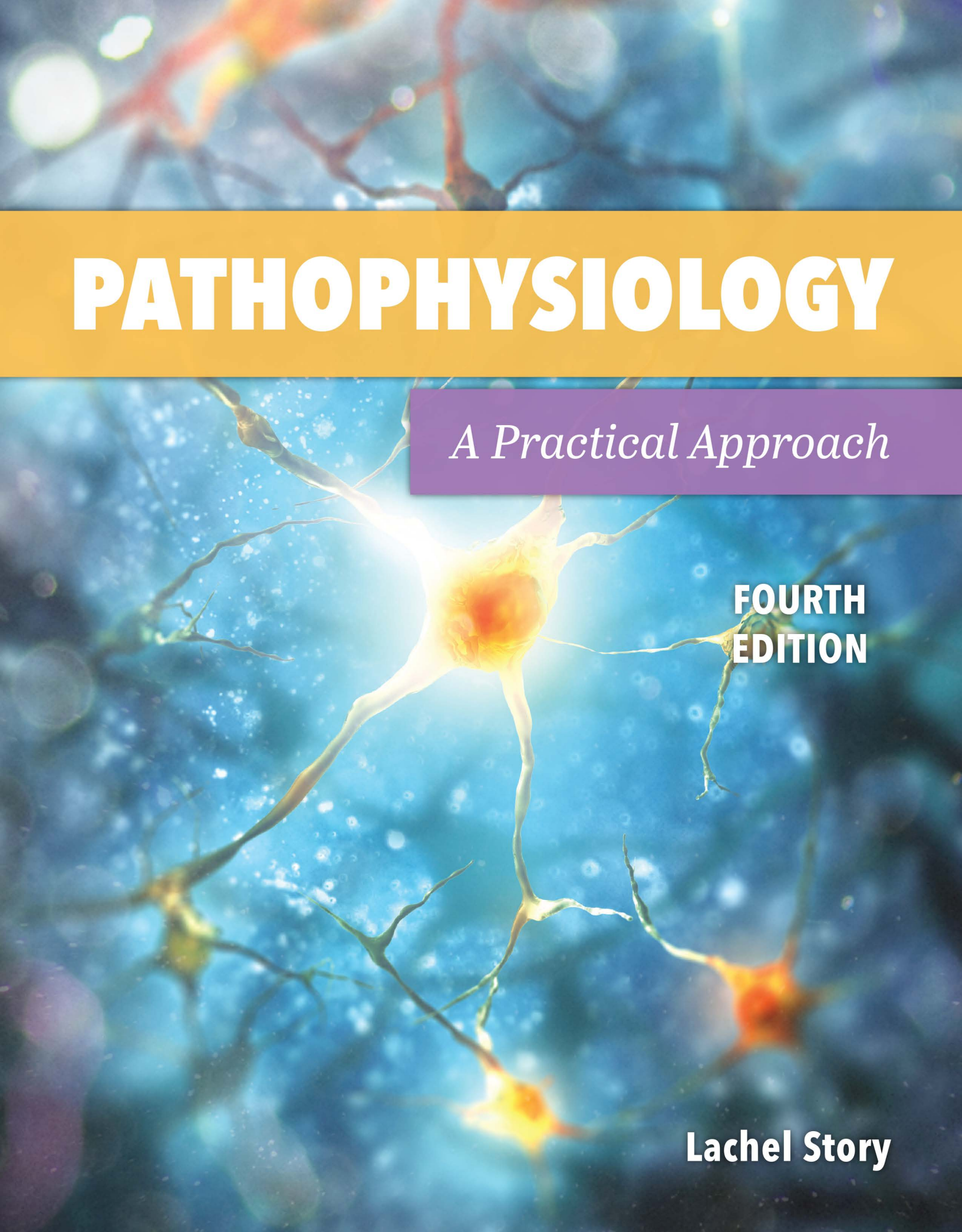
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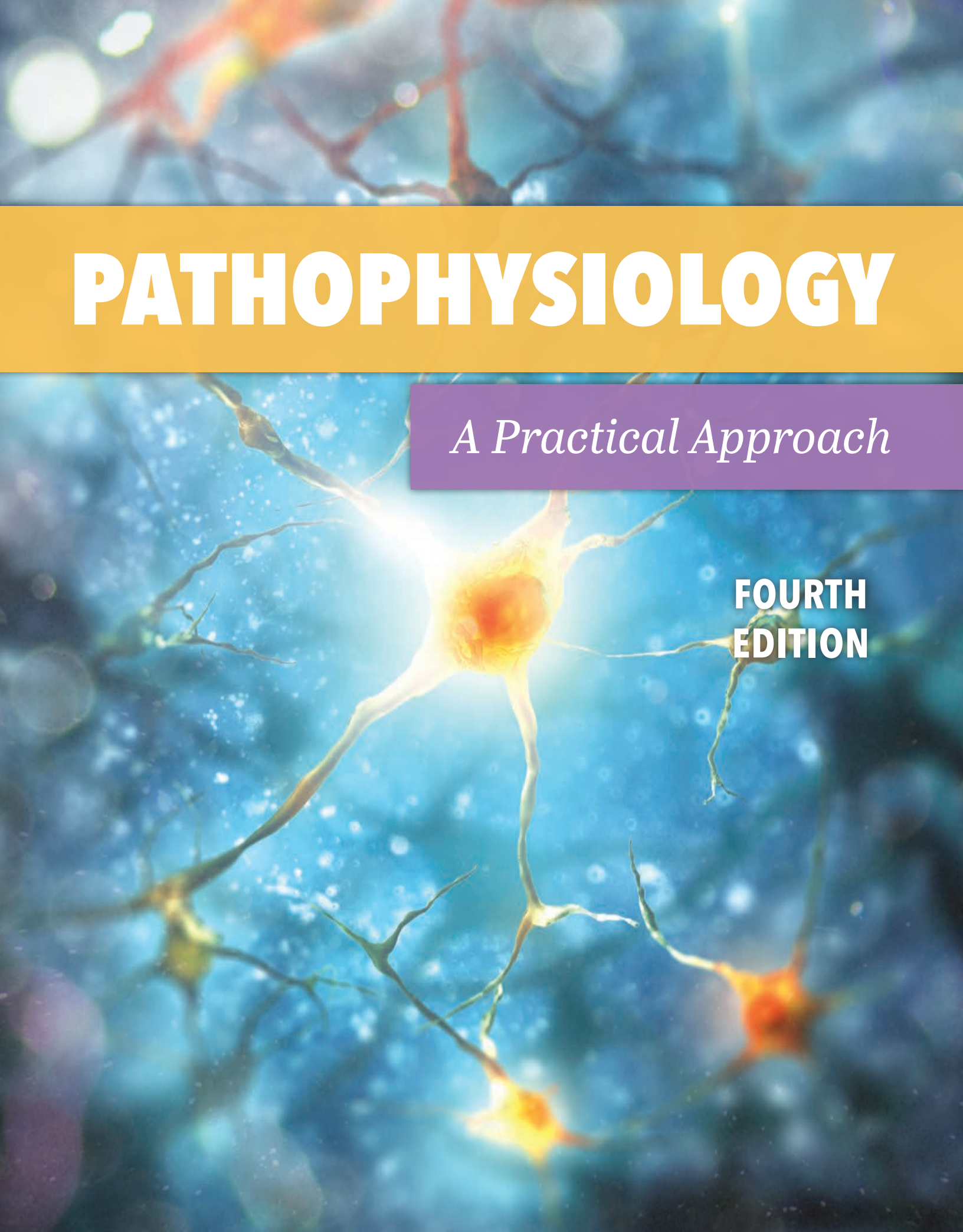
A Practical Approach
FOURTH EDITION
Lachel Story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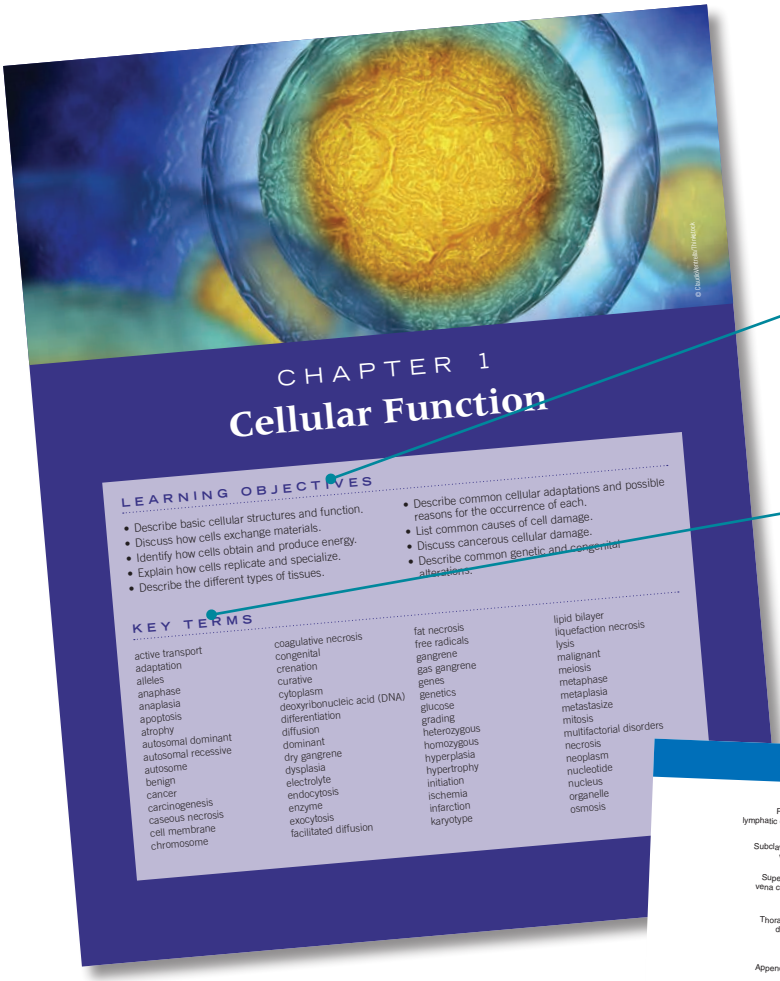
The Pedagogy

