomes from 25 different populations. The project catalogs the many small DNA-coding variations called *single nucleotide polymorphisms (SNPs)* as well as the larger structural variations in the human genome. Such information could lead to better understanding of the genetic basis of disease—and ultimately to effective treatments or cures.

Information obtained about the human genome can be expressed in a variety of ways. As you can see in Figure 37-2, an **ideogram** (ID-ee-oh-gram), or simple cartoon of a chromosome, is often used in genomics to show the overall physical structure of a chromosome. The constriction in the ideogram shows the relative position of the chromosome's centromere. The shorter segment of the chromosome is called the **p-arm** and the longer segment is called the **q-arm.**

The bands in an ideogram of a chromosome show staining landmarks and help identify the regions of the chromosome. Sometimes physical maps of genes will show exact positions of individual genes on the p-arm and q-arm of a chromosome. A more detailed representation of a gene would show the actual sequence of nucleotide bases, abbreviated *a*, *c*, *g*, and *t* for *adenine*, *cytosine*, *guanine*, and *thymine*, as shown in Figure 37-2.

Distribution of Chromosomes to Offspring

MEIOSIS

Each cell of the human body contains 46 chromosomes. The only exceptions to this principle are the **gametes**—male *spermatozoa* and female *ova*. Recall from Chapter 36 that a special form of nuclear division called **meiosis** (see Figure 36-1 on p. 1098) produces gametes with only 23 chromosomes—exactly one half the usual number. This number is called the **haploid** number. This process follows a basic principle of genetics first discovered by Gregor Mendel called the **principle of segregation.** This principle simply states that the two members of a pair of chromosomes separate, or *segregate*, during meiosis.

When a sperm (with its 23 chromosomes) unites with an ovum (with its 23 chromosomes) at conception, a *zygote* with 46 chromosomes is formed. Thus the zygote has the same number of chromosomes (46, the **diploid** number) as each typical body cell in the parents.

As the karyotype in Figure 37-2 shows, the 46 human chromosomes can be arranged in 23 pairs according to size. One pair called the **sex chromosomes** may not match, but the remaining 22 pairs of **autosomes** always appear to be nearly identical to each other.

PRINCIPLE OF INDEPENDENT ASSORTMENT

Because one half of an offspring's chromosomes are from the mother and one half are from the father, a unique blend of inherited traits is formed. According to another of Mendel's principles, each chromosome assorts itself independently during meiosis. This **principle of independent assortment** states that as sperm are formed, and chromosome pairs separate (the principle of segregation), the maternal and paternal chromosomes get mixed up and redistribute themselves independently of the other chromosome pairs (Figure 37-3). Thus each sperm is likely to have a *different* set of

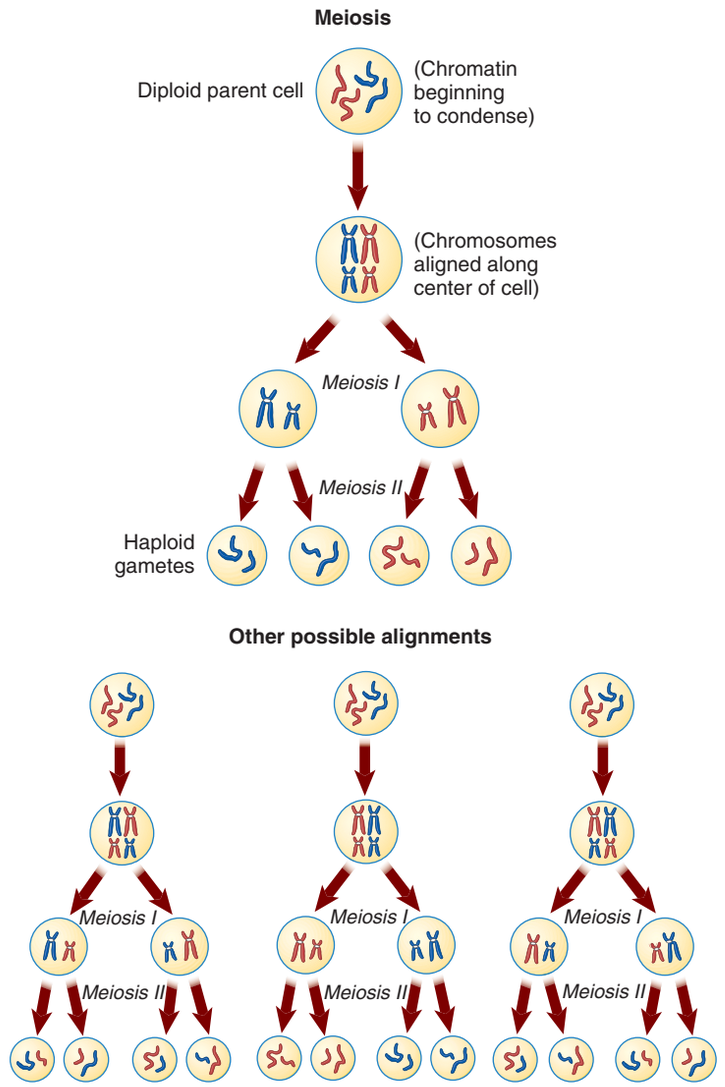


FIGURE 37-3

Meiosis and the principle of independent assortment. In meiosis, a series of two divisions results in the production of gametes with one half the number of chromosomes of the original parent cell. In both meiotic divisions shown here, the original cell has four chromosomes and the gametes each have two chromosomes. During the first division of meiosis, pairs of similar chromosomes line up along the cell's equator for even distribution to daughter cells. Because different pairs assort independently of each other, four (2^2) different alignments of chromosomes can occur. Because human cells have 23 pairs of chromosomes, more than 8 million (2^{23}) different combinations are possible.

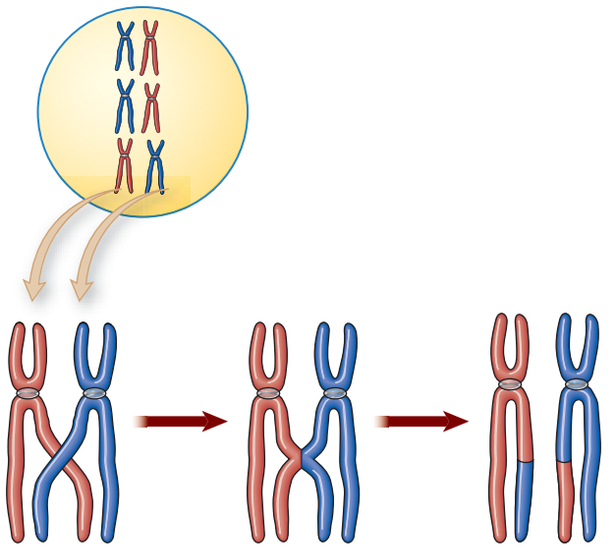


FIGURE 37-4

Crossing over. Genes (or linked groups of genes) from one chromosome are exchanged with matching genes in the other chromosome of a pair during meiosis.

23 chromosomes. Because the ova are formed in the same manner, each ovum is likely to be genetically different from the ovum that preceded it. Independent assortment of chromosomes ensures that each offspring from a single set of parents is very likely to be genetically unique—a phenomenon known as *genetic variation.*

According to the principle of **gene linkage,** genes on an individual chromosome tend to stay together. An important application of this principle occurs during one phase of meiosis, when pairs of matching chromosomes line up along the equator of the cell and exchange genes or groups of linked genes with one another. This process is called **crossing over** because genes from a particular location cross over to the same location on the matching chromosome (Figure 37-4). Crossing over introduces additional opportunities for genetic variation among the offspring of a single set of parents.

When one considers the genetic variation that is produced by independent assortment and crossing over, it is easy to understand the tremendous variation seen in the human population.

| QUICK CHECK |

1. How do genes produce biological traits?
2. Who might be considered the founder of the scientific study of genetics?
3. What is the difference between an autosome and a sex chromosome?
4. List some mechanisms that increase genetic variation among human offspring.

GENE EXPRESSION

Hereditary Traits

DOMINANT AND RECESSIVE TRAITS

Mendel discovered that the genetic units we now call genes may be expressed differently among individual offspring. After rigorous experimentation with pea plants, he discovered that each inherited trait is controlled by two sets of similar genes, one from each parent. Each autosome in a pair matches its partner in the type of genes it contains. In other words, if one autosome has a gene for hair color, its partner will also have a gene for hair color—in the same location on the autosome. Although both genes specify hair color, they may not specify the *same* hair color. Mendel discovered that some genes are *dominant* and some are *recessive.* A **dominant gene** is one whose effects are seen and whose effects are capable of masking the effects of a **recessive gene** for the same trait.

Consider the example of **albinism,** a total lack of melanin pigment in the skin and eyes (Figure 37-5). Because people with this condition lack dark pigmentation, they have difficulty seeing in bright light and must avoid direct sunlight to protect themselves from burns. The genes that cause albinism are recessive; the genes that cause normal melanin production are dominant. By convention, dominant genes are represented by uppercase letters and recessive genes by lowercase letters. One can represent the gene for albinism as *a* and one of the genes for normal skin pigmentation as A. An individual with the gene combination AA has two dominant genes—and so will exhibit a normal skin color. The code AA is called a **genotype.** A person with a genotype of two identical forms of a trait is said to be **homozygous** (from *homo-*, "same," and *-zygo*, "joined") for that trait.



FIGURE 37-5

Albinism. There are several forms of albinism in humans. The type shown here, tyrosinase-negative oculocutaneous albinism, results from the inheritance of two abnormal genes for tyrosinase—the enzymes required to convert tyrosine to melanin pigments. Melanin is normally present in the skin as well as in the eye, where its absence produces vision problems that include sensitivity to light. This African woman would otherwise have dark skin, dark hair, and normal vision. However, as she looks away from the bright camera light as she is photographed, you can see the abnormally light hair and skin typical of this type of albinism.

The manner in which a genotype is expressed is called the **phenotype.** Thus a person who is homozygous dominant (*AA*) for skin color will have a normal phenotype (i.e., normal skin pigmentation). Someone with the gene combination *Aa* will also have normal skin color because the normal gene *A* is dominant over the recessive albinism gene *a*. A person with genotype *Aa* is said to be **heterozygous** (from *hetero-*, "different," and *-zygo*, "joined") and will express the normal phenotype. Only a person with the homozygous recessive genotype of *aa* will have the abnormal phenotype, albinism, because there is no dominant gene to mask the effects of the two recessive genes.

In the example of albinism, a person with the heterozygous genotype of *Aa* is said to be a genetic **carrier** of albinism. This means that the person can transmit the albinism gene, *a*, to offspring. Thus two normal parents, each having the heterozygous genotype *Aa*, can produce both normal children and children who have albinism (Figure 37-6).

POLYGENIC TRAITS

It is important to note that melanin pigmentation in human skin is actually governed by several different pairs of genes. The gene for the form of albinism discussed here, *tyrosinase-negative oculocutaneous albinism*, involves just one of the gene pairs that regulate skin color. Inherited characteristics, such as skin color and height, which are determined by the combined effect of many different gene pairs, are often called **polygenic** ("many genes") traits to distinguish them from **monogenic,** or single-gene, traits.

Polygenic traits are often hard to study in the phenotype because they are so variable. You can think of a polygenic trait as a "combined trait" because it results from the combined activity of several different genes. Each gene may be dominant or recessive in character. Because each gene is only one of several that govern the combined trait, however, the phenotype may be any of a large number of different variations of the trait. Using skin color as an example, the form of albinism described above involved only one of several genes that govern pigmentation of the skin and eyes. But that one gene is critical; it negates the effects of all the other genes that govern skin color. However, if the dominant form of that critical gene is in place, then it is possible for variations in any of the other genes that regulate skin color to exert influence on skin pigmentation.

CODOMINANT TRAITS

What happens if two different dominant genes occur together? Suppose there is a gene A^1 for light skin and a gene A^2 for dark skin. In a form of dominance called **codominance,** they will simply have equal effects, and a person with the heterozygous geno-type A^1A^2 will exhibit a phenotype of skin color that is something between light and dark. Recall from Chapter 20 (Box 20-2, p. 602) that the genes for sickle cell anemia behave this way. A person with two sickle cell genes will have *sickle cell anemia*, whereas a person with one normal gene and one sickle cell gene will have a milder form of the disease called *sickle cell trait*.

The case of sickle cell inheritance is a good example of how the mechanism of codominance works. The hemoglobin molecules within all red blood cells (RBCs) are quaternary proteins that each include four polypeptide chains—two alpha chains and two beta chains (see Figure 20-5 on p. 602). The sickle cell gene is actually an abnormal version of the gene that contains the code for the beta chains of the hemoglobin molecule. Any beta chain that is produced by this code has one (of 146) amino acid replaced by the wrong amino acid—making it different enough to drastically alter its function. The RBCs of a person with one sickle cell gene and one normal beta-chain gene contain hemoglobin in which about one half the total number of beta chains are abnormal and about one half are normal. The RBCs of a person with two sickle cell genes contain hemoglobin in which all the beta chains are abnormal. Thus in sickle cell trait only some hemoglobin molecules are defective, but in sickle cell anemia *all* of the hemoglobin molecules are defective.

The frequency of occurrence of the abnormal sickle cell gene is an example of an interesting epidemiological phenomenon. Because sickle cell trait provides resistance to the parasite that causes the most deadly form of **malaria** (*Plasmodium falciparum* malaria), sickle cell disorders persist in areas of the world in which

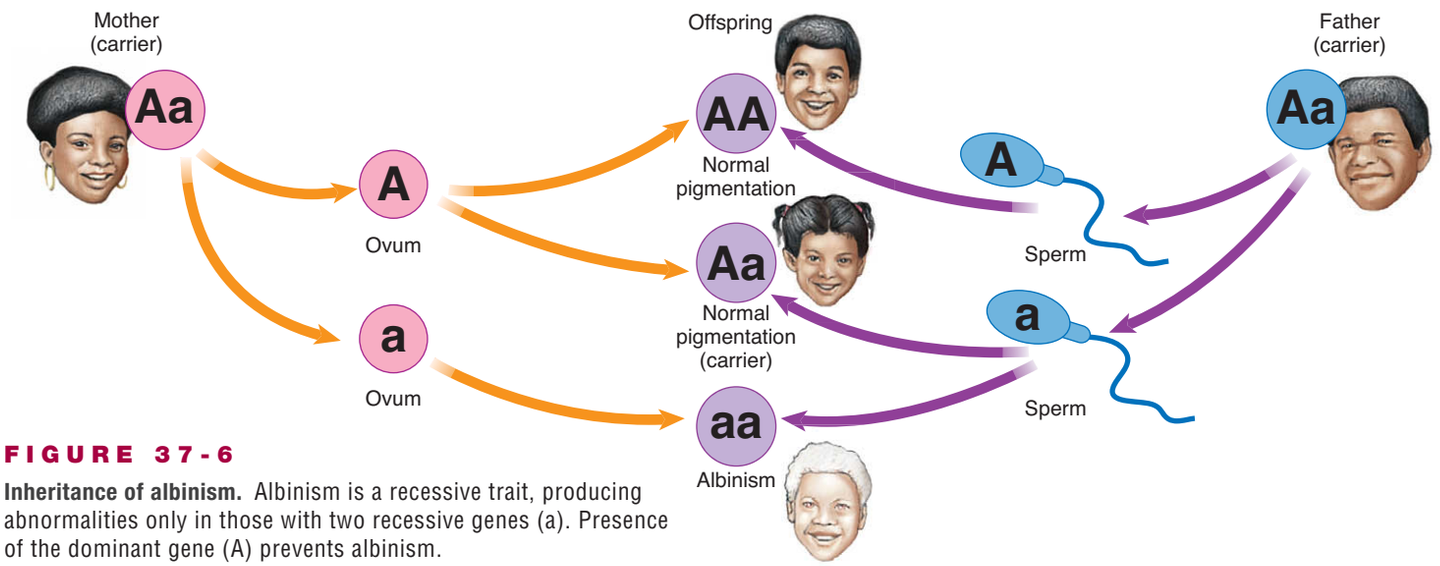


FIGURE 37-6

Inheritance of albinism. Albinism is a recessive trait, producing abnormalities only in those with two recessive genes (a). Presence of the dominant gene (A) prevents albinism.

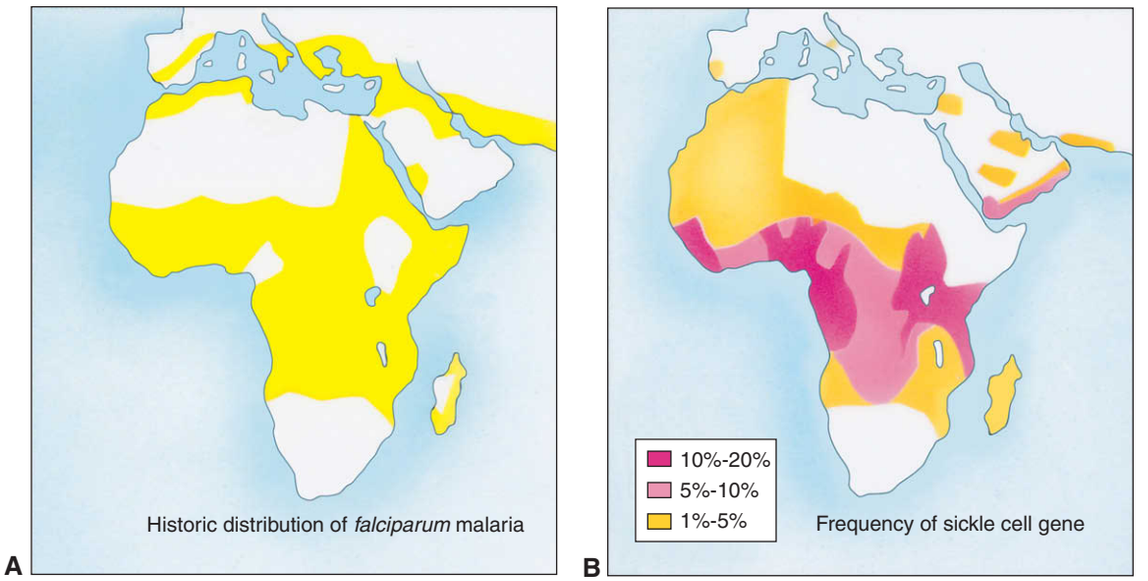


FIGURE 37-7

Relationship between the frequency of sickle cell trait and the distribution of malaria. A, The distribution of the most deadly form of malaria in Africa correlates closely with the frequency of occurrence of the sickle cell gene, **B.** The sickle cell trait provides resistance to malaria, and thus heterozygous individuals are more likely than homozygous individuals to survive and reproduce—spreading the abnormal gene further in the population.

malaria is still prevalent (Figure 37-7). Malaria is a sometimes fatal condition caused by blood cell parasites (*Plasmodium* species) and is characterized by fever, **anemia,** swollen spleen, and possible relapse months or years later. The unique distribution of *P. falciparum* malaria results from the fact that people without sickle cell trait more often die of this condition before producing offspring than those with the malaria-resistant sickle cell trait. Thus the "bad" sickle cell gene is more likely to be transmitted to the next generation than the "good" genes for normal hemoglobin.

The sickle cell/malaria relationship points to an important concept in medical genetics: "disease" genes often provide some biological advantage for a human population in certain circumstances. It is only when circumstances change that the gene is seen to do more harm than good. Genes for many other hereditary diseases (e.g., *thalassemia* and *Tay-Sachs disease*) are now known to impart protection against pathogenic conditions in heterozygous individuals.

Sex-Linked Traits

Recall from our earlier discussion that besides the 22 pairs of autosomes, there is one pair of sex chromosomes. Notice in the lower right portion of the karyotype in Figure 37-2 that the chromosomes of this pair do not have matching structures. The larger sex chromosome is called the X *chromosome*, and the smaller one is called the Y *chromosome*. The X chromosome is sometimes called the "female chromosome" because it includes genes that determine female sexual characteristics. If a person has only X chromosomes, she is genetically a female. The Y chromosome is often called the "male chromosome" because anyone possessing a Y chromosome is genetically a male. Thus all normal females have the sex chromosome combination XX, and all normal males have the combination XY (Box 37-2). Because men produce both X-bearing and Y-bearing sperm, any two parents can produce male or female children (Figure 37-8).

The large X chromosome contains many genes besides those needed for female sexual traits. Genes for producing certain clotting factors, photopigments in the retina of the eye, and many other proteins are also found on the X chromosome. The tiny Y chromosome, on the other hand, contains few genes other than those that determine male sexual characteristics. Thus both males and females need at least one normal X chromosome—otherwise genes for clotting factors and other essential proteins would be missing. Traits carried on sex chromosomes are called **sex-linked traits.** Some sex-linked traits are called *X-linked traits* because they are determined by genes in the large X chromosome. Other sex-linked traits are called *Y-linked traits* because they are determined by genes in the tiny Y chromosome.

Dominant X-linked traits appear in each person, as one would expect for any dominant trait. In females, recessive X-linked genes

Box 37-2 | FYI

Timing and Sex Determination

Research has shown that X-bearing sperm swim more slowly than Y-bearing sperm. An interesting hypothesis stems from this fact. If insemination occurs on the day of ovulation, Y-bearing sperm, being faster than X-bearing sperm, should reach the ovum first. Therefore a Y-bearing sperm would be more apt to fertilize the ovum. And because Y-bearing sperm produce males, there should be a greater probability of having a baby boy when insemination occurs on the day of ovulation. Statistical evidence supports this view.

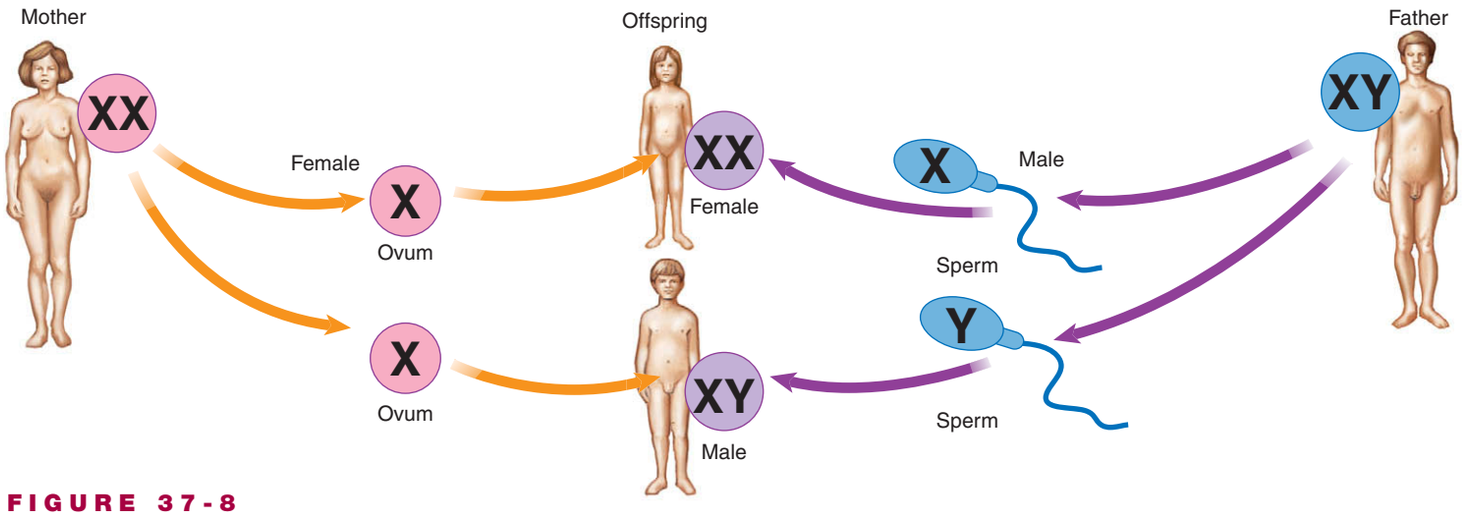


FIGURE 37-8

Sex determination. The presence of the Y chromosome specifies maleness. In the absence of a Y chromosome, an individual develops into a female.

are masked by dominant genes in the other X chromosome. Only females with two recessive X-linked genes can exhibit the recessive trait. Since males inherit only one X chromosome (from the mother), the presence of only one recessive X-linked gene is enough to produce the recessive trait. In short, in males there are no matching genes in the Y chromosome to mask recessive genes in the X chromosome. For this reason, X-linked recessive traits appear much more frequently in males than in females.

An example of a recessive X-linked condition is *red-green color blindness*, which involves a deficiency of normal photopigments in the retina (see Box 17-6, p. 533). In this condition, male children of a parent who carries the recessive abnormal gene on an X chromosome may be color blind (Figure 37-9). A female can inherit this form of color blindness only if her father is color blind *and* her mother is either color blind (homozygous recessive) or a color-blindness carrier (heterozygous). The X chromosome

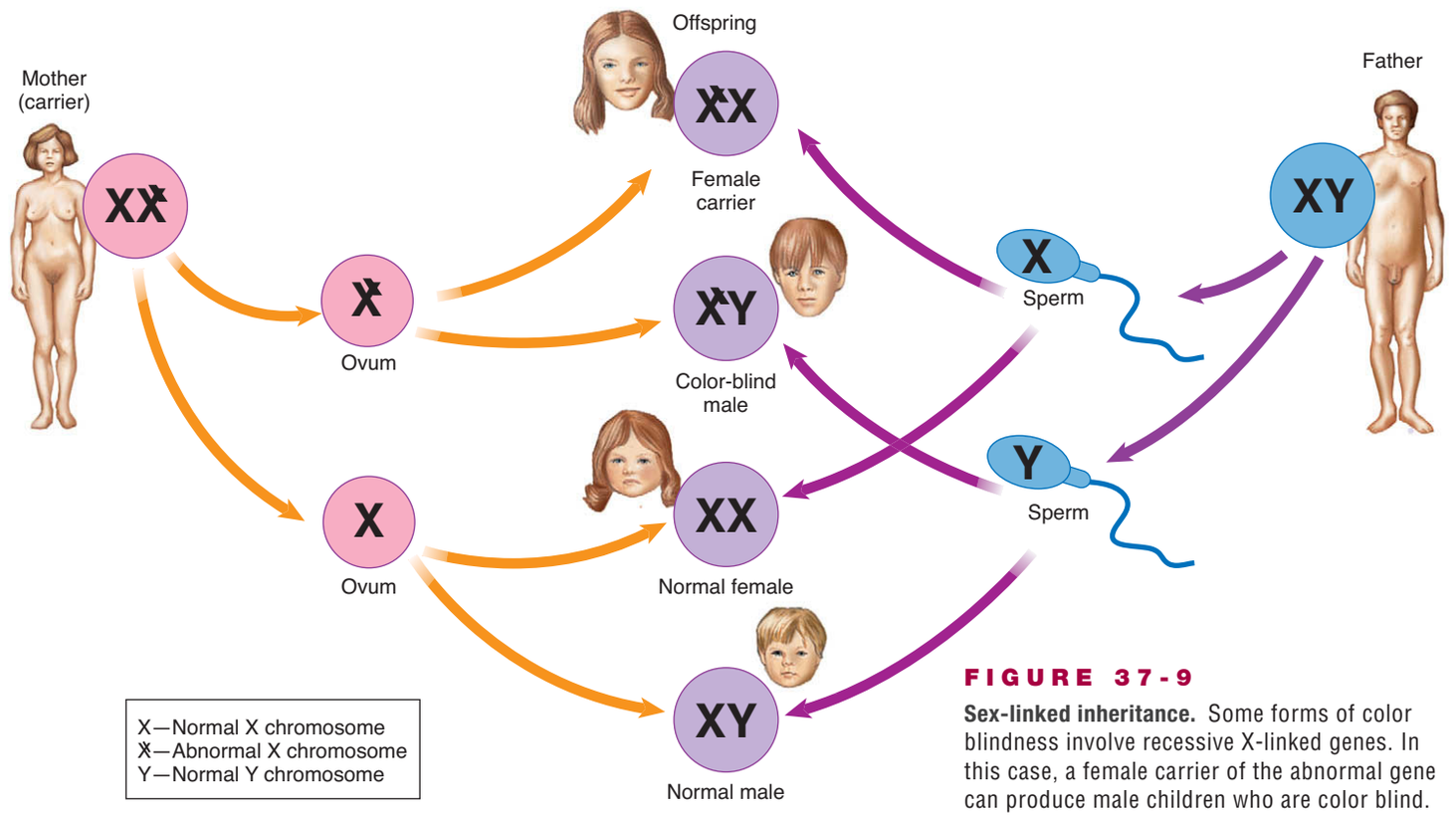


FIGURE 37-9

Sex-linked inheritance. Some forms of color blindness involve recessive X-linked genes. In this case, a female carrier of the abnormal gene can produce male children who are color blind.

has been studied in great detail, and general locations for genes causing dozens of distinct X-linked diseases have been identified (Figure 37-10).

Only one clinically significant Y-linked condition has been identified by geneticists. A missing part of q-arm of the Y chromosome may cause inheritable problems with spermatogenesis—and possible reduced fertility. Such a Y-linked condition may be passed from father to son.

Genetic Mutations

The term *mutation* simply means "change." A **genetic mutation** is a change in an individual's genetic code. Some mutations involve a change in the genetic code within a single gene, perhaps a slight rearrangement of the nucleotide sequence. A mutation called a **deletion** occurs when one or more nucleotide bases in a sequence are missing. An **insertion** mutation occurs when one or more nucleotides appear within the usual sequence of nucleotide bases in a gene. With either type of mutation, the cell cannot read the genetic code normally, and thus the encoded protein cannot be made in its usual form. Other mutations involve damage to a portion of a chromosome or a whole chromosome. For example, a portion of a chromosome may completely break away.

Mutations may occur spontaneously without the influence of factors outside the DNA itself. However, most genetic mutations are believed to be caused by **mutagens**—agents that cause changes in the genetic code by damaging DNA molecules. Genetic mutagens include chemicals, some forms of radiation, and even viruses.

If mutations occur in reproductive cells or their precursors, they may be inherited by offspring. Beneficial mutations allow organisms to adapt to their environments. Because such mutant genes benefit survival, they tend to spread throughout a population over the course of several generations.

Harmful mutations inhibit survival and therefore are not likely to spread widely through the population. Most harmful mutations kill the organism in which they occur or at least prevent successful reproduction—and so are never passed to offspring. Harmful mutations that are recessive, however, may persist at low frequencies in a population indefinitely because they do not cause problems for individuals who inherit just one of these genes. If a harmful dominant mutation is only mildly harmful, it may persist in a population over many generations.

Consider also the case of the mutations that cause sickle cell anemia, thalassemia, and Tay-Sachs disease—the heterozygous genotype produces a phenotype that resists a specific disease, and the homozygous genotype produces a phenotype characterized by emergence of a completely different disease condition.

| QUICK CHECK |

5. What is a dominant genetic trait? A recessive trait?
6. What is codominance?
7. How can a mutant gene benefit a human population?
8. What is X-linked inheritance?

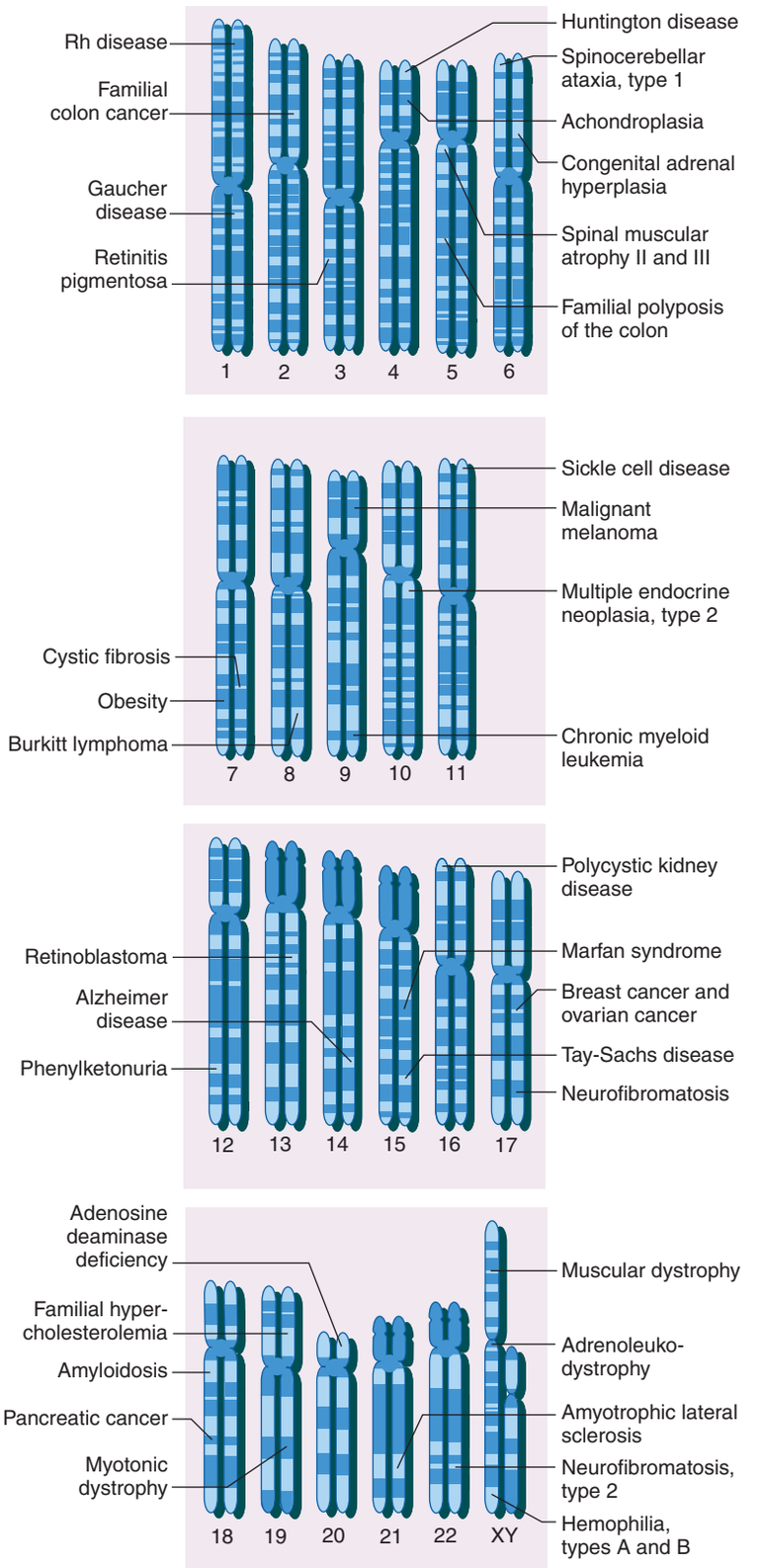


FIGURE 37-10

Disease map of chromosomes. This ideogram of each chromosome outlines just a few locations of the many genes whose mutations are responsible for genetic disorders.

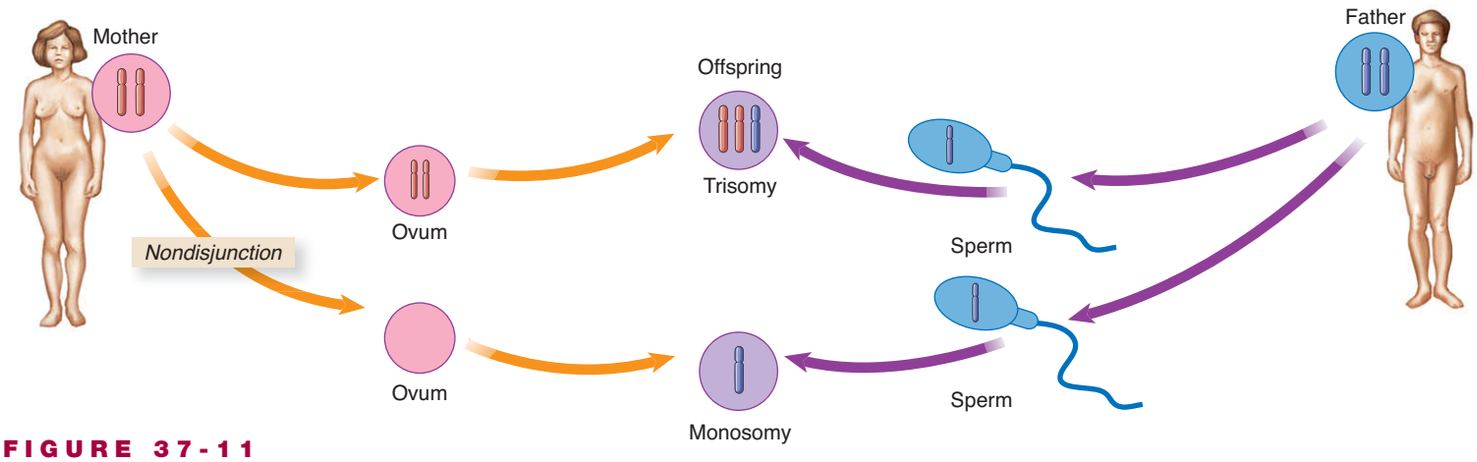


FIGURE 37-11

Effects of nondisjunction. Nondisjunction, failure of a chromosome pair to separate during gamete production, may result in trisomy or monosomy in the offspring.

MEDICAL GENETICS

Mechanisms of Genetic Diseases

As science writer Matt Ridley repeatedly and emphatically stated in his best-selling book *Genome: The Autobiography of a Species in 23 Chapters*, "GENES ARE NOT THERE TO CAUSE DISEASE." Although we often hear of new "disease genes" being discovered—and the pace is rapidly increasing—the function of these genes is not to cause disease any more than the function of an arm is to cause bone fractures. If you break an arm, a normal bone is broken and fails to serve its usual function. In genetic disorders, a normal gene or chromosome is broken (mutated) and fails to serve its usual function. Such a gene is sometimes called a "disease gene" because when it is broken, it is involved in the mechanism of a particular disease. Keep this simple—but often overlooked—principle in mind as you read the following paragraphs.

NUCLEAR INHERITANCE

Single-Gene Diseases

As we just stated, genetic diseases are diseases produced by an abnormality in the genetic code. Many genetic diseases are caused by individual mutant genes in the nuclear DNA that is passed from one generation to the next—making them **single-gene diseases.** In single-gene diseases, the mutant gene may make an abnormal product that causes disease or it may fail to make a product required for normal function. As discussed previously, some disease conditions result from the combined effects of inheritance and environmental factors. Because they are not solely caused by genetic mechanisms, such conditions are not genetic diseases in the usual sense of the word—they are instead said to involve a *genetic predisposition.*

Chromosomal Genetic Diseases

Some genetic diseases do not result from an abnormality in a single gene. Instead, these diseases result from chromosome breakage or from the abnormal presence or absence of entire chromosomes. For example, a condition called **trisomy** may occur in which there is a triplet of autosomes rather than a pair. Trisomy results from a mistake in meiosis called **nondisjunction** when a pair of chromosomes fails to separate. This produces a gamete with two autosomes that are "stuck together" instead of the usual one. When this abnormal gamete joins with a normal gamete to form a zygote, the zygote has a triplet of autosomes (Figure 37-11). Trisomy of any autosome pair is usually fatal. However, if trisomy occurs in autosome pair 13, 15, 18, 21, or 22, a person may survive for a time—but with profound developmental defects. **Monosomy,** the presence of only one autosome instead of a pair, may also result from conception involving a gamete produced by nondisjunction (see Figure 37-11). As with trisomy, monosomy may produce life-threatening abnormalities. Because most trisomic and monosomic individuals die before they can reproduce, these conditions are not usually passed from generation to generation. Trisomy and monosomy are congenital conditions that are sometimes referred to as **chromosomal genetic diseases** (Box 37-3).

Box 37-3 | FYI

Congenital Disorders

A congenital disorder is any pathological condition present at birth. As explained in Chapter 36, congenital disorders may have a genetic cause. For example, one form of a facial deformity known as cleft palate is an X-linked inherited condition (see Figure 37-9). However, some congenital disorders are not inherited. For example, fetal alcohol syndrome is a group of congenital deformities that result from exposing a developing fetus to alcohol consumed by the mother (see Box 21-3, p. 666). Thus not all congenital disorders are inherited disorders.

MITOCHONDRIAL INHERITANCE

Mitochondria are tiny, bacteria-like organelles present in every cell of the body (see Figure 3-11 on p. 77). The major exception, of course, is the red blood cell, which does not reproduce itself. As with a bacterium, each mitochondrion has its own circular DNA molecule, sometimes called **mitochondrial DNA (mDNA** or **mtDNA).** Figure 37-12 shows an ideogram of the structure of a mitochondrial chromosome.

Besides being a simple circle, mtDNA differs slightly from nuclear DNA in other ways. For example, a usual stop codon (UGA) instead codes for the amino acid tryptophan (see Figure 5-6 on p. 118).

Inheritance of mtDNA occurs only through one's mother because the few mitochondria that a sperm may contribute to the ovum during fertilization do not survive. Because mtDNA contains the only genetic code for several important enzymes, it has the potential for carrying mutations that produce disease. *Mitochondrial inheritance* is known to transmit genes for several degenerative nerve and muscle disorders. One such disease is *Leber hereditary optic neuropathy.* In this disease, young adults begin losing their eyesight as the optic nerve degenerates—resulting in total blindness by 30 years of age. Some medical researchers believe that at least some forms of several other diseases are associated with mtDNA mutations. These diseases include **Parkinson disease, Alzheimer disease (AD), diabetes mellitus (DM)** with deafness, and maternally inherited forms of deafness, myopathy, and cardiomyopathy.

| QUICK CHECK |

9. How are single-gene diseases different from chromosomal conditions?
10. What is *nondisjunction?* How can it cause trisomy?
11. What is mitochondrial inheritance?

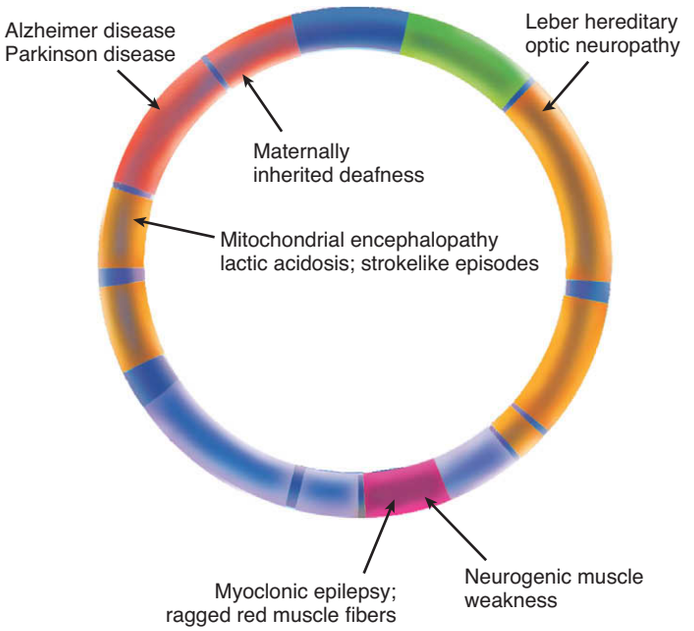


FIGURE 37-12

Map of mitochondrial DNA (mtDNA). Ideogram showing locations of some mtDNA genes associated with various diseases.

Single-Gene Diseases

There are many examples of single-gene diseases. Only a few of the many single-gene diseases are discussed here and summarized in Table 37-1.

Cystic fibrosis (CF), briefly mentioned in Chapter 4 (pp. 108–109), is caused by a recessive gene in chromosome 7 that codes for *CFTR (CF transmembrane conductance regulator).* CFTR normally regulates the transfer of sodium across cell membranes and serves as a chloride channel. When this gene has a deletion of a single codon, the abnormal version of CFTR causes impairment of chloride ion transport across cell membranes. Disruption of chloride transport causes exocrine cells to secrete thick mucus and concentrated sweat. The thickened mucus is especially troublesome in the gastrointestinal (GI) and respiratory tracts, where it can cause obstruction that leads to death. This condition is often treated by the continuous use of drugs and other therapies that relieve the symptoms. CF occurs most commonly among Caucasians. The mutation that causes CF is thought to protect carriers of the gene from potentially fatal cases of diarrhea, as in cholera and serious *Escherichia coli* infections.

Phenylketonuria (PKU) is caused by a recessive gene that fails to produce the enzyme *phenylalanine hydroxylase.* This enzyme is needed to convert the amino acid phenylalanine into another amino acid, tyrosine. Thus phenylalanine absorbed from ingested food accumulates in the body—resulting in the abnormal presence of phenylketone in the urine (hence the name phenylketonuria). A high concentration of phenylalanine destroys brain tissue; babies born with this condition are at risk of progressive mental retardation and, perhaps, death. Many PKU victims are identified at birth by state-mandated screening tests. After being identified, PKU victims are put on diets low in phenylalanine—thus avoiding a toxic accumulation of this amino acid. You may be familiar with the printed warning for people with phenylketonuria commonly seen on products that contain aspartame (NutraSweet) or other substances made from phenylalanine. The mutant PKU gene may have originated among the Celts in western Europe, where it offered protection against the toxic effects of molds growing on grains stored in cold, damp climates.

Tay-Sachs disease (TSD) is a recessive condition involving failure to make a subunit of an essential lipid-processing enzyme, hexosaminidase. Abnormal lipids accumulate in the brain tissue of Tay-Sachs victims, causing severe retardation and death by 4 years of age. There is currently no specific therapy for this condition.

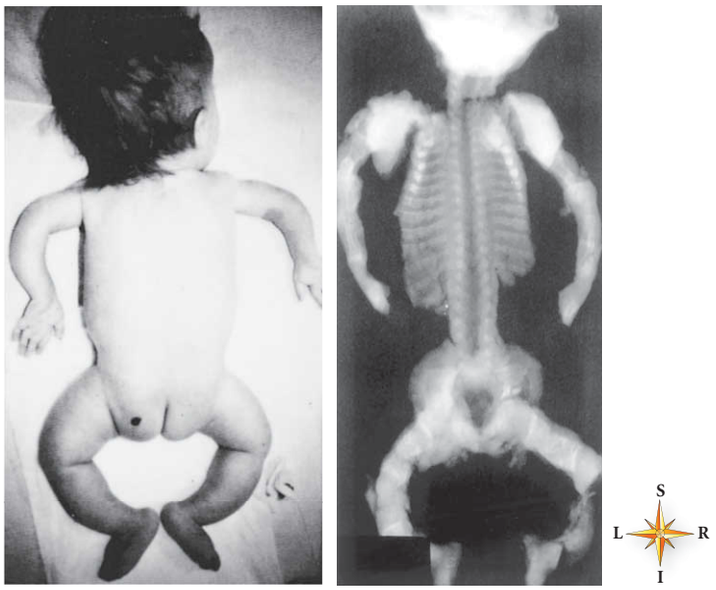
TSD is most prevalent among certain Jewish populations. Some epidemiologists believe that this ethnic distribution is related to the hypothesis that heterozygous carriers of the Tay-Sachs gene have a higher than normal resistance to tuberculosis (TB)—a potentially fatal disease that once killed millions in the crowded Jewish ghettos of many large cities. Residents of these TB-infested areas who carried the Tay-Sachs gene apparently survived longer—and reproduced more frequently—than noncarriers.

Tay-Sachs is also found in higher than average frequencies in French Canadians in southeastern Quebec and Cajun French families in southern Louisiana—probably due to the gene's presence in several founders of these family groups, rather than natural selection by the threat of TB.

Osteogenesis imperfecta is a dominant genetic disorder of connective tissues. Its name, which means "imperfect bone formation,"

TABLE 37-1 Examples of Genetic Conditions

CHROMOSOME LOCATION	DISEASE	DESCRIPTION
Single-Gene Inheritance (Nuclear DNA)		
Dominant		
1p, or 3p, or 7q, or 17q	Osteogenesis imperfecta	Group of connective tissue disorders is characterized by imperfect skeletal development that produces brittle bones
17q	Neurofibromatosis	Disorder is characterized by multiple, sometimes disfiguring benign tumors of the neuroglia that surround nerve fibers
1p, or 2p, or 19p	Hypercholesterolemia (familial)	High blood cholesterol may lead to atherosclerosis and other cardiovascular problems
4p	Huntington disease (HD)	Degenerative brain disorder is characterized by chorea (purposeless movements) progressing to severe dementia and death generally by age 55 years
4q or 16p	Polycystic kidney disease, autosomal dominant form (ADPKD)	Polycystic kidney disease or PKD (both dominant and recessive forms) is the most common single-gene genetic disorder; clusters of fluid-filled sacs occur in kidneys and other organs, causing kidney failure, hypertension, liver problems, and heart valve problems
Codominant		
11p	Sickle cell anemia Sickle cell trait	Blood disorder in which abnormal hemoglobin causes red blood cells (RBCs) to deform into a sickle shape; sickle cell anemia is the severe form, and sickle cell trait the milder form
11p or 16p	Thalassemia (a or b type)	Group of inherited hemoglobin disorders is characterized by production of hypochromic, abnormal RBCs
Recessive (Autosomal)		
7q	Cystic fibrosis (CF)	Condition is characterized by excessive secretion of thick mucus and concentrated sweat, often causing obstruction of gastrointestinal or respiratory ducts
15q	Tay-Sachs disease (TSD)	Fatal condition in which abnormal lipids accumulate in the brain and cause tissue damage leading to death by age 4 years
12q	Phenylketonuria (PKU)	Excess of phenylketones in the urine is caused by accumulation of phenylalanine in the tissues; it may cause brain injury and death if phenylalanine (amino acid) intake is not restricted
11q	Albinism (total)	Lack of the dark brown pigment *melanin* in the skin and eyes results in vision problems and susceptibility to sunburn and skin cancer
20q	Severe combined immune deficiency (SCID)	Failure of the lymphocytes to develop properly causes failure of the immune system's defense of the body; it is usually caused by adenosine deaminase (ADA) deficiency
6p	Polycystic kidney disease, autosomal recessive form (ARPKD)	See description listed for dominant form of PKD
Recessive (X Linked)		
23(X)q	Hemophilia	Group of blood clotting disorders is caused by failure to form clotting factors VIII, IX, or XI
23(X)p	Duchenne muscular dystrophy (DMD)	Muscle disorder is characterized by progressive atrophy of skeletal muscle without nerve involvement
23(X)q	Red-green color blindness	Inability to distinguish red and green light results from a deficiency of photopigments in the cone cells of the retina
23(X)q	Fragile X syndrome	Mental retardation results from breakage of X chromosome in males
23(X)p	Ocular albinism	Form of albinism in which the pigmented layers of the eyeball lack melanin results in hypersensitivity to light and other problems
23(X)q	Androgen insensitivity	Inherited insensitivity to androgens (steroid sex hormones associated with maleness) results in reduced effects of these hormones
23(X)q	Cleft palate, X-linked form (CPX)	One form of a congenital deformity in which the skull fails to develop properly, characterized by a gap in the palate (plate separating mouth from nasal cavity)
23(X)p	Retinitis pigmentosa (RP, X-1 form)	Condition causes blindness, characterized by clumps of melanin in retina of eyes
Single-Gene Inheritance (Mitochondrial DNA [mtDNA])		
mtDNA	Leber hereditary optic neuropathy	Optic nerve degeneration in young adults results in total blindness by age 30 years
mtDNA	Parkinson disease	Nervous disorder is characterized by involuntary trembling and muscle rigidity



A B

FIGURE 37-13

Osteogenesis imperfecta. A, The infantile form of this inherited disease is characterized by imperfect bone development that results in the appearance of this child: curved, brittle bones in the limbs and a thin, enlarged skull. **B,** This radiograph of a fetus with osteogenesis shows the many bone fractures that produce an accordion-like shortening of the limbs.

describes its chief characteristic. The bones of people with osteogenesis imperfecta do not have normal collagen and thus are often so brittle that the slightest trauma can result in serious fractures. There are different forms of the disease. In its most severe form, it results in fractures of the fetal skeleton in utero—often progressing to death shortly after birth. In a form seen in infancy, this disease is characterized by short, deformed limbs, a thin, enlarged skull, and easily fractured bones (Figure 37-13). In a less severe form, symptoms appear when a child begins to walk and become milder until after puberty—when the symptoms usually disappear.

Neurofibromatosis is a dominant genetic disorder discussed in Chapter 13 (p. 412). This disorder is characterized by multiple, sometimes disfiguring, skin spots and benign tumors of the glial cells that surround nerve fibers. Although usually inherited, it often arises from spontaneous mutations of DNA—which can then be inherited by offspring.

Other important inherited disorders include **Duchenne muscular dystrophy (DMD), hypercholesterolemia, sickle cell anemia, albinism,** certain forms of **hemophilia,** and **Huntington disease (HD).** These and other conditions are summarized in Table 37-1.

| A&P CONNECT |

Huntington disease (HD) is a dominant inherited disorder that has different forms, depending on whether it was inherited from the mother or the father. This occurs when temporary changes to the DNA expression are passed along to offspring. Such non-DNA inheritance is called **epigenetics.** Find out more about it in ***Epigenetics*** online at ***A&P Connect.***

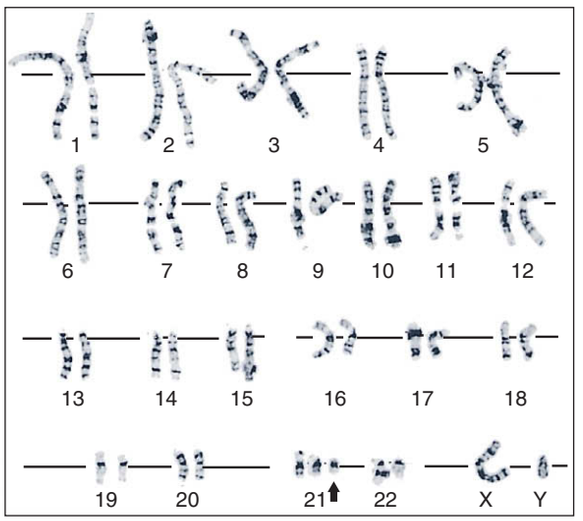
evolve

Chromosomal Diseases

As described earlier, some genetic disorders are not inherited in the usual sense but result from nondisjunction during formation of the gametes. As Figure 37-11 shows, nondisjunction results in gametes that produce either trisomy or monosomy in the cells of offspring. At least 10% of all human sperm and at least 25% of all mature oocytes have extra, missing, or broken chromosomes. Most zygotes and embryos with chromosomal abnormalities do not survive beyond a few days—and thus the mother is not even aware that conception occurred. Of the pregnancies that last long enough to become aware of, between 15% and 20% are spontaneously aborted (miscarried)—with about one half of those having chromosomal abnormalities.

A few of the major chromosomal disorders are summarized here and in Table 37-1.

The most well-known chromosomal disorder is *trisomy 21,* which produces a group of symptoms called **Down syndrome.** As Figure 37-14, A, shows, in this condition there is a triplet of chromosome 21 rather than the usual pair. In the general population, trisomy 21 occurs in only 1 of every 600 or so live births. After age 35 years, however, a mother's chances of producing a trisomic child increase dramatically—to as high as 1 in 80 births by age 40 years. One hypothesis that explains this phenomenon states that



A



B

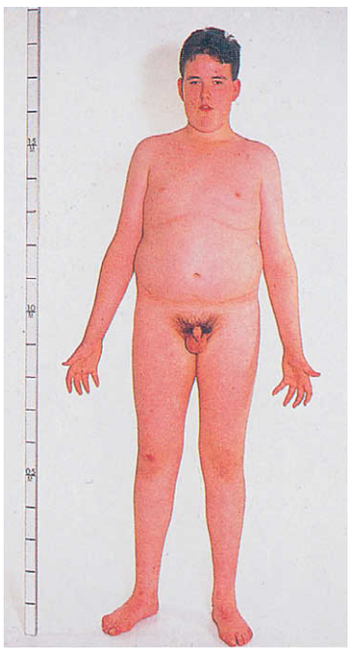
FIGURE 37-14

Down syndrome. A, Down syndrome is usually associated with trisomy of chromosome 21 (see Figure 37-11). **B,** A child with Down syndrome sitting on his father's knee. Notice the distinctive anatomical features: exaggerated epicanthal folds around the eyes, flattened nose, round face, and small hands with short fingers.

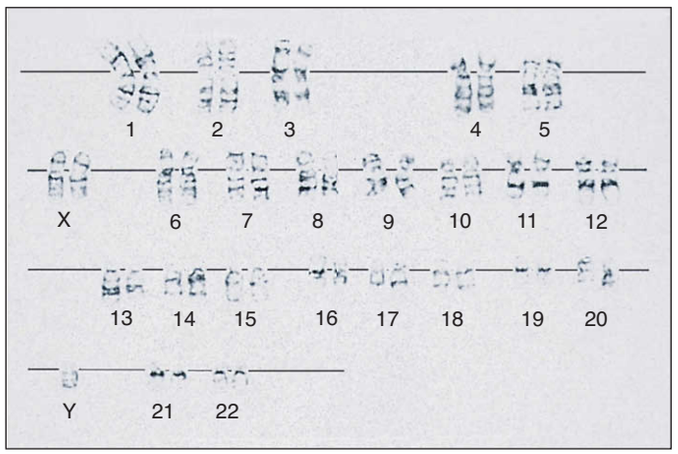
as a woman ages, her reproductive system becomes less likely to spontaneously abort abnormal blastocysts that have implanted in the endometrium. Thus nondisjunction may occur equally among young and middle-aged women, even though the number of live births may differ.

Down syndrome results from trisomy 21 and rarely from other genetic abnormalities (which can be inherited). This syndrome is characterized by mental retardation (ranging from mild to severe) and multiple defects that include distinctive facial appearance (Figure 37-14, *B*), enlarged tongue, short hands and feet with stubby digits, congenital heart disease, and susceptibility to acute leukemia. People with Down syndrome have a shorter than average life expectancy but can survive to old age.

Klinefelter syndrome is another genetic disorder resulting from nondisjunction of chromosomes. This disorder occurs in males with a Y chromosome and at least two X chromosomes, typically the XXY genotype. Characteristics of Klinefelter syndrome include long legs, enlarged breasts, low intelligence, small testes, sterility, and chronic pulmonary disease (Figure 37-15).



A



B

FIGURE 37-15

Klinefelter syndrome. **A,** This young man exhibits many of the characteristics of Klinefelter syndrome: small testes, some development of the breasts, sparse body hair, and long limbs. **B,** This syndrome results from the presence of two or more X chromosomes with a Y chromosome (genotypes XXY or XXXY, for example).

Turner syndrome, sometimes called *XO syndrome*, occurs in females with a single sex chromosome, X. As with the conditions described previously, the syndrome results from nondisjunction during gamete formation. Turner syndrome is characterized by failure of the ovaries and other sex organs to mature (causing sterility), cardiovascular defects, dwarfism or short stature, a webbed neck, and possible learning disorders (Figure 37-16). Symptoms of Turner syndrome can be reduced by hormone therapy using estrogens and growth hormone. Cardiovascular defects may be repaired surgically.

Genetic Basis of Cancer

Recall from Chapter 6 that some forms of cancer are thought to be caused, at least in part, by abnormal genes called **oncogenes.** Oncogenes are altered (mutated) forms of normal genes.

One hypothesis states that most normal cells contain such cancer-causing genes. However, it is uncertain how these genes become activated and produce cancer. Perhaps oncogenes can



A



B

FIGURE 37-16

Turner syndrome. **A,** This young woman exhibits many of the characteristics of Turner syndrome, including short stature, webbed neck, and sexual immaturity. **B,** As this karyotype shows, Turner syndrome results from monosomy of sex chromosomes (genotype XO).

transform a cell into a cancer cell only when certain environmental conditions occur. It has also been shown that viruses can transmit oncogenes to human cells.

Another hypothesis states that normal cells contain another class of genes, sometimes called **tumor suppressor genes.** According to this hypothesis, such genes regulate cell division so that it proceeds normally. When a tumor suppressor gene is nonfunctional because of a genetic mutation, it then allows cells to divide abnormally (or fail to die)—possibly producing cancer.

Yet another possible genetic basis for cancer relates to the genes that govern the cell's ability to repair damaged DNA. For example, a rare genetic disorder called **xeroderma pigmentosum** is characterized by the inability of skin cells to repair genetic damage caused by the ultraviolet (UV) radiation in sunlight. Individuals with this condition nearly always develop skin cancer when exposed to direct sunlight. In this condition, the genetic abnormality does not cause skin cancer directly but inhibits the cell's cancer-preventing mechanisms.

These three hypotheses regarding the genetic basis of cancer are not mutually exclusive. They are undoubtedly all important factors in the genesis of cancer. Cancer researchers are now working intensely to determine the exact role various genes play in the development of cancer. The more we understand the genetic basis of cancer, the more likely it is that we will find effective treatments—or even cures.

| QUICK CHECK |

12. How does avoidance of phenylalanine in the diet reduce the problems associated with phenylketonuria (PKU)?
13. Briefly describe the mechanism of Tay-Sachs disease.
14. What is trisomy 21?
15. How might the genetic code be involved in the development of cancer?

PREVENTION AND TREATMENT OF GENETIC DISEASES

Genetic Counseling

The term *genetic counseling* refers to professional consultations with families regarding genetic diseases. Trained genetic counselors may help a family determine the risk of producing children with genetic diseases.

Genetic counselors may also help evaluate whether any offspring already have a genetic disorder and offer advice on treatment or care. A growing list of tools is available to genetic counselors, some of which are described in the following section.

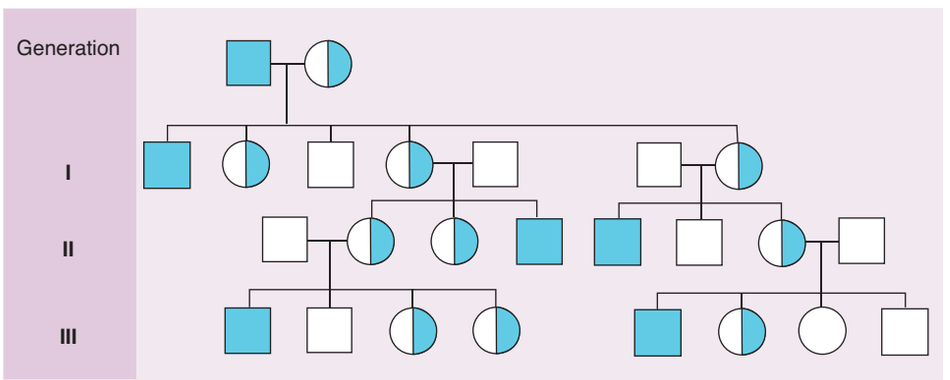
PEDIGREE

A **pedigree** is a chart that illustrates genetic relationships in a family over several generations (Figure 37-17). Using medical records and family histories, genetic counselors assemble the chart beginning with the client and moving backward through as many generations as are known. Squares represent males; circles represent females. Fully shaded symbols represent affected individuals, and unshaded symbols represent normal individuals. Partially shaded symbols represent carriers of a recessive trait. A horizontal line between symbols designates a sexual relationship that produced offspring.

The pedigree is useful in determining the possibility of producing offspring with certain genetic disorders. It also may tell a person whether he or she might have a genetic disorder that appears late in life, such as Huntington disease. In either case, a family can prepare emotionally, financially, and medically before a crisis occurs.

PUNNETT SQUARE

The **Punnett square,** named after the English geneticist Reginald Punnett, is a grid used to determine the mathematical *probability*



A



B

FIGURE 37-17

Pedigree. A, Pedigrees chart the genetic history of family lines. Squares represent males, and circles represent females. Fully shaded symbols indicate affected individuals, partly shaded symbols indicate carriers, and unshaded symbols indicate unaffected noncarriers. Roman numerals indicate the order of generations. This pedigree reveals the presence of an X-linked recessive trait. **B,** This huge pedigree compiled by Dr. Nancy Wexler of Columbia University and the Hereditary Disease Foundation traces Huntington disease (HD) over several generations of a large family in Venezuela. Dr. Wexler and other researchers collaborated in using information from this pedigree, along with techniques of molecular biology, to find the gene responsible for this disease and develop a test to detect the presence of the gene before the disease becomes apparent. Dr. Wexler became interested in this disease after her mother's death from HD.

of inheriting genetic traits. As Figure 37-18, *A*, shows, genes in the mother's gametes are represented along the horizontal axis of the grid and genes in the father's gametes along the vertical axis. The ratio of different gene combinations in the offspring predicts their probability of occurrence in the next generation. Thus offspring produced by two carriers of PKU (a recessive disorder) have a one in four (25%) chance of inheriting this recessive condition (see Figure 37-18, *A*).

The same grid shows that there is a two in four (50%) chance that a child produced will be a PKU carrier. Figure 37-18, *B*, however, shows that offspring of a carrier and a noncarrier cannot inherit PKU. What is the chance of an individual offspring being a PKU carrier in this case? The grid in Figure 37-18, *C*, shows the probability of producing an affected offspring when a PKU victim and a PKU carrier have children. Figure 37-18, *D*, shows the genetic probability when a PKU victim and a noncarrier produce children.

KARYOTYPE

Disorders that involve trisomy (extra chromosomes), monosomy (missing chromosomes), and broken chromosomes can be detected after a **karyotype** is produced.

The first step in producing a karyotype is getting a sample of cells from the individual to be tested. This can be done by scraping

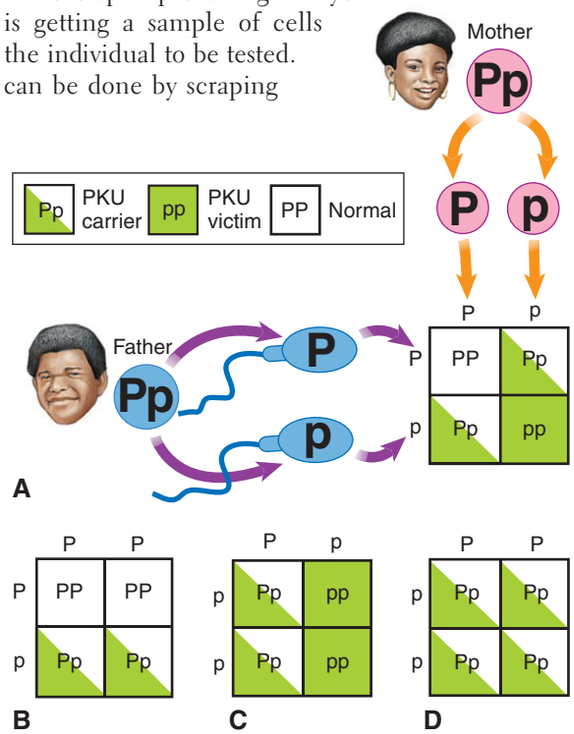


FIGURE 37-18

Punnett square. The Punnett square is a grid used to determine relative probabilities of producing offspring with specific gene combinations. Phenylketonuria (PKU) is a recessive disorder caused by the gene *p*. *P* is the normal gene. **A,** Possible results of cross between two PKU carriers. Because one in four of the offspring represented in the grid have PKU, a genetic counselor would predict a 25% chance that this couple will produce a PKU baby at each birth. **B,** Cross between a PKU carrier and a normal noncarrier. **C,** Cross between a PKU victim and a PKU carrier. **D,** Cross between a PKU victim and a normal noncarrier.

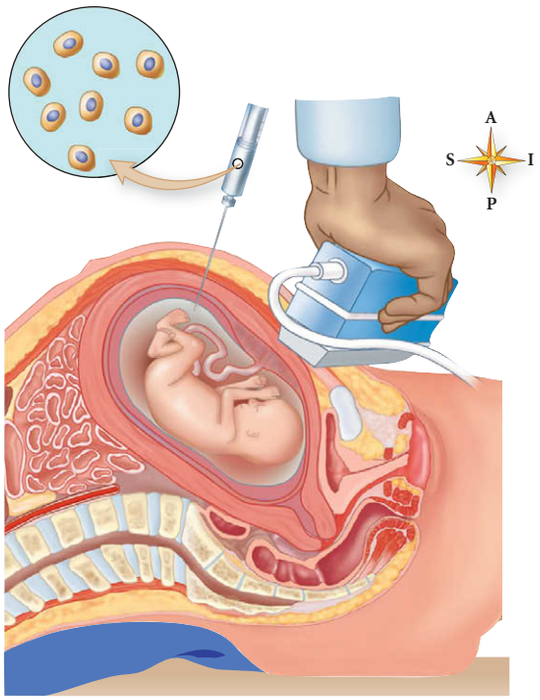


FIGURE 37-19

Amniocentesis. In amniocentesis, a syringe is used to collect amniotic fluid. Ultrasound imaging is used to guide the tip of the syringe needle to prevent damage to the placenta and fetus. Fetal cells in the collected amniotic fluid can then be chemically tested or used to produce a karyotype of the developing baby.

cells from the lining of the cheek or from a blood sample containing white blood cells (WBCs). Fetal tissue can be collected by **amniocentesis,** a procedure in which fetal cells floating in the amniotic fluid are collected with a syringe (Figure 37-19). **Chorionic villus sampling (CVS)** is a newer procedure in which cells from chorionic villi that surround a young embryo (see Chapter 36, p. 1105) are collected through the opening of the cervix.

Collected cells are grown in a special culture medium and allowed to reproduce. Cells in metaphase (when the chromosomes are most distinct) are stained and photographed using a microscope. The chromosomes are cut out of the photo and pasted on a chart in pairs according to size, as in Figures 37-2 and 37-15, *B*. More advanced techniques use digital imaging and computers to automatically generate a karyotype.

Genetic counselors then examine the karyotype, looking for chromosome abnormalities. What chromosome abnormality is visible in Figure 37-15, *B*? Is this a male or female karyotype?

| A&P CONNECT |

Many tools for discovering the secrets of a particular sample of DNA are available, such as *DNA fingerprinting* and **gene chips.** To see how these techniques work, check out ***DNA Analysis*** online at ***A&P Connect.***

| QUICK CHECK |

16. What is genetic counseling?
17. How are pedigrees used by genetic counselors?
18. How is a Punnett square used to predict mathematical probabilities of inheriting specific genes?
19. How is a karyotype prepared? What is its purpose?

Treating Genetic Diseases

Until fairly recently, the only hope of treating any genetic disease was to treat the symptoms. In some diseases, such as PKU, this works well. If PKU victims simply avoid large amounts of phenylalanine in their diets, especially during critical stages of development, severe complications can be avoided. In Klinefelter syndrome and Turner syndrome, hormone therapy and surgery can alleviate some symptoms. However, there are no effective treatments for the majority of genetic disorders. Fortunately, medical science now offers us some hope of treating genetic disorders through **gene therapy.**

In a therapy sometimes called **gene replacement,** genes that specify production of abnormal, disease-causing proteins are replaced by normal or "therapeutic" genes. To get the therapeutic genes to cells that need them, researchers are using genetically altered viruses as carriers. Recall that viruses are easily capable of inserting new genes into the human genome. If the therapeutic genes behave as expected, a cure may result. Thus the goal of gene replacement therapy is to genetically alter existing body cells in the hope of eliminating the cause of a genetic disease. Although called "gene replacement," this therapy does not actually replace the defective genes—it instead inserts normal genes so that normal proteins can "replace" abnormal or missing proteins in the body's metabolic pathways.

In a therapy called **gene augmentation,** normal genes are introduced with the hope that they will augment (add to) the production of the needed protein. In one form of gene augmentation, virus-altered cells are injected into the blood or implanted under the skin of a patient to produce increased amounts of the missing protein. Some researchers have proposed grafting synthetic skin containing cells with therapeutic genes. Another approach is to use bacterial DNA rings called **plasmids** that have been altered by recombinant DNA techniques to carry the therapeutic gene or genes. Another approach uses the **human engineered chromosome (HEC).** In the HEC strategy, a set of therapeutic genes is incorporated into a separate strand of DNA that is inserted into a cell's nucleus, thus acting like an extra, or forty-seventh, chromosome. Gene augmentation attempts to add genetically altered cells to the body, rather than change existing body cells, as in gene replacement therapy.

| A&P CONNECT |

Can gene therapy be used to extend the human life span? Check out ***Genes and Longevity*** online at ***A&P Connect.***



There have been tragic setbacks in some clinical trials of gene therapies with the result that there are not yet any approved gene therapies available. Despite setbacks and concerns, there are currently hundreds of ongoing gene therapy trials for diverse genetic disorders, cancer, and even aging. Thousands of laboratory experiments in anticipation of human trials are also currently under way. Hurdles that must be overcome before we will see widespread success of gene therapies include our lack of detailed knowledge regarding many of the "disease genes" and how best to effectively treat multiple-genes diseases—not to mention the high costs and risks involved with these therapies. Currently, gene therapy is experimental—there are no approved treatments available to the general public. It is too early to say for sure, but there may soon come a time when many genetic diseases are routinely treated—or even cured—with gene therapy.

| A&P CONNECT |

Experimentation with gene therapy in humans began as far back as 1990. Learn more about the early efforts at gene therapy in ***Using Gene Therapy*** online at ***A&P Connect.***



RNA interference (RNAi) may also become a weapon against genetic disorders in an approach called **RNAi therapy.** Recall from Box 5-2 (p. 120) that RNAi is a method of silencing particular genes. When harnessed in the laboratory, RNAi can turn off one gene at a time—greatly increasing the chances of figuring out which protein is encoded by that gene and what the function of that protein is.

The possibilities of RNAi therapy are very exciting. Work is already under way to find an effective means of using RNAi for creating antiviral creams containing short interfering RNA (siRNA) to protect against HIV and other viruses. Some researchers are using RNAi to knock out genes that permit permanent tissue damage during heart attacks, kidney failure, and stroke. In one proposal, RNAi would be used to silence the abnormal huntingtin gene that causes Huntington disease (HD). In animal studies, RNAi successfully blocked a gene causing high blood cholesterol—without any apparent side effects. Researchers are also attempting to harness the power of RNAi to treat cancer and many types of infection.

However, developing a large set of RNAi therapies may be thwarted by the possibility that they may also silence genes needed for normal function or trigger unwanted side effects in the body's immune defenses.

| QUICK CHECK |

20. How are most genetic disorders treated today?
21. How does gene replacement therapy work?

the BIG picture

Genetics, Heredity, and the Whole Body

The study of human genetics and heredity provides an amazingly clear view of the "big picture" of the structure and function of the human body. In fact, the genetic view extends from the molecular level all the way to the context of the whole human species and beyond.

At the molecular level, the genetic perspective reveals the importance of nucleic acids—especially DNA. DNA molecules serve as tiny data storage devices that contain *all* the information needed to manufacture the molecules needed to build and maintain the human body. Each cell, tissue, organ, and system in the body is built of, and directed by, molecules that have been synthesized with recipes contained in the genes of each of our DNA molecules.

At the molecular level, we see that DNA in concert with various forms of RNA directs the synthesis of structural and functional proteins. Some of the functional proteins, in turn, trigger and direct the synthesis of all other biomolecules that form and regulate the body—lipids, carbohydrates, and so on.

This vast collection of different kinds of molecules also includes the enzymes and other molecules needed to gather and assimilate chemicals from the external environment outside the body. These external chemicals include water, oxygen, vitamins, minerals, sugars, starches, amino acids, fats, and other nutrients. Some of the molecules that ultimately owe their existence in the body to DNA also include those that help us rid the body of wastes such as urea, carbon dioxide, and bile.

If DNA directs all the chemical activity of the body, then it certainly directs cellular metabolism. And, of course, cellular metabolism is the foundation of the function of each tissue, organ, and system in the body. Our study of medical genetics has shown us that even one mistake in one codon of a gene can upset the chemistry of the body enough to shut down an entire system—and thus threaten the survival of the entire body.

LANGUAGE OF SCIENCE *(continued from p. 1131)*

genetics
(jeh-NET-iks)
[*gen-* **produce,** *-ic* **relating to**]

genome
(JEE-nohm)
[*gen-* **produce (gene),** *-ome* **entire collection**]

genomics
(jeh-NO-miks)
[*gen-* **produce (gene),** *-om-* **entire collection,** *-ic* **relating to**]

genotype
(JEN-oh-type)
[*gen-* **produce (gene),** *-type* **kind**]

haploid
(HAP-loyd)
[*haplo-* **single,** *-oid* **of or like**]

heterozygous
(het-er-oh-ZYE-gus)
[*hetero-* **different,** *-zygo-* **union or yoke,** *-ous* **characterized by**]

histone
(HISS-tohn)
[*histo-* **tissue,** *-one* **unit**]

homozygous
(hoh-moh-ZYE-gus)
[*homo-* **same,** *-zygo-* **union or yoke,** *-ous* **characterized by**]

Human Genome Project

ideogram
(ID-ee-oh-gram)
[*ide-* **idea,** *-gram* **drawing**]

insertion

karyotype
(KAIR-ee-oh-type)
[*karyo-* **nucleus,** *-type* **kind**]

meiosis
(my-OH-sis)
[*meiosis* **becoming smaller**]

mitochondrial DNA (mDNA, mtDNA)
(my-toh-KON-dree-al D N A)
[*mito-* **thread,** *-chondrion-* **granule,** *-al* **relating to)**

monogenic
(mon-oh-JEN-ik)
[*mono-* **single,** *-gen-* **produce (gene),** *-ic* **relating to**]

monosomy
(MON-oh-so-mee)
[*mono-* **single,** *-som-* **body (chromosome),** *-y* **state**]

mutagen
(MYOO-tah-jen)
[*muta-* **change,** *-gen* **produce**]

nucleosome
(NOO-klee-oh-sohm)
[*nucleo-* **kernel (nucleus),** *-som-* **body**]

p-arm
[*p* **petite (small)**]

pedigree
(PED-i-gree)
[*pied de grue* **crane's foot pattern**]

phenotype
(FEE-no-type)
[*pheno-* **appear,** *-type* **kind**]

polygenic
(pahl-ee-JEN-ik)
[*poly-* **many,** *-gen-* **produce,** *-ic* **relating to**]

principle of independent assortment

principle of segregation

proteome
(PRO-tee-ohm)
[*prote-* **protein,** *-ome* **entire collection**]

proteomics
(proh-tee-OH-miks)
[*prote-* **first rank (protein),** *-om-* **entire collection,** *-ic* **relating to**]

pseudogene
(SOOD-oh-jeen)
[*pseudo-* **false,** *gene* **produce**]

Punnett square
(PUN-it)
[*Reginald C. Punnett* **English geneticist**]

q-arm
[*q* **follows p in Roman alphabet**]

recessive gene
[*recess-* **retreat,** *-ive* **relating to,** *gene* **produce**]

sex chromosome
(KROH-moh-sohm)
[*chrom-* **color,** *-som-* **body**]

sex-linked trait

transcriptome
(tran-SKRIPT-ome)
[*trans-* **across,** *-script-* **written document,** *-ome* **entire collection**]

transcriptomics
(tran-skript-OHM-iks)
[*trans-* **across,** *-script-* **written document,** *-om-* **entire collection,** *-ic* **relating to**]

trisomy
(TRY-so-mee)
[*tri-* **three,** *-som-* **body (chromosome),** *-y* **state**]

LANGUAGE OF MEDICINE *(continued from p. 1149)*

albinism
(AL-bi-niz-em)
[*alb-* **white**, *-in-* **characterized by**, *-ism* **state**]

Alzheimer disease (AD)
(AHLZ-hye-mer)
[*Alois Alzheimer* **German neurologist**]

amniocentesis
(AM-nee-oh-sen-TEE-sis)
[*amnio-* **birth membrane**, *-centesis* **a pricking**]

anemia
(ah-NEE-mee-ah)
[*an-* **without**, *-emia* **blood condition**]

chorionic villus sampling (CVS)
(koh-ree-ON-ik VIL-lus)
[*chorion-* **skin**, *-ic* **relating to**, *villus* **shaggy hair**]

chromosomal genetic disease
(kroh-moh-SOH-mal jeh-NET-ik)
[*chrom-* **color**, *-soma-* **body**, *-al* **relating to**, *gen-* **produce**, *-ic* **relating to**]

cystic fibrosis (CF)
(SIS-tik fye-BROH-sis)
[*cyst-* **sac**, *-ic* **relating to** *fibr-* **fiber**, *-osis* **condition**]

diabetes mellitus (DM)
(dye-ah-BEE-teez MELL-i-tus)
[*diabetes* **passer through or siphon**, *mellitus* **honey-sweet**]

DNA fingerprinting

Down syndrome
(SIN-drohm)
[*John L. Down* **English physician**, *syn-* **together**, *-drome* **running or (race)course**

Duchenne muscular dystrophy (DMD)
(doo-SHEN MUSS-kyoo-lar DISS-troh-fee)
[*Guillaume B. A. Duchenne de Boulogne* **French neurologist**, *mus-* **mouse**, *-cul-* **little**, *-ar* **relating to**, *dys-* **bad**, *-troph-* **nourishment**, *-y* **state**]

gene augmentation
(jeen awg-men-TAY-shun)
[*gen-* **produce or generate**]

gene chip
(jeen chip)
[*gen-* **produce or generate**]

gene replacement
[*gen-* **produce or generate**]

gene therapy
(jeen THER-ah-pee)
[*gen-* **produce or generate**]

hemophilia
(hee-moh-FIL-ee-ah)
[*hemo-* **blood**, *-phil-* **love**, *-ia* **condition**]

human engineered chromosome (HEC)
[*chrom-* **color**, *-som-* **body**]

Huntington disease (HD)
(HUNT-ing-ton)
[*George S. Huntington* **American physician**]

hypercholesterolemia
(hye-per-koh-les-ter-ohl-EE-mee-ah)
[*hyper-* **excessive**, *-chole-* **bile**, *-stero-* **solid**, *-ol-* **alcohol**, *-emia* **blood condition**]

Klinefelter syndrome
(KLINE-fel-ter SIN-drohm)
[*Harry F. Klinefelter* **American physician**, *syn-* **together**, *-drome* **running or (race)course**]

malaria
(mah-LAIR-ee-ah)
[*mal-* **bad**, *-ar-* **air**, *-ia* **condition**]

neurofibromatosis
(noo-roh-fye-broh-mah-TOH-sis)
[*neuro-* **nerve**, *-fibr-* **fiber**, *-oma-* **tumor**, *-t-* **combining form**, *-osis* **condition**]

nondisjunction
(non-dis-JUNK-shun)
[*non-* **not**, *-dis-* **split in two**, *-junction* **joint**]

oncogene
(ON-koh-jeen)
[*onco-* **swelling or mass (cancer)**, *-gen-* **produce or generate**]

osteogenesis imperfecta
(os-tee-oh-JEN-eh-sis im-per-FEK-tah)
[*osteo-* **bone**, *-gen-* **produce**, *-esis* **process**, *imperfecta* **not perfect**]

Parkinson disease
(PARK-in-son)
[*James Parkinson* **English physician**]

phenylketonuria (PKU)
(fen-il-kee-toh-NOO-ree-ah)
[*phen-* **shining (phenol)**, *-yl-* **chemical**, *-keton-* **acetone**, *-ur-* **urine**, *-ia* **condition**]

plasmid
(PLAS-mid)
[*plasmid* **something formed**]

RNAi therapy
[*RNA* **ribonucleic acid**, *i* **interference**, *therapy* **treatment**]

sickle cell anemia
(SIK-ul sell ah-NEE-mee-ah)
[*sickle* **crescent**, *cell* **storeroom**, *an* **without**, *-emia* **blood condition**]

single-gene disease
[*gen-* **produce or generate**]

Tay-Sachs disease (TSD)
(TAY-saks)
[*Warren Tay* **English ophthalmologist**, *Bernard Sachs* **American neurologist**]

tumor suppressor gene
[*tumor* **swelling**, *suppress-* **press down**, *-or* **agent**, *gen-* **produce or generate**]

Turner syndrome
(TUR-ner SIN-drohm)
[*Harry H. Turner* **American endocrinologist**, *syn-* **together**, *-drome* **running or (race)course**]

xeroderma pigmentosum
(zeer-oh-DER-mah pig-men-TOH-sum)
[*xero-* **dry**, *-derma* **skin**, *pigment-* **paint**, *-osum* **characterized by**]

CASE study

Carlos and Maria were ecstatic to have two healthy babies. Within the first hour, the babies had been cleaned, measured, and their heels pricked for blood samples. These initial blood tests were to assess for PKU (phenylketonuria), thyroid hormone levels, cystic fibrosis, and several other metabolic disorders. To their surprise, their new daughter tested positive for PKU. Neither Carlos nor Maria had PKU.

1. What are the chances that their son will have PKU as well?
   a. 25%
   b. 50%
   c. 75%
   d. 0%

Thankfully, their son tested negative for PKU. But, as they were discussing genetic testing, Maria remembered that her father had been color blind. She wondered whether that meant her son would also be color blind.

2. They couldn't tell yet, but what were the chances that Maria and Carlos' son would be color blind?
   a. 25%
   b. 50%
   c. 75%
   d. 0%

Carlos and Maria were so happy with their new twins. They were thinking about trying to have more children…maybe in a few years.

3. Having had one boy and one girl, what are Carlos and Maria's chances of having another boy?
   a. Depends on the timing of the fertilization
   b. 25%
   c. 50%
   d. 75%

HINT *To solve a case study, you may have to refer to the glossary or index, other chapters in this textbook,* ***A&P Connect,*** *and other resources.*

CAREER choices

Genetic Counselor

Genetic counseling is the process of helping people understand and adapt to the medical, psychological, and familial implications of genetic contributions to disease. I work in a private, not-for-profit medical facility. I see prenatal, pediatric, neurology, and cancer patients and their families. For specific details see information from our national support organization (National Society of Genetic Counselors [NSGC]) at nsgc.org).

I have always had an interest in the medical professions. However, genetic counseling was first introduced to me in an "Ethics of Healthcare" course in my undergraduate studies. After this course sparked my interest, I used job-shadowing opportunities to learn more about what is involved in the field. As I learned more about it, I was convinced that genetic counseling was the profession that I wanted to pursue. I now hold a Master of Science in Human Genetics and Genetic Counseling.

The current trends in my field include positions in research and nontraditional areas, such as positions with insurance companies and clinical laboratories. We are learning about genetic contributions to many multifactorial conditions like heart disease, diabetes, high blood pressure. The area of *pharmacogenetics*—the study of inherited responses to drugs—is rapidly expanding. Counselors can develop specialties in many areas, including prenatal, pediatric, oncology, and neurology clinics.

The variety of patients that I see, the challenges of each case, and the fact that I'm always learning are the greatest rewards of my job. I love working with families through difficult situations by helping to provide risk assessments or to establish a diagnosis, and helping them process what this means for themselves and their family. At times, I spend many hours working with one family, which is different from most other medical fields. We focus on not only the presenting problem but also the implications for the family as a whole.

Understanding anatomy and physiology is helpful when working with a clinical geneticist to establish a diagnosis. Genetic conditions are often complex, multisystem disorders, and understanding anatomy and physiology is vital. I recommend using repetition, flash cards, and hands-on laboratory activities for studying anatomy and physiology.

For other careers related to genetics, see ashg.org/education.



Christina Zaleski, MS, CGC

CHAPTER SUMMARY

To download an MP3 version of the chapter summary for use with your iPod or portable media player, access the ***Audio Chapter Summaries*** *online at evolve.elsevier.com.*

HINT

Scan this summary after reading the chapter to help you reinforce the key concepts. Later, use the summary as a quick review before your class or before a test.

THE SCIENCE OF GENETICS

A. Genetics—scientific study of inheritance; developed to explain how normal biological characteristics are inherited
B. Directly inherited diseases are often called *hereditary diseases*

CHROMOSOMES AND GENES

A. Mechanism of gene function
   1. Genetic code transmitted by way of genes, which are segments of DNA
   2. DNA (deoxyribonucleic acid) (Figure 37-1)
      a. Chromosome—compact form of DNA that exists only during cell division
      b. Chromatin—strand form of DNA made up of subunits called *nucleosomes*, which are like small spools of DNA wound around proteins called *histones*
   3. Each gene is a sequence of nucleotide bases in the DNA molecule, which the cell transcribes to an RNA molecule
   4. Each mRNA molecule associates with a ribosome, which translates the code to form one or more specific polypeptide molecules
   5. Genes determine the structure and function of the human body by producing a set of specific regulatory RNA and protein molecules—along with specific structural proteins
B. The human genome (Figure 37-2)
   1. Genome—entire set of human chromosomes (46 in nucleus of each cell, 1 mitochondrial chromosome)
      a. Map of the entire human genome (nearly all nucleotides in sequence) was completed in 2003
      b. Contains about 20,000 to 25,000 genes and large amounts of noncoding DNA
         (1) Genes can encode proteins or other functional products such as tRNA, rRNA, ribozymes
         (2) DNA sequences called *exons* join to form a gene; the same exons may be part of different genes
         (3) Pseudogenes—bits of formerly functional genes that make up part of noncoding "junk" DNA
      c. Less than 2% of genome codes for proteins
         (1) Some DNA codes for regulatory RNAs
         (2) Much of the DNA ("junk DNA") includes pseudogenes that are remnants of functional genes
   2. Genomics—analysis of the sequence contained in the genome
   3. Transcriptomics—analysis of the mRNA codes actually transcribed from genes in the genome
   4. Proteomics—analysis of the entire group of proteins encoded by the genome and transcriptome, a group of proteins called the *human proteome*
   5. Genomic information can be expressed in various ways
      a. Ideogram—cartoon of a chromosome showing the centromere as a constriction and the short segment (p-arm) and long segment (q-arm)
      b. Genes are often represented as their actual sequence of nucleotide bases expressed by the letters a, c, g, and t
C. Distribution of chromosomes to offspring
   1. Meiosis (see Figure 36-1)
      a. Produces gametes with the haploid number of chromosomes (23)
      b. When a sperm and an ovum unite at conception, they form a zygote with 46 chromosomes
   2. Principle of independent assortment
      a. As sperm and ovum are formed during meiosis, two members of a pair of homologous chromosomes separate (the principle of segregation) and the maternal and paternal chromosomes get mixed up and redistributed independently in each gamete, with each thus having a different set of 23 chromosomes (Figure 37-3)
      b. Genetic variation—independent assortment of chromosomes ensures that each offspring from a single set of parents is genetically unique
      c. Applies to individual genes or groups of genes
      d. Crossing over—during one phase of meiosis, pairs of matching chromosomes line up along the equator and exchange genes with one another (Figure 37-4)
      e. Gene linkage—sometimes an entire group of genes stays together and crosses over as a single unit

GENE EXPRESSION

A. Hereditary traits
   1. Dominant and recessive traits
      a. Each inherited trait is controlled by two sets of similar genes, one from each parent
      b. Each autosome in a pair matches its partner in the type of gene it contains
      c. Different types of genes (Figures 37-5 and 37-6)
         (1) Dominant gene—effects are seen; capable of masking the effects of a recessive gene for the same trait
         (2) Recessive gene—effects are masked by the effects of a dominant gene for the same trait
      d. Genotype—combination of genes within the cells of an individual
         (1) Homozygous—genotype with two identical forms of a gene
         (2) Heterozygous—genotype with two different forms of a gene
      e. Phenotype—manner in which genotype is expressed; how an individual looks because of genotype
      f. Carrier—person who possesses the gene for a recessive trait but does not exhibit the trait

2. Polygenic traits—when more than one gene is involved in producing a particular trait; a "combined trait" because it results from a combination of genes
3. Codominant traits—when two different dominant genes occur together, each will have an equal effect
4. Abnormal "disease" genes that persist in a population often provide some biological advantage, as in the case of the sickle gene that protects against malaria (Figure 37-7)

B. Sex-linked traits (Figures 37-8 and 37-9)
1. X chromosome—"female chromosome"; larger than Y chromosome; includes genes that determine female sexual characteristics, as well as nonsexual characteristics (Figure 37-10)
2. Y chromosome—"male chromosome"; smaller than X chromosome; contains few genes other than male sexual characteristics
3. Sex-linked traits—traits carried on sex chromosomes; also known as X-linked traits

C. Genetic mutations
1. Mutation—change in the genetic code
   a. Deletion—missing information in the genetic code
   b. Insertion—extra information in the genetic code
   c. Insertions and deletions result in a failure to make the usual protein encoded by a particular gene
2. Mutations can occur without outside influence
3. Mutagens—agents that cause most genetic mutations

MEDICAL GENETICS

A. Mechanisms of genetic disorders
1. Nuclear inheritance
   a. Single-gene diseases—caused by individual mutant genes in nuclear DNA that pass from one generation to the next
   b. Genetic predisposition—disease occurring because of combined effects of inheritance and environmental factors
   c. Chromosomal genetic diseases—congenital conditions such as trisomy and monosomy that often produce life-threatening abnormalities; trisomic and monosomic individuals may die before they can reproduce (Figure 37-11)
2. Mitochondrial inheritance
   a. Mitochondrial DNA (mtDNA)—each mitochondrion has its own DNA molecule (Figure 37-12)
   b. Inheritance of mtDNA occurs through one's mother because sperm does not contribute mitochondria to the ovum during fertilization
   c. mtDNA contains the only genetic code for several important enzymes

B. Single-gene diseases
1. Cystic fibrosis
   a. Results because of recessive genes in chromosome pair 7
   b. Impairment of chloride ion transport across cell membranes causes exocrine cells to secrete thick mucus and concentrated sweat; thickened mucus may obstruct respiratory and gastrointestinal tracts, leading to death
   c. Treatment—use of drugs and other therapies
2. Phenylketonuria (PKU)
   a. Results from recessive genes that fail to produce phenylalanine hydroxylase
   b. Phenylalanine cannot be converted into tyrosine and thus accumulates
   c. High concentrations of phenylalanine destroy brain tissue
   d. Treatment—diets low in phenylalanine
3. Tay-Sachs disease (TSD)
   a. Recessive condition involving failure to make an essential lipid-processing enzyme; carrying one TSD gene may be protective against TB
   b. Abnormal lipids accumulate in the brain, causing severe retardation and death by 4 years of age
   c. No specific therapy available
4. Osteogenesis imperfecta (Figure 37-13)
   a. Dominant genetic disorder of connective tissues resulting in imperfect bone formation
   b. Bones do not have normal collagen and are very brittle
5. Neurofibromatosis
   a. Group of dominant genetic disorders; often inherited but can result from spontaneous mutations of DNA
   b. Characterized by multiple spots and benign tumors of glial cells that surround nerve fibers

C. Chromosomal diseases—genetic disorders resulting from nondisjunction during formation of the gametes; produce either trisomy or monosomy
1. Trisomy 21—triplet of chromosome 21 rather than a pair; characterized by Down syndrome's mental retardation and multiple defects (Figure 37-14)
2. Klinefelter syndrome—occurs in males with a Y chromosome and at least two X chromosomes; characteristics include long legs, enlarged breasts, low intelligence, small testes, sterility, and chronic pulmonary disease (Figure 37-15)
3. Turner syndrome—XO syndrome; occurs in females with a single X chromosome; characterized by failure of ovaries and other organs to mature, sterility, cardiovascular defects, dwarfism, webbed neck, and learning disorders; symptoms can be reduced by hormone therapy (Figure 37-16)

D. Genetic basis of cancer
1. Oncogenes—abnormal genes thought to cause some forms of cancer
2. Tumor suppressor genes regulate cell division so it proceeds normally; when nonfunctional because of a genetic mutation, it allows cells to divide abnormally
3. Also, genetic abnormalities may inhibit the cell's cancer-preventing mechanisms

PREVENTION AND TREATMENT OF GENETIC DISEASES

A. Genetic counseling—professional consultations with families regarding genetic diseases
1. Pedigree—chart that illustrates genetic relationships in a family over several generations; helpful in determining the possibility of producing offspring with certain genetic disorders (Figure 37-17)

2. Punnett square—grid used to determine the mathematical probability of inheriting genetic traits (Figure 37-18)
3. Karyotype—ordered arrangement of photographs of chromosomes from a single cell; used in genetic counseling to identify chromosomal disorders

B. Treating genetic diseases (Figure 37-20)
1. A few genetic conditions can be alleviated by avoiding triggers or treating symptoms
2. Gene therapy involves changing the genetic code of cells to replace normal proteins that are absent in genetic disorders; still experimental
   a. Gene replacement—abnormal, disease-causing proteins are replaced by "therapeutic" genes; goal is to genetically alter existing body cells in the hope of eliminating the cause of a genetic disease
   b. Gene augmentation—normal genes are introduced to augment the production of the needed protein
3. RNA interference (RNAi) therapy—disease-causing genes can be "silenced" by introducing specific short interfering RNA (siRNA) sequences into the body; still experimental

REVIEW QUESTIONS



Write out the answers to these questions after reading the chapter and reviewing the Chapter Summary. If you simply think through the answer without writing it down, you won't retain much of your new learning.

1. Who was the first person to discover the basic mechanism by which traits are transmitted from parents to offspring?
2. Describe albinism in relation to dominance, recessiveness, and genotype.
3. Explain the difference between a genotype and a phenotype.
4. Define codominance, and give an example of a condition that demonstrates codominance.
5. If a certain trait is identified as X-linked recessive, describe the genotype of a female expressing the given trait.
6. Identify several genetic mutagens.
7. How can mutations be beneficial to a species?
8. What role do environmental factors play in relation to certain genetic diseases?
9. Explain the "mistake" in meiosis that results in the condition called *trisomy*.
10. Describe the genetic inheritance of cystic fibrosis, phenylketonuria (PKU), and Tay-Sachs disease.
11. Identify the chromosomal disorder that involves trisomy 21.
12. Differentiate between oncogenes and tumor suppressor genes.
13. How are gene replacement and gene augmentation therapies used to treat genetic diseases?
14. Define the term *genome*.
15. When is a disorder classified as congenital?

CRITICAL THINKING QUESTIONS



After finishing the Review Questions, write out the answers to these more in-depth questions to help you apply your new knowledge. Go back to sections of the chapter that relate to concepts that you find difficult.

1. Genes regulate protein synthesis. Why is the production of specific proteins so important to the structure and function of the body?
2. Differentiate among the text usage of chromatin, chromosomes, and genes.
3. Explain the processes that increase the variability of the genetic code in the offspring.
4. Explain why the structure of the X and Y chromosomes would predict a greater occurrence of sex-linked disorders in males.
5. Explain what is meant by a pedigree. Explain what is meant by a karyotype. Which of these would be most helpful in the diagnosis of Down syndrome? In the diagnosis of Huntington disease?

Glossary

A

abdominal aorta (ab-DOM-i-nal ay-OR-tah) portion of the descending aorta that passes through the abdominal cavity [*abdomin-* belly, *-al* relating to, *aort-* lifted, *-a* thing] *pl.*, aortae or aortas

abdominal reflex (ab-DOM-i-nal) drawing in of the abdominal wall in response to stroking the side of the abdomen [*abdomin-* belly, *-al* relating to, *re-* again, *-flex* bend]

abdominal thrusts (ab-DOM-i-nal) *see* **Heimlich maneuver** [*abdomin-* belly, *-al* relating to]

abdominopelvic cavity (ab-DOM-i-no-PEL-vik KAV-i-tee) term used to describe the single cavity containing the abdominal and pelvic organs [*abdomin-* belly, *-pelv-* basin, *cav-* hollow, *-ity* state]

abducens nerve (ab-DOO-sens) cranial nerve VI; motor nerve; controls movement of the eye and proprioception [*ab-* away, *-duc-* lead, *-ens* process]

abduction (ab-DUK-shun) moving away from the midline of the body; opposite motion of adduction [*ab-* away, *-duct-* lead, *-tion* process]

abnormal constituent (ab-NOR-mal kon-STICH-yoo-ent) any substance present in a body fluid that is not normally found there [*ab-* away from, *-norma* the rule]

abruptio placentae (ab-RUP-shee-oh plah-SEN-tay) separation of normally positioned placenta from the uterine wall; may result in hemorrhage and death of the fetus and/or mother [*ab-* away from, *-ruptio* rupture, *placentae* of flat cake (placenta)]

abscess (AB-ses) cavity, often pus filled, formed by disintegration of tissues [*ab-* away, *-cess* to go]

absolute refractory period (AB-so-loot ree-FRAK-toh-ree) time during which the local area of the membrane has surpassed the threshold potential and will not respond to any stimulus [*absolut-* unrestricted, *refract-* break apart, *-ory* relating to, *period* circuit]

absorption (ab-SORP-shun) passage of a substance through a membrane such as skin or mucosa; often refers to passage of nutrients into blood [*absorp-* swallow, *-tion* process]

accessory gland (ak-SES-oh-ree) a gland that assists organs in accomplishing their functions [*access-* extra, *-ory* relating to, *gland* acorn]

accessory hemiazygos vein (ak-SES-oh-ree hem-EE-ah-ZYE-gos) connects some of the superior intercostal veins with the azygos vein [*hemi-* half, *-a-* without, *-zygo-* union or yoke]

accessory nerve (ak-SES-oh-ree) cranial nerve XI (motor nerve) [*access-* extra, *-ory* relating to]

accessory organ (ak-SES-oh-ree) an organ that assists other organs in accomplishing their functions [*access-* extra, *-ory* relating to, *organ* instrument]

accessory spleen (ak-SES-oh-ree) a small version of the spleen commonly found in the mesentery that connects the spleen and stomach (the gastrosplenic ligament); *see* **spleen** [*access-* extra, *-ory* relating to]

accommodation (ah-kom-oh-DAY-shun) mechanism that allows the normal eye to focus on objects closer than 20 feet [*accommoda-* adjust, *-ation* process]

acetoacetic acid (ass-ih-toh-ah-SEE-tik ASS-id) an acidic ketone body that accumulates during the incomplete breakdown of fats; influences acid-base balance [*acet-* vinegar, *-acid-* sour, *-ic* relating to]

acetone (ASS-ah-tohn) an acidic ketone body that accumulates during the incomplete breakdown of fats; influences acid-base balance [*acet-* vinegar, *-one* chemical]

acetylcholine (ACh) (ass-ee-til-KOH-leen) type of neurotransmitter used by motor neurons at neuromuscular junctions to stimulate muscle contraction at or in some autonomic synapses (in ganglionic synapses, at all parasympathetic effectors, and at some sympathetic effectors) [*acetyl-* vinegar, *-chole-* bile, *-ine* made of]

acetylcholinesterase (ass-ee-til-koh-lin-ES-ter-ase) enzyme that rapidly inactivates acetylcholine bound to postsynaptic receptors [*acetyl-* vinegar, *-chole-* bile, *-in-* made of, *-ester-* vinegar, *-ase* enzyme]

acid (ASS-id) substance that ionizes in water to release hydrogen ions; substance with a pH of less than 7.0 [*acid* sour]

acid-forming food (ASS-id) any food that lowers the pH after it is absorbed into the body [*acid-* sour]

acidic ketone body (ah-SID-ik KEE-tohn) contributes hydrogen ions to the extracellular fluid; influences acid-base balance [*acid-* sour, *-ic* relating to, *keto-* acetone, *-one* chemical]

acidity (ah-SID-ih-tee) the amount of acid in a solution or the state of having a low pH [*acid-* sour, *-ity* state]

acidophil (ASS-id-oh-fil) cell that stains easily with acid dyes [*acid-* sour, *-phil* love]

acidosis (ass-i-DOH-sis) condition in which there is an excessive proportion of acid in the blood and thus an abnormally low blood pH; opposite of alkalosis [*acid-* sour, *-osis* condition]

acini (ASS-i-nee) any cell of a compound gland that secretes a watery fluid; also called *acinar cells* [*acinus-* grape-like]

acne (AK-nee) *see* **acne vulgaris** [*akme-* point]

acne vulgaris (AK-nee vul-GAR-is) inflammatory skin condition affecting sebaceous gland ducts; occurs most commonly in adolescent years; *see* **comedo** [*akme-* point, *vulgus-* common people]

acoustic nerve (ah-KOOS-tik) cranial nerve VIII; *see* **vestibulocochlear nerve** [*acoust-* hear, *-ic* relating to]

acoustic neuroma (ah-KOOS-tik noo-ROH-mah) glial tumor of the Schwann cells surrounding cranial nerve VIII, causing progressive hearing loss and dizziness [*acoust-* hear, *-ic* relating to, *neuro-* nerve, *-oma* tumor]

acquired cortical color blindness (ah-KWYERD KOHR-tih-kahl) loss of normal color vision caused by damage to the cortex of the cerebrum [*cortic-* bark, *-al* relating to]

acquired immune deficiency syndrome (AIDS) (ah-KWYERD IM-yoon deh-FISH-en-see SIN-drohm) collection of abnormalities caused by advanced HIV infection and characterized by a depression of T-cell immunity [*syn-* together, *-drome* running or (race) course]

acquired immunity (ah-KWYERD i-MYOO-ni-tee) immunity that is obtained after birth through exposure to a specific harmful agent; *see* **adaptive immunity** [*-immun* free, *-ity* state]

acromegaly (ak-roh-MEG-ah-lee) condition caused by hypersecretion of growth hormone after puberty, resulting in enlargement of facial features (e.g., jaw, nose), fingers, and toes [*acro-* extremities, *-mega-* great, *-aly* state]

acrosome (AK-roh-sohm) structure on the tip of the sperm head containing enzymes that break down the covering of the ovum to facilitate conception [*acro-* top or tip, *-some* body]

acrosome reaction (AK-roh-sohm) biochemical reaction that releases digestive enzymes from the sperm head (acrosome) after it attaches to the outer layers of an ovum [*acro-* top or tip, *-some* body]

actin (AK-tin) contractile protein found in the thin myofilaments of skeletal muscle; *see* **sliding filament model** [*act-* act or do, *-in* substance]

action potential (AK-shun poh-TEN-shal) nerve impulse; membrane potential fluctuation of an actively conducting axon [*potent-* power, *-ial* relating to]

active site any location on the surface of a molecule that reacts with another molecule [*actus-* moving]

active transport movement of a substance into or out of a living cell requiring the use of cellular energy [*actus-* moving, *trans-* across, *-portare* carry]

actual osmotic pressure (os-MOT-ik) current osmotic pressure of a solution; *see* **osmotic pressure** [*osmo-* push, *-ic* relating to]

acute (ah-KYOOT) intense; short in duration, as in acute disease [*acut* sharp]

acute anemia (ah-KYOOT ah-NEE-mee-ah) condition of a precipitous drop in the red blood cell count [*acut-* sharp, *an-* without, *-emia* blood condition]

acute bronchitis (ah-KYOOT brong-KYE-tiss) acute form of inflammation of the bronchi of the pulmonary tract [*acut-* sharp, *bronch-* windpipe, *-itis* inflammation]

acute glomerulonephritis (ah-KYOOT gloh-mer-yoo-loh-neh-FRY-tis) most common form of kidney disease; may be caused by a delayed immune response to streptococcal infection [*acut-* sharp, *glomer-* ball, *-ul-* little, *-nephr-* kidney, *-itis* inflammation]

acute lymphocytic leukemia (ALL) (ah-KYOOT LIM-foh-sit-ik loo-KEE-mee-ah) blood cancer that decreases the production of red blood cells, platelets, and nonmalignant lymphocyte cells [*acu-* sharp, *lymph-* water (lymphatic system), *-cyt-* cell, *-ic* relating to, *leuk-* white, *-emia* blood condition]

acute myeloid leukemia (AML) (ah-KYOOT MY-eh-loyd loo-KEE-me-ah) blood cancer that is caused by pathologic transformation of myeloid stem cells [*acu-* sharp, *myel-* marrow, *-oid* like, *leuk-* white, *-emia* blood condition]

acute pain (ah-KYOOT) intense pain [*acut-* sharp]

adaptation (ad-ap-TAY-shun) condition of many sensory receptors in which the magnitude of a receptor potential decreases over a period of time in response to a continuous stimulus [*adapt-* fit to, *-tion* process]

adaptive immunity (ah-DAP-tiv i-MYOO-ni-tee) type of immunity in which specific antigens or particles are recognized, then targeted for destruction; also called *acquired immunity* or *specific immunity* [*adapt-* fit to, *-ive* relating to, *immun-* free, *-ity* state]

Addison disease (AD-i-son) life-threatening condition caused by the hyposecretion of adrenal cortical hormones; caused by tuberculosis, autoimmunity, or other factors [*Thomas Addison* English physician]

adduction (ad-DUK-shun) moving toward the midline of the body; opposite motion of abduction [*ad-* toward, *-duct-* lead, *-tion* process]

adenine (AD-eh-neen) one of the nitrogenous bases of the nucleotides in RNA, DNA, and related molecules [*aden-* gland]

adenocarcinoma (ad-eh-no-kar-si-NO-mah) cancer of glandular epithelium [*adeno-* gland, *-carcin-* cancer, *-oma* tumor]

adenofibroma (ad-eh-no-fye-BROH-mah) benign neoplasm formed in epithelial and connective tissues [*adeno-* gland, *-fibra* fiber, *-oma* tumor]

adenohypophysis (ad-eh-no-hye-POF-i-sis) anterior pituitary gland, which has the structure of an endocrine gland [*adeno-* gland, *-hypo-* under or below, *-physis* growth] *pl.*, adenohypophyses

adenoid (AD-eh-noyd) literally, glandlike; adenoids, or enlarged pharyngeal tonsils, are paired lymphoid structures in the nasopharynx [*adeno-* gland, *-oid* like]

adenoma (ad-eh-NO-mah) benign tumor of glandular epithelium [*adeno-* gland, *-oma* tumor]

adenosine deaminase deficiency (ah-DEN-oh-seen dee-AM-i-nayse) inherited condition that produces immune deficiency [*adenosine* blend of adenine and ribose, *de-* remove, *-amin-* ammonia, *-ase* enzyme]

adenosine triphosphate (ATP) (ah-DEN-oh-seen try-FOS-fayt) chemical compound that provides energy for use by body cells [blend of *adenine* and *ribose*, *tri-* three, *-phosph-* phosphorus, *-ate* oxygen]

adenyl cyclase (AD-eh-nil SYE-klays) enzyme that promotes ATP change into cyclic AMP [*cycl-* recurring, *-ase* enzyme]

adipocyte (AD-i-poh-syte) fat-storing cell [*adipo-* fat, *-cyte* cell]

adipose tissue (AD-i-pohs) fat tissue [*adipo-* fat, *-ose* full of, *tissu-* fabric]

adolescence (ad-oh-LESS-ens) period between puberty (the onset of reproductive maturity) and adulthood [*adolesc-* grow up, *-ence* state]

adrenal (ah-DREE-nal) near the kidney, as in adrenal gland [*ad-* toward, *-ren-* kidney, *-al* relating to]

adrenal cortex (ah-DREE-nal KOR-teks) outer portion of adrenal gland that secretes hormones called *corticoids* [*ad-* toward, *-ren-* kidney, *-al* relating to, *cortex* bark] *pl.*, cortices

adrenal gland (ah-DREE-nal) endocrine gland that rests on the top of each kidney; made up of cortex and medulla regions [*ad-* toward, *-ren-* kidney, *-al* relating to, *gland* acorn]

adrenal medulla (ah-DREE-nal meh-DUL-ah) inner portion of adrenal gland that secretes epinephrine and norepinephrine [*ad-* toward, *-ren-* kidney, *-al* relating to, *medulla* middle] *pl.*, medullae or medullas

adrenaline (ah-DREN-ah-len) *see* **epinephrine** [*ad-* to, *-ren-* kidney, *-al* relating to, *-ine* chemical]

adrenergic (ad-ren-ER-jik) describes axons whose terminals release norepinephrine and epinephrine [*ad-* toward, *-ren-* kidney, *-erg-* work,*-ic* relating to]

adrenocorticotropic hormone (ACTH) (ah-dree-no-kor-teh-koh-TROH-pic HOR-mohn) hormone that stimulates the adrenal cortex to secrete larger amounts of hormones

[*adreno-* gland, *-cortic-* bark, *-trop-* nourish, *-ic* relating to, *hormon-* excite]

adult respiratory distress syndrome (ARDS) (RES-per-ah-tohr-ee dis-TRESS SIN-drohm) syndrome resulting from impairment or removal of surfactant in the alveoli [*re-* again, *-spir-* breathe, *-tory* relating to *syn-* together, *-drome* running or (race) course]

adult stem cell undifferentiated cell found in adults that is capable of producing specialized daughter cells [*adultus-* grown up, *-stem* tree, trunk, *-cell* storeroom]

adulthood (ah-DULT-hood) developmental period after adolescence [*adultus-* grown up]

adventitia (ad-ven-TISH-ah) shortened form of *tunica adventitia* [*adventitia* coming from abroad]

aerobic (air-OH-bik) relating to the use of oxygen, as in aerobic respiration [*aer-* air, *-bi-* life, *-ic* relating to]

aerobic respiration (air-OH-bik res-pi-RAY-shun) catabolic process; the stage of cellular respiration requiring oxygen [*aero-* air, *-b-* (from -bio-) life, *-ic* relating to, *re-* again, *-spir-* breathe, *-tion* process]

aerobic training (air-OH-bik) continuous vigorous exercise requiring the body to increase its consumption of oxygen and develop the muscles' ability to sustain activity over a long time; also known as *endurance training* [*aer-* air, *-bi-* life, *-ic* relating to]

afferent (sensory) neuron (AF-fer-ent NOO-ron) neuron that carries impulses toward the central nervous system from the periphery; sensory neuron [*a[d]-* toward, *-fer-* carry, *-ent* relating to, *neuron-* nerve]

afferent division (AF-fer-ent) sensory division (incoming pathways) of the nervous system [*a[d]-* toward, *-fer-* carry, *-ent* relating to]

afferent impulse (AF-fer-ent IM-pulse) impulse traveling toward the central nervous system [*a[d]-* toward, *-fer-* carry, *-ent* relating to]

afferent nervous system (AF-fer-ent) subdivision of the peripheral nervous system; consists of all incoming sensory nerves [*a[d]-* toward, *-fer-* carry, *-ent* relating to]

agglutinogen (ah-gloo-TIN-oh-jen) substance that stimulates agglutination (clumping), particularly of red blood cells; antigens present on red blood cell membranes [*agglutin-* glue, *-gen* produce]

aggregated lymphoid nodules (ag-rah-GAYT-ed LIM-foyd NOD-yools) isolated nodules of lymphatic tissue in the intestinal wall; also called *Peyer's patches* [*a[d]-* to, *-grega-* collect, *lymph-* water, *-oid* like, *nod-* knot, *-ule* small]

agonist (AG-ah-nist) agent that works like or with (rather than against) another agent [*agon-* struggle, *-ist* agent]

agranulocyte (ah-GRAN-yoo-loh-syte) white blood cells without cytoplasmic granules [*a-* without, *-granul* little grains or granules, *-cyte* cell]

air-contrast barium enema study (BAHR-eeum EN-e-mah) diagnostic study that outlines the bowel with barium and then adds air to enhance the presence of lesions [*contra-* against, *barys-* heavy, *enienai-* to send in]

alarm reaction the initial response to stress [*arma-* to arm, *re-* again, *-agere* to act]

albinism (AL-bi-niz-em) recessive, inherited condition characterized by a lack of the dark brown pigment melanin in the skin, eyes, and hair, resulting in vision problems and susceptibility to sunburn and skin cancer; ocular albinism is a lack of pigment in the layers of the eyeball [*alb-*white, *-in-* characterized by, *-ism* state]

albumin (al-BYOO-min) plasma protein that aids in the regulation of the osmotic concentration of the blood [*alb-* white]

aldosterone (AL-doh-steh-rohn *or* al-DAH-stair-ohn) hormone that stimulates the kidney to retain sodium, ions, and water; only physiologically important mineralocorticoid [*aldo-* aldehyde, *-stero-* solid or steroid derivative, *-one* chemical]

aldosterone mechanism (al-DOS-ter-own MEK-ah-niz-em) homeostatic mechanism that restores normal extracellular fluid volume when it decreases below normal [*aldo-* aldehyde, - *stero-* solid or steroid derivative, *-one* chemical, *mechan-* machine, *-ism* state]

aldosteronism (al-doh-STAIR-on-iz-em) hypersecretion of aldosterone [*aldo-* aldehyde, *-stero-* solid or steroid derivative, *-on-* chemical, *-ism* state]

alimentary canal (al-eh-MEN-tar-ee kah-NAL) the digestive tract as a whole [*aliment-* nourishment, *-ary* relating to]

alkaline (AL-kah-lin) refers to a substance that in solution has a pH of greater than 7.0 [*alkal-* ashes, *-ine* relating to]

alkalinity (al-kah-LIN-ih-tee) state of having a high pH; amount of base or alkaline in a solution [*alkal-* ashes, *-in-* relating to, *-ity* state]

alkalosis (al-kah-LOH-sis) condition in which there is an excessive proportion of alkali (base) in the blood; opposite of acidosis [*alkal-* ashes, *-osis* condition]

allergen (AL-er-jen) any substance that produces an allergic reaction [*all-* other, *-erg-* work, *-gen* produce]

allergy (AL-er-jee) a type of hyperimmunity [*all-* other, *-erg-* work, *-y* state]

allostasis (al-lo-STAY-sis) the physiological processes used by the body to restore homeostasis during stress [*allo-* different, *-stasis* standing still]

allosteric effector (al-oh-STEER-ik ee-FEKT-or) an agent that alters the function of an enzyme by changing the shape of the enzyme's active site [*allo-* another or different, *-ster-* solid, *-ic* relating to, *effect* to accomplish]

alopecia (al-o-PEE-sha) loss of hair; baldness [*alopec-* fox, *-ia* condition]

alpha (α) receptor (AL-fah ree-SEP-tor) adrenergic receptor for norepinephrine [*alpha* first letter of Greek alphabet, *recept-* receive, *-or* agent]

alpha cell (AL-fah) pancreatic islet cell that secretes glucagon; also called *A cell* [*alpha* (α) first letter of Greek alphabet, *cell* storeroom]

alpha motor neuron (AL-fah MOH-tor NOO-ron) generator of efferent impulses that stimulate regular muscle fibers to contract [*alpha* (α) first letter of Greek alphabet, *mot-* movement, *-or* agent, *neuron* nerve]

alpha particle (AL-fah PAR-ti-kul) radioactive particle consisting of two protons plus two neutrons [*alpha* (α) first letter of Greek alphabet]

alpha-fetoprotein (AFP) (AL-fah-fee-toh-PRO-teen) normal fetal protein; presence in adult suggests liver or germ cell cancer [*alpha-* first letter of Greek alphabet (α), *feto-* offspring (fetus)]

alveolar (al-VEE-oh-lar) relating to a small cavity, such as an alveolus of lung [*alveo-hollow, -ola-* little, *-ar* relating to]

alveolar cell (al-VEE-oh-lar) milk-producing cell that releases secretions into ducts of the breast [*alveo- hollow, -ola-* little, *-ar* relating to]

alveolar duct (al-VEE-oh-lar) airway that branches from the smallest bronchioles; alveolar sacs arise from alveolar ducts [*alve-* hollow, *-ol-* little, *-ar* relating to]

alveolar ventilation (al-VEE-oh-lar ven-ti-LAY-shun) volume of inspired air that actually reaches the alveoli [*alve-* hollow, *-ol-* little, *-ar* relating to, *vent-* fan or create wind, *-tion* process]

alveolus (al-VEE-oh-lus) literally, a small cavity; alveoli of lungs are microscopic sac-like dilations of terminal bronchioles; gas exchange in the lungs occurs across the membranes of the alveoli [*alve-* hollow, *-olus* little] *pl.*, alveoli

Alzheimer disease (AD) (AHLZ-hye-mer) syndrome characterized by dementia, usually beginning in mid to late adulthood and caused by a combination of factors, including genetic and environmental [*Alois Alzheimer* German neurologist, *dis-* opposite of, *-ease* comfort]

amenorrhea (ah-men-oh-REE-ah) absence of normal menstruation [*a-* without, *-men-* month, *-rrhea* flow]

amine (AM-een) organic compound containing nitrogen; neurotransmitter synthesized from amino acid molecules [*amine* ammonia compound]

amino acid (ah-MEE-no) type of chemical unit from which proteins are built; also have other functions made up of a carbon atom to which are bonded an amino group and carboxyl group [*amino* NH_2, *acid* sour]

amino acid derivative hormone (ah-MEE-no ASS-id deh-RIV-ah-tiv HOR-mohn) category of nonsteroid hormones; each hormone is derived from a single amino acid molecule [*amino* NH_2, *acid* sour, *hormon-* excite]

amniocentesis (am-nee-oh-sen-TEE-sis) procedure in which a sample of amniotic fluid is removed with a syringe for use in genetic testing, often to produce a karyotype of the fetus [*amnio-* birth membrane, *-centesis* a pricking]

amniotic cavity (am-nee-OT-ik KAV-i-tee) cavity within the blastocyst that eventually becomes a fluid-filled sac in which the embryo will float during development [*amnio-* fetal membrane, *-ic* relating to, *cav-* hollow, *-ity* state]

amphiarthrosis (am-fee-ar-THROH-sis) slightly movable joint such as the one that connects the two pubic bones [*amphi-* both sides, *-arthr-* joint, *-osis* condition] *pl.*, amphiarthroses (am-fee-ar-THROH-seez)

ampulla (am-PUL-ah) saclike dilation of a tube or duct; found at end of each semicircular duct, contains crista ampullaris [*ampu-* flask, *-ulla* little] *pl.*, ampullae

amygdaloid nucleus (ah-MIG-dah-loyd NOO-klee-us) basal nucleus (region of gray matter of the deep cerebrum) at the tip of the caudate nucleus [*amygdal-* almond, *-oid* like] *pl.*, nuclei

amylase (AM-eh-lays) enzyme that digests carbohydrates [*amyl-* starch, *-ase* enzyme]

anabolic hormone (an-ah-BOL-ik HOR-mohn) hormone that stimulates anabolism in the target organ [*anabol-* build up, *-ic* relating to, *hormon-* excite]

anabolic steroid (an-ah-BOL-ik STAYR-oyd) any steroid (lipid) hormone that promotes anabolism, such as testosterone [*anabol-* build up, *-ic* relating to, *stero-* solid, *-oid* like]

anabolism (ah-NAB-oh-liz-em) cells making complex molecules (e.g., hormones) from simpler compounds (e.g., amino acids); opposite of catabolism [*anabol-* build up, *-ism* action]

anaerobic (an-air-OH-bik) relating to a process that requires no oxygen [*an-* without, *-aer-* air, *-bi-* life, *-ic* relating to]

anaerobic pathway (an-air-OH-bik) catabolic process; stage of cellular respiration not requiring oxygen; although it is actually a type of fermentation, it is often called "anaerobic respiration" [*an-* without, *-aero-* air, *-b-* (from *-bio-*) life, *-ic* relating to]

anal canal (AY-nal kah-NAL) passage from the colon to the outside of the body [*an-* ring (anus), *-al* relating to]

anal fissure (AY-nal FISH-ur) minor lacerations in the lining of the anus or anal canal [*an-* ring (anus), *-al* relating to, *fissur-* cleft]

anal fistula (AY-nal FISS-tyoo-lah) passageway that often develops between the rectal wall and skin surrounding the anus [*an-* ring (anus), *-al* relating to, *fistula* pipe] *pl.*, fistulae *or* fistulas

anal triangle (AY-nal TRY-ang-gul) area surrounding anus [*an-* ring (anus), *-al* relating to]

anaphase (AN-ah-fayz) latter stage of mitosis; duplicate chromosomes move to poles of dividing cell [*ana-* apart, *-phase* stage]

anaphylactic shock (an-ah-fih-LAK-tik) type of severe allergic reaction characterized by severe circulatory failure [*ana-* without, *-phylact-* protection, *-ic* relating to]

anaplasia (an-ah-PLAY-zee-ah) growth of abnormal (undifferentiated) cells, as in a tumor or neoplasm [*ana-* without, *-plasia* shape]

anastomosis (ah-nas-toh-MOH-sis) connection between vessels that allows collateral circulation [*ana-* anew, *-stomo-* mouth, *-osis* condition] *pl.*, anastomoses

anatomical dead space (an-ah-TOM-i-kal) air passageways that contain air that does not reach the alveoli [*ana-* apart, *-tom-* cut, *-ical* relating to]

anatomical position (an-ah-TOM-i-kal po-ZISH-un) the standard reference position for the body; standing with arms hanging at sides with palms forward, gives meaning to directional terms [*ana-* apart, *-tom-* cut, *-ical-* relating to, *posit-* place, *-tion* state]

anatomy (ah-NAT-o-mee) study of the structure of an organism and the relationships of its parts [*ana-* apart, *-tom-* cut, *-y* action]

androgen (AN-droh-jen) hormone that promotes development and maintenance of male characteristics [*andro-* male, *-gen* produce]

androgen-binding protein (ABP) (AN-droh-jen-BYND-ing PRO-teen) specialized protein that binds to testosterone and increases concentration within the seminiferous tubules [*andro-* male, *-gen* produce, *prote-* first rank, *-in* substance]

anemia (ah-NEE-me-ah) deficient number of red blood cells, or deficient hemoglobin [*an-* without, *-emia* blood condition]

anemia of chronic disease (ah-NEE-mee-ah KRON-ik) condition of abnormally low hemoglobin secondary to a long-lasting illness [*an-* without, *-emia* blood condition, *chron-* time, *-ic* relating to]

anesthesia (an-es-THEE-zhah) state in which a person lacks the feeling of pain [*an-* absence, *-esthesia* feeling]

anesthetic (an-es-THET-ik) substance that reduces or eliminates the sensation of pain [*an-* absence, *-esthesia* feeling, *-ic* pertaining to]

aneurysm (AN-yoo-riz-em) abnormal widening of the arterial wall; aneurysms promote formation of thrombi and also tend to burst [*aneurysm* widening]

angina pectoris (an-JYE-nah PEK-tor-iss) severe chest pain resulting when the myocardium is deprived of sufficient oxygen [*angina* strangling, *pector-* breast, *-is* relating to]

angiogenesis (an-jee-oh-JEN-es-is) physiological process in which new blood vessels are formed [*angi-* vessel *-genesis* origin]

angiography (an-jee-AH-graf-ee) radiography in which radiopaque contrast medium is injected into a vessel to make it more visible in a medical image (angiogram); in arteries the image is called *arteriogram*; in veins, a *venogram* or *phlebogram*; in lymphatic vessels, a *lymphangiogram* [*angi-* vessel, *-graph-* draw, *-y* process]

angioplasty (AN-jee-oh-plass-tee) medical procedure in which vessels occluded by arteriosclerosis are opened (i.e., the channel for blood flow is widened) [*angio-* vessel, *-plasty* surgical repair]

angiotensin I (an-jee-oh-TEN-sin) substance formed by conversion of angiotensinogen by renin; causes vasoconstriction and an increase in blood pressure [*angio-* vessel,

-tens- pressure or stretch, *-in* substance, *I* Roman numeral one]

angiotensin II (an-jee-oh-TEN-sin) substance formed in the lungs by enzyme conversion of angiotensin I; ultimately stimulates secretion of aldosterone; causes vasoconstriction [*angio-* vessel, *-tens-* pressure or stretch, *-in* substance, *II* Roman numeral two]

angiotensinogen (an-jee-oh-TEN-sin-oh-jen) normal constituent of blood; a precursor to angiotensin [*angio-* vessel, *-tens-* pressure or stretch, *-in-* substance, *-gen* produce]

angular movement (ANG-gyoo-lar) body movement that increases or decreases the angle of a joint [*angulus-* angle, *movere-* to move]

anion (AN-eye-on) negatively charged molecule (negative ion) [*ana-* up, *-ion* to go (ion)]

ankle jerk reflex extension of the foot in response to tapping of the Achilles tendon [*re-* again, *-flex* bend]

annulus fibrosis (AN-yoo-lus fye-BROH-sis) tough outer edge of intervertebral disk; surrounds nucleus pulposus [*annulus* ring, *fibrosis* fibrous]

anorexia (an-oh-REK-see-ah) loss of appetite (a symptom, rather than a distinct disorder) [*an-* without, *-orex-* appetite, *-ia* condition]

anorexia nervosa (an-oh-REK-see-ah ner-VOH-sah) behavioral eating disorder characterized by chronic refusal to eat, often related to an abnormal fear of becoming obese [*an-* without, *-orex-* appetite, *-ia* condition, *nerv-* nerve, *-osa* relating to]

anorexigenic (an-oh-rek-sih-JEN-ik) relating to an agent that reduces appetite [*an-* without, *-orex-* appetite, *-gen-* produce, *-ic* relating to]

anosmia (AN-oz-mee-ah) inability to smell [*an-* without, *-osm-* smell, *-ia* condition]

antagonism (an-TAG-oh-niz-em) situation in which one agent (such as a hormone or muscle) produces the opposite effect of another agent [*ant-* against, *-agon-* struggle, *-ism* condition of]

antagonist (an-TAG-oh-nist) agent that has an opposing effect or works against another agent [*ant-*against, *-agon* struggle, *-ist* agent]

antagonist muscle (an-TAG-oh-nist) muscle that directly opposes prime movers; for example, muscles that flex the arm are antagonists to muscles that extend it [*ant-*against, *agon* struggle, *-ist* agent, *mus-*mouse, *-cle* small]

antenatal medicine (an-tee-NAY-tal) therapy used on an embryo or fetus [*ante-* before, *-nat-* birth, *-al* relating to]

anterior (an-TEER-ee-or) front, or ventral; opposite of posterior, or dorsal [*ante-* front, *-er-* more, *-or* quality]

anterior cavity (of eye) (an-TEER-ee-or) entire space located in front of the lens of the eye; divided into anterior and posterior chambers [*ante-* front, *-er-* more, *-or* quality, *cav-* hollow, *-ity* state]

anterior corticospinal tract (an-TEER-ee-or KOR-ti-koh-spy-nal) coordinates individual or small groups of muscles (hands, fingers, feet, toes) of the same side [*ante-* front, *-er-* more, *-or* quality, *cortic-* bark, *-spin-* backbone, *-al* relating to, *tract-* trail]

anterior cul-de-sac (an-TEER-ee-or kul-deh-sak) space created by the protrusion of the cervix into the lumen of the vagina; formed by the anterior ligament [*ante-* front, *-er-* more, *-or* quality, *cul-de-sac* bottom of the bag] *pl.*, culs-de-sac or cul-de-sacs

anterior fornix (an-TEER-ee-or FOR-niks) space created by the protrusion of the cervix into the lumen of the vagina; increases probability of reproductive success by retaining seminal fluid [*ante-* front, *-er-* more, *-or* quality, *fornix* arch] *pl.*, fornices

anterior ligament (an-TEER-ee-or LIG-ah-ment) fold of peritoneum formed by the extension of the peritoneum on the anterior surface of the uterus to the posterior surface of the bladder [*ante-* front, *-er-* more, *-or* quality, *liga-* bind, *-ment* condition]

anterior spinothalamic tract (an-TEER-ee-or SPY-no-tha-lam-ik) responds to crude touch and pressure [*ante-* front, *-er-* more, *-or* quality, *spino-* backbone, *-thalam-* inner chamber, *-ic* relating to]

anterior tibial vein (an-TEER-ee-or TIB-ee-al) vein along the front of the leg (shin) [*ante-* front, *-er-* more, *-or* quality, *tibia* shin bone, *-al* relating to]

anthrax (AN-thraks) bacterial infection caused by *Bacillus anthracis*, ordinarily affecting herbivores (sheep, cattle, goats, antelope) and often killing them; occurs rarely in humans through accidental or intentional exposure to bacterial spores through inhalation or skin contact; inhalation anthrax is life-threatening but can be treated successfully with drugs; cutaneous anthrax is less serious, characterized by a reddish-brown patch on the skin that ulcerates and then forms a dark, nearly black scab, followed by muscle pain, internal hemorrhage (bleeding), headache, fever, nausea, and vomiting [*anthrax* boil]

antianemic principle (an-tee-an-NEE-mik) factor that maintains a normal number of red blood cells; vitamin B_{12} [*anti-* against, *-an-* without, *-emia-* blood condition, *-ic* relating to]

antiangiogenesis agent (AN-tee-AN-jee-oh-jen-eh-sis) class of chemotherapy drugs used in cancer treatment that inhibits development of new blood vessels in a tumor; *see* **rational drugs** [*anti-* against, *angi-* vessel, *-genesis* origin]

antibody (AN-ti-bod-ee) plasma protein produced by B-lymphocytes that destroys or inactivates a specific substance (antigen) that has entered the body [*anti-* against]

antibody titer (AN-ti-bod-ee TYE-ter) measurement of the amount of antibody in the plasma [*anti-* against, *titer* proportion (in a solution)]

antibody-mediated immunity (AN-ti-bod-ee-MEE-dee-ayt-ed i-MYOO-nih-tee) immunity that is produced when antibodies render antigens unable to harm the body; also called *humoral immunity* [*anti-* against, *medi-* middle, *-ate* process, *immun-* free, *-ity* state]

anticoagulant (an-tee-koh-AG-yoo-lant) agent that opposes blood clotting [*anti-*against, *-coagul-* curdle, *-ant* agent]

anticoagulant drug treatment (an-tee-koh-AG-yoo-lant) therapy involving the use of anticlotting agents in the blood [*anti-*against, *-coagul-* curdle, *-ant* agent]

antidepressant (an-tee-deh-PRESS-ant) drug that inhibits feelings of depression or sadness [*anti-* against, *-de-* down, *-press-* press, *-ant* agent]

antidiuresis (an-tee-dye-yoo-REE-sis) opposing the production of a large urine volume [*anti-* against, *-dia-* through, *-uret-* urination, *-esis* condition]

antidiuretic hormone (ADH) (an-tee-dye-yoo-RET-ik HOR-mohn) hormone produced in the posterior pituitary gland to regulate the balance of water in the body by accelerating reabsorption of water in the kidney tubules; also called *arginine vasopressin (AVP)* [*anti-* against, *-dia-* through, *-uret-* urination, *-ic* relating to, *hormon-* excite]

antigen (AN-ti-jen) substance, usually a protein fragment, that causes an immune response [*anti-* against, *-gen* produce]

antigen-antibody complex (AN-ti-jen-AN-ti-bod-ee KOM-pleks) combination of an antigen with its complementary antibody [*anti-* against, *-gen* produce, *anti-* against, body, *complex* embrace]

antigenic determinant (AN-ti-jen-ik dih-TUR-mah-nant) region of an antibody molecule that binds to an antigen particle [*anti-* against, *-gen* produce, *-ic* relating to, *determin-* limit, *-ant* agent of]

antigen-presenting cell (APC) (AN-ti-jen) any of a variety of immune cells that present protein fragments (antigens) on their surface and thus allow recognition and reaction by other immune system cells; include macrophages and dendritic cells (DCs) and B cells [*anti-* against, *-gen* produce, *presenting*, *cell* storeroom]

antihistamine (an-ti-HISS-tah-meen) agent that inhibits the histamine, an inflammation agent [*anti-* against, *-histo-* tissue, *-amine* ammonia compound]

antioxidant (an-tee-OK-seh-dent) agent that inhibits chemical oxidation [*anti-* against, *-oxi-* sharp (oxygen), *-ant* agent]

antiplatelet drug treatment (an-tee-PLAYT-let) therapy that inhibits platelets [*anti-* against, *-plate-* flat, *-let* small]

anuria (ah-NOO-ree-ah) lack or failure to produce urine [*a-* not, *-ur-* urine, *-ia* condition]

aorta (ay-OR-tah) largest systemic artery; extends directly from the left ventricle [*aort-* lifted, *-a* thing] *pl.*, aortae *or* aortas

aortic arch (ay-OR-tik) 180-degree curve of the aorta, shortly after it leaves the left ventricle [*aort-* lifted, *-ic* relating to]

aortic baroreceptor (ay-OR-tik bar-oh-ree-SEP-tor) stretch receptor located in the aorta that is sensitive to changes in blood pressure [*aort-* lifted, *-ic* relating to, *baro-* pressure, *-recept-* receive, *-or* agent]

aortic body (ay-OR-tik) small cluster of chemosensitive cells that respond to changes in blood levels of carbon dioxide and oxygen [*aort-* lifted, *-ic* relating to]

aortic reflex (ay-OR-tik REE-fleks) increase or decrease in heart rate as a result of sensory nerve fibers in the wall of aorta responding to blood pressure [*aort-* lifted, *-ic* relating to, *re-* back or again, *-flex* bend]

aortic regurgitation (ay-OR-tik ree-gur-jih-TAY-shun) reflux of blood from the aorta to the ventricle [*aort-* lifted, *-ic* relating to, *re-* again, *-gurgit-* flow, *-ation* process]

aortic (semilunar) valve (ay-OR-tic [sem-i-LOO-nar]) valve between the aorta and left ventricle that prevents blood from flowing back into the ventricle [*aort-* lifted, *-ic* relating to]

apatite (AP-ah-tyte) crystals of calcium and phosphate that contribute to the hardness of bone [*apat-* deceit, *-ite* mineral]

Apgar score (AP-gar) system of assessing general health of newborn infant, in which heart rate, respiration, muscle tone, skin color and response to stimuli are scored (a perfect total score is 10) [*Virginia Apgar* American physician]

apex (AY-peks) the point or tip of a structure; *see also* **apical** [*apex* tip] *pl.*, apices

aphasia (ah-FAY-zee-ah) language deficit caused by damage in speech centers of the brain [*a-* without, *-phasia* speech]

apical (AY-pik-al) relating to the apex (tip) of an organ, cell, or other structure; in a cell, often refers to the surface facing the lumen of the organ [*apic-* tip, *-al* relating to]

aplastic anemia (a-PLAS-tik ah-NEE-mee-ah) abnormally low number of red blood cells caused by destruction of bone marrow by drugs, toxic chemicals, or radiation [*a-* without, *-plast-* form, *-ic* relating to, *a-* without, *-nemia* condition of red blood cell deficiency]

apnea (AP-nee-ah) temporary cessation of breathing [*a-* not, *-pne-* breathe, *-a* condition]

apneusis (ap-NYOO-sis) cessation of breathing in the inspiratory position [*a-* not, *-pneu-* breathe, *-sis* condition]

apneustic center (ap-NYOO-stik) regulatory area located in the pons; stimulates the inspiratory center to increase the length and depth of inspiration [*a-* not, *-pneus-* breathing, *-ic* relating to]

apocrine gland (AP-oh-krin) gland that collects its secretions near the apex of the cell and then releases them by pinching off the distended end; for example, mammary gland [*apo-* from, *-crin-* secrete, *gland* acorn]

apocrine sweat gland (AP-oh-krin) sweat glands located in the axillae and genital regions; these glands enlarge and begin to function at puberty [*apo-* from, *-crin-* secrete, *gland* acorn]

aponeurosis (ap-oh-nyoo-ROH-sis) broad, flat sheet of connective tissue [*apo-* from, *-neur-* sinew, *-osis* condition] *pl.*, aponeuroses

apoptosis (app-o-TOH-sis *or* app-op-TOH-sis) nonpathological, programmed cell death in which specific biochemical steps within the cell lead to the fragmentation of the cell and removal of the pieces by phagocytic cells; occurs when cells are no longer needed and is the normal process by which our tissues remodel themselves [*apo-* away, *-ptosis* falling]

appendicitis (ah-pen-di-SYE-tis) inflammation of the vermiform appendix [*appendic-* hang upon, *-itis* inflammation]

appendicolith (ah-pen-DIK-oh-lith) hardened nodule that may form within the appendix [*appendic-* hang upon, *-lith* a stone]

appendicular skeleton (ah-pen-DIK-yoo-lar SKEL-eh-ton) bones of the upper and lower extremities of the body [*append-* hang upon, *-ic-* relating to , *-ul-* little, *-ar* relating to]

appetite center (AP-ah-tyte) cluster of neurons in the lateral hypothalamus whose impulses cause an increase in appetite [*appetere-* to long for]

appositional growth (ap-oh-ZISH-un-al) process by which a flat bone or cartilage grows in size by addition of bony cartilage at its surface; also called *exogenous growth* [*apposit-* to put near, *-ion* process, *-al* relating to]

aqueous humor (AY-kwee-us HYOO-mor) watery fluid that fills the anterior chamber of the eye, in front of the lens [*aqu-* water, *-ous* relating to]

arachnoid (ah-RAK-noyd) weblike; particularly the middle layer of the meninges [*arachn-* spider(web), *-oid* like]

arbor vitae (AR-bor VI-tay) internal white matter of the cerebellum [*arbor* tree, *vitae* of life] *pl.*, arbores vitae

areola (ah-REE-oh-lah) region of skin of the breast that surrounds the nipple [*are-* area or space, *-ola* little] *pl.*, areolae, areoles, *or* areolas

areolar tissue (ah-REE-oh-lar) a type of connective tissue consisting of fibers and a variety of cells embedded in a loose matrix of soft, sticky gel [*are-* open space, *-ola-* little, *-ar* relating to *tissue-* fabric]

arginine vasopressin (AVP) (AHR-jih-neen vas-oh-PRES-in) see **antidiuretic hormone** [*arginine* type of amino acid, *vas-* vessel, *-press-* pressure, *-in* substance]

arrector pili muscle (ah-REK-tor PYE-lye) smooth muscles of the skin, attached to hair follicles; when contraction occurs, the hair stands up, resulting in "goose bumps" [*arrector* raiser, *pili* of hair, *mus-* mouse, *-cle* small]

arrhythmia (ah-RITH-mee-ah) term referring to any abnormality of cardiac rhythm ; also called **dysrhythmia** [*a-* without, *-rhythmos* rhythm, *-ia* condition]

arterial anastomosis (ar-TEER-ee-al ah-nas-toh-MOH-sis) junction between two arteries [*arteria-* vessel, *-al* relating to, *ana-* anew, *-stomo-*mouth, *-osis* condition] *pl.*, anastomoses

arterial blood Po_2 (ar-TEER-ee-al) partial pressure of oxygen in the blood of arteries [*arteri-* airpipe (artery), *-al* relating to; *P* pressure, O_2 oxygen]

arterial blood pressure (ar-TEER-ee-al) hydrostatic pressure of the blood in the arteries [*arteri-* airpipe (artery), *-al* relating to]

arteriogram (ar-TEER-ee-oh-gram) *see* **angiography** [*arteri-* artery, *-gram* drawing]

arteriole (ar-TEER-ee-ohl) small branch of an artery [*arteri-* vessel, *-ole* little]

arteriosclerosis (ar-tee-ree-oh-skleh-ROH-sis) hardening of arteries; materials such as lipids (as in atherosclerosis) accumulate in arterial walls, often becoming hardened via calcification [*arteri-* vessel (artery), *-sclero-* harden, *-osis* condition]

arteriovenous anastomosis (ar-teer-ee-oh-VEE-nus ah-nas-teh-MOH-sis) connection between an artery and a vein [*arteri-* vessel, *-ven-* vein, *-ous* relating to, *ana-* anew, *-stomo-*mouth, *-osis* condition] *pl.*, anastomoses

artery (AR-ter-ee) vessel carrying blood away from the heart [*arteri-* vessel]

arthritis (ar-THRY-tis) inflammation of joint structures [*arthr-* joint, *-itis* inflammation]

arthroplasty (AR-throh-plas-tee) the total or partial replacement of a diseased joint with an artificial device (prosthesis) [*arthr-* joint, *-plasty* surgical repair]

articular cartilage (ar-TIK-yoo-lar KAR-ti-lij) layer of hyaline cartilage covering the joint surfaces of epiphyses [*artic-* joint, *-ul-* little, *-ar* relating to, *cartilag* cartilage]

articulation (ar-tik-yoo-LAY-shun) joint [*artic-* joint, *-ul-* little, *-ation* state]

artificial immunity (ar-ti-FISH-al i-MYOO-ni-tee) immunization; deliberate exposure to potentially harmful antigens; as opposed to natural immunity [*artific-* not natural, *-al* relating to; *immun-* free, *-ity* state of]

artificial pacemaker (ar-ti-FISH-al PAYS-maykers) an electrical device that is implanted into the heart to treat problems with heart conduction [*artific-* not natural, *-al* relating to]

arytenoid (ar-eh-TEH-noyd) either of a pair of cartilages found in the supporting framework of the larynx [*aryten-* ladle, *-oid* like]

ascending aorta (ah-SEND-ing ay-OR-tah) portion of the aorta extending from the aortic valve to the aortic arch [*a[d]-* toward, *-scend-* climb, *aort-* lifted, *-a* thing] *pl.*, aortae *or* aortas

ascending colon (ah-SEND-ing KOH-lon) portion of the colon extending from the cecum to the hepatic flexure [*a[d]-* toward, *-scend-* climb, *colon* large intestine]

ascending tract (ah-SEND-ing) spinal cord tract that conducts impulses up the cord to the brain [*a[d]-* toward, *-scend-* climb,, *tract-* trail]

ascites (ah-SYE-tees) effusion (inflow of watery fluid) in the abdominal cavity; abdominal bloating [*askos-* bag]

aspiration biopsy cytology (ass-pih-RAY-shen BYE-op-see SYE-TOL-oh-jee) procedure that draws myeloid tissue into a syringe; allows for examination of tissue to confirm or reject diagnosis [*a-* act of, *-spir-* breathe, *-ation* process, *bio-* life, *-ops-* view, *-y* act of, *cyt-* cell, *-o-* combining form, *-log-* words (study of), *-y* activity]

assimilation (ah-sim-i-LAY-shun) the process of incorporation of a substance into the body [*assimila-* make alike, *-tion* process]

association tract (ah-so-see-AY-shun) most common cerebral tract; extends from one convolution to another in the same hemisphere [*associare-* to unite; *tractus-* trail]

aster (AS-ter) a starlike formation of microtubules (astral fibers) radiating outward from the centrosome (containing centrioles) during cell division; astral fibers anchor the centrosome and the spindle as chromosomes are pulled apart [*aster*, star]

asthma (AZ-mah) chronic obstructive pulmonary disorder characterized by recurring spasms of muscles in bronchial walls accompanied by edema and mucus production, making breathing difficult [*asthma* panting]

astigmatism (ah-STIG-mah-tiz-em) irregular curvature of the cornea or lens that impairs formation of a well-focused image in the eye [*a-* not, *-stigma-* point, *-ism* condition]

astrocyte (ASS-troh-syte) star-shaped neuroglial cell [*astro-* star shaped, *-cyte* cell]

astrocytoma (ass-troh-sye-TOH-mah) slow-growing neoplasm of astrocyte cells in the central nervous system [*astro-* star, *-cyt-* cell, *-oma* tumor]

atherectomy (ath-er-EK-to-mee) type of percutaneous coronary intervention (PCI) that uses a catheter to introduce lasers, drills, or spinning loops of wire to remove atherosclerotic plaque from an artery and thus clear the way for normal blood flow [*ather-* gruel, *-ec-* out, *-tom-* cut, *-y* action]

atherosclerosis (ath-er-oh-skleh-ROH-sis) type of "hardening of the arteries" in which lipids and other substances build up on the inside wall of blood vessels [*ather-* meal, *-sclero-* harden, -osis condition]

atom (AT-om) smallest particle of a chemical element that retains the properties of that element; particles that combine to form molecules (chemical building blocks) [*atom* indivisible]

atomic force microscopy (AFM) (ah-TOM-ik fors my-KRAH-skah-pee) form of microscopy in which an extremely fine-tipped needle drags over the surface to reveal the outer limits of the atoms and molecules that make up the surface [*atom-* indivisible, *-ic* relating to, *micro-* small, *-scop-* see, *-y* activity]

atomic mass (ah-TOM-ik) number of protons plus the number of neutrons in an atom of an element; also called *mass number* [*atom-* indivisible, *-ic* relating to]

atomic number (ah-TOM-ik) number of protons in an atom of an element [*atom-* indivisible, *-ic* relating to]

atomic weight (ah-TOM-ik) average (or range of) atomic mass of an atom of an element as it is found in nature; atomic weights are usually found in the periodic table of elements [*atom-* indivisible, *-ic* relating to]

ATP synthase (SIN-thays) enzyme that produces ATP molecules [*ATP* adenosine triphosphate, *syn-* together, *-ase* enzyme]

atrial fibrillation (A-fib or AF) (AY-tree-al fibril-LAY-shun) frequent, chaotic premature contractions of the atrium [*atri-* entrance courtyard, *-al* relating to, *fibr-* fiber, *-illa-* little, *-ation* process]

atrial natriuretic hormone (ANH) (AY-tree-al nay-tree-yoo-RET-ik HOR-mohn) hormone produced by the atrium that promotes secretion of sodium into the urine and therefore loss of water from the body [*atria-*entrance courtyard (atrium of heart), *-al* relating to, *natri-* natrium (sodium), *-uret-* urination, *-ic* relating to, *hormon-* excite]

atrioventricular (AV) bundle (ay-tree-oh-ven-TRIK-yoo-lar BUN-del) bundle of specialized cardiac muscle fibers that extend from the AV node to the subendocardial branches (Purkinje fibers); involved in coordination of heart muscle contraction [*atrio-* entrance courtyard, *-ventr-* belly, *-icul-* little, *-ar* relating to]

atrioventricular (AV) node (ay-tree-oh-ven-TRIK-yoo-lar) a small mass of special cardiac muscle tissue; part of the conduction system of the heart [*atrio-* entrance courtyard, *-ventr-* belly, *-icul-* little, *-ar* relating to, *-ar* relating to, *nod-* knot]

atrioventricular (AV) valve (ay-tree-oh-ven-TRIK-yoo-lar) either of two valves that separate the atrial chambers from the ventricles; also called *cuspid valve* [*atrio-* entrance courtyard, *-ventr-* belly, *-icul-* little, *-ar* relating to]

atrium (AY-tree-um) one of the upper chambers of the heart; receives blood from either the systemic or pulmonary circulation [*atrium* entrance courtyard] *pl.*, atria

atrophy (AT-ro-fee) wasting away of tissue; decrease in size of a part; sometimes referred to as *disuse atrophy* [*a-* without, *-troph-* nourishment, *-y* state]

auditory (AW-di-toh-ree) pertaining to hearing or the ear [*audit-* hear, *-ory* relating to]

auditory nerve (AW-di-toh-ree) cranial nerve VIII; *see* **vestibulocochlear nerve** [*audit-* hear, *-ory* relating to]

auditory ossicle (AW-di-toh-ree OS-ik-ul) any of the tiny bones in middle ear: malleus, incus, and stapes; they function to amplify sound waves passing from the eardrum to the membranes of inner ear [*audit-* hear, *-ory* relating to, *os-* bone, *-icle* little]

auditory tube (AW-di-toh-ree) tube that connects the throat with the middle ear and equalizes pressure between the middle ear and the exterior; also known as *Eustachian tube* [*audit-* hear, *-ory* relating to]

augmented lead (AWG-men-ted) one of three electrocardiogram leads based on combinations of the standard (appendicular) cardiogram leads [*augumentare-* to increase]

auricle (AW-ri-kul) part of the ear attached to the side of the head; earlike appendage of each atrium of the heart [*auricula-* little ear]

autocrine (AW-toh-krin) a type of hormone that regulates activity in the secreting cell itself [*auto-* self, *-crin* secrete]

autoimmune disease (aw-toh-i-MYOON) disorder in which the immune system reacts against cells of one's body [*auto-* self, *-immun-* free (immunity), *dis-* opposite of, *-ease* comfort]

autoimmunity (aw-toh-i-MYOO-ni-tee) immune system reaction against normal body structures (self-antigens) [*auto-* self, *-immun-*free, *-ity* state]

autologous transfusion (aw-TAHL-eh-gus) re-infusion of blood into your own body [*auto-* self, *-log-* word or proportion, *-ous* relating to]

autonomic (visceral) reflex (aw-toh-NOM-ik [VISS-er-al] REE-fleks) feedback regulatory mechanism of the autonomic nervous system in which autonomic (visceral) sensory receptors trigger a regulatory response [*auto-* self, *-nomo-* law *-ic* relating to, *viscer-* internal organ, *-al* relating to, *re-* again, *-flex* bend]

autonomic effector (aw-toh-NOM-ik ef-FEK-tor) tissues to which efferent (motor) autonomic neurons conduct impulses [*auto-* self, *-nomo* law, *-ic* relating to, *efficere-* to accomplish]

autonomic nervous system (ANS) (aw-toh-NOM-ik) division of the nervous system that monitors and regulates subconscious (involuntary) functions [*auto-* self, *-nom-* rule, *-ic* relating to, *nerv-* nerves, *-ous* relating to]

autopoiesis (aw-toe-poy-EE-sis) concept of self-organization and self-maintenance as a characteristic of all living organisms [*auto-* self, *-poiesis* making]

autoregulation (aw-toh-reg-yoo-LAY-shun) *see* **intrinsic control** [*auto-* self, *regula-* rule]

autorhythmic (aw-toh-RITH-mic) relating to the characteristic of certain cells (such as involuntary muscle fibers) to display a self-regulated repeating pattern of action, as when heart cells beat in a rhythm without external stimulation [*auto-* self, *-rhythm-* rhythm, *-ic* relating to]

autosome (AW-toh-sohm) one of the 44 (22 pairs) chromosomes in the human genome besides the two sex chromosomes; means "same body," in reference to each member of a pair of autosomes matching the other in size and other structural features [*auto-* self, *-som-* body]

avascular (ah-VAS-kyoo-lar) free of blood vessels [*a-* without, *-vas- vessel*, *-ula-* little, *-ar* relating to]

avitaminosis (ay-vye-tah-mi-NO-sis) general name for any condition resulting from a vitamin deficiency [*a-* without, *-vita-* life, *-amin-* ammonia compound, *-osis* condition]

avulsion fracture (ah-VUL-shun) type of bone fracture in which bone fragments have pulled away from the underlying bone surface or bone is torn completely from the body part [*avuls-* pull away, *-sion* process, *fracture* a breaking]

axial skeleton (AK-see-all SKEL-eh-ton) the bones of the head, neck, and torso [*axi-* axis, *-al* relating to]

axillary lymph node (AK-sil-lair-ee limf nohd) lymph node in the region at or near the armpit [*axilla-* wing, *-ary* relating to, *lymph* water, *nod-* knot]

axillary tail (of Spence) (AK-si-lar-ee tail of Spens) lateral extension of breast tissue that is in physical contact with several very large lymph nodes [*axilla-* wing, *-ary* relating to]

axillary vein (AK-si-lair-ee) vein of the armpit region [*axilla* wing, *-ary* relating to]

axon (AK-son) in a neuron, the single process that extends from the axon hillock and transmits impulses away from the cell body [*axon* axle]

axon collateral (AK-son koh-LAT-er-al) one or more side branches from the axon [*axon-* axle, *co-* with, together, *-lateralis* side]

axon hillock (AK-son HILL-ok) portion of the cell body from which the axon extends [*axon* axle, *hill-* hill *-ock* little]

axonal transport (AK-soh-nal trans-PORT) process of transporting vesicles, small organelles, and other structures along pathways inside the axon of a neuron [*axon* axle, *-al* relating to, *trans-* across, *-port* carry]

azygos vein (AZ-i-gohs) vein in the thorax [*a-* without, *-zygo-* union or yoke]

B

B cell immune system cell that produces antibodies against specific antigens; same as *B lymphocyte* [*B* bursa-equivalent tissue, *cell* storeroom]

B lymphocyte (B LIM-foh-syte) immune system cell that produces antibodies against specific antigens [*B* bursa-equivalent tissue, *lympho-* the lymph, *-cyte* cell]

Babinski reflex (bah-BIN-skee REE-fleks) *see* **plantar reflex** [*Joseph F.F. Babinski* French neurologist, *re-* again, *-flex* bend]

Babinski sign (bah-BIN-skee) extension of the great toe (with or without fanning of the other toes in response to stimulation of the outer margin of the foot, instead of the usual plantar reflex in which the toes curl in flexion; normal in infants but a sign of nerve dysfunction in adults [*Joseph F.F. Babinski* French neurologist]

bacterium (bak-TEE-ree-um) microorganism capable of causing disease; a primitive, single-celled organism without membranous organelles [*bacterium* small staff] *pl.*, bacteria

ball-and-socket joint spheroid joint, such as shoulder or hip joint; most movable type of joint [*soket* spearhead]

balloon angioplasty (AN-jee-oh-plas-tee) medical procedure in which vessels occluded by arteriosclerosis are opened (that is, the channel for blood flow is widened) by use of a balloon at the tip of a catheter (tube) inside the affected vessel; as the balloon is inflated, the blockage is pushed aside; *see* **angioplasty** [*angio-* vessel, *-plasty* surgical repair]

balloon kyphoplasty (KYE-foh-plas-tee) orthopedic procedure used to treat vertebral compression fracture [*kypho-* hump, *-plasty* surgical repair]

Bard endoscopic suturing system (en-doh-SKOP-ic) minimally invasive procedure used for treating serious cases of GERD [*endo-* within, *-scope* to look, *sutura-* a seam, *systema-* complex or organized whole]

baroreceptor (bar-oh-ree-SEP-tor) sensory neuron sensitive to changes in blood pressure [*baro-* pressure, *-recept-* receive, *-or* agent]

baroreflex (bar-oh-REE-fleks) feedback loop in which feedback from pressure receptors in arteries produces a regulatory effect such as a change in heart rate to restore normal blood pressure; also called *pressoreflex* [*baro-* pressure, *re-* again, *-flex* bend]

barrel (BARE-ul) cell organelle that resembles a tiny capsule and is thought to shuttle substances from place to place within a cell; also called *vault* [*barel-* barrel]

Barrett esophagus (eh-SOF-ah-gus) condition related to untreated gastroesophageal reflux disease; may develop precancerous changes in the esophageal lining [*Norman R. Barrett* English surgeon, *es-* will carry, *-phag-* food (eat)] *pl.*, esophagi

basal (BAY-sal) relating to the base or widest part of an organ or other structure; in a cell, pertains to the surface facing away from the lumen of an organ [*bas-* base, *-al* relating to]

basal cell (BAY-sal) cell of the base layer of a structure [*bas-* foundation, *-al* relating to, *cell* storeroom]

basal cell carcinoma (BAY-sal cell kar-si-NOH-mah) one of the most common forms of skin cancer; usually occurs on the upper face [*bas-* base, *-al* relating to, *cell* storeroom, *carcin-* cancer, *-oma* tumor]

basal ganglia (BAY-sal GANG-glee-ah) islands of gray matter located in the cerebrum of the brain that are responsible for automatic movements and postures; now known more properly as *basal nuclei* [*bas-* foundation, *-al* relating to *ganglion-* knot]

basal lamina (BAY-sal LAM-i-nah) glycoprotein material secreted by epithelial cells [*bas-*foundation, *-al* relating to *lamina-* thin plate]

basal metabolic rate (BMR) (BAY-sal met-ah-BAHL-ik) number of calories of heat that must be produced per hour by catabolism to keep the body alive, awake, and comfortably warm [*bas-* basis, *-al* relating to, *metabol-* change, *-ic* relating to]

basal nuclei (BAY-sal NOO-klee-eye) islands of gray matter located in the cerebrum of the brain that are responsible for automatic movements and postures; formerly known as *basal ganglia;* also known as *cerebral nuclei* [*bas-* foundation, *-al* relating to, *nucle-* nut or kernel] *sing.*, nucleus

base substance that ionizes in water to decrease the number of hydrogen ions; also known as *alkaline* [*bas-* foundation]

base pair adenine-thymine or cytosine-guanine; occurs when complementary bases from each helical chain of DNA are held together by hydrogen bonds [*bas-* foundation, *paria-* equal]

base-forming food food that produces a rise in pH inside the body [*bas-* foundation]

basement membrane the connective tissue layer of the serous membrane that holds and supports epithelial cells [*base-* base, *-ment* thing, *membrane* thin skin]

basic residue (BAYS-ick REHZ-ih-doo) remains or product of a chemical process that have a high pH [*bas-* foundation, *-ic* relating to, *residu-* remainder]

basilar membrane (BAYS-i-lar) *see* **spiral membrane** [*bas-* foundation, *-ar* relating to, *membran-* thin skin]

basilic vein (bah-SIL-ik) a vein of the forearm [*bas-* foundation, *-ic* relating to]

basophil (BAY-so-fil) white blood cell that stains readily with basic (alkaline) dyes [*bas-*foundation, *-phil* love]

basophilic erythroblast (BAY-so-fil-ik eh-rith-roh-BLAST) produced during red blood cell formation; results from the mitotic division of proerythroblast [*bas-* foundation, *-phil- love*, *-ic* relating to, *erythro-* red, *-blast* bud]

belly the central portion of a organ, such as a skeletal muscle [*beig-* bag]

benign (bee-NYNE) refers to a tumor, neoplasm, or other condition that does not metastasize (spread to different tissues) or otherwise cause serious harm [*benign* kind]

benign paroxysmal positional vertigo (BPPV) (be-NYNE par-ock-SIZ-mul poh-ZISH-i-nal VER-ti-go) type of vertigo associated with inner ear problems [*benign* kind, *paroxysm-* irritation, *-al* relating to, *vertigo* turning]

benign prostatic hypertrophy (BPH) (be-NYNE pro-STAT-ik hye-PER-troh-fee) a nonmalignant enlargement of the prostate gland [*benign* kind, *pro-* before, *-stat-* set or place, *-ic* relating to, *hyper-* excessive or above, *-troph-* nourishment, *-y* state]

beta blocker (BAY-tah) drug that blocks beta receptors and therefore prevents dilation of blood vessels and increased contraction of heart muscle [*beta* second letter of Greek alphabet]

beta cell (BAY-tah) pancreatic islet cell that secretes insulin; also called *B cell* [*beta* (β) second letter of Greek alphabet, *cell* storeroom]

beta particle (BAY-tah PAR-tih-kul) electrons formed in a radioactive atom's nucleus by a neutron breaking down into a proton and an electron [*beta* (β)- second letter of Greek alphabet, *particula-* small part]

beta (β) receptor (BAY-tah ree-SEP-tor) adrenergic receptor that, when stimulated, causes vessels to dilate and heart muscle to contract faster and stronger [*beta* second letter of Greek alphabet, *recept-* receive, *-or* agent]

beta-adrenergic blocker (BAY-tah-ad-ren-ER-jik) *see* **beta blocker** [*beta* (β) second letter of Greek alphabet, *ad-* toward, *-ren-* kidney, *-erg-* work, -ic relating to]

beta-hydroxybutyric acid (BAY-tah-hye-DROK-see-boo-teh-rik ASS-id) acidic ketone body that accumulates during the incomplete breakdown of fats [*beta* (β) second letter of Greek alphabet, *-hydro-* hydrogen, *-oxy-* oxygen, *-butyr-* butter , *-ic* relating to, *acid-* sour]

biaxial joint (bye-AK-see-al) skeletal articulation that has two axes of movement [*bi-* two, *-axi-* axle, *-al* relating to]

bicarbonate (bye-KAR-boh-nayt) *see* **bicarbonate ion** [*bi-* two, *-carbon*, coal (carbon), *-ate* oxygen compound]

bicarbonate ion (bye-KAR-boh-nayte EYE-on) HCO_3^-; an ion that serves an important role in maintaining normal blood pH [*bi-*twice, *-carbo-* coal, *-ate* oxygen]

bicarbonate loading (bye-KAR-boh-net) practice in which a person ingests bicarbonates to counteract the buildup of acids in the body [*bi-* two, *-carbon-* coal (carbon), *-ate* oxygen]

bicuspid (bye-KUSS-pid) having two cusps [*bi-* double, *-cusp-* point, *-id* characterized by]

bilateral symmetry (bye-LAT-er-al SIM-e-tree) concept of the right and left sides of the body being approximate mirror images of each other [*bi-* two, *-later-* side, *-al* relating to, *sym-* together, *-metr-* measure, *-ry* condition of]

bile (byle) mixture of excretions and secretions produced by the liver and released into the digestive tract [*bilus-* fluid secreted by the liver]

bile salt (byle) an emulsifying agent found in bile [*bilus-* fluid secreted by the liver]

bilirubin (bil-ih-ROO-bin) yellowish pigment formed when the heme group is removed from the hemoglobin molecule and stripped of its iron atom; a product of the breakdown of red blood cells [*bili-* bile, *-rub-* red, *-in* substance]

binge-purge syndrome (binj-purj SIN-drohm) eating disorder in which a person overeats and then induces vomiting [*syn-* together, *-drome* running or (race) course]

biochemistry (bye-oh-KEM-is-tree) science of chemistry of living organisms [*bio-* life, *-chemeia* alchemy]

biofeedback (bye-oh-FEED-bak) method of learning to consciously control autonomic effectors by monitoring autonomic biological functions [*bio-* life]

biological clock (bye-oh-LOJ-i-kal) internal timing mechanism that governs hunger, sleeping, reproduction, and behavior [*bio-*life, *-o-* combining form, *-log-* words (study of), *-ical* relating to]

biopsy (BYE-op-see) procedure in which living tissue is removed from a patient for laboratory examination, as in determining the presence of cancer cells [*bio-* life, *-opsy-* view, *-y* act of]

Biot's breathing (bee-OHS) breathing pattern characterized by repeated sequences of deep gasps and apnea due to increased intracranial pressure [*Camille Biot* French physician]

bioterrorism (bye-oh-TAIR-or-iz-em) act of using biological weapons such as disease pathogens to spread terror among civilian populations for the purpose of creating fear, panic, and general social disruption [*bio-*life, *terrere-* to frighten, *-ism* condition of]

bipolar neuron (bye-POH-lar NOO-ron) neuron with only one dendrite and only one axon [*bi-* two, *-pol-* pole, *-ar* relating to, *neuron* nerves]

blackhead sebum that accumulates, darkens, and enlarges a duct of the sebaceous glands, as in the case of acne; also known as a *comedo* [*blakkr-* dark]

blastocyst (BLASS-toh-sist) stage of developing embryo that implants in uterine wall; consists of hollow ball of cells plus an inner cell mass [*blasto-* bud, *-cyst* pouch]

bleaching (BLEECH-ing) process when opsin and retinal open and separate in the presence of light [*blechen-* bleach]

blepharoplasty (blef-ar-oh-PLAS-tee) surgical procedure that corrects a drooping eyelid [*blepharo-* eyelid or eyelash, *-plasty* surgical repair]

blind spot point on retina where blood vessels and nerves exit the eyeball; "blind" portion of visual field resulting from no photoreceptors present in that portion of retina; also known as *optic disk* [*blesti-* to become dark, *spotte-* speck]

blister (BLIS-ter) fluid-filled skin lesion; *see* **vesicle** [*blestre-* boil]

blood boosting *see* **blood doping**

blood clotting *see* **blood coagulation** [*clott-* lump]

blood coagulation (koh-ag-yoo-LAY-shun) process by which ruptured vessels are plugged up to stop bleeding and prevent loss of precious body fluids [*coagulare-* to curdle]

blood colloid osmotic pressure (BCOP) (blud KOL-loyd os-MOT-ik) filtration pressure that tends to draw fluid back to the capillaries [*coll-* glue, *-oid* like, *osmo-* push, *-ic* relating to]

blood doping (DOH-ping) practice of increasing the hematocrit by transfusing additional blood or by the use of erythropoietin to boost hematocrit [*dyppan-* to dip]

blood hydrostatic pressure (BHP) (hye-droh-STAT-ik) pressure of blood against the wall of a blood vessel [*hydro-* water, *-stat-* standing, *-ic* relating to]

blood loss anemia (ah-NEE-mee-ah) deficiency of red blood cells and hemoglobin caused by a loss of blood from the cardiovascular system [*an-* without, *-emia* blood condition]

blood serum (SEER-um) in a sample of blood, the pale yellowish liquid left after a clot forms [*serum* watery fluid] *pl.*, sera

blood test clinical laboratory examination of blood components [*testum-* test]

blood type one of the four different types of blood; identified by certain antigens on red blood cells (A, B, AB, and O) [*tupos-*impression]

blood urea nitrogen (BUN) test (yoo-REE-ah NYE-troh-jen) clinical laboratory measurement of the amount of nitrogen in urea present in the blood and used as a measure of the efficiency of the kidney's ability to clear urea from the body [*ure-* urine, *nitro-*soda, *-gen* produce]

blood-brain barrier (BBB) structural and functional barrier formed by astrocytes and blood vessel walls in the brain; it prevents some substances from diffusing from the blood into brain tissue [*barrere-* barrier]

blood-testis barrier (BTB) (blud-TES-tis) functional barrier between the testis and the rest of the body, thus protecting developing sperm from attack by the immune system [*testis-* witness (male gonad), *barrere-*barrier]

blowout fracture bone fracture of the eye orbit [*fracture* a breaking]

body the structure of the entire organism; also, the main part of an organ, cell, or other structure [*bodig-* body]

body composition (com-poh-ZISH-un) percentages of the body made of lean tissue and fat tissue [*componere-* to assemble]

body mass index (BMI) method used to assess whether a person's body weight is proportional to height [*indicare-* to make known]

body plane imagined flat surface that cuts through the body at any of various angles; *see* **coronal plane, sagittal plane, transverse plane** [*bodig-* body, *planum-* flat surface]

Bohr effect (BOR) when increased P_{CO_2} decreases the affinity between hemoglobin and oxygen [*Christian Bohr* Danish physiologist]

boil (BOY-el) carbuncle; pus-filled lesion of the skin [from *bile*]

bolus (BOW-lus) rounded mass of food that is swallowed [*bolos-* lump]

bone age method using the number of ossification centers visible on a radiograph to determine the maturation of bone

bone marking specific structural feature on an individual bone

bone marrow transplant (MAIR-oh TRANS-plant) medical procedure in which bone marrow tissue from a donor is placed in a recipient in hopes that it will produce healthy blood cells [*marow-* marrow, *transplantare-* transplant]

bone matrix (MAY-triks) intercellular material of the bone tissue [*matrix* womb] *pl.*, matrices (MAY-trih-seez)

bone scan medical imaging technique in which the density of bone is visualized

bone tamp inflatable balloon-like device used in balloon kyphoplasty; stabilizes and seals fractures [*tamp* pack down]

bone type of connective tissue whose matrix is hard and calcified

bone-seeking isotope (EYE-soh-tohp) radioactive element that will substitute for calcium in apatite crystals of bone; causes damage to red marrow and other tissues by radioactive emissions [*iso-* equal, *-topos* place]

booster shot additional vaccination that boosts the immune response against a particular antigen

Bouchard node (boo-SHAR) swelling deformity of the proximal interphalangeal joint [*Charles J. Bouchard* French physician, *nod-* knot]

bovine spongiform encephalopathy (BOH-vyne SPUNJ-i-form en-SEF-al-ah-path-ee) also known as *BSE* or "mad cow disease"; a

degenerative disease of the central nervous system caused by prions that convert normal proteins of the nervous system into abnormal proteins, causing loss of nervous system function; the abnormal form of the protein also may be inherited; *see* **prion** [*bos-* ox *spongi-* like a sponge, *form* specialized shape *encephal-* brain, *-pathy* disease]

Bowman capsule (BOH-men KAP-sul) in the kidney, the cup-shaped top of a nephron that surrounds the glomerulus; also called *glomerular capsule* [*William Bowman* English anatomist]

Boyle's law (boils) principle of physics that states that the pressure of a gas is proportional to its volume [*Robert Boyle* English scientist]

brachial plexus (BRAY-kee-all PLEK-sus) nerve plexus located deep in the shoulder that innervates the lower part of the shoulder and the entire arm [*brachi-* arm, *-al* relating to, *plexus* network] *pl.*, plexi or plexuses

brachial vein (BRAY-kee-al) vein of the arm [*brachi-* arm, *-al* relating to]

brachiocephalic artery (brayk-ee-oh-seh-FAL-ik AR-ter-ee) artery of the upper thorax [*brachi-* arm, *-cephal-* head, *-ic* relating to, *arteri-*vessel]

brachiocephalic vein (brayk-ee-oh-seh-FAL-ik) vein of the upper thorax [*brachi-* arm, *-cephal-* head, *-ic* relating to]

bradycardia (bray-dee-KAR-dee-ah) slow heart rhythm (below 50 beats/min) [*brady-* slow, *-cardi-* heart, *-ia* condition]

bradykinin (brad-ee-KYE-nin) chemical mediator released after tissue injury and cellular death [*brady-* slow or dull, *-kinin* move]

brain electrical activity map (BEAM) color-coded graphic image of the brain generated on a video screen [*electron-* amber, *acitivus-* active]

brain part of central nervous system contained within the cranium; consists of medulla oblongata, cerebellum, and cerebrum [*bragen-* brain]

brain waves fluctuating electrical activity occurring in the brain [*bragen-* brain]

brainstem part of brain containing the midbrain, pons, and medulla oblongata [*bragen-* brain, *-stem* tree or trunk]

breast cancer malignant neoplasm (tumor) of the breast [*cancer* crab or malignant tumor]

broad ligament (LIG-ah-ment) double fold of parietal peritoneum that forms a partition across the pelvic cavity [*liga-* bind, *-ment* condition]

bronchial tree (BRONG-kee-al) the trachea, two primary bronchi, and their many branches [*bronch-* windpipe, *-al* relating to]

bronchial vein (BRONK-kee-al) vein of the pulmonary airways [*bronch-* windpipe, *-al* relating to]

bronchiole (BRONG-kee-ohl) small branch of a bronchus [*bronch-* windpipe, *-ol-* little]

bronchitis (brong-KYE-tis) inflammation of the bronchi of the lungs, characterized by edema and excessive mucus production that causes coughing and difficulty in breathing (especially expiration) [*bronch-* windpipe, *-itis* inflammation]

bronchogram (BRONG-koh-gram) medical image of the pulmonary airways [*bronch-* windpipe, *-gram* drawing]

bronchopulmonary segment (brong-koh-PUL-moh- nair-ee) region of the lung supplied by a tertiary bronchus [*bronch-* windpipe, *-pulmon-* lung, *-ary* relating to]

bruits (BROO-eez) blood vessel noise caused by turbulence of blood flow [*bruits* noise]

brush border lining of small intestine that resembles bristles of a brush; formed by microvilli [*brusshe-* brush, *border-* to border]

buccal cavity (BUK-al KAV-i-tee) oral cavity [*bucca-* cheek]

buccinator muscle (BUK-si-NAY-tor) muscle of the cheek [*buccinator* trumpeter, *mus-* mouse, *-cle* little]

buffer (BUFF-er) compound that combines with an acid or with a base to form a weaker acid or base, thereby lessening the change in hydrogen ion concentration that would occur without the buffer; often operates as buffer pairs [*buffe-* cushion, *-er* actor]

buffer pair (BUFF-er) a chemical system of two chemicals that together act as a buffer, minimizing changes in pH of a solution [*buffe-* cushion, *-er* agent]

buffy coat found in a centrifuged sample of blood, the thin layer of leukocytes and platelets located at the interface between packed red cells and plasma [*buffe-* cushion]

bulboid corpuscle (BUL-boyd KOR-pus-ul) skin receptor that detects sensations of touch, low-frequency vibration, and texture differences; also known as *Krause end bulb* [*bulb-* swollen root, *-oid* like, *corpus-* body, *-cle* little]

bulbospongiosus muscle (bul-boh-spun-jee-OH-ses) muscle of the base of the penis [*bulbo-* swollen root (bulb), *-spongiosus* spongy, *mus-* mouse, *-cle* little]

bulbourethral gland (BUL-boh-yoo-REE-thral) either of two small glands at the base of the penis that contributes a small amount of fluid to semen; also called *Cowper gland* [*bulb-* swollen root, *-ure-* urine, *-thr-* agent or channel (urethra), *-al* relating to]

bulbous corpuscle (BUL-bus KOR-pus-ul) sensory receptor that senses deep pressure and continuous touch; located in dermis of the skin; also known as *Ruffini corpuscle* [*bulb-* swollen root, *-ous* relating to, *corpus-* body, *-cle* little]

bulimia (boo-LEE-mee-ah) eating disorder characterized by intentional purging of food by induced vomiting, laxatives, or other means [*bu-* ox, *-lim-* hunger, *-ia* condition]

bursa (BER-sah) small, cushion-like sac found between moving body parts, making movement easier [*bursa* purse] *pl.*, bursae (BER-see or BER-say)

bursitis (ber-SYE-tiss) inflammation of a bursa [*bursa-* purse, *-itis* inflammation]

bypass surgery (BYE-pass SUR-jah-ree) *see* **coronary bypass surgery** [*bi-* alongside, *surgery-* treatment of illness or deformity]

C

C cell type of cell of the thyroid gland that produces calcitonin [C for calcitonin, *cell* storeroom]

CA-125 tumor antigen associated with ovarian cancer [C cancer, A antigen]

cachexia (kah-KEKS-ee-ah) syndrome involving loss of weight, loss of appetite, and general weakness; usually associated with cancer [*kakos-* bad, *-hexis* state]

cadaver (kah-DAV-er) corpse preserved for anatomical study [*cadaver* dead body]

calcaneal tendon (kal-KAH-nee-al) connects gastrocnemius to calcaneus; Achilles tendon [*calcane-* heel, *-al* relating to, *tend-* pulled tight, *-on* unit]

calcitonin (CT) (kal-sih-TOH-nin) hormone secreted by the thyroid that decreases calcium levels in the blood [*calci-* lime (calcium), *-ton-* tone, *-in* substance]

calcitriol (kal-SIT-ree-ol) hormone that regulates calcium homeostasis in the body [*calci-* lime (calcium), *-tri-* three, *-ol* alcohol (after *1,25-D*$_3$ or *1,25-dihydroxycholecalciferol*)]

calcium (KAL-see-um) important mineral involved in bone formation, tooth formation, muscle contraction, synaptic transmission, and other vital processes of the body [*calc-*lime, *-um* thing or substance]

calcium channel blocker (KAL-see-um CHAN-al) agent that inhibits the opening of calcium channels in cell membranes [*calc-* lime, *-um* thing or substance]

calcium pump (KAL-see-um) energy-consuming structure embedded in a cell membrane that moves calcium ions through the membrane against their concentration gradient (that is, from an area of low concentration to an area of high concentration) [*calc-*lime, *-um* thing or substance]

calendar rhythm method method of fertility management based on timing of the female reproductive cycle [*calenda-* account book, *meta-* after, *-hodos* journey]

callus (KAL-us) bony tissue that forms a sort of collar around the broken ends of fractured bone during the healing process; in the skin, abnormally thick stratum corneum found at points of friction [*callus* hard skin]