Pathophysiology: A Practical Approach, Fourth Edition focuses on driving comprehension through a variety of strategies that meet the learning needs of students while generating enthusiasm about the topic. This interactive approach addresses different learning styles, making this the ideal text to ensure mastery of key concepts. The pedagogical aids that appear in most chapters include the following:



CHAPTER 1

Cellular Function

LEARNING OBJECTIVES

- Describe basic cellular structures and function.
- Discuss how cells exchange materials.
- Identify how cells obtain and produce energy.
- Explain how cells replicate and specialize.
- Describe the different types of tissues.
- Describe common cellular adaptations and possible reasons for the occurrence of each.
- List common causes of cell damage.
- Discuss cancerous cellular damage.
- Describe common genetic and congenital alterations.

KEY TERMS

active transport
adaptation
alleles
anaphase
anaplasia
apoptosis
atrophy
autosomal dominant
autosomal recessive
autosome
benign
cancer
carcinogenesis
caseous necrosis
cell membrane
chromosome
coagulative necrosis
congenital
crenation
curative
cytoplasm
deoxyribonucleic acid (DNA)
differentiation
diffusion
dominant
dry gangrene
dysplasia
electrolyte
endocytosis
enzyme
exocytosis
facilitated diffusion
fat necrosis
free radicals
gangrene
gas gangrene
genes
genetics
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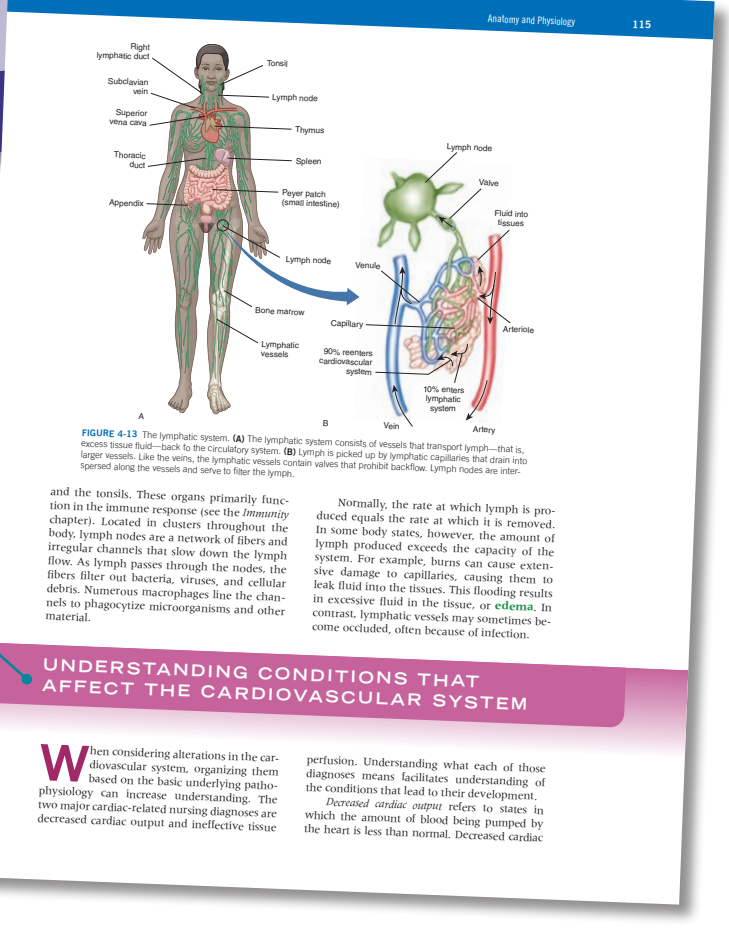
heterozygous
homozygous
hyperplasia
hypertrophy
initiation
ischemia
infarction
karyotype
lipid bilayer
liquefaction necrosis
lysis
malignant
meiosis
metaphase
metaplasia
metastasize
mitosis
multifactorial disorders
necrosis
neoplasm
nucleotide
nucleus
organelle
osmosis

Learning Objectives These objectives provide instructors and students with a snapshot of key information they will encounter in each chapter. They can serve as a checklist to help guide and focus study.

Key Terms Found in a list at the beginning of each chapter and appearing in bold throughout the text, these terms will create an expanded vocabulary in pathophysiology.



Anatomy and Physiology 115

FIGURE 4-13 The lymphatic system. **(A)** The lymphatic system consists of vessels that transport lymph—that is, excess tissue fluid—back to the circulatory system. **(B)** Lymph is picked up by lymphatic capillaries that drain into larger vessels. Like the veins, the lymphatic vessels contain valves that prohibit backflow. Lymph nodes are interspersed along the vessels and serve to filter the lymph.

and the tonsils. These organs primarily function in the immune response (see the *Immunity* chapter). Located in clusters throughout the body, lymph nodes are a network of fibers and irregular channels that slow down the lymph flow. As lymph passes through the nodes, the fibers filter out bacteria, viruses, and cellular debris. Numerous macrophages line the channels to phagocytize microorganisms and other material.

Normally, the rate at which lymph is produced equals the rate at which it is removed. In some body states, however, the amount of lymph produced exceeds the capacity of the system. For example, burns can cause extensive damage to capillaries, causing them to leak fluid into the tissues. This flooding results in excessive fluid in the tissue, or **edema**. In contrast, lymphatic vessels may sometimes become occluded, often because of infection.

UNDERSTANDING CONDITIONS THAT AFFECT THE CARDIOVASCULAR SYSTEM

When considering alterations in the cardiovascular system, organizing them based on the basic underlying pathophysiology can increase understanding. The two major cardiac-related nursing diagnoses are decreased cardiac output and ineffective tissue perfusion. Understanding what each of those diagnoses means facilitates understanding of the conditions that lead to their development.

Decreased cardiac output refers to states in which the amount of blood being pumped by the heart is less than normal. Decreased cardiac

Concept-Based Learning Each chapter is organized by overarching concepts, providing a framework for study and deepening understanding of content.

Learning Points Quick facts are called out to highlight important topics within each chapter.

Emerging Research Found in select chapters, these snapshots provide state-of-the-science insights into cutting-edge topics.

Myth Busters Common myths and misconceptions highlighted and debunked.

Application to Practice Found in select chapters, these vignettes provide critical-thinking challenges for students.

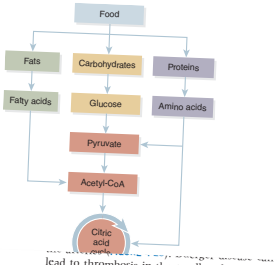
Summary Included at the end of each chapter, these provide a concise review of material covered in each chapter.

and particularly phagocytosis, to consume and destroy bacteria and other foreign material. **Exocytosis** is the release of materials from the cell, usually with the assistance of a vesicle (a membrane-bound sac) (Figure 1-8). Often glands secrete hormones using exocytosis.