Calorie (C) (KAL-or-ree) heat unit; kilocalorie (kcal); the amount of heat needed to raise the temperature of 1 kilogram of water 1° C [*calor-* heat, *-ie* full of]

calorie (cal) (KAL-or-ee) heat unit; the amount of heat needed to raise the temperature of 1 gram of water 1° C [*calor-* heat, *-ie* full of]

calvarium (kal-VAIR-ee-um) name for the upper dome of the cranium of the skull [*calvarium* skull] *pl.*, calvaria or calvariums

calyx (KAY-liks) cup-shaped branch of the renal pelvis [*calyx* cuplike] *pl.*, calyces (KAY-lis-eez)

canal of Schlemm (kah-NAL of shlem) *see* **scleral venous sinus** [*canal-* channel, *Friedrich Schlemm* German anatomist]

canaliculi (kan-ah-LIK-yoo-lye) an extremely narrow tubular passage or channel in compact bone; radiates from lacunae and connects with other lacunae and the central (Haversian) canal of the osteon [*canal-* channel, *-iculi* little] *sing.*, canaliculus

canaliculus (kan-ah-LIK-yoo-lus) singular of **canaliculi** [*canal-* channel, *-uculus* little]

canalith (KAN-ih-lith) crystalline structure of the semicircular canals of the inner ear [*canal-* channel, *-lith* stone]

canalith repositioning procedure (KAN-ih-lith) procedure to restore the proper position of crystalline structures of the semicircular canals of the ear and thus eliminate balance perception problems such as vertigo [*canal-* channel, *-lith* stone]

cancellous bone (KAN-seh-lus) bone containing tiny, branchlike trabeculae; also known as *spongy bone* or *trabecular bone* [*cancel-* lattice, *-ous* characterized by]

cancellous bone tissue (KAN-seh-lus) *see* **cancellous bone** [*cancel-* lattice, *-ous* characterized by, *tissu-* fabric]

cancer malignant cellular neoplasm (tumor) that invades other cells and often metastasizes to many parts of the body [*cancer* malignant tumor]

cancer of the uterus (YOO-ter-us) malignancy of uterine tissue [*cancer* crab or malignant tumor]

candidiasis (kan-dih-DYE-eh-sis) infection caused by *Candida* yeast [*candid-* white, *-asis* condition]

capacitance (kah-PASS-i-tens) the ease of stretch (distensibility) of a blood vessel wall [*capacit-* space or volume, *-ance* state]

capacitation (kah-pass-i-TAY-shun) process occurring after ejaculation of semen and needed for a mature sperm to become capable of fertilizing an ovum [*capacit-* space or volume, *-tion* process]

capillary (KAP-i-lair-ee) tiny vessels that connect arterioles and venules; gas exchange from blood to tissues occurs in capillaries [*capill-* hair, *-ary* relating to]

capillary exchange (KAP-i-lair-ee) process of moving molecules into and out of the blood of a capillary [*capill-* hair, *-ary* relating to]

capitulum (kah-PITCH-uh-lum) rounded knob on the humerus bone below the lateral epicondyle [*capit-* head, *-ulum* little]

carbaminohemoglobin (kahr-bam-ih-no-hee-moh-GLOH-bin) carbonated form of hemoglobin [*carb-* coal (carbon), *-amino-* ammonia compound (amino acid), *-hemo-* blood, *-glob-* ball, *-in* substance]

carbohydrate (kar-bo-HYE-drate) organic compounds containing carbon, hydrogen, and oxygen in certain specific proportions; for example, sugars, starches, and cellulose [*carbo-* carbon, *-hydr-* hydrogen, *-ate* oxygen]

carbon monoxide (CO) (KAR-bon mon-OKS-ide) molecule made up of one carbon atom and one oxygen atom [*mono-* single, *-ox-* sharp (oxygen), *-ide* chemical]

carbon monoxide poisoning (KAR-bon mon-OK-side POY-son-ing) condition in which exposure to carbon monoxide results in the molecule tightly binding to hemoglobin and thereby preventing oxygen transport by the blood [*carbon* coal, *mono-* single, *-ox* sharp (oxygen)]

carbonic acid (kar-BON-ik ASS-id) product of the reaction between carbon dioxide and water [*carbon-* coal (carbon), *-ic* relating to, *acid* sour]

carbonic anhydrase (CA) (kar-BON-ik an-HYE-drays) the enzyme that converts carbon dioxide into carbonic acid (and also reverses the reaction) [*carbo-* coal, *-ic* relating to, *a-* without, *-hydr-* water, *-ase* enzyme]

carbuncle (KAR-bung-kul) a mass of connected boils, pus-filled lesions associated with hair follicle infections; *see* **furuncle** [*carbunculus-* little coal]

carcinoembryonic antigen (CEA) (kar-sin-oh-em-bree-AHN-ik AN-ti-jen) tumor marker found normally in the fetus and elevated colorectal and other adult cancers [*carcino-* cancer, *-em-* in, *-bryo-* fill to bursting, *-ic* relating to, *anti-* against, *-gen* produce]

carcinogen (kar-SIN-oh-jen) substance that promotes the development of cancer [*carcino-* cancer, *-gen* produce]

carcinoma (kar-si-NO-mah) malignant tumor that arises from epithelial tissue [*carcin-* cancer, *-oma* tumor]

cardia (KAR-dee-ah) small collarlike section of the stomach near the junction with the esophagus, so-called because of its nearness to the heart; also called *cardiac part* or *cardial part* [*cardia* heart]

cardiac cycle (KAR-dee-ak) complete heartbeat consisting of diastole and systole of both atria and both ventricles [*cardi-* heart, *-ac* relating to, *cycle* circle]

cardiac muscle tissue (KAR-dee-ak) muscle tissue type that makes up the heart [*cardia-* heart, *-ac* relating to, *mus-* mouse, *-cle* small, *tissu-* fabric]

cardiac nuclear scanning (KAR-dee-ak NOO-klee-ar) medical image of the heart produced when radioactive materials flow through the coronary vessels [*cardi-* heart, *-ac* relating to, *nucle-* nut or kernel, *-ar* relating to]

cardiac output (CO) (KAR-dee-ak) volume of blood pumped by one ventricle per minute (example, L/min or ml/min) [*cardi-* heart, *-ac* relating to]

cardiac part (KAR-dee-ak) see **cardia** [*cardi-* heart, *-ic* relating to]

cardiac plexus (KAR-dee-ak PLEK-sus) combination of sympathetic and parasympathetic nerves that are located near the aortic arch [*cardi-* heart, *-ac* relating to, *plexus-* network]

cardiac pressoreflex (KAR-dee-ak pres-oh-REE-fleks) feedback regulatory mechanism in which pressure receptors in arteries trigger a change in heart rate to restore normal blood pressure [*cardi-* heart, *-ac* relating to, *press-* pressure, *-re-* back or again, *-flex* bend]

cardiac sphincter (KAR-dee-ak SFINGK-ter) a ring of muscle between the stomach and esophagus that prevents food from

reentering the esophagus when the stomach contracts [*cardi-* heart, *-ic* relating to, *sphinc-*bind tight, *-er* agent]

cardiac tamponade (KAR-dee-ak tam-po-nodd) compression of the heart caused by fluid buildup in the pericardial space, as in pericarditis or mechanical damage to the pericardium [*cardi-* heart, *-ac* relating to, *tampon-* plug, *-ade* process]

caries (KAIR-ees) decay, especially tooth decay [*caries* decay]

cardiogenic shock (kar-dee-oh-JEN-ik) condition characterized by low cardiac output; can result from any type of heart failure [*cardi-* heart, *-gen-* produce, *-ic* relating to]

cardiomyopathy (kar-dee-oh-my-OP-ah-thee) general term for disease of the myocardium (heart muscle) causing enlargement [*cardi-* heart, *-myo-* muscle, *-path-* disease, *-y* state]

cardiopulmonary resuscitation (CPR) (kar-dee-oh-PUL-moh-nair-ree ree-sus-i-TAY-shun) combined external cardiac (heart) massage and artificial respiration [*cardio-* heart, *pulmon-* lung, *resuscitare-* to revive]

caries (KAIR-eez) decay of teeth or of bone [*caries-* decay]

carotene (KAR-oh-teen) yellowish pigment; contributes to skin color [*carota-* carrot]

carotid sinus reflex (kah-ROT-id SYE-nus REE-fleks) homeostatic mechanism that involves baroreceptors that relay feedback information to cardiac control center; maintains blood pressure [*caro-* heavy sleep, *-id* relating to, *sinus* hollow, *re-* back or again, *-flex* bend]

carpal bone (KAR-pul) any of the bones of the wrist [*carp-* wrist, *-al* relating to]

carpal tunnel syndrome (KAR-pul TUN-el SIN-drohm) muscle weakness, pain, and tingling in the radial side (thumb side) of the wrist, hand, and fingers, perhaps radiating to the forearm and shoulder; caused by compression of the median nerve within the carpal tunnel (a passage along the ventral concavity of the wrist) [*carp-* wrist, *-al* relating to, *syn-* together, *-drome* running or (race) course]

carpometacarpal joint (kar-pol-met-ah-KAR-pal) skeletal articulation between a wrist (carpal) bone and hand (metacarpal) bone [*carpo-* wrist, *-meta-* beyond, *-carp-*wrist, *-al* relating to]

carrier (KARE-ee-er) in genetics, a person who possesses the gene for a recessive trait but who does not actually exhibit the trait; in cell biology, a protein structure in the membrane that facilitates transport of ions and other molecules [*carier-* to transport in a vehicle]

carrier-mediated passive transport (KARE-ee-er MEE-dee-ayt-ed PASS-iv TRANS-port) type of facilitated diffusion, in which solutes move down their concentration gradient through carrier mechanisms in the membrane wall [*mediat-* to be in the middle, *passus-* capable of suffering, *trans-* across, *-portare* to carry]

cartilage (KAR-tih-lij) connective tissue type that has the consistency of a firm plastic or gristle-like gel [*cartilag-* cartilage]

cartilaginous joint (kar-tih-LAJ-in-us joynt) articulation between bones that is primarily composed of cartilage [*cartilag-* cartilage, *-in-* substance, *-ous* characterized by]

catabolism (kah-TAB-oh-liz-em) breakdown of food compounds or cytoplasmic constituents into simpler compounds; opposite of anabolism [*cata-* against, *-bol-* to throw, *-ism* condition]

catalyst (KAT-ah-list) chemical that speeds up reactions without being changed itself [*cata-* lower, *-lys-* loosen, *-st* agent]

cataracts (KAT-ah-rakts) areas of opacity in the lens of the eye [*cataract* waterfall]

catecholamine (kat-eh-KOHL-ah-meen) chemical category of neurotransmitters that include norepinephrine, epinephrine, and dopamine [*catech-* melt, *-ol-* alcohol, *-amine* ammonia compound]

catheter (KATH-eh-ter) thin, flexible tube often used in medical procedures [*cathe-* send down, *-er* agent]

catheterization (kath-eh-ter-i-ZAY-shun) passage of a flexible tube (catheter) into the body through an exterior opening (as into the bladder through the urethra for the withdrawal of urine) [*cathe-* send down, *-er* agent, *-tion* process of]

cation (KAT-eye-on) positively charged particle [*cat-* down, *-ion* to go (ion)]

cauda equina (KAW-da eh-KWY-nah) lower end of spinal cord with its attached spinal nerve roots [*caud-* tail, *equina* of a horse] *pl.*, caudae equinae

caudate nucleus (KAW-dayt NOO-klee-us) one of the basal nuclei, gray matter areas in the inner region of the cerebrum of the brain [*caud-* tail, *-ate* of or like, *nucleus* nut or kernel] *pl.*, nuclei

caveola (kav-ee-OH-la) tiny indentation of a raft in the cell's plasma membrane that traps substances and shuttles them into or through the cell [*cave-* hollow, *-ola* little] *pl.*, caveolae

CD system international system for naming surface markers on red blood cells [*C* cluster, *D* differentiation]

celiac ganglion (SEE-lee-ak GANG-glee-on) solar plexus; collateral ganglion that lies just below the diaphragm [*cel-* belly, *-ac* relating to, *ganglion* knot]

cell basic biological and structural unit of the body consisting of a nucleus surrounded by cytoplasm and enclosed by a membrane [*cell* storeroom]

cell agranulocyte (ah-GRAN-yoo-loh-syte) one of two types of white blood cells; lymphocyte or monocyte [*a-* without, *-gran-* grain, *-ul-* little, *-cytes* cells]

cell body the main part of a cell, ordinarily containing the nucleus; in the neuron, the cell body is also called the *soma* or *perikaryon* [*cell* storeroom]

cell cycle *see* **cell life cycle** [*cell-* storeroom, *cycle* circle]

cell life cycle the repeating process of a cell's growth and reproduction, producing successive generations of cells and proceeding through the first growth phase (G1), DNA replication (S), second growth phase (G_2), and mitotic cell division (M); also called *cell cycle* [*cell-* storeroom, *lif-* life, body, *cycle-* circle]

cell theory concept proposed more than 100 years ago that all living organisms are made up of biological units called *cells*; *see* **cell** [*cell* storeroom, *theor-* look at, *-y* act of]

cell-mediated immunity (sell-MEE-dee-ayt-ed i-MYOO-nih-tee) type of adaptive immunity in which T-lymphocytes act directly on antigens to protect the body [*cell* storeroom, *medi-* middle, *-ate* process, *immun-* free, *-ity* state]

cellular immunity (SELL-yoo-lar i-MYOO-ni-tee) see **cell-mediated immunity** [*cell* storeroom, *-ular* relating to, *immun-* free, *-ity* state]

cellular respiration (SELL-yoo-lar res-pih-RAY-shun) set of biochemical reactions of a cell that transfer energy from nutrient molecules to ATP molecules [*cell* storeroom, *-ular* relating to, *respire-* to breathe, *-ation* process]

cellulose (SEL-yoo-lohs) dietary fiber; major component of most plant tissue; nondigestable by humans [*cell-* storeroom (cell), *-ul-* small, *-ose* carbohydrate]

central relating to the center of the body, as in *central nervous system* [*centr-* center, *-al* relating to]

central canal canal in the osteon (Haversian system) of bone that runs parallel to the long axis; contains blood vessels and nerves; also called *osteonal canal* or *Haversian canal* [*centr-* center, *-al* relating to, *canal-* channel]

central nervous system (CNS) the brain and spinal cord [*centr-* center, *-al* relating to, *nerv-* nerves, *-ous* relating to]

central sulcus (fissure of Rolando) (SUL-kus [FISH-ur of roh-LAHN-doh]) groove between frontal and parietal lobes of the cerebrum [*sulcus* trench, *Luigi Rolando* Italian physician] *pl.*, sulci

centriole (SEN-tree-ohl) one of a pair of tiny cylinders in the centrosome of a cell; believed to be involved with the spindle fibers formed during mitosis [*centr-* center, *-ole* small]

centromere (SEN-troh-meer) a beadlike structure that attaches one chromatid to another during the early stages of mitosis [*centro-* center, *-meros* part]

centrosome (SEN-troh-sohm) area of the cytoplasm near the nucleus that coordinates the building and breaking up of microtubules in the cell [*centr-* center, *-som-* body]

cephalic phase (seh-FAL-ik fayz) stage in regulation of stomach secretion in which mental factors stimulate gastric juice secretion [*cephal-* head, *-ic* relating to]

cephalic vein (seh-FAL-ik) vein of the head [*cephal-* head, *-ic* relating to]

cerebellum (sair-eh-BELL-um) second largest part of the human brain; plays an essential role in the production of normal movements [*cereb-* brain, *-ellum* small thing] *pl.*, cerebella or cerebellums

cerebral cortex (seh-REE-bral KOR-teks) thin layer of gray matter made up of neuron dendrites and cell bodies that compose the surface of the cerebrum [*cerebr-* brain (cerebrum), *-al* relating to, *cortex* bark] *pl.*, cortices

cerebral hemisphere (seh-REE-bral HEM-is-feer) either of the two right and left halves of the cerebrum [*cerebr-* brain, *-al* relating to, *hemi-* half, *-sphere* globe]

cerebral localization (seh-REE-bral) principle of brain function that states that specific cerebral functions are likely to be located in the cerebral cortex at specific, often predictable, locations [*cerebr-* brain, *-al* relating to, *loc-* place, *-al-* relating to, *-ization* process]

cerebral nuclei (seh-REE-bral NOO-klee-eye) *see* **basal nuclei** [*cerebr-* brain, *-al* relating to, *nucleus-* nut or kernel]

cerebral palsy (seh-REE-bral PAWL-zee) disorder in which damage to motor control areas of the brain cause abnormally high skeletal muscle tone (and thus, mobility problems) in one or more areas of the body [*cerebr-* brain, *-al* relating to, *palsy* paralysis (*para-* beyond, *-lysis* loosening)]

cerebral peduncle (seh-REE-bral peh-DUNG-kul) white matter tracts in the brain connecting the cerebellum to the cerebrum [*cerebr-*brain, *-al* relating to, *ped-* foot, *-uncl-* little]

cerebral plasticity (seh-REE-bral plas-TIS-i-tee) characteristic of the cerebrum that permits the relocation of functions from one area of the cerebral cortex to another area [*cerebr-* brain, *-al* relating to, *plastic-* moldable, *-ity* state]

cerebrospinal fluid (CSF) (seh-ree-broh-SPY-nal FLOO-id) plasmalike fluid that fills the subarachnoid space in the brain and spinal cord and in the cerebral ventricles [*cerebr-* brain, *-spin-* backbone, *-al* relating to]

cerebrovascular accident (CVA) (SAIR-eh-broh-VAS-kyoo-lar) event in which hemorrhage or cessation of blood flow caused by an embolism or ruptured aneurysm in brain blood vessel results in ischemia of brain tissue and destruction of neurons; commonly called a *stroke* [*cerebr-* brain, *-vas-* vessel, *cul-* little, *-ar* relating to]

cerebrum (SAIR-eh-brum) largest and uppermost part of the human brain that controls consciousness, memory, sensations, emotions, and voluntary movements [*cerebrum* brain] *pl.*, cerebra or cerebrums

cerumen (seh-ROO-men) ear wax [*cera* wax]

ceruminous gland (seh-ROO-mi-nus) gland that produces a waxy substance called *cerumen* (ear wax) [*cera-* wax, *-ous* relating to, *gland* acorn]

cervical cancer (SER-vi-kal) malignancy of the neck (cervix) of the uterus [*cervic-* neck, *-al* relating to, *cancer* crab or malignant tumor]

cervical plexus (SER-vih-kal PLEK-sus) plexus located deep within the neck; innervates muscles and skin of the neck, upper shoulder, and part of the head [*cervic-* neck, *-al* relating to, *plexus* network] *pl.*, plexi or plexuses

cervical vertebra (SER-vi-kal VER-teh-bra) one of the seven spinal (vertebral) bones of the neck [*cervi-* neck, *-al* relating to, *vertebra* that which turns] *pl.*, **vertebrae**

cervix (SER-viks) neck; particularly the inferior necklike portion of the uterus [*cervix* neck] *pl.*, cervices or cervixes

cesarean section (seh-SAIR-ee-an SEK-shun) surgical removal of a fetus through an incision of the skin and uterine wall; also called *C-section* [*Julius Caesar* Roman emperor, *-ean* of]

channel-mediated passive transport (CHAN-al MEE-dee-ayt-ed PASS-iv TRANS-port) any membrane transport mechanism in which molecules move down a concentration gradient through membrane channels

chaperonin (shap-er-OHN-in) any of a group of globular proteins that are present in every body cell and direct the intracellular steps required for other proteins to achieve the often twisted and convoluted shape required for them to function [*chaperon-* hood]

Charles's law (CHARLZ-ez law) gas law that states that volume is directly proportional to temperature when pressure is held constant; sometimes called *Gay-Lussac's law* (gay lus-SAKS law) after French physical scientist Joseph L. Gay-Lussac who first published it, crediting Jacques Charles with its discovery [*Jacques Alexandre César Charles* French physicist]

cheek facial prominence shaped by the underlying zygomatic bone [*cece-* jawbone]

chemical bond energy relationship joining two or more atoms; involves sharing or exchange of electrons [*chemeia-* alchemy]

chemical buffer combines with added acids or alkali in the body; changes hydrogen ion concentration and pH [*chemeia-* alchemy, *buffe-* cushion, *-er* agent]

chemical digestion (dye-JES-chun) changes in chemical composition of food as it passes through the alimentary canal [*chemeia-* alchemy, *digest-* break down, *-tion* process]

chemoreceptor (kee-moh-ree-SEP-tor) receptor that responds to chemicals; responsible for taste and smell and monitoring concentration of specific chemicals in the blood [*chemo-* chemical, *-recept-* receive, *-or* agent]

chemoreceptor reflex (kee-moh-ree-SEP-tor REE-fleks) nerve reflex in which chemical changes such as a change in blood pH trigger a reflexive change in physiology, such as a change in heart rate or respiratory rate, to restore a homeostatic balance [*chemo-* chemical, *-recept-* receive, *-or* agent, *re-* back or again, *-flex* bend]

chemotactic factor (kee-moh-TAK-tik) chemical that attracts a mobile cell such as a neutrophil or macrophage to a specific location, as in an immune response [*chemo-* chemical, *-tact-* movement, *-ic* relating to]

chemotaxin (kee-moh-TAK-sin) chemotactic factor [*chemo-* chemical, *-tax-* movement or reaction, *-in* substance]

chemotaxis (kee-moh-TAK-sis) process by which a substance attracts cells or organisms into (or away from) its vicinity;

for example, when inflammation mediators attract white blood cells; sometimes called *positive chemotaxis*; *see* **chemotactic factor** [*chemo-* chemical, *-taxis* movement or reaction]

chemotherapy (kee-moh-THAYR-ah-pee) technique of using chemicals to treat disease (e.g., infections, cancer) [*chemo-* chemical, *-therapy* treatment]

chest lead (leed) diagnostic procedure that records information about heart function; also called *precordial lead* [*chest-* box]

chest x-ray diagnostic procedure that exams the lungs, mediastinal contents, and bony thorax [*chest-* box]

Cheyne-Stokes respiration (chain stokes respih-RAY-shun) pattern of breathing associated with critical conditions such as brain injury or drug overdose and characterized by cycles of apnea and hyperventilation [*John Cheyne* Scots physician, *William Stokes* Irish physician]

chief cell cells lining the gastric glands of the stomach that secrete pepsinogen and intrinsic factor; also called *zymogenic cell* [*cell*-storeroom]

childhood period of human development from infancy to puberty [*cilde-* child]

chiropractic (kye-roh-PRAK-tik) system of therapy based on principle that alignment of the skeleton promotes healing [*chiro-* hand, *-practic* practical]

chloride channel (KLOR-ide CHAN-nul) a pore in a cell membrane that allows only chloride ions to permeate, or pass through, the membrane [*chlor-* green, *-ide* chemical, *canalis-* pipe]

chloride shift (KLOR-ide) diffusion of chloride ions into red blood cells as bicarbonate ions diffuse out; maintains electrical neutrality of red blood cells [*chlor-* green, *-ide* chemical]

chlorine (KLOR-een) important negative ion surrounding cells; has one unpaired electron plus three paired electrons [*chlor-* green, *-ine* chemical]

cholecystectomy (koh-leh-sis-TEK-toh-mee) surgical removal of the gallbladder [*chole-* bile, *-cyst-* bag, *-ec-* out, *-tom-* cut, *-y* action]

cholecystitis (koh-leh-sis-TYE-tis) inflammation of the gallbladder [*chole-* bile, *-cyst-*bag, *-itis* inflammation]

cholecystokinin (CCK) (koh-lee-sis-toh-KYE-nin) hormone secreted from the intestinal mucosa of the duodenum that stimulates contraction of the gallbladder, resulting in bile flowing into the duodenum [*chole-* bile, *-cyst-*bag, *-kin-* movement, *-in* substance]

cholelithiasis (koh-leh-lih-THEE-ah-sis) gallstone formation [*chole-* bile, *-lith-* stone, *-iasis* condition]

cholera (KAHL-er-ah) potentially fatal, infectious bacterial disease characterized by severe diarrhea, vomiting, cramps, dehydration [*chole-* bile, *-a* state]

cholesterol (koh-LESS-ter-ol) steroid lipid found in many body tissues and in animal fats [*chole-* bile, *-steros* solid, *-ol* oil]

cholinergic (koh-lin-ER-jik) having to do with acetylcholine [*chole-* bile, *-erg* to work, *-ic* relating to]

chondral fracture (KON-dral) fracture of an articular (cartilage) surface in a synovial joint [*condr-* cartilage, *-al* relating to, *fracture* a breaking]

chondrification center (kon-dri-fi-KAY-shun) area of specialized mesenchymal cells; site of future cartilage formation [*chondr-* cartilage, *-fication* to make]

chondrocyte (KON-droh-syte) cartilage cell [*chondro-* cartilage, *-cyte* cell]

chondroitin sulfate (kon-DROY-tin SUHL-fayt) type of proteoglycan that helps thicken and hold together the matrix of connective tissue; *see* **proteoglycan** [*chondr-* cartilage, *-oid* of or like, *-in* substance, *sulf-* sulfur, *-ate* oxygen]

chondroma (kon-DROH-mah) benign tumor of cartilage [*chondr-* cartilage, *-oma* tumor]

chondromalacia patellae (kon-droh-mah-LAY-shee-ah pah-TEL-ee) degenerative process that results in a softening of the articular surface of the patella [*chondro-* cartilage, *-malacia* softening, *pat-* dish, *-ella* small]

chordae tendineae (KOR-dee ten-DIN-ee) stringlike structures that attach the AV valves to the wall of the heart [*chorda* string or cord, *tendinea* pulled tight] *sing.*, chorda tendinea

chorion (KOH-ree-on) outermost fetal membrane; contributes to tissues in the placenta [*chorion* skin]

chorionic villi (koh-ree-ON-ik VIL-eye) connection between blood vessels of the chorion and those of the placenta [*chorion-* skin, *-ic* relating to]

chorionic villus sampling (CVS) (koh-ree-ON-ik VIL-lus) procedure in which a tube is inserted through the (uterine) cervical opening and a sample of the chorionic tissue surrounding a developing embryo is removed for karyotyping [*chorion-* skin, *-ic* relating to, *villus* shaggy hair]

choroid (KOH-royd) middle layer of the eyeball; contains a dark pigment that prevents the scattering of incoming light rays [*chorio-* skin, *-oid* like]

choroid plexus (KOH-royd PLEK-sus) tuft of capillaries in ventricles of the brain that secrete cerebrospinal fluid [*chorio-* skin, *-oid* like, *plexus* network] *pl.*, plexi or plexuses

chromatid (KROH-mah-tid) either of the two DNA strands joined by a centromere existing after DNA has replicated (before cell division) but before the centromere has divided [*chrom-* color, *-id* structure or body]

chromatin (KROH-mah-tin) threadlike form of DNA, making up the genetic material in the nucleus [*chrom-* color, *-in* substance]

chromosomal genetic disease (kroh-moh-SOH-mal jeh-NET-ik) disease that results from chromosomal breakage or from abnormal presence or absence of entire chromosomes [*chrom-* color, *-soma-* body, *-al* relating to, *gen-*produce, *-ic* relating to, *dis-*opposite of, *-ease* comfort]

chromosome (KROH-meh-sohm) compact, barlike bodies of chromatin (DNA) that have coiled to form a compact mass during mitosis or meiosis; each chromosome is composed of regions called *genes*, each of which transmits hereditary information [*chrom-* color, *-som-* body]

chromosome territory (CT) (KROH-meh-sohm TAIR-it-or-ee) defined location within a cell's nucleus for a specific chromosome (chromatin strand) [*chrom-* color, *-som-*body, *terri-* land, *-ory* place]

chronic (KRON-ik) long-lasting, as in "chronic disease" [*chron-* time, *-ic* relating to]

chronic glomerulonephritis (KRON-ik gloh-mer-yoo-loh-neh-FRY-tis) noninfectious glomerular disorder characterized by progressive kidney damage leading to renal failure [*chron-* time, *-ic* relating to, *glomer-*ball, *-ul-*little, *-nephr-* kidney, *-itis* inflammation]

chronic lymphocytic leukemia (CLL) (KRON-ik LIM-foh-sit-ik loo-KEE-mee-ah) white blood cell disorder that produces large numbers of malignant precursor B lymphocytes [*chron-* time, *-ic* relating to, *lymph-* water (lymphatic system), *-cyte* cell, *leuk-*white, *-emia* blood condition]

chronic myeloid leukemia (CML) (KRON-ik MY-eh-loyd loo-KEE-mee-ah) white blood cell disorder that results from cancerous transformation of granulocytic precursor cells in the bone marrow [*chronos-* time, *-ic* relating to, *myel-* bone marrow, *leuk-*white, *-emia* blood condition]

chronic obstructive pulmonary disease (COPD) (KRON-ik ob-STRUK-tiv PUL-moh-nair-ee) general term referring to a group of disorders characterized by progressive, irreversible obstruction of airflow in the lungs; *see* **asthma, bronchitis, emphysema** [*chron-* time, *-ic* relating to, *pulmon-*lung, *-ary* relating to, *dis-* opposite of, *-ease* comfort]

chronic pain (KRON-ik) pain that continues over a prolonged time [*chron-* time, *-ic* relating to]

chronic renal failure (KRON-ik REE-nal FAIL-yoor) slow, progressing condition resulting from gradual loss of nephrons [*chron-* time, *-ic* relating to, *ren-* kidney, *-al* relating to]

chronological age (KRON-ah-lodg-i-kul) age of an individual expressed in years [*chrono-*time, *-logos* reason, *-al* relating to]

chyle (kile) milky fluid; the fat-containing lymph in the lymphatics of the intestine [*chyl-* juice]

chylomicron (kye-loh-MYE-kron) small fat droplet [*chylo-* juice (chyle), *-micro-* small, *-on* particle]

chyme (kyme) partially digested food mixture leaving the stomach [*chym-* juice]

chymotrypsin (kye-moh-TRIP-sin) pancreatic enzyme that digests proteins in the digestive tract [*chymo-* juice, *-tryps-* pound, *-in* substance]

cilia (SIL-ee-ah) hairlike projections of cells [*cili-* eyelid] *sing.*, cilium

ciliary body (SIL-ee-air-ee) thickening of the choroid that is located between the anterior margin of the retina and the posterior margin of the iris [*ciliary* eyelids or eyelashes]

ciliary muscle (SIL-ee-air-ee) smooth muscle in the ciliary body of the eye that suspends the lens and functions in accommodation [*ciliary* eyelids or eyelashes, *mus-* mouse, *-cle* little]

cilium (SIL-ee-um) *see* **cilia** [*cili-* eyelid] *pl.*, cilia

circular movement arclike rotation of structure around an axis [*circulare-* circle]

circular muscle muscle that circles a body tube or opening; sometimes called *sphincter* [*circulare-* circle, *mus-* mouse, *-cle* little]

circulatory shock (SER-kyoo-lah-tor-ee) failure of the circulatory system to adequately deliver oxygen to the tissues [*circulat-* go around, *-ory* relating to]

circulatory system (SER-kyoo-lah-tor-ee) system composed of the heart, blood vessels, and lymphatic vessels; permits transportation of material to and from all the cells of the body [*circulat-* go around, *-ory* relating to]

circumcision (ser-kum-SIH-zhun) surgical removal of the foreskin, or prepuce, of the penis [*circum-* around, *-cision* cutting]

circumduction (ser-kum-DUK-shun) moving a part so its distal end moves in a circle [*circum-* around, *-duct* lead]

circumvallate papilla (ser-kum-VAL-ayt pah-PIL-ah) huge, dome-shaped bumps of the tongue mucosa that form a transverse row near the back of the tongue surface; each one contains thousands of taste buds [*circum-* around, *-vall-* post or stake, *-ate* relating to, *papilla* nipple] *pl.*, papillae

cirrhosis (sih-ROH-sis) degeneration of liver tissue characterized by the replacement of damaged liver tissue with fibrous or fatty connective tissue [*cirrhos-* yellow-orange, *-osis* condition]

cisterna (sis-TER-na) tiny, membranous sacs, such as those that make up the Golgi apparatus [*cisterna* vessel] *pl.*, cisternae

cisterna chyli (sis-TER-nah KYE-lye) an enlarged pouch on the thoracic duct that serves as a storage area for lymph moving toward its point of entry into the venous system [*cisterna* vessel, *chyli* of juice]

citric acid cycle (SIT-rik ASS-id) second series of chemical reactions in the process of glucose metabolism in which carbon dioxide is formed and energy is released; it is an aerobic process; *see* **Krebs cycle** [*citr-* lemony, *-ic* relating to, *acid* sour, *cycle* circle]

clavicle (KLAV-i-kul) collar bone [*clavi-* key, *-cle* little]

cleavage line (KLEEV-ij) pattern of dense bundles of white collagenous fibers that characterize the reticular layers of dermis; also called *Langer lines* [*cleave-* to split]

cleft lip (kleft) a congenital defect that affects the mouth; failure of structures in the upper lip to fuse properly during embryonic development [*cleft-* split]

cleft palate (kleft PAL-ett) facial deformity that is an X-linked inherited condition; when the palatine bones fail to unite completely [*cleft-* split, *palate-* plate]

climacteric (klye-MAK-ter-ik) *see* **menopause** [*climacter-* critical point in life, *-ic* relating to]

clitoris (KLIT-oh-ris) small, erectile body located within the vestibule of the vagina; also called *glans clitoris* [*clitoris-* to shut] *pl.*, clitorides

clonal selection theory (KLOH-nal) process through which a B or T cell, once sensitized through contact with an antigen, divides rapidly to create a colony of clones that destroys the "selecting" antigen [*klon-* a plant cutting, *-al* relating to, *theorein-* to look at]

clone (klohn) any of a family of many identical cells descended from a single "parent" cell [*klon* a plant cutting]

closed fracture *see* **simple fracture** [*fracture-*a breaking]

closed reduction process by which a fracture is properly aligned without the need for surgery [*reducere-* to lead back]

coagulation (koh-ag-yoo-LAY-shen) *see* **blood coagulation** [*coagul-* curdle, *-ation* process]

cocaine (koh-KAYN) drug that blocks the uptake of dopamine (neurotransmitter) by neurons, thus inhibiting pain signals or producing a temporary feeling of well-being [*coca-* type of shrub, *-ine* made of]

coccygeus muscle (kohk-SIJ-ee-us) one of the muscles that form the pelvic floor [*coccygeus* coccyx (cuckoo), *mus-* mouse, *-cle* little]

coccyx (KOK-sis) last bone of the vertebral column, made up of 4 or 5 vertebrae that have fused together [*coccyx* cuckoo (beak)]

cochlea (KOHK-lee-ah) snail shell-like structure in the inner ear that houses the spiral organ (organ of Corti), which is responsible for sense of hearing [*cochlea-* snail shell]

cochlear duct (KOHK-lee-ar membranous tube within the bony cochlea; only part of the internal ear concerned with hearing [*cochlea-* snail shell, *ducere-* to lead]

cochlear nerve (KOHK-lee-ar) part of vestibulocochlear nerve (cranial nerve VIII); sensory nerve responsible for hearing [*cochlea-*snail shell]

codominance (koh-DOM-i-nance) in genetics, a form of dominance in which two dominant versions of a trait are both expressed in the same individual [*co-* together, *-domina-* rule, *-ance* state]

codon (KOH-don) in RNA, a triplet of three base pairs that codes for a particular amino acid [*caudex-* book]

coenzyme (koh-EN-zyme) organic, nonprotein catalyst that acts as molecule carrier [*co-* together, *-en-* in, *-zyme* ferment]

coenzyme A (CoA) (koh-EN-zyme) molecule that is converted from pyruvic acid in cell respiration; allows for the transition to the citric acid cycle from glycolysis [*co-* together, *-en-* in, *-zyme* ferment, A first letter of Roman alphabet]

cofactor (KOH-fak-ter) a nonprotein unit attached to an enzyme molecule than enables the enzyme to function properly [*co-*together, *-factor* maker]

colitis (koh-LYE-tis) any inflammatory condition of the colon and/or rectum [*col-* colon, *-itis* inflammation]

collagen (KAHL-ah-jen) principal organic constituent of connective tissue [*colla-* glue, *-gen* produce]

collagenous dense fibrous tissue (kah-LAJ-eh-nus dense FYE-brus TISH-yoo) flexible but strong connective tissue; for example, tendons [*colla-* glue, *-gen* produce, *dense* thick, *fibro-* fiber, *-ous* relating to, *tissu-* fabric]

collateral ganglion (koh-LAT-er-al GANG-glee-on) sympathetic, prevertebral ganglion; named for nearby blood vessels [*co-* together, *-later-* side, *-al* relating to, *gangli-* knot, *-on* unit] *pl.*, ganglia

collecting duct (koh-LEK-ting) in the kidney, straight tubule joined by the distal tubules of several nephrons [*colligere-* to gather, *ducere-* to lead]

Colles fracture (KOL-ez) fracture of the distal end of the radius [*Abraham Colles*, Irish surgeon, *fracture* a breaking]

colloid (KOL-oyd) dissolved particles that resist separation from the gas, liquid, or solid medium in which they are dissolved [*coll-* glue, *-oid* resembling]

colloid osmotic pressure (KOL-oyd os-MOT-ik) *see* **blood colloid osmotic pressure** [*coll-*glue, *-oid* like, *osmo-* push, *-ic* relating to]

colon (KOH-lon) division of the large intestine; divided into ascending, transverse, descending, and sigmoid portions [*colon* large intestine]

colonoscopy (koh-lon-AH-skah-pee) medical procedure in which the lining of the colon is checked for colorectal cancer or other abnormalities by inserting a flexible scope through the anus and into the colon [*colon* large intestine, *-scop-* **see,** *-y* activity]

color Doppler mapping (DOP-ler) variation of ultrasonography that converts recorded flow frequencies into different colors; color images are then superimposed on M-mode or 2-D echocardiograms [*Christian Doppler* Australian physicist/mathematician]

colorectal cancer (koh-loh-REK-tal) malignancy of the colon or rectum [*colo-* colon, *-rect-* straight, *-al* relating to, *cancer* crab or malignant tumor]

columnar (koh-LUM-nar) cell classification by shape in which cells are higher than they are wide [*column-* column, *-ar* relating to]

coma (KOH-mah) altered state of consciousness from which an individual cannot be aroused [*coma* deep sleep]

combining site two small concave regions on the surface of an antibody molecule [*com-* together, *-bine* two at a time]

comedo (KOM-ee-doh) inflamed, plugged sebaceous gland duct, common in acne conditions; *see also* **blackhead** [*comedere-*to consume]

comminuted fracture (kom-i-NOO-ted) fracture that results in small, crushed bone fragments between or near the broken ends of the bone [*commin-* break into pieces, *-ute* perform action, *fracture* a breaking]

commissural tract (kom-MIS-yoo-ral) nerve tissue that connects the left and right hemispheres of the brain; *see* **corpus callosum** [*commissura-* a connection, *-al* relating to, *tractus-* trail]

common bile duct (KOM-on byle) duct from the liver that empties into the duodenum; made up of the merging of the hepatic duct with the cystic duct [*bilus-* bile, *ducere-* to lead]

common carotid artery (kah-ROT-id AR-ter-ee) blood vessel that supplies the region of the head and neck [*caro-* heavy sleep, *-id* relating to, *arteri-* vessel]

communicable (kom-MYOO-ni-kah-bil) able to spread from one individual to another [*communic* common, *-able* capacity for]

compact bone tissue dense bone; contains structural units called *osteons* or *Haversian systems* [*compact* to put together, *tissu-* fabric]

compensation (kom-pen-SAY-shun) physiological process in which the body's functions compensate, or counterbalance, a deviation from the normal set-point value of a characteristic of the body's internal environment—for example, pH [*compens-* balance, *-tion* process]

complement (KOM-pleh-ment) any of several proteins normally present in blood plasma that when activated kill foreign cells by puncturing them [*comple-* complete, *-ment* result of action]

complementary (base) pairing bonding purines and pyrimidines in DNA; adenine always binds with thymine, and cytosine always binds with guanine [*comple-* complete, *-ment-* process, *-ary* relating to]

complete blood cell count (CBC) clinical blood test that usually includes standard red blood cell, white blood cell, thrombocyte counts, the differential white blood cell count, hematocrit, and hemoglobin content [*complere-* to fill up, *cell-* storeroom]

complete fracture fracture that totally divides a bone into separate pieces [*complere-* to fill up, *fracture* a breaking]

compliance (kahm-PLY-ans) the ease of stretch of a material—as in lung compliance, the ease of stretch of the lung tissues [*compli-* complete, *-ance* act of]

composite cell (kahm-PAH-zit) artistic representation of a cell that includes features from many different types of cells [*composite* to assemble, *cell* storeroom]

compound a chemical combination of two or more elements [*compound* put together]

compound fracture type of bone fracture in which broken bone projects through surrounding tissue and skin, thereby inviting the possibility of osteomyelitis; also called *displaced* or *open fracture* [*compound* to put together, *fracture* a breaking]

computed tomography (CT) (kom-PYOO-ted toh-MOG-rah-fee) x-ray technique that produces an image representing a detailed cross section of a body structure [*tomo-* cut, *-graph-* draw, *-y* process]

concentration gradient (kahn-sen-TRAY-shun GRAY-dee-ent) measurable difference in concentration from one area to another [*con-*together, *-centr-* center, *-ation* process, *gradi-*step, *-ent* state]

concentric contraction (kon-SEN-trik kon-TRAK-shun) contraction in which the movement results in shortening of the muscle; type of isotonic contraction or dynamic tension [*con-* together, *-centr-* center, *-ic* relating to, *con-* together, *-tract-* drag or draw, *-tion* process]

contraction (kon-TRAK-shun) tension of muscle fibers produced by sliding of cytoskeletal filaments and producing either shortening of the muscle fiber, pull on a load, or both [*con-* together, *-tract-* drag or draw, *-tion* process]

concha (KONG-kah) scroll-shaped bone that forms a ledge projecting into the nasal cavity from its lateral wall [*concha* sea shell] *pl.*, conchae

condensation (kon-den-SAY-shun) see **dehydration synthesis** [*con-* together, *-dense-* thick or crowded, *-tion* process]

conduction in human anatomy, the transfer of heat energy to the skin and then the external environment [*con-* with, *duct-* lead, *-tion* process]

conductive keratoplasty (CK) (kon-DUK-tiv ker-ah-toh-PLAS-tee) treatment for the correction of farsightedness [*con-* with, *duct-* lead, *-ive* relating to, *kera-* horn, *-plasty* surgical repair]

conductivity (kon-duk-TIV-uh-tee) ability of living cells and tissues to selectively transmit a wave of excitation from one point to another within the body [*con-* with, *duct-* lead, *-iv-* relating to, *-ity* state]

condyloid joint (KON-di-loyd) ellipsoidal joint [*condylo-* knuckle, *-oid* resembling, *jungere-* to join]

cone receptor cell located in the retina that is stimulated by bright light [*konos-* cone]

congenital abnormality (kon-JEN-i-tall ab-nor- MAL-i-tee) *see* **congenital disorder** [*con-* with, *-genit-* born, *-al* relating to]

congenital disorder (kon-JEN-i-tall) refers to a condition present at birth; congenital conditions may be inherited or may be acquired in the womb or during delivery [*con-* with, *-genit-* born, -al relating to]

congestive heart failure (CHF) (kon-JES-tive) left heart failure; inability of the left ventricle to pump effectively, resulting in congestion in the systemic and pulmonary circulations [*congest-* crowd together, *-ive* relating to]

conjunctiva (kon-junk-TI-vah) mucous membrane that lines the eyelids and covers the sclera (white portion of the eye) [*con-*together, *-junct* join]

conjunctivitis (kon-junk-ti-VYE-tis) inflammation of the conjunctiva, usually caused by irritation, infection, or allergy [*con-* together, *-junct-* join, *-iv-* relating to, *-itis* inflammation]

connective tissue most abundant and widely distributed tissue in the body [*con-* together, *-nect-* bind, *-ive* relating to, *tissu-* fabric]

connective tissue membrane body membrane that lines movable joint cavities; for example, synovial [*con-* together, *-nect-*bind, *-ive* relating to, *tissu-* fabric, *membrane* thin skin]

connectome (kon-NEK-tohm) map of all the neural connections of the brain [*con-* together, *-nect-* bind, *-ome* complete set]

consciousness state of awareness of one's self and environment and other beings [*conscire-* to know wrong]

constipation (kon-sti-PAY-shun) condition that results when extra water is absorbed from the fecal mass, producing a hardened stool [*constipa-* crowd together, *-ation* process]

contact dermatitis (der-mah-TYE-tis) local skin inflammation lasting a few hours or days after being exposed to an antigen [*contingere-* to touch, *derma-* skin, *-itis* inflammation]

contact digestion (dye-JES-chun) when substrates bind onto enzymes located on the surface of the brush border and complete carbohydrate digestion [*contingere-* to touch, *diges*t- break down, *-tion* process]

continuous ambulatory peritoneal dialysis (CAPD) (AM-byoo-lah-tor-ee pair-i-toh-NEE-al dye-AL-i-sis) technique used in the treatment of renal failure [*continuare-* to unite, *ambulat-* walk, *-ory* relating to, *peritone-* peritoneum, *-al* relating to, *dia-*through, *-lysis* loosening]

continuous capillary (KAP-i-lair-ee) capillaries that have a continuous lining of endothelial cells with only small openings between them [*continuare-* to unite, *capill-*hair, *-ary* relating to]

continuous positive airway pressure (CPAP) special type of mechanical respirator used to treat infant respiratory distress syndrome [*continuare-* to unite, *premere-* to press]

contractility (kon-trak-TIL-i-tee) ability, as of muscle cell, to contract or shorten to produce movement [*con-* together, *-tract-* drag or draw, *-il-* of or like, *-ity* quality of]

contralateral (kon-trah-LAT-er-al) on the opposite side of the body [*contra-* against, *lateralis-* side]

contralateral reflex arc (kon-trah-LAT-er-al REE-fleks ark) reflex arc whose receptor and effectors are located on opposite sides of the body [*contra-* against, *lateralis-* side, *re-* again, *-flex* bend]

contusion (kon-TOO-zhun) a bruise; an injury in which the skin or surface of an organ is not broken but underlying blood vessels rupture and leak into interstitial space [*contus-* bruise, *-sion* result]

conus medullaris (KOH-nus MED-yoo-lair-is) tapered end of the spinal cord [*conus* cone, *medulla* middle] *pl.*, coni medullares

convection (kon-VEK-shun) in human anatomy, transfer of heat energy to air that is flowing away from the skin [*convergere-* to bring together]

convergence (kon-VER-jens) a coming together, as in movement of the two eyeballs inward so that their visual axes come together at the same point on the object viewed; also, when more than one presynaptic axon synapses with a single postsynaptic neuron [*con- together, -verg-* incline, *-ence* state]

convergent muscle (kon-VER-jent) muscle that radiates out from a small to a wider point of attachment; for example, pectoralis major [*con-* together, *-verg-* incline, *-ent* state, *mus-* mouse, *-cle* little]

convolution (kon-voh-LOO-shun) *see* **gyrus** [*con-* together, *-volut-* roll, *-tion* process]

convulsion (kon-VUL-shun) abnormal, uncoordinated tetanic contractions of varying groups of muscles; also called *seizure* [*convuls-* pull violently, *-sion* result]

cor pulmonale (kohr pul-mah-NAL-ee) failure of the right atrium and ventricle to pump blood effectively, resulting from obstruction of pulmonary blood flow [*cor* heart, *pulmon-* lung, *-ale* relating to]

cornea (KOR-nee-ah) transparent, anterior portion of the sclera [*corneus-* horny]

corneal reflex (KOR-nee-al) blinking in response to the cornea being touched [*corn-*horn, *-al* relating to, *re-* again, *-flex* bend]

corneocyte (KOR-nee-o-site) dead, flattened keratinocyte (epidermal cell of skin) that has filled with keratin and formed a dense, waterproof epidermal layer called *stratum corneum* [*cornu-* horn, *-cyte* cell]

corona radiata (ko-ROHN-ah ray-dee-AH-tah) layer surrounding ovum and its zona pellucida; made up of cumulus cells derived from the ovarian follicle [*corona* crown, *radiata* radiant (with rays)]

coronal plane (ko-RO-nal) frontal plane; divides the body into front and back portions [*corona-* crown, *-al* relating to]

coronary artery (KOHR-oh-nair-ee AR-ter-ee) blood vessel that provides blood to the myocardial cells [*corona-* crown, *-ary* relating to, *arteri-* vessel]

coronary artery disease (CAD) (KOR-oh-nair-ee AR-ter-ee) condition that results from reduced blood flow to the myocardial tissue [*corona-* crown, *-ary* relating to, *arteri-* vessel, *dis-* opposite of, *-ease* comfort]

coronary bypass surgery (KOR-oh-nair-ee) surgery to relieve severely restricted coronary blood flow; veins are taken from other parts of the body and grafted in to bypass the blockage [*corona-* crown, *-ary* relating to]

coronary sinus (KOR-oh-nair-ee SYE-nus) area that receives deoxygenated blood from the coronary veins and empties into the right atrium [*corona-* crown, *-ary* relating to, *sinus-* hollow]

coronoid fossa (KOR-uh-noyd FOSS-ah) depression at the distal end of the humerus bone, into which the coronoid process of the ulna fits (last part of the humerus-ulna articulation) [*coron-* crown, *-oid* like, *fossa* ditch] *pl.* fossae (FOSS-ee)

corpora cavernosa (KOHR-pohr-ah kav-er-NO-sah) *see* **corpus cavernosum** [*corpora-*bodies, *cavern-* hollow space]

corpora quadrigemina (KOHR-pohr-ah kwod-ri- JEM-i-nah) midbrain landmark composed of inferior and superior colliculi [*corpora* bodies, *quadri-* fourfold, *-gemina* twin]

corpus albicans (KOHR-pus AL-bi-kans) white scar on ovary that replaces the degenerated corpus luteum [*corpus* body, *albli-cans* whitening] *pl.*, corpora albicantia

corpus callosum (KOHR-pus kah-LOH-sum) nerve tissue connecting the right and left cerebral hemispheres; also called *commissural tract* [*corpus* body, *callosum* callous] *pl.*, corpora callosa

corpus cavernosum (KOHR-pus kav-er-NO-sum) either of two columns of erectile tissue in the shaft of the penis [*corpus* body, *cavern-* large hollow, *-os-* relating to, *-um* thing] *pl.*, corpora cavernosa

corpus luteum (KOHR-pus LOO-tee-um) a hormone-secreting glandular structure formed after ovulation at the site of the ruptured follicle; it secretes chiefly progesterone with some estrogen [*corpus* body, *lute-*yellow, *-um* thing] *pl.*, corpora lutea

corpus spongiosum (KOHR-pus spun-jee-OH-sum) a column of erectile tissue surrounding the urethra in the penis [*corpus* body, *spong-* sponge,*-os-* relating to, *-um* thing] *pl.*, corpora spongiosa

correction process in which a function is made to work properly, as in adjusting refraction of light in the eye to improve focusing an image on the retina [*corrigere-* to correct]

corrugator supercilii muscle (COR-uh-gay-tor soo-per-SIL-ee-eye) muscle that draws the eyebrows together [*corrugator* wrinkler, *super-* above, *-cilli-* eyelash, *mus-* mouse, *-cle* little]

cortex (KOHR-teks) outer part of an internal organ; for example, the outer part of the cerebrum or the outer portion of the kidneys [*cortex* bark] *pl.*, cortices

cortical (KOR-tik-al) to the cortex, or outer area of an organ or structure [*cortic-* bark, *-al* relating to]

cortical nephron (KOHR-ti-kal NEF-rons) nephron located in the renal cortex [*cortic-* bark (cortex), *-al* relating to, *nephro-* kidney, *-on* unit]

cortical nodule (KOHR-ti-kal NOD-yool) located within sinuses along the cortex of the lymph node; packed with lymphocytes surrounding the germinal center [*cortic-* bark (cortex), *-al* relating to, *nod-* knot, *-ule* small]

corticoid (KOHR-tih-koyd) hormone secreted by the adrenal cortex [*cortic-* cortex or bark, *-oid* like]

corticosteroid (kohr-ti-koh-STER-royd) glucocorticoid secreted by zona fasciculata of the adrenal cortex [*cortico-* cortex or bark, *stero-* solid, *-oid* resembling]

corticotroph (kohr-tih-koh-TROHF) cell type of the adenohypophysis (anterior pituitary) that secretes ACTH (adrenocorticotropic hormone) and tiny amounts of melanocortins such as α-MSH (alpha melanocyte-stimulating hormone) [*cortic-* bark, *-troph* nourish]

cortisol (KOHR-tih-sol) glucocorticoid secreted by zona fasciculata of the adrenal cortex; also known as *hydrocortisone* [*cortis-* bark, *-ol* alcohol]

cortisone (KOHR-ti-sohn) *see* **cortisol** [*corti-* cortex or bark]

costal cartilage (KOS-tal KAR-ti-lij) cartilage that attaches ribs two through ten to the body of the sternum [*costa-* rib, *-al* relating to, *cartilago-* cartilage]

costal surface (KOS-tal) region of the lungs that lies against the ribs; rounded to match contour of thoracic cavity [*costa-* rib, *-al* relating to]

cotransmission (koh-tranz-MISH-un) theory of efferent autonomic synaptic transmission that states that all or most postganglionic fibers release either norepinephrine or acetylcholine along with NANC (nonadrenergic-noncholinergic) transmitters or modulators and that each substance combines with postsynaptic and/or presynaptic receptors to produce regulatory effects [*co-* together, *-trans-* across, *-miss-* send, *-ion* process]

cotransport (koh-TRANZ-port) carrier that moves two or more solute types across the plasma membrane in the same direction; also called *symport* [*co-* together, *-trans-* across, *-port* carry]

cough reflex epiglottis and glottis close and contract in response to foreign matter in the trachea or bronchi [*re-* back or again, *-flex* bend]

coumarin (KOO-mar-in) compound that retards blood coagulation; often given as medication to prevent heart attacks [*coumarou-* tonka bean tree]

countercurrent mechanism (KON-ter-kerrent MEK-a-niz-em) system in which renal tubule filtrate flows in opposite directions; facilitates urine concentration [*counter-* against, *-current* flow]

countertransport (KON-ter-tranz-port) carrier that moves two different types of molecules in opposite directions across the plasma membrane; also called *antiport* [*counter-*against, *-trans-* across, *-port* carry]

covalent bond (ko-VAYL-ent) chemical bond formed by two atoms sharing one or more pairs of electrons [*co-* with, *-valen-* power, *bond* band]

Cowper gland (KOW-per) *see* **bulbourethral gland** [*William Cowper* English anatomist]

COX inhibitor (KOKS in-HIB-it-or) drug that slows or stops the activity of the COX enzyme, which produces prostaglandins that stimulate an inflammatory response [*COX* acronym for *cycloxygenase*]

coxal bone (KOK-sal) hip bone [*coxa-* hip, *-al* relating to]

CPL (C P L) a submicroscopic vesicle (bubble or membrane) within cells that acts as a "compartment for peptide loading (CPL)," in which proteins are altered in structure [shortened form of *compartment for peptide loading*]

cramps painful muscle spasms (involuntary twitches) that result from irritating stimuli, as in mild inflammation, or from ion imbalances [*crammian-* to fill]

cranial nerve (KRAY-nee-al) any of twelve pairs of nerves that attach to the undersurface of the brain and conduct impulses between the brain and structures in the head, neck, and thorax [*crani-* skull, *-al* relating to]

cranial reflex (KRAY-nee-al REE-fleks) reflex response mediated within the brain [*crani-* skull, *-al* relating to, *re-* again, *-flex* bend]

craniosacral division (kray-nee-oh-SAY-kral) parasympathetic division of the autonomic nervous system [*cranio-* skull, *-sacer* sacred, *-al* relating to, *dividere-* to divide]

cranium (KRAY-nee-um) bony vault, made up of eight bones, that encases the brain [*cranium* skull]

C-reactive protein (CRP) (C re-AK-tiv PRO-teen) blood marker for inflammation; elevated levels suggest cardiac disease [*re-* again, *-agere* to act, *prote-* first rank, *-in* substance]

creatine phosphate (CP) (KREE-ah-tin FOS-fayt) substance found in muscle cells and used for the temporary storage of chemical energy to supply ATP and ultimately for muscle contraction [*creat-* flesh, *-ine* relating to, *phosph-* phosphorus, *-ate* oxygen]

cremaster muscle (kreh-MASS-ter) muscle responsible for elevating the testes [*cremastos-* hanging, *mus-* mouse, *-cle* little]

crepitus (KREP-i-tus) sound of bone fragments rubbing together [*crepitus* crackling]

cretinism (KREE-tin-iz-em) dwarfism caused by hyposecretion of the thyroid gland [*cretin-* idiot, *-ism* condition]

Creutzfeldt-Jakob Disease (CJD) (KROYTS-felt YAH-kobe) *see* **variant Creutzfeldt-Jakob disease (vCJD)** [*Hans G. Cruetzfeldt* German neurologist, *Alfons M. Jakob* German neurologist, *dis-* opposite of, *-ease* comfort]

cribriform plate (KRIB-ri-form) perforated portion of ethmoid bone that separates the nasal and cranial cavities [*cribr-* sieve, *-form* shape]

crista (KRIS-tah) fold, for example, any of the folds of the inner membrane of a mitochondrion [*crista* crest or fold] *pl.*, cristae

crista ampullaris (KRIS-tah am-pyoo-LAIR-iss) fold that serves as a sensory receptor organ located within the ampulla of the semicircular ducts; detects head movements [*crista* ridge, *ampu-* flask, *-ulla-* little, *-aris* relating to] *pl.*, cristae ampulares

Crohn disease (krohn) type of autoimmune colitis affecting the small intestine [*Burrill B. Crohn* American physician, *dis-* opposite of, *-ease* comfort]

cross bridge junction of a thick myofilament with a thin myofilament in the myofibril of a muscle fiber, where the head of a myosin molecule in the thick filament binds to the active site of an actin molecule in the thin filament [*crux-* cross, *brigge-* bridge]

crossing over phenomenon that occurs during meiosis when pairs of homologous chromosomes synapse and exchange genes [*crux-* cross]

croup (kroop) syndrome characterized by labored inspiration and a harsh vibrating cough [*croup* croak]

crown topmost part of an organ or other structure [*corona-* crown]

cruciate ligament (KRU-shee-ayt) either of two crossed ligaments inside the knee joint cavity that connect the tibia to the femur; the *anterior cruciate ligament (ACL)* and the *posterior cruciate ligament (PCL)* [*cruci-* cross, *-ate* of or like]

cryopreservation (krye-oh-prez-er-VAY-shun) deep freezing technique; used for reimplantation of parathyroid tissue [*cryo-* cold, *-preserv-* to keep, *-tion* process]

cryptorchidism (krip-TOR-ki-diz-em) condition resulting in undescended testes [*crypt-* hidden, *-orchid-* testis, *-ism* condition]

cuboidal (KYOO-boyd-al) cell classification by shape in which cells resemble a cube [*cub-* cube, *-oid* like, *-al* relating to]

cupula (KYOO-pyoo-lah) structure found within the crista ampullaris of the semicircular duct; the gelatinous ridge in which the hair cells are embedded [*cup-* tub, *-ula* little] *pl.*, cupulae

Cushing syndrome (KOOSH-ing SIN-drohm) condition caused by hypersecretion of glucocorticoids from the adrenal cortex [*Harvey W. Cushing* American neurosurgeon, *syn-* together, *-drome* running or (race) course]

cuspid valve (KUS-pid) *see* **atrioventricular valve** [*cusp-* point, *-id* characterized by]

cutaneous membrane (kyoo-TAYN-ee-us) primary organ of the integumentary system; the skin [*cut- skin, -aneous* relating to]

cuticle (KYOO-ti-kul) skin fold covering the root of the nail [*cut-* skin, *-icle* little]

cyanosis (sye-ah-NO-sis) condition of blueness, particularly of the skin, resulting from inadequate oxygenation of the blood [*cyan-* blue, *-osis* condition]

cyclic AMP (SIK-lik A M P) one of several second messengers that delivers information inside the cell and thus regulates the cell's activity [*kyklos-* circle, *-ic* relating to]

cyclin (SYE-klin) any of several regulatory proteins in the cell that influence the function of activating enzymes called *cyclin-dependent kinases* that drive the cell forward from phase to phase in the cell life cycle and thus regulate the cell's growth and reproduction [*kyklos-* circle, *-in* neutral substance]

cyclin-dependent kinase (CDK) (SYE-klin dee-PEND-ent KI-nays) any of several activating enzymes that drive the cell through the various phases of its life cycle; "cyclin-dependent" refers to the CDK itself being regulated by cellular proteins called *cyclins* [*kyklos-* circle, *-in* neutral substance, *de-* away, *-pendere* to hang upon, *kinesis-* motion, *-ase* enzyme]

cystic duct (SIS-tik) joins with the common hepatic duct to form the common bile duct [*cyst-* sac, *-ic* relating to, *ducere-* to lead]

cystic fibrosis (CF) (SIS-tik fye-BROH-sis) inherited disease involving abnormal chloride ion (Cl^-) transport (CFTR chloride channel); causes secretion of abnormally thick mucus and other problems [*cyst-* sac, *-ic* relating to *fibr-* fiber, *-osis* condition]

cystitis (sis-TYE-tis) inflammation of a sac-like structure such as the urinary bladder [*cyst-* bag, *-itis* inflammation]

cystoscope (SIS-toh-skohp) device used to look into a bladder, such as the urinary bladder [*cyst-* bag, *-scop-* see]

cytokine (SYE-toh-kyne) chemical released from cells to trigger or regulate innate and adaptive immune responses [*cyto-* cell, *-kine* movement]

cytokinesis (sye-toe-kin-EE-sis) process by which a dividing cell splits its cytoplasm and plasma membrane into two distinct daughter cells; cytokinesis happens along with mitosis (or meiosis) during the cell division process [*cyto-* cell, *-kinesis* movement]

cytology (sye-TOL-oh-jee) study of cells [*cyto-* cell, *-ology* study of]

cytolysis (sye-TOL-i-sis) literally, "cell bursting"; often occurs when ions and water rush into a cell, causing it to burst [*cyto-* cell, *-lysis* loosening]

cytoplasm (SYE-toh-plaz-em) gel-like substance of a cell exclusive of the nucleus and plasma membrane; includes organelles (except nucleus) and cytosol (intracellular fluid) [*cyto-* cell, *-plasm* to mold]

cytoskeleton (sye-toh-SKEL-eh-ton) cell's internal supporting, moving framework [*cyto-* cell, *-skeleto-*dried body]

cytosol (SYE-toh-sawl) solution of water and other substances of a cell (outside the nucleus) in which the organelles and cellular inclusions are suspended; it is the liquid portion of the living cell substance known as *cytoplasm* [*cyto-* cell, *-ol* oil]

cytotoxic T cell (sye-toh-TOK-sik) "cell killing" T cell [*cyto-* cell, *-toxic* poison, *T* thymus gland, *cell* storeroom]

D

Dalton's law (DAL-tenz) gas law that states that the total pressure exerted by a mixture of gases is the sum of the pressure of each individual gas; also called *law of partial pressure* [*John Dalton* English chemist and physicist]

deamination (dee-am-i-NAY-shun) removal of an amino group from an amino acid to form a molecule of ammonia and one of keto acid; occurs in the liver as first step in protein catabolism [*de-* undo, *-amin-* ammonia compound, *-ation* process]

decarboxylase (dee-kar-BOK-si-lays) enzyme that removes carbon dioxide [*de-* undo, *-carbo* carbon, *-oxy* sour, *-ase* enzyme]

deciduous teeth (deh-SID-yoo-us) commonly referred to as "baby teeth"; 20 teeth that are shed at a certain age before development of permanent teeth [*decid-* fall off, *-ous* relating to]

decomposition reaction (dee-KAHM-poh-sih-shun ree-AK-shun) chemical reaction that breaks down a substance into two or more simpler substances [*de-* opposite of, *-compo-* to assemble, *-tion* process, *re-* again, *-action* action]

decubitus ulcer (deh-KYOO-bi-tus UL-ser) area of destroyed tissue resulting from inadequate blood supply that often develops when body lies in one position for prolonged periods [*decubitus* a lying down position, *ulcer* sore]

deep farther away from the body's surface, as opposed to superficial [*deep-* deep]
deep vein vein that is farther away from the surface, as opposed to a superficial vein [*vena-* vein]
defecation (def-eh-KAY-shun) expelling feces from the digestive tract [*de-* remove, *-feca-* waste (feces), *-tion* process]
defibrillation (deh-fib-ri-LAY-shun) application of an electric shock to force cardiac muscle fibers to contract in unison [*de-*undo, *-fibrilla* little thread, *-tion* process of]
deglutition (deg-loo-TISH-un) swallowing [*deglut-* swallow, *-tion* process]
dehydration (dee-hye-DRAY-shun) an abnormal loss of fluid from the body's internal environment [*de-* remove, *-hydro* water, *-ation* process]
dehydration synthesis (dee-hye-DRAY-shun SIN-the-sis) anabolic process by which molecules are joined to form larger molecules; often called *condensation* reaction because it joins molecules together into a denser mass [*de-* from, *-hydrat-* water, *-tion* process, *synthesis* putting together]
deletion (deh-LEE-shun) genetic mutation that occurs within a DNA molecule when one or more nucleotide bases in a sequence are missing, causing a misreading of the genetic code and a failure to produce a normal protein needed for body function [*deletionum-* destruction]
delta cell (DEL-tah) pancreatic islet cell that secretes somatostatin; also called *D cell* [*delta* (δ) fourth letter of Greek alphabet, *cell* storeroom]
deltoid (DEL-toyd) triangular muscle that covers the shoulder joint, abducting the arm [*delta-* triangle, *-oid* like]
dementia (de-MEN-shah) degenerative disease that can result in destruction of neurons in the brain [*de-* off, *-mens-* mind, *-ia* condition of]
denature (de-NAYT-shur) to alter the shape of a protein by a change in pH, heat, or some other manner to change its chemical properties [*de-* remove, *-nature* nature]
dendrite (DEN-dryte) branching or treelike nerve cell process that receives input from other neurons and transmits toward the cell body (or toward the axon in a unipolar neuron) [*dendr-* tree, *-ite* part (branch) of]
dendritic cell (DC) (DEN-dri-tik) phagocytic cells in the skin [*dendrit-* tree branch, *-ic* relating to, *cell* storeroom]
dens (denz) upward projection from the body of the second cervical vertebra that furnishes an axis for rotating the head; also called *odontoid process* [*dens* tooth]
dense fibrous tissue (FYE-brus) tissue consisting of fibers packed densely in the matrix [*dense* thick, *fibro-* fiber, *-ous* relating to, *connect-* bind, *-ive* relating to, *tissu-* fabric]
dentate fracture (DEN-tayt) type of bone fracture in which fracture components are jagged and fit together like teeth on a gear [*dent-* tooth, *-ate* of or like, *fracture* a breaking]
dentate nucleus (DEN-tayt NOO-klee-us) either of paired cerebellar gray matter structures that are connected by tracts with the thalamus, as well as motor areas of the cerebral cortex [*dent-* tooth, *-ate* of or like, *nucleus* nut or kernel] *pl.*, nuclei
deoxyribonucleic acid (DNA) (dee-ok-see-rye-boh-nook-lay-ik ASS-id) genetic material of the cell that carries the chemical "blueprint" of the body [*de-* removed, *-oxy-* oxygen, *-nucle-*nucleus (kernel), *-ic* relating to, *acid* sour]
deoxyribose (dee-ok-see-RYE-bohs) sugar in DNA whose molecules contain only five carbons [*deoxy-* containing a decreased amount of oxygen, *-ribose* 5 carbon sugar]
depolarization (dee-poh-lar-i-ZAY-shun) electrical activity that triggers a contraction of the heart muscle [*de-* opposite, *-pol-* pole, *-ar-* relating to, *-ization* process]
depressed fracture (dee-PREST) type of bone fracture in which skull bone is partly "caved in" from the fracture of skull bones [*de-*down, *-premere* to press, *fracture* a breaking]
depression (dee-PRESH-un) movement that lowers or depresses a part, moving it in the opposite direction from elevation [*de-*down, *-press-* press, *-sion* process]
dermal papilla (DER-mal pah-PIL-ah) any of the many small bumps in the surface of the papillary layer of the dermis and which form the ridges and grooves of fingerprints [*derma-* skin, *-al* relating to, *papilla* nipple] *pl.*, papillae
dermatitis (der-mah-TYE-tis) general term referring to any inflammation of the skin [*derma-* skin, *-itis* inflammation]
dermatology (der-mah-TOL-oh-jee) study of the integument and its diseases [*derma-* skin, *-ology* science of]
dermatome (DER-mah-tohm) skin surface areas supplied by a single spinal nerve [*derma-* skin, *-tome* cut segment or region]
dermatosis (der-mah-TOH-sis) general term meaning "skin condition" [*derma-* skin, *-osis* condition]
dermis (DER-mis) the deeper of the two major layers of the skin, composed of dense fibrous connective tissue interspersed with glands, nerve endings, and blood vessels [*derma* skin]
dermoepidermal junction (DEJ) (DER-mo-EP-i-dermal) thin, gluelike layer that binds the epidermis of the skin to the underlying dermis; also called d*ermal-epidermal junction* [*derma-* skin, *-al* relating to, *epi-* on or upon]
descending aorta (ay-OR-tah) conducts blood downward from the arch of the aorta to the abdominal cavity [*desend-* move downward, *aort-* lifted, *-a* thing] *pl.*, aortae or aortas
descending colon (dih-SEND-ing KOH-lon) portion of the colon that lies in the vertical position, on the left side of the abdomen; extends from below the stomach to the iliac crest [*desend-* move downward, *colon* large intestine]
descending tract (dih-SEND-ing) bundle of axons in the spinal cord that conducts impulses down the cord from the brain [*descend-* move downward, *tract-* trail]
desmosome (DES-moh-sohm) category of cell junction that holds adjacent cells together; consists of dense plate or band of connecting structures at point of adhesion [*desmo-* band, *-som-* body]
desquamation (des-kwah-MAY-shun) shedding of epithelial elements from the skin surface [*de-* to remove, *-squama-* scale, *-tion* process]
detrusor muscle (dee-TROO-sor) smooth muscle tissue making up the wall of the bladder [*detrus-* thrust, *-or* agent, *mus-*mouse, *-cle* little]
developmental anatomy *see* **developmental biology** [*developper-* to unfold, *ana-* not or without, *-tomy* a cut]
developmental biology branch of biology that studies the process of change over the life cycle [*developper-* to unfold, *bio-* life, *-log-* words (study of), *-y* activity]
deviated septum (DEE-vee-ay-ted SEP-tum) abnormal condition in which the nasal septum is far from its normal position, possibly obstructing normal nasal breathing [*devia-*turn aside, *-ate* process, *septum* partition] *pl.*, septa
diabetes insipidus (dye-ah-BEE-teez in-SIP-i-dus) condition resulting from hyposecretion of ADH in which large volumes of urine are formed [*diabetes* siphon, *insipidus* without zest]
diabetes mellitus (DM) (dye-ah-BEE-teez MELL-i- tus) condition resulting when the pancreatic islets secrete too little insulin, resulting in increased levels of blood glucose [*diabetes* passer through or siphon, *mellitus* honey-sweet]
diabetic ketoacidosis (dye-ah-BET-ik kee-toh-ass-i-DOH-sis) results from an accumulation of ketone bodies in the blood [*diabet-* siphon (diabetes mellitus), *-ic* relating to, *keto-* acetone, *-acid-* sour, *-osis* condition]
diabetic neuropathy (dye-ah-BET-ik nyoo-ROP-ah-thee) nerve damage caused by diabetes mellitus [*diabet-* siphon, *-ic* relating to, *neuro-* nerve, *-path-* disease, *-y* state]
diabetic retinopathy (dye-ah-BET-ik ret-in-AH-path-ee) retinal damage caused by diabetes mellitus [*diabet-* siphon, *-ic* relating to, *ret-* net, *-ina* relating to, *-path-* disease, *-y* state]
diad (dye-AD) double structure of sarcoplasmic reticulum and T tubules in cardiac muscle fiber [*diad-* across]
dialysis (dye-AL-i-sis) separation of smaller (diffusible) particles from larger (nondiffusible) particles through a semipermeable membrane [*dia-* apart, *-lysis* loosening]
diapedesis (dye-ah-peh-DEE-sis) passage of any formed elements within blood through the vessel wall, as in movement of white cells into an area of injury and infection [*dia-* apart or through, *-pedesis* oozing]
diaphragm (DYE-ah-fram) the flat muscular sheet that separates the thorax and abdomen; a major muscle of respiration [*dia-* across, *-phrag-* enclose]
diaphysis (dye-AF-i-sis) shaft of a long bone [*dia-* through or apart, *-physis* growth] *pl.*, diaphyses
diarrhea (dye-ah-REE-ah) abnormally frequent defecation of liquid or semi-liquid feces [*dia-* through, *-rrhea* flow]
diarthrosis (dye-ar-THROH-sis) freely movable joint [*dia-* between, *-arthr-* joint, *-osis* condition] *pl.*, diarthroses
diastasis (dye-ASS-tah-sis) reduced ventricular filling of the heart [*diastasis-* separation]
diastole (dye-ASS-toh-lee) relaxation of the heart (especially the ventricles), during which it fills with blood; opposite of systole [*dia-* through, *-stole* contraction]
diastolic blood pressure (dye-ah-STOL-ik) blood pressure in arteries during diastole (relaxation) of the heart; clinically more important than systolic pressure [*dia-* apart or through, *-stol-* contraction, *-ic* relating to]
diencephalon (dye-en-SEF-ah-lon) "between" brain; parts of the brain between the cerebral hemispheres and the mesencephalon, or midbrain [*di-* between, *-en-* within, *-cephalon* head] *pl.*, diencephala or diencephalons
differential white blood cell count (dif-er-EN-shal) percentage enumeration of the different types of leukocytes in a stained blood smear [*different-* difference, *cell-* storeroom]
differentiate (dif-er-EN-shee-ayt) act of *differentiation*, the process of the development of diverse types of cells with specialized structures and functions [*different-* difference, *-iate* act of]
differentiation (dif-er-EN-shee-AY-shun) *see* **differentiate** [*different-* difference, *-ation* process]
diffusion (dih-FYOO-shun) spreading; natural tendency of small particles to spread out evenly within any given space; for example, scattering of dissolved particles [*diffus-*spread out, *-sion* process]
digestion (dye-JES-chun) breakdown of food materials either mechanically (through chewing) or chemically (via digestive enzymes) [*digest-* break down, *-tion* process]
digestive system (dye-JES-tiv) system composed of mouth, pharynx, esophagus, stomach, small intestine, large intestine, rectum, and anal canal
digitalis (dij-i-TAL-is) *see* **digoxin** [*digit-* finger, *-alis* relating to (from finger-shaped flowers of foxglove plant)]
digoxin (di-JOK-sin) drug used to treat atrial fibrillation [*dig-* finger (from digitalis or foxglove), *-oxin* poison or toxin]
diploe (DIP-lo-EE) region of cancellous (spongy) bone within the wall of a flat bone of the cranium; also spelled *diploë* [*diploe* folded over (doubled)]
diploid number (DIP-loyd) normal number of chromosomes per somatic cell (46 in humans) [*diplo-* twofold, *-oid* of or like]
diplopia (di-PLOH-pee-ah) double vision [*di-*double, *-op-* vision, *-ia* condition]
dislocation (dis-low-KAY-shun) condition in which the articular surfaces of bones forming a joint are no longer in proper contact [*dis-* apart, *-locat-* to place, *-tion* process]
displaced fracture *see* **compound fracture** [*displace-* to remove, *fracture-* a breaking]
dissection (di-SEK-shun) cutting technique used to separate body parts for study [*dissect-* to cut apart, *-tion* process]
dissociate (di-SOH-see-ayt) when a compound breaks apart in solution forming ions that are surrounded by solvent molecules [*dis-* apart, *-socia-* unite, *-ate* action]
distal (DIS-tal) toward the end of a structure; opposite of proximal [*dist-* distance, *-al* relating to]
distal convoluted tubule (DCT) (DIS-tall KON-vo-LOO-ted TOO-byool) in the kidney, the part of the tubule distal to the ascending limb of the Henle loop that terminates in a collecting duct; main portion of *distal tubule* [*dist-* distance, *-al* relating to, *con-* together, *-volut-* roll, *tub-* tube, *-ul-* little]
distal interphalangeal (DIP) (DIS-tal in-ter-fah-LAN-gee-al) joint between the middle and distal phalanges [*dist-* distance, *-al* relating to, *inter-* between, *-phalang-* finger bones (ref. from rows of soldiers), *-al* relating to]
distal tubule (DIS-tall TOO-byool) *see* **distal convoluted tubule** [*dist-* distance, *-al* relating to, *tub-* tube, *-ul-* little]
disuse atrophy (DIS-yoos AT-roh-fee) loss of muscle tissue mass after a period of few or no contractions, resulting in weakness [*dis-* absence of, *a-* without, *-troph* nourishment]
diuretic (dye-yoo-RET-ik) substance that promotes or stimulates the production of urine [*dia-* through, *-ure-* urine, *-ic* relating to]
divergence (dye-VER-jens) when a single presynaptic axon synapses with more than one different postsynaptic neuron [*di-* to separate, *-verg-* incline, *-ence* state]
diverticulitis (dye-ver-tik-yoo-LYE-tis) inflammation of diverticula (abnormal outpouchings) of the large intestine, possibly causing constipation [*diverticul-* turn aside, *-itis* inflammation]
diverticulosis (dye-ver-tik-yoo-LOH-sis) condition resulting in the presence of abnormal saclike outpouchings of the intestinal wall [*diverticul-* turn aside, *-osis* condition]
diving reflex (DYE-ving REE-fleks) protective physiological response of the body to cold water immersion [*re-* back or again, *-flex* bend]
DNA fingerprinting technique used to analyze the genetic makeup of individuals; compares nucleotide sequences using electrophoresis [*fingraz-* finger]
dominant (DOM-i-nant) in genetics, term referring to genes that have effects that appear in the offspring (dominant forms of a gene are often represented by upper case letters); *see* **recessive** [*dominant-* to rule]
dopamine (DOH-pah-meen) chemical neurotransmitter
domain (doh-mayn) a specific three-dimensional region within a tertiary protein that acts as a functional unit [*doma-* house or estate]
dominant gene (DOM-i-nant jeen) gene whose effects are seen; capable of masking

the effects of a recessive gene for the same trait [*dominant-* to rule, *gene-* to produce]

dopaminergic (doh-pah-min-ER-jik) relating to a neuron that releases dopamine (neurotransmitter) or to a receptor molecule that is activated by dopamine [*dopa-* amino acid, *-amine* ammonia, *-ic* relating to]

Doppler ultrasonography (ul-trah-son-OG-rah-fee) diagnostic study that uses sound or frequency ultrasound to record the direction of blood flow through the heart [*Christian Doppler* Australian physicist/mathematician, *ultra-* beyond, *-sono-* sound, *-graph-* draw, *-y* process]

dorsal (DOR-sal) pertaining to the back; in a direction toward the back of the body; see **posterior**[*dors-* back, *-al* relating to]

dorsal (posterior) nerve root (DOR-sal) bundle of nerve fibers that carry sensory information into the spinal cord [*dors-* back, *-al* relating to]

dorsal cavities (DOR-sal KAV-ih-teez) body cavities on the dorsal side of the body, which include the cranial cavity and the spinal cavity; not a standard anatomical term, but used here to help organize the body for the beginning student [*dors* back, *-al* relating to, *cav-* hollow, *-ity* state]

dorsal ramus (DOR-sal RAY-mus) branch of spinal nerve that supplies somatic motor and sensory fibers to several smaller nerves [*dors-* the back, *-al* relating to, *ramus* branch] *pl.*, rami

dorsal root (DOR-sal) posterior branch of the attachment of a spinal nerve to the spinal cord [*dors-* the back, *-al* relating to]

dorsal root ganglion (DOR-sal root GANG-glee-on) small region of gray matter in dorsal nerve root made up of cell bodies of unipolar sensory neurons [*dors-* the back, *-al* relating to, *ganglion-* knot]

dorsiflexion (dor-si-FLEK-shun) ankle movement in which the top of the foot is elevated (brought toward the front of the leg) with toes pointing upward [*dorsi-* back, *-flex-* bend, *-ion* process]

double bond covalent chemical bond in which two pairs of electrons are shared [*double-* two, *bond-* to bind]

Down syndrome (SIN-drohm) group of symptoms usually caused by trisomy of chromosome 21; characterized by mental retardation and multiple structural defects, including facial, skeletal, and cardiovascular abnormalities [*John L. Down* English physician, *syn-* together, *-drome* running or (race) course]

down-regulation process in which hormone receptors in a target cell are reduced in number by some stimulus [*regula-* rule, *-tion* process]

Duchenne muscular dystrophy (DMD) (doo-SHEN MUSS-kyoo-lar DISS-troh-fee) common form of muscular dystrophy also called *pseudohypertrophy* (meaning "false muscle growth") because the atrophy of muscle is masked by excessive replacement of muscle by fat and fibrous tissue; characterized by mild leg muscle weakness that progresses rapidly to include the shoulder muscles; caused by mutated gene for dystrophin (needed to hold muscle fiber together during contraction) on the X chromosome, thus making DMD more common in boys than girls [*Duchenne* Guillaume B.A. Duchenne de Boulogne, French neurologist, *muscul-* little mouse (muscle), *-ar* relating to, *dys-* bad, *-troph-* nourishment, *-y* state]

ductus arteriosus (DA) (DUK-tus ar-teer-ee-OH-sus) in the developing fetus, this arterial duct connects the aorta and the pulmonary artery, allowing most blood to bypass the fetus' developing lungs [*ductus* duct, *arteri-*vessel, *-osus* relating to]

ductus deferens (DUK-tus DEF-er-enz) vas deferens [*ductus-* duct, *deferens-* carrying away]

ductus venosus (DUK-tus veh-NO-sus) continuation of the umbilical vein that shunts blood returning from the placenta past the fetus' developing liver directly into the inferior vena cava [*ductus* duct, *ven-* vein, *-osus* relating to]

duodenum (doo-oh-DEE-num) first subdivision of the small intestine; where most chemical digestion occurs [*duodeni-* 12 fingers, shortened from *intestinum duodenum digitorum* intestine of 12 finger-widths] *pl.*, duodena or duodenums

dura mater (DOO-rah MAH-ter) literally "strong" or "hard mother"; outermost layer of the meninges [*durus-* hard, *mater-* mother]

dural sinus (DOO-ral SYE-nus) name for a large vein of cranial cavity [*durus-* hard, *-al* pertaining to, *sinus-* hollow]

dwarfism (DWARF-iz-em) condition of abnormally small stature, sometimes resulting from hyposecretion of growth hormone [*dweraz-* tiny, *-ism* condition]

dynamic equilibrium (dye-NAM-ik ee-kwi-LIB-ree-um) maintaining balance when the head or body is rotated or suddenly moved [*dynam-* power, *-ic* relating to, *equi-* equal, *-libr-* balance]

dynamic tension (dye-NAM-ik TEN-shun) another name for isotonic contraction [*dynam-* power, *-ic* relating to, *tendere-* to stretch]

dysfunctional uterine bleeding (DUB) (dis-FUNK-shun-al YOO-ter-in) irregular or excessive uterine bleeding; results from structural problem or hormonal imbalance [*dys-* difficult, *-function-* performance, *-al* relating to, *uter-* womb, *-ine* relating to]

dysmenorrhea (dis-men-oh-REE-ah) menstrual cramps [*dys-* painful, *-men-* month, *-rhea* flow]

dysplasia (diss-PLAY-zha) abnormal changes in size, shape, and organization of cells in a tissue associated with neoplasms (tumors) [*dys-* disordered, *-plasia* to mold]

dyspnea (DISP-nee-ah) difficult or labored breathing [*dys-* painful, *-pne-* breathe, *-a* condition]

dysrhythmia (dis-RITH-mee-ah) abnormal heart rhythm; also called **arrhythmia** [*dys-* disordered, *-rhythm-*rhythm, *-ia* condition]

dystrophin (DIS-trof-in) protein molecule that forms strands in each skeletal muscle fiber and helps to hold the cytoskeleton to the sarcolemma to keep the muscle fiber from breaking during contractions; normal dystrophin is missing in Duchenne muscular dystrophy (DMD) and related conditions and thus cells break apart more easily, causing the symptoms of DMD [*dys-* bad, *-troph-* nourishment, *-in* substance]

dysuria (dis-YOO-ree-ah) painful urination

E

eardrum *see* **tympanic membrane** [*eare-* ear]

eccentric contraction (ek-SENT-rik kon-TRAK-shun) type of isotonic muscle contraction in which muscle lengthens while it is contracting [*ec-* out of, *-centr-* center, *-ic* relating to, *con-* together, *-tract-* drag or draw, *-tion* process]

eccrine sweat gland (EK-rin) water-producing exocrine sweat glands widely dispersed throughout the skin [*ec-* out, *-crin-* secrete, *gland* acorn]

echocardiography (ek-oh-kar-dee-OG-rah-fee) diagnostic technique that uses ultrasound waves that reflect off the heart to produce images of heart function [*echo-* reflect sound, *-cardi-* heart, *-graph-* draw, *-y* activity]

eclampsia (eh-KLAMP-see-ah) potentially fatal condition associated with toxemia of pregnancy; characterized by convulsions and coma [*ec-* out, *-lamp-* shine forth, *-sia* condition]

ectoderm (EK-toh-derm) outermost of the primary germ layers that develops early in the first trimester of pregnancy; gives rise to the skin and the nervous system [*ecto-* outside, *-derm* skin]

ectomorph (EK-toh-morf) thin, lean body type [*ecto-* outside, *-morph* form]

ectopic pacemaker (ek-TOP-ik PAYS-mayk-er) pacemaker other than the SA node [*ec-* out of, *-top-* place, *-ic* relating to]

ectopic pregnancy (ek-TOP-ik) pregnancy in which the fertilized ovum develops in some place other than in the uterus [*ec-* out of, *-top-* place, *-ic* relating to]

eczema (EK-zeh-mah) inflammatory skin condition associated with various diseases and characterized by erythema, papules, vesicles, and crusts [*eczema* to boil over]

edema (eh-DEE-mah) accumulation of fluid in a tissue, as in inflammation; swelling [*edema* a swelling]

Edmonton protocol (ED-mon-ton PRO-toh-kol) islet cell transplant technique used in the treatment of type 1 diabetes [*Edmonton* city in Canada]

effector B cell (ef-FEK-tor) cell that differentiates from a B cell; synthesizes and secretes huge amounts of antibodies [*effect-* accomplish, *-or* agent, *B* bursa-equivalent tissue, *cell* storeroom]

effector cell (ef-FEK-tor) type of lymphocyte that attacks antigens [*effect-* accomplish, *-or* agent, *cell* storeroom]

effector (ef-FEK-tor) organ, gland, or muscle that responds to a nerve stimulus [*effect-* accomplish, *-or* agent]

effector T cell (ef-FEK-tor) cell that differentiates from a T cell; cause contact killing of a target cell [*effect-* accomplish, *-or* agent, *T* thymus gland, *cell* storeroom]

efferent (motor) neuron (EF-fer-ent NOO-ron) nerve cell that transmits impulses away from the central nervous system to or toward muscles or glands [*e-* away, *-fer-* carry, *-ent* relating to]

efferent division (EF-fer-ent di-VI-shun) the motor division (outgoing pathways) of the nervous system [*e-* away, *-fer-* carry, *-ent* relating to]

efferent ductule (EF-fer-ent DUKT-yool) series of sperm ducts that drain the rete testis and pierce the tunica albuginea [*e-* away, *-fer* carry, *ducere-* to lead, *-ule* small one]

efferent nervous system (EF-fer-ent) subdivision of the peripheral nervous system (PNS) that consists of all outgoing motor nerves [*e-* away, *-fer-* carry, *-ent* relating to, *nerv-* nerve, *-ous* relating to]

efferent neuron (EF-fer-ent NOO-ron) neuron that transmits nerve impulses away from the central nervous system to muscles or glands (effectors) [*e-* away, *-fer-* carry, *-ent* relating to, *neuron-* nerve]