Learning Points

Active Transport

To understand active transport, consider the overfilled elevator again. If the door opens and someone from outside the elevator attempts to get in, it will require a great deal of effort (energy) to enter the already full elevator. The sodium–potassium pump is an example of active transport in the body. Energy is required both to move sodium out of a cell, where the concentrations are high, and to move potassium into a cell, where the concentrations are high.



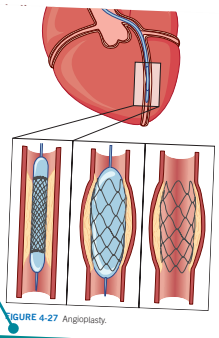


FIGURE 4-27 Angioplasty.

lead to thrombosis in the small and medium-sized arteries of the arms and legs, eventually occluding them. Buerger disease most commonly occurs in men between ages 20 and 40 who smoke.

Raynaud disease is a result of vasospasm of the arteries, most often of the hands, that occurs because of sympathetic stimulation (FIGURE 4-29). Raynaud phenomenon describes the situation in which such vasospasm occurs in association with an autoimmune disease (e.g., systemic lupus erythematosus and scleroderma). This condition most commonly occurs in women between ages 18 and 30. As vessel occlusion increases, the ischemia to the affected tissue worsens.

Chronic venous insufficiency is a condition in which one or more veins do not return blood from the legs back to the heart due to valve damage in the veins, so blood pools in segments of the veins. Thrombophlebitis refers to a thrombus in an inflamed vein, most often in the legs.

Emerging Research: Heart Disease Risk Factors

Most people are familiar with the traditional risk factors for heart disease—for example, hypertension, diabetes mellitus, dyslipidemia, obesity, physical inactivity, and smoking. In recent years, research has linked other health and lifestyle issues with an increased risk of developing heart disease, especially in the presence of the traditional risk factors. These issues include sleep disturbances, pregnancy complications, mental health problems, and periodontal disease.

Sleep apnea has been linked with high blood pressure and arrhythmias (Kadoya et al., 2018). Sleeping less than seven hours per night can lead to increased blood pressure, truncal obesity, and stress hormones. Additionally, not getting sufficient sleep can disrupt metabolism, causing increased lipid levels and making diabetes mellitus and hypertension more difficult to control.

Women who have a history of gestational diabetes have nearly a three times greater risk of developing coronary artery disease, hypertension, and type 2 diabetes mellitus (Daly et al., 2018). Women who have preeclampsia have a higher risk of developing hypertension and are twice as likely to develop cardiovascular disease by midlife.

Chronic mental health problems (e.g., depression, anxiety, anger, loneliness, and stress) can increase the risk for developing heart disease over time (Hegeman et al., 2018; Liu, Hernandez, Trout, Kleiman, & Bozzay, 2017). The connection between mental health and cardiovascular disease may be due in part to the fact that individuals experiencing these issues generally do not engage in healthy behaviors (e.g., regular exercise, proper diet) as well as increased levels of stress hormones.

Moderate to severe periodontal disease is associated with a significantly increased risk for developing cardiovascular disease (Holmlund, Lampa, & Lind, 2017; Singer et al., 2018).

Myth 2: I can get HIV from mosquitoes.

Although HIV spreads through blood, several studies have shown that mosquitoes cannot transmit HIV, even in areas with high numbers of mosquitoes and HIV cases. Mosquitoes do not inject the blood they consume into the next person they bite, and the virus lives only a short time in the insect.

Myth 3: If I'm receiving treatment, I can't spread the HIV virus.

Effective treatment can decrease the viral load in the blood, even to the point that the virus cannot be detected by a blood test. However, the virus can hide in other areas of the body, waiting for an opportunity to increase its replication again. The risk of transmission is lower when the viral load is lower, but transmission is still possible.

Myth 4: My partner and I are both HIV positive, so there's no reason to practice safer sex.

Continued exposure to HIV can increase the viral load and introduce another strain—both factors that can accelerate the disease's progression. Practicing safer sex (e.g., wearing condoms and using other barriers) can limit exposure to HIV and other sexually transmitted infections.

Myth 5: You can't get HIV from oral sex.

It is true that the risk of transmission through oral sex is lower than with other types of sex, but HIV can be transmitted by having oral sex with either a man or woman who is HIV positive.

application to practice

Let's put the things you have learned about the body's defenses into practice. Which of the following individuals would be at highest risk for impaired immune function?

- A 23-year-old female who weighs 5% more than her ideal body weight
- A 78-year-old male with poorly controlled diabetes mellitus
- An 89-year-old male with controlled hypertension
- A 45-year-old female who was recently widowed

When considering this type of question, you start by counting things that might impair the immune system. The patient with the most risk factors is at the greatest risk. Eliminate any information that does not increase risk. For instance, being male or female does not impair immune function, so eliminate that factor from your consideration.

Let's look at each of the example patients. The 23-year-old is not in an older age range and is fairly close to her ideal body weight; she has no risk factors. The 78-year-old is assigned one risk factor for his increased age and another for his chronic disease. Go ahead and give him another risk factor because his diabetes is uncontrolled—now he has three risk factors. The 89-year-old has one risk factor for his increased age and another for having a chronic disease, but his hypertension is controlled. He has two risk factors. Finally, the 45-year-old has only one risk factor, the stress of being recently widowed. After examining all of these patients, the 78-year-old male is at the most risk for impaired immune function owing to his three risk factors.

At-risk individuals and states that specifically put individuals at risk for an impaired immune system include the following:

- Very young or very old age
- Poor nutrition
- Impaired skin integrity
- Circulatory issues
- Alterations in normal flora due to antibiotic therapy
- Chronic diseases, especially diabetes mellitus
- Corticosteroid therapy
- Chemotherapy
- Smoking
- Alcohol consumption
- Immunodeficiency states

The following strategies can be employed to build a healthy immune system:

- Increasing fluid intake
- Eating a well-balanced diet
- Increasing antioxidants and protein intake
- Getting adequate sleep
- Avoiding caffeine and refined sugar
- Spending time outdoors
- Reducing stress

SUMMARY

The nervous system is a complex network that receives, organizes, and responds to internal and external stimuli—functions that are vital for achieving and maintaining homeostasis. The nervous system controls all sensory and motor functions. Damage to this system—even when minor—can result in significant neurologic deficits. The nature and severity of those deficits depend on the location and extent of damage. Such damage can result from trauma, infections, tumors, chemical imbalances, or genetic conditions. Regardless of the neurologic disorder, an affected individual may experience impaired social functioning, significant neurologic dysfunction, negative physical health consequences, and even death. Supporting neurologic health involves strategies such as observing safety precautions (e.g., wearing safety equipment), avoiding illicit drug use, minimizing alcohol consumption, getting vaccinations, and maintaining adequate nutrition.