Einthoven's triangle (EYN-to-venz) three-angle view of the heart's electrical activity [*Willem Einthoven* Dutch physiologist]

ejaculation (ee-jak-yoo-LAY-shun) sudden discharging of semen from the body [*e-* out or away, *-jacula-* throw, *-ation* process]

ejaculatory duct (ee-JAK-yoo-lah-toh-ree) duct formed by the joining of the ductus deferens and the duct from the seminal vesicle that allows sperm to enter the urethra [*e-* out or away, *-jacula* throw, *-ory* relating to, *ducere-*to lead]

ejection fraction (EF) (ee-JEK-shun) ratio of stroke volume (SV) of the heart to the end-diastolic volume (EDV); expressed as a percentage: EF = (SV/EDV) × 100; the EF refers to the ejection fraction of the left ventricle, unless specified otherwise, and decreases below 55% as the myocardium fails to contract normally—thus making EF an indicator of heart failure [*eject-* to cast out, *-tion* process, *fract-* a breaking, *-tion* process]

elastic artery (eh-LAS-tik AR-ter-ee) largest artery; includes aorta and some of its branches [*elast-* to drive or beat out, *-ic* relating to, *arteri-* vessel]

elastic cartilage (eh-LAS-tik KAR-ti-lij) cartilage with elastic, as well as collagenous, fibers; provides elasticity and firmness, as in, for example, the cartilage of the external ear [*elast-* drive or beat out, *-ic* relating to, *cartilag* cartilage]

elastic dense fibrous tissue form of dense (regular) fibrous tissue that contains mostly elastic fibers [*elast-* to drive or beat out, *-ic* relating to, *dense* thick, *fibr* fiber, *tissu-* fabric]

elastic filament in muscle fibers, microscopic protein filaments composed of *titin (connectin)* that anchor the ends of the thick filaments to the Z disk and give myofibrils their characteristic elasticity [*elas-* drive or beat out, *-ic* relating to, *fila-* thread, *-ment* thing]

elastic recoil tendency of the thorax and lungs to return to their preinspiration volume [*elast-* drive or propel, *-ic* relating to]

elastin (e-LAS-tin) protein found in elastic fiber [*elast-* to drive or beat out, *-in* substance]

electrocardiogram (ECG or EKG) (eh-lek-troh-KAR-dee-oh-gram) graphic record of the heart's action potentials [*electro-* electricity, *-cardio-* heart, *-gram* drawing]

electrocardiograph (eh-lek-troh-KAR-dee-oh-graf) machine that produces electrocardiograms [*electro-* electricity, *-cardio-* heart, *-graph* draw]

electrocardiography (eh-lek-troh-kar-dee-OG-rah-fee) process or technology that produces electrocardiograms [*electro-* electricity, *-cardio-* heart, *-graph-* draw, *-y* process]

electroencephalogram (EEG) (eh-lek-troh-en-SEF-ah-loh-gram) graphic representation of voltage changes in brain tissue used to evaluate nerve tissue function [*electro-*electricity, *-en-* within, *-cephal-* head, *-gram* drawing]

electroencephalography (eh-lek-troh-en-SEF-ah-log- rah-fee) diagnostic study that measures electrical activity produced by the brain [*electro-* electricity, *-en-* inside, *-cephal-* head, *-graph-* draw, *-y* activity]

electrolyte (eh-LEK-troh-lyte) substance that dissociates into ions in solution, rendering the solution capable of conducting an electric current [*electro-* electricity, *-lyt-* loosening]

electromyography (eh-lek-troh-my-OG-rah-fee) process or technology that records electrical impulses from muscles as they contract [*electro-* electricity, *-myo* muscle, *-graph* draw, *-y* activity]

electron (eh-LEK-tron) small, negatively charged subatomic particle [*electr-* electric, *-on* unit]

electron microscopy (EM) (eh-LEK-tron my-KRAH-skah-pee) technique of observing small structures by either passing a beam of electrons through a specimen (transmission electron microscopy, TEM) or reflecting a beam of electrons off a specimen (scanning electron microscopy, SEM) and focusing the resulting electron beam(s) to form a magnified image of the specimen [*electr-* electric, *-on* unit, *micro-* small, *-scop-* see, *-y* activity]

electron transport system (ETS) (eh-LEK-tron) carrier molecules embedded in the inner membrane of the mitochondria that take high-energy electrons from the citric acid cycle and form water and energy for oxidative phosphorylation; also called *electron transport chain (ETC)* [*electro-* electricity, *-on* subatomic particle, *trans-* across, *-port* carry]

electrophoresis (eh-lek-troh-foh-REE-sis) laboratory procedure in which different types of charged molecules are separated according to molecular weight using a weak electric current [*electro-* electricity, *-phoresis* a movement in a (specified) manner]

eleidin (eh-LEE-din) substance found in the dying cells of the stratum lucidum; transforms to keratin [*elei-* olive tree, *-in* substance]

element substance composed of only one type of atom that cannot be broken into simpler constituents by chemical means [*element* first principle]

elephantiasis (el-eh-fan-TYE-ah-sis) extreme lymphedema (swelling resulting from lymphatic blockage) in the limbs caused by a parasitic worm infestation; so called because the limbs swell to "elephantine proportions" [*elephant-* elephant, *-iasis* condition]

elevation (el-eh-VAY-shun) action that moves a part up [*e(x)-* up, *-lev-* raise, *-at-* perform, *-tion* process]

elimination defecation [*e-* out, *-limen-* threshold, *-ation* process]

embolism (EM-boh-liz-em) condition that results from a moving blood clot circulating in the bloodstream [*embol-* plug, *-ism* condition]

embolus (EM-boh-lus) a moving blood clot circulating in the bloodstream [*embolus* plug]

embryo (EM-bree-oh) animal in early stages of intrauterine development; in humans, the embryonic stage is the first 8 weeks after conception [*em-* in, *-bryo* fill to bursting]

embryology (em-bree-OL-oh-gee) study of the development of an individual from conception to birth [*em-* in, *-bryo-* fill to bursting, *-log-* words (study of), *-y* activity]

embryonic disk (em-bree-ON-ik) cells of the early embryo that differentiate into the three primary germ layers [*em-* in, *bryo* fill to bursting, *-ic* relating to]

embryonic stem cell (em-bree-ON-ik) nondifferentiated cells found in the embryo [*em-* in, *-bryo-* fill to bursting, *-ic* relating to]

emesis (EM-eh-sis) vomiting [*emesis* to vomit]

emission (ee-MISH-un) reflex movement of spermatozoa and secretions from genital ducts and accessory glands into prostatic urethra; precedes ejaculation [*e-* out or away, *-mis-* send, *-sion* process]

emmetropic (em-eh-TROHP-ik) relaxed normal eye [*emmetr-* the correct measure, *-opic* relating to a specific visual condition]

emphysema (em-fi-SEE-mah) abnormal condition characterized by trapping of air in alveoli of the lung that causes them to rupture and fuse to other alveoli; see also **chronic obstructive pulmonary disease** [*em-*in, *-physema* blowing or puffing up]

emulsified (ee-MULL-seh-fyde) dispersed fat molecules formed into tiny droplets before they can be digested [*e-* out, *-muls-* milk, *-i-* combining form, *-fy* process]

end-artery (end-AR-ter-ee) artery that diverges into a capillary [*-arteri-* vessel]

end-diastolic volume (EDV) (end-dye-ASS-toh-lik) the amount of blood in the heart at the end of diastole [*dia-* through, *-stol-* contraction, *-ic* relating to, *volume-* paper roll]

endemic (en-DEM-ik) refers to a disease native to a local region of the world [*en-* in, *-dem-* people, *-ic* relating to]

endocardium (en-doh-KAR-dee-um) thin layer of very smooth tissue lining each chamber of the heart [*endo-* within, *-cardi-* heart, *-um* thing]

endochondral ossification (en-doh-KON-dral os-i-fi-KAY-shun) process by which bones are formed by replacement of cartilage models [*endo-* inward or within, *-chondr-* cartilage, *-al* relating to, *oss-* bone, *-fication* to make]

endocrine (EN-doh-krin) secreting into blood or tissue fluid rather than into a duct; opposite of exocrine [*endo-* within, *-crin-* secrete]

endocrine cell (EN-doh-krin) glandular secretory cells located in the pancreas; found in pancreatic islets [*endo-* within, *-crin-* secrete, *cell* storeroom]

endocrine gland (EN-doh-krin) secretory structure that discharges hormones directly into the blood [*endo-* inward or within, *-crin-* secrete, *gland* acorn]

endocrine hormone (EN-doh-krin HOR-mohn) substance secreted by an endocrine gland into the bloodstream that acts on a specific target tissue to produce a given response [*endo-* inward or within, *-crin-* secrete *hormon-* excite]

endocrine reflex (EN-doh-krin) response that results from feedback loops within the endocrine system [*endo-* within, *-crin-* secrete, *re-* again, *-flex* bend]

endocrine system (EN-doh-krin) system composed of glands that secrete chemicals known as *hormones* directly into the blood [*endo-* inward or within, *-crin-* secrete]

endocrinology (en-doh-krin-OL-oh-jee) study of the endocrine glands and their hormones [*endo-* within, *-crin-* secrete, *re-again*, *-ology* study of]

endocytosis (en-doh-sye-TOH-sis) process that allows extracellular material to enter the cell without actually passing through the plasma membrane [*endo-* inward or within, *-cyto-* cell, *-osis* condition]

endoderm (EN-doh-derm) innermost layer of the primary germ layers that develops early in the first trimester of pregnancy; gives rise to digestive and urinary structures, as well as many other glands and organ parts [*endo-* within, *-derm* skin]

endogenous growth (en-DOJ-en-us) *see* **interstitial growth** [*endo-* within, *-genous* to originate from]

endolymph (EN-doh-limf) clear potassium-rich fluid that fills the membranous labyrinth of the inner ear [*endo-* within, *-lymph* water]

endometrial ablation (en-doh-MEE-tree-al ab-LAY-shun) minimally invasive technique used to destroy the endometrial lining and reduce excessive blood loss among women suffering from dysfunctional uterine bleeding [*endo-* within, *-metr-* womb, *-al* relating to, *ab-* away from, *-lat-* carry, *-tion* process]

endometrial cancer (en-doh-MEE-tree-al) cancer of the endometrium [*endo-* within, *-metr-* womb, *-al* relating to, *cancer* crab or malignant tumor]

endometriosis (en-doh-mee-tree-OH-sis) benign condition that affects the female reproductive tract ; characterized by functioning endometrial tissue outside the uterus [*endo-* within, *-metr-* womb, *-osis* condition]

endometrium (en-doh-MEE-tree-um) mucous membrane lining the uterus [*endo-* within, *-metr-* womb, *-um* thing] *pl.*, endometria

endomorph (EN-doh-morf) body type characterized by excessive fat [*endo-* within, *-morph* shape]

endomysium (en-doh-MEE-see-um) delicate connective tissue membrane covering the skeletal muscle fibers in a skeletal muscle organ [*endo-* within, *-mysium* muscle]

endoneurium (en-doh-NOO-ree-um) thin wrapping of fibrous connective tissue that surrounds each axon in a nerve [*endo-* inward, *-neuri-* nerve, *-um* thing] *pl.*, endoneuria

endoplasm (en-doh-PLAZ-im) material within a cell [*endo-* within, *-plasm* cell or tissue substance]

endoplasmic reticulum (ER) (en-doh-PLAZ-mik reh-TIK-yoo-lum) network of tubules and vesicles in cytoplasm that contributes to cellular protein manufacture (via attached ribosomes) and distribution [*endo-* inward or within, *-plasm-* to mold, *-ic* relating to, *ret-* net, *-ic-* relating to, *-ul-* little, *-um* thing] *pl.*, endoplasmic reticula

endorphin (en-DOR-fin) chemical in central nervous system that influences pain perception; a natural painkiller [*endo-* within, *-morphin* shape]

endoscopic cholangiography (en-doh-SKOP-ik koh-lan-jee-OG-rah-fee) procedure that uses x-rays to visualize the gallbladder and ducts that carry bile [*endo-* within, *-scop-* see, *chol-* bile, *angi-* vessel, *-graph-* draw, *-y* process]

endosteum (en-DOS-tee-um) fibrous membrane that lines the medullary cavity of long bones [*end-* within, *-osteum* bone]

endothelium (en-doh-THEE-lee-um) squamous epithelial cells that line the inner surface of the entire circulatory system and the vessels of the lymphatic system [*endo-* within, *-theli-* nipple, *-um* thing]

endotracheal intubation (en-doh-TRAY-kee-al in-too-BAY-shun) placing a tube in the trachea to ensure an open airway [*endo-* within, *-trache-* rough duct, *-al* relating to, *in-* within, *-tub-* tube, *-ation* process]

end-product inhibition (end-PROD-ukt inhib-ISH-un) process in a biochemical pathway in which the chemical product at the end of the pathway (the end product) becomes an allosteric effector, inhibiting the function of one or more enzymes in the pathway and thus inhibiting further production of the end product [*endo-* within, *producere-* bring forth, *inhibere-* restrain]

endurance training continuous vigorous exercise requiring the body to increase its consumption of oxygen and develop the muscles' ability to sustain activity over a prolonged period [*en-* in, *-durere* harden, *trahere-* to draw]

energy level limited region surrounding the nucleus of an atom at a certain distance containing electrons; also called a *shell* [*en-* in, *-erg-* work, *-y* state]

enkephalin (en-KEF-ah-lin) peptide chemical in the central nervous system that acts as a natural painkiller [*enkepalos-* brain, *-in* substance]

enteric nervous system (ENS) (en-TER-ik) complex arrangement of neurons that are interconnected with the central nervous system and with various divisions of the autonomic nervous system; for example, gastrointestinal muscles and mucous membranes [*enter-* intestine, *-ic* relating to]

enterogastric reflex (en-ter-oh-GAS-trik) nervous reflex causing inhibition of gastric peristalsis in response to the presence of acid and distention of duodenal mucosa; also may inhibit gastric secretion [*entero-* intestine, *-gastr-* stomach, *-ic* relating to, *re-* back or again, *-flex* bend]

enterogastrone (en-ter-oh-GAS-trown) hormone involved with decreasing gastric peristalsis [*entero-* intestine, *-gastr-* stomach]

enterokinase (en-ter-oh-KYE-nays) enzyme that activates trypsin in the intestinal lumen [*entero-* intestine, *-kin-* movement, *-ase* enzyme]

enzyme (EN-zyme) biochemical catalyst that allows chemical reactions to take place; functional proteins that regulate various metabolic pathways of the body [*en-* in, *-zyme* ferment]

eosinophil (ee-oh-SIN-oh-fil) white blood cell, readily stained by eosin (a reddish acid dye), that attacks large parasites and produces some allergic responses [*eosin-* reddish color, *-phil* love]

ependymal cell (eh-PEN-di-mal) cells that line the ventricles of the brain and the central canal of the spinal cord [*ep-* over, *-en-* on, *-dyma-* put, *-al* relating to, *cell* storeroom]

ependymoma (eh-pen-di-MOH-mah) tumor of glial cells called *ependyma* that line fluid spaces of the central nervous system [*ep-* over, *-en-* on, *-dyma-* put, *-oma* tumor]

epicardium (ep-i-KAR-dee-um) inner layer of the pericardium that covers the surface of the heart; it is also called the *visceral pericardium* [*epi-* on or upon, *-cardi-* heart, *-um* thing]

epidemic (ep-i-DEM-ik) refers to a disease that occurs in many individuals at the same time [*epi-* upon, *-dem-* people, *-ic* relating to]

epidemiology (EP-i-dee-mee-OL-o-jee) study of the occurrence, distribution, and transmission of diseases in human populations [*epi-* upon, *-dem-* people, *-o-* combining form, *-log-* words (study of), *-y* activity]

epidermis (ep-i-DER-mis) outermost layer of the skin; sometimes called the "false" skin [*epi-* on or upon, *-dermis* skin]

epididymis (ep-i-DID-i-miss) one of a pair of tightly, coiled male reproductive tubes that carry sperm to the vas deferens [*epi-* upon, *-didymis* pair] *pl.*, epididymes

epidural space (ep-i-DOO-ral) in the brain, the space above the dura mater [*epi-* upon, *-dura-* hard, *-al* relating to]

epigenetics (ep-i-jeh-NET-iks) any process of inheritance other than direct DNA inheritance, sometimes by adding a methyl group (or other chemical) to DNA, as in maternal/paternal imprinting of genes [*epi-* upon, *gen-* produce, *-ic* relating to]

epiglottis (ep-i-GLOT-iss) lidlike cartilage overhanging the entrance to the larynx [*epi-* upon, *-glottis* tongue] *pl.*, epiglottides or epiglottises

epiglottitis (EPP-ih-glaw-tye-tiss) form of laryngeal edema [*epi-* upon, *-glotti-* tongue (glottis), *-itis* inflammation]

epilepsy (EP-i-lep-see) chronic seizure disorder [*epilepsy-* seizure]

epimysium (ep-i-MIS-ee-um) coarse sheet of connective tissue that covers a muscle as a whole [*epi-* upon, *-mysium* muscle]

epinephrine (ep-i-NEF-rin) adrenaline; hormone secreted by the adrenal medulla [*epi-* upon; *-nephr-* kidney, *-ine* substance]

epineurium (ep-i-NOO-ree-um) fibrous coat surrounding a bundle of nerve fibers [tough fibrous sheath that covers the whole nerve [*epi-* upon, *-neuri-* nerve, *-um* thing] *pl.*, epineuria

epiphyseal fracture (ep-i-FEEZ-ee-al) when the epiphyseal plate is separated from the epiphysis or diaphysis; this type of fracture can disrupt normal growth of the bone [*epi-* on, *-phys-*growth, *-al* relating to, *fracture* to break]

epiphyseal plate (ep-i-FEEZ-ee-al) cartilage plate that is between the epiphysis and the diaphysis and allows growth to occur; sometimes referred to as a *growth plate* [*epi-* on, *-phys-* growth, *-al* relating to, *plate* flat]

epiphysis (eh-PIF-i-sis) end of a long bone; also, the pineal body of the brain [*epi-* on, *-physis* growth] *pl.*, epiphyses

episiotomy (eh-piz-ee-OT-oh-mee) surgical procedure used during birth to prevent a laceration of the mother's perineum or the vagina [*episi-* vulva, *-tom-* cut, *-y* action]

epispadias (ep-is-PAY-dee-us) congenital defect that involves the opening of the urethral meatus on the dorsal surface of the glans or penile shaft [*epi-* on or above, *-spad-* rip or split]

epistaxis (ep-i-STAK-sis) clinical term referring to a bloody nose [*epi-* upon, *-staxis* drip]

epithalamus (ep-i-THAL-ah-mus) small nuclei located outside the thalamus and hypothalamus; considered to be one of the structures of the diencephalon [*epi-* upon, *-thalamus* inner chamber] *pl.*, epithalami

epithelial membrane (ep-i-THEE-lee-al) membrane composed of epithelial tissue with an underlying layer of connective tissue [*epi-* on or upon, *-theli* nipple, *-al* relating to, *membrane* thin skin]

epithelial support cell (ep-i-THEE-lee-al) one of the types of cells that makes up the olfactory epithelium [*epi-* upon, *-theli* nipple, *-al* relating to]

epithelial tissue (ep-i-THEE-lee-al) tissue type that covers the body and its parts; lines various parts of the body; forms continuous sheets that contain no blood vessels; classified according to shape and arrangement [*epi-* on or upon, *-theli-* nipple, *-al* relating to, *tissu-* fabric]

epithelium (ep-i-THEE-lee-um) epithelial tissue [*epi-* on or upon, *theli-* nipple, *-um* thing] *pl.*, epithelia

epitope (EP-i-tohp) specific portion of an antigen that elicits an immune response [*epi-* on or upon, *-tope* place]

eponym (EP-o-nim) scientific term based on a person's name, such as *Islets of Langerhans* (equivalent to *pancreatic islets*); eponyms are avoided in modern usage [*epo-* above, *-nym* name]

epsilon cell (EP-sih-lon) type of endocrine cell found in the pancreatic islet and which secretes the hormone ghrelin [*epsilon* (ε) fifth letter of Greek alphabet, *cell* storeroom]

equatorial plate (eh-kwah-TOH-ree-al) plane at the "equator" of a cell during metaphase where the chromosomes align [*equate-* to make equal, *-al* relating to, *plat-* flat dish]

equilibration (eh-kwi-li-BRAY-shun) process of achieving equilibrium, a balance between opposing elements [*equilibr-* equal, *-tion* process]

equilibrium (e-kwi-LIB-ree-um) a balance between opposing elements [*equi-* equal, *-libr-*balance] *pl.*, equilibria [*equilibr-* equal, *-um* state]

erectile dysfunction (ED) (eh-REK-tyle) failure to achieve an erection of the penis adequate enough to permit sexual intercourse [*erect-* set up, *-ile* relating to, *dys-* bad or painful, *-func-*perform, *-tion* process]

erection (eh-REK-shun) condition of erectile tissue when filled with blood; often refers to enlargement of the penis during sexual arousal [*erect-* set up, *-tion* process]

erector spinae muscle (eh-REK-tor SPINE-ee) muscle group in the back consisting of a number of long, thin muscles that travel all the way down the back; the muscles extend (straighten or pull back) the vertebral column and rotate and flex the back laterally [*erector* that which makes rigid or upright, *spinae* of the spine, *mus-* mouse, *-cle* little]

erosive esophagitis (eh-ROH-siv eh-SOF-ah-jye-tis) narrowing or chronic inflammation of the esophagus [*es-* will carry, *-phag-* food (eat), *-itis* inflammation]

erythema (er-i-THEE-mah) reddening of the skin [*erythros-* red]

erythroblastosis fetalis (eh-rith-roh-blas-TOH-sis feh-TAL-is) condition of a fetus or infant caused by the mother's Rh antibodies reacting with the baby's Rh-positive red blood cells, characterized by massive agglutination of the blood and resulting in life-threatening circulatory problems for the infant [*erythro-*red, *-blast-* bud, *-osis* condition]

erythrocyte (eh-RITH-roh-syte) red blood cell [*erythro-* red, *-cyte* cell]

erythrocyte sedimentation rate (ESR) (eh-RITH-roh-syte sed-i-men-TAY-shen) the rate at which formed elements settle in a tube in 1 hour [*erythro-* red, *-cyte* cell]

erythropoiesis (eh-rith-roh-poy-EE-sis) process of red blood cell formation [*erythro-*red, *-poiesis* making]

erythropoietin (eh-RITH-roh-POY-eh-tin) glycoprotein secreted to increase red blood cell production in response to oxygen deficiency [*erythro-* red, *-poiet-* make, *-in* substance]

esophageal endoscope (eh-sof-ah-JEE-ul EN-doh-skohp) flexible tube used to insert and then remove the necessary electrode or suturing device required for treatment of gastroesophageal reflux disease [*es-* will carry, *-phag-* food (eat), *-al* relating to, *endo-* within, *-scop-* see]

esophageal vein (eh-sof-ah-JEE-al) small vein that returns blood from thoracic organs to the superior vena cava or azgos vein [*es-* will carry, *-phag-* food (eat), *-al* relating to]

esophagus (eh-SOF-ah-gus) muscular, mucus-lined tube that connects the pharynx with the stomach; also known as the *food pipe* [*es-*will carry, *-phagus* food] *pl.*, esophagi

essential fatty acid unsaturated fatty acid that must be provided by the diet; serves as a source within the body for prostaglandin synthesis [*acid* sour]

essential hypertension (hye-per-TEN-shun) high blood pressure condition with no identifiable pathological mechanism or reason [*hyper-* excessive, *-tens-* stretch or pull tight, *-sion* state]

essential organ primary organ; organ needed for the essential functions of a system [*organ* instrument]

essential reproductive organ reproductive organ that must be present for reproduction to occur; the gonads [*re-* again, *-producere* to produce, *organ-* instrument]

estrogen (ES-troh-jen) sex hormone secreted by the ovary that causes development and maintenance of female secondary sex characteristics and stimulates growth of the epithelial cells lining the uterus [*estro-* frenzy, *-gen* produce]

estrogenic phase (es-troh-JEN-ik) menstrual cycle phase that occurs between the end of menses and ovulation; also called *postmenstrual, preovulatory phase,* or *follicular phase* [*estr-* frenzy, *-gen-* produce, *-ic* relating to]

ethmoid (ETH-moyd) irregular cranial bone that lies anterior to the sphenoid and posterior to the nasal bones [*ethmo-* sieve, *-oid* like]

etiology (e-tee-OL-o-jee) theory, or study, of the factors involved in causing a disease [*etio-* cause, *-o-* combining form, *-log-* words (study of), *-y* activity]

eumelanin (yoo-MEL-ah-nin) type of melanin pigment that is dark brown in color [*eu-*true, *-melan-* black, *-in* substance]

eupnea (YOOP-nee-ah) normal respiration [*eu-* easily, *-pne-* breathe, *-a* condition]

eustachian tube (yoo-STAY-shun) auditory tube [*Bartolomeo Eustachio* Italian anatomist, *-an* relating to]

evaporation (ee-vap-oh-RAY-shun) in anatomy and physiology, heat lost from the body by vaporization of liquid (sweat) from the skin [*e-* out from, *-vapor* steam, *-ation* process]

eversion (ee-VER-shun) movement that turns the foot outward [*e(x)-* outward, *-ver-* turn, *-sion* process]

evoked potential (EP) measurement of the electrical activity of the brain; information can be analyzed by a computer and generated on a video screen (brain electrical activity map) [*potent-* power, *-ial* relating to]

excess postexercise oxygen consumption (EPOC) *see* **oxygen debt** [*excedere-* to go out, *post-* after, *-exercere* keep busy *oxy-* presence of oxygen, *-gen* produce, *consumere-*use up, *-tion* process]

exchange reaction chemical reaction that breaks down a compound and then synthesizes a new compound by switching portions of the molecules; for example, AB +CD Æ AD+BC [*ex-* from, *-change* to change, *re-* again, *-action* action]

excitability (ek-syte-eh-BIL-i-tee) ability of a muscle to be stimulated; also known as *irritability* [*excit-* arouse, *-abil-* capable, *-ity* state]

excitation (ek-sye-TAY-shun) electrical fluctuation (increase in voltage) occurring when a neuron or muscle fiber is stimulated and additional Na^+ channels open [*excit-*arouse, *-ation* process]

excitatory neurotransmitter (ek-SYE-tah-toh-ree noo-roh-TRANS-mit-er) neurotransmitter that causes excitation (and thus depolarization) of the postsynaptic neuron [*excita-* arouse, *-ory* relating to, *neuro-*nerves, *-trans- across, -mitt-* send, *-er* agent]

excitatory postsynaptic potential (EPSP) (ek-SYE-tah-toh-ree post-si-NAP-tik poh-TEN-shal) temporary depolarization of postsynaptic membrane following stimulation [*excita-* arouse, *-ory* relating to, *post-* after, *-syn-* together, *-apt-* join, *-ic* relating to, *potent-* power, *-ial* relating to]

excretion (eks-KREE-shun) removal of waste products produced during body functions; occurs by defecation, urination, and respiration and through the skin [*excret-* separate, *-tion* process]

exocrine (EKS-oh-krin) secreting into a duct, as in glands that secrete their products via ducts onto a surface or into a cavity; opposite of endocrine [*exo-* outside or outward, *-crin-* secrete]

exocrine gland (EK-soh-krin) secretory structure that discharges products into ducts [*exo-* outside or outward, *-crin-* secrete, *gland* acorn]

exocytosis (eks-o-sye-TOH-sis) process that allows large molecules to leave the cell without actually passing through the plasma membrane [*exo-* outside or outward, *-cyto* cell, *-osis* condition]

exogenous growth (eks-OJ-eh-nus) *see* **appositional growth**

experiment test (or series of tests) of a proposed scientific idea or hypothesis; a controlled experiment is one that accounts for, and eliminates, effects of influences other than those being tested [*exo-* outside, *-gen* produce, *-ous* relating to]

exon (EKS-ahn) segment of a gene in DNA that is used directly for protein synthesis; in the mRNA transcript of a gene, the intervening intron (noncoding) segments are removed and the remaining exon (coding) segments are spliced together to form the final, edited version of the mRNA transcript; *see* **ribonucleic acid (RNA), transcription** [*exo-* outside, *-on* unit]

exophthalmos (ek-soff-THAL-mus) protrusion of the eyeballs resulting, in part, from edema of tissue at the back of the eye socket [*ex-* outside, *-oph-* eye, *-thalm-* inner chamber, *-ic* relating to]

expiration (eks-pih-RAY-shun) exhaling [*ex-*out, *-pir-* breathe, *-tion* process]

expiratory center (eks-PYE-rah-tor-ee) one of the two most important respiratory control centers, located in the medulla [*ex-* out of, *-[s]pir-*breathe, *-tory* relating to, *centrum-*center]

expiratory muscles (eks-PYE-rah-tor-ee) muscles that allow more forceful expiration to increase the rate and depth of ventilation; internal intercostals and abdominal muscles [*ex-* out of, *-[s]pir-* breathe, *-tory* relating to, *musc-* mouse, *-cle* little]

expiratory reserve volume (ERV) (eks-PYE-rah-tor-ee) amount of air that can be forcibly exhaled after expiring the tidal volume (TV) [*ex-* out of, *-[s]pir-* breathe, *-tory* relating to, *volume-* paper roll]

extensibility (ek-STEN-si-BIL-i-tee) ability of a muscle to extend or stretch and return to resting length [*ex- outward, -tens-* stretch, *-abil-* capable, *-ity* state]

extension (ek-STEN-shun) increasing the angle between two bones at a joint; as opposed to flexion [*ex- outward, -tens-* stretch, *-sion* process]

extensor digitorum longus muscle (ek-STEN-ser dij-i-TOH-rum) dorsal flexor muscle on the anterior surface of the foot [*extensor* that which stretches, *digit* of the finger or toe, *longus* long, *mus-* mouse, *-cle* little]

external anal sphincter muscle (AY-nal SFINGK-ter) circular muscle located around the anus [*extern-* outside, *-al* relating to, *an-*ring (anus), *-al* relating to, *sphinc-* bind tight, *-er* agent, *mus-* mouse, *-cle* little]

external acoustic meatus (ak-OOS-tik mee-AY-tus) ear canal; a curved tube (approximately 2.5 cm) extending from the auricle into the temporal bone, ending at the tympanic membrane [*extern-* outside, *acust-*hearing, *-ic* relating to, *meatus-* channel]

external ear outer part of the ear: auricle and external auditory canal [*extern-* outside, *-al* relating to]

external genital (JEN-i-tall) any of the reproductive organs (usually the external organs); penis, scrotum, and related structures in males; vagina, vulva, and related structures in females [*extern-* outside, *-al* relating to, *genit-* birth or reproduction, *-al* relating to]

external iliac vein (IL-ee-ak) vein of the lower extremity [*extern-* outside, *-al* relating to, *ilium* flank]

external intercostal muscle (in-ter-KOS-tal) muscle of the thorax; elevates the ribs [*extern-* outside, *-al* relating to, *inter-* between, *-costa-* rib, *-al* relating to, *mus-* mouse, *-cle* little]

external jugular vein (JUG-yoo-lar) vein of the neck [*extern-* outside, *-al* relating to, *jugul-* neck, *-ar* relating to]

external oblique muscle (oh-BLEEK) muscle of the abdominal wall [*extern-* outside, *-al* relating to, *obliq-* slanted, *mus-* mouse, *-cle* little]

external os constricted end of the uterus [*extern-* outside, *-al* relating to, *os* mouth or opening] *pl.*, ora

external table outer wall of a flat bone of the cranium, made of compact bone; compare to *internal table* [*extern-* outside, *-al* relating to]

exteroceptor (eks-ter-oh-SEP-tor) somatic sense receptor located on the body surface [*exter-* outside, *-cept-* receive, *-or* agent]

extracellular (eks-trah-SELL-yoo-lar) space outside the cell [*extra-* outside, *-cell-* storeroom, *-ular* relating to]

extracellular fluid (ECF) (eks-trah-SELL-yoo-lar) liquid found outside of cells, located in two compartments: between cells (interstitial fluid) and in blood (plasma); lymph, cerebrospinal fluid, and joint fluids are also *extracellular fluids* [*extra-* outside, *-cell-* storeroom, *-ular* relating to]

extracellular matrix (ECM) (eks-trah-SEL-yoo-lar MAY-triks) material between cells in a tissue, made up of water and a variety of proteins and other molecules [*extra-* beyond, *-cell-* storeroom, *-ular* relating to, *matrix* womb] *pl.*, matrices

extrapyramidal tract (eks-trah-pi-RAH-midal) motor tract from the brain to the spinal cord anterior horn motor neurons, except for the corticospinal tract [*extra-* outside, *-pyramid-* pyramid, *-al* relating to, *tract-*trail]

extrinsic clotting pathway (eks-TRIN-sik) clotting mechanism that involves chemicals released from damaged tissue outside of the blood [*extr-* outside, *-sic* beside]

extrinsic control (eks-TRIN-sik) style of physiological regulation in which the control center (regulatory center) is outside, or extrinsic to, the tissue being regulated; for example, the brain's control of a leg muscle or the pituitary gland's regulation of the thyroid gland [*extr-* outside or beyond, *-insic* beside]

extrinsic eye muscle (eks-TRIN-sik) voluntary muscle that attaches the eyeball to the socket and produces movement of the eyeball [*extr-*outside, *-sic* beside, *mus-* mouse, *-cle* small]

extrinsic factor (eks-TRIN-sik) substance secreted in the stomach that allows vitamin B_{12} to be absorbed by the body [*extr-* outside, *-sic* beside]

extrinsic foot muscle (eks-TRIN-sik) leg muscle responsible for movement of the ankle and foot [*extrins-* outside, *-ic* relating to, *mus-* mouse, *-cle* little]

extrinsic muscle (eks-TRIN-sik) muscle originating from outside of the part of the

skeleton moved [*extrins-* outside, *-ic* relating to, *mus-* mouse, *-cle* little]

F

face front of the head [*fac-* appearance]
facet (fah-SET or FASS-et) flat, rounded face on a bone projection (as in vertebrae) [*fac-* appearance (face), *-et* small]
facial nerve (FAY-shal) cranial nerve VII, mixed nerve [*faci-* face, *-al* relating to]
facilitated diffusion (fah-SIL-i-tay-ted di-FYOO-shun) special type of diffusion; when movement of a molecule is made more efficient by action of carrier or channel mechanisms in the plasma membrane [*facili-* easy, *-ate* act of, *diffuse-* spread out, *-sion* process]
fallen arches (flatfoot) condition in which the *tendons* and ligaments of the foot weaken, allowing the normally curved arch to flatten out [*arcus-* arc]
fallopian tube (fal-LOH-pee-an) uterine tube; either of a pair of tubes that conduct the ovum from the ovary to the uterus [*Gabriello Fallopio*]
false pelvis (PEL-vis) structure above the pelvic inlet [*pelvis* basin] *pl.*, pelves (PEL-veez) or pelvises (PEL-vis-ez)
false vocal fold upper pair of folds of mucous membrane in the larynx; also called *vestibular fold* [*voca-* voice, *-al* relating to]
falx cerebelli (falks ser-eh-BEL-lee) small fold in the dura mater in the posterior cranial fossa, between the cerebellum and cerebrum [*falx* sickle, *cerebelli* of the cerebellum (small brain)] *pl.*, falces cerebelli
falx cerebri (falks SER-eh-bree) fold in the dura mater that separates the two cerebral hemispheres [*falx* sickle, *cerebri* of the cerebrum] *pl.*, falces cerebri
farsightedness *see* **hyperopia**
fascicle (FAS-i-kul) small bundle or cluster, especially of groups of skeletal muscle fibers bound together by perimysium [*fasci-* band or bundle, *-cle* small]
fascia (FASH-ee-ah) general name for the fibrous connective tissue masses located throughout the body [*fascia* band or bundle]
fasciculus cuneatus (fah-SIK-yoo-lus KYOO-nee-ay-tus) wedgelike bundle of spinal cord sensory tracts; carries information regarding discrimination touch and conscious sensation of body position and movement [*fasci-* bundles, *-iculus* little, *cuneatus* wedgelike] *pl.*, fasciculi
fasciculus gracilis (fah-SIK-yoo-lus GRAH-sil-iss) thin bundle of spinal cord sensory tracts that carry information for detecting touch and conscious sensation of position and movement of the body [*fasci-* bundles, *-iculus* little, *gracilis* thin]
fast (A) pain type of nerve fiber that carries pain impulses that result in sharp pain; associated with superficial injury or trauma [*fast-* quickly, swiftly, *poena-* punishment]
fast fiber *see* **fast muscle fiber** [*fibra-* fiber]
fast muscle fiber white muscle fiber; primarily relies on anaerobic processes to produce ATP; responds quickly [*mus-* mouse, *-cle* little, *fibra-* fiber]
fatty acid product of fat digestion; building block of fat molecules [*faettian-* fat, *acid-* sour]
fauces (FAW-seez) opening from the mouth into the oropharynx [*faux-* throat]
febrile (FEB-ril) referring to fever [*febris-* fever]
feces (FEE-seez) waste material discharged from the intestines [*feces* waste]
feedback control loop highly complex and integrated communication control network, classified as negative or positive; negative feedback loops are the most important and numerous homeostatic control mechanisms [*control-* to check]
feed-forward concept that information may flow ahead to another process to trigger a change in anticipation of an event that will follow [*fedan-* nourish, *-forward* toward the front]
femoral hernia (FEM-or-all HER-nee-ah) rupture of the lower abdominal wall at the femoral ring [*femor-* femur, *-al* relating to, *hernia* rupture] *pl.*, herniae or hernias
femoral vein (FEM-or-al) vein of the thigh [*femor-* thigh, *-al* relating to]
femur (FEE-mur) thigh bone [*femur* thigh]
fenestrated capillary (fen-es-TRAY-tid KAP-i-lair-ee) type of capillary that has intercellular clefts between their lining of endothelial cells and small holes through the plasma membrane [*fenestra-* window, *-ate* characterized by, *capill-* hair, *-ary* relating to]
fenestration (fen-es-TRAY-shun) perforation in the endothelium of a capillary, as in the glomerulus [*fenestra-* window, *-ation* process]
fertility drug (fer-TIL-i-tee) drug taken to correct ovulatory dysfunction [*fertil-* fruitful, *-ity* state]
fertility sign (fer-TIL-i-tee) structural or functional change in the body used to predict ovulation [*fertil-* fruitful, *-ity* state]
fertilization (FER-ti-li-ZAY-shun) union of an ovum and a sperm; conception [*fertil-* fruitful, *-ation* process]
fetal alcohol syndrome (FAS) (FEE-tal AL-koh-hol SIN-drohm) a condition that may cause congenital abnormalities in a baby; it results from a woman consuming alcohol during pregnancy [*fet-* offspring, *-al* relating to, *syn-* together, *-drome* running or (race) course]
fetal hemoglobin (FEE-tal hee-moh-GLOH-bin) oxygen-binding protein present in the fetus that is made up of two alpha chains and two gamma chains [*fet-* offspring, *-al* relating to, *hemo-* blood, *-glob-* ball, *-in* substance]
fetal programming (FEE-tal) process that refers to the relationship between events occurring during the course of fetal development and the appearance of specific anatomical, physiological, or disease states that develop later in life [*fet-* offspring, *-al* relating to]
fetus (FEE-tus) unborn young, especially in the later stages; in human beings, the fetal stage is from the third month of the intrauterine period until birth [*fetus-* fruitful]
fever unusually high body temperature [*febris-* fever]
fiber (FYE-ber) threadlike structure, as in a muscle fiber (a threadlike cell) or a collagen fiber (a threadlike protein strand) [*fibr-* thread or fiber]
fibrillation (fi-bri-LAY-shun) condition in which individual muscle fibers, or small groups of fibers, contract asynchronously (out of time) with other muscle fibers in an organ (especially the heart), producing no effective movement [*fibril-* small fiber, *-ation* process]
fibrin (FYE-brin) insoluble protein in clotted blood [*fibr-* fiber, *-in* substance]
fibrinogen (fye-BRIN-oh-jen) soluble blood protein that is converted to insoluble fibrin during clotting [*fibr-* fiber, *-gen* produce]
fibrinolysis (fye-brin-OL-i-sis) physiological mechanism that dissolves clots [*fibr-* fiber, *-lysis* loosening]
fibroblast (FYE-broh-blast) connective tissue cell that synthesizes interstitial fibers and gels [*fibro-* fiber, *-blast* bud]
fibrocartilage (fye-broh-KAR-ti-lij) cartilage with the greatest number of collagenous fibers; strongest and most durable type of cartilage [*fibro-* fiber, *-cartilag* cartilage]
fibroid (FYE-broyd) *see* **fibromyoma** [*fibr-* fiber, *-oid* of or like]
fibromyalgia (FM) (fye-broh-my-AL-jah) syndrome of chronic, widespread musculoskeletal pain accompanied by distress and other symptoms; resulting primarily from overamplification of pain in the central nervous system [*fibr-* fiber, *-my-* muscle, *-algia* pain]
fibromyoma (fye-broh-my-OH-mah) benign tumor of uterine fibrous or smooth muscle tissue [*fibro-* fiber, *-my-* muscle, *-oma* tumor]
fibromyositis (fye-broh-my-oh-SYE-tis) tendon inflammation with myositis (muscle inflammation), as in a charley horse [*fibro-* fiber, *-myos-* muscle, *-itis* inflammation]
fibrosarcoma (fye-broh-sar-KOH-mah) cancer of fibrous connective tissue [*fibro-* fiber, *-sarco* flesh, *-oma* tumor]
fibrous connective tissue (FYE-brus) strong, nonstretchable, white collagen fibers that make up tendons [*fibr-* fiber, *-ous* relating to, *connect-* bind, *-ive* relating to, *tissu-* fabric]
fibrous joint (FYE-brus joynt) connection between bones made primarily by bands of fibrous connective tissue [*fibr-* fiber, *-ous* relating to]
fibrous pericardium (FYE-brus pair-i-KAR-dee-um) tough, loose-fitting, and inelastic sac around the heart [*fibr-* fiber, *-ous* relating to, *peri-* around, *-cardi-* heart, *-um* thing]
fibula (FIB-yoo-lah) leg bone; lateral to tibia [*fibula* clasp] *pl.*, fibulae or fibulas
fibular (peroneal) vein (FIB-yoo-lar [per-oh-NEE-al]) vein of the leg [*fibula-* clasp, *-ar* relating to, *perone-* brooch, *-al* relating to]
fibularis tertius muscle (per-oh-NEE-us TER-shee-us) leg muscle that flexes and everts the foot; also **peroneous tertius** [*fibularis* relating to a clasp (fibula), *tertius* third, *mus-* mouse, *-cle* little]
fight-or-flight reaction changes produced by increased sympathetic impulses allowing the body to deal with any type of stress [*feohtan-* fight, *flyhte-* flight, *re-* again, *-action* action]
filaria (fi-LAR-ee-a) taxonomic group of organisms that includes parasitic worms [*fila-* thread, *-ar-* like, *-ia* things] *pl.*, filariae
filiform papilla (FIL-ih-form pah-PIL-ah) bumps of the tongue mucosa with tiny, threadlike projections; these papillae are scattered among the fungiform papillae; they do not contain taste buds but allow us to experience food texture and "feel" [*fili-* thread, *-form* shape, *papilla* nipple] *pl.*, papillae
filtrate (FIL-trayt) substance remaining in a liquid after it has passed through a filter [*filtr-* strain, *-ate* result]
filtration (fil-TRAY-shun) movement of water and solutes through a membrane because of a higher hydrostatic pressure on one side [*filtr-* strain, *-ation* process]
filum terminale (FYE-lum ter-mi-NAL-ee) slender filament formed by the pia mater that blends with the dura mater and then the periosteum of the coccyx [*filum* thread, *termin-* boundary, *-al* relating to] *pl.*, fila terminales
fimbria (FIM-bree-ah) fringe of tiny finger-like projections around the opening of each fallopian (uterine) tube; the projections help move an ovum into the fallopian tube [*fimbria* fringe] *pl.*, fimbriae
first polar body small, nonfunctional cell produced during meiotic divisions in the formation of the female gamete [*pol-* pole, *-ar* relating to]
first-degree burn partial-thickness burn, actual tissue destruction is minimal [*degree-* step or rank]
fissure (FISH-ur) groove [*fissure-* cleft]
fixator muscle (fik-SAY-tor) muscle that functions as a joint stabilizer [*fixator* fastener, *mus-* mouse, *-cle* little]
fixed-membrane-receptor model *see* **second-messenger model** [*figere-* to fasten, *membran-* thin skin, *recept-* receive, *-or* agent]
flaccid muscle (FLAK-sid) muscle with less tone than normal [*flac-* flabby, *-id* structure or body, *mus-* mouse, *-cle* little]
flagellum (flah-JEL-um) single projection extending from the cell surface similar to a cilium; only example in human is the "tail" of the male sperm [*flagellum* whip] *pl.*, flagella
flat bone broad and thin bone with a flattened and often curved surface
flavin adenine dinucleotide (FAD) (FLAY-vin AD-en-een dye-NOO-klee-oh-tyde) molecule that serves as an electron carrier in the electron transport system [*flav-* yellow, *-in* substance, *aden-* gland, *-ine* chemical, *di-*two, *nucleo-* kernel (nucleus), *-t-* combining form, *-ide* chemical]
flexion (FLEK-shun) act of bending; decreasing the angle between two bones at the joint; opposite of extension [*flex-* bend, *-ion* process]
flow-volume loop a type of spirogram (breathing graph) that shows the flow rate (L/min) of breathing along one axis and volume of breathing (L) along the other axis, thus forming a loop or circle with each respiratory cycle
fluid and electrolyte balance (eh-LEK-troh-lyte) constancy of body fluid and electrolyte levels [*electro-* electricity, *-lyt-*loosening]
fluid balance homeostasis of fluids; the volumes of interstitial fluid, intracellular fluid, and plasma and total volume of water remain relatively constant [*fluere-* to flow, *bilancia-* balance]
fluid compartment area in the body where fluid is located; interstitial fluid, plasma, and intracellular fluid compartments are the major fluid compartments of the body [*fluere-* to flow, *com-* together, *partiri-* to share]
fluid mosaic model (moh-ZAY-ik) theory of plasma membrane composition in which molecules of the membrane are bound tightly enough to form a continuous layer but loosely enough so molecules can slip past one another [*fluere-* to flow, *Musa-* mosaic]
fluorescence microscopy (FM) (flor-ESS-ens my-KRAH-skah-pee) type of light microscopy that uses a certain wavelength of light (such as UV) to trigger special fluorescent stains in a microscopic specimen to glow brightly [*fluor-* fluorite (fluorescent mineral), *-escence* state, *micro-* small, *-scop-* see, *-y* activity]
folate deficiency anemia (FOH-layt deh-FISH-en-see ah-NEE-mee-ah) condition in which there is a decrease in the red blood cell count resulting from a vitamin deficiency [*fol-* leaf, *-ate* relating to, *an-* without, *-emia* blood condition]
folia (FOH-lee-ah) thin, delicate gyri (raised ridges) of the surface of the cerebellum [*folia* leaves] *sing.*, folium
foliate papilla (FOL-ee-ayt pah-PIL-ah) red, leaflike ridges of mucosa on the lateral edges of the posterior tongue surface; each contains about a hundred or so taste buds [*foli-* leaf, *-ate* relating to, *papilla* nipple] *pl.*, papillae
follicle (FOL-lih-kul) general name for a pocket or bubble structure; for example, ovarian structure consisting of oocyte surrounded by numerous supporting cells (follicle cells); also, pocketlike structures from which a hair grows; also, a small hollow sphere with a wall of glandular epithelium, found in thyroid tissue [*foll-* bag, *-icle* little]
follicle-stimulating hormone (FSH) (FOL-lih-kul-STIM-yoo-lay-ting HOR-mohn) hormone present in males and females; in males, FSH stimulates the production of sperm; in females, FSH stimulates the ovarian follicles to mature and follicle cells to secrete estrogen [*foll-* bag, *-icle* little, *hormon-* excite]
follicular cell (foh-LIK-yoo-lar) cell that produces thyroid colloid [*foll-* bag, *-icul-* small, *-ar* relating to, *cell* storeroom]

follicular phase (foh-LIK-yoo-lar) postmenstrual phase of the female reproductive cycle; also called *preovulatory* or ***estrogenic phase*** [*foll-* bag, *-icul-* little, *-ar* relating to]
fontanel (FON-tah-nel) "soft spot" where ossification in the cranium is incomplete at birth [*fontam-* fountain, *-el* little]
foot distal extremity of the leg specially adapted to supporting weight [*fot-* foot]
foramen (foh-RAY-men) hole or opening, as in a bone (for blood vessels and nerves) [*foramen* opening] *pl.*, foramina (foh-RAM-in-ah) or foramens (foh-RAY-menz)
foramen ovale (foh-RAY-men oh-VAL-ee) in the developing fetus, opening that shunts blood from the right atrium directly into the left atrium, allowing most blood to bypass the baby's developing lungs [*foramen* opening, *ovale* egg shaped] *pl.*, foramina ovales
forced expiratory volume (FEV) (eks-PYE-rah-tor-ee) maximum volume (mL or L) of air that can be breathed out; also called *forced vital capacity (FVC)* [*ex-* out of, *-[s]pir-* breathe, *-tory* relating to, *volume-* paper roll]
formed element any of the cells of the blood tissue: red blood cells, white blood cells, and platelets in blood [*form-* having a specific shape, *element-* first principle]
fornix (FOR-niks) corner of the vagina where it meets the cervix of the uterus [*fornix-* arch]
fossa (FOSS-ah) slight depression, as in a bone [*fossa* ditch] *pl.*, fossae (FOSS-ee)
fourth-degree burn burn involving underlying muscles, fasciae, or bone [*degree-* step or rank]
fovea centralis (FOH-vee-ah sen-TRAL-is) small depression in the macula lutea where cones are most densely packed; vision is sharpest where light rays focus on the fovea [*fovea* pit, *centralis* center] *pl.*, foveae centrales
fractal geometry (FRAK-tal jee-OM-eh-tree) study of surfaces with a seemingly infinite area, such as the lining of the small intestine [*fract-* a breaking, *-al* relating to, *geometry-* measurement of earth or land]
fundoplication (fun-doh-plih-KAY-shun) surgical procedure performed to strengthen the lower esophageal sphincter [*fundus* bottom, *-plicare* to fold]
fraternal twin (frah-TERN-al) offspring that results from the fertilization of two different ova by two different spermatozoa [*frater-* brother, *-al* relating to, *twin* twofold]
free fatty acid (FFA) fatty acid combined with albumin to be transported by the blood to other cells [*acidus* sour]
free nerve endings sensory receptors in the skin that respond to pain [*freo-* free]
friction ridge raised underlying dermal papillae; form fingerprints [*fric-* rub, *-tion* process]
frontal bone forehead bone [*front-* forehead, *-al* relating to]
frontal plane lengthwise plane running from side to side, dividing the body into anterior and posterior portions [*front-* forehead, *-al* relating to, *plane-* broad]
frostbite local damage to tissues caused by extremely low temperature [*frost-* freezing]
full-thickness burn third-degree burn; skin is severely damaged and nerve endings are destroyed [*thick-* not thin, *-ness* state of]
functional group small cluster of atoms in an organic molecule that gives the molecule particular functional characteristics such as certain chemical binding properties; often represented generically by the letter R [*function-* to perform, *-al* relating to]
functional MRI (fMRI) (procedure that detects which areas of the brain are most active by measuring oxygen consumption by neurons [*MRI* magnetic resonance imaging]
functional protein category of proteins that affect the functional operations of a cell; contrast to *structural protein* [*function-* to perform, *-al* relating to, *prote-* primary, *-in* substance]
functional residual capacity (FRC) amount of air left in the lungs at the end of a normal expiration [*function-* to perform, *-al*, *residu-* left over, *-al* relating to]
fundus (FUN-duss) one of three divisions of the stomach; enlarged portion to the left and above the opening of the esophagus into the stomach [*fundus* bottom] *pl.*, fundi
fungiform papilla (FUN-jih-form pah-PIL-ah) large, mushroom-shaped bumps of the tongue mucosa found in the anterior two thirds of the tongue surface; each one contains one or a few taste buds [*fungi-* mushroom, *-form* shape, *papilla* nipple] *pl.*, papillae
fungus (FUNG-us) organism similar to plants but lacking chlorophyll and capable of producing mycotic (fungal) infections [*fungus* mushroom] *pl.*, fungi (FUNG-eye)
funiculus (fuh-NIK-yoo-lus) large bundle of nerve fibers divided into smaller bundles called *spinal tracts* [*funi-* rope, *-icul-* little] *pl.*, funiculi
furuncle (FUR-un-kul) boil; pus-filled cavity formed by some hair follicle infections; see also **carbuncle** [*furuncle-* little thief]
fusiform muscle (FYOO-si-form) muscle that has fascicles close to parallel in the center of the muscle but converge to a tendon at one or both ends [*fusi-* spindle, *-form* shape, *mus-* mouse, *-cle* little]

G

G protein protein in the plasma membrane of a target cell (such as a postsynaptic cell) involved in signal transduction of a message from outside the cell [G for guanine nucleotide binding, *prote-* first rank, *-in* substance]
G-protein–coupled receptor (GPCR) (jee-PROH-teen–kup-eld ree-SEP-ter) receptor mechanism embedded in plasma membranes of cells that receives chemical messengers (such as neurotransmitters and nonsteroid hormones) and initiates signal transduction to the cell by way of a G protein, which triggers the resulting changes in the cell [G for guanine nucleotide binding, *-prote-* first rank, *-in* substance, *recept-* receive, *-or* agent]
G_0 phase step of the cell life cycle in which a newly formed daughter cell grows in size and then maintains itself for some time, but fails to proceed onward to prepare for later reproduction (cell division); G_0 phase follows the M phase (mitotic division) and represents the cell "opting out" of further reproduction; *see* **cell life cycle** [G- *growth* or *gap*, *phase* appearance]
G_1 phase step of the cell life cycle in which a newly formed daughter cell grows in size, in anticipation of later reproduction (cell division); G_1 phase follows the M phase (mitotic division) and precedes the S phase (DNA replication); *see* **cell life cycle** [G- *growth* or *gap*, *phase* appearance]
G_2 phase step of the cell life cycle in which a cell grows in size after having replicated its DNA and prepares for mitotic reproduction (cell division); G_2 phase follows the S phase (DNA replication) and precedes the M phase (mitotic division); *see* **cell life cycle** [G- *growth* or *gap*, *phase* appearance]
galactokinetic hormone (gal-ak-toh-ki-NET-ik HOR-mohn) any hormone that promotes milk ejection into ducts of the breast by stimulating myoepithelial cells surrounding alveoli [*galact-* milk, *-kinesis* motion, *-ic* relating to, *hormon-* excite]
galactopoietic hormone (gal-ak-toh-poy-ET-ik HOR-mohn) any hormone that maintains milk production in the breast (after it has already started) [*galact-* milk, *-poiet-* make, *-ic* relating to, *hormon-* excite]
gamete (GAM-eet) sex cells; spermatozoa and ova [*gamet-* sexual union or marriage partner]
gamma motor neuron (GAM-mah MOH-tor NOO-roon) stimulate contraction of the striated ends of the muscle spindle fiber (intrafusal fiber) [*gamma (γ)* third letter of Greek alphabet, *mot-* movement, *-or* agent, *neuron* nerve]
gamma ray (GAM-mah) electromagnetic radiation; more penetrating than alpha and beta particles [*gamma (γ)* third letter of Greek alphabet]
ganglion (GANG-lee-on) in peripheral nerves, a region of gray matter made up of unmyelinated fibers [*gangli-* knot, *-on* unit] *pl.*, ganglia
ganglion neuron (GANG-glee-ON) sensory neurons in the retina of the eye that collect information from rods and cones and also act as photoreceptors themselves [*gangli-* knot, *-on* unit *neuron* nerve]
gangrene (GANG-green) tissue death (necrosis) that involves decay of tissue [*gangren-* gnawing sore]
gap junction cell connection formed when membrane channels of adjacent plasma membranes adhere to each other [*junction* to join]
gastric inhibitory peptide (GIP) (GAS-trik in-HIB-i-tor-ee PEP-tyde) hormone produced by the intestinal mucosa that inhibits gastric secretion and motility; because it also enhances pancreatic insulin secretion in the presence of high plasma glucose, it has been more recently called *glucose-dependent insulinotropic polypeptide (GIP)* [*gastr-* stomach, *-ic* relating to, *inhibit-* restrain, *-ory* relating to, *pept-* digest, *-ide* chemical]
gastric juice (GAS-trik) stomach secretion containing acid and enzymes; aids in the digestion of food [*gastr-* stomach, *-ic* relating to]
gastric phase (GAS-trik) during this phase the stomach releases gastrin, which accelerates secretion of gastric juice [*gastr-* stomach, *-ic* relating to]
gastrin (GAS-trin) gastrointestinal (GI) hormone that plays an important regulatory role in the digestive process by stimulating gastric secretion [*gastr-* stomach, *-in* substance]
gastrocnemius muscle (GAS-trok-NEE-mee-us) calf muscle [*gastro-* belly, *-cnemius* leg, *mus-* mouse, *-cle* little]
gastroenteritis (gas-troh-en-ter-EYE-tis) inflammation of the stomach and intestines [*gastr-* stomach, *-enter-* intestine, *-itis* inflammation]
gastroenterology (gas-troh-en-ter-AHL-oh-jee) study of the stomach and intestines and their diseases [*gastr-* stomach, *-entero-* intestine, *-o-* combining form, *-log-* words (study of), *-y* activity]
gastroesophageal reflux disease (GERD) (gas-troh-eh-sof-eh-JEE-all REE-fluks) condition that results when stomach acid enters into the esophagus [*gastro-* stomach, *-es-* will carry, *-phag-* food (eat), *-al* relating to, *re-* again or back, *-flux* flow, *dis-* opposite of, *-ease* comfort]
gastrointestinal (GI) tract (gas-troh-in-TES-ti-nul) alimentary canal; tube formed by the major organs of digestion [*gastr-* stomach, *-intestin-* intestine, *-al* relating to, *tractus* trail]
gastrulation (gas-troo-LAY-shun) process by which blastocyst cells move and then differentiate into the three primary germ layers [*gastr-* belly, *-ula-* little, *-tion* process]
gated channel channel in the plasma membrane that can be opened and closed to alter membrane permeability [*gate-* opening or passage, *chanel-* groove]
gene one of many segments of a chromosome (DNA molecule); each gene contains the genetic code for synthesizing a protein molecule such as an enzyme or hormone or to make a functional RNA molecule such as tRNA or rRNA [*gen-* produce or generate]
gene augmentation (awg-men-TAY-shun) therapeutic technique that introduces genes with the hope that they will add to the production of a needed protein [*gen-* produce or generate]
gene chip DNA analysis technique [*gen-* produce or generate]
gene linkage when a whole group of genes stay together during the crossing-over process [*gen-* produce or generate]
gene replacement therapeutic technique that replaces genes that specify production of abnormal proteins with normal genes [*gen-* produce or generate]
gene therapy manipulation of genes to cure genetic problems; most forms of gene therapy have not yet proven to be effective in humans [*gen-* produce or generate]
general adaptation syndrome (GAS) (ad-ap-TAY-shun SIN-drum) group of changes that make the presence of stress in the body known [*general-* relating to all, *adapt-* fit to, *-tion* process, *syn-* together, *-drome* running or (race) course]
general sense organ structure that consists of microscopic receptors widely distributed throughout the body [*general-* relating to all, *organ-* instrument]
genetic counseling (jeh-NET-ik) professional consultations with families regarding genetic diseases [*genesis-* origin, *council-* plan]
genetic factor (jeh-NET-ik) inherited trait [*genesis* origin]
genetic mutation (jeh-NET-ik myoo-TAY-shun) change in the genetic material within a genome; may occur spontaneously or as a result of mutagens [*gene-* produce, *-ic* relating to, *muta-* change, *-ation* process]
genetic predisposition (jeh-NET-ik pree-dis-poh-ZIH-shun) likelihood due to inherited genes of developing a condition even though the condition itself may not be solely caused by genetic mechanisms [*gene-* produce, *-ic* relating to, *pre-* before, *dispose-* put in order, *-tion* process]
genetics (jeh-NET-iks) scientific study of heredity and the genetic code [*gen-* produce, *-ic* relating to]
geniculate body (jeh-NIK-ye-lit BOD-ee) either of two groups of cerebral nuclei comprising the thalamus; located in posterior region of each lateral mass; play role in processing auditory and visual input [*gen-* knee or knot, *-icul-* small, *-ate* of or like]
genital (JEN-i-tall) reproductive organ [*gen-* produce, *-al* relating to] *pl.*, genitals or genitalia
genital duct (JEN-i-tall) conveys sperm to the outside of the body; also called *reproductive duct* [*gen-* produce, *-al* relating to]
genitalia (jen-i-TAIL-yah) reproductive organs (*see* **genital**) [*gen-* produce, *-al* relating to]
genome (JEE-nohm) entire set of chromosomes in a cell; the *human genome* refers to the entire set of human chromosomes [*gen-* produce (gene), *-ome* entire collection]
genomics (jeh-NO-miks) field of endeavor involving the analysis of the genetic code contained in the human or another species' genome [*gen-* produce (gene), *-om-* entire collection, *-ic* relating to]
genotype (JEN-oh-type) alleles present at one or more specific loci on a chromosome of a given individual; *see* **phenotype** [*gen-* produce (gene), *-type* kind]
germinal epithelium (JER-mi-nal ep-i-TH-EE-lee-um) small epithelial cells that are on the surface of the ovaries [*germ* sprout, *-al* relating to, *epi-* on or upon, *-theli-* nipple, *-al* relating to]
germinal matrix (JER-mi-nal MAY-triks) cap-shaped cluster of cells at the bottom of a

hair follicle [*germ* sprout, *-al* relating to, *matrix* womb] *pl.*, matrices

gerontology (jair-on-TAHL-oh-jee) study of the aging process [*geronto-* old age, *-log-* words (study of), *-y* activity]

gestation period (jes-TAY-shun) length of pregnancy, approximately 9 months in humans [*gesta-* bear, *-tion* process]

ghrelin (GHRL) (GRAY-lin) hormone secreted by epithelial cells lining the stomach; ghrelin boosts appetite, slows metabolism, and reduces fat burning; may be involved in the development of obesity [*ghrel-* grow (also acronym for growth hormone releasing peptide), *-in* substance]

gigantism (jye-GAN-tiz-em) condition produced by hypersecretion of growth hormone during the early years of life; results in a child who grows to gigantic size [*gigant-* great, *-ism* condition]

gingivitis (jin-ji-VYE-tis) inflammation of the gum (gingiva), often as a result of poor oral hygiene [*gingiv-* gum, *-itis* inflammation]

gland secreting structure [*gland* acorn]

glandular (GLAN-dyoo-lar) resembling a gland [*gland-* acorn (gland), *-ula-* little, *-ar* relating to]

glans penis (glans PEE-nis) slightly bulging structure formed by the distal end of the corpus spongiosum; head of the penis; covered by the foreskin in uncircumcised males [*glans* acorn, *penis* male sex organ] *pl.*, glandes penes

glans clitoris (glans KLIT-oh-ris) *see* **clitoris** [*glans* acorn, *clitoris-* to shut]

glaucoma (glaw-KOH-mah) disorder characterized by elevated pressure in the eye; can lead to permanent blindness [*glauco-* gray or silver, *-oma* tumor (growth)]

glia (GLEE-ah) nonexcitable supporting cells of nervous tissue; formerly called *neuroglia* [*glia* glue] *sing.*, glial cell

gliding (movement) movement that results when the articular surface of one bone moves over the articular surface of another without any angular or circular movement [*glidan-* move along smoothly and easily]

glioblastoma multiforme (glye-oh-blas-TOH-ma mul-ti-FOR-mee) malignant tumor of astrocyte cells of the brain [*glio-* glue, *-blasto-*bud, *-oma* tumor, *multi-* many, *-form-* shape]

glioma (glee-OH-mah) any tumor of neuroglia (glial) cells in nerve tissue [*glio-* neuroglia, *-oma* tumor]

globin (GLOH-bin) chain of four proteins; binds to a red pigment (heme) to form hemoglobin [*glob-* ball, *-in* substance]

glomerular capsular membrane (gloh-MER-yoo-lar KAP-soo-lahr) membrane made up of glomerular endothelium, basement membrane, and visceral layer of the Bowman capsule; function is filtration [*glomer-* ball, *-ul-*little, *-ar* relating to, *caps-* box, *-ula-* little, *-ar* relating to, *membran-* thin skin]

glomerular filtration rate (GFR) (gloh-MER-yoo-lar fil-TRAY-shun) the rate of movement of fluid out of the glomerulus and into the capsular space [*glomer-* ball, *-ul-* little, *-ar* relating to, *filtr-* strain, *-ation* process]

glomerulonephritis (gloh-mer-yoo-loh-neh-FRY-tis) inflammatory disease of the glomerular-capsular membranes of the kidney [*glomer-* ball, *-ul-* little, *-nephr-* kidney, *-itis* inflammation]

glomerulus (gloh-MAIR-yoo-lus) compact cluster, particularly when referring to the tuft of capillaries forming part of the nephron [*glomer-* ball, *-ulus* little] *pl.*, glomeruli

glossopharyngeal nerve (glos-oh-fah-RIN-jee-al) cranial nerve IX; mixed nerve [*glosso-* tongue, *-pharyng-* throat, *-al* relating to]

glottis (GLOT-iss) composed of the true vocal cords and the space between them [*glottis* tongue] *pl.*, glottides or glottises

glucagon (GLOO-kah-gon) hormone secreted by alpha cells of the pancreatic islets; increases activity of phosphorylase [*gluca-* sweet (glucose), *-agon* lead or bring]

glucocorticoid (GC) (gloo-koh-KOR-ti-koyd) hormone that influences food metabolism; secreted by the adrenal cortex [*gluco-* sweet (glucose), *-cortic* bark or cortex, *-oid* like]

gluconeogenesis (gloo-koh-nee-oh-JEN-eh-sis) formulation of glucose or glycogen from protein or fat compounds [*gluco-* sweet (glucose), *-neo-* new, *-gen-* produce, *-esis* process]

glucosamine (gloo-KOHS-ah-meen) component of some proteoglycans that thicken and hold together connective tissues such as cartilage [*glucos-* sweetness or glucose, *-amine* ammonia compound]

glucose (GLOO-kohs) monosaccharide, or simple sugar; principal blood sugar used by cells [*gluco-* sweet, *-ose* carbohydrate (sugar)]

glucose-dependent insulinotropic polypeptide (GIP) (GLOO-kohs dih-PEN-dent in-suh-LIN-oh-troph-ik poh-lee-PEP-tyde) *see* **gastric inhibitory peptide** [*gluco-* sweet, *-ose* carbohydrate (sugar), *depend-* to hang upon, *insula-* island, *-troph* nourishment, *-ic* relating to]

glucose phosphorylation (GLOO-kohs fos-for-i-LAY-shun) process of converting glucose to glucose-6-phosphate; prepares glucose for further metabolic reactions [*gluco-* sweet, *-ose* carbohydrate (sugar), *phos-* light, *-phor-*carry, *-yl-* chemical, *-ation* process]

glutamate (GLOO-tah-mayt) glutamic acid; amino acid believed to be responsible for up to 75% of the excitatory signals in the brain [*glutamate-* sticky substance]

gluteal muscle (GLOO-tee-al) buttock muscle; moves the thigh [*glut-* buttocks, *-al* relating to, *mus-* mouse, *-cle* little]

glycerol (GLIS-er-ol) product of fat digestion [*glyce-* sweet, *-ol* alcohol]

glycine (GLYE-seen) amino acid; most widely distributed inhibitory neurotransmitter in the spinal cord [*gly-* sweet, *-amine* ammonia]

glycogen (GLYE-koh-jen) polysaccharide (complex carbohydrate); main carbohydrate stored in animal cells [*glyco-* sweet, *-gen* produce]

glycogenesis (glye-koh-JEN-eh-sis) anabolic pathway of glycogen formation; formation of glycogen from glucose or from other monosaccharides, fructose, or galactose [*glyco-* sweet, *-gen-* produce, *-esis* process]

glycogenolysis (glye-koh-jeh-NOL-ih-sis) hydrolysis of glycogen to glucose-6-phosphate or to glucose [*glyco-* sweet (glucose), *-gen-* produce, *-o-* combining form, *-lysis* loosening]

glycolipid (glye-koh-LIP-id) lipid molecule with attached carbohydrate group [*glyco-* sweet (glucose), *-lipid* fat]

glycolysis (glye-KAHL-i-sis) first series of chemical reactions in carbohydrate catabolism; changes glucose to pyruvic acid in a series of anaerobic reactions [*glyco-* sweet (glucose), *-o-*combining form, *-lysis* loosening]

glycophospholipid (glye-koh-fos-foh-LIP-id) molecule that is part sugar and part phospholipid; formed in epidermal cells of the skin to produce a waterproof barrier [*glyco-* sweet (glucose), *phos-* light, *-pho* to bear, *-lipid* fat]

glycoprotein (glye-koh-PROH-teen) substance made of molecules that are a combined form of carbohydrate and protein [*glyco-* sweet (glucose), *-prote-* first rank, *-in* substance, *hormon-* excite]

glycoprotein hormone (glye-koh-PRO-teen HOR-mohn) hormone made of molecules that are a combined form of carbohydrate and protein [*glyco-* sweet (glucose), *-prote-* first rank, *-in* substance, *hormon-* excite]

glycosuria (glye-koh-SOO-ree-ah) glucose in urine; a sign of diabetes mellitus [*glyco-* sweet (glucose), *-ur-* urine, *-ia* condition]

goblet cell (GOB-let) epithelial cell that produces and secretes large amounts of mucus [*goblet-* small bowl, *cell-* storeroom]

Golgi apparatus (GOL-jee ap-ah-RA-tus) organelle consisting of small sacs stacked on one another near the nucleus that makes carbohydrate compounds, combines them with protein molecules, and packages the product for distribution from the cell [*Camillo Golgi* Italian histologist]

Golgi tendon organ (GOL-jee TEN-don OR-gan) sensory organ imbedded in muscle tendons made up of sensory neurons (Golgi tendon receptors) that are encapsulated with collagen bundles; also called *tendon organ* [*Camillo Golgi* Italian histologist, *tend-* pulled tight, *-on* unit]

Golgi tendon receptor (GOL-jee TEN-don ree-SEP-tor) sensory stretch receptor neuron (part of the Golgi tendon organ) that is responsible for proprioception (muscle tension); stimulated by excessive muscle contraction; also called *tendon receptor* [*Camillo Golgi* Italian histologist, *tend-* pulled tight, *-on* unit, *recept-*receive, *-or* agent]

Golgi tendon reflex (GOL-jee) spinal nerve reflex that protects muscles from tearing internally or pulling away from their tendinous points of attachment to bone because of excessive contractile force by relaxing a muscle when its tension becomes too great; also called *tendon reflex* [*Camillo Golgi* Italian histologist, *tend-* pulled tight, *-on* unit, *re-* back or again, *-flex* bend]

gomphosis (gom-FOH-sis) fibrous joint where a process is inserted into a socket; for example, the joint between the tooth and mandible [*gomphos-* bolt, *-osis* condition] *pl.*, gomphoses

gonad (GO-nad) sex gland in which reproductive cells are formed; ovary in women, testis in men [*gon-* offspring, *-ad* relating to]

gonadotroph (go-NAD-oh-trohf) cell type of the adenohypophysis (anterior pituitary) that secretes the gonadotropins luteinizing hormone (LH) and follicle-stimulating hormone (FSH) [*gon-* offspring, *-ad-* relating to, *-troph* nourish]

gonadotropin (go-nah-doh-TROH-pin) any of the hormones (FSH and LSH) produced by the anterior pituitary or embryonic tissue (hCG) that stimulate growth and maintenance of the testes or ovaries [*gon-* offspring, *-ad-* relating to, *-trop-* nourish, *-in* substance]

goniometer (gon-ee-OM-eh-ter) instrument used to measure range of motion (ROM) angles of a joint [*gonio-* angle, *-meter* measure]

gout (gowt) condition characterized by excessive levels of uric acid in the blood that are deposited in the joints [*gout-* drop]

gouty arthritis (gow-TEE ar-THRY-tis) metabolic disorder in which excess blood levels of uric acid are deposited within the synovial fluid of joints and other tissues [*gout-* drop, *-y* of or like, *arthr-* joint, *-itis* inflammation]

graafian follicle (GRAH-fee-en FOL-li-kul) a secondary follicle; consists of a mature ovum surrounded by granulosa cells at boundary of fluid-filled antrum [*Reijnier de Graaf* Dutch physician, *-an* relating to, *foll-* bag, *-icle* little]

graded potential local potentials that vary according to strength of stimulus and distance on membrane from source [*grade-* step, *potent-* power, *-ial* relating to]

graded strength principle skeletal muscles contract with varying degrees of strength at different times [*grade-* step, *strength-* power, *principle-* beginning, first part]

gradient (GRAY-dee-ent) measurable difference between two points of a given variable such as molecular concentration, pressure, or electrical charge [*grade-* step]

graft-versus-host rejection rejection of grafted tissue that occurs when donated tissue attacks the recipient's human leukocyte antigens [*graft-* stylus, *versus-* turned toward or against, *host-* guest, *re-* again, *-ject* to throw, *ion* process]

granulation tissue (gran-yool-AY-shun TISH-yoo) fibrous connective tissue with a rich blood supply and high number of immune cells that forms in a wound as a blood clot dissolves; it is a normal tissue present during the healing process [*gran-* grain, *-ul-*little, *-ation* process, *tissue* fabric]

granule cell (GRAN-yool) inhibits action potentials in the olfactory bulb [*gran-* grain, *-ule* little, *cell-* storeroom]

granulocyte (GRAN-yoo-loh-syte) leukocyte with granules in cytoplasm [*gran-* grain, *-ul-* little, *-cyte* cell]

granulosa cell (gran-yoo-LOH-sah) develop around each primary oocyte forming a primary follicle [*gran-* grain, *-ul-* little, *-osa* relating to, *cell* storeroom]

Graves disease inherited, possibly autoimmune endocrine disorder characterized by hyperthyroidism accompanied by exophthalmos (protruding eyes) [*Robert J. Graves* Irish physician, *dis-* opposite of, *-ease* comfort]

gray column any one of the three longitudinal areas (anterior, lateral, posterior) of the spinal cord that contain gray matter [*column-* pillar]

gray commissure (KOHM-is-shoor) middle band of gray matter that joins the left and right columns [*commissur-* a joining]

gray fiber unmyelinated nerve fiber; component of gray matter (*fiber-* thread]

gray matter type of nerve tissue characterized by a relative lack of myelin and often includes many neuron cell bodies and synapses that process information; contrast with *white matter* [*materia-* something from which something is made]

gray ramus (RAY-muss) short branch by which some postganglionic axons return to a spinal nerve [*ramus-* branch]

great saphenous vein (sah-FEE-nus) vein of the lower extremity; drains much of the superficial leg and foot [*saphen-* manifest, *-ous* relating to]

greater omentum (oh-MEN-tum) pouch-like extension of the visceral peritoneum extending from greater curvature of the stomach to the transverse colon; often called "the lace apron" [*omentum* fatty covering of intestines] *pl.*, omenta

greater vestibular gland (ves-TIB-yoo-lar) either of the glands on each side of the vaginal orifice that secrete a lubricating fluid; also called *Bartholin's glands* [*vestibul-* entrance hall, *-ar* relating to, *gland* acorn]

greenstick fracture type of incomplete bone fracture in which bone is bent but broken only on one side (common in children) [*fracture* a breaking]

gross anatomy the study of the larger structures of an organism, such as organs and systems, that are large enough to be seen without magnification; also called *macroscopic anatomy*; compare to **microscopic anatomy** [*gross* large, *ana-* apart, *-tom-* cut, *-y* action]

ground substance organic matrix of bone and cartilage [*substancia-* material]

growth hormone (GH) (HOR-mohn) hormone secreted by the anterior pituitary gland that controls the rate of skeletal and visceral growth [*hormon-* excite]

growth normal increase in size or number of cells [*growan-* to grow]

gustatory (GUS-tah-tor-ee) refers to taste [*gusta-* taste, *-ory* relating to]

gustatory cell (GUS-tah-tor-ee s) chemoreceptors in tongue that sense taste [*gusta-* taste, *-ory* relating to, *cell* storeroom]

gustatory hair (GUS-tah-tor-ee) cilia-like structure projecting from gustatory cells and into taste pores [*gusta-* taste, *-ory* relating to]

Guthrie test (GUH-three) blood test to detect phenylketonuria (PKU) [*Robert Guthrie* American microbiologist]

gynecology (gye-neh-KOL-oh-jee) study of the female reproductive system [*gyneco-* woman or female gender, *-logy* study of]

gyrus (JYE-rus) convoluted ridge, usually refers to rounded elevations of the brain surface; also called *convolution* [*gyro-* circle]

H

hair cells mechanoreceptors in the ear that are responsible for balance and hearing [*cell-* storeroom]

hair follicle (FOHL-i-kul) small blind-end tube extending from the dermis through the epidermis that contains the hair root and where hair growth occurs; sebaceous and apocrine skin glands have ducts leading into the follicle [*foll-* bag, *-icle* little]

hair papilla (pah-PIL-ah) small, cap-shaped cluster of cells located at the base of the follicle where hair growth begins [*papilla* nipple] *pl.*, papillae

hairline fracture type of bone fracture common in the skull—fracture components are small and aligned; if the fracture is pushed downward, called a *depressed fracture* [*fracture* a breaking]

Haldane effect (HAWL-dayne) phenomenon that refers to the increased CO_2 loading caused by a decrease in Po_2 [*John Scott Haldane* Scots physiologist]

hangman's fracture bone fracture of the posterior elements in the upper cervical spine, especially the axis [*fracture* a breaking]

haploid (number) (HAP-loyd) halved number of chromosomes in gametes resulting from meiosis; in humans, 23 chromosomes per sex cell [*haplo-* single, *-oid* of or like]

hard palate (PAL-et) portions of four bones (two maxillae and two palatines) that make up the roof of the mouth [*palatum-* roof of the mouth]

Haversian canal (hah-VER-shun) *see* **central canal** (of bone) [*Clopton Havers,* English physician]

Haversian system (hah-VER-shun) *see* **osteon** [*Clopton Havers,* English physician]

heart block blockage of impulse conduction from atria to ventricles so that the heart beats at a slower rate than normal [*block-* solid piece]

heart failure inability of the heart to pump returned blood sufficiently

heart murmur abnormal heart sound that may indicate valvular insufficiency or stenosing of the valve [*murmur* hum]

heart organ of circulatory system that pumps the blood; composed of cardiac muscle tissue [*heorte-* heart]

heat exhaustion condition caused by fluid loss resulting from activity of thermoregulatory mechanisms in a warm external environment [*heat-* hot, *exhaust-* to draw off or out, *-ion* process]

heat stroke life-threatening condition characterized by high body temperature; failure of thermoregulatory mechanisms to maintain homeostasis in a very warm external environment [*heat-* hot, *stroke-* the Stroke of God's hand]

Heberden node (HEB-er-den) swelling deformity of the distal interphalangeal joints [*William Heberden* English physician, *nod-* knot]

Heimlich maneuver (HYME-lik mah-NOO-ver) lifesaving technique that can be used to open a windpipe that suddenly becomes obstructed [*Henry J. Heimlich* American physician]

helper T cell (TH cell) immune system cells that help B cells differentiate into antibody-secreting plasma cells; also help coordinate cellular immunity through direct contact with other immune cells [helper, *T* thymus gland, *cell* storeroom]

hematocrit (hee-MAT-oh-krit) volume percent of blood cells in whole blood; packed cell volume [*hemato-* blood, *-crit* separate]

hematopoiesis (hee-mat-oh-poy-EE-sis) process of blood cell formation [*hemo-*blood, *-poiesis* making]

hematopoietic stem cell (hee-mah-toh-poy-ET-ik) nucleated cell in the red bone marrow that develops into a red blood cell [*hem-* blood, *-poiesis* making, *stem-* tree or trunk, *cell-* storeroom]

hematopoietic tissue (hee-mah-toh-poy-ET-ik) connective tissue type that is responsible for formation of blood cells and lymphatic system cells; in red bone marrow, spleen, tonsils, and lymph nodes [*hema-* blood, *-poie-* to make, *-ic* relating to, *tissu-* fabric]

hematuria (hem-ah-TOO-ree-ah) blood in the urine [*hema-* blood, *-ur-* urine, *-ia* condition]

heme (heem) iron-containing chemical group found in hemoglobin; temporarily binds to oxygen [*hem-* blood]

heme group (heem) *see* **heme** [*hem-* blood]

hemiazygos vein (hem-ee-AZ-i-gohs) vein of the thorax [*hemi-* half, *-a-* without, *-zygo-* union or yoke]

hemiplegia (hem-ee-PLEE-jee-ah) condition that refers to paralysis of one whole side of the body [*hemi-* half, *-plegia* stroke]

hemisphere (HEM-iss-feer) one half of a generally spherical structure, as in the left and right hemispheres of the cerebellum or cerebrum [*hemi-* half, *-sphere* globe]

hemisphericity (HEM-i-sfeer-is-i-tee) different specialization of function in each hemisphere of an organ, as in the cerebral hemispheres [*hemi-* half, *-spher-* globe, *-ic-* relating to, *-ity* state]

hemocytoblast (hee-moh-SYE-toh-blast) bone marrow stem cell from which all formed elements of blood arise [*hemo-* blood, *-cyto* cell, *-blast* embryonic state of development]

hemodialysis (hee-moh-dye-AL-i-sis) therapy involving separation of smaller (diffusible) particles from larger (nondiffusible) particles in blood through a semipermeable membrane, usually employed when a patient's kidneys fail to remove these particles from the blood [*hemo-* blood, *-dia-* through or between, *-lysis* loosening]

hemodynamics (hee-moh-dye-NAM-iks) study of the mechanisms that influence dynamic circulation of blood [*hemo-* blood, *-dynami-* force, *-ic* relating to]

hemoglobin (hee-moh-GLOH-bin) iron-containing protein in red blood cells responsible for their oxygen-carrying capacity [*hemo-*blood, *-glob-* ball, *-in* substance]

hemolytic anemia (hee-moh-LIT-ik ah-NEE-mee-ah) inherited blood disorder that is characterized by abnormal types of hemoglobin [*hemo-* blood, *-lyt-* loosen, *-ic* relating to, *an-* without, *-emia* blood condition]

hemophilia (hee-moh-FIL-ee-ah) X-linked inherited disorder that decreases the production of one or more plasma proteins responsible for blood clotting [*hemo-* blood, *-phil-* love, *-ia* condition]

hemorrhoid (HEM-eh-royd) varicose vein in the rectum; also called *piles* [*hema-* blood, *-rhoi-* flow]

hemostasis (hee-moh-STAY-sis) stoppage of blood flow [*hemo-* blood, *-stasis* standing]

Henle loop (HEN-lee) extension of the proximal tubule of the nephron; also called *loop of Henle* or *nephron loop* [*Friedrich Gustave Henle* German anatomist]

Henry's law gas law that describes how the pressure of a gas relates to the concentration of that gas in a liquid solution [*William Henry* English chemist]

heparin (HEP-ah-rin) substance obtained from the liver; inhibits blood clotting [*hepar-* liver, *-in* substance]

hepatic (heh-PAT-ik) relating to the liver [*hepa-* liver, *-ic* relating to]

hepatic duct (heh-PAT-ik) one of two ducts that drains bile out of the liver [*hepa-* liver, *-ic* relating to, *ducere-* to lead]

hepatic lobule (heh-PAT-ik LOB-yool) anatomical units of the liver [*hepa-* liver, *-ic* relating to, *lob-* pod, *-ule* small]

hepatic portal circulation (heh-PAT-ik PORtal) the route of blood flow through the liver [*hepa-* liver, *-ic* relating to, *port-* doorway, *-al* relating to, *circulat-* go around, *-tion* process]

hepatitis (hep-ah-TYE-tis) inflammation of the liver; may be caused by toxins, viruses (e.g., hepatitis A, hepatitis B), bacteria, or parasites [*hepat-* liver, *-itis* inflammation]

heredity (heh-RED-i-tee) transmission of characteristics from parents to offspring [*heredity-* inheritance]

Hering-Breuer reflex (HER-ing BROO-er REE- fleks) stretch reflex to control respirations—especially rate and rhythmicity [*Heinrich E. Hering* German physiologist, *Joseph Breuer* Australian physician, *re-* back or again, *-flex* bend]

herniated disk (HER-nee-ayt-ed) condition of the vertebral disk when the annulus fibrosis becomes disrupted, allowing the nucleus pulposus to protrude [*hernia-* rupture, *-ate* act of]

herpes zoster (HER-peez ZOS-ter) "shingles," viral infection that affects the skin of a single dermatome [*herpe* creep, *zoster* girdle]

heterozygous (het-er-oh-ZYE-gus) genotype with two different forms of a trait [*hetero-* different, *-zygo-* union or yoke, *-ous* characterized by]

hexose (HEK-sohs) monosaccharide molecule with six carbons [*hex-* six, *-ose* sugar]

hiatal hernia (hye-AY-tal HER-nee-ah) condition in which a portion of the stomach is pushed through the hiatus (opening) of the diaphragm, often weakening or expanding the cardiac sphincter at the inferior end of the esophagus [*hiat-* gap, *-al* relating to, *hernia* rupture] *pl.*, herniae or hernias

hiccup (HIK-up) involuntary spasmodic contraction of the diaphragm [*hiccup* imitation of sound made when hiccupping]

high-density lipoprotein (lip-oh-PROH-teen) a blood lipid fraction (plasma protein) composed of cholesterol, about 50% protein, and triglycerides; often called "good cholesterol" because it carries cholesterol out of the blood to the liver for elimination [*dense-* thick, *-ity* state, *lipo-* fat, *-protein* first rank]

high-energy bond chemical bond that requires an input of energy to form and when broken can result in the transfer of useful energy to cellular processes, as in ATP [*en-* in, *-erg* work, *-y* state, *bond* band]

hilum (HYE-lum) slit on medial surface of each lung where primary bronchi and pulmonary vessels enter; slit on medial surface of each kidney where blood vessels and other structures enter the kidney [*hilum* least bit] *pl.*, hila

hinge joint (hinj joynt) type of diarthrotic synovial joint that allows movement around a single axis in the manner of a hinge

histamine (HIS-tah-meen) inflammatory chemical [*hist-* tissue, *-amine* ammonia compound]

histogenesis (hiss-toh-JEN-eh-sis) formation of tissues from primary germ layers of embryo [*histo-* tissue, *-gen-* produce, *-esis* process]

histology (his-TOL-oh-jee) branch of microscopic anatomy that studies tissues; biology of tissues [*histo-* tissue, *-o-* combining form, *-log-* words (study of), *-y* activity]

histone (HISS-tohn) protein that organizes chromatin into nucleosomes [*histo-* tissue, -one unit]

histophysiology (his-toh-fiz-ee-OL-oh-jee) study of microscopic anatomy of cells and tissues and how structural information correlates with function [*histo-* tissue, *-o-* combining form, *-physio-* nature (function), *-o-* combining form, *-log-* words (study of), *-y* activity]

H-K pump ion pump in the gastric parietal cells [*H* hydrogen, *K* potassium]

Hodgkin disease (HOJ-kin) type of lymphoma (malignant lymph tumor) characterized by painless swelling of lymph nodes in the neck, progressing to other regions [*Thomas Hodgkin* English physician, *dis-* opposite of, *-ease* comfort]

Hodgkin lymphoma (HOJ-kin lim-FOH-mah) *see* **Hodgkin disease** [*Thomas Hodgkin* English physician, *lymph-* water, *-oma* tumor]

holocrine gland (HOH-loh-krin) gland that collects secretory product inside its cells, which then rupture completely to release it; for example, sebaceous glands of the skin [*holo-* whole, *-crine* to secrete]

homeostasis (ho-me-o-STAY-sis) relative constancy of the normal body's internal (fluid) environment [*homeo-* same or equal, *-stasis* standing still]

homeostatic control mechanisms (hoh-mee-oh-STAH-tik) devices for maintaining or restoring homeostasis [*homeo-* same or equal, *-static* relating to standing still]

homologous transfusion (ho-MOL-oh-gus) blood transfused into the body of another individual [*homo-* same, *-log-* word or proportion, *-ous* relating to]

homozygous (hoh-moh-ZYE-gus) genotype with two identical forms of a trait [*homo-* same, *-zygo-* union or yoke, *-ous* characterized by]

horizontal fissure (hor-i-ZON-tal FISH-ur) separates the superior lobe of the right lung from the middle lobe [*fissur-* cleft]

horizontal plane (hor-i-ZON-tal) transverse plane; divides the body into superior and inferior portions [*plane-* flat surface]

hormone (HOR-mohn) substance secreted by an endocrine gland into the bloodstream that acts on a specific target tissue to produce a given response [*hormon-* excite]

hormone-receptor complex (HOR-mohn ree-SEP-tor) when a steroid hormone combines to a receptor site in the target cell and then moves into the nucleus of the target cell [*hormon-* excite, *recept-* receive, *-or* agent, *complex-* surrounding or environment]

host-versus-graft rejection rejection of grafted tissue that occurs when the recipient's immune system recognizes foreign human leukocyte antigens and attacks them, destroying the donated tissue [*host-* guest, *versus-* turned toward or against, *graft-* stylus, *re-* again, *-ject* to throw, *ion* process]

human chorionic gonadotropin (HCG or hCG) (HYOO-man KOH-ri-on-ik go-nad-oh-TROH-pin) hormone secreted early in pregnancy by the placenta that serves to maintain the uterine lining [*human-* of or belonging to a man, *chorion-* skin, *-ic* relating to, *gon-* offspring, *-ad-* relating to, *-trop-* nourish, *-in* substance]

human engineered chromosome (HEC) (KROH-meh-sohm) gene augmentation procedure that inserts therapeutic genes into a separate strand of DNA that is inserted into nucleus of cell [*human-* of or belonging to a man, *chrom-* color, *-som-* body]

Human Genome Project (HGP) (JEE-nome) a worldwide collaborative effort of scientists and others to map out the entire human genome and study the biological, medical, and ethical aspects of their discoveries; the HGP is largely funded by U.S. government sources such as the

DOE (Department of Energy) and the NIH (National Institutes of Health); *see* **genome, genomics** (*human-* of or belonging to a man, *gen-* to produce, *-ome* from chromosome]

human immunodeficiency virus (HIV) (im-yoo-no-deh-FISH-en-see) a retrovirus that contains RNA that produces its own DNA inside infected cells; results in acquired immune deficiency syndrome (AIDS) [*human-* of or belonging to man, *immuno-* free (immunity), *virus* poison]

human leukocyte antigen (HLA) (LOO-koh-syte AN-ti-jen) protein involved in transplant rejection [*human-* of or belonging to man, *leuko-* white, *-cyte* cell, *anti-*against, *-gen* produce]

human placental lactogen (hPL) (plah-SEN-tal lak-TOH-jen) hormone released by the placenta; promotes development of mammary glands during pregnancy and regulates energy balance in fetus [*human-* of or belonging to man, *placenta* flat cake, *-al* relating to, *lacto-* milk, *-gen* produce]

humerus (HYOO-mer-us) arm bone [*humer-us* arm] *pl.*, humeri

humoral immunity (HYOO-mor-al i-MYOO-ni-tee) antibody-mediated immunity occurring within blood plasma and other body fluids [*humor-* liquid, *-al* relating to, *immun-*free, *-ity* state]

huntingtin (HUN-ting-tin) a protein normally present in all cells; an abnormal version of huntingtin is produced in people with Huntington disease (HD), clinging to molecules too tightly in the brain and thus preventing normal function [*George S. Huntington* American physician]

Huntington disease (HD) (HUN-ting-ton) an inherited disease characterized by chorea (involuntary, purposeless movements) that progresses to severe dementia and death; *see* **huntingtin** [*George S. Huntington* American physician, *dis-* opposite of, *-ease* comfort]

hyaline cartilage (HYE-ah-lin KAR-ti-lij) most common type of cartilage; appears gelatinous and glossy [*hyaline* glass, *cartilag* cartilage]

hyaline membrane disease (HMD) (HYE-ah-lin) condition that results from a deficiency of surfactant in premature infants [*hyal-* glass, *-ine* of or like, *membrane-* thin skin, *dis-* opposite of, *-ease* comfort]

hyaluronic acid (hye-al-yoo-RAHN-ik ASS-id) type of proteoglycan that helps thicken and hold together the matrix of connective tissue; *see* **proteoglycan** [*hyal-* glass, *uron-*urine, *-ic* relating to, *acid-* sour]

hybridoma (hye-brid-OH-mah) hybrid cell formed by fusion of cancerous cell with a lymphocyte to mass produce a specific antibody (monoclonal antibodies) [*hybrid-*mixed offspring, *-oma* tumor]

hydrase (HYE-drays) enzyme that adds water to a molecule without splitting it [*ase-*enzyme]

hydrocele (HYE-dro-seel) accumulation of fluid that causes scrotal swelling [*hydro-*water, *-cele* tumor]

hydrocephalus (hye-droh-SEF-ah-lus) condition that results from an accumulation of cerebrospinal fluid in the subarachnoid space around the brain [*hydro-* water, *-cephalus* head]

hydrocortisone (hye-droh-KOHR-ti-zohn) hormone secreted by the adrenal cortex; cortisol; compound [*hydro-* water, *-cortisone* cortex of adrenal gland]

hydrogen bond (HYE-droh-jen) weak chemical bond that occurs between the partial positive charge on a hydrogen atom covalently bound to a nitrogen or oxygen atom and the partial negative charge of another polar molecule [*hyro-* water, *-gen* produce]

hydrogen ion (HYE-droh-jen EYE-on) a proton or a hydrogen atom without its electron; occurs in water and water solutions; produces an acidic solution; has a positive charge (H^+) [*hyro-* water, *-gen* produce, *ion-*to go]

hydrolase (HYE-droh-lays) hydrolyzing enzyme [*hydro-* water, *-ase* enzyme]

hydrolysis (hye-DROHL-i-sis) chemical process in which a compound is split by addition of H^+ and OH^- portions of a water molecule [*hydro-* water, *-lysis* loosening]

hydronephrosis (hye-droh-neh-FROH-sis) condition resulting when urine backs up into the kidney, causing a swelling of the renal pelvis and calyces [*hydro-* water, *-nephr-* kidney, *-osis* condition]

hydrophilic (hye-dro-FIL-ik) "water-loving" [*hydro-* water, *-phil-* love, *-ic* relating to]

hydrophobic (hye-droh-FOH-bik) "water-fearing" [*hydro-* water, *-phob-* fear, *-ic* relating to]

hydrosalpinx (hye-droh-SAL-pinks) condition that results from obstruction of the uterine tube and marked dilation at the end of the tube caused by accumulation of fluid that cannot escape [*hydro-* water, *-salpinx* tube] *pl.*, hydrosalpinges

hydrostatic pressure (hye-droh-STAT-ik) force of a fluid pushing against some surface [*hydro-* water, *-static* relating to standing still, *pressure-* act of pressing]

hydrostatic pressure gradient (hye-droh-STAT-ik PRESH-ur GRAY-dee-ent) situation in which a difference in pressure is caused by the force of a fluid as it moves from one point to another [*hydro-* water, *-static* relating to standing still, *pressure-* act of pressing, *grade-* step]

hymen (HYE-men) Greek for "membrane"; mucous membrane that may partially or entirely occlude the vaginal outlet [*hymen* Greek god of marriage]

hyoid bone (HYE-oyd bohn) U-shaped bone of the neck between the mandible and the larynx [*hy-* Greek letter upsilon (Υ or υ), *-oid* like]

hypercapnia (hye-per-KAP-nee-ah) excessive carbon dioxide in the blood [*hyper-* above, *-capn-* vapor (CO_2), *-ia* condition]

hypercholesterolemia (hye-per-koh-les-ter-ohl-EE-mee-ah) elevated blood cholesterol that my lead to atherosclerosis and other cardiovascular problems [*hyper-* excessive, *-chole-* bile, *-stero-* solid, *-ol-* alcohol, *-emia* blood condition]

hyperchromic (hye-per-KROH-mik) abnormally high hemoglobin content [*hyper-* excessive, *-chrom-* color, *-ic* relating to]

hyperextension (hye-per-ek-STEN-shun) stretching an extended part beyond its anatomical position; may clinically refer to abnormal extension beyond normal range of motion [*hyper-* excessive, *-ex-* out, *-ten-*stretch, *-sion* process]

hyperglycemia (hye-per-glye-SEE-mee-ah) higher than normal blood glucose concentration [*hyper-* excessive, *-glyc-* sweet (glucose), *-emia* blood condition]

hyperkalemia (hye-per-kah-LEE-mee-ah) excessive potassium in the blood [*hyper* excessive, *-kal-* potassium, *-emia* blood condition]

hyperkeratosis (hye-per-ker-ah-TOH-sis) thickening of the horny layer of the skin [*hyper* excessive, *-kera-* horn, *-osis* condition]

hypernatremia (hye-per-nah-TREE-mee-ah) excessive sodium in the blood [*hyper-* excessive, *-natri-* sodium, *-emia* blood condition]

hyperopia (hye-per-OH-pee-ah) refractive disorder of the eye caused by a shorter-than-normal eyeball; results in ability to see objects at a distance better than objects nearer; also called *farsightedness* [*hyper-* excessive or above, *-op-* vision, *-ia* condition]

hyperpituitarism (hye-per-pih-TYOO-i-tar-iz-em) disorder that results from benign tumors in the pituitary gland [*hyper-* excessive, *-pituitar-* phlegm (pituitary gland), *-ism* condition]

hyperplasia (hye-per-PLAY-zee-ah) growth of an abnormally large number of cells at a local site, as in a neoplasm or tumor [*hyper-* excessive, *-plasia* shape]

hyperpnea (hye-PERP-nee-ah) abnormal increase in respiratory rate and depth [*hyper-* excessive, *-pne-* breathe, *-a* condition]

hyperpolarization (hye-per-pol-lar-i-ZAY-shun) increase in electrical charges separated by the cell membrane; causes change further below 0 mV [*hyper-* excessive, *-pol-*pole, *-ar-* relating to, *-ization* process]

hypersecretion (hye-per-seh-KREE-shun) too much secretion of a substance [*hyper-*excessive, *-secret-* separate, *-tion* process]

hypersensitivity (hye-per-SEN-sih-tiv-i-tee) type of inappropriate or excessive response of the immune system [*hyper-* excessive, *sensitiv-* able to feel, *-ity* state]

hypertension (HTN) (hye-per-TEN-shun) abnormally high blood pressure [*hyper-* excessive, *-tens-* stretch or pull tight, *-sion* state]

hyperthyroidism (hye-per-THYE-royd-iz-em) hypersecretion of thyroid hormone [*hyper-*excessive, *-thyr-* shield (thyroid gland), *-oid* like, *-ism* condition]

hypertonic (hye-per-TON-ik) adjective used to describe a solution that has a higher potential osmotic pressure than a solution to which it is being compared; a hypertonic solution tends to have high osmolality and thus tends to gain water (by way of osmosis) from the solution to which it is compared; solution containing a higher level of salt (NaCl) than is found in a living red blood cell (above 0.9% NaCl); causes cells to shrink [*hyper-* excessive, *-ton-* tension, *-ic* relating to]

hypertrophic cardiomyopathy (hye-PER-troh-fik KAR-dee-oh-my-OP-ah-thee) genetic condition that causes an abnormal enlargement of the heart [*hyper-* excessive, *-troph-* nourishment, *-ic* relating to, *cardi-*heart, *-myo-* muscle, *-path-* disease, *-y* state]

hypertrophy (hye-PER-tro-fee) increased size of an organ or part caused by an increase in the size of its cells [*hyper-* excessive, *-troph-*nourishment, *-y* state]

hyperventilation (hye-per-ven-ti-LAY-shun) very rapid, deep respirations [*hyper-* excessive, *-vent-* fan or create wind, *-tion* process]

hypervitaminosis (hye-per-vye-tah-mih-NO-sis) general name for any condition resulting from an abnormally high intake of vitamins [*hyper-* excessive, *-vita-* life, *-amin-*ammonia compound, *-osis* condition]

hypervolemia (hye-per-voh-LEE-mee-ah) abnormally increased blood volume [*hyper-*excessive, *-vol-* volume, *-emia* blood condition]

hypoallergenic (hye-poh-AL-er-jen-ik) refers to having a lower potential for producing allergic reactions [*hypo-* under or below, *-aller-* other, *-gen-* produce, *-ic* relating to]

hypocalcemia (hye-poh-kal-SEE-mee-ah) abnormally low calcium levels in the blood [*hypo-* under or below, *-calc-* lime (calcium), *-emia* blood condition]

hypochloremia (hye-poh-kloh-REE-mee-ah) abnormally low levels of chloride in the blood associated with potassium loss [*hypo-*under or below, *-chlor-* green (chlorine), *-emia* blood condition]

hypodermis (hye-poh-DER-mis) loose layer fascia under the skin, rich in fat and areolar tissue located beneath the dermis; also called *subcutaneous layer* or *superficial fascia* [*hypo-* under or below, *-dermis* skin]

hypoglossal (hye-poh-GLOS-al) under the tongue [*hypo-* under or below, *-gloss-*tongue, *-al* relating to]

hypoglossal nerve (hye-poh-GLOS-al) cranial nerve XII; motor nerve; responsible for tongue movement [*hypo-* under or below, *-gloss-*tongue, *-al* relating to]

hypoglycemia (hye-poh-gly-SEE-mee-ah) lower than normal blood glucose concentration [*hypo-* under or below, *-glyc-* sweet (glucose), *-emia* blood condition]

hypokalemia (hye-poh-kah-LEE-mee-ah) abnormally low serum potassium level [*hypo-*under or below, *-kal-* potassium, *-emia* blood condition]

hyponatremia (hye-poh-nah-TREE-mee-ah) abnormally low sodium levels in the blood [*hypo-* under or below, *-natri-* sodium, *-emia* blood condition]

hypophyseal portal system (hye-poh-FIZ-ee-al POR-tal) complex of small blood vessels through which releasing hormones travel from the hypothalamus to the pituitary [*hypo-* under or below, *-physis-* growth, *-al* relating to, *portal* doorway]

hypophysectomy (hye-poff-i-SEK-toh-mee) surgical removal of the pituitary gland [*hypo-* under or below, *-phys-* growth, *-ec-*out, *-tom-* cut, *-y* action]

hypophysis (hye-POF-i-sis) pituitary gland; also called *hypophysis cerebri* [*hypo-* under or below, *-physis-* growth]

hypopotassemia (hye-poh-poh-tah-SEE-mee-ah) potassium deficit [*hypo-* under or below, *-potass* potassium, *-emia* blood]

hyposecretion (hye-poh-seh-KREE-shun) too little secretion of a substance [*hypo-* under or below, *-secret-* separate, *-tion* process]

hypospadias (hye-poh-SPAY-dee-us) congenital condition that is characterized by the opening of the urethral meatus on the underside or ventral surface of the glans or penile shaft [*hypo-* under or below, *-spad-*rip or split]

hypothalamic-pituitary-adrenal axis (HPA) (hye-poh-THAL-ah-mik pi-TOO-i-tair-ee ah-DREE-nal) process that activates a stress mechanism that stimulates the sympathetic nervous system and pituitary gland [axis axle]

hypothalamus (hye-poh-THAL-ah-muss) important autonomic and neuroendocrine control center located inferior to the thalamus in the brain [*hypo-* under or below, *-thalamus* inner chamber] *pl.*, hypothalami

hypothermia (hye-poh-THER-mee-ah) failure of thermoregulatory mechanisms to maintain homeostasis in a very cold external environment; results in abnormally—sometimes life-threatening—low body temperature [*hypo-* under or below, *-therm-*heat, *-ia* abnormal condition]

hypothesis (hye-POTH-eh-sis) idea or scientific concept, usually based on previous ideas or observations, that is proposed as a possible explanation of nature or a natural process; hypotheses undergo intense testing before being accepted widely in the scientific community; *see* law, science, theory [*hypo-* under or below, *-thesis* placing or proposition] *pl.*, hypotheses (hye-POTH-eh-seez)

hypotonic (hye-poh-TON-ik) adjective used to describe a solution that has a lower potential osmotic pressure than a solution to which it is being compared; a hypotonic solution tends to have low osmolality and thus tends to lose water (by way of osmosis) to the solution to which it is compared [*hypo-* under or below, *-ton-* tension, *-ic* relating to]

hypoventilation (hye-poh-ven-ti-LAY-shun) slow and shallow respirations [*hypo-* under or below, *-vent-* fan or create wind, *-tion* process]

hypovolemia (hye-poh-voh-LEE-mee-ah) inadequate fluid volume in the extracellular compartment; dehydration [*hypo-* under or below, *-vol-* volume, *-emia* blood condition]

hypovolemic shock (hye-poh-voh-LEE-mik) condition when dehydration results in multiple organ failure [*hypo-* under or below, *-vol-* whirl, *-emi(a)-* blood condition, *-ic* relating to]

hypoxia (hye-POK-see-ah) deficiency of oxygen in the blood [*hypo-* under or below, *-ox-* oxygen, *-ia* condition]

hysterosalpingogram (his-ter-oh-sal-PING-go-gram) x-ray technique used to produce images of the uterus and uterine tube [*hyster-* uterus, *-salping-* tube, *-gram* drawing]

I

ideal gas gas whose molecules are so far apart that the molecules rarely collide with one another [*idea-* form, *gas-* empty space]

identical twin one of two siblings born as a result of the splitting of embryonic tissue from the same zygote early in development [*identic-* the same, *-al* relating to, *twin-* twofold]

ideogram (ID-ee-oh-gram) a graphic representation of any idea; in genomics, a simple cartoon of a chromosome often used to show the overall physical structure of a chromosome; *see* chromosome, genomics [*ide-* idea, *-gram* drawing]

idiopathic (id-ee-o-PATH-ik) refers to a disease of undetermined cause [*idio-* peculiar, *-path-* disease, *-ic* relating to]

ileum (IL-ee-um) distal portion of the small intestine [*ileum* groin or flank] *pl.,* ilea

iliac lymph node (ILL-ee-ak limf nohd) pelvic and groin lymph node [*ilia-* loin or gut (ileum), *-ac* relating to, *lymph* water, *nod-* knot]

ilium (IL-ee-um) largest and uppermost coxal bone [*ilium* flank] *pl.,* ilia (IL-ee-ah)

immune deficiency (i-MYOON deh-FISH-en-see) failure of immune system mechanisms to defend against pathogens; also called *immunodeficiency* [*immun-* free (immunity)]

immune system (i-MYOON) body's defense system against disease [*immun-* free (immunity)]

immunization (i-myoo-ni-ZAY-shun) deliberate artificial exposure to disease for the purpose of producing acquired immunity [*immun-* free (immunity), *-tion* process of]

immunoglobulin (Ig) (i-myoo-noh-GLOB-yoo-lin) antibody [*immuno-* free (immunity), *-glob-* ball, *-ul-* small, *-in* substance]

immunological synapse (IS) (i-myoo-no-LOJ-ik-al SIN-aps) temporary junction between an immune cell and another cell, such as another immune cell or a target cell to be destroyed; compare to *synapse* [*immuno-* free (immunity), *-log-* words (study of), *-ical* relating to, *syn-* together, *-aps-* join]

immunology (i-myoo-NOL-oh-jee) study of immune system functions and mechanisms [*immuno-* free (immunity), *-logy* study of]

immunosuppressive drugs (i-myoo-no-soo-PRES-iv) drugs that suppress the immune system's ability to attack the foreign antigens in the donated tissue [*immuno-* free (immunity), *-suppress-* press down, *-ive* relating to]

immunotherapy (im-yoo-no-THAYR-ah-pee) therapeutic technique that bolsters a person's immune system in an attempt to control a disease [*immuno-* free, *-therapy* treatment]

impacted fracture type of bone fracture in which one end of the fracture is driven into the diaphysis of the other fragment [*impact-***to push into,** *fracture* **a breaking**]

imperforate hymen (im-PER-fah-rayt HYE-men) condition in which the hymen completely covers the vaginal outlet [*im-* not, *-perfor-* pierce, *-ate* state, *hymen* Greek god of marriage]

impermeable (im-PERM-ee-ah-bul) adjective used to describe a membrane that does not allow substances to move through (permeate) it [*im-* not, *-permeable* pass through]

impermeant (im-PERM-ee-ent) adjective used to describe a substance that is not able to move through (permeate) a membrane [*im-* not, *-permeable* pass through]

impetigo (im-peh-TYE-go) highly contagious bacterial skin infection that occurs most often in children [*impetigo* an attack]

implantation (im-plan-TAY-shun) process in which developing offspring tissue connects to the uterine wall of the mother [*im-* in, *-planta-* set or place, *-ation* process]

impotence (IM-poh-tense) *see* erectile dysfunction (ED) [*im-* not, *-poten-* power, *-ence* state]

impulse (IM-puls) an electrical signal; *see* action potential [*impulse-* to drive]

in vitro fertilization (IVF) (in VEE-troh FER-ti-li-ZAY-shun) artificial union of sperm and egg "in glass" in a laboratory dish [*in* in, *vitro* glass, *fertil-* fruitful, *-ation* process]

inborn errors of metabolism (IN-born AIR-ors meh-TAB-oh-liz-em) group of genetic conditions involving a deficiency or absence of a particular enzyme [*metabol-* change, *-ism* action]

inborn immunity (IN-born i-MYOO-ni-tee) inherited immunity to disease [*in-* within, *-born* brought forth, *immuno-* free (immunity)]

inclusion an unidentified particle within a cell or other structure [*in-* within, *-clus* to shut, *-ion* process]

incomplete fracture type of bone fracture in which some fracture components are still partially joined [*fracture* a breaking]

incomplete tetanus (TET-ah-nus) tetanus with very short periods of relaxation occurring between peaks of muscle tension [*tetanus-* extreme tension]

incontinence (in-KON-ti-nens) involuntary voiding of urine [*incontinentia-* inability to retain]

incretin (IN-kre-tin) any GI hormone that triggers the release of insulin from the pancreatic islets; examples, glucagon-like peptide 1 (GLP-1) and gastric inhibitory peptide [glucose-dependent insulinotropic peptide] (GIP) [*in-* in, *-cret-* secrete, *-in* substance]

incubation (in-kyoo-BAY-shun) early, latent stage of an infection, during which an infection has begun but signs or symptoms have not yet developed in the host [*in-* in or on, *-cubat-* lie, *-tion* condition of]

indirect calorimetry (kal-oh-RIM-eh-tree) method used to determine body mass index (BMR) [*in-* not, direct, *calor-* heat, *-metr-* measuring, *-y* process]

infancy period of human development from birth to about 18 months of age [*infan-* unable to speak, *-y* state]

infant respiratory distress syndrome (IRDS) (RES-per-ah-toh-ree di-STRESS SIN-drohm) leading cause of death in premature babies, caused by a lack of surfactant in the alveolar air sacs, inferior lower portion; opposite of superior [*infan-* unable to speak, *re-* again, *-spir-* breathe, *-tory* relating to, *distress-* restraint, *syn-* together, *-drome* course]

infectious mononucleosis (in-FEK-shuss mah-noh-noo-klee-OH-sis) a viral (noncancerous) white blood cell (WBC) disorder common in young adults; characterized by leukocytosis of atypical lymphocytes and severe fatigue [*infect-* stain, *-ous* relating to, *mono-* single, *-nucle-* nut, *-osis* condition]

inferior lower; opposite of superior [*infer-* lower, *-or* quality]

inferior cerebellar peduncle (SAIR-eh-bell-ar peh-DUNG-kul) tract that enters the cerebellum from the medulla and cord [*infer-* lower, *-or* quality, *cerebellar* relating to the cerebellum (small brain), *ped-* foot, *-uncl-* little]

inferior colliculi (koh-LIK-yoo-lee) form the posterior, upper part of the midbrain [*infer-* lower, *-or* quality, *colli-* hill, *-iculus* small] *sing.,* colliculus

inferior nasal concha (KONG-ke) *see* concha [*infer-* lower, *-or* quality, *nas-* nose, *-al* relating to, *concha* sea shell] *pl.,* conchae (KONG-kee or KONG-kay)

inferior vena cava (VEE-nah KAY-vah) vein of the thorax; drains blood from the lower trunk and extremity [*infer-* lower, *-or* quality, *vena* vein, *cava* hollow] *pl.,* venae cavae

infertility (in-fer-TIL-i-tee) failure to conceive after 1 year of regular unprotected intercourse [*in-* not, *-fertil-* fruitful, *-ity* state]

inflammation (in-flah-MAY-shun) group of responses to a tissue irritant marked by signs of redness, heat, swelling, and pain [*inflam-* set afire, *-tion* process]

inflammatory exudate (in-FLAM-ah-toh-ree EK-soo-dayt) substance that accumulates in the interstitial spaces as a result of increased permeability of blood vessels, increased blood flow, and migration and accumulation of white blood cells [*inflam-* set afire, *-ory* relating to, *exudate* to sweat out]

inflammatory joint disease (in-FLAM-ah-toh-ree) joint condition that involves inflammation of the synovial fluid [*inflam-* set afire, *-ory* relating to, *dis-* opposite of, *-ease* comfort]

inflammatory response (in-FLAM-ah-toh-ree) specific process involving tissues and blood vessels in response to injury [*inflam-* set afire, *-ory* relating to]

infraspinatus muscle (IN-frah-spy-nah-tus) one of the four rotator cuff muscles around the shoulder joint [*infra-* below, *-spina-* spine, *mus-* mouse, *-cle* little]

infundibulum (in-fun-DIB-yoo-lum) stalk that connects the pituitary gland to the hypothalamus [*infundibulum* funnel] *pl.,* infundibula

ingestion (in-JES-chun) taking in of complex foods, usually by mouth [*in-* within, *-gest-* carry, *-tion* process]

inguinal hernia (ING-gwi-nal HER-nee-ah) rupture of the lower abdominal wall at the inguinal canal [*inguin-* groin, *-al* relating to, *hernia* rupture] *pl.,* herniae or hernias

inguinal lymph node (ING-gwi-nal limf nohd) pelvic and groin lymph node [*inguin-* groin, *-al* relating to, *lymph* water, *-atic* relating to, *nod-* knot]

inherited immunity (in-HAIR-i-ted i-MYOO-ni-tee) inborn immunity; occurs when immune mechanisms are put in place by genetic mechanisms during the early stages of human development [*in-* within, *-herit* to make an heir, *immun-* free (immunity)]

inhibin (in-HIB-in) glycoprotein hormone produced by the ovary to regulate FSH secretion by the anterior pituitary (adenohypophysis) [*inhib-* inhibit, *-in* substance]

inhibitory (in-HIB-i-tor-ee) something that slows or stops a process [*inhib-* to restrain, *-ory* relating to]

inhibitory neurotransmitter (in-HIB-i-tor-ee noo-roh-TRANS-mit-er) neurotransmitter that causes hyperpolarization of the postsynaptic membrane, thereby decreasing chances of impulse propagation [*inhib-* restrain, *-ory* relating to, *neuro-* nerve, *-trans-* across, *-mitt-* send, *-er* agent]

inhibitory postsynaptic potential (IPSP) (in-HIB-i-tor-ee post-si-NAP-tik poh-TEN-shal) temporary hyperpolarization that makes the inside of the membrane even more negative than at the resting potential [*inhib-* restrain, *-ory* relating to, *post-* after, *-syn-* together, *-apt-* join, *-ic* relating to, *potent-* power, *-ial* relating to]

innate immunity (IN-ayt i-MYOO-ni-tee) type of immunity that exists prior to exposure to a specific antigen and that can recognize and destroy a variety of harmful agents or conditions; also called *nonspecific immunity* [*innat-* inborn, *immun-* free, *-ity* state]

inner cell mass layer of cells in the blastocyst [*inner-* within, *cell-* storeroom]

inner ear region of the ear consisting of a bony labyrinth and a membranous labyrinth; also called *labyrinth* [*inner-* within]

inorganic compounds (in-or-GAN-ik) chemical constituents that do not contain both carbon and hydrogen; for example, water, carbon dioxide, and oxygen [*in-* not, *-organic* natural, *compound-* to assemble]

inspiratory capacity (IC) (in-SPY-rah-tor-ee kah-PAS-i-tee) maximal amount of air an individual can inspire following a normal expiration [*in-* in, *-spir* to breathe, *-tory* relating to, *capac-* able to hold much, *-ity* state]

insertion (muscle insertion) attachment of a muscle to the bone that it moves when contraction occurs (as distinguished from its origin); (insertion mutation) a type of genetic mutation that occurs when one or more nucleotide bases appear within the usual sequence of nucleotide bases in a gene; in insertion mutations, the cell cannot read the genetic code normally and thus the encoded protein cannot be made in its usual form; *see* deletion [*in-* in, *-ser-* join, *-tion* process]

inspiration (in-spih-RAY-shun) process of bringing air into the lungs [*in-* in, *-spir-* breathe, *-ation* process]

inspiratory capacity (IC) (in-SPY-rah-tor-ee) maximum amount of air an individual can inspire after a normal expiration [*in-* in, *-spir-* breathe, *-tory* relating to]

inspiratory center (in-SPY-rah-tor-ee) one of the two most important control centers located in the medulla; the other is the expiratory center [*in-* in, *-spir-* breathe, *-tory* relating to]

inspiratory reserve volume (IRV) (in-SPY-rah-tor-ee) amount of air that can be forcibly inspired over and above a normal inspiration [*in-* in, *-spir-* breathe, *-tory* relating to, *volume-* paper roll]

insula (IN-soo-lah) lobe of the cerebral cortex; lies hidden from view in the lateral fissure [*insula* island] *pl.,* insulae

insulin (IN-suh-lin) hormone secreted by beta cells of the pancreatic islets that increases the uptake of glucose and amino acids by most body cells [*insul-* island, *-in* substance]

integral membrane protein (IMP) (IN-tegrel MEM-brayn PROH-teen) any of the numerous kinds of proteins embedded within cellular membranes [*integr-* whole, *-al* relating to, *membran-* thin skin, *prote-* primary, *-in* substance]

integrin (in-TEG-rin) type of protein that acts as a connector to bind structural proteins in a way that connects a cell's cytoskeleton to surrounding structures such as other cells [*integr-* whole, *-in* substance]

integument (in-TEG-yoo-ment) skin; the body's largest organ [*in-* on, *-teg-* cover, *-ment* result of action]

integumentary system (in-teg-yoo-MEN-tar-ee) skin and its related structures [*in-* on, *-teg-* cover, *-ment* result of action, *-ary* relating to]

interatrial bundle (in-ter-AT-tree-al) conducting fibers that facilitate rapid conduction to the left atrium [*inter-* between, *-atri-* entrance courtyard, *-al* relating to]

intercalated disk (in-TER-kah-lay-ted) any of the disk-like connections between ends of adjacent cardiac muscle fibers characterized by gap junctions and often appearing as tiny, darkly stained lines in micrographs [*intercalate-* to insert]

intercarpal joint (in-ter-KAR-pal) articulation between the eight carpal bones [*inter-* between, *-carp-* wrist, *-al* relating to]

interferon (IFN) (in-ter-FEER-on) small protein produced by the immune system that inhibits virus multiplication [*inter-* between, *-fer-* strike, *-on* substance]

interleukin (IL) (in-ter-LOO-kin) any of a class of about a dozen cytokines, regulatory chemicals secreted by leukocytes and other

cells, that are involved in regulating a wide variety of immune functions in different cell types; each interleukin is named by the IL acronym with its number, such as IL-1, IL-2, and so on [*inter-* between, *-leuko-*white (blood cell), *-in* substance]

intermediate fiber (in-ter-MEE-dee-it) muscle fiber exhibiting characteristics between fast and slow fibers [*inter-* between, *-medi-* middle, *-ate* of or like]

intermediate filament (in-ter-MEE-dee-it FIL-ah-ment) twisted strands of protein, slightly larger than microfilaments that make up part of the cell's internal skeleton (the cytoskeleton) [*inter-* between, *-mediate* to divide, *fila-* threadlike *-ment* process]

intermittent claudication (in-ter-MIT-tent klaw-dih-KAY-shen) condition that causes cramplike pain in the calves after walking and is caused by intermittent arterial occlusion by platelet plugs [*inter-* between, *-mitt-* send, *claudica-* limping, *-ation* process]

internal capsule large mass of white matter associated with the basal nuclei [*intern-* inside, *-al* relating to, *caps-* box, *-ul-* little]

internal intercostal muscle (in-ter-KOS-tal) muscle attached to ribs; contraction depresses ribs [*intern-* inside, *-al* relating to, *inter-* between, *-costal-* rib, *-al* relating to, *mus-* mouse, *-cle* little]

internal jugular vein (JUG-yoo-lar) deep vein of the neck [*intern-* inside, *-al* relating to, *jugul-* neck, *-ar* relating to]

internal oblique muscle (oh-BLEEK) abdominal muscle [*intern-* inside, *-al* relating to, *obliq-* slanted, *mus-* mouse, *-cle* little]

internal os cavity of the uterus that opens into the cervical canal [*intern-* inside, *-al* relating to, *os* mouth or opening] *pl.*, ora

internal table inner wall of a flat bone of the cranium, made of compact bone; compare to *external table* [*intern-* inside, *-al* relating to]

interneuron (in-ter-NOO-ron) in a three-neuron reflex arc, nerve cell that conducts impulses from a sensory neuron to a motor neuron [*inter-* between, *-neuron* nerve]

internodal bundle (in-ter-NOH-dal) conducting fibers that allow for complete contraction of both atrial chambers before the impulse reaches the ventricles [*inter-*between, *-nod-* knot, *-al* relating to]

interoceptor (in-ter-oh-SEP-tor) *see* visceroceptor [*inter-* inward, *-cept-* receive, *-or* agent]

interosseous muscle (in-ter-OSS-ee-us) muscle of the hand [*inter-* between, *-os-* bone, *-ous* relating to, *mus-* mouse, *-cle* little]

interphalangeal joint (in-ter-fah-LAN-jee-al) articulation that exists between the heads of the phalanges and the bases of the more distal phalanges [*inter-* between, *-phalang-* finger bones (ref. from rows of soldiers), *-al* relating to]

interphase (IN-ter-fayz) mitotic phase immediately before visible condensation of the chromosomes during which the DNA of each chromosome replicates itself [*inter-* between, *-phase* stage]

interspinales group (in-ter-spy-NAH-leez) group of back muscles that connect one vertebra to the next—also helping to extend the back and neck or flex them to the side [*inter-* between, *-spina-* spine, *-al* relating to]

interstitial (in-ter-STISH-al) in an in-between location, as between tissue cells [*inter-* between, *-stit-* stand, *-al* relating to]

interstitial cell (in-ter-STISH-al) any of the small cells in the testes found between seminiferous tubules and that secrete the male sex hormone, testosterone; also called *Leydig cell* [*inter-* between, *-stit-* stand, *-al* relating to, *cell* storeroom]

interstitial cystitis (in-ter-STISH-al sis-TYE-tis) form of bladder inflammation that occurs without evidence of bacterial infection [*inter-*between, *-stit-* stand, *-al* relating to, *cyst-* bag, *-itis* inflammation]

interstitial fluid (IF) (in-ter-STISH-al) fluid located in microscopic spaces between cells [*inter-* between, *-stit-* stand, *-al* relating to]

interstitial fluid colloid osmotic pressure (IFCOP) (in-ter-STISH-al KOL-oyd os-MAH-tik) one of four types of pressure that serve as a control mechanism for water exchange between plasma and interstitial fluid; draws fluid back out of the capillaries [*inter-* between, *-stit-* stand, *-al* relating to, *coll-* glue, *-oid* like, *osmo-* push, *-ic* relating to]

interstitial fluid hydrostatic pressure (IFHP) (in-ter-STISH-al hye-droh-STAT-ik) one of four types of pressure that serve as a control mechanism for water exchange between plasma and interstitial fluid; tends to force fluid out of the interstitial fluid into the capillaries [*inter-* between, *-stit-* stand, *-al* relating to, *hydro-* water, *-stat-* stand, -ic relating to]

interstitial growth (in-ter-STISH-al) cartilage growth following mitosis and secretion of matrix by chondrocytes; interstitial growth of epiphyseal plate results in growth in length of long bones; also called *endogenous growth* [*inter-* between, *-stit-* stand, *-al* relating to]

intestinal flora (in-TES-ti-nal FLOR-ah) community of various bacterial populations that normally inhabit the colon [*intestin-* intestine, *-al* relating to, *flora-* flowers]

intestinal juice (in-TES-ti-nal) refers to the sum total of intestinal secretions [*intestin-*intestine, *-al* relating to]

intestinal phase (in-TES-ti-nal) stage of gastric secretion triggered when material leaves the stomach and enters the small intestine [*intestin-* intestine, *-al* relating to, *phase* appearance]

intestine (in-TES-tin) part of the digestive tract into which food passes after it leaves the stomach; separated into two segments, the small and the large [*intestin-* intestine]

intracellular (in-trah-SELL-yoo-lar) relating to the interior of the cell [*intra-* occurring within, *-cell-* storeroom, *-ular* relating to]

intracellular control (in-tra-SELL-yoo-lar) level of homeostatic control of body processes that occurs within cells, as in genetic regulation or enzymatic regulation of the cell [*intra-* inside or within, *-cell* storeroom]

intracellular fluid (ICF) (in-trah-SELL-yoo-lar) water inside the cell [*intra-* occurring within, *-cell-* storeroom, *-ular* relating to]

intracellular fluid (ICF) compartment (in-trah-SELL-yoo-lar) fluid located within cells; largest fluid compartment [*intra-* occurring within, *-cell-* storeroom, *-ular* relating to, *com-* together, *-partiri* to share]

intramembranous ossification (in-trah-MEM-brah-nus os-i-fi-KAY-shun) process by which most flat bones are formed within connective tissue membranes [*intra-* within, *-membran-* thin skin, *-ous* characterized by, *os-* bone, *-fication* to make]

intramural plexus (in-trah-MYOO-ral PLEK-sus) complex arrangement of neurons in the gastrointestinal tract [*intra-* within, *-mura-*wall, *-al* relating to, *plexus* network] *pl.*, plexi or plexuses

intramuscular injection (in-trah-MUSS-kyoo-lar in-JEK-shun) administration of medication into the muscle [*intra-* within, *mus-* mouse, *-cle* little, *-ar* relating to]

intratracheal injection (in-trah-TRAY-kee-al in-JEK-shun) administration of surfactant through a tube directly into the airways [*intra-* within, *-trache-* rough duct, *-al* relating to]

Intrauterine device (IUD) (in-trah-YOO-ter-in) contraceptive device that works by inducing an immune response toxic to gametes; some IUDs also release progesterone and thus have an action similar to other hormonal contraceptives [*intra-* inside or within, *-uter-* womb, *-ine* relating to]

intravenous injection (in-trah-VEE-nus in-JEK-shun) administration of medication into veins [*intra-* within, *-ven-* vein, *-ous* relating to, *in-* in, *-ject* throw, *-tion* process]

intrinsic clotting pathway (in-TRIN-sik) series of reactions that begin with factors normally present in the blood [*intr-* within, *-sic* beside]

intrinsic control (in-TRIN-sik) level of homeostatic control of body processes that occurs within a particular tissue or organ, as when local regulators such as prostaglandins regulate local physiology; may be called *local control* or *autoregulation* [*intr-* inside or within, *-insic* beside]

intrinsic eye muscle (in-TRIN-sik) involuntary muscle located within the eye; responsible for size of the iris and shape of the lens [*intr-* within, *-sic* beside, *mus-* mouse, *-cle* small]

intrinsic factor (in-TRIN-sik) binds to molecules of B_{12}, protecting them from the acids and enzymes of the stomach; secreted by parietal cells [*intr-* inside or within, *-insic* beside]

intrinsic foot muscle (in-TRIN-sik) muscle located within the foot [*intrins-* inward, *-ic* relating to, *mus-* mouse, *-cle* little]

intrinsic muscle (in-TRIN-sik) muscle that is actually within the part moved [*instrins-* inward, *-ic* relating to, *mus-* mouse, *-cle* little]

intrinsic rhythm (in-TRIN-sik RITH-em) phenomenon of specialized cells in the sinoatrial (SA) node that produce regular impulses without stimulation from the brain or spinal cord [*instrins-* inward, *-ic* relating to, *rhythm-* measure flow or movement]

intron (IN-trahn) segment of a gene in a DNA molecule that is not used to code for a protein; introns are removed from mRNA transcripts of the gene and the remaining exons are spliced together to form the final, edited version of the mRNA transcript; *see* exon, RNA [*intra-* within, *-on* unit]

inversion (in-VER-shun) movement that turns the sole of the foot inward [*in- inward, -ver-* turn, *-sion* process]

involuntary muscle (in-VOL-un-tair-ee) smooth muscle not under conscious control and found in organs such as the stomach, small intestine, and ureters [*in-* not, *volunt-* will, *mus-* mouse, *-cle* little]

involution (in-voh-LOO-shun) return of an organ to its normal size after enlargement; also after retrograde or degenerative change [*in-* in, *-volu-* roll, *-tion* state]

ion (EYE-on) electrically charged atom or group of atoms [*ion* to go]

ion channel (EYE-on) transport proteins in the plasma membrane that move sodium or potassium ions [*ion* to go, *channel-* water pipe]

ionic bond (eye-ON-ik) electrocovalent bond; bond formed by transferring of electrons from one atom to another [*ion* to go, *bond* band]

ionizing radiation (EYE-on-eyz-ing) form of radioactivity, or radiation energy, resulting from alpha or beta particles or gamma rays emitted from radioactive atoms scoring direct hits on other atoms and thus ionizing the atoms by knocking electrons out of their outer energy levels; the effect of ionization may injure, kill, or change living cells; *see* radiation, radiation sickness

ipsilateral (ip-si-LAT-er-al) on the same side [*ion-* to go, *-ize* to make, *radia-* to shine, *-tion* process]

ipsilateral reflex arc (ip-si-LAT-er-al REE-fleks ark) reflex arc whose receptors and effectors are located on the same side of the body [*ipsi-* same, *-later* side, *-al* relating to, *re-* again, *-flex* bend, *arc-* bow]

iris (EYE-ris) colored portion of the eye [*iris* rainbow]

iron deficiency anemia (deh-FISH-en-see ah-NEE-mee-ah) condition in which there are inadequate levels of iron in the diet causing less hemoglobin to be produced [*iron-* holy metal, *an-* without, *-emia* blood condition]

irregular bone bone that has no particular size or shape [*ir-* not, *-regula-* rule, -ar relating to]

irritability ability of a muscle to be stimulated; *see* excitability [*irrita-* tease, *-ble* able or tending to, *-ity* state]

irritable bowel syndrome (SIN-drohm) common chronic noninflammatory condition that is often caused by stress; characterized by diarrhea or constipation with or without pain [*irrita-* tease, *-ble* able or tending to, *bowel* sausage, *syn-* together, *-drome* running or (race) course]

ischemia (is-KEE-mee-ah) decreased blood supply to a tissue resulting in impairment of cell function [*ische-* hold back, *-emia* blood condition]

ischemic (is-KEE-mik) relating to ischemia [*ischem-* hold back, *-ic* relating to]

ischiocavernosus muscle (iss-kee-oh-KAV-er-no-sus) muscle of the pelvic floor; form the urogenital triangle [*ischio-* hip joint, *-cavern-* hollow space, *-osus* relating to, *mus-* mouse, *-cle* little]

ischium (IS-kee-um) lowermost coxal bone [*ischium* hip joint] *pl.*, ischia (IS-kee-ah)

islets of Langerhans (EYE-lets of lahn-GER-hans) pancreatic islets [*isl-* island, *-et* little, *Paul Langerhans* German pathologist]

isoimmunity (eye-soh-i-MYOO-ni-tee) normal but undesirable reaction of the immune system to antigens from a different individual of the same species [*iso-* equal, *-immun-* free, *-ity* state]

isometric contraction (eye-soh-MET-rik) type of muscle contraction in which muscle does not alter the distance between two bones; *see* isotonic contraction

isotonic (eye-soh-TON-ik) two fluids that have the same potential osmotic pressure [*iso-* equal, *-ton-* tension, *-ic* relating to]

isotonic contraction (eye-soh-TON-ik) type of muscle contraction in which the muscle sustains the same tension or pressure and a change in the distance between two bones occurs [*iso-* equal, *ton-* stretch or tension, *-ic* relating to, *con-* together, *-tract-* drag or draw, *-tion* process]

isotope (EYE-so-tohp) atoms with the same atomic number but different atomic masses [*iso-* equal, *-tope* place]

isthmus (ISS-muss) constriction between two larger parts of an organ; for example, isthmus of thyroid [*isthmus* narrow connection or passage]

J

jaundice (JAWN-dis) abnormal yellowing of skin, mucous membranes, and white of eyes [*jaun-* yellow, *-ice* state]

jejunum (jeh-JOO-num) middle third of the small intestine [*jejun-* empty, *-um* thing]

joint capsule sleevelike extension of the periosteum of each of the bones at an articulation [*joint-* to join, *caps-* box, *-ule* little]

joint cavity small space between articulating surfaces of the two bones of the joint [*joint-* to join, *cavus-* hollow, *-ity* state]

joint junction between two or more bones; articulation [*joint-* to join]

joule (J or j) (jool) unit of measuring energy; *see* calorie [*James Prescott Joule* English physicist]

juvenile rheumatoid arthritis (JRA) (JOO-veh-ney-el ROO-mah-toyd ar-THRY-tis) systemic autoimmune disease that results in severe deterioration and deformity of joints [*juven-* youth, *-ile* of or like, *rheuma-* flow, *-oid* like, *arthr-* joint, *-itis* inflammation]

juxtaglomerular apparatus (juks-tah-gloh-MER-yoo-lar app-ah-RAT-us) in the nephron, the complex of cells from the distal

tubule and the afferent arteriole, which helps regulate blood pressure by secreting renin in response to blood pressure changes in the kidney; located near the glomerulus; also called *juxtaglomular complex* [*juxta-* near or adjoining, *-glomer-* ball, *-ul-*little, *-ar* relating to]

juxtaglomerular (JG) cell (jux-tah-gloh-MER-yoo-lar) cell of the juxtaglomerular apparatus [*juxta-* near or adjoining, *-glomer-* ball, *-ul-*little, *-ar* relating to, *cell* storeroom]

juxtamedullary nephron (jux-tah-MED-oo-lair-ee NEF-ron) region of the nephron that lies near the junction of the cortical and medullary layers of the kidney [*juxta-* near or adjoining, *-medulla-* middle, *-ary* relating to, *nephro-* kidney, *-on* unit]

K

Kaposi sarcoma (KAH-poh-see sar-KOH-mah) rare malignant neoplasm of the skin that often spreads to lymph nodes and internal organs; Kaposi sarcoma is often found in AIDS patients [*Moritz K. Kaposi* Hungarian dermatologist, *sarco-* flesh, *-oma* tumor]

karyotype (KAIR-ee-oh-type) ordered arrangement of photographs of chromosomes from a single cell used in genetic counseling to identify chromosomal disorders such as trisomy or monosomy [*karyo-* nucleus, *-type* kind]

Kegel exercise (KEE-gel) noninvasive treatment used to reduce urinary stress incontinence [*Arnold Kegel* American gynecologist]

keloid (KEE-loyd) unusually thick fibrous scar on the skin [*kel-* claw, *-oid* like]

keratin (KER-ah-tin) tough, fibrous protein substance in hair, nails, outer skin cells, and horny tissues [*kera-* horn, *-in* substance]

keratinization (ker-ah-tin-i-ZAY-shun) process by which cells of the stratum corneum become fitted with keratin and move to the surface [*kera* horn, *-in-* substance, *-iz-* to cause, *-ation* process]

keratinocyte (keh-RAT-i-no-syte) epidermal cell responsible for synthesizing keratin [*kera-* horn, *-in-* substance, *-cyte* cell]

keratohyalin (ker-ah-toh-HYE-ah-lin) staining granules located within the stratum lucidum; required for surface keratin formation [*kera-* horn, *-hyaline* glass]

ketogenesis (kee-toh-JEN-eh-sis) process that produces ketone bodies [*keto-* acetone, *-gen-*produce, *-esis* process]

ketone body (KEE-tohn) acid produced during fat catabolism [*keto-* acetone, *-one* chemical]

ketosis (kee-TOH-sis) large amount of ketone bodies present in the blood of a person with uncontrolled diabetes mellitus [*keto-*acetone, *-osis* condition]

kidney (KID-nee) one of the two organs that cleanses the blood of waste products continually produced by metabolism; the kidneys produce urine [*kidnere-* kidney]

killer T cells cytotoxic T lymphocytes [*kill-*to deprive of life, *cell-* storeroom]

kilocalorie (Kcal) (KIL-oh-kal-oh-ree) 1000 calories; *see* Calorie [*kilo-* one thousand, *-calor* heat]

kinase (KYE-nayz) substance that converts proenzymes to active enzymes [*kin-* motion, *-ase* enzyme]

kinesiopathology (kih-nee-see-oh-PATH-ol-oh-jee) existence of or study of any abnormality of motion of the musculoskeletal system of the body [*kines-* movement, *-path-*disease, *-o-* combining form, *-log-* words (study of), *-y* activity]

kinesthesia (kin-es-THEE-zee-ah) "muscle sense"; that is, sense of position and movement of body parts [*kines-* movement, *-thesia-* seeking]

kinin (KYE-nin) chemical compound that is released from injured tissues; results in vasodilation and increases the permeability of blood vessels [*kin-* move, *-in* substance]

Klinefelter syndrome (KLINE-fel-ter SIN-drohm) genetic disorder caused by the presence of two or more X chromosomes in a male (typically trisomy XXY); characterized by long legs, enlarged breasts, low intelligence, small testes, sterility, and chronic pulmonary disease [*Harry F. Klinefelter* American physician, *syn-* together, *-drome* running or (race) course]

knee jerk reflex extension of the leg in response to tapping of the patellar tendon; also called *patellar reflex* [*re-* again, *-flex* bend]

Korotkoff sound (kor-ROT-koff) sound of blood turbulence heard when measuring arterial blood pressure with a sphygmomanometer [*Nicolai Korotkoff* Russian physician]

Krause end bulb (KROWS) *see* bulboid corpuscle [*Wilhelm J. F. Krause* German anatomist]

Krebs cycle also called *tricarboxylic acid (TCA) cycle*; *see* citric acid cycle [*Sir Hans Adolf Krebs* British biochemist, *cycl-* circle]

Kupffer cell (KOOP-fer) macrophage found in spaces between liver cells [*Karl W. von Kupffer* German surgeon, *cell-* storeroom]

kwashiorkor (kwah-shee-OR-kor) nutritional disorder that results from a protein deficiency in the presence of sufficient calories [*kwashiorkor* one who is displaced (from the breast)]

kyphosis (kye-FOH-sis) abnormally exaggerated thoracic curvature of the vertebral column [*kypho-* hump, *-osis* condition]

L

labia majora (LAY-bee-ah mah-JOH-rah) large lateral folds of the vulva; [*labia* lips, *majora* large] *sing.*, labium majus

labia minora (LAY-bee-ah mih-NO-rah) small medial folds of the vulva [*labia* lips, *minora* small] *sing.*, labium minor

labor process of expulsion of the fetus and the placenta; childbirth [*labor-* work]

labyrinth (LAB-i-rinth) bony cavities and membranes of the inner ear [*labyrinth* maze]

lacrimal apparatus (LAK-ri-mal app-ah-RAT-us) in the eye, the tear (lacrimal) gland plus associated ducts that form tears [*lacrima-*tear, *-al* relating to, *apparatus-* equipment, preparation]

lacrimal bone (LAK-ri-mal) facial bone that joins the maxilla, frontal bone, and ethmoid bone [*lacrima-* tear, *-al* relating to]

lactase (LAK-tayse) enzyme needed to digest lactose [*lact-* milk, *-ase* enzyme]

lactation (lak-TAY-shun) milk production [*lact-* milk, *-ation* process]

lacteal (LAK-tee-al) lymphatic vessel located in each villus of the intestine; serves to absorb fat materials from chyme passing through the small intestine [*lact-* milk, *-al* relating to]

lactic acid (LAK-tik ASS-id) product of anaerobic energy metabolism that accumulates in muscle tissue during exercise and causes a burning sensation [*lac-* milk, *-ic* relating to, *acid* sour]

lactic acidosis (LAK-tik ass-ih-DOH-sis) condition characterized by elevated blood lactate levels, electrolyte imbalances, and decreased blood pH [*lac-* milk, *-ic* relating to, *acid-* sour, *-osis* condition]

lactogenic hormone (lak-toh-JEN-ik HOR-mohn) any hormone that initiates milk production by secretory cells of breast alveoli [*lact-* milk, *-gen-* produce, *-ic* relating to, *hormon-* excite]

lactose intolerance (LAK-tohs in-TOL-er-ans) condition in which one lacks the enzyme lactase, resulting in an inability to digest lactose (a disaccharide in milk and dairy products) [*lact-* milk, *-ose* carbohydrate (sugar), *in-* not, *-toler-* bear, *-ance* state]

lactotroph (lak-toh-TROHF) cell type of the adenohypophysis (anterior pituitary) that secretes prolactin [*lacto-* milk, *-troph* nourish]

lacuna (lah-KOO-nah) space or cavity; for example, lacunae in bone contain bone cells [*lacuna* pit] *pl.*, lacunae

lamella (lah-MEL-ah) thin layer, as of bone [*lam-* plate, *-ella* little] *pl.*, lamellae

lamellar corpuscle (lah-MEL-ar KOR-pus-ul) sensory receptor with a layered encapsulation found deep in the dermis that detects pressure on the skin surface; also known as *Pacini corpuscle* [*lam-* plate, *-ella-* little, *-ar* relating to, *corpus-* body, *-cle* little]

lamina propria (LAM-in-ah PROH-pree-ah) fibrous connective tissue underlying the epithelium in mucous membranes (*lamina* thin plate, *propria* proper]

laminar flow (LAM-i-nar) the manner in which blood flows through a smooth vessel [*lamina-* plate, *-ar* relating to]

Langer lines (LANG-er) pattern of dense bundles of white collagenous fibers that characterize the reticular layers of dermis; also called *cleavage lines* [*Karl Langer-* Austrian anatomist]

Langerhans cell (LAHNG-er-hanz) epidermal dendritic cell; cell that plays a role in immunology of the skin and thus serves as defense mechanism for the body [*Paul Langerhans* German pathologist, *cell* storeroom]

lanugo (lah-NOO-go) extremely fine and soft hair coat on developing fetus [*lanugo* down]

laparoscope (LAP-ah-roh-skope) fiberoptic viewing instrument [*laparo-* abdomen, *-scop-* see]

LaPlace, Law of (lah-PLAHS) *see* Young-LaPlace Law [*Pierre S. de Laplace* French physicist]

laryngitis (lar-in-JYE-tis) inflammation of the mucous tissues of the larynx (voice box) [*laryng-* voice box (larynx), *-itis* inflammation]

laryngopharynx (lah-ring-go-FAIR-inks) lowest part of the pharynx [*laryng-* voice box (larynx), *-pharynx* throat] *pl.*, laryngopharynges or laryngopharynxes

larynx (LAIR-inks) voice box located just below the pharynx; the largest piece of cartilage making up the larynx is the thyroid cartilage, commonly known as the *Adam's apple* [*larynx* voice box] *pl.*, larynges or larynxes

laser therapy (LAY-zer) procedure that uses an intense beam of light to destroy a tumor [*laser* shortened "light amplification by stimulated emission of radiation"]

laser-assisted *in situ* keratomileusis (LASIK) (LAY-zer ah-SIS-ted in-SYE-too kair-at-oh-mill-YOO-sis) refractive eye surgery to correct myopia [*in* in, *situ* place, *kera-* horn, *-mileusis* carving]

latent period (LAY-tent) period between time a muscle fiber is stimulated and when it contracts; precedes the contraction phase [*latent-* to lie hidden]

lateral (LAT-er-al) of or toward the side; opposite of medial [*later* side, *-al* relating to]

lateral corticospinal tract (LAT-er-al kohr-ti-koh-SPY-nal) spinal motor tract that controls the contraction of individual or small group of muscles, particularly those moving hands, fingers, feet, and toes on opposite side of the body [*later-* side, *-al* relating to, *cortico-* bark, *-spin-* backbone, *-al* relating to, *tract-* trail]

lateral fissure (fissure of Sylvius) (LAT-er-al FISH-ur [FISH-ur of SIL-vi-us]) deep groove between the temporal lobe below and the frontal and parietal lobes of the brain [*later-* side, *-al* relating to, *Franciscus Sylvius* German medical professor]

lateral lobe (LAT-er-al) one of two large lobes of the thyroid gland [*later-* side, *-al* relating to]

lateral longitudinal arch (LAT-er-al lon-jih-TOO-di-nal) supportive arch of the foot; shaped by the calcaneus, cuboid tarsals, and the fourth and fifth metacarpals [*later-*side, *-al* relating to, *longitud-* length, *-al* relating to]

lateral spinothalamic tract (LAT-er-al spy-no-tha-LAM-ik) sensory tract that integrates crude touch, pain, and temperature [*later-*side, *-al* relating to, *spino-* backbone, *-thalam-*inner chamber, *-ic* relating to, *tract-* trail]

law scientific idea or explanation that is viewed with a very high degree of confidence or certainty after rigorous testing and observation; compare to hypothesis and theory [*lagu-* law]

law of partial pressures *see* Dalton's law [*pars-*parts, *-al* relating to, *pressure-* to press]

lecithin (LES-i-thin) substance in bile that emulsifies dietary oils, and fats in the lumen of the small intestine [*lecith-* yolk, *-in* substance]

Le Fort fracture (leh-FOHR) bone fracture of the face and/or base of the skull (also called *Guérin fracture*) [*Rene Le Fort* French surgeon, *Alphonse F.M. Guérin*, French surgeon, *fracture* a breaking]

legionnaires' disease (LEE-jen-airs) form of bacterial pneumonia caused by infection with the *Legionella pneumophila* organism [originally named for American Legion, convention location at which first outbreak was noted]

length-tension relationship maximum strength that a muscle can develop bears a direct relationship to the initial length of its fibers [*length-* long, *tens-* stretch, *-ion* process of]

lens refracting mechanism of the eye that is located directly behind the pupil [*lens-* lentil]

lentiform nucleus (LEN-ti-form NOO-klee-us) mass of gray matter in the interior of each cerebral hemisphere; consists of the putamen and the pallidum [*lent-* lentil (lens), *-form* shape, *nucleus* nut or kernel] *pl.*, nuclei

leptin (LEP-tin) a protein hormone produced by fat-storing cells in adipose tissue that plays a role in inhibiting food intake by regulating the satiety center in the hypothalamus; leptin also plays a role in reducing fat storage in nonadipose cells in the liver and skeletal muscles; because of its role in fat storage, it may play a role in future treatments for diabetes, obesity, and other conditions related to fat metabolism; *see* satiety center; leptin also helps regulate some immune and neuroendocrine functions and plays a role in development [*lept-*thin, *-in* substance]

lesser omentum (oh-MEN-tum) extension of the peritoneum that is attached from the liver to the lesser curvature of the stomach and the first part of the duodenum [*omentum* fatty covering of intestines]

lesser vestibular gland (ves-TIB-yoo-lar) tiny mucous gland located near the female's urinary meatus by way of two small ducts; also called *Skene's glands* [*vestibul-* entrance hall, *-ar* relating to, *gland* acorn]

leukemia (loo-KEE-mee-ah) blood cancer; affects white blood cells [*leuk-* white, *-emia* blood condition]

leukocyte (LOO-koh-syte) white blood cell [*leuko-* white, *-cyte* cell]

leukocytosis (loo-koh-SYE-toh-sis) abnormally high white blood cell numbers in the blood [*leuko-* white, *-cyt-* cell, *-osis* condition]

leukocytosis-promoting (LP) factor (look-oh-sye-TOH-sis) substance released by injured tissue; stimulates the release of white cells from storage areas and increases the num-

ber of circulating white blood cells [*leuko-* white, *-cyto-* cell, *-osis* condition]

leukopenia (loo-koh-PEE-nee-ah) abnormally low white blood cell numbers in the blood [*leuko-* white, *-penia* lack]

leukoplakia (loo-koh-PLAY-kee-ah) precancerous change in the mucous membrane characterized by thickened, white, and slightly raised patches of tissue [*leuko-*white, *-plak-* flat area, *-ia* condition]

leukoreduction (loo-koh-ree-DUK-shen) filtering process that removes leukocytes from blood [*leuko-* white, *-reduc-* lead back, *-tion* process]

leukorrhea (loo-koh-REE-ah) whitish vaginal discharge [*leuko-* white, *-rrhea* flow]

leukotriene (loo-koh-TRY-een) cytokine compound that functions as an inflammation mediator [*leuko-* white, *-tri-* three, *-ene* chemical]

levator ani muscle (leh-VAY-tor A-nye) muscle of the pelvic floor [*levator* lifter, *ani* of the anus, *mus-* mouse, *-cle* little]

levator scapulae (leh-VAY-tor SCAP-yoo-lee) shoulder girdle muscle that elevates the scapula [*levator* lifter, *scapulae* of the shoulder blade]

lever (LEV-er) any rigid bar free to turn about a fixed point [*lev-* lift, *-er* agent]

lever system (LEV-er) simple mechanical device that makes the work of moving a weight or other load easier [*lev-* lift, *-er* agent]

levodopa (L-dopa) (LEEV-oh-doh-pah) a molecule derived from tyrosine in neurons that is used to produce the neurotransmitter dopamine [*levo-* left (form of molecule), *-dopa* acronym denoting 3.4- *d*ihydroxy*p*henyl*a*lanine]

Leydig cell (LYE-dig) *see* interstitial cell [*Franz von Leydig* German anatomist, *cell* storeroom]

ligament (LIG-ah-ment) band of white fibrous tissue connecting bones to other bones [*liga-* bind, *-ment* result of action]

light micrograph (LM) (MYK-roh-graf) photographic image of a microscopic structure using a light microscope [*micro-* small, *-graph* drawing]

light microscope (LM) (MYK-roh-skope) magnifying device made of glass lenses that use light transmitted through or reflected from a specimen [*micro-* small, *-scop-* see]

limb lead (lim leed) electrode placed on limbs during electrocardiography [*lim-* limb, branch of tree, *lead-* to go]

limbic system (LIM-bik) parts of the brain involved in emotions and sense of smell; plays key role in coupling sensory inputs to short- and long-term memory; consists of the hippocampus, the hypothalamus, and several other structures [*limb-* edge, *-ic* relating to]

limited-field radiation treatment procedure for early-stage cancers that have not spread [*limes-* limit, *feld-* open land, *radiare-* to shine, *-tion* process]

linea alba (LIN-ee-ah AL-bah) tough band of connective tissue that covers the rectus abdominis muscle [*linea* line, *alba* white]

linear fracture (LIN-ee-ar) type of bone fracture in which fracture line is parallel to the bone's long axis [*linea-* line, *-ar* relating to, *fracture* a breaking]

lingual tonsil (LING-gwal TAHN-sil) tonsil located at the base of the tongue [*lingua-* tongue, *-al* relating to]

lip region that lines the mouth and continues into the oral cavity [*lip-* edge]

lipase (LYE-pays) fat-digesting enzyme [*lip-* fat, *-ase* enzyme]

lipid (LIP-id) class of organic compounds that includes fats, oils, and related substances [*lip-* fat, *-id* form]

lipogenesis (lip-oh-JEN-eh-sis) formation of body fat from food sources [*lipo-* fat, *-gen-* produce, *-esis* process]

lipoma (li-POH-mah) benign tumor of adipose (fat) tissue [*lip-* fat, *-oma* tumor]

lipoprotein (lip-oh-PROH-teen) substance that is part lipid and part protein; produced mainly in the liver [*lipo-* fat, *protein* first rank]

lithotripsy (LITH-oh-trip-see) technique that pulverizes kidney stones [*litho-* stone, *-trips-* pound, *-y* action]

lithotriptor (LITH-oh-trip-tor) ultrasound generator used in lithotripsy; also spelled "lithotripter" [*litho-* stone, *-trip-* pound, *-or* agent]

litmus (LIT-mus) pigment used to test for acidity and alkalinity [*litmus-* colored herb]

lobar (LOH-bar) referring to a lobe [*lob-*lobe, *-ar* relating to]

lobectomy (loh-BEK-toh-mee) surgical removal of a single lobe of an organ, as in the removal of one lobe of a lung [*lob-* lobe, *-ectomy* surgical removal]

local potential (poh-TEN-shal) slight shift from resting membrane potential in a specific region of the plasma membrane [*potent-* power, *-ial* relating to]

lock-and-key model description of how a specific enzyme will fit into only a specific substrate, like a key fits into a lock [*lock-* fastening, *model-* mode]

long bone bone that is characterized by its extended longitudinal axis and unique articular ends

longissimus capitis muscle (lon-JIS-i-mus KAP-i-tis) muscle of the head [*longissumus* longest or very long, *capit-* head, *mus-* mouse, *-cle* little]

longitudinal arch (lon-ji-TOO-dih-nal) two arches, the medial and lateral, that extend lengthwise in the foot [*longitud-* length, *-al* relating to]

longitudinal fissure (lon-ji-TOO-dih-nal FISH-ur) deepest groove in the cerebrum; divides the cerebrum into two hemispheres [*longitud-* length, *-al* relating to]

loose fibrous connective tissue *see* areolar tissue [*loose-*free, *con-* together, *-nect-* bind, *-ive* relating to, *fibr-* thread, *-ous*, characterized by, *tissu-* fabric]

lordosis (lor-DOH-sis) abnormally exaggerated lumbar curvature of the vertebral column [*lordos-* bent backward, *-osis* condition]

low-density lipoprotein (lip-oh-PROH-teen) a blood lipid fraction (plasma protein) composed of relatively more cholesterol and triglycerides than protein; often call "bad cholesterol" because high levels contribute to atherosclerotic plaque formation and arterial wall damage [*lipo-* fat, *-protein* first rank]

lower esophageal sphincter (LES) (eh-SOF-eh-JEE-ul SFINGK-ter) muscle located at the junction between the terminal portion of the esophagus and the stomach; also called *cardiac sphincter* [*es-* will carry, *-phag-* food (eat), *-al* relating to, *sphinc-* bind tight, *-er* agent]

lower respiratory tract (RES-pih-rah-tor-ee) region of the respiratory tract that consists of the trachea, all segments of the bronchial tree, and the lungs [*re-* again, *-spir-* breathe, *-tory* relating to, *tractus* trail]

lumbar plexus (LUM-bar PLEK-sus) spinal nerve plexus located in the low back [*lumb-* loin, *-ar* relating to, *plexus* network] *pl.*, plexi or plexuses

lumbar puncture (LUM-bar) clinical procedure in which some cerebrospinal fluid is withdrawn from the subarachnoid space in the lumbar region of the spinal cord for analysis [*lumb-* loin, *-ar* relating to]

lumbar vertebra (LUM-bar VER-teh-bra) lower five bones of the vertebral column; support the small of the back [*lumb-* loin, *-ar* relating to, *vertebra* that which turns] *pl.*, vertebrae

lumbrical muscle (LUM-bri-kal) intrinsic muscle of the foot [*lumbrical* like a worm, *mus-* mouse, *-cle* little]

lumen (LOO-men) the hollow area of a hollow organ such as the stomach, blood vessel, or urinary bladder; *see also* luminal [*lumen* light] *pl.*, lumina

luminal (LOO-min-al) relating to the hollow part, or lumen, of a hollow organ such as the urinary bladder or small intestine; *see also* lumen [*lumin-* light, *-al* relating to]

lumpectomy (lump-EK-toh-mee) surgical removal of a tumor from breast tissue [*lump-* mass, *-ec-* out, *-tom-* cut, *-y* action]

lung cancer malignancy of pulmonary tissue [*cancer* crab or malignant tumor]

lunula (LOO-nyoo-lah) crescent-shaped white area under the proximal nail bed [*luna-* moon, *-ula* small]

luteal phase (LOO-tee-al) phase of the menstrual cycle that occurs between ovulation and the onset of menses; also called *premenstrual phase*, *postovulatory phase*, or *secretory phase* [*lute-* yellow, *-al* relating to]

luteinization (loo-tee-in-i-ZAY-shun) formation of a golden body (corpus luteum) in the ruptured follicle [*lute-* yellow, *-ization* process]

luteinizing hormone (LH) (loo-tee-in-EYE-zing HOR-mohn) in females, acts in conjunction with follicle-stimulating hormone (FSH) to stimulate follicle and ovum maturation, release of estrogen, and ovulation; known as the *ovulating hormone*; in males, causes testes to develop and secrete testosterone [*lute-* yellow, *-izing* process, *hormon-* excite]

lymph (limf) watery fluid drained from the tissue spaces that returns excess fluid and protein molecules to the blood via the lymphatic vessels [*lymph* water]

lymph node (limf nohd) small structure that performs biological filtration of lymph on its way to the circulatory system [*lymph* water, *nod-* knot]

lymphangiography (lim-fan-jee-OG-reh-fee) method using x-rays and radiopaque material to examine lymphatic vessels [*lymph-* water, *-angi-* vessel, *-graph-* draw, *-y* process]

lymphangitis (lim-fan-JYE-i-tis) inflammation of lymph vessels, usually caused by infection, characterized by fine red streaks extending from the site of infection; may progress to septicemia (blood infection) [*lymph-* water, *-angi-* vessel, *-itis* inflammation]

lymphatic capillary (lim-FAT-ik KAP-i-lair-ee) microscopic blind-end vessels that transport lymph [*lymph-* water, *-atic* relating to, *capill-* hair, *-ary* relating to]

lymphatic vessel (lim-FAT-ik) any vessel of a system of blind-ended vessels that collect lymph and deliver it to the circulatory system via the thoracic duct and the right lymphatic duct [*lymph-* water, *-atic* relating to]

lymphedema (lim-fah-DEE-mah) swelling caused by lymphatic vessel blockage [*lymph-* water, *-edema* swelling]

lymphocyte (LIM-foh-syte) one type of white blood cell; *see* B lymphocyte, T lymphocyte [*lymph-* water (lymphatic system), *-cyte* cell]

lymphokine (LIM-foh-kyne) chemical compounds released by antigen-bound sensitized T cells [*lymph-* water, *-kine* motion]

lymphoid neoplasm (LIM-foyd NEE-oh-plazem) *see* lymphoma [*lymph-* water (lymphatic system), *-oid* like, *neo-* new, *-plasm* substance]

lymphoid tissue (LIM-foyd) type of reticular tissue that contains lymphocytes and other specialized cells [*lymph-* water, *-oid* like, *tissu* fabric]

lymphokinesis (lim-foh-kih-NEE-sis) flow of lymph [*lymph-* water, *-kinesis* activation]

lymphoma (lim-FOH-mah) cancer of lymphatic tissue [*lymph-* water, *-oma* tumor]

lymphotoxin (lim-foh-TAWK-sin) powerful poison that quickly kills any cells it attacks [*lympho-* water (lymphocyte), *-tox-* poison, *-in* substance]

lysosome (LYE-so-sohm) membranous organelle containing various enzymes that can dissolve most cellular compounds; called *digestive bags* or *suicide bags of cell* [*lyso-* dissolution, *-som-* body]

M

M line region of the sarcomere where myosin filaments are held together and stabilized by protein molecules [*M mittel* middle]

M phase step of the cell life cycle in which a cell divides through the process of mitosis (mitotic cell division); M phase follows the G_2 phase (second growth phase) and occurs along with cytokinesis (splitting of the cell's cytoplasm into two daughter cells); *see* cell life cycle [*phase* appearance]

macromolecule (mak-roh-MOL-eh-kyool) large, complex chemical made of combinations of molecules [*macro-* large, *molec-* mass, *-ule* small]

macronutrients (MAK-roh-NOO-tree-ents) nutrients needed in large amounts; carbohydrates, fats, and proteins [*macro-* large, *nutri-* nourish, *-ent* agent]

macrophage (MAK-roh-fayj) phagocytic cell in the immune system [*macro-* large, *-phag-* eat]

macula (MAK-yoo-lah) strip of sensory epithelium in the utricle and saccule; provides information related to head position or acceleration [*macula* spot] *pl.*, maculae or maculas

macula densa (MAK-yoo-lah DEN-sah) distal tubule cells in the juxtaglomerular apparatus that are dense and tightly packed [*macula* spot, *densa* thick] *pl.*, maculae densae

macula lutea (MAK-yoo-lah LOO-tee-ah) yellowish area near center of the retina where cones are densely distributed; also called simply "macula" [*macula* spot, *lutea* yellow] *pl.*, maculae luteae

magnesium (mag-NEE-see-um) element that is a component of many energy-transferring enzymes [*magne-* lodestone, *-um* thing or substance]

magnetic resonance imaging (MRI) (mag-NET-ik REZ-ah-nens IM-ah-jing) scanning technique that uses a magnetic field to induce tissues to emit radio waves that can be used by computer to construct a sectional view of a patient's body [*magnet-* lodestone, *-ic* relating to, *re-* again, *-sona-* sound, *-ance* state]

magnetoencephalography (MEG) (mag-NET-oh-en-sef-eh-LOG-reh-fee) method of measuring brain activity using a sensitivity machine called a *biomagnetometer*; detects very small magnetic fields generated by neural activity [*magneto-* lodestone, *-en-* within, *-cephalo-* head, *-graph-* draw, *-y* activity]

major histocompatibility complex (MHC) (HIST-oh-kom-PAT-ib-il-it-ee) set of genes in chromosome 6 that all code for antigen-presenting proteins and other immune system proteins; proteins produced by MHC genes in class I and class II also are called *human leukocyte antigens (HLAs)*; MHC proteins present different protein fragments (peptides) at the surface of the cell for possible recognition as either self or nonself antigens by immune system cells [*histo-* tissue, *-compatibil-* agreeable, *-ity* state, *complex* embrace]

malabsorption syndrome (mal-ab-SORP-shun SIN-drohm) refers to a group of symptoms resulting from the failure of the small intestine to absorb nutrients properly [*mal-* bad, *-absorp-* swallow, *-tion* process, *syn-* together, *-drome* running or (race) course]

malaria (mah-LAIR-ee-ah) sometimes fatal condition caused by blood parasites [*mal-* bad, *-ar-* air, *-ia* condition]

male pattern baldness common type of baldness that results when the gene for baldness is present and testosterone is present [*pat-*

tern that which is to be copied, *baldness*-balled state]

malignant (mah-LIG-nant) refers to a tumor or neoplasm that is capable of metastasizing, or spreading, to new tissues; cancer [*malign* bad]

malignant hyperthermia (MH) (mah-LIG-nant hye-per-THERM-ee-ah) inherited condition characterized by abnormally increased body temperature and muscle rigidity when exposed to certain anesthetics or muscle relaxants [*malign-* bad, *-ant* state, *hyper-* excessive, *-therm-* heat, *-ia* abnormal condition]

malignant melanoma (mah-LIG-nant mel-ah-NO-mah) most deadly type of skin cancer [*malign-* bad, *-ant* state, *melan*-black, *-oma* tumor]

malignant tumor (mah-LIG-nant TOO-mer) cancer that is not encapsulated and tends to spread to other regions of the body [*malign* bad, *-ant* state, *tumor* swelling]

malocclusion (mal-oh-CLEW-zhun) condition that occurs when missing teeth create wide spaces in the dentition, when teeth overlap, or when one or more teeth prevents correct alignment [*mal-* bad, *-occlu-*close up, *-sion* state]

maltase (MAL-tays) enzyme that catalyzes the final steps of carbohydrate digestion [*malt-* grain, *-ase* enzyme]

mammary gland (MAM-mah-ree) milk-producing glands of the breasts; classified as external accessory sex organs in females [*mamma-* breast, *-ry* relating to, *gland* acorn]

mammogenic hormone (mam-moh-JEN-ik HOR-mohn) any hormone that promotes breast tissue growth and development [*mammo-* breast, *-gen-* produce, *-ic* relating to, *hormon-* excite]

mammography (mam-OG-rah-fee) x-ray photography of the breast [*mammo-* breast, *-graphy* kind of printing or recording]

mandible (MAN-di-bal) jaw bone; largest and strongest bone of the face [*mandere* to chew]

mandibular nerve (man-DIB-yoo-lar) part of the trigeminal nerve [*mandere* to chew, *-lar* relating to]

marasmus (mah-RAZ-mus) form of protein-calorie malnutrition; results from an overall lack of calories and protein [*marasmus* a wasting]

marrow cavity (MAIR-oh KAV-i-tee) *see* medullary cavity [*marrow-* inner most, *cav*-hollow, *-ity* state]

mass number see **atomic mass**

masseter (mah-SEE-ter) facial muscle responsible for chewing [*masseter* chewer]

mast cell immune system cell to which antibodies become attached in early stages of inflammation [*mast* fattening, *cell* storeroom]

mastectomy (mas-TEK-toh-mee) surgical removal of the breast [*mast-* breast, *-ectomy* surgical removal]

mastication (mass-ti-KAY-shun) chewing [*mastica-* chew, *-ation* process]

mastitis (mass-TYE-tis) breast inflammation [*mast-* breast, *-itis* inflammation]

mastoidectomy (mass-toyd-EK-toh-mee) inflammation of the air spaces within the mastoid portion of the temporal bone [*mast-* breast, *-oid-* like, *-ec-* out, *-tom-* cut, *-y* action]

mastoiditis (mas-toyd-EYE-tis) inflammation of the air cells within the mastoid portion of the temporal bone; usually caused by infection [*mast-* breast, *-oid-* like, *-itis* inflammation]

matrix (MAY-triks) extracellular substance of a tissue; for example, the matrix of bone is calcified, whereas that of blood is liquid; *see also* extracellular matrix (ECM) [*matrix* womb] *pl.*, matrices

matter anything that has mass and occupies space [*matter-* something from which something is made]

maxilla (mak-SIH-lah) upper jaw bone [*maxilla* upper jaw] *pl.*, maxillae (mak-SIH-lee)

maxillary nerve (MAK-si-lair-ee) branch of the trigeminal nerve [*maxilla* upper jaw, *-ary* relating to]

McBurney's point (mak-BUR-neez) a point on the abdominal wall midway between the right anterior superior iliac spine and the umbilicus; site of pain in acute appendicitis [*Charles McBurney* American surgeon]

meatus (mee-AYT-us) any tubelike passageway or opening [*meatus* passage]

mechanical digestion process through which food is broken into smaller portions through chewing and movements of the alimentary canal; enables enzymes to act on a larger surface area to accomplish chemical digestion [*diges*t- break down, *-tion* process]

mechanoreceptor (mek-an-oh-ree-SEP-tor) receptors that respond to physical movement in the environment, such as sound waves; for example, equilibrium and balance sensors in the ears [*mechano-* machine (mechanical), *-cept-* receive, *-or* agent]

medial (MEE-dee-al) of or toward the middle; opposite of lateral [*media-* middle, *-al* relating to]

medial lemniscal system (MEE-dee-al lem-NIS-kal) posterior white columns of the spinal cord plus the medial lemniscus; functions in touch sensations and conscious proprioception [*media-* middle, *-al* relating to, *lemmis-* fillet, *cal-* relating to, *system-* arrangement]

medial longitudinal arch (MEE-dee-al lon-ji-TOO-dih-nal) inner lengthwise (anteroposterior) support structure of the foot [*medial* middle, *-al* relating to, *longitudo* length, *-al* relating to]

median cubital vein (KYOO-bi-tall) forearm vein [*medi-* middle, *-an* relating to, *cubit-* elbow, *-al* relating to]

mediastinum (MEE-dee-ass-TI-num) a portion of the thorax cavity in the middle of the thorax [*mediastinus-* midway]

medical imaging techniques that visualize tissues for medical study [*medic-* to heal, *-al* relating to, *image-* picture]

medulla (meh-DUL-ah) Latin for "marrow"; the inner portion of an organ in contrast to the outer portion, or cortex [*medulla* middle] *pl.*, medullae or medullas

medulla oblongata (meh-DUL-ah ob-long-GAH-tah) lowest part of the brainstem; an enlarged extension of the spinal cord; the vital centers are located within this area [*medulla* middle, *oblongata* oblong] *pl.*, medullae oblongatae

medullary (MED-oo-lar-ee) relating to the middle or center of an organ or structure [*medulla-* middle, *-ry* state]

medullary cavity (MED-oo-lair-ee) hollow area inside the diaphysis of the bone that contains yellow bone marrow [*medulla* middle, *cav-* hollow, *-ity* state]

medullary ischemic reflex (MED-uh-lair-ee is-KEE-mik REE-fleks) mechanism that exerts powerful control of blood vessels during emergency situations when blood flow to the brain drops below normal [*medulla-* middle, *-ary* relating to, *ischem-* hold back, *-ic* relating to, *re-* back or again, *-flex* bend]

medullary rhythmicity area (MED-eh-lair-ee rith-MIH-sih-tee) area in the brainstem that generates the basic rhythm of the respiratory cycle of inspiration and expiration [*medulla-* middle, *-ary* relating to, *rhythm*-rhythm, *-ic* relating to, *-ity* condition]

megakaryocyte (meg-ah-KAIR-ee-oh-syte) large cell in the spleen that contributes to formation of platelets [*mega-* huge, *-karyo* nut, *-cyte* cell]

meiosis (my-OH-sis) nuclear division in which the number of chromosomes is reduced to half their original number through separation of homologous pairs; produces gametes [*meiosis* becoming smaller]

Meissner corpuscle (MYZ-ner KOR-pus-ul) *see* tactile corpuscle [*George Meissner* German physiologist]

melacine (MEL-ah-seen) vaccine made from melanoma cancer cells; used for prevention of recurrence of malignant melanoma following initial treatment and as a less toxic alternative to chemotherapy for treatment of advanced melanoma [*mela-* black]

melanin (MEL-ah-nin) brown pigment primarily in skin and hair [*melan-* black, *-in* substance]

melanocyte (MEL-ah-no-syte) cell type in the stratum basale of the skin that produces melanin pigment granules, releasing them to other nearby skin cells [*melan-* black, *-cyte* cell]

melanocyte-stimulating hormone (MSH) (meh-LAN-oh-syte-STIM-yoo-lay-ting HOR-mohn) hormone secreted by the pituitary that increases production of melanin, leading to darker skin color [*melan*-black, *-cyte* cell, *hormon-* excite]

melanoma (mel-ah-NO-mah) cancer of pigmented epithelial cells [*melan-* black, *-oma* tumor]

melanosome (MEL-ah-no-sohm) pigment granule released by melanocytes [*melan-* black, *-som-* body]

melatonin (mel-ah-TOH-nin) important hormone produced by the pineal gland; it is believed to regulate onset of puberty and the menstrual cycle; also referred to as the *third eye* because it responds to levels of light and is thought to be involved with the body's internal clock [*mela-* black, *-ton-* tone, *-in* substance]

membrane thin, sheetlike structure [*membran-* thin skin]

membrane attack complex (MAC) molecules formed by the complement cascade; leads to cell lysis [*membran-* thin skin, *complex* embrace]

membrane bone bone formed within membranous tissues, such as the flat bones of the skull, instead of indirectly through endochondral ossification [*membran-* thin skin]

membrane channel pores within the cell membrane through which specific ions or other small, water-soluble molecules can pass [*membran-* thin skin, *channel-* water pipe]

membrane potential difference in electrical charge between inside and outside of the plasma membrane [*membran-* thin skin, *potent-* power, *-ial* relating to]

membranous (MEM-brah-nus) resembling a membrane [*membran-* thin skin, *-ous* characterized by]

membranous organelle (MEM-brah-nus or-gah-NELL) cell organ that is defined or bordered by a membrane [*membran-* thin skin, *-ous* characterized by, *organ-* instrument, *-ele* small]

memory B cell B cell that has been activated but is not an effector cell producing an active response [*memory-* remembering, *B* bursa-equivalent tissue, *cell* storeroom]

memory cell cell that remains in reserve in the lymph nodes until their ability to secrete antibodies is needed [*memory-* remembering, *cell-* storeroom]

memory T cell T cell that has been activated but is not an effector cell producing an active response [*memory-* remembering, *T* thymus gland, *cell* storeroom]

menarche (meh-NAR-kee) first menses occurring at the onset of puberty [*men-* month, *-arche* beginning]

Ménière disease (men-ee-AIR) chronic inner ear disease of unknown cause [*Prosper Ménière* French physician, *dis-* opposite of, *-ease* comfort]

meninges (meh-NIN-jeez) fluid-containing membranes surrounding the brain and spinal cord [*mening* membrane] *sing.*, meninx

meningitis (men-in-JYE-tis) inflammation of the meninges caused by various factors, including bacterial infection, mycosis, viral infection, and tumors [*mening-* membrane, *-itis* inflammation]

meniscus (meh-NIS-kus) articular cartilage disk [*meniscus* crescent] *pl.*, menisci (meh-NIS-eye or meh-NIS-kye)

menopause (MEN-oh-pawz) termination of menstrual cycles; also called *climacteric* [*men-* month, *-paus-* cease]

menotropin (men-oh-TROHP-in) drug used as an infertility treatment [*men-* month, *-trop*-nourish, *-in* substance]

menses (MEN-seez) periodic shedding of endometrial lining in uterus; occurs in cycles of about 28 days [*menses* months] *pl.*, menses

menstrual cycle (MEN-stroo-al) series of changes that regularly occurs in sexually mature, nonpregnant women that results in shedding of the uterine lining approximately once a month [*mens-* month, *-al* relating to, *cycle* circle]

menstrual period (MEN-stroo-al) *see* menses [*mens-* month, *-al* relating to]

menstruation (men-stroo-AY-shun) menses; regular event of the female reproductive cycle that allows the endometrium to renew itself [*mens-* month, *-ation* process]

Merkel cell (MER-kuhl) *see* tactile epithelial cell [*Friedrich Sigmund Merkel* German anatomist]

merocrine gland (MER-oh-krin) gland that discharges secretions directly through the cell or plasma membrane [*mero-* part, *-crine* to separate]

mesangial cell (mess-AN-jee-al) irregular cell that functions as a support and phagocytic cell; unique to renal corpuscles [*mes-* middle, *-angi-* vessel, *-al* relating to, *cell-*storeroom]

mesentery (MEZ-en-tair-ee) large double fold of peritoneal tissue that anchors the loops of the digestive tract to the posterior wall of the abdominal cavity [*mes-* middle, *-enter-* intestine]

mesoderm (MEZ-oh-derm) middle layer of the primary germ layers; gives rise to such structures as muscle, bones, and blood vessels [*meso-* middle, *-derm* skin]

mesomorph (MEZ-oh-morf) body type characterized by a muscular build [*meso-* middle, *-morph* form]

mesothelium (mez-oh-THEE-lee-um) epithelial lining of the pleura, pericardium, and peritoneum [*meso-* middle or median, *-theli-* nipple, *-um* thing] *pl.*, mesothelia

messenger RNA (mRNA) duplicate copy of a gene sequence on the DNA that passes from the nucleus to the cytoplasm; used by ribosomes to create specific proteins [*RNA*-ribonucleic acid]

metabolic acidosis (met-ah-BOL-ik ass-ih-DOH-sis) disturbance affecting the bicarbonate element of the bicarbonate-carbonic acid buffer pair in the blood; bicarbonate deficit [*metabol-* change, *-ic* relating to, *acid-* sour, *-osis* condition]

metabolic alkalosis (met-ah-BOL-ik al-kah-LOH-sis) disturbance affecting the bicarbonate element of the bicarbonate-carbonic acid buffer pair in the blood; bicarbonate excess [*metabol-* change, *-ic* relating to, *alkal-* ashes, *-osis* condition]

metabolic pathway (met-ah-BOL-ik) sequence of chemical reactions [*metabol-*change, *-ic* relating to]

metabolic rate (met-ah-BOL-ik) amount of energy released by catabolism in the body over a given period [*metabol-* change, *-ic* relating to]

metabolic syndrome (met-ah-BOL-ik SIN-drohm) collection of risk factors that

together increase the risk of coronary heart disease, stroke, and type 2 diabetes mellitus (e.g., central obesity, insulin resistance, high blood lipids, hypertension) [*metabol-* change, *-ic* relating to, *syn-* together, *-drome* running or (race)course]

metabolism (meh-TAB-oh-liz-em) complex, intertwining set of chemical processes by which life is made possible for a living organism; *see* anabolism, catabolism [*metabol-* change, *-ism* condition]

metacarpal bone (met-ah-KAR-pal) bone of the hand [*meta-* beyond,*-carp-* wrist, *-al* relating to]

metacarpophalangeal joint (met-ah-KAR-poh-fah-LAN-jee-al) type of joint with the rounded heads of the metacarpals and the concave bases of the proximal phalanges articulating with each other [*meta-* beyond, *-carpo-* wrist, *-phalang-* finger bones (ref. from rows of soldiers), *-al* relating to]

metaphase (MET-ah-fayz) second stage of mitosis, during which the nuclear membrane and nucleolus disappear and the chromosomes align on the equatorial plane [*meta-* change, *-phase* stage]

metarteriole (met-ar-TEER-ee-ohl) short connecting blood vessel that connects a true arteriole with the proximal end of dozens of capillaries [*meta-* change or exchange, *arteri-*vessel, *-ole* little]

metastasis (meh-TAS-tah-sis) process characteristic of cancer by which malignant tumor cells separate from a primary tumor and then migrate to a new tissue to initiate a secondary tumor [*meta-* change, *-stasis* standing]

micelle (my-SELL) droplet of lipid surrounded by bile salts, which makes the lipid temporarily water-soluble [*mic-* grain, *-elle* small]

microarray (mye-kroh-ar-RAY) DNA biotechnology technique that uses a tiny silicon plate with a grid made up of tiny wells [*micro-* small, *-array* arrangement in rows]

microbiome (mye-kroh-BYE-ohm) all the interacting ecosystems of microbes (bacteria, fungi, etc.) that live on or in the human body [*micro-* small, *-bio-* life, *-ome* entire collection]

microcephaly (my-kroh-SEF-ah-lee) congenital abnormality in which an infant is born with an abnormally small head [*micro-*small, *-ceph* head, *-aly* relating to]

microcirculation (my-kroh-sir-kyoo-LAY-shun) flow of blood through the capillary bed [*micro-* small, *circulat-* go around, *-tion* process]

microfilament (my-kroh-FIL-ah-ment) smallest cell fibers; "cellular muscles" [*micro* small, *-fila-* threadlike, *-ment* thing]

microglia (my-KROG-lee-ah) type of small neuroglial cell of nerve tissue that serves an immune system function by becoming an active phagocyte when stimulated [*micro-*small *-glia* glue] *sing.*, microglial cell

microkeratome (my-kroh-KAR-ah-tohm) surgical device used in automated lamellar keratoplasty (ALK) [*micro-* small, *-kera-*horn, *-tom-* cut]

micronutrient (MYE-kroh-NOO-tree-ent) nutrient needed by the body in very small quantity [*micro-* small, *nutri-* nourish, *-ent* agent]

microscopic anatomy (my-kroh-SKOP-ik ah-NAT-o-mee) the study of the smaller structures of an organism, such as cells and tissues, that are small enough to require significant magnification; compare to gross anatomy [*micro-* small, *-scop-* see, *-ic* relating to, *ana-* apart, *-tom-* cut, *-y* action]

microscopy (my-KRAH-skah-pee) any of several techniques used to visualize structures too small to be seen by the unaided human eye [*micro-* small, *-scop-* see, *-y* activity]

microtubule (my-kroh-TOOB-yool) thick cell fiber (compared to microfilament); hollow tube responsible for movement of substances within the cell or movement of the cell itself [*micro-* small, *-tubule* little tube]

microvillus (my-kroh-VIL-us) brushlike border made up of epithelial cells on each villus in the small intestine; increases the surface area for absorption of nutrients [*micro-* small, *-villi* shaggy hairs] *pl.*, microvilli

micturition (mik-too-RISH-un) urination, voiding [*mictur-* to urinate, *-tion* process]

midbrain region of the brainstem between the pons and the diencephalon [*mid-* middle]

middle cerebellar peduncle (SAIR-eh-bell-ar peh-DUNG-kul) tracts that enter the cerebellum from the pons [*cerebell-*cerebellum (small brain), -ar relating to, *ped- foot*, *-uncl-* little]

middle ear tiny and very thin epithelium-lined cavity in the temporal bone that houses the ossicles; in the middle ear, sound waves are amplified [*mid-* middle]

midsagittal plane (mid-SAJ-i-tal) cut, or plane, that divides the body or any of its parts into two equal (mirror-image) halves

migrating motor complex (MMC) (my-GRAYT-ing) wave of rhythmic contractions of the smooth muscle in the gastrointestinal tract during the fasting state [*migra-* wander, *-at-* process, *motor* move, *complex* embrace]

milliequivalent (mil-i-ee-KWIV-ah-lent) number of ionic charges or electrocovalent bonds in a solution; abbreviated mEq [*milli-* 1/1000 part, *-equi-* equal, *-val-* strength, *-ent* state]

Milwaukee brace (mil-WAWK-ee) supportive brace used to correct scoliosis [*Milwaukee* after the city in Wisconsin, U.S.A.]

mineralocorticoid (MC) (MIN-er-al-oh-KOR-ti-koyd) hormone that influences mineral salt metabolism; secreted by adrenal cortex; aldosterone is the chief mineralocorticoid [*mineral-* mine, *-cortic* bark or cortex, *-oid* like]

mineral inorganic element or salts occurring naturally in the earth, many of which are vital to proper functioning of the body and must be obtained in the diet [*mineral-*mine]

minute volume volume of blood circulating through the body per minute [*minut-* very small, *volume* paper roll]

mirror neuron (MEER-or NOO-ron) type of nerve cell in the cerebral cortex of the brain that is stimulated both when a person performs an action or when *another* person performs an action, thus enabling the brain to "mirror" the activity of another person's brain; may be partly responsible for the ability to imitate actions of others and to empathize with the feelings of others [*mirror-* to look at, *neuron-* nerve]

miscarriage (mis-KARE-ij) loss of an embryo or fetus before the twentieth week of pregnancy; after 20 weeks, the event is termed a *stillbirth* [*mis-* wrongly, *-carriage* carry]

mitochondrial DNA (mDNA, mtDNA) (my-toh-KON-dree-al D N A) DNA specifically in the mitochondrion that has the only genetic code for several important enzymes [*mito-* thread, *-chondrion-* granule, *-al* relating to)

mitochondrion (my-toh-KON-dree-on) organelle in which ATP generation occurs; often termed "powerhouse of cell" [*mito-*thread, *-chondrion* granule] *pl.*, mitochondria

mitosis (my-TOH-sis) complex process in which a cell's DNA is replicated and divided equally between two daughter cells [*mitos-* thread]

mitral valve (MY-tral) located between the left atrium and ventricle, this valve prevents backflow of blood into the left atrium; named for its resemblance to a bishop's hat (miter); also known as the *bicuspid valve* [*mitr-* bishop's hat, *-al* relating to]

mitral valve prolapse (MVP) (MY-tral valv PROH-laps) condition in which the bicuspid (mitral) valve extends into the left atrium, causing incompetence (leaking) of the valve [*mitr-* bishop's hat, *-al* relating to, *pro-*forward, *-laps-* fall]

mittelschmerz (MIT-el-schmertz) abdominal discomfort experienced by many women at the time of ovulation [*mittel-* middle, *-schmerz* pain]

mixed cranial nerve (KRAY-nee-al) bundle of axons that contain both sensory and motor neurons [*crani-* skull, *-al* relating to]

mixed nerve nerve with axons of both sensory and motor neurons [*micere-* to mix]