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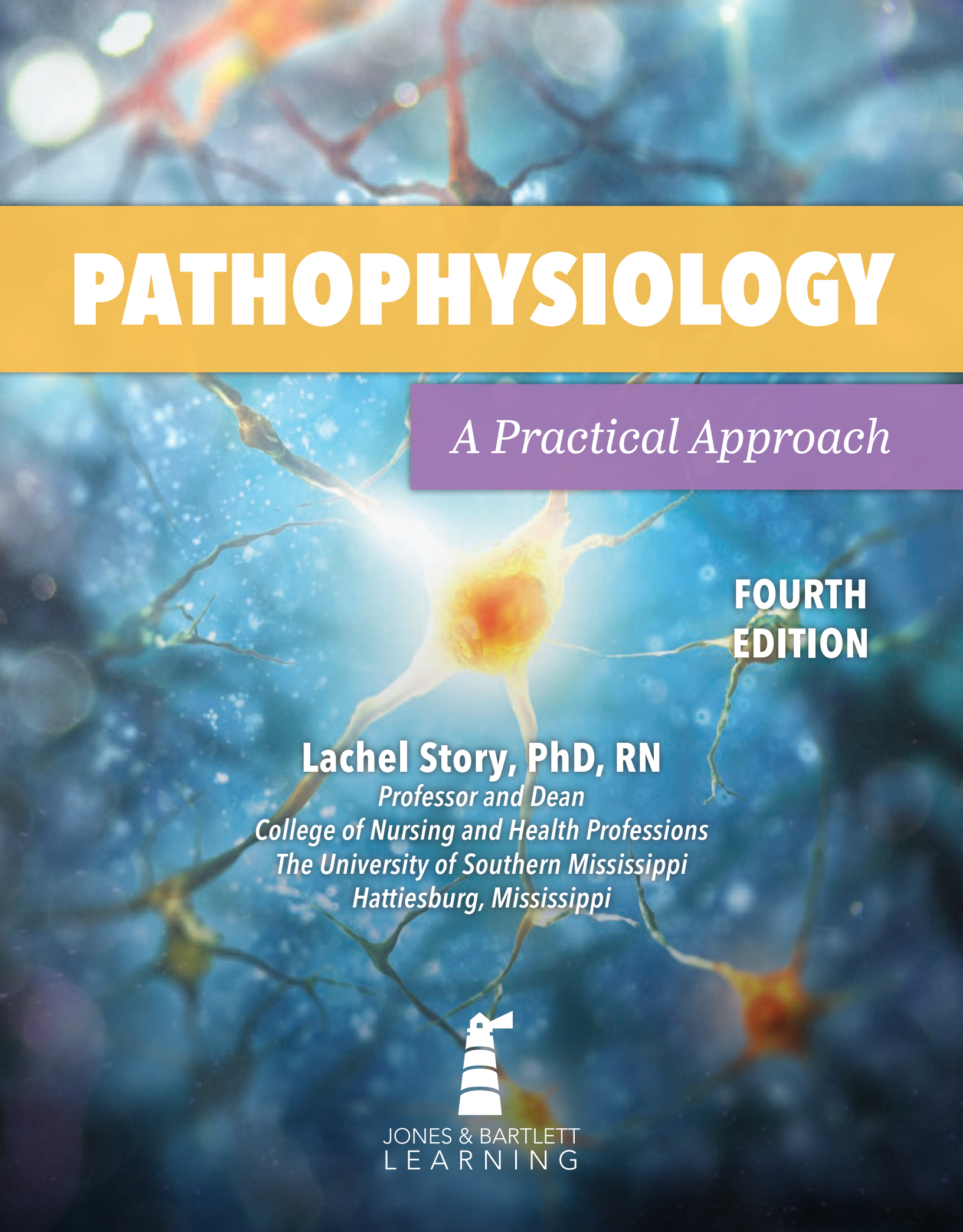

PATHOPHYSIOLOGY

A Practical Approach

FOURTH EDITION

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Contents

Preface

While teaching pathophysiology for more than 14 years and nursing for more than 25 years, I noticed a lack of pathophysiology books that students could relate to and encountered high student frustration with learning the sometimes convoluted material. Pathophysiology—while being the foundation of much of nursing education, from medical–surgical care to pharmacology—is often an insurmountable barrier for students. They face a copious amount of complicated information that they must weed through and synthesize. While some students become bogged down in an information marsh, others seek more information than is provided in a skeleton book that has been cut to the bone. Nursing faculty join the students on this frustrating Goldilocks journey by trying to make the available resources fit. Unfortunately, nursing students and faculty often have pathophysiology books available that provide either far too much information or far too little.

This text provides the right fit. It is a practical guide to pathophysiology that presents information in an understandable student-friendly way. Here, extraneous information is omitted, leaving only necessary information. The information in this text is also presented in a more accessible manner by considering readability, providing colorful graphics, and giving the content context and meaning.

This unique text will provide a springboard for faculty and students to come together as co-learners to explore this fascinating content. When such co-learning is stimulated, pathophysiology is no longer just mindlessly deposited into the students in a stifling manner; rather, learning for the students and the faculty becomes an empowerment pedagogy. This approach has been supported by experts at the Institute of Medicine (2011), the Robert Wood Johnson Foundation (Committee on the Robert Wood Johnson Foundation Initiative on the Future of Nursing at the Institute of Medicine, 2010), and nursing leaders (Benner, Sutphen, Leonard, & Day, 2010), among others, who have sought to change how nurses are educated to meet the changing landscape of health care and needs of new generations.

The fourth edition of this text organizes content in a conceptual manner to provide students with an understandable and practical resource for learning pathophysiology. New and updated material has been added to every chapter. Emerging research has been incorporated to provide state-of-the-science insights into selected topics. Life span considerations have been expanded throughout. New and updated case studies add to students' understanding and ability to apply their learning on a practical level. Instructor resources include active learning activities that support the "flipped" classroom approach. Faculty will appreciate having a resource that speaks to and engages students. Health professionals will also be able to refer to the text to refresh their memory on concepts in a pragmatic way.

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Introduction to Pathophysiology

LEARNING OBJECTIVES

- Define pathophysiology and identify its importance for clinical practice.
- Identify key health and disease concepts.

KEY TERMS

acute
chronic
compensatory mechanism
complication
congenital
convalescence
degenerative
developmental
diagnosis
disease
epidemic
epidemiology
etiology
exacerbation
genetic
health
hereditary
homeostasis
iatrogenic
idiopathic
inflammatory
insidious
manifestation
metabolic
morbidity
mortality
negative feedback system
neoplastic
pandemic
pathogenesis
pathophysiology
positive feedback systems
predisposing factor
prevention
prognosis
remission
signs
symptoms
syndrome
treatment

Pathophysiology Concepts

What is meant by **pathophysiology**? And why is it so important to understand, especially for nurses? Essentially, pathophysiology is the study of what happens when normal anatomy and physiology go wrong. Veering off this normal path can cause diseases or abnormal states. Pathophysiology is the foundation upon which all of nursing is built. It is the "why" that unlocks all the mysteries of the human body and its response to medical and nursing therapies. Understanding pathophysiology provides insight into why patients look the way they do when they have a certain disease, why the medicines we give them work, why the side effects of treatments occur, and why complications sometimes transpire. Pathophysiology provides the rationale for evidence-based medicine.

Why are so many students mystified by pathophysiology? Unfortunately, students often get lost in the minute details and the complicated nuances of pathophysiology. Pathophysiology, when brought back to the basics and framed in a practical context, can bring meaning and understanding to the world of health and disease in which people live.

Health and Disease

To understand disease, the definition of health must first be clarified. **Health** may be considered the absence of disease—but this concept can also be expanded to include wellness of mind, body, and spirit. The normal state may vary due to genetic, age, and gender differences, and it exists relative to the individual's baseline. Negative events in any one of these three areas can cause issues in the others—these areas coexist. Humans are complicated and do not live in a vacuum. Instead, just as the mind, body, and spirit are interrelated, so humans are interrelated with their environment, including their physical ecology as well as social factors. These external factors play a significant role in an individual's health, whether negatively or positively.

On the flip side of health is disease. **Disease** is a state in which a bodily function is no longer occurring normally. The severity of diseases ranges from merely creating temporary stress to causing life-changing complications. Health and disease may be considered as the two extremes of a continuum. At one end are severe, life-threatening disease states that cause significant physical and emotional issues; at the other end is optimal health that supports mind, body, and spirit well-being.

Diseases can be classified in several ways. First, a disease may be **hereditary**, meaning it is transmitted before birth. Disease may also be present at birth, or **congenital**. **Genetic** diseases are caused by abnormalities in the individual's genetic makeup, such as differences in chromosomal numbers or mutations (see the Cellular Function chapter). **Developmental** diseases occur as a result of an issue that arises during embryonic or fetal development. Other diseases may develop over the life span. **Inflammatory** diseases trigger the inflammatory response (see the Immunity chapter). **Degenerative** diseases include conditions that cause parts of the body to deteriorate (e.g., arthritis). Conditions that affect metabolism, such as diabetes mellitus, are referred to as **metabolic** diseases. **Neoplastic** diseases are caused by abnormal or uncontrolled cellular growth, which can lead to benign and malignant tumors (see the Cellular Function chapter).

Exploring concepts of homeostasis is a good place to start in understanding the origins of disease.

Homeostasis

Many words can be used to describe **homeostasis**, such as *equilibrium*, *balance*, *consistency*, and *stability*. Some examples of this relative consistency can be seen in vital signs such as blood pressure, pulse, and temperature. Every part of the human body—from the smallest cells to the largest organs—needs balance to maintain its usual functions. In some cases, such as with pH, even minimal changes can cause significant and life-threatening problems. The human body is constantly engaging in multiple strategies to maintain this balance and addressing external stressors, such as injury or organism invasion, that might tip the balance in one direction or another.