M-mode echocardiogram (ek-oh-KAR-dee-oh-gram) method of echocardiography that shows motion of the heart walls and valves over time as a transducer is held in a stable position [*M-* motion, *-mode* manner, *echo-*reflected sound, *-cardio-* heart, *-gram* drawing]

mobile-receptor model theory that a hormone enters a target cell where it binds to a free (nonstationary) receptor, thereby activating a gene and thus the beginning of mRNA transcription [*recept-* receive, *-or* agent]

modiolus (moh-DI-oh-lus) cone-shaped core of bone around which the tube of the cochlea is wound [*modiolus-* nave, hub]

molar (MOHL-ar) a tricuspid tooth, which is a relatively flat-topped tooth near the posterior of the jaw; *see also* mole [*mola-* millstone, *-ar* relating to]

mole (mohl) standard unit of measuring amount of a substance; one mole of a substance is made up of 6.02 10^{23} particles of that substance; moles per liter as a concentration of a solute in a solvent is expressed as "molar concentration" or M [*mole-* mass]

molecular genetics (moh-LEK-yoo-lar jeh-NET-iks) branch of genetics that studies DNA and RNA and the mechanisms by which they store and transmit hereditary information [*mole-* mass, *-cul-* small, *-ar* relating to]

molecular motor (mo-LEK-yoo-lar) small structures in the cell made up of one or two molecules and that act as mechanisms of movement [*mole-* mass, *-cul-* small, *-ar* relating to, *mot-* movement, *-or* agent]

molecule (MOL-eh-kyool) formed when two or more atoms join [*mole-* mass, *-cul-*small]

monoamine (mon-oh-ah-MEEN) category of small neurotransmitter molecule derived from a single amino acid [*mono-* single, *-amine* ammonia compound (amino acid)]

monoamine oxidase (MAO) (mon-oh-ah-MEEN OK-si-dase) enzyme located in synaptic knobs of postganglionic neurons; responsible for breaking down neurotransmitters [*mono-* single, *-amine* ammonia compound (amino acid), *oxi-* oxygen, *-ase* enzyme]

monoamine oxidase inhibitor (MAOI) (mon-oh-ah-MEEN OK-si-dase in-HIB-i-tor) class of antidepressant drugs that block the action of monoamine oxidase, the enzyme that inactivates dopamine and serotonin [*mono-* single, *-amine* ammonia compound (amino acid), *oxid-* oxygen compound, *-ase* enzyme, *inhibit-*prevent, *-or* agent]

monoclonal (mon-oh-KLONE-al) genetically identical; member of the same family or clone of cells [*mono-* single, *-clon-* plant cutting, *-al* relating to]

monoclonal antibody (MAb) (mon-oh-KLONE-al AN-ti-bod-ee) specific antibody produced from a population of identical cells; *see* hybridoma [*mono-* single, *-clon-*plant cutting, *-al* relating to, *anti-* against]

monocyte (MON-oh-syte) large white blood cell; an agranular leukocyte [*mono-* single, *-cyte* cell]

monogenic (mon-oh-JEN-ik) single-gene [*mono-* single, *-gen-* produce (gene), *-ic* relating to]

monosaccharide (mon-oh-SAK-ah-ride) simple sugar, such as glucose or fructose; building block of carbohydrates [*mono-* one, *-saccharide* sugar]

monosomy (MON-oh-so-mee) abnormal genetic condition in which cells have only one chromosome instead of a pair; usually caused by nondisjunction (failure of chromosome pairs to separate) during gamete production [*mono-* single, *-som-* body (chromosome), *-y* state]

mons pubis (monz PYOO-bis) skin-covered pad of fat over the pubic symphysis in the female [*mons* mountain, *pubis* groin] *pl.*, montes pubis

morula (MOR-yoo-lah) solid mass of cells formed by the divisions of a fertilized egg [*mor-* mulberry, *-ula* little] *pl.*, morulae

motif (moh-TEEF) specific pattern of structure within the secondary structure of a protein, such as a particular set of helices and/or folds, that imparts certain structural or functional characteristics in each protein where it appears; also called *supersecondary structure* [*motif* theme]

motilin (moh-TIL-in) hormone released from the endocrine cells in the duodenum; triggers the migrating motor complex [*mot-*move, *-il-* relating to, *-in* substance]

motility (moh-TIL-i-tee) ability to move spontaneously [*mot-* move, *-il-* relating to, *-ity* state]

motor cranial nerve (MOH-ter KRAY-nee-al nerv) nerve that consists mainly of motor neurons [*mot-*movement, *-or* agent, *crani-*skull, *-al* relating to]

motor endplate (MOH-ter END-playt) point at which motor neurons connect to the sarcolemma to form the neuromuscular junction [*mot-* movement, *-or* agent]

motor nerve (MOH-ter nerv) nerve containing motor neurons and thus transmits nerve impulses from the brain and spinal cord to muscles and glandular epithelial tissues [*mot-* movement, *-or* agent]

motor neuron (MOH-ter NOO-ron) nerve cell that transmits nerve impulses from the brain and spinal cord to muscles and glandular epithelial tissues [*mot-* movement, *-or* agent, *neuron* nerve]

motor program (MOH-ter PROH-gram) set of coordinated commands that control the programmed muscle activity mediated by extrapyramidal pathways [*mot-* movement, *-or* agent]

motor unit (MOH-ter YOO-nit) functional unit composed of a single motor neuron with the muscle cells it innervates [*mot-*movement, *-or* agent]

mouth oral cavity

mucosa (myoo-KOH-sah) innermost layer of the gastrointestinal wall [*muc-* slime, *-osa* relating to] *pl.*, mucosae

mucosal immune system (myoo-KOH-sal i-MYOON) immune system in the mucous membranes, protecting the external boundaries of the body [*mucos-* slime or mucus, *-al* relating to, *immun-* free]

mucosal-associated lymphoid tissue (MALT) (myoo-KOH-sal-ah-soh-she-AYT-ed LIM-foyd) location of the immune cells that make up the mucosal immune system [*mucos-* slime or mucus, *-al* relating to, *associa-* unite, *-ate* process, *lymph-* water, *-oid* like, *tissue-* fabric]

mucous membrane (MYOO-kus) epithelial membrane that lines body surfaces opening directly to the exterior and secretes mucus [*muc-* slime, *-ous* characterized by, *membran-* thin skin]

mucus (MYOO-kus) thick, slippery material secreted by mucous membranes that keeps the membrane moist and protected [*mucus* slime]

multiaxial joint (mul-tee-AK-see-al) joint that permits movement around three or more axes and in three or more planes [*multi-* many, *-axon* axle]
multicellular gland (mul-tih-SELL-yoo-lar) cluster or group of glandular epithelial cells [*multi-* many, *-cell-* storeroom, *-ular* relating to, *gland* acorn]
multifides group (mul-TIF-i-deez) group of back muscles that each connect one vertebra to the next, also helping to extend the back and neck or flex them to the side [*multi-* many, *-fides* split (into pieces)]
multiple myeloma (my-eh-LOH-mah) cancer of antibody-secreting B lymphocytes [*myel-* marrow, *-oma* tumor]
multiple sclerosis (MS) (skleh-ROH-sis) most common primary disease of the central nervous system, MS leads to demyelination of nerves, which commonly causes problems with vision, muscle control, and incontinence [*multi-* many, *-pl-* fold, *sclera-* hard, *-osis* condition]
multiple wave summation (sum-MAY-shun) condition in which a series of stimuli come in rapid enough succession that the muscle is not able to relax completely, and sustained or more forceful contraction results [*multi-* many, *-pl-* fold, *wave*, *summa-* total, *-tion* process]
multipolar neuron (NOO-rons) neuron with only one axon but several dendrites [*multi-* many, *-pol-* pole, *-ar* relating to, *neuron* nerve]
multiunit smooth muscle type of smooth muscle tissue composed of many independent single-fiber units that does not usually generate its own impulse but rather responds only to nervous input and is often found in bundles [*multi-* many, *mus-* mouse, *-cle* little]
mumps acute viral disease characterized by swelling of the parotid salivary glands [*mumps* grimace]
muscarinic (M) receptor (mus-kah-RIN-ik ree-SEP-tor) type of cholinergic receptor responding to muscarine, as well as acetylcholine [*musca-* fly, *-in-* substance, *-ic* relating to (after the toxic mushroom *A. muscaria*), *recept-* receive, *-or* agent]
muscle fatigue state of exhaustion produced by strenuous muscular activity [*mus-* mouse, *-cle* little, *fatig-* tire]
muscle spindle stretch receptor in muscle cells involved in maintaining muscle tone [*mus-* mouse, *-cle* small]
muscle strain muscle injury resulting from overexertion or trauma and involving overstretching or tearing of muscle fibers [*mus-* mouse, *-cle* small]
muscle tissue tissue type that produces movement [*mus-* mouse, *-cle* small, *tissu-* fabric]
muscle tone tonic contraction; characteristic of muscle of a normal individual who is awake [*mus-* mouse, *-cle* little, *ton-* stretch or tension]
muscular artery (AR-ter-ee) carry blood farther away from the heart to specific organs and areas of the body; also called *distributing artery* [*mus-* mouse, *-cul-* little, *-ar* relating to, *arteri-* vessel]
muscular dystrophy (DISS-troh-fee) group of genetic diseases characterized by atrophy of skeletal muscle tissue [*mus-* mouse, *-cul-* little, *-ar* relating to, *dys-* bad, *-troph-* nourishment, *-y* state]
muscular system the muscles of the body [*mus-* mouse, *-cul-* little, *-ar* relating to]
muscularis (mus-kyoo-LAIR-is) two layers of muscle surrounding the digestive tube that produce wavelike, rhythmic contractions, called *peristalsis,* that move food material along the digestive tract [*mus-* mouse, *-cul-* little, *-aris* relating to] *pl.*, musculares
mutagen (MYOO-tah-jen) agent capable of causing mutation (alteration) of DNA [*muta-* change, *-gen* produce]
mutation (myoo-TAY-shun) change in genetic material within a cell [*mutat-* change, *-tion* state]
myalgia (my-AL-jee-ah) muscle pain [*my-* muscle, *-algia* pain]
myasthenia gravis (my-es-THEE-nee-ah GRAH-vis) chronic autoimmune disease characterized by muscle weakness, especially in the face and throat, caused by immune attacks at the neuromuscular junction [*my-*muscle, *-asthenia* weakness, *gravis* severe]
myelin (MY-eh-lin) lipoprotein substance in the myelin sheath around many nerve fibers that contributes to high-speed conductivity of impulses [*myel-* marrow, *-in* substance]
myelin disorder (MY-eh-lin) any of several disorders characterized by loss or improper development of the myelin sheath that surrounds many axons of the nervous system [*myel-* marrow, *-in* substance]
myelin sheath (MY-eh-lin sheeth) whitish, fatty sheath surrounding nerve fibers; substance produced by Schwann cells [*myel-* marrow, *-in* substance]
myelin sheath gap (MY-eh-lin sheeth *see* node of Ranvier [*myel-* marrow, *-in* substance]
myelinated fiber (MY-eh-li-nay-ted) axon surrounded by a sheath of myelin formed by Schwann cells (PNS) or oligodendrocytes (CNS) [*myel-* marrow, *-in-* substance, *-ate* act of]
myeloid neoplasm (MY-eh-loyd NEE-oh-plaz-em) blood-related cancer [*myel-* marrow, *-oid* like, *neo-* new, *-plasm* substance]
myeloid tissue (MY-eh-loyd) red bone marrow; type of soft, diffuse connective tissue; the site of hematopoiesis [*myel-*marrow, *-oid* of or like, *tissu-* fabric]
myocardial infarction (MI) (my-oh-KAR-dee-al in-FARK-shun) death of cardiac muscle cells resulting from inadequate blood supply, as in coronary thrombosis; also called "heart attack" [*myo-* muscle, *-cardi-*heart, *-al* relating to, *in-* in, *-farc-* stuff]
myocardium (my-oh-KAR-dee-um) muscle of the heart [*myo-* muscle, *-cardi-* heart, *-um* thing] *pl.*, myocardia (my-oh-KAR-dee-ah)
myofascial meridian (my-oh-FAY-shul mer-ID-ee-an) line or chain of force or tension in the body formed by the continuous structures of a group of skeletal muscles and connective tissue (fascia) that are structurally and functionally linked [*myo-* muscle, *-fasci-* bundle, *-al* relating to, *meridi-* midday, *-an* relating to]
myofibril (my-oh-FYE-bril) very fine longitudinal fibers found in skeletal muscle cells; composed of thick and thin filaments [*myo-* muscle, *-fibr-* fiber, *-il* little]
myofilament (my-oh-FIL-ah-ment) ultramicroscopic, threadlike structures found in myofibrils; composed of myosin (thick) and actin (thin) [*myo-* muscle, *-fila-* thread, *-ment* thing]
myogenic mechanism (mye-oh-JEN-ik) smooth muscle autoregulatory mechanism that helps to maintain glomerular filtration rate [*myo-*muscle, *-gen-* produce, *-ic* relating to]
myoglobin (my-oh-GLO-bin) large protein molecule in the sarcoplasm of muscle cells that attracts oxygen and holds it temporarily [*myo-* muscle, *-glob-* ball, *-in* substance]
myography (my-OG-rah-fee) procedure in which the contraction of an isolated muscle is recorded [*myo-* muscle, *-graphy* process of recording]
myoma (my-OH-mah) benign tumor of the uterine fibrous or smooth muscle tissue [*my-* muscle, *-oma* tumor]
myometrium (my-oh-MEE-tree-um) middle muscle layer in the uterus [*myo-* muscle, *-metr-* womb, *-um* thing]
myopathology (mye-oh-PATH-ol-oh-jee) existence of or study of any abnormality of muscle tissue or muscle function [*myo-*muscle, *-path-* disease, *-o-* combining form, *-log-* words (study of), *-y* activity]
myopathy (my-OP-ah-thee) general term referring to any muscle disease [*myo-* muscle, *-path-* disease, *-y* state]
myopia (my-OH-pee-ah) refractive disorder of the eye caused by an elongated eyeball; nearsightedness [*myops-* nearsighted, *-op-*vision, *-ia* condition]
myosin (MY-oh-sin) contractile protein found in the thick filaments of skeletal muscle myofilaments [*myos-* muscle, *-in* substance]
myositis (my-oh-SYE-tis) inflammation of muscle tissue [*myos-* muscle, *-itis* inflammation]
myotome (MY-oh-tohm) skeletal muscle or group of muscles that receives motor axons from a given spinal nerve [*myo-*muscle, *-tome* cut segment or region]
myxedema (mik-seh-DEE-mah) firm swelling (edema) of the skin caused by deficiency of thyroid hormone in adults [*myx-* mucus, *-edema* swelling]

N

nail bed layer of epithelium under the nail [*naegl-* metal pin]
nail body visible part of the nail [*naegl-* metal pin]
nail multilayered, protective structure composed of epithelial cells containing hard keratin; located at the distal ends of fingers and toes [*naegl-* metal pin]
nail root part of the nail hidden by the cuticle [*naegl-* metal pin]
naïve (nye-EVE) refers to a B or T cell that is inactive [*naïve* natural]
naïve B cell (nye-EVE) *see* naïve [*naïve* natural, *B* bursa-equivalent tissue, *cell* storeroom]
nanobody (NAN-oh-bod-ee) antibody fragment [*nano* small]
nasal bone (NAY-zal) bone that gives shape to the nose; forms upper bridge of the nose [*nas-* nose, *-al* relating to]
nasal mucosa (NAY-zal myoo-KOH-sah) mucous membrane in the nose that air passes over [*nas-* nose, *-al* relating to, *mucus* slime] *pl.*, mucosae
nasolacrimal duct (nay-zoh-LAK-rih-mal) tube that extends from lacrimal sac into the inferior meatus of the nose [*naso-* nose, *-lacrim* tear, *-al* relating to, *duct-* to lead]
nasopharynx (nay-zoh-FAIR-inks) uppermost portion of the tube just behind the nasal cavities [*naso-* nose, *-pharynx* throat] *pl.*, nasopharynges or nasopharynxes
native state the final, folded and functional shape of a complete protein molecule [*native-* produced by birth]
natural family planning method of predicting the time of ovulation based upon the woman's cyclical changes [*nature-* free from affectation, *-al* relating to, *family-* household, *-plan* sketch]
natural immunity (i-MYOO-ni-tee) acquired immunity resulting from exposure to disease-causing agents in the course of daily living [*nature-* free from affectation, *-al* relating to, *immun-* free, *-ity* state]
natural killer (NK) cell type of lymphocyte that kills many types of tumor cells [*nature-*free from affectation, *-al* relating to, *kill-* to strike, *cell-* storeroom]
nausea (NAW-zee-ah) unpleasant sensation of the gastrointestinal tract that commonly precedes the urge to vomit; upset stomach [*nausea* seasickness]
near reflex constriction of the pupil for near vision [*re-* again, *-flex* bend]
necrosis (neh-KROH-sis) death of cells in a tissue, often resulting from ischemia (reduced blood flow) [*necr-* death, *-osis* condition]
negative feedback feedback control system in which the level of a variable is changed in the direction opposite to that of the initial stimulus
negative nitrogen balance (NYE-troh-jen) condition in which the amount of nitrogen in the urine exceeds the amount of nitrogen in the protein food ingested [*nitro-*soda, *-gen* produce]
neonatal period (nee-oh-NAY-tal) period of development immediately after birth [*neo-* new, *-nat-* birth, *-al* relating to]
neonatology (nee-oh-nay-TOL-oh-jee) diagnosis and treatment of disorders of the newborn [*neo-* new, *-nat-* born, *-log-* words (study of), *-y* activity]
neoplasm (NEE-oh-plaz-em) tumor or abnormal growth; may be benign or malignant [*neo-* new, *-plasm* formation]
nephritis (neh-FRY-tis) inflammatory kidney disease [*nephr-* kidney, *-itis* inflammation]
nephron (NEF-ron) anatomical and functional unit of the kidney, consisting of the renal corpuscle and the renal tubule [*nephro-* kidney, *-on* unit]
nephrotic syndrome (neh-FROT-ik SIN-drohm) collection of signs and symptoms that accompany various glomerular disorders [*nephr-* kidney, *-ic* relating to, *syn-* together, *-drome* running or (race) course]
nerve bundle of nerve fibers, plus surrounding connective tissue, located outside the brain or spinal cord [*nervus-* nerve]
nerve fiber axon of neuron in the nervous system [*fiber-* filament]
nerve impulse self-propagating wave of electrical depolarization that carries information along nerves; also called *action potential* [*impulse-* to drive]
nerve zero very thin nerve near each olfactory nerve; *see* terminal nerve [*zero-* naught]
nervous system brain, spinal cord, and nerves [*nerv-* nerves, *-ous* relating to]
nervous tissue tissue type consisting of neurons and glia that provides rapid communication and control of body function [*nerv-* nerves, *-ous* relating to, *tissu-* fabric]
neural network (NOOR-al) a network of interconnected neurons in nervous tissue, forming a web of pathways to process information [*neur-* nerves, *-al* relating to]
neuralgia (noo-RAL-jee-ah) general term referring to nerve pain [*neur-* nerve, *-algia* pain]
neurilemma (noo-ri-LEM-mah) sheath of Schwann; formed by the nonmyelinated out layer of the Schwann cell (neurolemmocyte) around the axon of a neuron [*neuri-*neuron, *-lemma* sheath] *pl.*, neurilemmae
neurilemmocyte (noo-ri-LEM-moh-syte) another name for the Schwann cell; also spelled *neurolemmocyte* [*neuro-* nerve, *-lemmo* sheath, *-cyte* cell]
neurobiology (noo-roh-bye-AHL-oh-jee) branch of biology that studies the basic science of the nervous system; compare to neurology [*neuro-* nerve, *-bio* life, *-ology* study of]
neuroblastoma (noo-roh-blas-TOH-mah) malignant tumor of sympathetic nervous tissue, found mainly in young children [*neuro-* nerve, *-blast* germ, *-oma* tumor]
neuroendocrine system (noo-roh-EN-doh-krin) endocrine and nervous systems working in concert to perform communication, integration, and control within the body [*neuro-* nerve, *-endo-* within, *-crin-* secrete]
neurofibril (noo-roh-FYE-bril) fine strands extending through the cytoplasm of each neuron; formed by cell's cytoskeleton [*neuro-* nerves, *-fibr-* fiber, *-il* small]
neurofibromatosis (noo-roh-fye-broh-mah-TOH-sis) group of genetic disorders characterized by multiple, sometimes disfiguring, benign tumors of the glia that surround

nerve fibers [*neuro-* nerves, *-fibr-* fiber, *-oma-* tumor, *-osis* condition]

neurogenic bladder (noor-oh-JEN-ik) disorder of the bladder that results in loss of control of normal voiding; due to disruption of nervous input to the bladder [*neuro-* nerves, *-gen-* produce, *-ic* relating to]

neurogenic shock (noo-roh-JEN-ik) condition that results from widespread dilation of blood vessels caused by an imbalance in autonomic stimulation of smooth muscle in vessel walls [*neuro-* nerve, *-gen-* produce, *-ic* relating to]

neuroglia (noo-ROG-lee-ah) nonexcitable supporting cells of nervous tissue; more properly called *glia* [*neuro-* nerve, *-glia* glue] *sing.*, neuroglial cell

neuroglobin (Ngb) (NOO-roh-gloh-bin) protein in neurons similar to hemoglobin used to temporarily store a "back up" supply of oxygen [neuro- nerves, *-glob-* ball, *-in* substance]

neurohypophysis (noo-roh-hye-POF-i-sis) posterior pituitary gland [*neuro-* nerve, *-hypo-* under or below, *-physis* growth] *pl.*, neurohypophyses

neurology (noo-ROL-oh-jee) branch of medical science that deals with the nervous system, especially its disorders and their treatments; compare to neurobiology [*neur-* nerves, *-ology* study of]

neuroma (noo-ROH-mah) any tumor arising from nervous tissue [*neur-* nerves, *-oma* tumor]

neuromodulator (noo-roh-MOD-yoo-lay-tor) "cotransmitter" that regulates the effects of neurotransmitter(s) released along with it [*neuron-* nerves, *-modul-* regulate, *-ate* act of]

neuromuscular junction (NMJ) (noo-roh-MUSS-kyoo-lar) point of contact between nerve endings and muscle fibers; *see* motor endplate [*neuro-* nerve, *- mus-* mouse, *-cul-* little, *-ar* relating to]

neuron (NOO-ron) nerve cell, including its processes (axons and dendrites) [*neuron* string or nerve]

neuron doctrine (NOO-ron DOK-trin) theory stating that the neuron is the basic structural and functional unit of the nervous system and that neurons are independent units connected by chemical synapses; now includes concepts of a larger neural network [*neuron* string or nerve]

neuropeptide (noo-roh-PEP-tyde) neurotransmitter with short strands of polypeptides [*neuro-* nerves, *-pept-* digest, *-ide* chemical]

neuropeptide Y (NOOR-oh-pep-tyde) type of neuropeptide; enhances blood vessel constriction, regulates energy balance, and learning and memory [*neuro-* nerve, *-pept-* digest, *-ide* chemical]

neurosecretory tissue (noo-roh-SEK-reh-tor-ee) modified neurons that secrete chemical messengers that diffuse into the bloodstream rather than across a synapse; for example, in the hypothalamus [*neuro-* nerve, *-secret-* secretion, *-ory* relating to, *tissu-* fabric]

neurotransmitter (noo-roh-trans-MIT-ter) chemicals by which neurons communicate; the substance is released by a neuron, diffuses across the synapse, and binds to the postsynaptic neuron [*neuro-* nerves, *-trans-* across, *-mitt-* send, *-er* agent]

neurotrophin (noo-roh-TROF-in) nerve growth factor [*neuro-* nerve, *-troph-* nutrition, *-in* substance]

neutron (NOO-tron) neutral subatomic particle located in the nucleus of an atom [*neuter-* neither]

neutrophil (NOO-troh-fil) white blood cell that stains readily with neutral dyes [*neuter-* neither, *-phil* love]

nevus (NEE-vus) small, pigmented benign tumor of the skin; a mole [*nevus-* birthmark]

nicotinamide adenine dinucleotide (NAD) (nik-oh-TIN-ah-myde AD-eh-neen dye-NOO-klee-oh-tyde) molecule that serves as an electron carrier in the electron transport system [*Jacque Nicot* French diplomat (brought tobacco to France), *-in-* substance (after plant genus *Nicotiana*), *-am-* ammonia, *-ide* chemical, *aden-* gland, *-ine* derived substance, *di-* two, *nucleo-* kernel (nucleus), *-t-* combining form, *-ide* chemical]

nicotinic (N) receptor (NIK-oh-tin-ik) type of cholinergic receptor [*Jean Nicot Villemain* French diplomat (brought tobacco to France), *-in-* substance, *-ic* relating to, (after plant genus *Nicotiana*) *recept-* receive, *-or* agent]

nipple small projection at the center of the areola on the anterior surface of the breast where the lactiferous ducts release milk [*nip-* beak, *-le* small]

Nissl bodies (NISS-ul) found in rough endoplasmic reticulum, provide protein molecules needed for transmission of nerve impulses from one neuron to another; also called *Nissl substance* [*Franz Nissl* German neurologist]

nitric oxide (NO) (NYE-trik AWK-side) small gas molecule used as a neurotransmitter that *diffuses backward* from a postsynaptic cell toward the presynaptic neuron, where it has its biochemical effects and gives the opportunity for feedback [*nitr-* nitrogen, *-ic* relating to, *ox-* oxygen, *-ide* chemical]

nitrogen balance (NYE-troh-jen) state in which the amount of nitrogen taken into the body equals the amount of nitrogen excreted [*nitro-* soda, *-gen* produce]

nitrogenous waste (nye-TROJ-i-nes) waste from protein catabolism; for example, urea, uric acid, ammonia, and creatinine [*nitro-* soda, *-gen- produce, -ous* relating to]

nitroglycerin (nye-troh-GLIS-eh-rin) heart medication that dilates coronary blood vessels thus improving supply of oxygen to myocardium [*nitro-* nitrogen, *-glyc-* sweet (sugar), *-in* substance]

nociceptor (noh-see-SEP-tor) receptor activated by intense stimuli of any type that results in tissue damage; pain receptor [*noci-* harm, *-cept-* receive, *-or* agent]

node of Ranvier (node of rahn-vee-AY) short space in the myelin sheath between adjacent Schwann cells; also called *myelin sheath gap* [*nod-* knot, *Louis A. Ranvier* French pathologist]

nonadrenergic-noncholinergic (NANC) transmission (non-AD-ren-er-jik non-KOHL-iner-jik tranz-MISH-un) neural synaptic transmission in the efferent autonomic pathways that involves transmitters other than the classical autonomic neurotransmitters norepinephrine and acetylcholine; NANC transmitters include GABA, ATP, neuropeptide Y, and others [*non-* not, *-ad-* toward, *-ren-* kidney, *-erg-*work, *-ic* relating to, *-non-* not, *-chole-* bile, *-erg-*work, *-ic* relating to]

nondisjunction (non-dis-JUNK-shun) occurs during meiosis when a pair of chromosomes fails to separate [*non-* not, *-dis-*split in two, *-junction* joint]

nondisplaced fracture *see* simple fracture [*non-* not, *-displace* to remove, *fracture-*a breaking]

nonelectrolyte (non-ee-LEK-troh-lyte) compound that does not dissociate in solution; for example, glucose [*non-* not, *-electro-* electricity, *-lyt-* loosening]

noninflammatory joint disease (non-in-FLAM-ah-toh-ree) joint disorder that does not involve inflammation of the synovial membrane [*non-* not, *- inflam-* set afire, *-ory* relating to, *joint-* to join, *dis-* opposite of, *-ease* comfort]

nonmembranous organelle (NON-membran-us or-gah-NELL) cell organ that is not defined or bordered by a membrane [*non-* without, *membran-* thin skin, *organ-* instrument, *-ele* small]

nonpolar describes a covalent chemical bond (or covalently bonded molecule) in which there is equal sharing of electrons and therefore no distinct areas of electrical charge [*non-* not, *-pol-* pole, *-ar* relating to]

nonself antigens (AN-ti-jens) foreign and tumor cell markers that a body's immune cells can recognize as being different from the self; also called *nonself markers* [*non-* not, *-self* one's own person, *anti-* against, *-gen* to produce]

nonself concept in immunology that the immune system agents can recognize certain cell-surface molecules or other molecules as not belonging to that individual and thus being a potential target for destruction or damage by the immune system [*non-* not, *-self* one's own person]

nonspecific immunity (non-speh-SIF-ik i-MYOO-ni-tee) mechanisms that resist various threatening agents or conditions, not just certain specific agents; *see* innate immunity [*non-* not, *-specif-* form or kind, *-ic* relating to, *immun-* free, *-ity* state]

nonsteroid (non-STAYR-oyd) hormone synthesized primarily from amino acids rather than from cholesterol [*non-* not, *-stero-* solid, *-oid* like]

nonsteroidal antiinflammatory drug (NSAID) (non-steh-ROID-al an-tee-in-FLAM-ah-tor- ee [EN-sed]) pain medication; for example, aspirin and ibuprofen [*non-* not, *-stero-* solid, *-oid-* like, *-al* relating to, *anti-*against, *-inflamm-* set afire, *-ory* relating to]

norepinephrine (NE, NR) (nor-ep-i-NEF-rin) hormone secreted by adrenal medulla that increases cardiac output; neurotransmitter released by sympathetic nervous system cells [*nor-* chemical prefix (unbranched C chain), *-epi-* upon, *-nephr-*kidney, *-ine* substance]

norepinephrine reuptake inhibitor (NRI) (nor-ep-i-NEF-rin ree-UP-tayk in-HIB-it-or) type of drug that stops the return of norepinephrine (neurotransmitter) to the presynaptic neuron, thus increasing the baseline amount of norepinephrine in the synapse and restoring the baseline to a normal neurotransmitter level [*nor-* chemical prefix (unbranched C chain), *-epi-* upon, *-nephr-*kidney, *-ine* substance, *re-* again, *inhib-* restrain, *-or* agent]

normal saline (SAY-leen) chloride-containing solution [*norm-* rule, *-al* relating to, *sal-* salt, *-ine* relating to]

nuclear envelope (NOO-klee-ar) the boundary of a cell's nucleus, made up of a double layer of cellular membrane [*nucle-* nucleus, *-ar* relating to]

nuclear magnetic resonance (NMR) (NOO-klee-ar mag-NET-ik REH-son-ans) *see* magnetic resonance imaging [*nucle-* nucleus, *-ar, magnet-* lodestone, *-ic* relating to, *re-* again, *-sona-* sound, *-ance* state]

nuclear pore complex (NPC) (NOO-klee-ar poor KOM-plex) complicated, channel-like structure in the nuclear envelope, the nuclear pore (as it is sometimes called) selectively transports molecules into or out of the nucleus [*nucle-* nucleus, *-ar, pore-*passage, *complex-* surrounding]

nuclease (NOO-klee-ayz) RNA and DNA digesting enzyme [*nucle-* nut or kernel (nucleic acid),*-ase* enzyme]

nucleic acid (noo-KLAY-ik ASS-id) any of the high-molecular-weight organic compounds composed of nucleotides, a ribose or deoxyribose sugar, and a phosphate group. See as examples deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) [*nucle-* nut kernel, *-ic* relating to, *acid* sour]

nucleic acid test (NAT) (noo-KLAY-ik ASS-id) blood-safety screening procedure that detects minute particles of genetic material found in infectious agents [*nucle-* nut or kernel, *-ic* relating to, *acid* sour]

nucleolus (noo-KLEE-oh-lus) dense, well-defined but membraneless body within the nucleus; critical to protein formation because it "programs" the formation of ribosomes in the nucleus [*nucleo-* nucleus (kernel), *-olus* little] *pl.*, nucleoli

nucleoplasm (NOO-klee-oh-plaz-im) substance inside a cell's nucleus [*nucleo-* kernel (nucleus), *-plasm* cell or tissue substance]

nucleosome (NOO-klee-oh-sohm) tightly wound subunit of chromatin and proteins (his-tones) [*nucleo-* kernel (nucleus), *-som-* body]

nucleotide (NOO-klee-oh-tide) monomer made up of three types of chemical groups (sugar, phosphate, nitrogen base) that can act alone or to make up a polymer (nucleic acid) [*nucleo-* nut or kernel, *-ide* chemical]

nucleus (NOO-klee-us) membranous organelle that contains most of the genetic material of the cell; also, group of neuron cell bodies in the brain or spinal cord [*nucleus* kernel] *pl.*, nuclei

nucleus pulposus (NOO-klee-us pul-POH-sus) gel-like center of the intervertebral disk; surrounded by annulus fibrosis [*nucleus* kernel, *pulp-* pith of wood]

nurse cell *see* **Sertoli cell** [*nurse-* that suckles, nourishes, *cell-* storeroom]

nutrition foods we eat and the nutrients they contain [*nutri-* nourish, *-tion* process]

nyctalopia (nik-tah-LOH-pee-ah) disorder of the retina that causes difficulty seeing at night or in dim light; also called *night blindness* [*nyct-* night, *-op-* vision, *-ia* condition]

O

obesity (oh-BEES-i-tee) abnormal increase in the proportion of fat in the body [*obes-* fatness, *-ity* state]

obligatory base pairing (oh-BLIG-ah-tor-ee) same nitrogen bases in the DNA structure pairing off with each other; adenine to thymine and cytosine to guanine [*oblige-* to bind]

oblique fissure (oh-BLEEK FISH-ur) fissure in the lungs that separates the inferior and medial lobes [*obliqu-* slanted, *fissur-* cleft]

oblique fracture (oh-BLEEK) type of bone fracture in which fracture line is slanted or diagonal to the longitudinal axis [*obliq-* slanted, *fracture* a breaking]

occipital bone (awk-SIP-it-al) posterior and inferior bone of the skull [*occipit-* back of head, *-al* relating to]

occipital lobe (ok-SIP-it-al) posterior and inferior lobe of the cerebrum [*occipit-* back of head, *-al* relating to]

occipitofrontalis (ok-sip-i-toh-fron-TAL-is) muscle that covers the frontal bone and occipital bone [*occipit-* back of head, *front-* forehead, *-al* relating to]

octet rule (ok-TET) general principle in chemistry whereby atoms usually form bonds in ways that will provide each atom with an outer shell of eight electrons [*octet* group of eight]

oculomotor nerve (awk-yoo-loh-MOH-tor) cranial nerve III; motor nerve; controls eye movements [*oculo-* eye, *mot-* movement, *-or* agent]

older adulthood postnatal period after adulthood [*adultus-* grown up]

olecranon (oh-LEK-rah-non) scoop-shaped process at distal end of ulna that articulates with the humerus at the elbow joint [*olecranon* elbow]

olecranon bursa (oh-LEK-rah-non BER-sah) cushion-like sac located just under the skin overlying the olecranon of the ulna [*olecranon* elbow, *bursa* purse] *pl.*, bursae

olecranon bursitis (oh-LEK-rah-non ber-SYE-tis) inflammation of the olecranon

bursa [*olecranon* elbow, *burs-* purse, *-itis* inflammation]

olecranon fossa (oh-LEK-rah-non FOSS-ah) depression in the posterior surface of the humerus bone to allow room for the olecranon of the ulna when the elbow joint extends [*olecranon* elbow, *fossa* ditch] *pl.*, fossae (FOSS-ee)

olfactory (ohl-FAK-tor-ee) relating to the sense of smell [*olfact-* smell, *-ory* relating to]

olfactory epithelium (ohl-FAK-tor-ee ep-ih-THEE-lee-um) lining of the upper surface of the nasal cavity [*olfact-* smell, *-ory* relating to, *epi-* upon, *theli-* nipple, *-um* thing] *pl.*, epithelia

olfactory nerve (ol-FAK-tor-ee) cranial nerve I; sensory nerve; responsible for the sense of smell [*olfact-* smell, *-ory* relating to]

olfactory receptor neuron (ol-FAK-tor-ee ree-SEP-tor NOO-ron) *see* olfactory sensory neuron [*olfact-* smell, *-ory* relating to, *re-cept*-receive, *-or* agent, *neuron* nerve]

olfactory sensory neuron (ol-FAK-tor-ee SEN-so-ree NOO-ron) afferent neuron in the roof of the nose mucosa that is adapted to detect odors [*olfact-* smell, *-ory* relating to, *neuron* nerve]

oligodendrocyte (ohl-i-go-DEN-droh-syte) small astrocyte with few cell processes; helps to form myelin sheaths around axons within the central nervous system [*oligo-* few, *-dendr-* part (branch) of, *-cyte* cell]

oligodendroglioma (ohl-i-go-DEN-droh-glee-OH-mah) tumor arising from oligodendrocytes (neuroglia of central nervous tracts) [*oligo-* few, *-dendro-* part (branch) of, *-glio-* glue, *-oma* tumor]

oligospermia (ol-i-go-SPER-mee-ah) disruption of the sperm-producing function of the seminiferous tubules [*oligo-* few or little, *-sperm-* seed, *-ia* condition]

oliguria (ohl-i-GOO-ree-ah) condition of reduced urine production [*olig-* few or little, *-ur-* urine, *-ia* condition]

olive oval projection located lateral to the pyramids [*oliva-* olive]

oncogene (ON-koh-jeen) gene (DNA segment) thought to be responsible for the development of a cancer [*onco-* swelling or mass (cancer), *-gen-* produce or generate]

oncologist (ong-KOL-oh-jist) cancer specialist [*onco-* swelling or mass (cancer), *-ist* practitioner of a science]

onycholysis (ahn-ik-oh-LYE-sis) separation of the nail from the nail bed [*onycho-* nail, *-lysis* loosen]

oocyte (OH-oh-syte) developing female sex cell contained within ovarian follicles [*oo-* egg, *-cyte* cell]

oogenesis (oh-oh-JEN-eh-sis) production of female gametes [*oo-* egg, *-gen-* produce, *-esis* process]

oogonium (oh-oh-GO-nee-um) primitive cell from which oocytes derive meiosis [*oo-*egg, *-gon-* offspring, *-um* thing] *pl.*, oogonia

open fracture *see* **compound fracture** [*open* uncovered, *fracture* a breaking]

open reduction surgical procedure that aligns the broken ends of the bone [*open* uncovered, *reducere-* to lead back]

ophthalmic nerve (op-THAL-mik) part of the trigeminal nerve [*oph-* eye or vision, *-thalm-* inner chamber, *-ic* relating to]

ophthalmology (off-thal-MOL-eh-jee) medical practice specialty concerned with pathologic conditions of the eye and the diagnosis and treatment of eye disorders [*oph-* eye or vision, *-thalm-* inner chamber, *-o-* combining form, *-log-* words (study of), *-y* activity]

ophthalmoscope (off-THAL-mah-skohp) instrument used to examine the retinal surface and internal eye structures [*oph-* eye or vision, *-thalmo-* inner chamber, *-scop-* see]

opponens pollicis muscle (oh-POH-nenz POL-i-cis) thumb muscle [*oppenens* opposing, *pollicis* pole, *mus-* mouse, *-cle* little]

opsin (OP-sin) protein produced by the breakdown of rhodopsin in rods and cones of the retina; involved in a chemical reaction that initiates an impulse that results in interpretation of light energy as vision [*ops-* vision, *-in* substance]

optic chiasma (OP-tik kye-AS-mah) region where right and left optic nerves enter the brain and cross each other, exchanging fibers [*opti-* vision, *-ic* relating to, *chiasma* crossed lines (from Greek letter chi, X)] *pl.*, chiasmata, chiasms, or chiasmas

optic disk (OP-tic) area in the retina where the optic nerve fibers exit the eye and where therefore no rods or cones are present; also known as a *blind spot* [*opti-* vision, *-ic* relating to]

optic nerve (OP-tik) cranial nerve II; sensory nerve; nerves that conduct visual information to the brain [*opt-* vision, *-ic* relating to]

optic tract (OP-tik) bundles of fibers formed after the optic nerves pass through the optic chiasma [*opt-* vision, *-ic* relating to, *tract-* trail]

oral contraceptive (OR-al kon-tra-SEP-tiv) medication that controls sex hormone levels and ovulation [*or-* mouth, *-al* relating to, *contra-* against, *-cept-* take or receive (conception), *-ive* agent]

oral hypoglycemic agent (OR-al hye-poh-glye-SEE-mik) treatment for type 2 diabetes that stimulates beta cells to increase insulin supplies [*or-* mouth, *-al* relating to, *hypo-* under or below, *-glyc-* sweet, *-emia* blood condition]

oral rehydration therapy (ORT) treatment of infant diarrhea by the administration of a liberal dose of sugar and salt solution [*or-* mouth, *-alis* relating to, *re-* back again, *-hydra-* water, *-ation* process]

orbicularis oculi muscle (or-bik-yoo-LAIR-is OK-yoo-lye) muscle that encircles the mouth; "kissing muscle" [*orbi-* circle, *-cul-* little, *-ar* relating to, *ocul-* eye, *mus-* mouse, *-cle* little]

orbicularis oris muscle (or-bik-yoo-LAR-is OR-iss) muscle that encircles and closes the eye [*orbi-* circle, *-cul-* little, *-ar* relating to, *oris* mouth, *mus-* mouse, *-cle* little]

orchitis (or-KYE-tis) testicular inflammation [*orchi-* testis, *-itis* inflammation]

orexigenic (oh-rek-sih-JEN-ik) appetite producing [*orex-* appetite, *-gen-* produce, *-ic* relating to]

orexin (oh-REK-sin) factor that stimulates appetite [*orex-* appetite, *-in* substance]

organ group of several tissue types that together perform a special function [*organ*-tool or instrument]

organ of Corti (KOR-tee) *see* spiral organ [*organ-* tool or instrument, *Alfonso Corti* Italian anatomist]

organelle (or-gah-NELL) any of many cell "organs" or organized structures; for example, a ribosome or mitochondrion [*organ-* tool or instrument, *-elle* small]

organic (or-GAN-ik) referring to chemicals that contain covalently bound carbon and hydrogen atoms and are involved in metabolic reactions [*organ-* tool or instrument, *-ic* relating to]

organism (OR-gah-niz-im) any living entity considered as a whole; may be unicellular (one-celled) or composed of many different cells and body systems working together to maintain life [*organ-* instrument, *-ism* condition]

organogenesis (or-gah-no-JEN-eh-sis) formation of organs from the primary germ layers of the embryo [*organ-* instrument (organ), *-gen*-produce, *-esis* process]

orgasm (OR-gaz-um) sexual climax [*orgasm* excitement]

origin attachment of a muscle to the bone, which does not move when contraction occurs; compare to *insertion* [*origin-* source]

oropharynx (or-oh-FAIR-inks) portion of the pharynx that is located behind the mouth [*oro-* mouth, *-pharynx* throat] *pl.*, oropharynges or oropharynxes

orthodontics (or-thoh-DON-tiks) branch of dentistry that deals with the prevention and correction of positioning irregularities of the teeth and malocclusion [*ortho-* straight or upright, *-odont-* tooth, *-ic* relating to]

orthopedics (or-thoh-PEE-diks) medical specialty dealing with skeletal injury and disease [*ortho-* straight or normal, *-ped-* feet, *-ic* relating to]

orthopnea (or-THOP-nee-ah) dyspnea (difficulty in breathing) that is relieved after moving into an upright or sitting position [*ortho-* straight or upright, *-pne-* breathe, *-a* condition]

orthostatic effect (or-thoh-STAT-ik) shift of the blood reservoir to the veins in the legs when standing [*ortho-* upright, *-stat-* standing, *-ic* relating to]

Osgood-Schlatter disease (OZ-good SCHLAYT-er) avulsion fracture of bone fragments from the surface of the tibial tuberosity [*Robert B. Osgood* American surgeon, *Carl Schlatter* Swiss surgeon]

osmolality (os-moh-LAL-i-tee) osmotic concentration of a solution; the number of moles of a substance per kilogram times the number of particles into which the solute dissociates [*osmo-* push (osmosis), *-al* relating to, *-ity* state]

osmoreceptor (os-moh-ree-SEP-tor) special receptors near the supraoptic nucleus that detect decreased osmotic pressure of blood when the body dehydrates [*osmo-* push (osmosis), *-cept-* receive, *-or* agent]

osmosis (os-MO-sis) movement of a fluid (usually water) through a semipermeable membrane from an area of lesser solute concentration to an area of greater concentration [*osmos-* push, *-osis* condition]

osmotic pressure (os-MOT-ik) water pressure that develops in a solution across a semipermeable membrane as a result of osmosis [*osmo-* push, *-ic* relating to]

osseous tissue (OS-ee-us) bone tissue [*os-* bone, *-ous* relating to]

ossification (os-i-fi-KAY-shun) bone formation [*os-* bone, *-fication* to make]

osteitis fibrosa cystica (os-tee-EYE-tis fye-BROH-sah SIS-ti-kah) bone disease caused by hypercalcemia [*oste-* bone, *-it is* inflammation, *fibr-* fiber, *cyst-* cyst, *-ica* relating to]

osteoarthritis (os-tee-oh-ar-THRY-tis) degenerative joint disease; a noninflammatory disorder of a joint characterized by degeneration of articular cartilage [*osteo-* bone, *-arthr-* joint, *-itis* inflammation]

osteoblast (OS-tee-oh-blast) bone-forming cell [*osteo-* bone, *-blast* bud]

osteoclast (OS-tee-oh-klast) bone-absorbing cell [*osteo-* bone, *-clast* break]

osteocyte (OS-tee-oh-syte) bone cell [*osteo-* bone, *-cyte* cell]

osteogenic stem cell (os-tee-oh-JEN-ik) cell that differentiates to produce different types of bone cells; *see also* stem cell [*osteo-* bone, *-gen-* produce, *-ic* relating to]

osteogenesis (os-tee-oh-JEN-eh-sis) combined action of osteoblasts and osteoclasts to mold bones into adult shape [*osteo-* bone, *-gen-* produce, *-esis* process]

osteogenesis imperfecta (os-tee-oh-JEN-eh-sis im-per-FEK-tah) dominant, inherited disorder of connective tissue characterized by imperfect skeletal development, resulting in brittle bones [*osteo-* bone, *-gen-* produce, *-esis* process, *imperfecta* not perfect]

osteoid (OS-tee-oid) organic matrix of bone [*oste-* bone, *-oid* like]

osteoma (os-tee-OH-mah) benign bone tumor [*oste-* bone, *-oma* tumor]

osteomalacia (os-tee-oh-mah-LAY-shah) metabolic skeletal disease [*osteo-* bone, *-malacia* softening]

osteomyelitis (os-tee-oh-my-eh-LYE-tis) bacterial (usually staphylococcal) infection of bone tissue [*osteo-* bone, *myel-* marrow, *-itis* inflammation]

osteon (AHS-tee-on) unit of compact bone tissue made up of a tapered cylinder with layered, concentric arrangements of calcified matrix and cells around a central canal for nerves and blood vessels; also called *Haversian system* [*osteo-* bone, *-on* unit]

osteonal canal (OS-tee-on) *see* central canal (of bone) [*osteo-* bone, *-on-* unit, *-al* relating to]

osteoporosis (os-tee-oh-poh-ROH-sis) bone disorder characterized by loss of minerals and collagen from bone matrix, reducing the volume and strength of skeletal bone [*osteo-* bone, *-poro-* pore, *-osis* condition]

osteosarcoma (os-tee-oh-sar-KOH-mah) bone cancer [*osteo-* bone, *-sarc* flesh, *-oma* tumor]

otitis (oh-TYE-tis) general term referring to inflammation or infection of the ear [*ot-* ear, *-itis* inflammation]

otitis media (oh-TYE-tis MEE-dee-ah) middle ear infection [*ot-* ear, *-itis* inflammation, *medi-* middle, *-al* relating to]

otolith (OH-toh-lith) tiny "ear stones" composed of protein and calcium carbonate in the maculae of the ear, which, by responding to gravity and changes in body position, trigger hair cells that initiate impulses resulting in sense of balance [*oto-* ear, *-lith* stone]

otosclerosis (oh-toh-skleh-ROH-sis) inherited bone disorder; impairs sound conduction by causing structural irregularities in the stapes; *see also* tinnitus [*oto-* ear, *-sclero-* hard, *-sis* condition]

otoscope (OH-toh-skohp) lighted instrument used to examine the external ear canal and outer surface of the tympanic membrane [*oto-* ear, *-scop-* see]

oval window small, membrane-covered opening that separates the middle and inner ear [*oval-* egg-shaped]

ovarian cancer (oh-VAIR-ee-an) cancer of the ovary [*ovum* egg, *cancer* crab or malignant tumor]

ovarian cortex (oh-VAIR-ee-an KOHR-teks) outer region of the ovary [*ov-* egg, *-arian* relating to, *cortex* bark] *pl.*, cortices

ovarian cyst (oh-VAIR-ee-an SIST) fluid-filled cyst on the ovary that develops from follicles that fail to rupture completely or from corpora lutea that fail to degenerate [*ov-* egg, *-arian* relating to, *cyst-* bag]

ovarian follicle (oh-VAIR-ee-an FOL-i-kul) spherical configuration of cells in the ovary that contains a single oocyte [*ov-* egg, *-arian* relating to, *foll-* bag, *-icle* little]

ovarian medulla (oh-VAIR-ee-an meh-DUL-ah) inner region of the ovary; contains supportive connective tissue cells, blood vessels, nerves, and lymphatics [*ov-* egg, *-arian* relating to, *medulla* middle] *pl.*, medullae or medullas

ovary (OH-var-ee) female gonad that produces ova (sex cells) [*ov-* egg, *-ar-* relating to, *-y* location of process]

overactive bladder refers to frequent urination characterized by urgency and pain [*over-* above, *-actus* active, *bledre-* bladder]

oviduct (OH-vi-dukt) *see* fallopian tube, uterine tube [*ovi-* egg, *-duct* to lead]

ovulation (ov-yoo-LAY-shun) release of an ovum from the ovary at the end of oogenesis [*ov-* egg, *-ation* process]

ovum (OH-vum) female sex cell (gamete) [*ovum* egg] *pl.*, ova

oxidative phosphorylation (ahk-si-DAY-tiv fos-for-i-LAY-shun) reaction that joins a phosphate group to ADP to form ATP [*oxi-* sharp (oxygen), *-id-* chemical (*-ide*), *-at-* action of (*-ate*), *-ive* relating to, *phos-* light, *-phor-* carry, *-yl-* chemical, *-ation* process]

oxygen debt (AHK-si-jen) additional oxygen required for ATP synthesis to remove excess lactic acid following anaerobic exercise; also called *excess postexercise oxygen consumption (EPOC)* [*oxy-* sharp, *-gen* produce, *debt* thing owed]

oxygen-hemoglobin dissociation curve (AHK-sih-jen hee-moh-GLOH-bin) graph representing the relationship between Po_2 and O_2 saturation of hemoglobin [*oxy-* sharp, *-gen* produce, *hemo-* blood, *-glob-* ball, *-in* substance, *dis-* reverse, *-socia-* unite, *-ation* process]

oxyhemoglobin (ahk-see-hee-moh-GLOH-bin) hemoglobin combined with oxygen [*oxy-* sharp (oxygen), *-hemo-* blood, *-glob-* ball, *-in* substance]

oxytocin (OT) (ahk-see-TOH-sin) hormone secreted by the posterior pituitary gland before and after delivering a baby; thought to initiate and maintain labor, as well as cause the release of breast milk into ducts of the mammary glands [*oxy-* oxygen, *-toc-* birth, *-in* substance]

P

P wave electrocardiogram deflection that represents depolarization of the atria [named for letter of Roman alphabet]

pacemaker (PAYS-may-ker) *see* sinoatrial node [*pace-* step; *-maker* to make]

Pacini corpuscle (pah-SIN-ee KOHR-pus-ul) *see* lamellar corpuscle [*Filippo Pacini* Italian anatomist, *corpus-* body, *-cle* little]

packed cell volume (PCV) *see* **hematocrit** [*pack-* bundle, *cell-* storeroom, *volume-* paper roll]

pain control area place in the pain conduction pathway where impulses from pain receptors can be inhibited [*pain-* punishment, *control-* regulate, *area-* open space]

palatine bone (PAL-ah-tine) bone that forms the posterior part of the hard palate and the lateral wall of the posterior part of each nasal cavity [*palat-* palate (roof of mouth), *-ine* relating to]

palatine tonsil (PAL-ah-tine TAHN-sil) tonsils located behind and below the pillars of the fauces [*palat-* palate, *-ine* relating to]

palmar venous arch (PAHL-mar VEE-nus) superficial vein of the hand [*palm-* palm of hand, *-ar* relating to, *ven-* vein, *-ous* relating to]

palpable (PAL-pah-bul) can be identified by touch, such as bony landmarks located beneath the skin [*palp-* touch gently, *-able* capable]

palpebrae (PAL-peh-bree) eyelids [*palpebra-* eyelid]

palpebral fissure (PAL-peh-bral FISH-ur) opening between the two eyelids [*palpebra-* eyelid, *-al* relating to, *fissure-* cleft]

pancreas (PAN-kree-ass) endocrine gland located in the abdominal cavity; contains pancreatic islets that secrete glucagon and insulin [*pan-* all, *-creas* flesh]

pancreatic cancer (pan-kree-AT-ik) cancer of the pancreas; usually a form of adenocarcinoma [*pan-* all, *-creat-* flesh, *-ic* relating to, *cancer* crab or malignant tumor]

pancreatic islet (pan-kree-AT-ik eye-let) endocrine portion of the pancreas; made up of alpha and beta cells, among others; source of insulin and glucagon; *also called* islets of Langerhans [*pan-* all, *-creat-* flesh, *-ic* relating to, *isl-* island, *-et* little]

pancreatic juice (pan-kree-AT-ik) digestive secretion; secreted by the exocrine acinar cells of the pancreas [*pan-* all, *-creat-* flesh, *-ic* relating to]

pancreatic polypeptide (pan-kree-AT-ik pol-ee-PEP-tyde) hormone produced in the periphery of the pancreatic islets; influences digestion and distribution of food molecules [*pan-* all, *-creat-* flesh, *-ic* relating to, *poly-* many, *-pept-* to digest, *-ide* chemical, *cell* storeroom]

pancreatitis (pan-kree-ah-TYE-tiss) inflammation of the pancreas [*pan-* all, *-creat-* flesh, *-itis* inflammation]

pandemic (pan-DEM-ik) refers to a disease that affects many people worldwide [*pan-* all, *-dem-* people, *-ic* relating to]

pannus (PAN-us) aggregation of inflammatory cells, granulation tissue, and fibroblasts that adheres to the articular cartilage; destroys articular cartilage and bridges the opposing bones [*pannus* tattered cloth]

Papanicolaou test (Pap smear) (pah-peh-nik-oh-LAH-oo) cancer-screening test in which cells swabbed from the uterine cervix are smeared on a glass slide and examined for abnormalities; also called *Pap smear* or *Pap test* [*George N. Papanicolaou* Greek physician]

papilla (pah-PIL-ah) small, nipple-shaped elevation [*papilla* nipple] *pl.*, papillae (pah-PIL-ee)

papillary (PAP-i-lair-ee) relating to papillae, as in the papillary layer of the dermis located at the dermal papillae [*papilla-* nipple, *-ary* relating to]

papilloma (pap-i-LOH-mah) benign skin tumor characterized by finger-like projections (e.g., a wart) [papilla- nipple, -oma tumor]

paracrine [agent or hormone] (PAIR-ah-krin) hormone that regulates activity in nearby cells within the same tissue as their source [*para-* beside, *-crin-* secrete]

parallel muscle long straplike muscles with parallel fascicles [*para-* beside, *-llel* one another, *mus-* mouse, *-cle* little]

paralysis (pah-RAL-i-sis) loss of power of motion, especially voluntary motion [*para-* beside, *-lysis* loosening]

paramyxovirus (pair-ah-MIK-soh-VYE-rus) virus responsible for mumps [*para-* beside, *-myx-* mucus, *-virus* poison]

paranasal sinus (pair-ah-NAY-zal SYE-nus) air-containing spaces that are connected by channels to the nasal cavity [*para-* beside, *-nas-*nose, *-al* relating to, *sinus* hollow]

paraplegia (pair-ah-PLEE-jee-ah) spastic paralysis that affects both legs [*para-* beside, *-plegia* stroke]

parasympathetic division (pair-ah-sim-pah-THET-ik) part of the autonomic nervous system; ganglia are connected to the brainstem and the sacral segments of the spinal cord; controls many autonomic effectors under normal ("rest and repair") conditions [*para-* beside, *-sym- together, -pathe-* feel, *-ic* relating to]

parathyroid gland (pair-ah-THYE-royd) endocrine gland located in the neck on the posterior aspect of the thyroid gland; secretes parathyroid hormone [*para-* beside, *-thyr-* shield, *-oid* like, *gland* acorn]

parathyroid hormone (PTH) (pair-ah-THYE-royd HOR-mohn) hormone released by the parathyroid gland that increases concentration of calcium in the blood [*para-* besides, *-thyr-*shield, *-oid* like, *hormon-* excite]

parenteral (therapy) (pah-REN-ter-al) administration of nutrients, special fluids, and/or electrolytes by injection [*par-* beside, *-enter-* intestine, *-al* relating to]

parietal (pah-RYE-ih-tal) refers to the walls of an organ or cavity [*pariet-* wall, *-al* relating to]

parietal bone (pah-RYE-i-tal) cranial bone [*parie-* wall,*-al* relating to]

parietal cell (pah-RYE-i-tal) cell located on the basement membrane of gastric glands of the stomach that secretes hydrochloric acid [*paires-* wall, *-al* relating to, *cell* storeroom]

parietal lobe (pah-RYE-eh-tal) lobe that occupies the lateral and medial surface of the cerebrum [*pariet-* wall, *-al* relating to]

parietal membrane (pah-RYE-i-tal) portion of the serous membrane that lines the wall of a body cavity [*pariet-* wall, *-al* relating to, *membran-* thin skin]

parietal peritoneum (pah-RYE-i-tal pair-i-TOH-nee-um) serous membrane that covers organs of the abdomen, pelvis, and thorax [*parie-* wall, *-al* relating to, *peri-* around, *-tone-* stretched, *-um* thing]

parietal pleura (pah-RYE-i-tal PLOO-rah) serous membrane that lines the entire thoracic cavity [*parie-* wall, *-al* relating to, *pleura* rib] *pl.*, pleurae

parietooccipital sulcus (pah-RYE-eh-toh-ok-SIP-i- tal SUL-kus) groove in the cerebrum that separates the occipital lobe from the parietal lobe; also *parietooccipital fissure* [*parieto-* wall, *-occipit-* back of head, *- al* relating to, *sulcus* trench] *pl.*, sulci

Parkinson disease (PD) (PARK-in-son) nervous disorder characterized by abnormally low levels of the neurotransmitter dopamine in parts of the brain that control voluntary movement—victims usually exhibit involuntary trembling and muscle rigidity [*James Parkinson* English physician]

p-arm the shorter segment of the chromosome, which is divided into two "arms" by the centromere (the longer segment is called the *q-arm*) [*p* petite (small), arm]

parotid (gland) (peh-RAH-tid) largest of the paired salivary glands [*par-* beside, *-ot-* ear, *-id* relating to]

parotitis (pair-oh-TYE-tis) *see* mumps [*par-* beside, *-ot-* ear (parotid salivary gland), *-itis* inflammation]

pars anterior (parz an-TEER-ee-or) major part of the anterior pituitary gland [*pars* part, *ante-* front, *-er-* more, *-or* quality]

pars intermedia (PARS in-ter-MEE-dee-ah) forms a small part of the anterior pituitary gland [*pars* part, *inter-* between, *-media* to divide]

partial pressure (PAR-shal) pressure exerted by any one gas in a mixture of gases or in a liquid [*pars-* part, *-al* relating to, *premere-* to press]

partial-thickness burn (PAR-shal) first-or second-degree burn [*pars-* part, *-al* relating to]

parturition (pahr-too-RIH-shun) act of giving birth [*parturi-* give birth, *-tion* process]

passive transport cellular process in which substances move through a cellular membrane with their own energy supplied directly by the cell or its membrane [*passives* passive, *trans-* across, *-portare* carry]

patella (pah-TEL-ah) knee cap [*pat-* dish, *-ella* small] *pl.*, patellae (pah-TEL-ee)

pathogen (PATH-oh-jen) microorganism that causes disease [*patho-*disease, *-gen* produce]

pathogenesis (path-o-JEN-e-sis) pattern of a disease's development [*patho-* disease, *-genesis* origin]

pathogenic animal (path-o-JEN-ik) animal, such as an insect, that causes disease in humans; *see also* vector [*patho-* disease, *-gen-* produce, *-ic* condition of]

pathological fracture (pah-THOL-lah-jik-al) bone fracture caused by weakening of the bone by a disease, thus making normal movements too stressful for the bone to bear; also called *spontaneous fracture* [*patho-* disease, *-log-* words (study of), *-ical* relating to, *fracture* a breaking]

pathology (pah-THOL-oh-jee) study of diseased body structures [*patho-* disease, *-o-* combining form, *-log-* words (study of), *-y* activity]

pathophysiology (path-o-fiz-ee-OL-o-jee) study of the underlying physiological aspects of disease [*patho-* disease, *-physio-* nature (function), *-o-* combining form, *-log-*words (study of), *-y* activity]

pavementing adherence of neutrophils and other phagocytes to a vessel's endothelial lining [*pavement-* beaten floor]

pectoral girdle (PEK-toh-ral GIRD-el) incomplete ring of bones formed by the scapulae and clavicles and providing structural support for the upper limbs; the shoulder girdle [*pector-* breast, *-al* relating to, *girdle* belt]

pectoralis minor (pek-toh-RAL-is) muscle that pulls the shoulder down and forward [*pector-* breast, *-al* relating to, *minor* lesser]

pedicel (PED-i-cel) branches of the podocytes of the Bowman capsule, packed tightly together with only filtration slits between them [*pedic-* feet, *-el* small]

pedigree (PED-i-gree) chart used in genetic counseling to illustrate genetic relationships over several generations [*pied de grue* crane's foot pattern]

pelvic girdle (PEL-vic GER-dul) bony structure formed by the coxal bones; supports the trunk and attaches the lower extremities to it [*pelvi-* basin, *-ic* relating to]

pelvic inflammatory disease (PID) (PEL-vik in-FLAM-ah-tor-ee) inflammatory condition caused by several pathogens that spreads upward from the vagina [*pelv-* basin, -ic relating to, *inflam-* set afire, *-ory* relating to]

penis (PEE-nis) mass of erectile tissue; forms part of the male genitalia; when sexually aroused, becomes stiff to enable it to enter and deposit sperm in the vagina [*penis* male sex organ] *pl.*, penes (PEE-neez) or penises (PEE-nis-ez)

pennate muscle (PEN-ayt) muscle with fascicle attachments that appear "feather-like" [*penn-* feather, *-ate* of or like, *mus-* mouse, *-cle* little]

pentose (PEN-tohs) five-carbon sugar such as ribose or deoxyribose [*pent-* five, *-ose* sugar]

pepsin (PEP-sin) protein-digesting enzyme [*peps-* digestion, *-in* substance]

pepsinogen (pep-SIN-oh-jen) proenzyme that is converted to pepsin by hydrochloric acid [*peps-* digestion, *-in* substance, *-o-* combining form, *-gen* produce]

peptidase (PEP-tyd-ayz) protease found in the intestinal brush border; hydrolyzes peptides to amino acids [*pept-* digestion, *-ide* chemical, *-ase* enzyme]

peptide (PEP-tyde) compound made of two or more amino acids connected by peptide bonds (compare to polypeptide)

peptide bond (PEP-tyde) bond that forms between the amino group of one amino acid and the carboxyl group of another [*pept-* digest, *-ide* chemical]

peptide hormone (PEP-tyde HOR-mohn) major category of nonsteroid hormones; smaller than protein hormones; made up of a short chain of amino acids; for example, antidiuretic hormone (ADH) [*pept-* to digest, *-ide* chemical, *hormon-* excite]

perception (per-SEP-shun) interpreting a sensation [*percept-* to perceive, *-ion* process]

percutaneous coronary intervention (PCI) (per-kyoo-TAYN-ee-us KOR-oh-nair-ee inter-VEN-shun) a group of procedures in which a catheter is inserted through the skin and along an artery to an atherosclerotic plaque and instruments are then passed along the catheter to push away or remove the plaque; examples include angioplasty and atherectomy [*per-* through, *cut-* skin, *-aneous* relating to, *corona-* crown, *-ary* relating to, *inter-* between, *-ven-* go, *-tion* process]

perfusion pressure (per-FYOO-shun) local pressure gradient needed to maintain blood flow in a tissue [*per-* through, *-fus-*pour, *-sion* process]

pericardial effusion (pair-ih-KAR-dee-all ef-FYOO-shen) accumulation of pericardial fluid, pus, or blood in the space between the two pericardial layers [*peri-* around, *-cardi-* heart, *-al* relating to, *e(x)*-outside, *-fus-* pour, *-sion* process]

pericardial fluid (pair-ih-KAR-dee-al) lubricating fluid secreted by the serous membrane; in pericardial space [*peri-* around, *-cardi-* heart, *-al* relating to]

pericardial space (pair-i-KAR-dee-al) space between the visceral layer and the parietal layer surrounding the heart, filled with pericardial fluid [*peri-* around, *-cardi-* heart, *-al* relating to]

pericardial vein (pair-ih-KAR-dee-al) vein of the thorax [*peri-* around, *-cardi-* heart, *-al* relating to]

pericardiocentesis (pair-ee-KAR-dee-oh-sen-TEE-sis) pericardial drainage [*peri-* around, *-cardi-* heart, *-centesis* pricking]

pericarditis (pair-ih-kar-DYE-tis) inflammation of the pericardium [*peri-* around, *-cardi-* heart, *-itis* inflammation]

pericardium (pair-ih-KAR-dee-um) membrane that surrounds the heart [*peri-* around, *-cardi-* heart, *-um* thing] *pl.*, pericardia

perichondrium (pair-ih-KON-dree-um) fibrous covering of cartilage structures [*peri-* around, *-chondr-* cartilage, *-um* thing] *pl.*, perichondria

perikaryon (pair-ih-KAR-ee-on) *see* cell body [*peri-* around, *-karyon* nut or kernel]

perilymph (PAIR-ih-limf) watery fluid that fills the bony labyrinth of the ear [*peri-* around, *-lymph* water]

perimetrium (pair-ih- MEE-tree-um) serous covering that partly covers the uterus; a portion of the parietal peritoneum [*peri-* around, *-metr-* womb, *-um* thing]

perimysium (pair-ih-MEE-see-um) tough, connective tissue surrounding fascicles [*peri-* around, *-mysium* muscle]

perineal body (pair-ih-NEE-al) node formed by fibers from several muscles that form the pelvic floor [*peri-* around, *-ine-* excrete (perineum), *-al* relating to]

perineum (pair-ih-NEE-um) area between anus and genitals [*peri-* around, *-ine-* excrete, *-um* thing] *pl.*, perinea (pair-IH-nee-ah)

perineurium (pair-ih-NOO-ree-um) connective tissue that encircles a bundle of nerve fibers within a nerve [*peri-* around, *-neuri-* nerve, *-um* thing] *pl.*, perineuria

periodontitis (pair-ee-oh-don-TYE-tis) inflammation of the periodontal membrane that anchors teeth to jaw bone; common cause of tooth loss among adults [*peri-* around, *-odont-* tooth, *-itis* inflammation]

periosteum (pair-ee-OS-tee-um) tough, connective tissue covering the bone [*peri-* around, *-osteum* bone] *pl.*, periostea

peripheral (pe-RIF-er-al) relating to the periphery, or outer boundaries of the body, as in peripheral nervous system [*peri-* around, *-phera-* boundary, *-al* relating to]

peripheral nervous system (PNS) (peh-RIF-er-al) nerves connecting brain and spinal cord to other parts of the body [*peri-* around, *-phera-* boundary, *-al* relating to, *nerv-* nerves, *-ous* relating to]

peripheral neuropathy (peh-RIF-er-al noo-ROP-ah- thee) general term for any disease or disorder that involves damage to peripheral nerves; also called *peripheral neuritis*, or if many nerves are involved, *polyneuropathy* or *polyneuritis* [*peri-* around, *-phera-* boundary, *-al* relating to, *neuro-* nerves, *-path-* disease, *-y* state]

peripheral resistance (peh-RIF-er-al) resistance to blood flow caused by friction of blood passing through blood vessels [*peri-* around, *-phera-* boundary, *-al* relating to]

peripheral vascular disease (PVD) (peh-RIF-er-al VAS-kyoo-lar) decrease in blood flow in the hands, legs, or feet [*peri-* around, *-pher-* boundary, *-al* relating to, *-vas-* vessel, *-ular* relating to, *dis-* opposite of, *-ease* comfort]

peristalsis (pair-i-STAL-sis) wavelike, rhythmic contractions of the stomach and intestines that move food material along the digestive tract [*peri-* around, *-stalsis* contraction]

peritoneum (pair-i-toh-NEE-um) large, moist, slippery sheet of serous membrane that lines the abdominopelvic cavity (parietal layer) and its organs (visceral layer) [*peri-* around, *-tone-* stretched, *-um* thing] *pl.*, peritonea

peritonitis (pair-i-toh-NYE-tis) inflammation of the serous membranes in the abdominopelvic cavity; sometimes a serious complication of an infected appendix [*peri-* around, *-ton-* stretch (peritoneum), *-itis* inflammation]

peritubular capillary (pair-ee-TOOB-yoo-lar KAP-i-lair-ee) capillaries around the tubules in the kidney [*peri-* around, *-tub-* tube, *-ul-* little, *-ar* relating to, *capill-* hair, *-ary* relating to]

permanent teeth set of 32 teeth that replaces deciduous teeth [*permanent-* to endure]

permeable (PERM-ee-ah-bil) adjective used to describe a membrane that allows substances to move through (permeate) it [*permeable-* able to pass through]

permeant (PERM-ee-ent) adjective used to describe a substance that is able to move through (permeate) a membrane [*permeable-* able to pass through]

permeate (PERM-ee-ayt) to move through or soak through, as water moving through the pores of a fabric or molecules diffusing through the pores of a cellular membrane [*permeable-* able to pass through]

permissiveness (per-MISS-iv-ness) hormone action that occurs when a small amount of one hormone allows a second hormone to have its full effect on a target cell [*permissive-* to permit, *-ness* state]

pernicious anemia (per-NISH-us ah-NEE-mee-ah) blood disorder characterized by a low number of red blood cells as a result of a dietary deficiency of vitamin B_{12} [*pernici-* destruction, *-ous* relating to, *an-* without, *-emia* blood condition]

pernicious vomiting (per-NISH-us) severe vomiting [*pernici-* destruction, *-ous* relating to]

peroneus tertius muscle (per-oh-NEE-us TER-shee-us) leg muscle that flexes and everts the foot; also fibularis tertius [*peroneus* relating to a boot, *tertius* third, *mus-* mouse, *-cle* little]

peroxisome (pe-ROKS-i-sohm) organelles that detoxify harmful substances that have entered cells [*peroxi-* hydrogen peroxide, *-soma* body]

perspiration transparent, watery liquid released by glands in the skin that eliminates ammonia and uric acid and helps maintain body temperature; also known as *sweat* [*per-* throughout or completely, *-spire* to breathe, *-ation* process]

pH units by which acid and base concentrations (relative H ion concentrations) are measured; scale ranges from O (extremely acidic; high H concentration) to 14 (extremely basic, or alkaline; low H concentration) [abbreviation for *potenz* power, *hydrogen* hydrogen]

phalanx (fah-LANKS) any of the bones of the fingers or toes [*phalanx* formation of soldiers in rows] *pl.*, phalanges (fah-LAN-jeez)

phagocytes (FAG-oh-sytes) white blood cells that engulf microorganisms and digest them [*phago-* eat, *-cyte-* cell]

phagocytosis (fag-oh-sye-TOH-sis) ingestion and digestion of particles by a cell [*phago-* eat, *-cyte-* cell, *-osis* condition]

pharyngeal tonsil (fah-RIN-jee-al TAHN-sil) tonsil located in the nasopharynx on its posterior wall; when enlarged, referred to as *adenoids* [*pharyng-* throat, *-al* relating to]

pharyngitis (fair-in-JYE-tis) sore throat; inflammation or infection of the pharynx [*pharyng-* throat (pharynx), *-itis* inflammation]

pharynx (FAIR-inks) tubelike structure that extends from the base of the skull to the esophagus; also called *throat* [*pharynx* throat] *pl.*, pharynges or pharynxes

phenotype (FEE-no-type) overt, observable expression of a genotype [*pheno-* appear, *-type* kind]

phenylalanine hydroxylase (fen-il-AL-ah-neen hye-DROK-seh-lays) enzyme needed to convert phenylalanine into tyrosine; its absence causes phenylketonuria [*phen-* shining (phenol), *-yl-* chemical, *-alanine* amino acid, *hydro-* water, *-oxy* oxygen, *-ase* enzyme]

phenylketonuria (PKU) (fen-il-kee-toh-NOO-ree-ah) recessive, inherited condition characterized by excess of phenylketone in the urine, caused by accumulation of phenylalanine (an amino acid) in the tissues; may cause brain injury and death if phenylalanine intake is not managed properly [*phen-* shining (phenol), *-yl-* chemical, *-keton-* acetone, *-ur-* urine, *-ia* condition]

pheomelanin (fee-oh-MEL-ah-nin) type of melanin pigment that is reddish in color [*pheo-* dusky, *-melan-* black, *-in* substance]

pheromone (fair-o-mohn) class of organic molecules found in apocrine sweat (possibly urine and other excretions) and which acts as sexual (or other) signals to other individuals [*pher-* carry, *-mone* hormone (excite)]

phimosis (fi-MOH-sis) condition in which the foreskin of the penis fits so tightly over the glans that it cannot be retracted [*phimosis* muzzle]

phlebitis (fleh-BYE-tis) inflammation of a vein [*phleb-* vein, *-itis* inflammation]

phosphatase (FOS-foh-tayse) enzyme that removes phosphate groups [*phospho-* phosphorus, *-ase* enzyme]

phospholipid (fos-fo-LIP-id) phosphate-containing fat molecule; an important constituent of cell membranes [*phospho-* phosphorus, *-lip-* fat, *-id* form]

phosphoric acid (foss-FOR-ik ASS-id) contributes hydrogen ions to the extracellular fluid; influences acid-base balance [*phos-* light, *-phor-* bear (phosphorus), *-ic* relating to, *acid* sour]

phosphorus (FOS-for-us) element that is the principal component in the backbone of nucleic acids; important in energy transfer [*phos-* light, *-phorus* bearer]

phosphorylase (fos-FOR-i-layse) enzyme that adds phosphate groups [*phos-* light, *-phor-* carry, *-yl-* chemical, *-ase* enzyme]

phosphorylation (fos-for-i-LAY-shun) process of adding a phosphate group to a molecule [*phos-* light, *-phor-* carry, *-yl-* chemical, *-ation* process]

photodynamic therapy (PDT) (foh-toh-dye-NAM-ik) less invasive treatment of certain types of lung cancer [*photo-* light, *-dynam-* force, -ic relating to]

photopigment (foh-toh-PIG-ment) chemicals in retinal cells that are sensitive to light [*photo-* light, *-pigment* paint]

photopupil reflex (foh-toh-PYOO-pul REE-fleks) constriction of the pupil in bright light to protect the retina from too intense or too sudden stimulation; also known as *pupillary light reflex* [*photo-* light, *-pupil* center of eye, *re-* again, *-flex* to bend]

photoreceptor (FOH-toh-ree-sep-tor) receptor only in the eye; responds to light stimuli if the intensity is great enough to generate a receptor potential [*photo-* light, *-cept-* receive, *-or* agent]

photorefractive keratectomy (FOH-toh-ree-frak-tiv kair-ah-TEK-toh-mee) laser surgery that uses a "cool" excimer laser beam to vaporize corneal tissue [*photo-* light, *-refract-* break apart, *-ive* relating to, *kera-* hard, *-ec-*out, *-tom-* cut, *-y* action]

phrenic nerve (FREN-ik) nerve that stimulates the diaphragm to contract [*phren-* mind, *-ic* relating to]

physiological buffer (fiz-ee-o-LOJ-i-kal) secondary defense against harmful shifts in pH of body fluids; comes into play after the chemical buffer system [*physio-* nature (function), *-o-* combining form, *-log-* words (study of), *-ical* relating to, *buffe-* cushion, *-er* agent]

physiological dead space (fiz-ee-oh-LOJ-i-kal) the anatomical dead space (pulmonary airway volume outside the alveoli) plus any alveolar dead space (i.e., obstructed or diseased alveoli); *see* anatomical dead space [*physio-* nature, *-log-* words (study), *-ical* relating to]

physiological fatigue (fiz-ee-oh-LOJ-i-kal fah-TEEG) fatigue caused by a relative lack of ATP, rendering the myosin cross bridges incapable of producing the force required for further muscle contractions [*physio-* nature, *-log-* words (study), *-ical* relating to, *fatigue-* to tire]

physiological polycythemia (fiz-ee-oh-LOJ-i-kal pol-ee-sye-THEE-mee-ah) elevated red blood cell numbers and hematocrit values in healthy individuals who live and work in high altitudes [*physi-* nature, *-o-* combining form, *-log-* words (study of), *-y* activity, *poly-* many, *-cyt-* cell, *-emia* blood condition]

physiology (fiz-ee-OL-o-jee) scientific study of an organism's body function [*physio-* nature (function), *-o-* combining form, *-log-* words (study of), *-y* activity]

physique (fi-ZEEK) body build [*physique-* natural, physics]

pia mater (PEE-ah MAH-ter) vascular innermost covering (meninx) of the brain and spinal cord [*pia-* tender, *mater-* mother]

pigment coloring material produced in the body; for example, melanin [*pigment-* paint]

pimple pustule on the skin, usually associated with acne

pineal body (PIN-ee-al) endocrine gland located in the diencephalon and thought to be involved with regulating the body's biological clock; produces melatonin; also called *pineal gland* [*pine-* pine, *-al* relating to, *gland* acorn]

pineal gland (PIN-ee-al) *see* pineal body [*pine-* pine, *-al* relating to, *gland* acorn]

pinna (PIN-nah) flap of the external ear [*pinna-* peak or point]

pinocytosis (pin-oh-sye-TOE-sis) active transport mechanism used to transfer fluids or dissolved substances into cells [*pino-* drink, *-cyto-* cell, *-osis* condition]

pitch number of sound waves that occur during a specific time unit (frequency) [*picchen-* pitch]

pitting edema (eh-DEE-mah) depressions in swollen subcutaneous tissue [*edema* swelling]

pituitary dwarfism (pih-TOO-i-tair-ee DWARF-iz-em) condition resulting from hyposecretion of growth hormone during the growth years [*pituita-* phlegm, *-ism* condition]

pituitary gland (pih-TOO-i-tair-ee) neuroendocrine gland located near base of the brain that has numerous and important regulatory functions; also called the *hypophysis* [*pituit-* phlegm, *-ary* relating to, *gland* acorn

pivot joint (PIV-it joynt) type of diarthrotic synovial joint in which a projection from one bone articulates with a ring or notch in another bone, allowing rotational movement

placenta (plah-SEN-tah) structure that anchors the developing fetus to the uterus and provides a "bridge" for the exchange of nutrients and waste products between the mother and developing baby [*placenta* flat cake] *pl.*, placentae or placentas

placenta previa (plah-SEN-tah PREE-vee-ah) abnormal condition in which a blastocyst implants in the lower uterus, developing a placenta that approaches or covers the cervical opening; placenta previa involves risk of placental separation and hemorrhage [*placenta* flat cake, *previa* gone before]

plantar flexion (PLAN-tar FLEK-shun) the bottom of the foot is directed downward; this motion allows a person to stand on tiptoe [*planta-* sole, *-ar* relating to, *flex-* bend, *-ion* process]

plantar reflex (PLAN-tar REE-fleks) reflex in which the toes curl in flexion in response to stimulation of the outer margin of the foot; the Babinski sign is extension of the great

toe (with or without fanning of the other toes) instead (normal in infants) [*planta-* sole, *-ar* relating to, *re-* again, *-flex* bend]

plaque (plak) raised skin lesion greater than 1 cm in diameter [*plaque-* patch]

plasma (PLAZ-mah) liquid part of the blood [*plasma* substance]

plasma cell (PLAZ-mah) *see* B lymphocyte [*plasma* something molded (blood plasma), *cell* storeroom]

plasma membrane (PLAZ-mah) membrane that separates the contents of a cell from the tissue fluid, encloses the cytoplasm, and forms the outer boundary of the cell [*plasma* substance, *membrane* thin skin]

plasmid (PLAS-mid) small circular ring of bacterial DNA [*plasmid* something formed]

platelet (PLAYT-let) flattened cell fragment found in the blood that functions in hemostasis; thrombocyte [*plate-* flat, *-let* small]

platelet plug (PLAYT-let) results when platelets undergo a change caused by an encounter with a damaged capillary wall, or with underlying connective tissue fibers; helps to stop the flow of blood into the tissues [*plate-* flat, *-let* small]

pleura (PLOO-rah) serous membrane in the thoracic cavity [*pleura* rib] *pl.*, pleurae

pleurisy (PLOOR-i-see) inflammation of the pleura [*pleur-* rib, *-itis* inflammation]

plexus (PLEK-sus) complex network formed by converging and diverging nerves, blood vessels, or lymphatics [*plexus* network] *pl.*, plexi or plexuses

pneumonectomy (noo-moh-NEK-toh-mee) surgical procedure in which an entire lung is removed [*pneumon-* lung, *-ec-* out, *-tom-* cut, *-y* action]

pneumonia (noo-MOH-nee-ah) abnormal condition characterized by acute inflammation of the lungs in which alveoli and bronchial passages become plugged with thick fluid (exudate) [*pneumon-* lung]

pneumotaxic center (noo-moh-TAK-sik) group of cells in the pons of the brain that affects the rate of respiration by inhibiting the inspiration center [*pneumo-* wind (breath), *-taxi-* movement or reaction, *-ic* relating to]

pneumothorax (noo-moh-THOH-raks) abnormal condition in which air is present in the pleural space surrounding the lung, possibly causing collapse of the lung [*pneumo-* air or wind, *-thorax* chest]

podocyte (POD-oh-syte) special epithelial cells making up the visceral layer of the Bowman capsule [*pod-* foot, *-cyte* cell]

Poiseuille's law (pwah-SWEEZ) volume of blood circulated per minute is directly related to mean arterial pressure minus central venous pressure and inversely related to resistance [*Jean L.M. Poiseuille* French physiologist]

polar molecule (POH-lar MOL-eh-kyool) molecule in which the electrical charge is not evenly distributed, causing one side of the molecule to be more positive or negative than the other [*pol-* pole, *-ar* relating to]

poliomyelitis (pol-ee-oh-my-eh-LYE-tis) viral disease that damages motor nerves, often progressing to paralysis of skeletal muscles [*polio-* gray, *-mye-* marrow, *-itis* inflammation]

polychromatic erythroblast (pahl-ee-kroh-MAT-ik ee-RITH-roh-blast) produced during red blood cell formation; produces hemoglobin [*poly-* many, *-chrom-* color, *-ic* relating to, *erythro-* red, *-blast* bud]

polycystic ovary disease (PCOD) (pahl-ee-SIS-tik OH-var-ee) condition that is characterized by ovaries usually twice the normal size and that are studded with fluid-filled cysts [*poly-* many, *-cyst-* bag, *-ic* relating to, *ov-* egg, *-ar-* relating to, *-y* location of process]

polycythemia (pahl-ee-sye-THEE-mee-ah) excess of red blood cells [*poly-* many, *-cyt-* cell, *-emia* blood condition]

polydipsia (pol-ee-DIP-see-ah) excessive and ongoing thirst [*poly-* many. *-dipsa-* thirst, *-ia* condition]

polygenic (pahl-ee-JEN-ik) refers to traits that are determined by the combined effect of many different pairs of genes [*poly-* many, *-gen-* produce, *-ic* relating to]

polymer (PAHL-i-mer) large molecule made up of many identical smaller molecules joined together in sequence [*poly-* many, *-mer* parts]

polymorphonuclearleukocyte (pahl-ee-mohr-foh-NYOO-klee-er LOO-koh-syte) another name for neutrophil, describing the two, three, or more lobes of their nuclei [*poly-* many, *-morph-* form , *-nucle-* nut or kernel, *-ar* relating to, *leuko-* white, *-cyte* cell]

polynucleotide (pahl-ee-NOOK-lee-oh-tyde) strand of nucleotides bound to each other by chemical bonds, as in the polynucleotide strand that makes up an mRNA molecule [*poly-* many, *nucleo-* nut or kernel, *-ide* chemical]

polypeptide (pahl-ee-PEP-tyde) compound made of many amino acids connected by peptide bonds [*poly-* many, *pept-* digest,*-ide* chemical]

polyphagia (pol-ee-FAY-jee-ah) intense and continuous hunger [*poly-* many, *-phag-* eat, *-ia* condition]

polyribosome (PAHL-ee-RYE-bo-sohm) temporary structure formed within a cell by many ribosomes following one another along a strand of mRNA during the process of translation [*poly-* many, *-som-* body]

polyuria (pahl-ee-YOO-ree-ah) frequent urination [*poly-* many, *-ur-* urine, *-ia* condition]

pons (ponz) part of the brainstem between the medulla oblongata and the midbrain [*pons* bridge] *pl.*, pontes (PON-tees)

popliteal vein (pop-lih-TEE-al) vein that runs behind the knee joint [*poplit-* back of knee, *-al* relating to]

portal system arrangement of blood vessels in which blood exiting one tissue is immediately carried to a second tissue before being returned to the heart and lungs for oxygenation and redistribution [*port-* doorway, *-al* relating to]

positive feedback (mechanism) feedback control system that is stimulatory; tends to amplify or reinforce a change in the internal environment [*positiv-* to place or to amplify]

positive nitrogen balance (NYE-troh-jen) nitrogen intake in foods is greater than nitrogen output in urine [*positiv-* to place or to amplify, *nitro-* soda, *-gen* produce]

positron-emission tomography (PET) (POZ-itron eh-MISH-un toh-MOG-rah-fee) variation of computed tomography scanning; radioactive substance is introduced into the blood supply of the brain projecting a bright spot on the image [*positron* positive electron, *e-* out, *-mission* send, *tomo-* cut, *-graph-* draw, *-y* activity]

posterior (pos-TEER-ee-or) located behind; opposite of anterior [*poster-* behind, *-or* quality]

posterior cavity (of eye) (pohs-TEER-ee-or KAV-i-tee) all the space posterior to the lens of the eye; contains vitreous body [*poster-* behind, *-or* quality, *cav-* hollow, *-ity* state]

posterior chamber (of eye) (pohs-TEER-ee-or CHAM-ber) subdivision of the anterior cavity of the eye; small space behind the iris and anterior to the lens [*poster-* behind, *-or* quality, *chamber-* vaulted enclosure]

posterior cul-de-sac (of Douglas) (pohs-TEER-ee-or kul-deh-sak) a deep pouch between the uterus and the anus; formed by the posterior ligament [*poster-* behind, *-or* quality, *cul-de-sac* end of the pouch, *James Douglas* Scots anatomist] *pl.*, culs-de-sac or cul-de-sacs

posterior fornix (pohs-teer-ee-or FOR-niks) space created by the protrusion of the cervix into the lumen of the vagina; increases probability of reproductive success by retaining seminal fluid [*poster-* behind, *-or* quality, *fornix* arch]

posterior ligament (pohs-TEER-ee-or LIG-ah-ment) fold of peritoneum extending from the posterior surface of the uterus to the rectum [*poster-* behind, *-or* quality, *liga-* bind, *-ment* condition]

posterior tibial vein (pohs-TEER-ee-or TIB-ee-al) deep vein of the leg [*poster-* behind, *-or* quality, *tibia* shin bone, *-al* relating to]

postganglionic neuron (post-gang-glee-ON-ik NOO-ron) efferent autonomic neuron that conducts nerve impulses from a ganglion to effectors such as cardiac or smooth muscle or glandular epithelial tissue [*post-* after, *-ganglion-* knot, *-ic* relating to, *neuron* nerve]

postinfectious glomerulonephritis (post-in-FEK-shus gloh-mer-yoo-loh-neh-FRY-tis) *see* acute glomerulonephritis [*post-* after, *-infec-*stain, *-ous* relating to, *glomer-* ball, *-ul-* little, *-nephr-* kidney, *-itis* inflammation]

postmenstrual phase (post-MEN-stroo-al) phase in the menstrual cycle that occurs between the end of menses and ovulation; also called *preovulatory phase* and *proliferative phase* [*post-* after, *-mens-* month, *-al* relating to]

postnatal period (POST-nay-tal) period after birth, ending at death [*post-* after, *-nat-* birth, *-al* relating to]

postovulatory phase (post-ov-yoo-lah-TOR-ee) *see* premenstrual phase [*post-* after, *-ov-* egg, *-ory* relating to]

postsynaptic (post-si-NAP-tik) adjective describing any structure after a synapse (junction) of one neuron to another or any function that occurs after synaptic transmission [*post-* after, *-syn-* together, *-apt-* join, *-ic* relating to]

postsynaptic neuron (post-si-NAP-tik NOO-ron) in neuron-to-neuron communication, the neuron that receives a stimulus via an adjacent neuron's transmission of neurotransmitters across the synapse [*post-* after, *-syn-* together, *-apt-* join, *-ic* relating to]

postsynaptic potential (post-sih-NAP-tik poh-TEN-shal) local potential produced by opening of ion channels in the postsynaptic membrane [*post-* after, *-syn-* together, *-apt-* join, *-ic* relating to, *potent-* power, *-ial* relating to]

posture position of the body; often refers to the erect position of the body maintained unconsciously [*postur-* position]

potassium (poh-TAS-ee-um) mineral element that forms the ion K [*potass-* potash, *-um* thing or substance]

potassium channel (poh-TASS-ee-um CHAN-el) a pore in a cell membrane that allows only potassium ions to permeate, or pass through, the membrane [*potass-* potash, *-um* thing or substance, *channel-* groove]

potential osmotic pressure (po-TEN-shal os-MOT-ik) maximum osmotic pressure that could develop in a solution when it is separated from pure water by a selectively permeable membrane [*potent-* power, *-ial* relating to, *osmo-* push, *-ic* relating to]