Homeostasis is a self-regulating, give-and-take system that responds to minor changes in the body through compensation mechanisms. Compensation mechanisms attempt to counteract those changes and return the body to its normal state (FIGURE I-1). Several brain structures are instrumental in maintaining this balance, including the medulla oblongata, hypothalamus, reticular formation, and pituitary gland. The medulla oblongata is located in the brainstem and controls vital functions such as

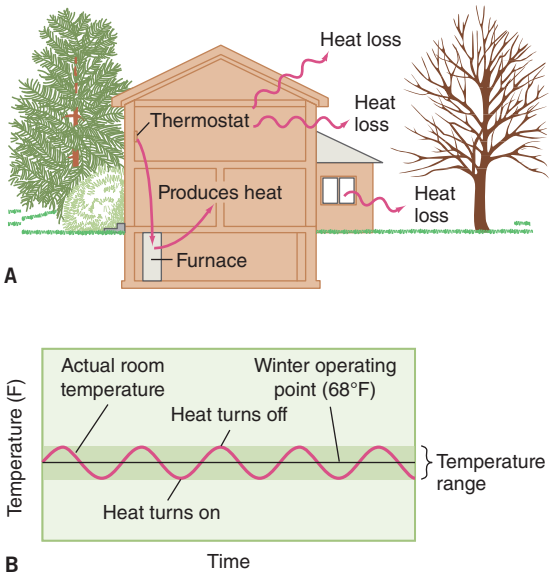

FIGURE I-1 Homeostasis is like a house. **(A)** Heat is maintained in a house by a furnace, which compensates for heat loss. **(B)** A hypothetical temperature graph.

blood pressure, temperature, and pulse. The reticular formation is a network of nerve cells in the brain stem and the spinal cord that also controls vital functions; it relays information to the hypothalamus. The hypothalamus, in turn, controls homeostasis by communicating information to the pituitary gland. The pituitary gland, also known as the master gland, regulates other glands that contribute to growth, maturation, and reproduction.

Two types of feedback systems exist to maintain homeostasis: negative and positive. A **negative feedback system**—the most common type—works to maintain a deficit in the system. Such negative feedback mechanisms work to resist any change from normal. Examples include temperature and glucose regulation. **Positive feedback systems**, though few in number, move the body away from homeostasis. With this type of feedback, an amplified response occurs in the same direction as the original stressor. Examples of positive feedback systems include childbirth, sneezing, and blood clots.

Disease Development

Etiology is the study of disease causation. Etiologic factors may include infectious agents, chemicals, and environmental influences, to name a few. Etiologic factors may also be unknown, or **idiopathic**. Additionally, diseases can be caused by an unintended, or **iatrogenic**, effect of a medical treatment.

Predisposing factors are tendencies that put an individual at risk for developing certain diseases. Examples of predisposing factors are similar to etiologic factors and may include dietary imbalances and carcinogen exposure.

Identifying the etiology and predisposing factors for a disease can be instrumental in preventing the disease by distinguishing at-risk populations who can be targeted with prevention measures. Today, the healthcare system is focusing more on disease prevention because investing resources before a disease develops can decrease the long-term financial burden associated with its treatment.

How a disease develops is referred to as **pathogenesis**. Some diseases are self-limiting, whereas others are chronic and never resolve. Some diseases cause reversible changes, while others cause irreparable damage. To limit the damage from diseases, the body activates **compensatory mechanisms**—that is, physiological strategies the body employs in the midst of homeostatic imbalance to maintain normalcy. When those mechanisms can no longer maintain relative consistency, disease occurs.

Sometimes, the onset of the disease may be sudden or acute. Acute onset of a disease may include pronounced indicators such as pain or vomiting. By comparison, a gradual, or **insidious**, onset may be associated with only vague signals. Hypertension, for example, can occur in this subtle manner.

Disease duration is another important concept to consider. A disease may be short term, or **acute**, occurring and resolving quickly. Gastroenteritis and tonsillitis are examples of acute diseases. When an acute disease does not resolve after a short period, it may move into a chronic state. A **chronic** disease often has fewer notable signs and occurs over a longer period. Chronic diseases may not ever resolve but may sometimes be manageable. Diabetes mellitus and depression are examples of chronic diseases. Additionally, people with chronic diseases can experience an acute event of that disease, complicating care. An example of this phenomenon can be seen when a patient with asthma (a chronic disease) has an acute asthma attack.

Recognition of a disease when it is encountered is important in **diagnosis**, or identification, of disease. **Manifestations** are the clinical effects or evidence of a disease. They may include both **signs**—what can be seen or measured—and **symptoms**—what the patient describes but is not visible to the healthcare

practitioner. Manifestations may include issues identified during a physical assessment (e.g., heart murmur), diagnostic results (e.g., laboratory levels), patient complaints (e.g., pain), and family reports (e.g., unusual behavior). A **syndrome** comprises a group of signs and symptoms that occur together. Some chronic diseases may include episodes of remission and exacerbation. **Remission** occurs when the manifestations subside, and **exacerbation** occurs when the manifestations increase again. Systemic lupus erythematosus and heart failure are examples of diseases that demonstrate remissions and exacerbations. Manifestations may vary depending on the point at which they occur in the pathogenesis. For instance, an early sign of shock may be tachycardia, whereas bradycardia occurs late in the disease process. Manifestations are often a critical component of disease diagnosis. Additionally, a detailed patient history may be used to facilitate accurate diagnosis.

Treatment refers to strategies used to manage or cure a disease. Treatment may focus on eliminating the cause of the disease, or it may be used to alleviate the disease's clinical manifestations. For example, an antibiotic may be prescribed to target the specific organism causing a patient's pneumonia, or an antiemetic may be administered to relieve vomiting associated with acute pancreatitis. Treatment regimens often require the services of an interdisciplinary team (e.g., nurses, nurse practitioners, dietitians, respiratory therapists, physical therapists, occupational therapists, physiotherapists, physicians, and pharmacists). Such a team is often necessary when a swift, aggressive approach is required or when long-term management is needed.

Some of the same treatment strategies are used for disease prevention. **Prevention** includes strategies to avoid the development of disease in individuals or groups. Such strategies may include screening, vaccinations, lifestyle changes, or prophylactic interventions (e.g., medication to reduce high cholesterol levels to prevent strokes, mastectomy in a person at high risk of developing breast cancer).

Recovering from a disease and limiting any residual effects are important aspects of disease management. **Convalescence** is the stage of recovery following a disease, which may last for days or months. **Prognosis** refers to an individual's likelihood of making a full recovery or regaining normal functioning. The death rate from a particular disease is referred to as **mortality**. **Complications** are new problems that arise because of a disease. For example, renal failure can be a complication of uncontrolled hypertension or diabetes mellitus.

Understanding the factors that affect the health and diseases experienced by populations is the cornerstone to understanding prevention and containment. **Epidemiology** is the branch of science that analyzes patterns of diseases in a group of people. Such tracking of disease patterns includes the occurrence, incidence, prevalence, transmission, and distribution of a disease. **Morbidity** refers to disease rates within a group. **Epidemics** occur when increasing numbers of people have a certain disease within a specific group. When the epidemic expands to a larger population, it becomes a **pandemic**.

Summary

Pathophysiology is the basis for understanding the intricate world of the human body, its response to disease, and the rationale for treatment. Understanding pathophysiology can assist the nurse to better anticipate situations, correct issues, and provide appropriate care. The concepts of health and disease, although complex, need not cause stress to nursing students or patients. Instead, these concepts can open a world of wonder of which to be in awe.