Pott fracture fracture of the lower part of the tibia [*Percival Pott*, English physician, *fracture* a breaking]

preauricular lymph node (pree-ah-RIK-yoo-lar limf nohd) lymphatic tissue located just in front of the ear [*pre-* before, *-auric-* ear, *-ula-*little, *-ar* relating to, *lymph* water, *nod-* knot]

precapillary sphincter (pree-CAP-pi-lair-ee SFINGK-ter) smooth muscle cells that guard the entrance to the capillary [*pre-* before, *-capill-* hair, *-ary* relating to]

precordial lead (pree-KOR-dee-al) *see* chest lead [*pre-* before, *-cordi-* heart, *-al* relating to]

preeclampsia (pree-ee-KLAMP-see-ah) syndrome of abnormal conditions of uncertain cause in pregnancy; symptoms include hypertension, proteinuria, and edema; also called *toxemia of pregnancy*, it may progress to eclampsia—severe toxemia that may cause death [*pre-* before, *-lamp-* shine forth, *-sia* condition]

preganglionic neuron (pree-gang-glee-ON-ik NOO-ron) efferent autonomic neuron that conducts nerve impulses between the spinal cord and a ganglion [*pre-* before, *-ganglion-* knot, *-ic* relating to, *neuron* nerve]

pregnancy-induced hypertension (PIH) (PREG-nan-see-in-DOOST hye-per-TEN-shun) a condition in which a woman's blood pressure rises after the twentieth week of pregnancy and remains elevated until the end of pregnancy; PIH may have a genetic component and may progress to *preeclampsia* [*hyper-* excessive, *-tens-* stretch or pull tight, *-sion* state]

premature contraction contraction that occurs before the next expected contraction in a series of cardiac cycles; also called *extrasystole* [*pre-* before, *-mature* to ripen, *con-* together, *-tract* to draw, *-tion* process]

premenstrual phase (pree-MEN-stroo-al) phase of the menstrual cycle that occurs between ovulation and the onset of the menses; also called *postovulatory phase*, *progesterone phase*, *luteal phase*, or *secretory phase* [*pre-* before, *-mens-* month, *-al* relating to]

premenstrual syndrome (PMS) (pree-MEN-stroo-all SIN-drohm) condition that involves a collection of symptoms that regularly occur in many women during the premenstrual phase [*pre-* before, *-mens-* month, *-al* relating to, *syn-* together, *-drome* running or (race) course]

prenatal period (PREE-nay-tal) developmental period after conception until birth [*pre-* before, *-nat-* birth, *-al* relating to]

preovulatory phase (pree-ov-yoo-lah-TOR-ee) *see* postmenstrual phase [*pre-* before, *-ov-* egg, *-ory* relating to]

prepatellar bursitis (pree-pah-TEL-er ber-SYE-tis) inflammation of the prepatellar bursa; also called "housemaid's knee" [*pre-* in front of, *-pat-* dish, *-ella* small, *-ar* relating to, *bursa-* purse, *-itis* inflammation]

prepuce (PREE-pus) foreskin, especially covering fold of skin over the glans penis [*pre-* before, *-puc-* penis]

presbycusis (pres-bih-KYOO-sis) progressive hearing loss as a result of nerve impairment; common among elderly [*presby-* elderly, *-cusis* hearing]

presbyopia (pres-bee-OH-pee-ah) farsightedness of old age [*presby-* aging, *-op-* vision, *-ia* condition]

pressoreflex (pres-oh-REE-fleks) *see* baroreflex pressure acuity (ah-KYOO-i-tee) sharpness of visual perception [*premere-* to press, *acu-* sharp, *-ity* state]

presynaptic (pree-si-NAP-tik) adjective describing any structure before a synapse (junction) of one neuron to another or any function that occurs before synaptic transmission [*press-* pressure, *-re-* back or again, *-flex* bend]

presynaptic neuron (pree-si-NAP-tik NOO-ron) in neuron-to-neuron communication, the neuron that transmits a signal to an adjacent neuron via release of neurotransmitters that cross the synapse and bind to the postsynaptic neuron [*pre-* before, *-syn-* together, *-apt-* join, *-ic* relating to]

prevertebral ganglion (pree-ver-TEE-bral GANG-glee-on) collateral ganglion; pairs of sympathetic ganglia located a short distance from the spinal cord [*pre-* before, *-vertebra* joint, *-al* relating to, *ganglion-* knot]

primary bronchus (PRY-mair-ee BRONG-kus) either of the two branches of the trachea that enter the lungs [*prim-* first, *-ary* relating to, *bronchus* windpipe] *pl.*, bronchi (BRONG-kye)

primary follicle (PRY-mair-ee FOL-i-kul) follicles present at puberty; formed from granulosa cell [*prim-* first, *-ary* state, *folli-* bag, *-cle* small]

primary germ layer (PRY-mair-ee) any of the three layers of developmental cells that give rise to definite structures as the embryo develops; *see* ectoderm, endoderm, mesoderm [*prim-* first, *-ary* state, *germ* sprout]

primary hyperparathyroidism (PRY-mair-ee hye-per-pair-ah-THY-royd-iz-em) condition that results when parathyroid gland fails to adjust its hormone output to compensate for changes in blood calcium levels [*prim-* first, *-ary* relating to, *hyper-* excessive, *-para-* beside, *-thyr-* shield (thyroid), *-oid* like, *-ism* condition]

primary oocytes (PRY-mair-ee OH-oh-sytes) developmental stage of the ova; formed from oogonia during the fetal period [*prim-* first, *-ary* state, *oo-* egg, *-cyte* cell]

primary ossification center (PRY-mair-ee os-i-fi-KAY-shun) where a blood vessel enters the cartilage of a developing bone at the midpoint of the diaphysis to initiate bone formation [*primary* first order, *os-* bone, *-fication* to make]

primary principle of ventilation (PRY-mair-ee) movement of air in the pulmonary airways from the area where the pressure is higher to the area where the pressure is lower [*prim-* first, *-ary* relating to, *princip-* foundation, *vent-* fan or create wind, *-tion* process]

primary sex characteristics (PRY-mair-ee) changes that involve the development of the gonads [*prim-*first, *-ary* state, *charassein* to engrave]

prime mover main muscle responsible for producing a particular movement [*prime* first order]

principle of independent assortment genetic principle that states as chromosome pairs separate, the maternal and paternal chromosomes redistribute themselves independently of the other chromosome pairs [*princip-* foundation, *in-* not, *-de-* remove entirely, *-pend* to hang upon, *assort-* to match into groups]

principle of segregation genetic principle that states that the two members of a pair of chromosomes separate during meiosis [*princip-* foundation, *segregate-* divide, *-ation* process of]

prion (PREE-ahn) a term that is short for "*pro*teinaceous *in*fectious particles," which are proteins that convert normal proteins of the nervous system into abnormal proteins, causing loss of nervous system function; the abnormal form of the protein also may be inherited; a newly discovered type of pathogen, not much is known about how the prion works; *see* bovine spongiform encephalopathy, variant Creutzfeldt-Jakob Disease (vCJD) [condensed from *proteinaceous infectious particle*]

process (PRAH-ses) 1. A series of actions having a result 2. A projection from a structure such as a bone [*process* advance or project (from)]

product molecules or atoms that result from a chemical reaction [*product-* to bring forth]

proctitis (prok-TYE-tis) inflammation of the rectal mucosa [*proct-* anus, *-itis* inflammation]

proenzyme (pro-EN-zime) inactive form in which many enzymes are synthesized [*pro-* first, *-en-* in, *-zyme* ferment]

proerythroblast (proh-eh-rith-roh-BLAST) maturation stage of the red blood cell; appearance of this cell begins differentiation in red blood cells [*pro-* first, *-erythro-* red, *-blast* bud]

progeria (proh-JEER-ee-ah) rare, inherited condition in which a young child appears to age rapidly, also called *Hutchinson-Gilford disease* [*pro-* early, *-ger-* old age, *-ia* condition]

progesterone (proh-JES-ter-ohn) steroid hormone produced by the ovaries (particularly the corpus luteum) that helps prepare the uterus for implantation; along with estrogen, helps maintain normal uterine and mammary gland function [*pro-* provide for, *-gester-* bearing (pregnancy), *-stero-* solid or steroid derivative, *-one* chemical]

progesterone phase (proh-JES-ter-ohn) *see* premenstrual phase [*pro-* provide for, *-gester-*bearing pregnancy), *-stero-* solid or steroid derivative, *-one* chemical]

prohormone (proh-HOR-mohn) hormone precursor [*pro-* first, *hormon-* excite]

projection tract extension of the sensory spinothalamic tracts and descending corticospinal tracts in the brain [*project-* thrown forward, *-ion* process, *tract-* trail]

prolactin (PRL) (proh-LAK-tin) hormone secreted by the anterior pituitary gland during pregnancy to stimulate the breast development needed for lactation [*pro-* provide for, *-lact-* milk, *-in* substance]

proliferative phase (PROH-lif-er-eh-tiv) *see* postmenstrual phase [*proli-* offspring, *-fer-*bear or carry, *-at-* process, *-ive* relating to]

pronation (proh-NAY- shun) movement that turns the palm of the hand down [*pronat-*bend forward, *-tion* process]

prophase (PRO-fayz) first stage of mitosis during which chromosomes become visible [*pro-* first, *-phase* stage]

proprioception (proh-pree-oh-SEP-shun) perception of movement and position of the body [*propri-* one's own, *-cept-* receive, *-tion* process]

proprioceptor (proh-pree-oh-SEP-tor) receptor located in the muscles, tendons, and joints; allows the body to perceive its position relative to surroundings [*propri-* one's own, *-cept-* receive, *-or* agent]

propulsion (proh-PUL-shen) continual pushing of chyme in the stomach toward the pyloric sphincter by peristaltic contractions [*pro-* in front, *-pul-* drive, *-sion* process]

prostaglandin (PG) (pross-tah-GLAN-din) any of a group of naturally occurring lipid-based substances that act in a hormone-like way to affect many body functions, including vasodilation, uterine smooth muscle contraction, and the inflammatory response [*pro-* before, *-stat-* set or place (prostate), *-gland-* acorn (gland), *-in* substance]

prostate (PROSS-tayt) exocrine gland that lies just below the bladder in the male; secretes a fluid that constitutes about 30% of the seminal fluid volume; helps activate sperm and helps them maintain motility [*pro-* before, *-stat-* set or place]

prostatectomy (pros-tah-TEK-toh-mee) surgical removal of the prostate [*pro-* before, *-stat-* set or place (prostate gland), *-ec-* out, *-tom-* cut, *-y* action]

prostate-specific antigen (PSA) (PROSS-tayt speh-SIF-ik AN-ti-jen) blood protein sometimes associated with prostate cancer [*pro-*before, *-stat-* set or place (prostate gland), *specif-* form, *-ic* relating to, *anti-*against, *-gen* produce]

prosthesis (pros-THEE-sis) artificial device that is used in the partial or total replacement of a diseased joint [*prosthesis* addition] *pl.*, prostheses (pros-THEE-seez)

protease (PRO-tee-ayz) enzyme that catalyzes the hydrolysis of proteins into intermediate compounds (proteoses and peptides) [*prote-*protein, *-ase* enzyme]

proteasome (PRO-tee-ah-sohm) cell structure that breaks down individual proteins [*protea-* protein, *-som-* body]

protein (PRO-teen) large molecules formed by linkage of amino acids by peptide bonds; one of the basic building blocks of the body [*prote-* primary, *-in* substance]

protein balance (PRO-teen) rate of protein anabolism equals or balances the rate of protein catabolism [*prote-* primary, *-in* substance]

protein hormone (PRO-teen HOR-mohn) long, folded chain of amino acids; for example, insulin and parathyroid hormone [*prote-* first rank, *-in* substance, *hormon-* excite]

protein-calorie malnutrition (PCM) (PRO-teen KAHL-ah-ree mal-noo-TRISH-un) abnormal condition resulting from a deficiency of calories in general and protein in particular [*mal-* poor, *-nutri-* nourish, *-tion* process]

proteoglycan (PRO-tee-oh-GLYE-kan) large molecule made up of a protein strand that forms a backbone to which are attached many carbohydrate molecules [*proteo-* protein, *-glycan* polysaccharide (from *-glyc-*sweet)]

proteome (PRO-tee-ohm) the entire group of proteins produced by a cell or by the entire body [*prote-* protein, *-ome* entire collection]

proteomics (proh-tee-OH-miks) the endeavor that involves the analysis of the proteins encoded by the genome, with the ultimate goal of understanding the role of each protein in the body [*prote-* first rank (protein), *-om-* entire collection, *-ic* relating to]

proton (PROH-ton) positively charged subatomic particle [*protos-* first, *-on* elementary atomic particle]

protozoan (pro-toe-ZO-an) single-celled organism with a nucleus and other membranous organelles that can infect humans [*proto-* first, *-zoan* animal] *pl.*, protozoa

protraction (proh-TRAK- shun) movement that moves a part forward [*pro-* forward, *-tract-* drag, *-tion* process]

proximal (PROK-si-mal) next or nearest; located nearest the center of the body or the point of attachment of a structure; opposite of distal [*proxima-* near, *-al* relating to]

proximal convoluted tubule (PROK-si-mal KON-vo-LOO-ted TOO-byool) second part of the nephron and the first segment of a renal tubule; major portion of the *proximal tubule* [*proxima-* near, *-al* relating to, *con-*together, *-volut-* roll, *tub-* tube, *-ul-* little]

proximal interphalangeal (PIP) (PROK-si-mal in-ter-fah-LAN-gee-al) joint between the proximal and middle phalanges [*proxima-* near, *-al* relating to, *inter-* between, *-phalang-* finger bones (ref. from rows of soldiers), *-al* relating to]

proximal tubule (PROK-si-mal TOO-byool) *see* proximal convoluted tubule [*proxima-*near, *-al* relating to, *tub-* tube, *-ul-* little]

pseudogene (SOOD-oh-jeen) nonfunctional "broken" genetic code found in "junk DNA" located between the functioning, coding genes of a DNA molecule; pseudogenes are thought to be genetic "fossils" remaining from our evolutionary past [*pseudo-* false, *gene* produce]

pseudostratified columnar epithelium (SOOD-oh-STRAT-i-fyed KAHL-um-nar ep-i-THEE-lee-um) type of tissue similar to simple columnar epithelium; forms a membrane made up of single layer of cells that are tall and narrow but have been squeezed together in a way that pushes the nuclei into two layers and thus gives the appearance that it is stratified [*pseudo-* false, *-strati-* layer, *-fied* to be made, *column-* column, *-ar* characterized by] *pl.*, epithelia

psoriasis (so-RYE-ah-sis) chronic, inflammatory skin disorder characterized by cutaneous inflammation and scaly plaques [*psor-* itching, *-iasis* condition]

psychological stressor (sye-koh-LOJ-i-kal STRESS-or) anything an individual perceives as a threat [*psycho-* the mind, *-logos-*words (study), *-al* relating to, *stress-* tighten, *-or* agent]

psychophysiology (sye-koh-fiz-ee-OL-oh-jee) scientific discipline that studies physiological responses of individuals being subjected to psychological stressors [*psycho-* the mind, *-physio* nature (function), *-o-* combining form, *-log-* words (study of), *-y* activity]

psychosomatic (sye-koh-so-MAT-ik) mind influencing the body

ptosis (TOH-sis) downward displacement of an organ; for example the lowered kidneys of very thin individuals [*psycho-* the mind, *-soma* body, *-ic* relating to]

pterygoid muscle (TER-i-goid) muscle of mastication; opens and protrudes the mandible while causing sideways movement [*ptery-* wing, *-oid* like, *mus-* mouse, *-cle* little]

puberty (PYOO-ber-tee) stage of adolescence in which a person becomes sexually mature [*pubert-* age of maturity, *-y* state]

pubis (PYOO-biss) most anterior coxal bone [*pubis* groin] *pl.*, pubes (PYOO-beez)

puerperal fever (pyoo-ER-per-al) condition caused by bacterial infection in a woman after delivery of an infant, possibly progressing to septicemia and death; also called "child-bed fever" [*puerp-* childbirth, *-al* relating to]

pulmonary artery (PUL-moh-nair-ee AR-ter-ee) artery that carries deoxygenated blood from the right ventricle of the heart to the lungs; exiting the heart is the trunk of the pulmonary artery (pulmonary trunk), which branches into a left and right pulmonary artery [*pulmon-* lung, *-ary* relating to, *arteri-* vessel]

pulmonary circulation (PUL-moh-nair-ee) blood flow from the right ventricle to the lung and returning to the left atrium [*pulmon-* lung, *-ary* relating to, *circulat-* go around, *-tion* process]

pulmonary edema (PUL-moh-nair-ee eh-DEE-mah) congestion of blood in the pulmonary circulation [*pulmon-* lung, *-ary* relating to, *edema* swelling]

pulmonary embolism (PUL-moh-nair-ee EM-boh-liz- em) blockage of the pulmonary circulation by a thrombus or other matter; may lead to death if blockage of pulmonary blood flow is significant [*pulmon-*lung, *-ary* relating to, *embol-* plug, *-ism* condition]

pulmonary radiology (PUL-moh-nair-ee RAY-dee-ohl-oh-gee) chest x-ray examination [*pulmon-* lung, *-ary* relating to, *radi-* ray or radiation, *-o-* combining form, *-log-* words (study of), *-y* activity]

pulmonary trunk (PUL-moh-nair-ee trunk) initial segment of the pulmonary artery, before it splits into left and right branches [*pulmon-* lung, *-ary* relating to]

pulmonary (semilunar) valve (PUL-moh-nair-ee [semi-LOO-nar]) valve located at the beginning of the pulmonary artery [*pulmon-* lung, *-ary* relating to, *semi-* half, *-luna* moon, *-ar* relating to, *valve-* folding door]

pulmonary vein (PUL-moh-nair-ee) any vein that carries oxygenated blood from the lungs to the left atrium [*pulmon-* lung, *-ary* relating to]

pulmonary ventilation (PUL-moh-nair-ee ven-tih-LAY-shun) breathing; process that moves air in and out of the lungs [*pulmon-*lung, *-ary* relating to, *vent-* fan or create wind, *-tion* process]

pulp cavity cavity in the dentin of a tooth that contains connective tissue, blood and lymphatic vessels, and sensory nerves [*pulp* flesh, *cav-* hollow, *-ity* condition]

pulse point where the pulse can be palpated; that is, wherever an artery lies near the surface and over a bone or other firm background; for example, radial artery [*pulse-* beat]

pulse pressure difference between systolic and diastolic blood pressure [*pulse* beat]

puncta (PUNK-ta) see punctum

punctum (PUNK-tum) opening into the lacrimal canals located at the inner canthus of the eye [*punctum* small point] *pl.*, puncta

Punnett square (PUN-it) grid used in genetic counseling to determine the probability of

inheriting genetic traits [*Reginald C. Punnett* English geneticist]

pupil opening in the center of the iris that regulates the amount of light entering the eye [*pup-* doll, *-il* little]

pupillary light reflex (PYOO-pih-lair-ee) photopupil reflex [*pup-* doll, *-il* little, *-ary* relating to, *re-* again, *-flex* bend]

purine base (PYOO-reen) one of two types of nitrogenous bases that are vital components of DNA derived from purine; adenine and guanine [*pur-* pure, *-ine* chemical]

Purkinje fibers (pur-KIN-jee) *see* subendocardial branches [*Johannes E. Purkinje* Czech physiologist]

pus accumulation of white blood cells, dead bacterial cells, and damaged tissue cells at site of an infection [*pus* corrupt matter]

pustule (PUS-tyool) small, raised skin lesion filled with pus [*pustule-* blister or pimple]

pyelonephritis (pye-eh-loh-neh-FRY-tis) inflammation of the renal pelvis and connective tissues of the kidney [*pyel-* renal pelvis, *-nephr-* kidney, *-itis* inflammation]

pyloric sphincter (pye-LOR-ik SFINGK-ter) sphincter (muscular valve) that prevents food from leaving the stomach and entering the duodenum [*pyl-* gate, *-or-* to guard, *-ic* relating to, *sphinc-* bind tight, *-er* agent]

pyloric stenosis (pye-LOR-ik steh-NO-sis) obstructive narrowing of the pylorus [*pyl-* gate, *-or-* guard, *-ic* relating to, *stenos-* narrow, *-osis* condition] *pl.*, stenoses

pylorospasm (pye-LOHR-oh-spaz-um) condition occurring in infants when the pyloric fibers do not relax normally to allow food to leave the stomach, and the infant vomits food instead of digesting and absorbing it [*pyl-* gate, *-or-* guard, *-spasm* twitch or involuntary contraction]

pylorus (pye-LOR-us) lower part of the stomach [*pyl-* gate, *-orus* guard]

pyramid (PEER-ah-mid) one of two bulges of white matter located on the ventral surface of the medulla [*pyramis-* pyramid]

pyramidal tract (pi-RAM-i-dal) fibers that come together in the medulla to form the pyramids; also called *corticospinal tract* [*pyrami-* pyramid, *-al* relating to, *tract-* trail]

pyramids (PEER-ah-mids) triangular-shaped divisions of the medulla of the kidney [*pyramis-* pyramid]

pyrimidine base (pi-RIM-i-deen) one of two types of nitrogenous bases that are vital components of DNA derived from pyrimidine; cytosine and thymine [*pyrimid-* nitrogen compound, *-ine* chemical]

pyrogen (PYE-roh-jen) systemic inflammatory response chemical that causes the thermostatic control centers of the hypothalamus to produce a fever [*pyro-* heat, *-gen* produce]

pyuria (pye-YOO-ree-ah) pus in urine [*py-* pus, *-ur-* urine, *-ia* condition]

Q

q-arm the longer segment of the chromosome, which is divided into two "arms" by the centromere (the shorter segment is called the p-arm) [*q* follows *p* in Roman alphabet]

QRS complex electrocardiogram deflection that represents depolarization of the ventricles [named for letters of Roman alphabet]

quadriplegia (kwod-ri-PLEE-jee-ah) paralysis that affects all four extremities [*quadri-* fourfold, *-plegia* stroke]

quaternary (KWAH-ter-nair-ee) fourth or relating to the fourth in a series, as in the quaternary structure of a protein, which is the fourth level of complexity in the structure of a protein molecule; a quaternary protein is a protein possessing a fourth level of complexity in its molecular structure [*quarti-* fourth, *-ary* relating to]

R

raccoon eyes (ra-KOON eyes) condition that may occur as a result of the fracture of the fragile bones of the eye orbit [*arocoun-* raccoon]

radial keratotomy (RAY-dee-al KAR-ah-tah-toh-mee) surgical placement of six or more radial slits in a spoke-like pattern around the cornea; flattens cornea and improves focus [*radi-* ray, *-al* relating to, *kera-* horn, *-tom-* cut, *-y* action]

radiation (ray-dee-AY-shun) electromagnetic energy, including light, x-rays, heat; in physiology, often refers to flow of excess heat energy away from the body via the blood [*radia-* send out rays, *-tion* process]

radiation sickness (ray-dee-AY-shun) a condition caused by ionizing radiation that can be mild to severe, or even fatal, depending on the level of radiation exposure and the length of time exposed; exposure at lower doses of radiation can result in headache, nausea and vomiting, appetite loss, and diarrhea; exposure to low doses for a longer period of time or a single high-level exposure may cause sterility, damage to fetal development, cancer (including leukemia), cataracts, hair loss (alopecia), and skin damage (radiation dermatitis); *see* ionizing radiation

radiation therapy (ray-dee-AY-shun) treatment often used to combat cancer; high-intensity (x-ray or gamma) radiation is used to destroy cancer cells; also called *radiotherapy* [*radia-* send out rays, *-tion* process, *therapy* treatment]

radical mastectomy (RAD-i-kal mas-TEK-toh-mee) procedure that removes the entire breast, nearby muscles and lymph nodes [*radic-* root, -al relating to, *mast-* breast, *-ec-* out, *-tom-* cut, *-y* action]

radioactive isotope (ray-dee-oh-AK-tiv EYE-so-tope) unstable isotope that spontaneously emits subatomic particles and electromagnetic radiation [*radio* send out rays, *iso-* equal, *-tope* place]

radioactivity (ray-dee-o-ak-TIV-it-ee) the ongoing process of emitting subatomic particles and electromagnetic radiation [*radio* send out rays]

radiocarpal joint (RAY-dee-oh-KAR-pal) the point of articulation where the radius distally articulates directly with the carpal bones [*radio-* ray, *-carp-* wrist, *-al* relating to]

radiofrequency ablation (RAY-dee-oh-FREE-kwen-see ab-LAY-shun) procedure that uses a gold-plated mesh fabric to fill the uterine cavity, which is then charged with radiofrequency energy to destroy bleeding endometrial cells [*radio-* ray, frequency, *ab-*away from, *-lat-* carry, *-tion* process]

radiography (ray-dee-OG-rah-fee) imaging technique using x-rays that pass through certain tissues more easily than others, allowing an image of tissues to form on a photographic plate [*radio-* ray, frequency, *-graphy* drawing]

radioisotope (ray-dee-oh-EYE-so-tope) an isotope that is unstable and undergoes nuclear breakdown [*radio-* send out rays, *-iso-* equal, *-tope* place]

radiotherapy (ray-dee-oh-THER-ah-pee) radiation therapy [*radio-* send out rays, *-therapy* treatment]

radioulnar joint (RAY-dee-oh-UL-nur) articulation of the head of the radius and the radial notch of the ulna [*radio-* ray, *-ulna-* elbow or arm, *-ar* relating to]

radius (RAY-dee-us) forearm bone; located on thumb side [*radius* ray] *pl.*, radii (RAY-dee-eye)

raft a structure made up of groupings of molecules (cholesterol, certain phospholipids, proteins) within a cell membrane that travel together on the surface of the cell, something like a log raft on a lake; also called *lipid raft* [*raft-* floating platform]

ramus (RAY-mus) large branch of a spinal nerve as it emerges from the spinal cavity [*ramus* branch] *pl.*, rami

range of motion (ROM) extent of movement of a joint [*range-* to place in a row, *motus-* to move, *-ion* process]

rapid eye movement (REM) sleep stage of sleep characterized by rapid movements of the eye; associated with vivid dreaming [*rapid-* hasty, *move-* set in motion]

rate law law of mass action [*ratus-* reckoned]

ratio (RAY-shee-oh) the relationship of one quantity to one or more other quantities expressed as a proportion of one to the others [*ratio* a reckoning]

rational drugs chemotherapy drugs that target only those specific molecules, enzymes, or receptors unique to cancer cells or tumor growth, thereby affecting only the cancer and sparing normal cells, increasing efficiency and reducing side effects [*ratio-* reason, *-al* relating to]

reabsorption (ree-ab-SORP-shun) movement of substances back into the bloodstream, as when bone calcium is dissolved by osteoclasts and diffuses into the bloodstream, or when solutes in renal filtrate (in the nephron) move back into the bloodstream [*re-* back again, *-absorp-* swallow, *-tion* process]

reactant (ree-AK-tant) participant in a chemical reaction that is changed by the reaction [*re-* again, *-actant* to act]

receptor portion of a sensory neuron that responds to an external stimulus; also, any molecule on the surface of a cell that binds specifically to other molecules (such as cell markers, hormones, neurotransmitters) [*recept-* receive, *-or* agent]

receptor potential potential that develops in the receptor's membrane when an adequate stimulus has been received [*recept-* receive, *-or* agent, *potent-* power, *-ial* relating to]

recessive (ree-SES-iv) in genetics, refers to genes that have effects that do not appear in the offspring when they are masked by a dominant gene (recessive forms of a gene are represented by lowercase letters); *see* dominant [*recess-* retreat, *-ive* relating to]

recombinant DNA (ree-KOM-bih-nant D N A) joining together of hereditary material into new, biologically functional combinations [*re-* again, *-comb* together, *-bini* two by two]

recessive gene (ree-SES-iv j) gene that has effects that do not appear in the offspring when they are masked by the dominant gene [*recess-* retreat, *-ive* relating to, *gene* produce]

recruit (ree-KROOT) to supply with new members, as in stimulating additional muscle fibers to contract simultaneously in a muscle in order to strengthen the contraction force [*re-* again, *-cruit* grow]

rectouterine pouch (rek-toh-YOO-ter-in) *see* posterior cul-de-sac (of Douglas) [*recto-* straight, *-uter-* womb, *-ine* relating to]

rectum (REK-tum) distal region of the intestinal tube [*rect-* straight, *-um* thing]

rectus abdominis muscle (REK-tus ab-DOM-i-nus) muscle that runs down the middle of the abdomen; compresses abdomen [*rectus* straight, *abdominis* abdomen, *mus-* mouse, *-cle* little]

rectus sheath (REK-tus sheeth) layer of aponeuroses that cover the rectus abdominis muscle [*rectus* straight]

red fiber muscle fibers that contain large amounts of myoglobin and have a deep red appearance [*fibra-* fiber]

red marrow (MAIR-oh) bone marrow found in the ends of long bones and in flat bones; so named because of its function in the production of red blood cells [*marrow-* inner most]

reduction division meiosis when the diploid chromosome number (46) is reduced to the haploid number (23) [*re-* back, *-duce* bring, *-tion* process of, *divis-* to divide, *-ion* process of]

reduction proper alignment of a fractured bone; in chemistry, the gain of one or more electrons by a molecule (as in oxidation-reduction reactions) [*re-* back, *-duce* bring, *-tion* process of]

referred pain pain felt on or near the surface of the body that results from stimulation of nociceptors in deep structures; for example, experiencing pain in the left arm when heart muscle receptors signal pain, as during a heart attack [*referre-* to bring back, *poena-* punishment]

reflex automatic involuntary reaction to a stimulus resulting from a nerve impulse passing over a reflex arc [*re-* again, *-flex* bend]

reflex arc impulse conduction route to and from the central nervous system; smallest portion of nervous system that can receive a stimulus and generate a response [*re-* back or again, *-flex* bend, *arc* curve]

refraction (ree-FRAK-shun) bending of a ray of light as it passes from a medium of one density to one of a different density; occurs as light rays pass through the eye [*refract-* break apart, *-tion* process]

regeneration (ree-jen-er-AY-shun) process of replacing missing tissue with new tissue by means of cell division [*re-* again, *generat-* produce, *-tion* process]

regulator T cell (T-reg) *see* **suppressor T cell** [*regula-* rule, *T* thymus gland, *cell* storeroom]

Reissner membrane (RYZ-ner) *see* vestibular membrane [*Ernst Reissner* German anatomist, *membran-* thin skin]

rejection syndrome (reh-JEK-shun SIN-drohm) reaction of immune system against foreign antigens in grafted tissue [*re-* again, *-ject* to throw, *-tion* process of, *syn-* together, *-drome* running or (race) course]

relative refractory period (ree-FRAK-tor-ee) in muscle cell contraction, the few milliseconds after the absolute refractory period; time during which the membrane is repolarizing and restoring the resting membrane potential [*refract-* break apart, *-ory* relating to, *period* circuit]

relaxation state of lessened tension [*relax-* to ease, *-ation* process of]

relaxin (reh-LAK-sin) hormone that inhibits contractions during pregnancy and softens pelvic joints to facilitate childbirth [*relax-* relaxation, *-in* substance]

releasing hormone (HOR-mohn) hormone produced by the hypothalamus that causes the pituitary gland to release its hormones [*hormon-* excite]

remission (ree-MISH-un) stage of a disease during which a temporary recovery from symptoms occurs [*re-* back or again, *-miss-* to send, *-sion* condition of]

renal artery (REE-nal AR-ter-ee) large branch of the abdominal aorta that brings blood into each kidney [*ren-* kidney, *-al* relating to, *arteri-* vessel]

renal calculus (REE-nal KAL-kyoo-lus) crystallized mineral chunks that develop in the renal pelvis or calyces; also called *kidney stones* [*ren-* kidney, *-al* relating to, *calculi* little stone] *pl.*, calculi

renal cell carcinoma (REE-nal cell kar-si-NO-mah) malignant neoplasm of the kidney [*ren-* kidney, *-al* relating to, *cell* storeroom, *carcino-* cancer, *-oma* tumor]

renal clearance (REE-nal) amount of a substance removed from the blood by the kidneys per minute [*ren-* kidney, *-al* relating to]

renal columns (REE-nal) within the kidneys, the cortical tissue in the medulla between the pyramids [*ren-* kidney, *-al* relating to]

renal corpuscle (REE-nal KOR-pus-ul) within the nephron, the glomerulus plus the Bowman capsule surrounding it [*ren-* kidney, *-al* relating to, *corpus-* body, *-cle* little]

renal cortex (REE-nal KOR-teks) outer portion of the kidney [*ren-* kidney, *-al* relating to, *cortex* bark] *pl.*, cortices

renal diabetes (REE-nal dye-ah-BEE-teez) when the maximum cotransport capacity of the kidney is greatly reduced and glucose appears in the urine even though the blood sugar level may be normal; also called *renal glycosuria* [*ren-* kidney, *-al* relating to, *diabetes* siphon]

renal failure (REE-nal) failure of the kidney to properly process blood plasma and form urine [*ren-* kidney, *-al* relating to]

renal medulla (REE-nal meh-DUL-ah) inner portion of the kidney [*ren-* kidney, *-al* relating to, *medulla* middle] *pl.*, medullae or medullas

renal pelvis (REE-nal PEL-vis) basin-like upper end of the ureter that is located inside the kidney into which the calyces drain [*ren-* kidney, *-al* relating to, *pelvis* basin] *pl.*, pelves (PEL-veez) or pelvises (PEL-vis-ez)

renal ptosis (REE-nal TOH-sis) condition in which one or both kidneys drop from their normal position [*ren-* kidney, *-al* relating to, *ptosis* falling]

renal pyramid (REE-nal PIR-ah-mid) any of the distinct triangular wedges that make up most of the medullary tissue in the kidney [*ren-* kidney, *-al* relating to]

renal tubule (REE-nal TOOB-yool) a principal part of the nephron; consists of the proximal convoluted tubule, the Henle loop, and the distal tubule; receives filtrate from Bowman capsule and transports it to collecting ducts while filtrate is reabsorbed and additional substances are secreted into it in the process of urine formation [*ren-* kidney, *-al* relating to, *tube-* pipe, *-ule* small]

renal vein (REE-nal) kidney vein [*ren-* kidney, *-al* relating to]

renature (ree-NAYT-shur) to reverse the alteration (denaturation) of a protein and thus restore its normal shape and chemical properties [*re-* again, *-nature* born]

renin (REE-nin) enzyme produced by the juxtaglomerular apparatus of the kidney nephrons that catalyzes the formation of angiotensin, a substance that increases blood pressure; *see* renin-angiotensin-aldosterone system (RAAS) [*ren-* kidney, *-in* substance]

renin-angiotensin mechanism (REE-nin an-jee-oh-TEN-sin) *see* renin-angiotensin-aldosterone system [*ren-* kidney, *-in* substance, *angio-* vessel, *-tens-* pressure or stretch, *-in* substance, *mechan-* machine, *-ism* state]

renin-angiotensin-aldosterone system (RAAS) (REE-nin–an-jee-oh-TEN-sin–al-DAH-stair-ohn) causes changes in blood plasma volume mainly by controlling aldosterone secretion [*ren-* kidney, *-in* substance, *angio-* vessel, *-tens-* pressure or stretch, *-in* substance, *aldo-* aldehyde, *-stero-* solid or steroid derivative, *-one* chemical]

repolarization (ree-poh-lah-ri-ZAY-shun) phase of the action potential in which the membrane potential changes from its maximum degree of depolarization toward the resting state potential [*re-* back or again, *-pol-* pole, *-ar* relating to, *-zation* process]

reproduction formation of a new individual; formation of new cells in the body to permit growth [*re-* again, *-produce* to bring forth, *-tion* process]

reproductive system system in both sexes that is composed of the gonads, genital ducts, accessory glands, and genitals [*re-* again, *-produce* to bring forth, *-tive* relating to]

residual volume (ree-ZID-yoo-al) amount of air that remains in the lungs after the most forceful expiration [*residu-* remainder, *-al* relating to, [*volume-* paper roll]

resistin (reh-SIS-tin) hormone that reduces sensitivity to insulin and thus raises blood glucose levels [*resist-* resistance, *-in* substance]

respiration (res-pi-RAY-shun) processes that result in the absorption, transport, and utilization or exchange of respiratory gases between an organism and its environment [*re-* again, *-spir-* breathe, *-ation* process of]

respiratory acidosis (RES-pih-rah-tor-ee ass-ih-DOH-sis) retention of carbon dioxide in the blood [*re-* again, *-spir-* breathe, *-tory* relating to, *acid-* sour, *-osis* condition]

respiratory alkalosis (RES-pih-rah-tor-ee alkah-LOH-sis) excessive loss of carbonic acid from the blood [*re-* again, *-spir-* breathe, *-tory* relating to, *alkal-* ashes; *-osis* condition]

respiratory arrest (RES-pih-rah-tor-ee ah-REST) cessation of breathing without resumption [*re-* again, *-spir-* breathe, *-tory* relating to]

respiratory center (RES-pih-rah-tor-ee) control center located in the medulla and pons that stimulates muscles of respiration [*re-* again, *-spir-* breathe, *-tory* relating to]

respiratory cycle (RES-pih-rah-tor-ee) the alternating pattern of inspiration and expiration (inhalation/exhalation) of breathing [*re-* again, *-spir-* breathe, *-tory* relating to, *cycle-* circle]

respiratory distress syndrome (RDS) (RES-pih-rah- tor-ee di-STRESS SIN-drohm) difficulty in breathing caused by absence or failure of the surfactant in fluid lining the alveoli of the lung; IRDS is infant respiratory distress syndrome; ARDS is adult respiratory distress syndrome [*re-* again, *-spir-*breathe, *-tory* relating to, *syn-* together, *-drome* running or (race) course]

respiratory membrane (RES-pih-rah-tor-ee) single layer of cells that makes up the wall of the alveoli [*re-* again, *-spir-* breathe, *-tory* relating to, *membran-* thin skin]

respiratory mucosa (RES-pih-rah-tor-ee myoo-KOH-sah) mucus-covered membrane that lines tubes of the respiratory tree [*re-* again, *-spir-* breathe, *-tory* relating to, *mucus* slime]

respiratory physiology (RES-pih-rah-tor-ee fiz-ee-OL-oh-jee) study of the function of the respiratory system [*re-* again, *-spir-* breathe, *-tory* relating to, *physio-* nature, *-log-* words (study), *-y* process]

respiratory portion (of nasal passage) (RES-pih-rah-tor-ee) area within the nasal passage that extends from the inferior meatus to the small funnel-shaped orifices of the *posterior nares* [*re-* again, *-spir-* breathe, *-tory* relating to]

respiratory system (RES-pih-rah-tor-ee) system composed of the nose, pharynx, larynx, trachea, bronchi, and lungs [*re-* again, *-spir-* breathe, *-tory* relating to]

respiratory tract (RES-pih-rah-tor-ee) organs of the respiratory system, divided into lower and upper respiratory tracts [*re-* again, *-spir-* breathe, *-tory* relating to, *tract-* trail]

responsiveness characteristic of life that permits an organism to sense, monitor, and respond to changes in its external environment [*response-* reply, *-ive* relating to, *-ness* state of]

resting membrane potential (RMP) membrane potential maintained by a nonconducting neuron's plasma membrane; approximately 70 mV [*membran-* thin skin, *potent-* power, *-ial* relating to]

retention (ree-TEN-shun) inability to void urine even though the bladder contains an excessive amount of urine [*retent-* to hold, *-ion* process]

reticular (reh-TIK-yoo-lar) resembling a netlike pattern [*ret-* net, *-icul-* little, *-ar* relating to]

reticular activating system (RAS) (reh-TIK-yoo-lar) complex processing system in the neural network (reticular formation) in the brain responsible for maintaining consciousness [*ret-* net, *-ic-* relating to, *-ul-* little, *-ar* characterized by]

reticular formation (reh-TIK-yoo-lar) neural network located in the brainstem where it is involved in arousal (reticular activating system) [*ret-* net, *-ic-* relating to, *-ul-* little, *-ar* characterized by]

reticular theory (reh-TIK-yoo-lar) concept that the nervous system is best understood as a large integrated network—one endless piece [*ret-* net, *-ic-* relating to, *-ul-* little, *-ar* characterized by, *theor-* look at, *-y* act of]

reticular tissue (reh-TIK-yoo-lar) meshwork of netlike tissue that forms the framework of the spleen, lymph nodes, and bone marrow [*ret-* net, *-ic-* relating to, *-ul-* little, *-ar* characterized by, *tissu-* fabric]

reticulin (reh-TIK-yoo-lin) type of collagen found in reticular fibers [*ret-* net, *-ic-* relating to, *-ul-* little, *-in* substance]

reticulocyte (reh-TIK-yoo-loh-syte) immature red blood cells [*ret-* net, *-ic-* relating to, *-ul-* little, *-cyte* cell]

reticulocyte count (reh-TIK-yoo-loh-syte) medical procedure used to determine the rate of erythropoiesis cells [*ret-* net, *-ic-* relating to, *-ul-* little, *-cyte* cell]

reticulospinal tract (reh-TIK-yoo-loh-SPY-nal) spinal cord motor tract that helps maintain posture during skeletal muscle movement [*ret-* net, *-ic-* relating to, *-ul-* little, *-spin-* backbone, *-al* relating to, *tract-* trail]

reticulum (reh-TIK-yoo-lum) intricate network of fibers [*ret-* net, *-ic-* relating to, *-ul-* little, *-um* thing]

retina (RET-i-nah) innermost layer of the eyeball; contains rods and cones and continues posteriorly with the optic nerve [*ret-*net, *-ina* relating to]

retinal (RET-i-nal) light-absorbing portion of all photopigments [*ret-* net, *-ina-* relating to, *-al* relating to]

retinal detachment (RET-ih-nal) condition that occurs when part of the retina falls away from the tissue supporting it [*ret-* net, *-ina-* relating to, *-al* relating to]

retraction movement that moves a part back [*re-* back, *-tract-* drag, *-tion* process]

retrograde pyelogram (RET-roh-grayd PYE-eh-loh-gram) an x-ray image produced as a result of contrast material injected through a catheter [*retro-* backward, *-grad-* step, *pyelo-* renal pelvis, *-gram* drawing]

retrograde signaling (RET-roh-grayd SIG-nah-ling) type of synaptic transmission in which chemical signals are sent from the postsynaptic neuron back to the presynaptic neuron, usually to facilitate or inhibit further presynaptic signals [*retro-* backward, *-grad-* step, *sign-* mark, *-al* relating to]

retroperitoneal (reh-troh-pair-i-toh-NEE-al) area outside of the peritoneum [*retro-* backward, *peri-* around, *-tone-* stretched, *-al* relating to]

retropulsion (ret-roh-PUL-shen) process of chyme being forced to move backward behind a closed pyloric sphincter [*retro-* backward, *-pul-* drive, *-sion* process]

reversible reaction (ree-VER-si-bl ree-AK-shun) when the products of a chemical reaction change back to the original reactants; generally, an equilibrium of products and reactants exists [*re-* again, *-vers-* turn, *-ible* able to, *re-* again, *-action* action]

Rh factor (R h FAK-tor) antigen present on the red blood cells of Rh^+ individuals; so named because it was first studied in the rhesus monkey [*Rh*: rhesus monkey]

rheumatic fever (roo-MAT-ik) delayed inflammatory response to streptococcal infection that, if not properly treated, may allow the cardiac valves to become inflamed [*rheuma-* flow, *-ic* relating to]

rheumatic heart disease (roo-MAT-ik) cardiac damage (especially to the endocardium, including the valves) resulting from a delayed inflammatory response to streptococcal infection; *see* rheumatic fever [*rheuma-* flow, *-ic* relating to, *dis-* opposite of, *-ease* comfort]

rheumatoid arthritis (RA) (ROO-mah-toyd ar-THRY-tis) form of systemic autoimmune disease that involves chronic inflammation of many different tissues and organs of the body [*rheuma-* flow, *-oid* like, *arthr-* joint, *-itis* inflammation]

rhinitis (rye-NYE-tis) inflammation of the nasal mucosa often caused by nasal infections [*rhin-* nose, *-itis* inflammation]

rhodopsin (roh-DOP-sin) photopigment in rods [*rhodo-* red, *-ops-* vision, *-in* substance]

rhomboid major/minor muscle (ROM-boyd) upper limb muscle that adducts and elevates the scapula [*rhombo-* flatfish or equilateral parallelogram (rhombus), *-oid* like, *major* greater, *minor* lesser, *-oid* like, *mus-* mouse, *-cle* little]

ribonucleic acid (RNA) (rye-boh-noo-KLAY-ik ASS-id) nucleic acid found in both nucleus and cytoplasm of cells; involved in transmission of genetic information from nucleus to cytoplasm and in cytoplasmic assembly of proteins [*ribo-* ribose (sugar), *nucle-* nucleus, *-ic* pertaining to, *acid-* sour]

ribose (RYE-bohse) five-carbon sugar; the sugar in RNA [*ribose-* 5 carbon sugar]

ribosome (RYE-boh-sohm) organelle in the cytoplasm of cells that synthesizes proteins; sometimes called "protein factory" [*ribo-* ribose or RNA, *-som-* body]

ribozyme (RYE-boh-zyme) form of RNA (ribonucleic acid) that acts like an enzyme to promote or regulate chemical reactions in the cell [*ribo-* ribose or RNA, *-zyme* enzyme]

rickets (RIK-ets) condition primarily seen in infants and children caused by vitamin D deficiency; disease results in soft, pliable bones and skeletal deformities caused by abnormal calcium metabolism [unknown origin]

right lobe the right portion of an organ, such as the liver [*lob-* pod or hull, husk, or pod]

right lymphatic duct (lim-FAT-ik) main lymphatic duct [*lymph-* water, *-atic* relating to]

righting reflexes muscular responses that restore the body and its parts to their normal position when they have been displaced [*re-* again, *-flex* to bend]

rigor mortis (RIG-or MOR-tis) literally "stiffness of death"; the permanent contraction of muscle tissue after death caused by the depletion of ATP during the actin-myosin reaction, preventing myosin from releasing actin to allow relaxation of the muscle [*rigor* stiffness, *mortis* of death]

RNA *see* **ribonucleic acid** [*RNA-* ribonucleic acid]

RNA interference (RNAi) (RNA in-ter-FEER-enz) a regulatory process of the cell in which a small molecule of dsRNA (double-stranded RNA) called *siRNA* (small interfering RNA) joins with a RISC (RNA-induced silencing complex) protein structure to break down a specific mRNA (messenger RNA) transcript and thus effectively silence the gene encoded by the mRNA; RNAi is a natural regulatory process thought to be involved with regulating gene expression, as in inhibiting viral infections, but is also used as a research technique to study the human genome [*RNA-* ribonucleic acid]

RNAi therapy any medical procedure in which RNAi techniques are used to silence (disable) the effects of a disease-causing gene; *see also* RNA interference [*RNA* ribonucleic acid, *i* interference, *therapy* treatment]

rod photoreceptor cell responsible for night vision [*rod-* pole]

root blunt tip of the tongue; portion of the tooth that fits into the socket of the alveolar process of either the upper or lower jaw [*root-* underground part of plant]

rotation joint movement around a longitudinal axis; for example, shaking your head "no" [*rot-* turn, *-ation* process]
rotator cuff (ROH-tay-tor) musculotendinous cuff resulting from fusion of the tendons of the supraspinatus, infraspinatus, teres minor, and subscapularis (SITS muscles); adds to the stability of the glenohumeral (shoulder) joint [*rot-* turn, *-ator* agent, *mus-* mouse, *-cle* little]
rotator cuff muscle (roh-TAY-tor) a muscle of the rotator cuff group [*rot-* turn, *-ator* agent, *mus-* mouse, *-cle* little]
round ligament (LIG-ah-ment) fibromuscular cord that extends from the upper, outer angles of the uterus through the inquinal canals and terminating in the labia majora [*liga-* bind, *-ment* condition]
round window opening into inner ear; covered by a membrane [*window-* wind, eye]
rubrospinal tract (roo-broh-SPY-nal) spinal cord nerves that transmit impulses that coordinate body movements and maintain posture [*rubro-* red, - *spin-* backbone, *-al* relating to, *tract-* trail]
Ruffini corpuscle (roo-FEE-nee KOR-pus-ul) *see* bulbous corpuscle [*Angelo Ruffini* Italian anatomist, *corpus-* body, *-cle* little]
rule of nines frequently used method to estimate extent of a burn injury in an adult; the body is divided into areas that are multiples and fractions of 9% [*rule-* guide]

S

S phase step of the cell life cycle in which a growing cell synthesizes a second copy of its nuclear DNA molecules, a process also called *DNA replication*, in anticipation of later reproduction (cell division); S phase follows the G_1 phase (first growth phase) and precedes the G_2 phase (second growth phase); *see* cell life cycle [S- synthesis, *phase* appearance]
saccule (SAK-yool) part of the membranous labyrinth in the inner ear; contains sensory structure called a *macula*, which functions in sensation of static equilibrium [*sac-* bag, *-ule* small]
sacral plexus (SAY-kral PLEK-sus) plexus formed by fibers from the fourth and fifth lumbar nerves and the first four sacral nerves [*sacr-* sacred, *-al* relating to (sacrum), *plexus* network] *pl.*, plexi (PLEK-sye) or plexuses (PLEK-sus-ez)
sacrum (SAY-krum) bone of the lower vertebral column between the last lumbar vertebra and the coccyx, formed by the fusion of five sacral vertebrae [*sacr-* sacred, *-um* thing]
sagittal plane (SAJ-i-tal) longitudinal plane that divides the body or a part into left and right sides [*sagitta* arrow, *-al* relating to]
saliva (sah-LYE-vah) secretion of the salivary glands that is made up of water, mucus, amylase, sodium bicarbonate, and lipase [*saliva-* spittle]
salpingitis (sal-pin-JYE-tis) inflammation of the uterine tubes [*salping-* tube, *-itis* inflammation]
saltatory conduction (SAL-tah-tor-ee) process in which a nerve impulse travels along a myelinated fiber by jumping from one node of Ranvier to the next [*salta-* leap, *-ory* relating to]
sarcolemma (sar-koh-LEM-ah) plasma membrane of a striated muscle fiber [*sarco-* flesh, *-lemma* sheath] *pl.*, sarcolemmae
sarcoma (SAR-koh-mah) tumor of muscle tissue [*sarco-* flesh, *-oma* tumor]
sarcomere (SAR-koh-meer) contractile unit of muscle cells; length of a myofibril between two Z disks [*sarco-* flesh, *-mere* part]
sarcoplasm (SAR-koh-plaz-em) cytoplasm of muscle fibers [*sarco-* flesh, *-plasm* substance]
sarcoplasmic reticulum (SR) (sar-koh-PLAZ-mik reh-TIK-yoo-lum) network of tubules and sacs in muscle cells; similar to endoplasmic reticulum of other cells [*sarco-* flesh, *-plasm-* substance, *-ic* relating to, *ret-* net, *-ic-* relating to, *-ul-* little, *-um* thing] *pl.*, reticula
satellite cell a type of Schwann cell (neuroglial cell) that surrounds the cell bodies of neurons of the peripheral nervous system [*satell-* attendant, *-ite* relating to, *cell* storeroom]
satiety center (sah-TYE-eh-tee) cells in the hypothalamus that send impulses to decrease appetite so that an individual feels satisfied; also see leptin [*sati-* enough, *-ety* state]
saturated condition when all available bonds of a hydrocarbon chain are filled with hydrogen atoms [*saturate-* to fill]
saturated fat fats containing triglycerides in which fatty acid chains contain no double bonds (because they are "saturated" with hydrogen atoms) [*saturate-* to fill]
scala tympani (SKAH-lah TIM-pah-nee) lower portion of the cochlear duct lying below the basilar membrane [*scala-* to climb, *tympani-* drum]
scala vestibuli (SKAH-lah ves-TIB-yoo-lye) upper portion of the cochlear duct scar-thickened mass of tissue, usually fibrous connective tissue, that remains after a damaged tissue has been repaired [*scala-* to climb, *vestibuli-* courtyard]
scanning electron microscopy (SEM) (eh-LEK-tron my-KRAH-skah-pee) procedure that uses a beam of electrons to scan the surface of a specimen; the electrons reflected from, or knocked off of, the surface are detected by a special sensor producing an image of the specimen's surface on a video monitor [*electro-* electric, *-on* subatomic particle, *micro-* small, *-scop-* see, *-y* activity]
scapula (SKAP-yoo-lah) upper extremity bone; shoulder blade [*scapula* shoulder blade] *pl.*, scapulae (SKAP-yoo-lee)
scar dense fibrous mass of tissue that remains after a damaged tissue has been repaired [*scar-* scab]
Scheuermann disease (SHOY-er-man) abnormal skeletal condition developing in puberty that is characterized by increased roundness in the thoracic curvature (kyphosis) [*Holger W. Scheuermann*, Danish surgeon]
Schwann cell (shwon *or* shvon) any of the large nucleated cells that form myelin around the axons of neurons; also called *neurilemmocyte* [*Theodor Schwann* German anatomist]
sciatica (sye-AT-i-kah) neuralgia of the sciatic nerve [*sciatica-* of pain in the hip]
science field of inquiry that uses rational or logical methods to determine the nature of the universe; biology is the branch of science that specifically studies the living organisms of the universe [*scientia-* knowledge]
sclera (SKLEH-rah) white outer coat of the eyeball [*scler-* hard]
scleral venous sinus (SLEH-ral VAY-nus SYE-nus) a ring-shaped venous sinus located deep within the anterior portion of the sclera; also called *canal of Schlemm* [*scler-* hard, *-al* relating to, *ven-* vein, *-ous* of or like, *sinus* hollow]
scleroderma (skleer-oh-DER-mah) rare disorder affecting vessels and connective tissue of skin and other tissues, characterized by tissue hardening [*sclero-* hard, *-derma* skin]
scoliosis (skoh-lee-OH-sis) abnormal lateral (side-to-side) curvature of the vertebral column [*scolio-* twisted or crooked, *-osis* condition]
scotoma (skoh-TOH-mah) form of neuritis (nerve inflammation), often associated with multiple sclerosis; can cause loss of only the center of the visual field [*scoto-* darkness, *-oma* tumor]
scrotum (SKROH-tum) pouchlike sac that contains the testes [*scrotum* bag] *pl.*, scrota or scrotums
seasonal affective disorder (SAD) mental disorder in which a patient suffers severe depression only in winter; linked to the pineal gland [*season-* period of year, *-al* relating to, *affect-* act on, *-ive* relating to, *dis-* without, *-order* arrangement]
sebaceous gland (seh-BAY-shus) any of the oil-producing glands in the skin [*seb-* tallow (hard animal fat), *-ous* relating to, *gland* acorn]
sebum (SEE-bum) secretion of sebaceous glands
second messenger model theory of hormone action in which the hormone binds to receptors of the target cell, which then triggers a second molecule within the cell (such as cyclic AMP) to accomplish its function; also called *fixed-membrane receptor model* [*sebum* tallow (hard animal fat)]
secondary bronchi (BRONG-kye) *see* secondary bronchus [*second-* second, *bronch-* windpipe]
secondary bronchus (BRONG-kus) branch of the pulmonary airway formed when the primary bronchus enters the lung on its respective side and immediately splits into smaller bronchioles [*second-* second, *bronchus* windpipe] *pl.*, bronchi
secondary follicle (FOL-i-kul) *see* graafian follicle [*second-* second, *-ary* relating to, *folli-* bag, *-cle* small]
secondary hypertension (hye-per-TEN-shun) high blood pressure resulting from a specific condition [*second-* second, *-ary* relating to, *hyper-* excessive, *-tens-* stretch or pull tight, *-sion* state]
secondary oocyte (OH-oh-site) oocyte that arises from a primary oocyte after it completes Meiosis I [*second-* second, *-ary* relating to, *oo-* egg, *-cyte* cell]
secondary ossification center (os-i-fih-KAY-shun) growth center located in the epiphyses of long bones; *see* primary ossification center [*secondary* second ,*-ary* relating to, *os-* bone, *-fication* to make]
secondary sexual characteristics external physical characteristics of sexual maturity resulting from action of sex hormones; include male and female patterns of body hair and fat distribution, as well as development of external genitals [*secondary-* second, *-ary* relating to, *sexual-* relating to sex, *charassein* to engrave]
second-degree burn burn involving deep epidermal layers of the skin but not causing irreparable damage [*degree-* rank]
second-messenger model model that explains nonsteroid hormone mechanism of action; nonsteroid hormone is "first messenger" acting on cell membrane; intracellular "second messenger"—often cyclic AMP—triggers specific cellular action; also called *fixed-membrane-receptor model*
secretin (seh-KREE-tin) gastrointestinal hormone; first hormone discovered [*secret-* secretion, *-in* substance]
secretion process by which a substance is released outside the cell [*secret-* separate, *-tion* process]
secretory phase (SEEK-reh-toh-ree) *see* premenstrual phase [*secret-* separate, *-ory* relating to, *phase-* appearance]
secretory vesicle (SEEK-reh-toh-ree VES-i-kil) bubble made of cellular membrane; contains products of cell metabolism that moves from inside the cell to the plasma membrane, where it breaks open and secretes the products outside of the cell [*secret-* separate, *-ory* relating to, *vesi-* bladder or blister, *-cle* small]
segmental reflex (seg-MEN-tal) reflex whose mediating reflexes enter and leave the same segment of the spinal cord [*segment-* cut section, *-al* relating to, *re-* again, *-flex* bend]
segmentation (seg-men-TAY-shun) occurs when digestive reflexes cause a forward-and-backward movement within a single region of the GI tract [*segment-* cut section, *-ation* process]
seizure (SEE-zhur) *see* convulsion [*seize-* sudden attack of illness]
selectively permeable (sel-EK-tiv-lee PERM-ee-ah-bil) adjective used to describe a living membrane that allows only certain substances to move through (permeate) it and only at certain times [*select-* to choose, *-ive* relating to, *perme-* to pass through, *-able* ability]
self concept in immunology that proposes the immune system agents can recognize certain cell surface molecules as belonging to that individual, which thus makes them "safe" from destruction or damage from the immune system [*self* one's own person]
self-antigen (AN-ti-jen) molecule located on the plasma membrane of all body cells that identifies all normal cells of the body for the immune system; also called *self-marker* [*self-* one's own person, *anti-* against, *-gen* produce]
self-examination process of looking at one's own body to screen for health abnormalities, as in breast self-examination or testicular self-examination [*self-* one's own person, *exam-* test or try, *-ation* process]
self-tolerance ability of our immune system to attack abnormal or foreign cells but spare our own normal cells [*self-* one's own person, *tolerare-* to endure]
semen (SEE-men) ejaculate from the penis that contains spermatozoa plus fluids from the testes, seminal vesicles, bulbourethral glands, and prostate [*semen* seed]
semicircular canal (sem-i-SIR-kyoo-lar) three bony, tubelike structures located in the temporal bone, making up part of the inner ear; each structure contains a membranous semicircular duct that functions in the sense of equilibrium [*semi-* half, *-circulare* to go around, *-lar* relating to, *canal* channel]
semilunar (SL) valve (sem-i-LOO-nar) valve located between each ventricle and the large artery that carries blood away from it; valves in the veins are sometimes referred to as *semilunar valves* [*semi-* half, *-luna* moon, *valve-* folding door]
seminal vesicle (SEM-i-nal VES-i-kul) highly convoluted pouch that secretes an alkaline, viscous, creamy-yellow liquid that constitutes about 60% of semen volume [*semen-* seed, *-al* relating to, *vesic-* blister, *-cle* little]
seminiferoustubule(seh-mih-NIF-er-usTOOB-yools) long, coiled structure that forms the bulk of the testicular mass and in which spermatozoa develop [*semin-* seed, *-fer-* bear or carry, *-ous* relating to, *tub-*tube, *-ul-* little]
senescence (seh-NES-enz) older adulthood; aging [*senesc-* grow old, *-ence* state]
sensation interpretation of sensory nerve impulses by the brain as an awareness of an internal or external event; for example, feeling pain [*sens-* feel, *-ation* process]
sensory cranial nerve (KRAY-nee-al) cranial nerve that consists of only sensory axons [*sens-* feel, *-ory* relating to, *crani-* skull, *-al* relating to]
sensory nerve nerve that contains primarily sensory neurons [*sens-* feel, *-ory* relating to]
sensory neurons (NOO-rons) neurons that transmit impulses to the spinal cord and brain from all parts of the body [*sens-* feel, *-ory* relating to, *neuron* string or nerve]
sensory projection brain function that pinpoints the area of the body from which a receptor potential was initiated [*sens-* feel, *-ory* relating to, *project-* thrown forward, *-ion* process]
sensory receptor sense organs in the peripheral nervous system that enable the body to respond to stimuli caused by changes in its

internal or external environment [*sens-* feel, *-ory* relating to, *recept-* receive, *-or* agent]

sentinel lymph node (SLN) (SEN-tin-el limf nohd) lymph node that is the first to receive a metastasized cancer cell from a nearby tumor [*sentinel* lookout, *lymph* water, *nod-* knot]

septic shock (SEP-tik) condition that results from complications of septicemia [*septi-* putrid, *-ic* relating to]

septicemia (sep-ti-SEE-mee-ah) blood poisoning [*septic-* putrid, *-emia* blood condition]

septum (SEP-tum) a wall that divides two areas; for example, nasal septum [*septum* wall] *pl.*, septa

serosa (see-ROH-sah) outermost covering of the digestive tract; composed of the parietal pleura in the abdominal cavity [*ser-* watery fluid, *-osa* relating to] *pl.*, serosae

serotonin (sair-oh-TOH-nin) neurotransmitter that belongs to a group of compounds called *catecholamines* [*sero-* watery body fluid, *-ton-* tension, *-in* substance]

serotonin and norepinephrine reuptake inhibitor (SNRI) (sair-oh-TOH-nin and nor-ep-i-NEF-rin ree-UP-tayk in-HIB-it-or) type of drug that stops the return of serotonin and norepinephrine (neurotransmitters) to the presynaptic neuron, thus increasing the baseline amount of serotonin and/or norepinephrine in the synapse and restoring the baseline to a normal neurotransmitter level [*sero-* serum (watery fluid), *-ton-* tension, *-in* substance, *nor-* chemical prefix (unbranched C chain), *-epi-* upon, *-nephr-* kidney, *-ine* substance, *re-* again, *inhib-* restrain, *-or* agent]

serotonin-specific reuptake inhibitor (SSRI) (sair-oh-TOH-nin speh-SIF-ik ree-UP-tayk in-HIB-it-or) type of drug that stops the return of serotonin (neurotransmitter) to the presynaptic neuron, thus increasing the baseline amount of serotonin in the synapse and restoring the baseline to a normal serotonin level [*sero-* serum (watery fluid), *-ton-* tension, *-in* substance, *specif-* kind, *-ic* relating to, *re-* again, *inhib-* restrain, *-or* agent]

serous membrane (SEE-rus) two-layer epithelial membrane that lines body cavities and covers surfaces of organs) [*sero-* watery body fluid, *-ous* characterized by, *membran-* thin skin]

serous pericardium (SEER-us pair-i-KAR-dee-um) part of pericardial coverings of the heart; made up of a parietal layer and a visceral layer [*sero-* watery fluid, *-ous* relating to, *peri-* around, *-cardi-* heart, *-um* thing] *pl.*, pericardia

serratus anterior muscle (ser-RAY-tus) anterior chest wall muscle [*serra-* saw teeth, *ante-* front, *-er-* more, *-or* quality, *mus-* mouse, *-cle* little]

Sertoli cell (ser-TOH-lee) testis cell found within walls of the seminiferous tubules; provides mechanical support and protection for the developing sperm; also called *sustentacular cell* or *nurse cell* [*Enrico Sertoli* Italian histologist, *cell* storeroom]

sesamoid bone (SES-ah-moyd) small seed-shaped bones imbedded in tendons; the patella is the largest and most consistently found in the human skeleton [*sesam-* sesame seed, *-oid* like]

set point normal reading or range of normal [*point-* distinguishing feature]

severe combined immune deficiency (SCID) (i-MYOON deh-FISH-en-see) condition in which stem cells are missing or are unable to grow properly; humoral immunity and cell-mediated immunity are defective [*immun-* free]

sex chromosome (KROH-moh-sohm) pair of chromosomes in the human genome that determine gender; normal males have one X chromosome and one Y chromosome (XY); normal females have two X chromosomes (XX) [*chrom-* color, *-som-* body]

sex hormone (seks HOR-mohn) hormone that targets reproductive tissue; examples include estrogen, progesterone, and testosterone [*hormon-* excite]

sex-linked trait nonsexual, inherited trait governed by genes located in a sex chromosome (X or Y); most known sex-linked traits are X-linked [*link-* joint, *trait-* feature]

sexually transmitted diseases (STDs) any communicable disease that is commonly transmitted through sexual contact [*sexual-* relating to sex, *transmit-* transfer, dis- opposite of, ease]

shaft *see* **diaphysis** [*shaft-* slender rod]

shingles (SHING-guls) *see* herpes zoster [from *cingulum* girdle (inflammation often extends around the middle of the body, like a girdle]

short bone cube- or box-shaped bone that is about as broad as it is long; for example, carpals and tarsals [*short-* stunted]

shoulder girdle clavicle and scapula, which form the only bony attachment of the upper extremity to the trunk [*girdle-* belt or sash]

shunt tube used to drain the flow of a body fluid from one cavity or vessel to another [*shunt-* to shun]

sickle cell anemia (SIK-ul sell ah-NEE-mee-ah) severe, possibly fatal, hereditary disease in which red blood cells become sickle-shaped because of presence of an abnormal type of hemoglobin [*sickle* crescent, *cell* storeroom, *an-* without, *-emia* blood condition]

sickle cell trait (SIK-ul sell trayt) condition that occurs when only one gene for sickle cell is inherited and only a small amount of abnormal hemoglobin is produced [*sickle* crescent, *cell* storeroom, *trait-* feature]

sigmoid colon (SIG-moyd) portion of the large intestine that courses downward below the iliac crest [*sigm-* sigma (Σ or σ)18th letter of Greek alphabet (Roman S), *-oid* like, *colon* colon]

sign objective deviation from normal that marks the presence of a disease [*sign* mark]

signal transduction (tranz-DUK-shen) process of changing a signal such as a hormone or neurotransmitter into another form such as enzymatic reaction within the cell receiving the signal (thus the extracellular hormone signal is transduced, or changed, to an intracellular enzymatic signal) [*trans-* across, *-duc-* transfer, *-tion* process]

signal transduction inhibitor (tranz- DUK-shen in-HIB-ih-tor) any agent that blocks normal processing (transduction) of physiological signaling at a membrane receptor [*trans-* across, *-duc-* transfer, *-tion* process, *inhibit-* prevent, *-or* agent]

silent gallstone gallstone that does not cause a problem [*gall* bile]

simple diffusion movement of molecules through a membrane by means of the natural tendency of the molecules to spread and the ability of the spreading molecules to move through, or permeate [*simple* not mixed, *diffus-* spread out, *-sion* process]

simple epithelium (ep-i-THEE-lee-um) arrangement of epithelial cells in a single layer [*simple* not mixed, *epi-* on, *-theli-* nipple, *-um* thing] *pl.*, epithelia

simple fracture type of bone fracture in which broken bone does not project through surrounding tissue and skin; also called *nondisplaced* or *closed fracture* [*simple* not mixed, *fracture* a breaking]

simple goiter (GOY-ter) condition in which the thyroid enlarges because iodine is lacking in the diet [*simple* not mixed, from *gutter* throat]

single unit smooth muscle most common type of smooth muscle tissue; smooth muscle tissue in which gap junctions join individual smooth muscle fibers into large, continuous sheets that contract together in an autorhythmic fashion; also called *visceral muscle* [*mus-* mouse, *-cle* little]

single-gene disease disease caused by individual mutant genes in nuclear DNA that pass from one generation to the next [*gen-* produce or generate, *dis-* opposite of, *-ease* comfort]

single-photon emission computed tomography (SPECT) (toh-MOG-rah-fee) method of scanning that is used to visualize blood flow patterns in the brain [*photo-* light, *e-* out, *-mission* send, *tomo-* cut, *-graph-* draw, *-y* activity]

sinoatrial (SA) node (sye-no-AY-tree-al) the heart's pacemaker; where the impulse conduction of the heart normally starts; located in the wall of the right atrium near the opening of the superior vena cava [*sin-* hollow (sinus), *atri-* entrance courtyard, *-al* relating to, *nod-* knot]

sinus (SYE-nus) space or cavity [*sinus* hollow]

sinus dysrhythmia (SYE-nus dis-RITH-mee-ah) variation in rhythm of heart rate during the breathing cycle (inspiration and expiration) [*sinus* hollow, *dys-* disordered, *-rhythm-*rhythm, *-ia* condition]

sinusitis (sye-nyoo-SYE-tis) sinus inflammation [*sinus-* hollow, *-itis* inflammation]

sinusoid (SYE-nah-soyd) capillary that has a much larger lumen and more winding or tortuous course than other capillary vessels [*sinus-* hollow, *-oid* like]

Sjögren syndrome (SHOW-grin SIN-drohm) autoimmune disease in which the body's immune system targets salivary and tear glands for destruction [*Henrik S.C. Sjögren* Swedish ophthalmologist, *syn-* together, *-drome* running or (race) course]

skeletal muscle muscle under willed or voluntary control; *see* skeletal muscle tissue [*skeleto-* dried body, *-al* relating to, *mus-* mouse, *-cle* small]

skeletal muscle tissue also known as *voluntary* or *striated voluntary muscle*; includes muscle fibers under willed or voluntary control [*skeleto-* dried body, *-al* relating to, *mus-* mouse, *-cle* small, *tissu-* fabric]

skeletal system bones, cartilage, and ligaments that provide the body with a rigid framework for support and protection [*skeleto-* dried body, *-al* relating to]

skin *see* **cutaneous membrane** [*skin-* animal hide]

sleep apnea (APP-nee-ah) transitional period of sleep characterized by loud snoring to variable periods of complete cessation of breathing [*a-* not, *-pnea* breathe]

sliding filament model theory of muscle contraction in which sliding of thin filaments toward the center of each sarcomere quickly shortens the muscle fiber and thereby the entire muscle

slow (B) pain type of nerve fiber that carries impulses that result in dull, aching pain; originates in deep body structures [*slow-* inactive, sluggish, *poena-* punishment]

slow muscle fiber red muscle fiber; also called *slow-twitch muscle fiber* [*mus-* mouse, *-cle* small, *fiber-* thread]

slow-wave sleep (SWS) stage of sleep that is characterized by slow-frequency, high-voltage delta rays seen in the EEG during deep sleep [*sleep-* repose of death]

small saphenous vein (sah-FEE-nus) superficial vein of the lower extremity [*saphen-* manifest, *-ous* relating to]

smooth muscle muscle fibers that are not under conscious control; also known as *involuntary* or *visceral muscle*; forms the walls of blood vessels and hollow organs [*mus-* mouse, *-cle* small]

smooth muscle tissue *see* **smooth muscle** [*mus-* mouse, *-cle* small, *tissu-* fabric]

sneeze reflex a burst of air directed through the nose and mouth; stimulated by contaminants in the nasal cavity [*re-* back or again, *-flex* bend]

sodium important positive ion surrounding cells [*sod-* soda, *-um* thing or substance]

sodium channel a pore in a cell membrane that allows only sodium ions to permeate, or pass through, the membrane [*sod-* soda, *-um* thing or substance, *channel-* water pipe]

sodium cotransport (koh-TRANS-port) complex transport process in which carriers that bind both sodium ions and glucose molecules passively transport the molecules together out of the GI lumen [*sod-* soda, *-ium* chemical ending, *co-* with, *-trans-* across, *-port* carry]

sodium lactate (LAK-tayt) compound used to treat metabolic and respiratory acidosis [*sod-* soda, -um thing or substance, *lact-* milk, *-ate* chemical]

sodium-potassium pump active transport pump that operates in the plasma membrane of all human cells; transports both sodium ions and potassium ions but in opposite directions and in a 3:2 ratio, thereby maintaining a gradient across the plasma membrane [*sod-* soda, *-um* thing or substance, *potass-* potash, *-um* thing or substance]

soft palate (PAL-et) partition between the mouth and nasopharynx [*palate-* roof of mouth]

soleus muscle (SOH-lee-us) leg muscle that extends the foot [*soleus* sole of foot, *mus-* mouse, *-cle* little]

solubility (sol-yoo-BIL-i-tee) relative ability to dissolve [*solubili-* able to dissolve, *-ity* state]

solute (SOL-yoot) dissolved particles in solution [*solutus-* dissolved]

solution liquid made up of a mixture of molecule types, usually made of solutes (solids) scattered in a solvent (liquid), such as salt in water [*solutus-* dissolved, *-ion* process]

solvent (SOL-vent) liquid portion of a solution in which a solute is dissolved [*solvere-*to dissolve]

soma (SO-mah) body; for example, the body of a neuron; also called *perikaryon* [*soma* body]

somatic (so-MAH-tik) referring to the body [*soma-* body, *-ic* relating to]

somatic motor neuron (so-MAH-tik MOH-tor NOO-ron) motor neuron that stimulates a muscle fiber [*soma-* body, *-ic* relating to, *mot-* movement, *-or* agent, *neuron-* nerve]

somatic nervous system (SNS) (so-MAH-tik) motor neurons that control voluntary actions of skeletal muscles [*soma-* body, *-ic* relating to, *nerv-* nerves, *-ous* relating to]

somatic pain (so-MAH-tik) sharp "take your breath away" type of pain associated with superficial injury or trauma; also called *fast pain* [*soma-* body, *-ic* relating to]

somatic reflex (so-MAH-tik) reflexive contraction of skeletal muscles [*soma-* body, *-ic* relating to, *re-* again, *-flex* bend]

somatic sense (so-MAH-tik) sense that enables an individual to detect sensations such as pain, temperature, and proprioception [*soma-* body, *-ic* relating to, *sens-* feel]

somatic sensory division (so-MAH-tik) division of the nervous system made up of afferent (incoming) pathways from somatic sensory receptors (receptors involved in conscious perception) [*soma-* body, *-ic* relating to, *sens-* feel, *-ory* relating to]

somatopsychic (so-mah-toh-SYE-kik) refers to the body affecting the mind; physical disorder that produces mental symptoms; *see* psychosomatic [*soma-* body, *-psychic* relation between mind and body]

somatostatin (soh-mah-toh-STAT-in) hormone produced by delta cells of the pancreas that inhibits secretion of glucagon, insulin, and pancreatic polypeptide [*soma-* body, *-stat-* stand, *-in* substance]

somatotroph (soh-mah-toh-TROHF) cell type of the adenohypophysis (anterior pituitary) that secretes growth hormone (somatotropin) [*soma-* body, *-troph* nourish]

somatotropin (STH) (soh-mah-toh-TROH-pin) growth hormone [*soma-* body, *-trop-* nourish, *-in* substance]

somatotype (so-MAT-o-type) classification of body type determined on the basis of certain physical characteristics; *see* ectomorph, endomorph, mesomorph [*soma-* body, *-type* kind]

snRNP (snurp) small nuclear ribonucleotide; along with polypeptides, forms subunits of the spliceosome in a cell's nucleus

spastic paralysis (SPAS-tik pah-RAL-i-sis) type of paralysis characterized by involuntary contractions of affected muscles [*spast-* pull, *-ic* relating to, *para-* beyond, *-lysis* loosening]

spatial summation (SPAY-shal sum-MAY-shun) ability of the postsynaptic neuron to add together the inhibitory and stimulatory input received from numerous different presynaptic neurons and produce an action potential based on that collation of information [*spati-* space, -al relating to, *summa-* total, *-tion* process]

special movement unique or unusual movement that occurs only in a very limited number of joints [*species* form or kind, *-al* relating to]

special sense characterized by receptors grouped closely together or grouped in a complex sensory organ; for example, sense of smell, taste, hearing, equilibrium, or vision [*species* form or kind, *-al* relating to]

species resistance (SPEE-sheez ree-SIS-tens) genetic characteristics common to all organisms of a particular species that provide natural inborn immunity to a certain disease [*species* form or kind]

specific heat the amount of heat required to raise 1 gram of substance 1 degree centigrade [*specif-* form or kind, *-ic* relating to]

specific immunity (i-MYOO-ni-tee) protective mechanisms by which the immune system is able to recognize, remember, and destroy specific types of bacteria or toxins; *see* adaptive immunity [*specif-* form or kind, *-ic* relating to, *immun-* free, *-ity* state]

spermatic cord (sper-MAT-ik) cylindrical casings of white fibrous tissue formed by the ductus deferens and located in the inguinal canal between the scrotum and the abdominal cavity [*sperma-* seed, *-ic* relating to]

spectrin (SPEK-trin) unique protein on red blood cells that makes it possible for them to be flexible enough to pass through small blood capillaries [*spect-* look , *-in* substance]

spermatogenesis (sper-mah-toh-JEN-eh-sis) production of sperm cells [*sperm-* seed, *-gen-* produce, *-esis* process]

spermatogonium (sper-mah-toh-GO-nee-um) stem cell of a population that gives rise to sperm cells [*sperm-* seed, *-gonia* offspring] *pl.*, spermatogonia

spermatozoon (sper-mah-tah-ZOH-on) mature male gamete; sperm cell [*sperma-* seed, *-zoon* animal] *pl.*, spermatozoa

sphenoid bone (SFEE-noyd) keystone bone of the cranium; resembles a bat [*spheno-* wedge, *-oid* like]

sphincter urethrae muscle (SFINGK-ter yoo-REE-three) *see* urethral sphincter [*sphinc-* bind tight, *-er* agent, *ure-* urine, *-thr-* agent or channel (urethra), *mus-* mouse, *-cle* little]

sphygmomanometer (sfig-moh-mah-NOM-eh-ter) device for measuring blood pressure in the arteries of a limb [*sphygmo-* pulse, *-mano-* thin, *-meter* measure]

spinal cord portion of central nervous system that provides two-way conduction from the brain; major reflex center [*spin-* backbone, *-al* relating to]

spinal ganglion (GANG-glee-on) enlarged portion of the dorsal root of the spinal cord, where afferent nerve fibers from sensory receptors synapse with associated sensory neurons on their way to the brain or lower reflex centers [*spin-* backbone, *-al* relating to, *ganglion-* knot]

spinal meningitis (men-in-JYE-tis) inflammation of the spinal meninges [*spin-* backbone, *-al* relating to, *meninx-* membrane, *-itis* inflammation]

spinal nerve nerve that connects the spinal cord to peripheral structures such as the skin and skeletal muscles [*spin-* backbone, *-al* relating to]

spinal reflex reflex arc whose center is located in the spinal cord [*spine-* backbone, *-al* relating to, *re-* again, *-flex* bend]

spinal tract white columns of the spinal cord that provide conduction paths to and from the brain; ascending tracts carry information to the brain, whereas descending tracts conduct impulses from the brain [*spin-* backbone, *-al* relating to, *tract-* trail]

spindle fiber (SPIN-dul) network of tubules formed in the cytoplasm between the centrioles as they are moving away from each other during mitosis [*spinel-* to spin, *fiber-* thread]

spinocerebellar tract (SPY-no-sair-eh-BELL-ar) sensory tract that conveys information about subconscious kinesthesia [*spino-* backbone, *-cerebell-* cerebellum (small brain), *-ar* relating to, *tract-* trail]

spinotectal tract (SPY-no-TEK-tal) sensory tract that conveys information about touch that triggers visual reflexes [*spino-* backbone, *-tect-* roof, *-al* relating to, *tract-* trail]

spinothalamic pathway (spy-no-thah-LAM-ik) pathway that conducts impulses that produce sensations of crude touch and pressure [*spino-* backbone, *-thalam-* inner chamber, *-ic* relating to]

spinothalamic tract (spy-no-thah-LAM-ik) ascending tracts of the spinal cord that convey information about pain, temperature, deep pressure, and coarse touch; these tracts cross over in the spinal cord [*spino-* backbone, *-thalam-* inner chamber, *-ic* relating to, *tract-* trail]

spinous process (SPY-nus PRAH-ses) sharp projection from the laminae of vertebral bones, pointing posteriorly and inferiorly [*spino-* backbone, *-ous* relating to, *process* project (from)] *pl.*, processes (PRAH-ses-eez)

spiral fracture type of bone fracture in which fracture line spirals around the long axis [*spir-* coiled, *-al* relating to, *fracture* a breaking]

spiral membrane floor of the cochlear duct, this structure's vibrating response to sound frequencies leads to the transduction of sound waves into nerve impulses; also called *basilar membrane* [*spir-* coiled, *-al* relating, *membran-* thin skin]

spiral muscle muscle that has fibers twisted between their points of attachment; for example, latissimus dorsi [*spir-* coiled, *-al* relating to, *mus-* mouse, *-cle* little]

spiral organ organ of hearing located in the cochlea; consists of membranes and embedded hair cells capable of converting mechanical motion of sound waves into neural impulses; also called *organ of Corti* [*spir-* coiled, *-al* relating to, *organ* tool or instrument]

spirogram (SPY-roh-gram) graphic recording of the changing pulmonary volumes observed during breathing [*spir-* breathe, *-gram* drawing]

spirometer (spih-ROM-eh-ter) instrument used to measure the amount of air exchanged in breathing [*spir-* breathe, *-meter* measurement]

splanchnic nerve (SPLANK-nik) nerve that innervates the viscera [*splanchn-* internal organ, *-ic* relating to]

spleen largest lymphoid organ; filters blood, destroys worn out red blood cells, salvages iron from hemoglobin, and serves as a blood reservoir [*splen-* spleen]

splenectomy (spleh-NEK-toh-mee) surgical removal of the spleen [*splen-* spleen, *-ec-* out, *-tom-* cut, *-y* action]

splenius capitis (SPLEH-nee-us KAP-i-tis) deep muscle of the neck; extends the head [*splen-* patch, *capitis* head]

splenomegaly (spleh-no-MEG-ah-lee) condition of enlargement of the spleen [*splen-* spleen, *-mega* large, *-ly* relating to]

spliceosome (SPLISE-oh-sohm) small structure within the nucleus, about the size of a ribosome and made up of snRNPs (small nuclear ribonucleotides) along with polypeptides; removes introns from mRNA transcript and splices remaining exons into final version of mRNA [*splice-* cut rope and join remaining ends, *-som-* body]

spongy bone net-like arrangement of bone tissue found inside bones and which is often filled with red marrow; also called *cancellous bone* or *trabecular bone* [*spongia-* sponge]

spontaneous abortion (spon-TAY-nee-us ah-BOR-shun) *see* miscarriage [*ab-* away from, *-or-* be born, *-tion* process]

spontaneous fracture (spon-TAY-nee-us) *see* pathological fracture [*fracture-* a breaking]

spore form assumed by a bacterium that is resistant to heat, drying, and chemicals but can later become active to cause infection [*spore-* seed]

sprain injury to ligamentous joint structures often caused by twisting or wrenching movements [unknown origin]

squamous (SKWAY-muss) scalelike [*squam-* scale, *-ous* characterized by]

squamous cell carcinoma (SKWAY-muss sell kar-si-NO-mah) slow-growing skin cancer that arises in the epidermis [*squam-* scale, *-ous* characterized by, *cell* storeroom, *carcin-* cancer, *-oma* tumor]

stage of exhaustion third stage of the general adaptation syndrome; when the body can no longer cope or adapt to stressors [*exhaust-* to drain away, *-ion* process]

stage of resistance second stage of the general adaptation syndrome [*resist-* to withstand, *-ance* state]

staircase phenomenon (feh-NOM-eh-non) *see* treppe [*stair-* single step, *-case* box, *phenomenon-* that which appears or is seen]

standard lead one of three electrodes (lead *I*, lead *II*, or lead *III*) used in electrocardiography [*standard-* stand fast or firm]

Starling's law of the capillaries (STAR-lingz KAP-i-lair-eez) principle that states that a balance between inwardly directed forces and outwardly directed forces will determine whether fluids will move into or out of the plasma in the capillaries at any particular point [*Ernest H. Starling* English physiologist, *capill-* hair, *-ary* relating to]

Starling's law of the heart (STAR-lings) principle stating that as myocardial fibers are stretched, the force of contraction is increased [*Ernest H. Starling* English physiologist]

static equilibrium (ee-kwi-LIB-ree-um) sensing the position of the head relative to gravity; compare with dynamic equilibrium [*stat-* stand, *-ic* relating to, *equi-* equal, *-libr-* balance]

static tension another name for isometric (muscle) contraction [*stat-* stand, *-ic* relating to, *tendere-* to stretch]

steatorrhea (stee-eh-tah-REE-ah) foul-smelling stool as a result of impaired fat absorption [*steat-* fat, *-o-* combining form, *-rrhea* flow]

stem cell cells that have the ability to maintain a constant population of newly differentiating cells [*stem-* tree, trunk, *cell-* storeroom]

stenosed valve (steh-NOSD) valve that is narrower than normal, slowing blood flow from a heart chamber [*stenos-* narrow, *-osis* condition]

stent metal spring or mesh tube inserted into an affected artery to keep it open [*stent-* tube implanted temporarily]

stereognosis (steh-ree-og-NO-sis) awareness of an object's size, shape, and texture [*steros-* solid, *-gnosis* knowledge]

sterility (steh-RIL-i-tee) loss of reproductive function [*steril-* barren, *-ity* state]

sternocleidomastoid muscle (STERN-oh-KLYE-doh-MAS-toyd) muscle that flexes the head; "prayer" muscle [*sterno-* breastbone (sternum), *-cleid-* key (clavicle), *-masto-* breast (mastoid process), *-oid* like, *mus-* mouse, *-cle* little]

sternum (STER-num) breastbone [*sternum* breastbone] *pl.*, sterna or sternums

steroid (STAYR-oid) any of a class of lipids related to sterols and forming numerous reproductive and adrenal hormones [*ster-* sterol, *-oid* like]

steroid hormone (STAYR-oyd HOR-mohn) lipid-soluble hormone that passes intact through the cell membrane of the target cell and influences cell activity by acting on specific genes [*ster-* sterol, *-oid* like, *hormon-* excite]

stillbirth delivery of a dead fetus after the twentieth week of gestation; before 20 weeks it is termed a *spontaneous abortion* [*still-* motionless, *-birth* to bear]

stimulus excitant or irritating agent that induces a response [*stimulus* incitement]

stimulus-gated channel type of cell-membrane channel for the transport of molecules that is controlled by a gate that responds to a stimulus such as a sensory stimulus or chemical (neurotransmitter) stimulus [*stimulus* incitement, *channel-* groove]

stomach organ of the digestive system; an expansion of the digestive tract between the esophagus and small intestine, where some protein digestion begins and where food is churned and mixed with gastric juices before entering the small intestine [*stomach-* gullet]

stomach cancer gastric carcinoma [*stomach-* gullet, *cancer* crab or malignant tumor]

strabismus (strah-BIS-mus) abnormal condition in which lack of coordination of, or weakness in, the muscles that control the eye causes improper focusing of images on the retina, making depth perception difficult [*strab-* squinting, *-ismus* condition]

strain overexertion or trauma-type injury resulting in tearing of skeletal muscle fibers [*strain-* to stretch]

stratified epithelium (STRAT-i-fyde ep-i-THEE-lee-um) epithelial cells layered one on another [*strati-* layer, *epi-* on, *-theli-* nipple, *-um* thing] *pl.*, epithelia

stratum (STRAH-tum) layer [*stratum* layer] *pl.*, strata

stratum basale (STRAH-tum bay-SAH-lee) "base layer"; deepest layer of the epidermis; cells in this layer are able to reproduce themselves [*stratum* layer, *bas-* base, *-ale* relating to] *pl.*, strata

stratum compactum (STRAH-tum kom-PAKT-um) surface layer of the endometrium in the uterus [*stratum* layer, *compact-* concentrated, *-um* thing]

stratum corneum (STRAH-tum KOR-nee-um) tough outer layer of the epidermis; cells are filled with keratin [*stratum* layer *corneum* horn] *pl.*, strata

stratum germinativum (STRAH-tum jer-min-ah-TIV-um) synonym for stratum basale of the skin epidermis; sometimes used to denote stratum basale and stratum spinosum together [*stratum* layer, *germinativum* something that sprouts] *pl.*, strata

stratum granulosum (STRAH-tum gran-yoo-LOH-sum) "granular layer," layer in which the process of keratinization begins [*stratum* layer, *gran-* grain, *-ul-* little, *-osum* thing]

stratum lucidum (STRAH-tum LOO-see-dum) "clear" layer of the epidermis, in thick

skin between the stratum granulosum and the stratum corneum [*stratum* layer, *lucid-* clear, *-um* thing] *pl.*, strata

stratum spinosum (STRAH-tum spi-NO-sum) "spiny layer"; layer of epidermis that is rich in RNA to aid in protein synthesis required for keratin production [*stratum* layer, *spino-* spine, *-um* thing] *pl.*, strata

stratum spongiosum (STRA-tum spon-gee-OH-sum) middle layer of the endometrium (of uterus), composed of loose fibrous connective tissue [*stratum* layer, *spongia-* sponge, *-um* thing]

strength training contracting muscles against resistance to enhance muscle hypertrophy; *see* aerobic training, endurance training [*strength-* power, *train-* instruct]

stress any stimulus that directly or indirectly stimulates neurons of the hypothalamus to release corticotropin-releasing hormone [*stress-* tighten]

stress fracture bone fracture caused by mechanical stress (pressure) [*stress* tighten, *fracture* a breaking]

stress response *see* **stress syndrome** [*stress* tighten, *response* reply]

stress syndrome (SIN-drohm) signs and symptoms associated with the body's frequently maladaptive response to stressors; diverse changes initiated by [*stress* tighten, *syn-* together, *-drome* running or (race) course]

stress triad (TRYE-ad) three changes (hypertrophied adrenals, atrophied lymphatic organs, and bleeding gastrointestinal ulcers) as described by Selye that occur together characterize not any one particular kind of injury but all kinds of harmful stimuli [*stress* tighten, *triad* group of three]

stress-age syndrome (SIN-drohm) refers to a group of anatomical, neurohormonal, and immune system changes related to aging that influence both physiological and psychological stress responses [*stress-* tighten, *syn-* together, *-drome* running or (race) course]

stressor any agent or stimulus that produces stress [*stress-* tighten, *-or* agent]

stress-relaxation effect effect that occurs when overall blood pressure rises and the elastic nature of blood vessels allow them to expand and adapt to the higher pressure to maintain normal blood flow [*stress-* tighten, *relax-* loosen, *-ation* process]

stretch marks tiny silver-white scars resulting when elastic fibers in the dermis are stretched too much; also called *striae* [*stretch-* pull tight, *mark-* appearance]

stretch reflex automatic response in which the muscle reacts and tries to maintain a constancy of muscle length when a load is applied [*re-* again, *-flex* bend]