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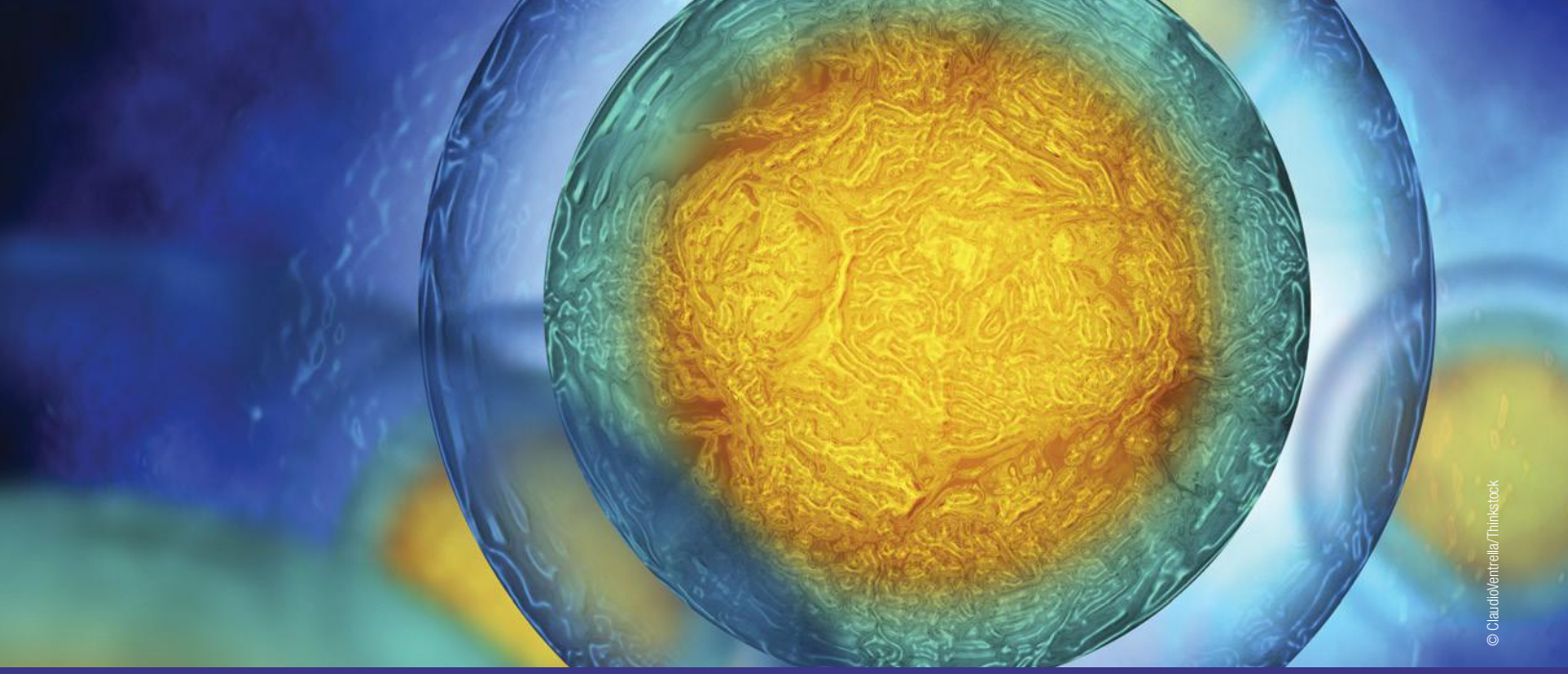


CHAPTER 1
Cellular Function

LEARNING OBJECTIVES

- Describe basic cellular structures and function.
- Discuss how cells exchange materials.
- Identify how cells obtain and produce energy.
- Explain how cells replicate and specialize.
- Describe the different types of tissues.
- Describe common cellular adaptations and possible reasons for the occurrence of each.
- List common causes of cell damage.
- Discuss cancerous cellular damage.
- Describe common genetic and congenital alterations.

KEY TERMS

active transport
adaptation
alleles
anaphase
anaplasia
apoptosis
atrophy
autosomal dominant
autosomal recessive
autosome
benign
cancer
carcinogenesis
caseous necrosis
cell membrane
chromosome
coagulative necrosis
congenital
crenation
curative
cytoplasm
deoxyribonucleic acid (DNA)
differentiation
diffusion
dominant
dry gangrene
dysplasia
electrolyte
endocytosis
enzyme
exocytosis
facilitated diffusion
fat necrosis
free radicals
gangrene
gas gangrene
genes
genetics
glucose
grading
heterozygous
homozygous
hyperplasia
hypertrophy
initiation
ischemia
infarction
karyotype
lipid bilayer
liquefaction necrosis
lysis
malignant
meiosis
metaphase
metaplasia
metastasize
mitosis
multifactorial disorders
necrosis
neoplasm
nucleotide
nucleus
organelle
osmosis

osmotic pressure
palliative
phagocytosis
phenotype
pinocytosis
plasma membrane
prognosis
programmed cell death
progression
proliferation
promotion
prophase
prophylactic
protoplasm
recessive
remission
selectively permeable
sex-linked
telophase
teratogens
TNM staging
tumor
wet gangrene

Pathophysiology understanding begins with exploring the basic building blocks of living organisms. Cells give organisms their immense diversity. Organisms can be made up of a single cell, such as with bacteria or viruses, or billions of cells, such as with humans. In humans, these building blocks work together to form tissues, organs, and organ systems. These basic units of life are also the basic units of disease. As understanding increases about specific diseases, many diseases can be explained at the cellular level. Diseases are likely to occur due to some loss of homeostatic control, and the impact is evident from the cellular level up to the system level. Understanding the various cellular dysfunctions associated with diseases has led to improved prevention and treatment of those diseases. Therefore, understanding basic cellular function and dysfunction is essential to understanding pathophysiology.

Basic Cell Function

Cells are complex mini-organisms resulting from millions of years of evolution. These mini-organisms come together to form specialized tissues with specific functions, and these tissues then form organs with precise purposes. Organs, in turn, form systems that are responsible for maintaining and performing complex actions and meeting the body's needs. This organized interaction is essential to life and optimal health.

Cells can arise only from another, preexisting cell. Genes interact with the cells to ensure they are specialized for a particular purpose—a process called differentiation. Although they vary greatly in size and shape (FIGURE 1-1), cells have the remarkable ability to exchange materials with their immediate surroundings, obtain energy from organic nutrients, synthesize complex molecules, and replicate themselves.

The basic components of cells include the cytoplasm, organelles, and cell membrane. The **cytoplasm**, or **protoplasm**, is a colorless, viscous liquid containing water, nutrients, ions, dissolved gases, and waste products; this liquid is where the cellular work takes place. The cytoplasm supports all of the internal cellular structures called **organelles** (FIGURE 1-2). Organelles ("little organs") perform the work that maintains the cell's life (TABLE 1-1). The cytoplasm also surrounds the nucleus. The **nucleus**, which acts as the control center of the cell, contains all the genetic information (deoxyribonucleic acid [DNA]) and is surrounded by a double membrane (FIGURE 1-3). The nucleus regulates cell growth, metabolism, and reproduction. The **cell membrane**, also called the **plasma membrane**, is the semipermeable boundary containing the cell and its components (FIGURE 1-4). A **lipid bilayer**, or fatty double covering, makes up the membrane. The interior surface of the bilayer is uncharged and primarily made up of lipids, whereas the exterior surface is charged and is less fatty than the interior surface (i.e., lipid bilayer). This fatty cover protects the cell from the aqueous environment in which it exists, while allowing it to be permeable to some molecules but not others.

Exchanging Material

Cellular permeability is the ability of the cell to allow passage of some substances through the membrane, while not permitting others to enter or exit. To accomplish this function, cells have gates that may be opened or closed by proteins, chemical signals, or electrical charges. Being **selectively permeable** allows the cell to maintain a state of internal balance, or homeostasis. Some substances have free passage in and out of the cells, including enzymes, glucose, and electrolytes. **Enzymes** are proteins that facilitate chemical reactions in cells, while **glucose** is a sugar molecule that provides energy. **Electrolytes** are chemicals that are charged conductors when they are dissolved in water. Passage across the cell

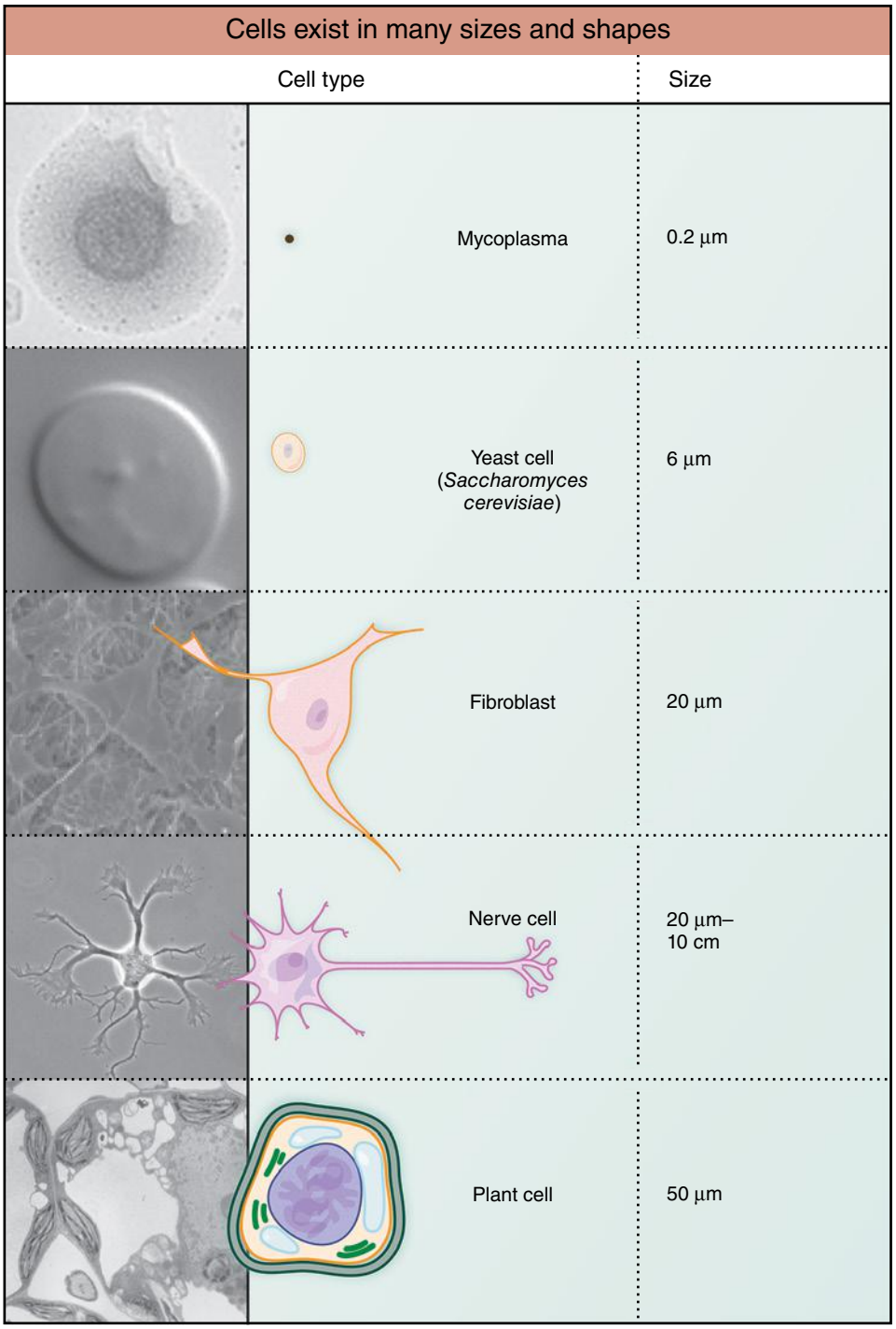


FIGURE 1-1 Cells vary greatly in size and shape. Some cells are spherical, while others are long extensions.

Courtesy of Tim Pietzcker, Universitat Ulm University.

Courtesy of Fred Winston, Harvard Medical School.

Courtesy of Junzo Desaki, Ehime University School of Medicine.

Courtesy of Gerald J. Obermair and Bernhard E. Flucher, Innsbruck Medical Universit.

Courtesy of Ming H. Chen, University of Alberta.

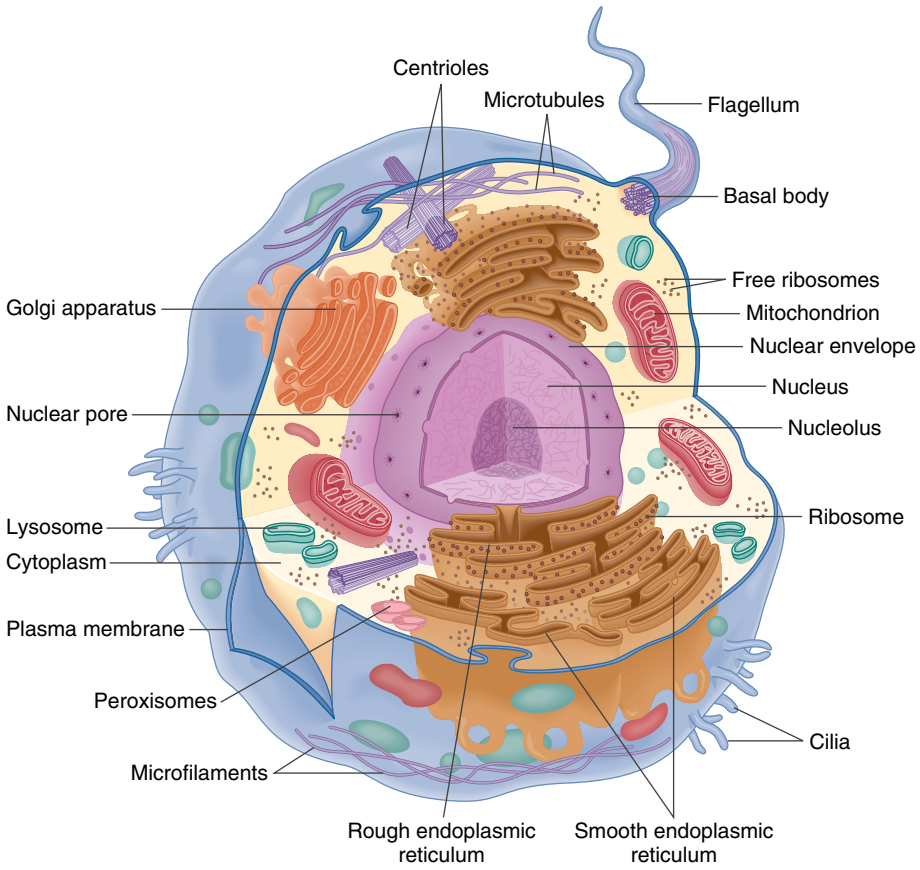


FIGURE 1-2 The basic human cell.

TABLE 1-1 Overview of Cell Organelles

Organelle	Structure	Function
Nucleus	Largest organelle. Round or oval body surrounded by a nuclear envelope (a lipid bilayer membrane that allows for communication with the rest of the cell).	Contains the genetic information necessary for control of the cell's structure, function, and replication. In the nucleus, histones (proteins) bind deoxyribonucleic acid (DNA) to form chromosomes, and DNA contains sections of genes that hold hereditary information.
Nucleolus	Round or oval body in the nucleus.	Produces ribosomal ribonucleic acid (RNA) subunits (rRNA) and sends them out into the cell, where they form ribosomes.
Endoplasmic reticulum (ER)	Network of membranous tubules in the cytoplasm of the cell that is a continuation or extension of the nucleus. Smooth endoplasmic reticulum (SER) contains no ribosomes. Rough endoplasmic reticulum (RER) is studded with ribosomes.	SER produces lipids and hormones, stores and metabolizes calcium ions, and performs a variety of other functions depending on the cell type (e.g., metabolizing wastes in the liver). RER is the site of the synthesis and transport of lysosomal enzymes and proteins for intracellular (e.g., Golgi apparatus) and extracellular use.
Ribosomes	Small particles found in the cytoplasm (free) or attached to the ER that are made of rRNA and protein.	Aid in protein production on the RER and form polysomes (clusters of ribosomes held together by messenger RNA).
Golgi complex	Series of flattened sacs usually located near the nucleus.	Sorts, chemically modifies, and packages proteins produced in the RER.