Stretta procedure (STRETT-ah) procedure for treating serious cases of GERD; uses radiofrequency energy emitted by a special electrode to produce small burns that tighten the muscular wall of the lower esophageal sphincter and reduce acid reflux from the stomach [*stretta* tight]

striated involuntary muscle (STRYE-ay-ted) cardiac muscle [*striated-* striped, *mus-* mouse, *-cle* little]

striated muscle (STRYE-ay-ted) *see* skeletal muscle [*striated-* striped, *mus-* mouse, *-cle* little]

stricture (STRIK-chur) abnormally narrowed passage [*stric-* tighten, *-ture* condition]

stroke event in which hemorrhage or cessation of blood flow caused by an embolism or ruptured aneurysm in brain blood vessel results in ischemia of brain tissue and destruction of neurons; *see* cerebrovascular accident (CVA) [*stroke-* apoplectic seizure (*Stroke of God's Hand*)]

stroke volume (SV) amount of blood that is ejected from the ventricles of the heart with each beat [*stroke* apoplectic seizure (*Stroke of God's Hand*), *volume* paper roll]

structural protein any of a category of proteins with the primary function of forming structures of the cell or tissue; contrast with *functional protein* [*structura-* arrangement, *-al* relating to, *prote-* primary, *-in* substance]

subarachnoid space (sub-ah-RAK-noyd) within the meninges, space under the arachnoid and outside the pia mater [*sub-* beneath, *-arachn-* spider, *-oid* like]

subareolar plexus (sub-ah-REE-oh-lar PLEKS-us) where the cutaneous plexus and large lymphatics that drain the secretory tissue and ducts of the breast come together [*sub-* beneath, *areola-* little space, *-ar* relating to, *plexus* network]

subatomic particles particles that make up atoms; for example, neutrons, protons, and electrons [*sub-* beneath, *-atom* indivisible, *-ic* relating to, *particula-* little bit]

subclavian artery (sub-KLAY-vee-an) artery of the upper extremity [*sub-* below, *-clavi-* key, *-ula* little, *arteri-* vessel]

subclavian vein (sub-KLAY-vee-an) deep vein of the upper extremity [*sub-* below, *-clavi-* key (clavicle bone), *-an* relating to]

subcutaneous injection (sub-kyoo-TAY-nee-us in-JEK-shun) administration of nutrients, special fluids, and/or electrolytes into the spongy and porous subcutaneous layer beneath the skin [*sub-* under, *cut-* skin, *-aneous* relating to, *in-* in, *-ject-* throw, *-tion* process]

subcutaneous layer (sub-kyoo-TAY-nee-us) *see* hypodermis [*sub-* beneath, *-cut-* skin, *-ous* relating to]

subdural space (sub-DOO-ral) within the meninges; the space between the dura mater and the arachnoid membrane [*sub-* beneath, *-dura-* hard or tough, *-al* relating to]

subendocardial branches (sub-en-doh-KAR-dee-al) conductive cardiac muscle fibers located in the walls of the ventricles; relay impulses from the AV node to the ventricles, causing them to contract [*sub-* under, *-endo-* within, *-cardi-* heart, *-al* relating to]

subfornical organ (SFO) (sub-FOR-nih-kal) highly specialized nerve cells located in the roof of the third ventricle in the brain; critical regulator of fluid homeostasis [*sub-* under, *-fornic-* arch, *-al* relating to]

sublingual gland (sub-LING-gwall) smallest of the three major salivary glands; produces a mucous type of saliva [*sub-* under, *-lingua-* tongue, *-al* relating to, *gland* acorn]

submandibular gland (sub-man-DIB-yoo-lar) salivary gland located just below the mandibular angle; contains enzyme and mucus-producing elements [*sub-* under, *-mandibul-* chew (mandible or jawbone), *-ar* relating to, *gland* acorn]

submandibular group (sub-man-DIB-yoo-lar) group of lymph nodes under the mandible [*sub-* beneath, *-mandibul-* chew (mandible or jawbone), *-ar* relating to]

submaxillary group (sub-MAK-sih-lair-ee) alternate name for *submandibular group* [*sub-* beneath, *-maxilla-* upper jaw, *-ary* relating to]

submental group (sub-MEN-tal) group of lymph nodes located in the floor of the mouth; lymph from the nose, lips, and teeth drains through these nodes [*sub-* beneath, *-ment-* chin, *-al* relating to]

submucosa (sub-myoo-KOH-sah) connective tissue layer containing blood vessels and nerves in the wall of the digestive tract [*sub-* under, *-muc-* slime, *-osa* relating to] *pl.*, submucosae

subscapularis muscle (sub-SKAP-yoo-lar-is) one of a group of muscles (rotator cuff) that serve as both a structural and functional cuff around the shoulder joint [*sub-* beneath, *-scapula-* shoulder blades, *-ar* relating to, *mus-* mouse, *-cle* little]

substantia nigra (sub-STAN-shee-ah NYE-grah) midbrain structure that consists of clusters of cell bodies of neurons involved in muscular control [*substantia-* essence, *nigra-* black]

substrate (SUB-strayt) substance on which an enzyme acts [*sub-* below, *-stratum* layer]

subtalar joint (sub-TAY-ler joynt) diarthrotic synovial joint formed by the talus bone of the ankle overlying the calcaneus bone and permits side-to-side motion of the foot [*sub-* below, *-tal-* ankle (talus), *-ar* relating to]

sucrase (soo-krays) enzyme that catalyzes the hydrolysis of sucrose and maltose [*sucr-* sugar, *-ase* enzyme]

sudoriferous gland (soo-doh-RIF-er-us) epidermal sweat glands [*sudo-* sweat, *-fer-* bear or carry, *-ous* relating to, *gland* acorn]

sulcus (SUL-kus) furrow, or groove, often associated with the cerebral cortex [*sulcus-* furrow]

sulfur (SUL-fur) component of many energy-transferring enzymes [*sulfur* brimstone]

sulfuric acid (sul-FYOOR-ik ASS-id) contributes hydrogen ions to the extracellular fluid; influences acid-base balance [*sulfur-* brimstone (sulfur), *-ic* relating to]

superficial near the body surface; opposite of deep [*super-* over or above, *-fici-* face, *-al* relating to]

superficial cervical lymph node (SER-vi-kal limf) lymph node that drains lymph from the head and neck; located in the neck along the sternocleidomastoid muscle [*super-* over or above, *-fici-* face, *-al* relating to, *cervic-* neck, *-al* relating to, *lymph* water, *nod-* knot]

superficial cubital lymph node (KYOO-bi-tal limf) lymph node located just above the bend of the elbow; lymph from the forearm passes through this node [*super-* over or above, *-fici-* face, *-al* relating to, *cubit-* elbow, *-al* relating to, *lymph* water, *nod-* knot]

superficial fascia (FAH-shah) hypodermis; subcutaneous layer beneath the dermis [*super-* over or above, *-fici-* face, *-al* relating to, *fascia* band]

superficial reflex reflexes elicited by stimulation of receptors located in the skin or mucosa [*super-* over or above, *-fici-* face, *-al* relating to, *re-* again, *-flex* bend]

superficial vein vein that lies near the surface [*super-* over or above, *-fici-* face, *-al* relating to]

superior higher; opposite of inferior [*super-* over or above, *-or* quality]

superior cerebellar peduncle (SAIR-eh-bel-lar peh-DUNG-kuls) internal white matter of the cerebellum composed principally of tracts from dentate nuclei in the cerebellum through the red nucleus of the midbrain to the thalamus [*super-* over or above, *-or* quality, *cerebell-* cerebellum (small brain), *-ar* relating to, *ped-* foot, *-uncl-* little]

superior colliculi (koh-LIK-yoo-lee) superior region of the corpora quadrigemina [*super-* over or above, *-or* quality, *colli-* hill, *-iculus* small] *sing.*, colliculus

superior intercostal vein (inter-KOS-tal) vein of the thorax [*super-* over or above, *-or* quality, *inter-* between, *-costa-* rib, *-al* relating to]

superior vena cava (VEE-nah KAY-vah) large vein of the upper extremity; drains blood into the right atrium of the heart [*super-* over or above, *-or* quality, *vena* vein, *cava* hollow] *pl.*, venae cavae

supination (soo-pi-NAY-shun) movement that turns the hand palm side up [*supin-* lying on the back, *-ation* process]

suppressor T cell T lymphocytes of the immune system that suppress B-cell differentiation into plasma cells, allow fine-tuning antibody-mediated immune responses; often called *regulator T cells (T-regs)* [*suppress-* press down, *-or* agent, *T* thymus gland, *cell* storeroom]

supraovulation (soo-prah-o-vyoo-LAY-shun) simultaneous rupture of multiple mature follicles [*supra-* above or over, *-ov-* egg, *-ation* process]

suprarenal (soo-prah-REE-nal) situated above a kidney [*supra-* above or over, *ren-* kidney, *-al* relating to]

suprarenal vein (soo-prah-REE-nal) abdominal vein; drains blood into the adrenal gland [*supra-* above or over, *-ren-* kidney, *-al* relating to]

supraspinatus muscle (SOO-prah-spy-nah-tus) one of a group of muscles (rotator cuff) that serve as both a structural and functional cuff around the shoulder joint [*supra-* above, *-spina-* spine, *mus-* mouse, *-cle* little]

supratrochlear lymph node (soo-prah-TRO-HK-lee-ar limf) *see* superficial cubital lymph node [*supra-* above, *-trochlea-* pulley, *-ar* relating to, *lymph* water, *nod-* knot]

surface film layer on the outer surface of skin made up of a mixture of secretions from sweat and sebaceous glands along with epithelial cells being shed from the epidermis; works as a protective barrier [*sur-* above, *-face* form]

surface tension the force of attraction between water molecules [*sur-* above, *-face* form, *tendere-* to stretch]

surfactant (sur-FAK-tant) substance covering the surface of the respiratory membrane inside the alveolus; it reduces surface tension and prevents the alveoli from collapsing [combination of *surf(ace) act(ive) a(ge)nt]*

surgical neck (SER-jik-el nek) region of the humerus bone of the arm just below the tubercles, so named because of its liability to fracture (*surg-* handwork, *-ical* relating to)

suspensory ligament (sus-PEN-so-ree LIG-ah-ment) fibers attached to the capsule of the lens that help hold it in place [*suspend-ere-* to hang, *-ory* relating to, *ligare-* to bind]

sustentacular cell (sus-ten-TAK-yoo-lar) *see* Sertoli cell [*sustent-* support, *-acular* relating to]

suture (SOO-chur) immovable joint, such as those between the bones of the skull [*sutur-* seam]

sweat gland gland in the skin that produces a transparent, watery liquid that eliminates ammonia and uric acid and helps maintain body temperature [*gland* acorn]

sympathetic division (sim-pah-THET-ik) part of the autonomic nervous system; ganglia are connected to the thoracic and lumbar regions of the spinal cord; functions in "fight-or-flight" response [*sym-* together, *-pathe-* feel, *-ic* relating to]

sympathetic trunk (sim-pah-THET-ik) arrangement of sympathetic axon collaterals that bridge the gap between adjacent ganglia that lie on the same side of the vertebral column [*sym-* together, *-pathe-* feel, *-ic* relating to]

symphysis (SIM-fi-sis) joint characterized by the presence of a pad or disk of fibrocartilage connecting the two bones [*sym-* together, *-physis* growth] *pl.*, symphyses

symptom subjective deviation from normal that marks the presence of a disease; sometimes used synonymously with *sign* [*sym-*together, *-tom* fall]

symptomatic gallstone (simp-toh-MAT-ik) gallstone that produces painful symptoms or other medical complications [*sym-* together, *-tom* fall, *sym-* together, *-tom* fall, *-ic* relating to, *gall* bile]

synapse (SIN-aps) membrane-to-membrane junction between a neuron and another neuron, effector cell, or sensory cell; functions to propagate nerve impulses (via neurotransmitters); two types: electrical and chemical; compare to immunological synapse [*syn-* together, *-aps-* join]

synaptic cleft (si-NAP-tik kleft) space between a synaptic knob and the plasma membrane of a postsynaptic neuron [*syn-* together, *-apt-*join, *-ic* relating to]

synaptic knob (si-NAP-tik nob) tiny bulge at the end of a terminal branch of a presynaptic neuron's axon that contains vesicles with

neurotransmitters [*syn-* together, *-apt-* join, *-ic* relating to]

synarthrosis (sin-ar-THROH-sis) joint in which fibrous connective tissue joins bones and holds them together tightly; commonly called *sutures* [*syn-* together, *-arthr-* joint, *-osis* condition] *pl.*, synarthroses

synchondrosis (SIN-kon-DROH-sis) joint characterized by the presence of hyaline cartilage between articulating bones [*syn-* together, *-chondr-* cartilage, *-osis* condition] *pl.*, synchondroses

syncytium (sin-SISH-ee-em) continuous, electrically coupled mass of cardiac fibers; allows an efficient, coordinated pumping action [*syn-* together, *-cyt-* cell, *-um* a thing] *pl.*, syncytia

syndesmosis (SIN-dez-MO-sis) fibrous joint [*syn-* together, *-desmo-* bond, *-osis* condition] *pl.*, syndesmoses

syndrome (SIN-drome) collection of signs or symptoms, usually with a common cause that defines or gives a clear picture of a pathological condition [*syn-* together, *-drome* running or (race) course]

synergism (SIN-er-jiz-em) with hormones, a combination of hormones has a greater effect on a target than the sum of effects that each would have if acting alone [*syn-* together, *-erg-* work, *-ism* condition of]

synergist (SIN-er-jist) muscle that assists a prime mover [*syn-* together, *-erg-* to work, *-ist* agent]

synovial fluid (si-NO-vee-all) thick, colorless lubricating fluid secreted by the synovial membrane in synovial joints [*syn-* together, *-ovi-* egg (white), *-al* relating to, *fluid* flow]

synovial membrane (si-NO-vee-all) connective tissue membrane lining spaces between bones and joints that secretes synovial fluid [*syn-* together, *-ovi-* egg (white), *-al* relating to, *membran-* thin skin]

synthesis (SIN-the-sis) combination, as in the combination of molecules to form a larger molecule [*synthes-* put together, *-is* process of]

synthesis reaction (SIN-the-sis reaction that combines two or more reactants to form a more complex structure [*synthes-* put together, *-is* process of, *re-* again, *-action* action]

system a group of organs that functions as a coordinated team; also called a *body system* [*system* organized whole]

systemic anatomy (sis-TEM-ik ah-NAT-oh-mee) study of anatomy that focuses on learning about body systems [*system* organized whole, *-ic* relating to, *ana-* apart, *-tom-* cut, *-y* action]

systemic circulation (sis-TEM-ik ser-kyoo-LAY-shun) blood flow from the left ventricle to all parts of the body and back to the right atrium [*system-* organized whole, *-ic* relating to, *circulat-* go around, *-tion* process]

systemic lupus erythematosus (SLE) (sis-TEM-ik LOO-pus er-i-them-ah-TOH-sus) autoimmune disease that affects many tissues in the body; red rash often develops on the faces of those afflicted with SLE [*lupus* wolf, *erythema-* redness, *-osus* condition]

systole (SIS-toh-lee) contraction of heart muscle [*systole* contraction]

systolic blood pressure (sis-TOL-ik) force with which blood pushes against artery walls when ventricles contract [*systole-* contraction, *-ic* relating to]

systolic discharge (sis-TOL-ik) volume of blood pumped by one contraction [*systole-* contraction, *-ic* relating to]

T

T cell *see* **T lymphocyte** [*T* thymus gland, *cell* storeroom]

T lymphocyte (LIM-foh-syte) cells of the immune system that have undergone maturation in the thymus; produce cell-mediated immunity [*T* thymus gland, *lymph-* water (lymphatic system), *-cyte* cell]

T tubule (TOOB-yool) transverse tubules unique to muscle cells; formed by inward extensions of the sarcolemma that allow electrical impulses to move deeper into the cell [*T* transverse, *tub-* tube, *-ul-* little]

T wave electrocardiogram deflection that reflects the repolarization of the ventricles [named for letter of Roman alphabet]

tachycardia (tak-i-KAR-dee-ah) rapid heart rhythm (above 100 beats/min) [*tachy-* rapid, *-cardi-* heart, *-ia* condition]

tactile corpuscle (TAK-tyle KOR-pus-ul) large, encapsulated sensory neuron of the skin for light or discriminative touch; also known as *Meissner corpuscle* [*tact-* touch, *-ile* relating to, *corpus-* body, *-cle* little]

tactile disk (TAK-tyle) flat-ended, unencapsulated sensory neuron of the skin for light or discriminative touch; also known as *Merkel disk* or *tactile meniscus* [*tact-* touch, *-ile* relating to]

tactile epithelial cell (TAK-tyle ep-i-THEE-lee-al) stiff epithelial cell of the epidermis of the skin that passes compression of the skin on to the sensory tactile disk neuron; also known as *Merkel cell* [*tact-* touch, *-ile* relating to, *cell* storeroom]

talus (TAY-lus) bone overlying the calcaneus bone and articulating with the tibia and fibula of the leg to form the ankle joint [*talus* ankle] *pl.*, tali (TAY-lye)

tamoxifen (teh-MOK-seh-fin) drug used extensively to prevent the recurrence of breast cancers fueled by estrogen. [*t-* trans (across), *-am-* amino (ammonia compound), *-oxi-* oxygen, *-fen* phenol (shining)]

target destination of a physiological agent such as a hormone or neurotransmitter [*target* small shield]

target cell cell that, when acted on by a particular hormone, responds because it has receptors to which the hormone can bind [*targuete-* small shield, *cell* storeroom]

target organ organ that is acted on and responds to a particular hormone [*targuete-* small shield, *organ-* instrument]

tarsal bone (TAR-sal bohn) any of the bones of the posterior region of the foot [*tars-* ankle, *-al* relating to]

tarsal plate (TAR-sal) border of thick connective tissue at the free edge of each eyelid [*tarsos-* flat surface, *plate-* flat, or broad]

taste bud chemical receptors in the tongue that generate nerve impulses, resulting in the sense of taste

Tay-Sachs disease (TSD) (TAY-saks) recessive, inherited condition in which abnormal lipids accumulate in the brain and cause tissue damage that leads to death by age 4 years [*Warren Tay* English ophthalmologist, *Bernard Sachs* American neurologist]

tectorial membrane (tek-TOH-ree-al) gelatinous membrane of inner ear that tops hair cells in the spiral organ (organ of Corti) [*tect-* roof, *-or-* quality, *-al* relating to, *membran-* thin skin]

tectospinal tract (tek-toh-SPY-nal) motor tract that conveys messages for head and neck movement related to visual reflexes [*tecto-* roof, *-spin-* backbone, *-al* relating to, *tract-* trail]

telodendrion (tel-oh-DEN-dree-on or tee-loh-DEN-dree-on) any of the distal tips of axons that form branches; each branch terminates in a synaptic knob [*telo-* end, *-dendr-* part (branch) of] *pl.*, telodendria

telomere (TEL-oh-meer or TEE-loh-meer) a strand of additional noncoding nucleotides that can be lost during normal DNA replication without affecting the coding part of the chromosome [*telo-* end, *-mer-* root]

telophase (TEL-oh-fayz or TEE-loh-fayz) last stage of mitosis [*telo-* end, *-phase* stage]

temporal bone (TEM-poh-ral) cranial bone located on lower side of cranium and part of its floor [*tempora-* temple (of head), *-al* relating to]

temporal summation (TEM-poh-ral sum-MAY-shun) when synaptic knobs stimulate a postsynaptic neuron in rapid succession and the effects add up over time to produce an action potential (also spatial summation) [*tempor-* time, *-al* relating to]

temporalis muscle (tem-poh-RAL-is) muscle of mastication; elevates and retracts the mandible [*tempo-* temple of head, *-al* relating to, *mus-* mouse, *-cle* little]

tendon bands or cords of fibrous connective tissue that attach a muscle to a bone or other structure [*tend-* pulled tight, *-on* unit]

tendon organ *see* **Golgi tendon organ** [*tend-* pulled tight, *-on* unit]

tendon receptor *see* **Golgi tendon receptor** [*tend-* pulled tight, *-on* unit, *recept-* receive, *-or* agent]

tendon reflex reflex stimulated by tapping on a tendon; *see also* Golgi tendon reflex [*tend-* pulled tight, *-on* unit, *re-* again, *-flex* bend]

tendon sheath (sheeth) tube-shaped structure lined with synovial membrane that encloses certain tendons [*tend-* pulled tight, *-on* unit]

tenosynovitis (ten-oh-sin-oh-VYE-tis) inflammation of a tendon sheath [*teno-* pulled tight (tendon), *-syn-* together, *-ovi-* egg white (joint fluid), *-itis* inflammation]

tension pressure or force, as in muscle contraction force or osmotic force [*tendere-* to stretch]

tensor fasciae latae muscle (TEN-sor FASH-ee-LAT-tee) muscle that moves the thigh and leg [*tensor* stretcher, *fascia* band or bundle, *lat-* side, *mus-* mouse, *-cle* little]

tentorium cerebelli (ten-TOR-ee-um sair-eh-BEL-lee) inward extension of the dura mater that separates the cerebellum from the cerebrum [*tentorium* tent, *cerebelli* of the cerebellum (small brain)] *pl.*, tentoria cerebelli

teratogen (TER-ah-toh-jen) physical or chemical agent that disrupts normal embryonic development and thus causes congenital defects [*terato-* monster, *-gen* produce]

teres minor (TER-eez) one of four rotator cuff muscles; forms a structural and functional cuff around the shoulder joint [*teres* rounded, *minor* lesser]

terminal ganglion (GANG-glee-on) ganglia that consists of parasympathetic fibers near or in the effectors in the chest and abdomen [*termin-* boundary, *-al* relating to, *ganglio-* knot, *-on* unit] *pl.*, ganglia

terminal hair coarse pubic and axillary hair that develops at puberty [*termin-* boundary, *-al* relating to]

terminal nerve pair of cranial nerves alongside the olfactory nerves, thought to be involved in sensing pheromones (sex signals); often called *nerve zero*, not usually found in the classic list of 12 cranial nerves [*termin-* boundary, *-al* relating to]

Terminologia anatomica (Ta or TA) (ter-mi-no-LOJ-ee-ah an-ah-TOM-ik-ah) literally "Terminology of Anatomy;" the official list of anatomical terms related to gross anatomy sponsored by the International Federation of Associations of Anatomists; lists all terms by number and name (in both Latin and English) as well as general principles of usage

Terminologia histologica (Th or TH) (ter-mi-no-LOJ-ee-ah his-to-LO-jik-ah) literally "Terminology of Histology;" the official list of anatomical terms related to microscopic anatomy sponsored by the International Federation of Associations of Anatomists; lists all terms by number and name (in both Latin and English) as well as general principles of usage

testicular self-examination (tes-TIK-yoo-lar) recommended procedure that involves palpating each testis, preferably after a warm shower or bath when the scrotum is relaxed and the testes are descended and accessible [*testi-* witness (testis), *-cul-* small, *-ar* relating to]

testis (TES-tis) male gonad [*testis* witness (male gonad)] *pl.*, testes

testosterone (tes-TOS-teh-rohn) male sex hormone produced by interstitial cells in the testes; the "masculinizing hormone" [*testo-* witness (testis), *-stero-* solid or steroid derivative, *-one* chemical]

tetanus (TET-ah-nus) smooth, sustained muscular contraction caused by high-frequency stimulation [*tetanus* tension]

tetraiodothyronine (T_4) (tet-rah-eye-oh-doh-THY-roh-neen) one of two hormones that compose the thyroid hormone; also called *thyroxine* [*tetra-* four, *-iodo-* violet (iodine), *-thyro-* shield (thyroid gland), *-ine* chemical]

thalamus (THAL-ah-muss) mass of gray matter located in diencephalon just above the hypothalamus; helps produce sensations, associates sensations with emotions, and plays a part in the arousal mechanism [*thalamus* inner chamber] *pl.*, thalami

thalassemia (thal-ah-SEE-mee-ah) group of inherited hemoglobin disorders characterized by production of abnormal red blood cells [*thalass-* sea, *-emia* blood condition]

theca cell (THEE-kah) specialized cell formed from the outer layer of granulosa cells; transforms into a fibrous capsule that secretes a hormone that ultimately converts into additional estrogen [*theca* sheath, *cell* storeroom]

theory a scientific idea or explanation that has a reasonably high degree of confidence after rigorous testing or observation; compare to hypothesis and law [*theor-* look at, *-y* act of]

thermal ablation (THUR-mal ab-LAY-shun) procedure that is used to treat women who suffer from dysfunctional uterine bleeding (DUB) [*therm-* heat, *-al* relating to, *ab-* away from, *-lat-* carry, *-tion* process]

thermoreceptor (ther-moh-ree-SEP-tor) sensory receptor activated by heat or cold [*thermo-* heat, *-cept-* receive, *-or* agent]

thermotaxis (ther-moh-TAK-sis) process in which a cell, such as a sperm cell, is attracted to heat and moves toward the source of heat [*therm-* heat, *-taxis* movement or reaction]

thick ascending limb (TAL) (thik ah-SEND-ing lim) thick-walled region of the limbs of the hairpin nephron loop (Henle loop) that conducts filtrate toward the distal tubule

thin ascending limb of Henle (tALH) (thin ah-SEND-ing lim ov HEN-lee) thin-walled region of the limbs of the hairpin nephron loop (Henle loop) that conducts filtrate toward the distal tubule

third-degree burn full-thickness burn; most serious of the three degrees of burns [*degree* step or rank]

thirst center region of the hypothalamus containing osmoreceptors that can detect an increase in solute concentration in extracellular fluid caused by water loss [*thurs-* dry]

thoracic aorta (thoh-RASS-ik ay-OR-tah) downward arch of the aorta through the thorax and ending at the diaphragm [*thorac-* chest, *-ic* relating to, *aort-* lifted, *-a* thing] *pl.*, aortae or aortas

thoracic cavity (thoh-RASS-ik KAV-i-tee) hollow space within the larger ventral body cavity that contains the lungs (in pleural cavities) and heart (in the mediastinum) [*thorac-* chest (thorax), *-ic* relating to, *cav-* hollow, *-ity* state]

thoracic duct (thoh-RASS-ik) largest lymphatic vessel in the body [*thorac-* chest (thorax), *-ic* relating to]

thoracic vertebra (thoh-RASS-ik VER-the-bra) vertebral bone located in the posterior part of the chest [*thorac-* chest, *-ic* relating to, *vertebra* that which turns] *pl.*, vertebrae

thoracolumbar division (thoh-rah-koh-LUM-bar) sympathetic division of the

autonomic nervous system [*thoraco-* chest, *lumb-* loin, *-ar* relating to]

thorax (THOH-raks) chest [*thorax* chest] *pl.*, thoraces (THOH-rah-seez)

thoroughfare channel (THUR-oh-fair CHAN-el) the distal end of a metarteriole that is devoid of precapillary sphincters, allowing blood to bypass a capillary bed

threshold potential (THRESH-hold poh-TEN-shal) magnitude of voltage across a membrane at which an action potential, or nerve impulse, is produced [*potent-* power, *-ial* relating to]

threshold stimulus (THRESH-hold STIM-yoo-lus) minimal level of stimulation required to cause a muscle fiber to contract [*stimul-* to excite, *-us* thing] *pl.*, stimuli

thrombocyte (THROM-boh-syte) cell fragments that play a role in blood clotting; also called *platelets* [*thrombo-* clot, *-cyte* cell]

thrombocytopenia (throm-boh-sye-toh-PEE-nee-ah) condition resulting from a decreased platelet count [*thrombo-* clot, *-cyto-*cell, *-penia* lack]

thrombophlebitis (throm-boh-fleh-BYE-tis) vein inflammation (phlebitis) accompanied by clot formation [*thrombo-* clot, *-phleb-*vein, *-itis* inflammation]

thrombopoiesis (throm-boh-poy-EE-sis) formation of platelets [*thromb-* clot, *-poiesis* making]

thrombosis (throm-BOH-sis) condition resulting from a clot (thrombus) that stays in one place [*thrombo-* clot, *-osis* condition]

thromboxane (throm-BOKS-ayne) prostaglandin-like substance in platelets that plays a role in hemostasis and blood clotting [*thrombo-* clot, *-oxa-* oxygen, *-ane* chemical]

thrombus (THROM-bus) a nonmoving or fixed blood clot attached to the lining of a vein or artery [*thrombus* clot] *pl.*, thrombi

thymic corpuscle (THYE-mik KOR-pus-ul) laminated spherical structures found in the thymus; composed of concentric layers of keratinized epithelial cells; also called *Hassall's corpuscles* [*thym-* thyme flower (thymus gland), *-ic* relating to, *corpus-* body, *-cle* little]

thymocyte (THY-moh-syte) cell in the thymus that develops into T lymphocytes [*thymo-* thyme flower (thymus gland), *-cyte* cell]

thymopoietin (thy-moh-POY-eh-tin) peptide that has a critical role in the development of the immune system; thought to stimulate the production of specialized lymphocytes involved in the immune response called *T cells* [*thymo-* thymus gland, *-poiet-* make, *-in* substance]

thymosin (THY-moh-sin) hormone produced by the thymus that is vital to the development and functioning of the body's immune system [*thymos-* thyme flower (thymus gland), *-in* substance]

thymus (THY-muss) endocrine gland located in the mediastinum; vital part of the body's immune system [*thymus* thyme flower] *pl.*, thymuses

thyroglobulin (thy-roh-GLOB-yoo-lin) protein-iodine complex that is a precursor of thyroid hormones [*thyro-* shield (thyroid gland), *-glob-* ball, *-ul-* small, *-in* substance]

thyroid cartilage (THY-royd KAR-ti-lij) largest cartilage of the larynx; Adam's apple [*thyr-* shield, *-oid* like]

thyroid colloid (THY-royd KOL-oyd) thick fluid that fills the interior of thyroid follicles [*thyro-* shield (thyroid gland), *-oid* like, *coll-* glue, *-oid* like]

thyroid gland (THY-royd) endocrine gland located in the neck that stores its hormones until needed; thyroid hormones regulate cellular metabolism [*thyro-* shield, *-oid* like, *gland* acorn]

thyroid hormone (THY-royd HOR-mohn) hormone that accelerates catabolism of glucose [*thyro-* shield, *-oid* like, *hormone-* excite]

thyroid-stimulating hormone (TSH) (THY-royd STIM-yoo-lay-ting HOR-mohn) a tropic hormone secreted by the anterior pituitary gland that stimulates the thyroid gland to increase its secretion of thyroid hormone [*thyro-* shield, *-oid* like, *hormon-* excite]

thyrotroph (thy-roh-TROHF) cell type of the adenohypophysis (anterior pituitary) that secretes thyroid-stimulating hormone (TSH) [*thyro-* shield (thyroid gland), *-troph* nourish]

thyroxine (thy-ROK-sin) thyroid hormone that stimulates cellular metabolism [*thyro-* shield (thyroid gland), *-ox-* oxygen, *-ine* chemical]

tibia (TIB-ee-ah) larger, stronger and more medially and superficially located of the two leg bones [*tibia* shin bone] *pl.*, tibiae (TIB-ee-ee) or tibias (TIB-ee-ahz)

tibialis anterior muscle (tib-ee-AL-is) dorsal flexor muscle of the foot; located on the anterior surface of the leg [*tibia* shinbone, *-al* relating to, *ante-* front, *-er-* more, *-or* quality, *mus-* mouse, *-cle* little]

tic douloureux (tik doo-loo-ROO) *see* trigeminal neuralgia [*tic douloureux-* painful spasm (French)]

tidal volume (TV) (TYE-dal) amount of air breathed in and out with each breath [*tid-* time, *-al* relating to, *volume* paper roll]

tight junction connection between cells in which they are joined by "collars" of tightly fused membrane [*tight-* strong, *junct-* to join, *-ion* process]

tinea (TIN-ee-ah) fungal infection of the skin [*tinea* worm]

tinnitus (tih-NYE-tus or TIN-nit-us) "ringing in the ear"; *see* otosclerosis [*tinnitis* a ringing or tinkling]

tissue group of similar cells that performs a common function [*tissu-* fabric]

tissue plasminogen activator (t-PA) (plaz-MIN-oh-jen) clot dissolving substance [*tissue-* fabric, *plasm-* substance (plasma), *-in-* substance, *-gen* produce]

TMR *see* **transmyocardial laser revascularization** [abbreviation of transmyocardial laser revascularization]

TNF blocker drug used in the treatment of rheumatoid arthritis [*TNF-* tumor necrosis factor]

Toll-like receptor (TLR) family of membrane receptors that act as pattern-recognition receptors in immunity to identify any of a large, nonspecific group of microbial antigen molecules and then trigger an innate immune response [*toll-* weird or amazing, *-like*, *recept-* receive, *-or* agent]

tongue solid mass of skeletal muscle components covered by a mucus membrane; manipulates food in the mouth and contains taste buds [*tunge-* organ of speech]

tonic contraction (TAHN-ik) type of skeletal muscle contraction used to maintain posture [*ton-* to stretch, *-ic* relating to, *con-* together, *-tract-* drag or draw, *-tion* process]

tonicity (toh-NIS-i-tee) potential osmotic pressure [*ton-* stretch or tension, *-ic* relating to, *-ty* state]

tonsillectomy (tahn-sih-LEK-toh-mee) surgical removal of the tonsils [*tonsil-* tonsil, *-ec-* out, *-tom-* cut, *-y* action]

tonsillitis (tahn-sih-LYE-tis) inflammation of the tonsils, usually due to infection [*tonsil-* tonsil, *-itis* inflammation]

tonsil (TAHN-sil) masses of lymphoid tissue; protect against bacteria; three types: palatine tonsils, located on each side of the throat; pharyngeal tonsils (adenoids), near the posterior opening of the nasal cavity; and lingual tonsils, near the base of the tongue [*tonsilla* tonsil]

tophus (TOH-fus) sodium urate crystal deposited within the synovial fluid of joints and in other tissues [*tophus* porous rock] *pl.*, tophi

total lung capacity (TLC) total volume of air a lung can hold [*capax-* able to hold much, *-ity* state]

total metabolic rate (TMR) (met-ah-BOL-ik) total amount of energy used by the body per day [*metabol-* change, *-ic* relating to]

total minute volume rate of pulmonary ventilation per minute [*minute-* sixtieth part of an hour, *volume* paper roll]

total peripheral resistance (TPR) (peh-RIF-er-al) cumulative arterial resistance to blood flow [*peri-* around, *-phera-* boundary, *-al* relating to, *-al* relating to, *resist-* withstand, *-ance* act of]

toxin (TOK-sin) poison; chemical that can cause sickness or damage in the body [*toxin* poison]

toxoid (TOK-soyd) form of bacterial toxin that stimulates production of antibodies [*tox-* poison, *-oid* like]

trabecula (trah-BEK-yoo-la) tiny branch-like threads in a tissue, such as the beams of spongy (cancellous) bone, that surround a network of spaces [*trab-* beam, *-ula* little] *pl.*, trabeculae

trabecula carnea (trah-BEK-yoo-la KAR-nee-ah) any of the branched columns of muscle visible in the lining of the ventricles of the heart [*trab-* beam, *-ula* little, *carne-* flesh (muscle)] *pl.*, trabeculae carneae

trabecular bone (trah-BEK-yoo-lar) *see* spongy bone, cancellous bone [*trab-* beam, *-ula-* little, *-ar* relating to]

trace element elements found in small amounts in the body [*element* first principle]

trachea (TRAY-kee-ah) windpipe; the tube extending from the larynx to the bronchi [*trachea* rough duct] *pl.*, tracheae or tracheas

tracheostomy (tray-kee-OS-toh-mee) surgical procedure in which an opening is cut into the trachea [*trache-* rough duct, *-os-*mouth or opening, *-tom-* cut, *-y* action]

trachoma (trah-KOH-mah) chronic infection of the reproductive tract [*trach-* rough, *-oma* tumor]

tract (trakt) bundle of nerve fibers within the central nervous system; unlike a nerve, a tract does not have connective tissue coverings [*trac-* course]

transabdominal pelvic ultrasound (tranz-ab-DOM-i-nal PEL-vik UL-trah-sound) imaging technique used to look at the uterus and adjacent reproductive structures [*trans-* across, *-abdomin-* belly, *-al* relating to, *pelv-* basin (pelvis), *-ic* relating to, *ultra-* beyond, sound]

transcription (trans-KRIP-shun) process in which DNA molecule is used as template to form mRNA [*trans-* across, *-script-* write, *-tion* process]

transcriptome (tran-SKRIPT-ome) mRNA codes transcribed from the human genome [*trans-* across, *-script-* written document, *-ome* entire collection]

transcriptomics (tran-skript-OHM-iks) analysis of all the mRNA codes actually transcribed from the human genome (transcriptome) [*trans-* across, *-script-* written document, *-om-* entire collection, *-ic* relating to]

transcutaneous electrical nerve stimulation (TENS) unit (trans-kyoo-TAY-nee-us) device used to stimulate skin touch receptors in a painful area; results in closure of the spinal cord pain gate and relief of pain [*trans-* across, *-cutan-* skin, *-ous* relating to]

transduction process of changing one form of energy or other physical event to another form, as when sound energy is changed to electrical energy in a microphone [*trans-* through, *-duct* to lead, *-ion* process]

transfer RNA (tRNA) RNA involved with protein synthesis; tRNA molecules carry amino acids to the ribosome for placement in the sequence prescribed by mRNA [*RNA-* ribonucleic acid]

transfusion reaction fatal event resulting from a mixture of agglutinogens (antigens) and agglutinins (antibodies) resulting in the agglutination of the donor and recipient blood [*trans-* across, *-fus-* pour, *-sion* process]

transitional epithelium (tran-ZISH-en-al epi-THEE-lee-um) stratified tissue typically found in body areas that are subjected to stress and tension changes [*trans-* across, *-tion* process, *epi-* on, *-theli-* nipple, *-um* thing] *pl.*, epithelia

translation process in which mRNA is used by ribosomes in the synthesis of a protein [*translat-* a bringing over, *-tion* process]

transmission electron micrograph (TEM) (MY-kroh-graf) photograph of an image produced by a transmission electron microscope [*trans-* across, *-miss-* send, *-ion* process, *electro-* electric, *-on* subatomic particle, *micro-* small, *-graph* drawing]

transmyocardial laser revascularization (TMR) (tranz-my-oh-KARD-ee-al LAY-zer ree-VAS-kyoo-lar-i-zay-shun) heart surgery used with patients suffering from severe angina (chest/heart pain) in which a laser beam makes toothpick-sized holes in the myocardium, which stimulates the growth of new blood vessels (angiogenesis) that relieves the angina [*trans-* across, *-myo* muscle, *-cardi* heart, *-al* relating to, *laser-* abbreviation for *light amplification by stimulated emission of radiation*, *re-* again, *-vasculum* little vessel, *-ar* relating to, *-ation* process]

transplant medical procedure in which tissue from a donor is surgically grafted into the body of another [*trans-* across, *-plant* plant]

transportation process of carrying essential materials within the body [*trans-* across, *-portare* to carry, *-tion* process]

transpulmonary pressure (trans-PUHL-moh-nair-ee) the pressure difference between the alveolar air pressure in the lungs and the fluid pressure in the intraplural space, that is, the pressure difference across the wall of the lung [*trans-* across, *pulmon-* lung, *-ary* relating to]

transurethral resection (TUR) (tranz-yoor-REE-thral rih-SEK-shun) surgical removal of swollen tissue surrounding the urethra [*trans-* across or through, *-ure-* urine, *-thr-* agent or channel (urethra), *-al* relating to, *re-* again, *-sect-* cut, *-tion* process]

transvenous approach (tranz-VEE-nus) method of inserting a permanent pacemaker [*trans-* across, *-ven-* vein, *-ous* relating to]

transverse canal (tranz-VERS kah-NAL) communicating canal between central (Haversian) canals that contains vessels to carry blood to the osteons; also carries nerves and lymphatic vessels; also called *Volkmann canal* [*trans-* across, *-vers-* turn]

transverse colon (tranz-VERS KOH-len) division of the colon that passes horizontally across the abdomen [*trans-* across, *-vers-* turn, *colon* large intestine]

transverse fracture (tranz-VERS FRAK-sher) type of bone fracture in which fracture line is at a right angle to the long axis of the bone [*trans-* across, *-verse* turn, *fracture* a breaking]

transverse mesocolon (tranz-VERS MEZ-oh-koh-lon) fold of peritoneum that attaches the transverse colon to the posterior abdominal wall [*trans-* across, *-vers-* turn, *meso-* middle, *-colon* large intestine]

transverse plane (tranz-VERS) horizontal plane that divides the body or any of its parts into upper and lower parts [*trans-* across or through, *-vers* turn]

transverse process (tranz-VERS PRAH-ses) any of the lateral projections of a vertebral bone [*trans-* across or through, *-vers* turn, *process* project (from)] *pl.*, processes (PRAH-ses-eez)

transversus abdominis muscle (ab-DAH-min-us) innermost muscle of the

anterolateral wall of the abdomen [*trans-* across, *-vers-* turn, *abdomin-* belly]

trapezius muscle (trah-PEE-zee-us) upper limb muscle that raises or lowers the shoulders and shrugs them [*trapezion* small table, *mus-* mouse, *-cle* little]

treppe (TREP-ee) gradual increase in the extent of muscular contraction following rapidly repeated stimulation; also called *staircase phenomenon* [*treppe* staircase]

triad (TRY-ad) triplet of tubules; allows an electrical impulse traveling along a T tubule to stimulate the membranes of adjacent sacs of the sarcoplasmic reticulum [*triad* group of three]

tricarboxylic acid (TCA) cycle (try-kar-bok-SIL-ik) aerobic metabolic pathway in which acetyl CoA (from other metabolic pathways) is converted into CO_2 and H_2O with the formation of ATP; also known as *citric acid cycle*, or *Krebs cycle* [*tri-* three, *-carbo-* carbon, *-oxy-* sharp(oxygen), *-yl-* chemical, *-ic* relating to, *acid* sour, *cyclo-* circle]

tricuspid valve (try-KUS-pid) heart valve located between right atrium and ventricle [*tri-* three, *-cusp-* point, *-id* characterized by]

trigeminal nerve (try-JEM-i-nal) cranial nerve V; responsible for chewing movements and sensations of the head and face [*tri-* three, *-gemina-* twin or pair, *-al* relating to]

trigeminal neuralgia (try-JEM-i-nal noo-RAL-jee-ah) pain in one or more (of three) branches of the fifth cranial nerve (trigeminal nerve) that runs along the face; also called *tic douloureux* [*tri-* three, *-gemina-* twins or pair, *-al* relating to, *neur-* nerves, *-algia* pain]

triglyceride (try-GLI-ser-ide) lipid that is synthesized from fatty acids and glycerol or from excess glucose or amino acids; stored mainly in adipose tissue cells [*tri-* three, *-glycer-* sweet, *-ide* chemical]

trigone (TRY-gohn) triangular structure, as in the three-cornered floor of the urinary bladder [*tri-* three, *-gon* corner]

triiodothyronine (T_3) (try-eye-oh-doh-THY-roh-neen) thyroid hormone that stimulates cellular metabolism [*tri-* three, *-iodo-* violet (iodine), *-thyro-* shield (thyroid gland), *-nine* chemical]

trimester three-month segments of the gestation period [*trimestris-* three months]

triplegia (try-PLEE-jee-ah) paralysis that affects both legs and one arm [*tri-* three, *-plegia* stroke]

trisomy (TRY-so-mee) abnormal genetic condition in which cells have three chromosomes (a triplet) where there should be a pair; usually caused by nondisjunction (failure of chromosome pairs to separate) during gamete production [*tri-* three, *-som-* body (chromosome), *-y* state]

trochlea (TROK-lee-ah) spool-shaped projection on the distal end of the humerus bone of the arm that articulates with the olecranon of the ulna [*trochlea* pulley] *pl.*, trochleae (TROK-lee-ee)

trochlear nerve (TROK-lee-ar) cranial nerve IV; motor nerve; responsible for eye movements [*trochlea-* pulley, *-al* relating to]

trophoblast (TROH-foh-blast) outer wall of the blastocyst; contributes in formation of the placenta [*tropho-* nourishment, *-blast* sprout]

tropic hormone (TROH-pik HOR-mohn) hormone that stimulates another endocrine gland to secrete its hormones [*trop-* nourish, *-ic* relating to, *hormon-* excite]

tropomyosin (troh-poh-MY-oh-sin) in sliding-filament theory of muscle cell contraction, the long protein molecule that covers the active sites of myosin; myofilament [*tropo-* to turn, *-myo-* muscle, *-in* substance]

troponin (troh-POH-nin) in sliding filament theory of muscle cell contraction, the molecules spaced at intervals along the thin filament that blocks troponin when the myofilament is at rest [*tropo-* turn, *-in* substance]

troponins test (TROH-poh-nins) diagnostic aid used to identify a specific biochemical marker present in cardiac disease [*tropo-* turn, *-in* substance]

true ankle joint (tru ANG-kel joynt) diarthrotic synovial joint formed at the distal ends of the medial malleolus of the tibia and the lateral malleolus of the fibula embracing the underlying talus, allowing up-and-down movement of the foot

true capillary (tru KAP-i-lair-ee) blood vessel that receives blood flowing out of metarterioles or other small arterioles [*capill-* hair, *-ary* relating to]

true pelvis (tru PEL-vis) structure forming a bony ring between the pelvic inlet and the pelvic outlet of the skeleton [pelvis basin] pl., pelves (PEL-veez) or pelvises (PEL-vis-ez)

true vocal cord *see* **vocal fold** [*voca-* voice, *-al* relating to]

trypsin (TRIP-sin) protein-digesting enzyme [*tryps-* pound, *-in* substance]

trypsinogen (trip-SIN-oh-gen) inactive proenzyme that is subsequently converted to active trypsin by enterokinase in the intestinal lumen [*tryps-* pound, *-in* substance, *-o-* combining form, *-gen* produce]

tubal pregnancy (TOO-bal) ectopic pregnancy that occurs in a uterine tube [*tub-* tube, *-al* relating to]

tuberculosis (TB) (too-ber-kyoo-LOH-sis) chronic bacterial (bacillus) infection of the lungs or other tissues caused by *Mycobacterium tuberculosis* organisms [*tuber-* swelling, *-cul-* little, *-osis* condition]

tubular (TOOB-yoo-lar) relating to a tube [*tub-* tube, *-ul-* little, *-ar* relating to]

tubular reabsorption (TOOB-yoo-lar ree-ab-SORP-shun) movement of molecules out of the various segments of the renal tubule and into the peritubular blood [*tub-* tube, *-ul-* little, *-ar* relating to, *re-* back again, *-absorp-* swallow, *-tion* process]

tubular secretion (TOOB-yoo-lar seh-KREE-shun) movement of molecules out of the peritubular blood and into the renal tubule for excretion [*tub-* tube, *-ul-* little, *-ar* relating to, *secret-* separate, *-tion* process]

tubuloglomerular feedback (toob-yoo-loh-glow-MER-yoo-lar) regulatory mechanism that helps protect the kidney from rapid systemic arterial pressure variations [*tub-* tube, *-ul-* little, *-glomer-*ball, *-ul-* little, *-ar* relating to]

tumor growth of tissues in which cell proliferation is uncontrolled and progressive [*tumor* swelling]

tumor marker abnormal antigen on cancer cells; also called *tumor-specific antigen* [*tumor* swelling]

tumor suppressor gene gene that works against the development of cancerous cells [*tumor* swelling, *suppress-* press down, *-or* agent, *gen-* produce or generate]

tumor-specific antigen (AN-ti-jen) *see* tumor marker [*tumor* swelling, *specif-* form, *-ic* relating to, *anti-* against, *-gen* produce]

tunica adventitia (TOO-nih-kah ad-ven-TISH-ah) outermost layer of arteries, veins, lymphatic vessels, and other organs; made of strong, flexible fibrous connective tissue; usually called *tunica externa* or simply *adventitia* [*tunica* tunic or coat, *adventitia* coming from abroad] *pl.*, tunicae adventitia

tunica albuginea (TOO-nih-kah al-byoo-JIN-ee-ah) tough, whitish membrane that surrounds each testis and enters the gland to divide it into lobules [*tunica* tunic or coat, *albuginea* white] *pl.*, tunicae albuginea

tunica externa (TOO-nih-kah ex-TER-nah) outermost layer of arteries, veins, lymphatic vessels, and other organs; made of strong, flexible fibrous connective tissue; sometimes called *tunica adventitia* [*tunica* tunic or coat, *extern-* outside] *pl.*, tunicae externae

tunica interna (TOO-nih-kah ex-TER-nah) *see* tunica intima [*tunica* tunic or coat, *intern-* inside] *pl.*, tunicae internae

tunica intima (TOO-nih-kah IN-tih-mah) layer made up of endothelium that lines blood vessels; also called *tunica interna* [*tunica* tunic or coat, *intima* innermost] *pl.*, tunicae intimae

tunica media (TOO-nih-kah MEE-dee-ah) muscular middle layer in blood vessels; the tunica media of arteries is more muscular than that of veins [*tunica* tunic or coat, *media* middle] *pl.*, tunicae media

turbinate (TUR-bih-nayt) *see* concha [*turbin-* top (spinning toy), *-ate* of or like]

turbulent flow (TER-byoo-lent) flow of blood that occurs normally at heart valves; contributes to the first and second heart sounds [*turbulentus-* full of commotion, restless]

turgor (TUR-ger) resiliency or fluid pressure in the cells of the skin, often lost during dehydration [*turg-* swollen, *-or* condition]

Turner syndrome (TUR-ner SIN-drohm) genetic disorder caused by monosomy of the X chromosome (XO) in females; characterized by immaturity of sex organs (causing sterility), webbed neck, cardiovascular defects, and learning disorders [*Harry H. Turner* American endocrinologist, *syn-* together, *-drome* running or (race) course]

twitch contraction quick jerk of a muscle produced by a single, brief threshold stimulus [*con-* together, *-tract-* drag or draw, *-tion* process]

two-point discrimination test procedure that tests the distribution of touch receptors in the skin [*discriminare-* to divide]

tympanic membrane (tim-PAN-ik) eardrum [*tympan-* drum, *-ic* relating to, *membran-* thin skin]

tympanotomy tube (tim-peh-NOT-eh-mee) surgical tool used to relieve pressure and permit drainage of the ear [*tympan-* drum, *-tom-* cut, *-y* action]

type 1 diabetes mellitus (dye-ah-BEE-teez MELLi-tus) condition resulting when the pancreatic islets secrete too little insulin, resulting in increased blood glucose [*diabetes* siphon, *mellitus* honey sweet]

type 2 diabetes mellitus (dye-ah-BEE-teez MELL-i-tus) condition resulting when cells of the body become less sensitive to the hormone insulin and perhaps the pancreatic islets secrete too little insulin, resulting in increased levels of blood glucose [*diabetes* siphon, *mellitus* honey sweet]

Type A blood type that has antigen A on red blood cells

Type AB blood type that has both antigen A and antigen B on red blood cells

Type B blood type that has antigen B on red blood cells

type II cell produces surfactant in the alveoli [*II* Roman numeral two, *cell-* storeroom]

Type O blood type that has neither antigen A nor antigen B on red blood cells

tyrosine kinase inhibitor (TYE-roh-seen KIN-ayz in-HIB-it-er) class of chemotherapy drugs that inhibit tyrosine-activating enzymes in cancer cells [*tyro-* cheese, *-sine* chemical, *kinesis-* motion, *-ase* enzyme, *inhibit-* restrain, *-or* relating to]

U

U wave electrocardiogram deflection that results from late repolarization of Purkinje fibers in the papillary muscle of the ventricular myocardium, or possibly from different durations of action potential in the ventricular myocardium producing a two-part T wave [named for letter of Roman alphabet]

ubiquitin (yoo-BIK-wit-in) a class of numerous, very small proteins used by the cell to tag proteins for destruction by the proteasome [*ubiqui-* everywhere, *-in* substance]

ulcer (UL-ser) necrotic open sore or lesion [*ulc-* sore]

ulna (UL-nah) forearm bone [*ulna* elbow] *pl.*, ulnae (UL-nee) or ulnas (UL-nahz)

ulnar deviation (UL-nur dee-vee-AY-shun) deformity of the hands as a result of rheumatoid arthritis [*ulna-* elbow, *-ar* relating to, *de-* out of, *-via-* road or path, *-ation* process]

ultrasonography (ul-trah-son-OG-rah-fee) imaging technique in which high-frequency sound waves are reflected off tissue to form an image [*ultra-* beyond, *-sono-* sound, *-graph-* draw, *-y* process]

ultrasound lithotripsy (UL-trah-sound LITH-oh-trip-see) procedure that uses an ultrasound generator to pulverize stones so that they can be flushed out of the urinary tract without surgery [*ultra-* beyond, sound, *litho-*stone, *-trips-* pound, *-y* action]

umbilical artery (um-BIL-i-kul AR-ter-ee) two small arteries that carry oxygen-poor blood from the developing fetus to the placenta [*umbilic-* navel, *-al* relating to, *arteri-* vessel]

umbilical cord (um-BIL-i-kul) flexible structure connecting the fetus with the placenta; contains umbilical arteries and vein [*umbilic-* navel, *-al* relating to]

umbilical hernia (um-BIL-i-kul HER-nee-ah) rupture of the anterior abdominal wall at the navel [*umbilic-* navel, *-al* relating to, *hernia* rupture] *pl.*, herniae or hernias

umbilical vein (um-BIL-i-kul) large vein carrying oxygen-rich blood from the placenta to the developing fetus [*umbilic-* navel, *-al* relating to]

umbilicus (um-BIL-i-kus) navel [*umbilic-*navel, *-us* singular]

uncompensated acidosis (un-KOM-pen-sayted ass-ih-DOH-sis) decrease in the ratio of base to acid; causes a decrease in pH [*acid-* sour, *-osis* condition]

uncompensated alkalosis (un-KOM-pen-sayted al-kah-LOH-sis) increase in the ratio of base to acid; causes an increase in pH [*alkal-* ashes, *-osis* condition]

uniaxial joint (yoo-nee-AK-see-al) synovial joint that permits movement around only one axis and in only one plane [*uni-* one, *-axi-* axle, *-al* relating to]

unicellular gland (yoon-ih-SEL-yoo-lar) single glandular epithelial cell [*uni-* one, *-cell-* storeroom, *-ular* relating to, *gland* acorn]

unipolar (pseudounipolar) neuron (yoo-nee-POH-lar [SOO-doh-yoo-nee-POH-lar] NOO-ron) structural category of neurons made up of cells that appear to have only one extension from the cell body [*uni-* single, *-pol-* pole, *-ar* relating to, *pseudo-* false, *neuron* nerve]

unmyelinated fiber (un-MY-eh-lin-ay-ted) nerve fiber that does not have a myelin sheath; also referred to as *gray fiber* [*un-* not, *-myel-* marrow, *-in-* substance, *-ate* act of, *fiber-* thread]

unsaturated fat (un-SATCH-yoo-ray-ted) fat-containing fatty acid chains in which there are some double bonds, not all sites for hydrogen are filled; usually liquid at room temperature [*un-* not, *-saturate-* to fill, *-ate* act of]

upper esophageal sphincter (UES) (eh-SOF-ah- JEE-ul SFINGK-ter) ring of muscular tissue at proximal end of esophagus; helps prevent air from entering the esophagus during respiration [*es-* will carry, *-phag-* food (eat), *-al* relating to, *sphinc-* bind tight, *-er* agent]

upper respiratory infection (RES-pih-rah-tor-ee) infection localized in the muscosa of the upper respiratory tract [*re-* again, *-spir-* breathe, *-tory* relating to, *infec-* stain, *-tion* process]

upper respiratory tract (RES-pih-rah-tor-ee) respiratory organs that are not contained within the thorax; includes nasal cavity,

pharynx, and associated structures [*re-* again, *-spir-* breathe, *-tory* relating to, *tract-* trail]

up-regulation phenomenon that occurs when a target cell has more receptors and thus can be more sensitive to a hormone [*up-* increase, *regula-* rule, *-tion* process]

urea (yoo-REE-ah) nitrogen-containing waste product [*urea-* urine]

uremia (yoo-REE-mee-ah) condition in which blood urea concentration is abnormally elevated, expressed as a high blood urea nitrogen (BUN) value; uremia is often caused by renal failure; also called *uremic syndrome* [*ur-* urine, *-emia* blood condition]

uremic syndrome (yoo-REE-mik SINdrohm) *see* uremia [*ur-* urine, *-(h)em-* blood, *-ic* relating to, *syn-* together, *-drome* running or (race) course]

ureter (YOOR-eh-ter) long tube that carries urine from kidney to bladder [*ure-* urine, *-ter* agent or channel]

urethra (yoo-REE-thrah) passageway from bladder to exterior; functions in elimination of urine; in males, also acts as a genital duct that carries sperm to the exterior [*ure-* urine, *-thr-* agent or channel]

urethral sphincter (yoo-REE-thral SFINGKter) circular muscle of the pelvic floor that constricts around the urethra, thus regulating urine flow from the bladder and out of the body [*ure-* urine, *-thr-* agent or channel (urethra), *-al* relating to, *sphinc-* bind tight, *-er* agent]

urethral stricture (yoo-REE-thral STRIKchur) narrowing or blockage of the urethra [*ure-* urine, *-thr-* agent or channel (urethra), *-al* relating to, *stric-* tighten, *-ture* condition]

urethritis (yoo-reh-THRY-tis) inflammation or infection of the urethra [*ure-* urine, *-thr-* agent or channel (urethra), *-itis* inflammation]

urinary bladder (YOOR-i-nair-ee) collapsible saclike organ that collects urine from the kidneys and stores it before elimination [*urin-* urine, *-ary* relating to]

urinary meatus (YOOR-i-nair-ee mee-AY-tus) external opening of the urethra [*urin-* urine, *-ary* relating to, *meatus* passage] *pl.*, meatus or meatuses

urinary system (YOOR-i-nair-ee) system responsible for excreting most liquid wastes from the body [*urin-* urine, *-ary* relating to]

urination (yoor-i-NAY-shun) passage of urine from the body; emptying of the bladder; also called *micturition* [*urin-* urine, *-ation* process]

urine (YOOR-in) fluid waste excreted by kidneys [*ur-* urine, *-ine* chemical]

urochrome (YOOR-oh-krohm) pigments from the breakdown of old red blood cells in the liver and elsewhere that are found in the urine [*uro-* urine, *-chroma* color]

urodynamics (yoo-roh-dye-NAM-iks) force of urine flow in the urinary tract [*uro-* urine, *dynam-* force, *-ic* relating to]

urogenital triangle (YOO-roh-JEN-ih-tal) region of the perineum that contains the external genitals (labia, vaginal orifice, clitoris) and urinary opening, and the anal triangle, which surrounds the anus [*uro-* urine, *-genit-* reproduction, *-al* relating to, *tri-*three, *-angle* corner]

urticaria (er-ti-KAIR-ee-ah) hives; allergic or hypersensitive response characterized by raised red lesions [*urtica-* nettle, *-ia* abnormal condition]

uterine artery embolization (YOO-ter-in ARter-ee em-boh-lih-ZAY-shun) technique that involves snaking a small catheter through an artery in the groin into the arterial vessel supplying blood to a fibroid; procedure results in dramatic shrinkage of the treated fibroid and a reduction in symptoms, including hemorrhage [*uter-* womb, *-ine* relating to, *arteri-* vessel, *embol-* plug, *-ation* process]

uterine fibroid (YOO-ter-in FYE-broyd) abnormal muscular growth in the uterus that may result in dysfunctional uterine bleeding [*uter-* womb, *-ine* relating to, *fibr-* fiber, *-oid* of or like]

uterine tube (YOO-ter-in) fallopian tube [*uter-* womb, *-ine* relating to]

uterosacral ligament (yoo-ter-oh-SAK-ral LIG-ah-ment) foldlike extension of the peritoneum from the posterior surface of the uterus to the sacrum [*uter-* womb, *sacr-* sacred (sacrum), *-al* relating to (sacrum), *liga-* bind, *-ment* condition]

uterus (YOO-ter-us) hollow, muscular organ that holds and sustains developing offspring until birth [*uterus* womb]

utricle (YOO-tri-kul) part of membranous labyrinth of inner ear; involved with sensation of static equilibrium [*utricle-* small bag]

uvula (YOO-vyoo-lah) cone-shaped process hanging from the soft palate that helps prevent food and liquid from entering the nasal cavities [*uva-* grape]

V

vaccination (vak-si-NAY-shun) method used to achieve active immunity by triggering the body to form antibodies against specific pathogens [*vaccin-* cow (cowpox), *-ation* process]

vaccine (VAK-seen) application of killed or attenuated (weakened) pathogens (or portions of pathogens) to a patient to stimulate immunity against that pathogen [*vaccin-* cow (cowpox)]

vagina (vah-JYE-nah) internal tube from uterus to vulva [*vagina* sheath]

vaginal orifice (VAH-ji-nal OR-i-fis) opening of the vagina to the outside of the body [*vagina-* sheath, *-al* relating to, *ori-* mouth, *-fice-* something made]

vaginitis (vaj-i-NYE-tis) inflammation of the vagina [*vagin-* sheath (vagina), *-itis* inflammation]

vagus nerve (VAY-gus) cranial nerve X; mixed nerve; sensations and movements of organs [*vagus* wanderer]

valvuloplasty (VAL-vyoo-loh-plas-tee) procedure that replaces damaged or defective cardiac valves [*valv-* folding door (valve), *-plasty* surgical repair]

variant Creutzfeldt-Jakob Disease (vCJD) (VAR-ee-ant KROYTS-felt YAH-kobe) degenerative disease of the central nervous system caused by prions (*pr*oteinaceous *in*fectious particles) that convert normal proteins of the nervous system into abnormal proteins, causing loss of function; *see* prion [*Hans G. Cruetzfeldt* German neurologist, *Alfons M. Jakob* German neurologist]

varicose vein (VAIR-i-kohse) enlarged vein in which blood pools; also called *varix* [*varic-* swollen vein, *-ose* characterized by] *pl.*, varices

varix (VAIR-ix) varicose vein [*varix* swollen vein] *pl.*, varices

vas deferens (vas DEF-er-enz) reproductive duct that extends from the epididymis to the ejaculatory duct; also called *ductus deferens* [*vas* duct or vessel, *deferens* carrying away] *pl.*, vasa deferentia

vasa recta (VAH-sah REK-tah) the long, hairpin-shaped arterioles of the kidney leading from the efferent arteriole and following the nephron loop; also called *straight arterioles (of kidney)* [*vas-* vessel, *rect-* straight] *sing.*, vas rectum

vasa vasorum (VAS-ah vah-SOR-um) tiny blood vessels that supply the smooth muscles that surround the walls of larger blood vessels [*vasa* vessel, *vaso-* vessel or duct, *-um* small one]

vascular anastomosis (VAS-kyoo-lar ah-nastoh-MOH-sis) condition when blood moves from veins to other veins or arteries to other arteries without passing through an intervening capillary network [*vas-* vessel, *-ular* relating to, *ana-* anew, *-stomo-* mouth, *-osis* condition] *pl.*, anatomoses

vasectomy (va-SEK-toh-mee) surgical severing of the vas deferens to render a male sterile [*vas-* vessel (vas deferens), *-ec-* out, *-tom-* cut, *-y* action]

vasoactive intestinal peptide (VIP) (vay-so-AK-tiv in-TES-ti-nal PEP-tyde) hormone involved with controlling intestinal secretion [*vas-* vessel, *-act* to do, drive, *-tive* state, *intestin-* intestine, *-al* relating to, *pept-* digest, *-ide* chemical]

vasoconstriction (vay-soh-kon-STRIK-shun) reduction in vessel diameter caused by increased contraction of the muscular coat [*vas-* vessel, *-constrict-* draw tight, *-tion* state]

vasodilation (vay-soh-DYE-lay-shun) increase in vessel diameter caused by relaxation of vascular muscles [*vaso-* vessel, *-dilat-* widen, *-tion* state]

vasodilator (vay-so-DYE-lay-tor) class of drugs that trigger the smooth muscles of arterial walls to relax, causing the arteries to dilate [*vas-* vessel or duct, *-dilat-* widen, *-or* agent]

vasodilatory shock (vay-soh-DYE-lah-tor-ee) *see* neurogenic shock [*vas-* vessel, *-dilat-* widen, *-ory* relating to]

vasomotor chemoreflex (vay-so-MOH-tor kee-moh-REE-fleks) chemoreceptors located in the aortic and carotid bodies are sensitive to hypercapnia, hypoxia, and decreased arterial blood pH [*vas-* vessel, *-motor* move, *chemo-* chemical, *-re-* back or again, *-flex* bend]

vasomotor mechanism (vay-so-MOH-tor) feedback regulation of the diameter of arterioles [*vas-* vessel, *-motor* move, *mechan-* machine, *-ism* state]

vasomotor pressoreflex (vay-so-MOH-tor press-oh-REE-fleks) reflex that occurs in response to a change in arterial blood pressure [*vas-* vessel, *-motor* move, *press-* pressure, *-re-* back or again, *-flex* bend]

vault *see* **barrel** [*voute* arch]

vector (VEK-tor) arthropod that carries an infectious pathogen from one organism to another [*vector-* carrier]

vein vessel carrying blood from capillaries toward the heart [*vena* blood vessel]

vellus (VEL-us) strong, fine, and less pigmented hair [*vellus* wool]

venous pump (VEE-nus) blood-pumping action of respirations and skeletal muscle contractions facilitate venous return by increasing pressure gradient between peripheral veins and venae cavae [*ven-* vein, *-ous* relating to]

venous return (VEE-nus) amount of blood returned to the heart by the veins [*ven-* vein, *-ous* relating to]

venous sinus (VEE-nus SYE-nus) large specialized venous structures that have very thin endothelial walls [*ven-* vein, *-ous* relating to, *sinus* hollow]

ventilation (ven-tih-LAY-shun) rate and depth of breathing [*vent-* fan or create wind, *-tion* process]

ventral (anterior) nerve root (VEN-tral) bundle of nerve fibers that carry motor information out of the spinal cord [*ventr-* belly, *-al* relating to]

ventral (VEN-tral) of or near the belly; in humans, front or anterior; opposite of dorsal or posterior [*ventr-* belly, *-al* relating to]

ventral cavities (VEN-tral KAV-ih-teez) body cavities on the ventral side of the body, which include the thoracic cavity and abdominopelvic cavity; not a standard anatomical term, but used here to help organize the body for the beginning student [*ventr-* belly, *-al* relating to, *cav-* hollow, *-ity* state]

ventral ramus (VEN-tral RAY-mus) large, complex branch of each spinal nerve [*ventr-* belly, *-al* relating to *ramus* branch] *pl.*, rami

ventral root (VEN-tral) motor branch of a spinal nerve, by which it is attached to the spinal cord [*ventr-* belly, *-al* relating to]

ventricle (VEN-tri-kul) a cavity, such as the large, fluid-filled spaces within the brain or the chambers of the heart [*ventr-* belly, *-icle* little]

ventricular fibrillation (ven-TRIK-yoo-lar fibril-LAY-shun) an immediately life-threatening condition caused by the lack of ventricular pumping suddenly stopping flow of blood to vital organs [*ventr-* belly, *-icul-* little, *-ar* relating to, *fibr-* fiber, *-illa-* little, *-ation* process]

venule (VEN-yool) small blood vessels that collect blood from capillaries and join to form veins [*ven-* vein, *-ule* little]

vermiform appendix (VERM-i-form ah-PEN-diks) hollow, tubular structure attached to the cecum (of the colon) and thought to be a breeding ground for beneficial intestinal bacteria [*vermi-* worm, *-form* shape, *append-* hang upon, -ix thing] *pl.*, appendices

vermis (VER-mis) central section of the cerebellum [*vermis* worm] *pl.*, vermes

vertebra (VER-teh-bra) any of the bones that make up the spinal column [*vertebra* that which turns] *pl.*, vertebrae (VER-the-bray or VER-teh-bree)

vertebral column (ver-TEE-bral) the spinal column, made up of a series of separate vertebrae that form a flexible, curved rod; made up of the cervical, thoracic, lumbar, sacral, and coccygeal segments [*vertebra* that which turns, *-al* relating to, *columna-* pillar]

vertebral foramen (ver-TEE-bral for-AY-men) the central opening in the vertebral column that contains the spinal cord [*vertebra* that which turns, *-al* relating to, *foramen* hole]

vertebroplasty (ver-tee-broh-PLAS-tee) orthopedic procedure used to treat the vertebral compression fractures that occur in osteoporosis; involves injecting bone cement, but without using a balloon [*vertebra* that which turns, *-plasty* surgical repair]

vertigo (VER-ti-go) abnormal sensation of spinning; dizziness [*vertigo* turning]

vesicle (VES-i-kul) any tiny membranous bubble within a cell; clinical term referring to blisters, fluid-filled skin lesions; see also blister [*vesic-* blister, *-cle* little]

vesicouterine pouch (ves-i-koh-YOO-ter-in) *see* anterior cul-de-sac [*vesic-* blister, *-uter-* womb, *-ine* relating to]

vestibular fold (ves-TIB-yoo-lar) either of the lower of two pairs of lateral folds of the mucosa in the larynx, just above the vocal folds; also called *false vocal fold* or *false vocal cord*; compare to vocal fold [*vestibul-* entrance hall, *voca-* voice, *-al* relating to]

vestibular membrane (ves-TIB-yoo-lar) roof of the cochlear duct; also called *Reissner's membrane* [*vestibule-* entrance hall, *-ar* relating to, *membran-* thin skin]

vestibular nerve (ves-TIB-yoo-lar) division of the vestibulocochlear nerve (eighth cranial nerve)

vestibule (VES-ti-byool) located in the bony labyrinth of the inner ear; portion adjacent to the oval window between the semicircular canals and the cochlea [*vestibul-* entrance hall]

vestibulocochlear nerve (ves-TIB-yoo-lohkok-lee-ar) cranial nerve VIII; sensory nerve; responsible for hearing and equilibrium [*vestibulo-* entrance hall, *-cochle-* snail shell, *-ar* relating to]

vestibulospinal tract (ves-TIB-yoo-loh-SPYnal) descending, or motor, tract that conveys neural messages that coordinate posture and balance [*vestibul-* entrance hall, *-spino-* backbone, *-al* relating to, *tract* trail]

vibrissa (VYE-BRISS-ah) coarse hair found in the skin of the vestibule of the nose [*vibrissa* nostril hair] *pl.*, vibrissae

villus (VIL-us) any of the fingerlike folds covering the plicae of the small intestines [*villus* shaggy hair], *pl.*, villi
Vincent infection (VIN-sent) bacterial (spirochete) infection of the gum, producing gingivitis; also called *Vincent angina* and *trench mouth* [*Henri Vincent* French physician]
virion (VYE-ree-on) a complete viral particle (genetic material and protein capsule) [*vir-* poison, *-on* unit]
virus (VYE-rus-ez) microscopic, intracellular parasitic entity consisting of a nucleic acid bound by a protein coat and sometimes a lipoprotein envelope [*virus* poison]
viscera (VISS-er-ah) internal organs [*visc-* internal organ] *sing.*, viscus
visceral (VISS-er-al) relating to the viscera (internal organs); toward or on the internal organs (opposite of parietal) [*viscer-* internal organ, *-al* relating to]
visceral membrane (VISS-er-al) serous membrane that covers the surface of the viscera [*viscer-* internal organ, *-al* relating to, *membran-* thin skin]
visceral pericardium (VISS-er-al pair-i-KAR-dee-um) the serous membrane that adheres to and covers the heart; also called the *epicardium* [*viscer-* internal organ, *-al* relating to, *peri-* around, *-cardi-* heart, *-um* thing]
visceral pleura (VISS-er-al PLOO-rah) the serous membrane that adheres to and covers the lung [*viscer-* internal organ, *-al* relating to, *pleura* rib] *pl.*, pleurae
visceral portion (VISS-er-al) serous membrane that covers the surfaces of organs in the body cavity [*viscer-* internal organ, *-al* relating to]
visceral reflex (VISS-er-al REE-fleks) autonomic reflex; contractions of smooth or cardiac muscles or secretion by glands [*viscer-* internal organ, *-al* relating to, *re-* again, *-flex* bend]
visceral sensory division (VISS-er-al) division of the nervous system made up of afferent (incoming) pathways from autonomic sensory receptors (receptors involved in subconscious perception) of the internal organs (viscera) [*viscer-* internal organs, *-al* relating to, *sens-* feel, *-ory* relating to]
visceroceptor (viss-er-oh-SEP-tors) somatic sense receptors located in the internal visceral organs; also called *interoceptor* [*viscero-* internal organs, *-cept-*receive, *-or* agent]
viscosity (vis-KOS-i-tee) thickness of a fluid [*viscos-* sticky, *-ity* state]
vital capacity (VC) (largest amount of air that can be moved in and out of the lungs in one inspiration and expiration [*vita-* life, *-al* relating to]
vitamin organic molecules needed in small quantities to help enzymes operate effectively [*vita-* life, *-amin* ammonia compound]
vitamin D compound that influences several important chemical reactions in the body; for example, formation of bones and teeth [*vit-* life, *-amine* chemical group]
vitiligo (vit-i-LYE-go) acquired condition that results in loss of pigment in certain areas of the skin [*vitiligo* blemish]
vitreous body (VIT-ree-us) sac filled with jelly-like fluid in the eye, posterior to the lens [*vitre-* glassy, *-ous* of or like]
vocal cord *see* **vocal fold** [*voca-* voice, *-al* relating to]
vocal fold lower pair of lateral folds of mucosa in the larynx, responsible for vocalization; also called *true vocal fold* or *true vocal cord* or *vocal cord*; compare to false vocal fold [*voca-* voice, *-al* relating to]
voiding (VOYD-ing) emptying the bladder [*void-* empty]
volar (VOH-lar) palm of the hand or sole of the foot [*vola-* palm, sole]
Volkmann canal (VOLK-man) *see* transverse canal (of bone) [*Richard von Volk-mann,* German surgeon]
voltage-gated channel type of cell-membrane channel for the transport of molecules that is controlled by a gate that responds to a change in voltage (difference in charge across the cell membrane) [*volt-* unit of electrical force (after *Alessandro Volta* Italian physicist), *-age* amount]
volume measurement of the amount of space taken up by a substance [*volume* paper roll]
voluntary muscle *see* **skeletal muscle** [*mus-* **mouse**, *-cle* **little**]
vomer bone (VOH-mer) bone that forms the lower and posterior part of the nasal septum [*vomer* plowshare]
vomeronasal organ (VNO) (voh-mer-oh-NAY-sal) sensory organ for detecting pheromones (sex signal molecules) located in the muscosa of the nasal septum [*vomer-* plowshare (vomer bone), *nas-* nose, *-al* relating to, *organ* instrument]
vulva (VUL-vah) external genitals of the female [*vulva* wrapper]
vulvitis (vul-VYE-tis) inflammation of the vulva (external female genitals)

W

wart nipplelike neoplasm of the skin; caused by papilloma virus [*wart* swelling]
white fibers muscle fibers containing little myoglobin; also called *fast fibers*; nerve fibers with a thick myelin sheath [*fiber* thread]
white matter nerves covered with white myelin sheath [*materia-* something from which something is made]
white ramus (RAY-mus) small branch of myelinated sympathetic preganglionic fibers [*ramus* branch]
windpipe trachea [*wind-* blowing, *-pipe* small reed]
withdrawal reflex reflex that moves a body part away from an irritating stimulus [*with-* away, *-draw* to draw, *-al* relating to, *re-* again, *-flex* bend]

X

X chromosome (KROH-moh-sohm) sex chromosome, which, in females, is paired with another X chromosome; as opposed to being paired to a Y chromosome as in males [*chromo-* color, *-some* body]
xeroderma pigmentosum (zeer-oh-DER-mah pig-men-TOH-sum) rare genetic disorder characterized by the inability of skin cells to repair genetic damage caused by the ultraviolet (UV) radiation in sunlight [*xero-* dry, *-derma* skin, *pigment-* paint, *-osum* characterized by]
xerostomia (zee-oh-STOH-mee-ah) condition that results from a dramatic reduction of production of saliva and tears; dry mouth [*xero-* dryness, *-stom-* mouth, *-ia* condition]
X-linked trait genetic trait associated with the female (X) chromosome [*trait* trace]
x-ray photography method of noninvasive imaging of internal body structures; uses energy in the x band of the radiation spectrum beamed through the body to photographic film; also called *radiography* [*x* unknown, *photo-* light, *-graph-* draw, *-y* activity]

Y

Y chromosome (KROH-moh-sohm) sex chromosome that contains genes that determine maleness [*chromo-* color, *-some* body]
yawn slow, deep inspiration through an unusually widened mouth [*yawn* gape]
yeast (yeest) single-celled fungus (compared to mold, which is a multicellular fungus) [*yeast* foam, froth]
yellow marrow (MAIR-oh) connective tissue rich in fat that is found in the medullary cavity of the long bones of an adult; inactive in red cell production [*marrow* inner most]
Y-linked trait genetic trait associated with the male (Y) chromosome [*trait* trace]
yolk sac in humans, involved with production of blood cells in the developing embryo [*yoke* joining]
Young-LaPlace law (law of LaPlace) principle that states that air pressure (P) in a bubble is inversely proportional to the radius (r) and directly proportional to the surface tension (T) summarized by the equation P = 2T/r [*Thomas Young* English physician, *Pierre Simon de LaPlace* French physicist]

Z

Z disk also called Z *line*; microscopic structure within the myofibril of a muscle fiber where the thin filaments unite with each other and form a netlike disk; serves as boundary of sarcomere unit [Z *zwischen* between]
zona fasciculata (ZOH-nah fas-sic-yoo-LAY-tah) middle zone of the adrenal cortex that secretes glucocorticoids [*zona* belt, *fasiculata* having little bundles] *pl.*, zona fasciculatae
zona glomerulosa (ZOH-nah gloh-mair-yoo-LOH-sah) outer zone of the adrenal cortex that secretes mineralocorticoids [*zona* belt, *glomerulosa* having small balls] *pl.*, zonae glomerulosae
zona pellucida (ZP) (ZOH-nah pah-LOO-sih-dah) thick, clear jelly-like film surrounding the ovum, beneath the cumulus cells of the corona radiata [*zona* belt or girdle, *pellucida* transparent] *pl.*, zonae pellucidae
zona reticularis (ZOH-nah reh-tik-yoo-LAIR-is) inner zone of the adrenal cortex that secretes small amounts of sex hormones [*zona* belt, *reticularis* having little nets] *pl.*, zonae reticulares
zone of calcification (kal-si-fi-KAY-shun) deepest layer of the epiphyseal plate; composed of cartilage undergoing rapid calcification [*zone-* belt, *calc-* lime, *-fica* to make, *-tion* process]
zone of hypertrophy (hye-PER-troh-fee) third layer of the epiphyseal plate; composed of older, enlarged cartilage cells that are undergoing degenerative changes associated with calcium deposition [*zone-* belt, *hyper-* excessive, *-troph* nourishment, *-y* state]
zone of proliferation (proh-LIF-er-ay-shun) second layer of the epiphyseal plate; composed of cartilage cells undergoing active mitosis [*zone-* belt, *proles-* offspring, *-fera* to bear, *-tion* process]
zygomatic bone (zye-goh-MAT-ik) cheek bone; also called *malar bone* [*zygo-* union or yoke, *-ic* relating to]
zygomaticus major muscle (zye-goh-MAT-ik-us) muscle that elevates corners of the mouth and lips; also known as the "smiling muscle" [*-zygo-* union or yoke, *-ic* relating to, *major* greater, *mus-* mouse, *-cle* little]
zygote (ZYE-goht) original cell of an offspring, formed by the union of an ovum and sperm [*zygot-* union or yoke]
zymogenic cell (zye-moh-JEN-ik) *see* chief cell [*zym-* ferment (enzyme), *-o-* combining form, *-gen-* produce *-ic* relating to, *cell-* storeroom]

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Pain Control Areas: Discusses pain control areas, areas where pain signals heading toward the conscious brain can be inhibited, and how they have led to pain-reducing therapies.

Pheromones and the Vomeronasal Organ: Describes pheromones, signaling molecules that other individuals detect, and the vomeronasal organ, which is thought to detect them.

Photodynamic Therapy: Outlines this treatment of certain lung cancers, in which photosensitizing drugs are injected into the patient and a laser causes a chemical reaction with the drugs, thereby destroying cancerous cells.

Protective Strategies of the Respiratory Tract: Provides a table summarizing the important protective mechanisms that operate in each segment of the respiratory airways.

Pulmonary Radiology: Explains the types of x-ray studies that can be done to detect bronchial and lung disorders, including standard x-rays, bronchiograms, and arteriograms.

Radioactivity: Describes how radioactivity works and what effects it can have on the human body.

Refractive Eye Surgery: Discusses the common refractive eye surgeries and how they are performed.

Retrograde Signaling: Explains the process of retrograde signaling, or signals being sent backward at a synapse.

Sexually Transmitted Diseases: Illustrates and describes some of the sexually transmitted diseases that occur in both males and females.

Skeletal Radiography: Illustrates skeletal radiography, or x-ray photography, with a description and radiographs of several parts of the body.

Skeletal Variations: Describes the natural variations in the human skeleton, including male and female variations and age-related variations.

Skin Cancer: Explains and illustrates the different types of skin cancer and how they are treated.

Sleep: Outlines the stages of the sleep cycle, including what happens to the body during each of the stages.

Specialization of Cerebral Hemispheres: Explains the specialization of the two hemispheres of the brain and illustrates some of the suggested "special talents" attributed to each side of the brain.

Stem Cell Research: Discusses a controversial topic of scientific research, including the different types of stem cells and how stem cell research could help in cell therapy, the use of special cells to treat disease.

Summary of Gas Exchange: Summarizes some of the essential concepts of gas exchange with a description and a simplified illustration.

Swollen Larynx: Describes and illustrates syndromes that involve a swollen larynx, a potentially lethal condition.

Tools of Microscopic Anatomy: Explains and gives examples of the most common tools in microscopic anatomy: light microscopy, scanning and transmission electron microscopy, and atomic force microscopy.

Tracing Blood Flow in the Kidney: Summarizes the flow of blood in the kidney by providing a simplified flow chart and comparing it to the flow of the blood through the body.

Using Gene Therapy: Summarizes the origins and early history of using gene therapy to treat genetic disorders.

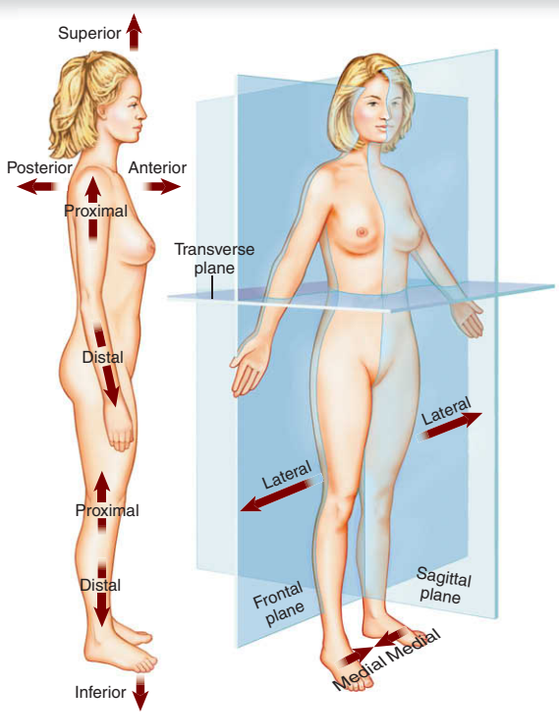
Vertigo and Ear Rocks: Describes the sensation of vertigo, how "ear rocks" can cause this condition, and how to treat them.

Visualizing the Urinary Tract: Explains two methods of medical imaging used to examine the urinary tract: retrograde pyelogram and intravenous pyelogram.

Whole-Body Muscle Mechanics: Discusses how muscles are made up of muscle fibers and many layers of connective tissues, all working together to provide movement and maintain posture.

Anatomical Directions

DIRECTIONAL TERM	DEFINITION	EXAMPLE OF USAGE
Left	To the left of body (not *your* left, the subject's)	The stomach is to the *left* of the liver.
Right	To the right of the body or structure being studied	The *right* kidney is damaged.
Lateral	Toward the side; away from the midsagittal plane	The eyes are *lateral* to the nose.
Medial	Toward the midsagittal plane; away from the side	The eyes are *medial* to the ears.
Anterior	Toward the front of the body	The breastbone (sternum) is *anterior* to the heart.
Posterior	Toward the back (rear) of the body	The heart is *posterior* to the breastbone (sternum).
Superior	Toward the top of the body	The shoulders are *superior* to the hips.
Inferior	Toward the bottom of the body	The stomach is *inferior* to the heart.
Dorsal	Along (or toward) the vertebral surface of the body	Her scar is along the *dorsal* surface.
Ventral	Along (toward) the belly surface of the body	The navel is on the *ventral* surface.
Caudad (caudal)	Toward the tail (used for 4-legged animals)	The neck is *caudad* to the skull.
Cephalad	Toward the head (used for 4-legged animals)	The neck is *cephalad* to the tail.
Proximal	Toward the trunk (describes relative position in a limb or other appendage)	The joint is *proximal* to the toenail.
Distal	Away from the trunk or point of attachment	The hand is *distal* to the elbow.
Visceral	Toward an internal organ; away from the outer wall (describes positions inside a body cavity)	This organ is covered with the *visceral* layer of the membrane.
Parietal	Toward the wall; away from the internal structures	The abdominal cavity is lined with the *parietal* peritoneal membrane.
Deep	Toward the inside of a part; away from the surface	The thigh muscles are *deep* to the skin.
Superficial	Toward the surface of a part; away from the inside	The skin is a *superficial* organ.
Medullary	Refers to an inner region, or medulla	The *medullary* portion contains nerve tissue.
Cortical	Refers to an outer region, or cortex	The *cortical* area produces hormones.
Ipsilateral	On the same side of the body as	The left knee is *ipsilateral* to the left ankle.
Contralateral	On the opposite side of the body	The left knee is *contralateral* to the right knee.



To make the reading of anatomical figures a little easier, an anatomical compass is used throughout this book. On many figures, you will notice a small compass rosette similar to those on geographical maps. Rather than being labeled *N*, *S*, *E*, and *W*, the anatomical rosette is labeled with abbreviated anatomical directions.



A = Anterior	**P** (opposite A) = Posterior
D = Distal	**P** (opposite D) = Proximal
I = Inferior	**S** = Superior
L (opposite M) = Lateral	**M** = Medial
L (opposite R) = Left	**R** = Right

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Oxygen Supplements: Explains how oxygen therapy can be used to treat disease and improve athletic performance, and can even be used recreationally at "oxygen bars."

Oxygen-Binding Proteins: Explains the oxygen-binding proteins other than hemoglobin that are important to human physiology.

Pain Control Areas: Discusses pain control areas, areas where pain signals heading toward the conscious brain can be inhibited, and how they have led to pain-reducing therapies.

Pheromones and the Vomeronasal Organ: Describes pheromones, signaling molecules that other individuals detect, and the vomeronasal organ, which is thought to detect them.

Photodynamic Therapy: Outlines this treatment of certain lung cancers, in which photosensitizing drugs are injected into the patient and a laser causes a chemical reaction with the drugs, thereby destroying cancerous cells.

Protective Strategies of the Respiratory Tract: Provides a table summarizing the important protective mechanisms that operate in each segment of the respiratory airways.

Pulmonary Radiology: Explains the types of x-ray studies that can be done to detect bronchial and lung disorders, including standard x-rays, bronchiograms, and arteriograms.

Radioactivity: Describes how radioactivity works and what effects it can have on the human body.

Refractive Eye Surgery: Discusses the common refractive eye surgeries and how they are performed.

Retrograde Signaling: Explains the process of retrograde signaling, or signals being sent backward at a synapse.

Sexually Transmitted Diseases: Illustrates and describes some of the sexually transmitted diseases that occur in both males and females.

Skeletal Radiography: Illustrates skeletal radiography, or x-ray photography, with a description and radiographs of several parts of the body.

Skeletal Variations: Describes the natural variations in the human skeleton, including male and female variations and age-related variations.

Skin Cancer: Explains and illustrates the different types of skin cancer and how they are treated.

Sleep: Outlines the stages of the sleep cycle, including what happens to the body during each of the stages.

Specialization of Cerebral Hemispheres: Explains the specialization of the two hemispheres of the brain and illustrates some of the suggested "special talents" attributed to each side of the brain.

Stem Cell Research: Discusses a controversial topic of scientific research, including the different types of stem cells and how stem cell research could help in cell therapy, the use of special cells to treat disease.

Summary of Gas Exchange: Summarizes some of the essential concepts of gas exchange with a description and a simplified illustration.

Swollen Larynx: Describes and illustrates syndromes that involve a swollen larynx, a potentially lethal condition.

Tools of Microscopic Anatomy: Explains and gives examples of the most common tools in microscopic anatomy: light microscopy, scanning and transmission electron microscopy, and atomic force microscopy.

Tracing Blood Flow in the Kidney: Summarizes the flow of blood in the kidney by providing a simplified flow chart and comparing it to the flow of the blood through the body.

Using Gene Therapy: Summarizes the origins and early history of using gene therapy to treat genetic disorders.

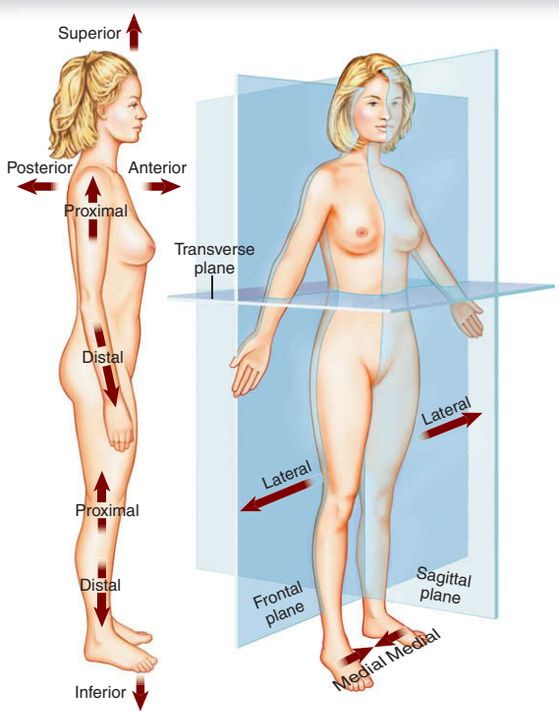
Vertigo and Ear Rocks: Describes the sensation of vertigo, how "ear rocks" can cause this condition, and how to treat them.

Visualizing the Urinary Tract: Explains two methods of medical imaging used to examine the urinary tract: retrograde pyelogram and intravenous pyelogram.

Whole-Body Muscle Mechanics: Discusses how muscles are made up of muscle fibers and many layers of connective tissues, all working together to provide movement and maintain posture.

Anatomical Directions

DIRECTIONAL TERM	DEFINITION	EXAMPLE OF USAGE
Left	To the left of body (not *your* left, the subject's)	The stomach is to the *left* of the liver.
Right	To the right of the body or structure being studied	The *right* kidney is damaged.
Lateral	Toward the side; away from the midsagittal plane	The eyes are *lateral* to the nose.
Medial	Toward the midsagittal plane; away from the side	The eyes are *medial* to the ears.
Anterior	Toward the front of the body	The breastbone (sternum) is *anterior* to the heart.
Posterior	Toward the back (rear) of the body	The heart is *posterior* to the breastbone (sternum).
Superior	Toward the top of the body	The shoulders are *superior* to the hips.
Inferior	Toward the bottom of the body	The stomach is *inferior* to the heart.
Dorsal	Along (or toward) the vertebral surface of the body	Her scar is along the *dorsal* surface.
Ventral	Along (toward) the belly surface of the body	The navel is on the *ventral* surface.
Caudad (caudal)	Toward the tail (used for 4-legged animals)	The neck is *caudad* to the skull.
Cephalad	Toward the head (used for 4-legged animals)	The neck is *cephalad* to the tail.
Proximal	Toward the trunk (describes relative position in a limb or other appendage)	The joint is *proximal* to the toenail.
Distal	Away from the trunk or point of attachment	The hand is *distal* to the elbow.
Visceral	Toward an internal organ; away from the outer wall (describes positions inside a body cavity)	This organ is covered with the *visceral* layer of the membrane.
Parietal	Toward the wall; away from the internal structures	The abdominal cavity is lined with the *parietal* peritoneal membrane.
Deep	Toward the inside of a part; away from the surface	The thigh muscles are *deep* to the skin.
Superficial	Toward the surface of a part; away from the inside	The skin is a *superficial* organ.
Medullary	Refers to an inner region, or medulla	The *medullary* portion contains nerve tissue.
Cortical	Refers to an outer region, or cortex	The *cortical* area produces hormones.
Ipsilateral	On the same side of the body as	The left knee is *ipsilateral* to the left ankle.
Contralateral	On the opposite side of the body	The left knee is *contralateral* to the right knee.



To make the reading of anatomical figures a little easier, an anatomical compass is used throughout this book. On many figures, you will notice a small compass rosette similar to those on geographical maps. Rather than being labeled *N*, *S*, *E*, and *W*, the anatomical rosette is labeled with abbreviated anatomical directions.



A = Anterior	**P** (opposite A) = Posterior
D = Distal	**P** (opposite D) = Proximal
I = Inferior	**S** = Superior
L (opposite M) = Lateral	**M** = Medial
L (opposite R) = Left	**R** = Right