Organelle	Structure	Function
Secretory vesicles	Membrane-bound vesicles containing proteins produced by the RER and repackaged by the Golgi complex. Contain protein hormones or enzymes.	Store protein hormones or enzymes in the cytoplasm, awaiting a signal to release them from the cell.
Food vacuole	Membrane-bound vesicle containing material engulfed by the cell.	An intercellular stomach that stores ingested material and combines it with lysosomes to be broken down.
Lysosome	Round, membrane-bound structure containing digestive enzymes.	Combines with food vacuoles and digests materials (e.g., bacterial and viruses) engulfed by cells. Also digests excessive or worn-out organelles.
Peroxisomes	Small structures containing enzymes.	Contain enzymes crucial for metabolic activity. Break down various potentially toxic intracellular molecules (e.g., fatty acids). Also play a role in alcohol digestion.
Mitochondria	Round, oval, or elongated structures with a double membrane. The inner membrane is shaped into folds.	Primarily responsible for cellular respiration and energy production. Act much like the digestive system, by consuming nutrients, breaking them down, and creating energy-rich molecules for the cell. Complete the breakdown of glucose, producing nicotine adenine dinucleotide and adenosine triphosphate (ATP) for cellular energy (a process called cellular respiration).
Cytoskeleton	Network of microtubules and microfilaments in the cell.	Gives the cell internal support, helps transport molecules and some organelles inside the cell, and binds to enzymes of metabolic pathways.
Cilia	Small projections of the cell membrane containing microtubules. Found on a limited number of cells.	Propel materials along the surface of certain cells.
Flagella	Large projections of the cell membrane containing microtubules. In humans, found only on sperm cells.	Provide motive force for sperm cells.
Centrioles	Small cylindrical bodies composed of microtubules arranged in nine sets of triplets. Found in animal cells, but not in plant cells.	Help organize the spindle apparatus necessary for cell division.

membrane may occur through several mechanisms, including diffusion, osmosis, facilitated diffusion, active transport, endocytosis, and exocytosis. Exchanging material is critical in maintaining bodily functions, so disruption of any of these mechanisms can result in disease development.

Diffusion, or simple diffusion, is the movement of solutes—that is, particles dissolved in a solvent (i.e., liquid)—from an area of higher concentration to an area of lower concentration (**FIGURE 1-5**). The degree of diffusion depends on the permeability of the membrane and the concentration gradient, which is the difference in the concentrations of substances on either side of the membrane. Simple diffusion will continue to occur until

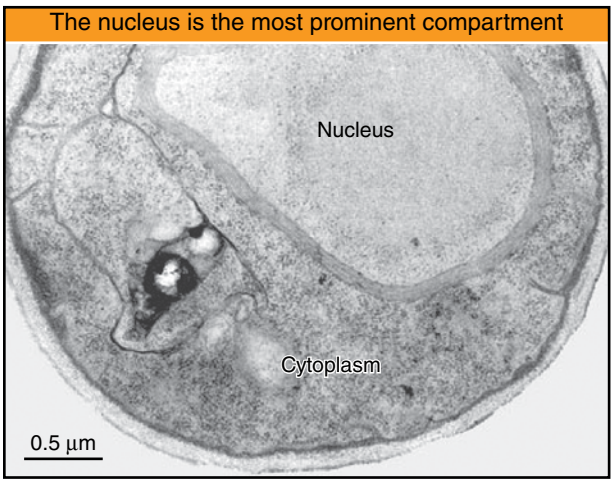


FIGURE 1-3 Although the proportion of the cell that is taken up by the nucleus varies according to cell type, the nucleus is usually the largest and most prominent cellular compartment.

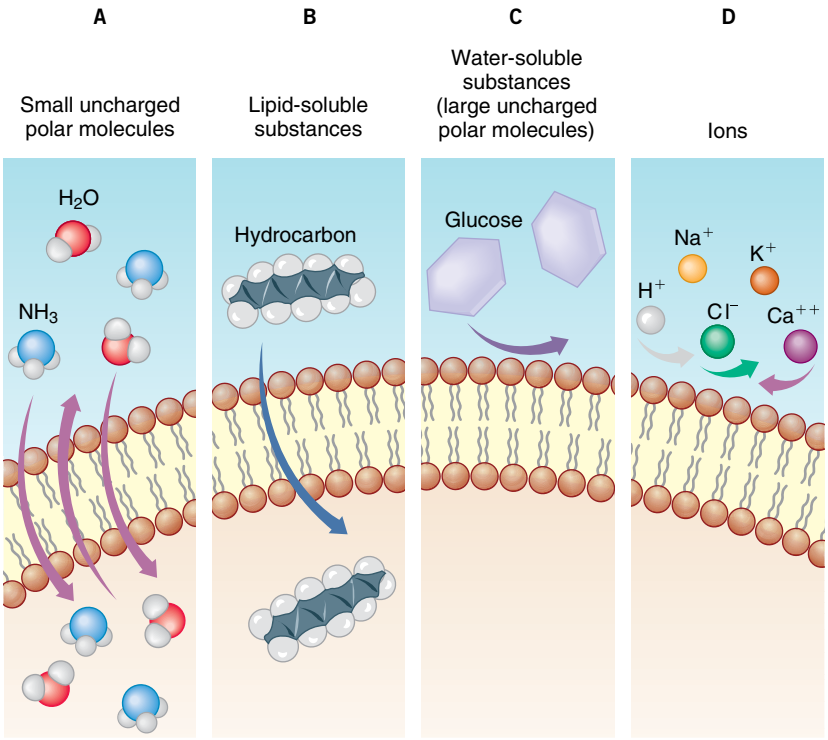


FIGURE 1-4 A selectively permeable membrane maintains homeostasis by allowing some molecules to pass through, while preventing others from entering or exiting.

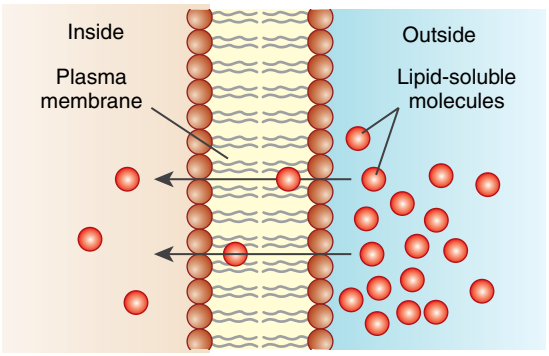


FIGURE 1-5 Lipid-soluble substances pass through the membrane directly by simple diffusion.

the concentrations of particles are equal on both sides of the membrane. Smaller particles (e.g., water) and lipid-soluble particles (e.g., steroids) diffuse more easily than larger ones, and less viscous solutions diffuse more rapidly than thicker solutions. Additionally, the thinner and more permeable the membrane, the faster particles will diffuse across. Many substances, such as oxygen, enter the cell through diffusion.

Learning Points

Simple Diffusion

To illustrate simple diffusion, consider an elevator filled beyond capacity with people. When the door opens, the people near the door naturally fall out—moving from an area of high concentration to an area with less concentration without exerting any effort or energy. In the body, gases are exchanged in the lungs by diffusion. Unoxygenated blood enters the pulmonary capillaries (low concentration of oxygen, high concentration of carbon dioxide), where it picks up oxygen from the inhaled air of the alveoli (high concentration of oxygen, low concentration of carbon dioxide), while dropping off carbon dioxide to the alveoli to be exhaled.

Learning Points

Osmosis

To understand osmosis, envision a plastic bag filled with sugar water and with holes punched in it that allow only water to pass through them. If this bag is submerged in distilled water (which contains no impurities), the bag will begin to swell because the water is attracted to the sugar. The water shifts to the areas with higher concentrations of sugar in an attempt to dilute the sugar concentrations (**FIGURE 1-6**). In our bodies, the process of osmosis allows the cells to remain hydrated.

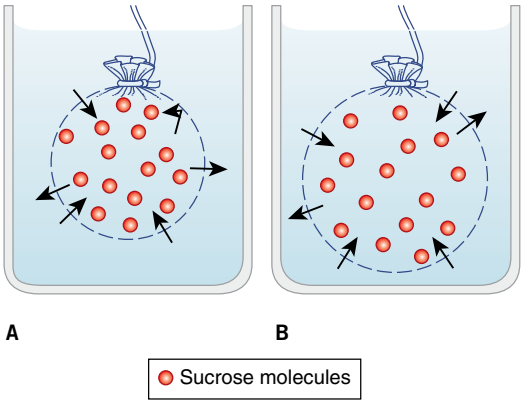


FIGURE 1-6 **(A)** When a bag of sugar water is immersed in a solution of pure water, **(B)** water will diffuse into the bag toward the lower concentrations of water, causing the bag to swell.

Facilitated diffusion is the movement of substances from an area of higher concentration to an area of lower concentration with the assistance of a carrier molecule (**FIGURE 1-7**). Energy is not required for this process, and the number of molecules that can be transported in this way is directly equivalent to the concentration of the carrier molecule. Insulin transports glucose into the cells using this method.

Water is critical to cellular survival. **Osmosis** is the passive movement of water or another solvent across the cellular membrane from an area of low solute concentration to an area of high solute concentration. The membrane is permeable to the solvent (liquid) but

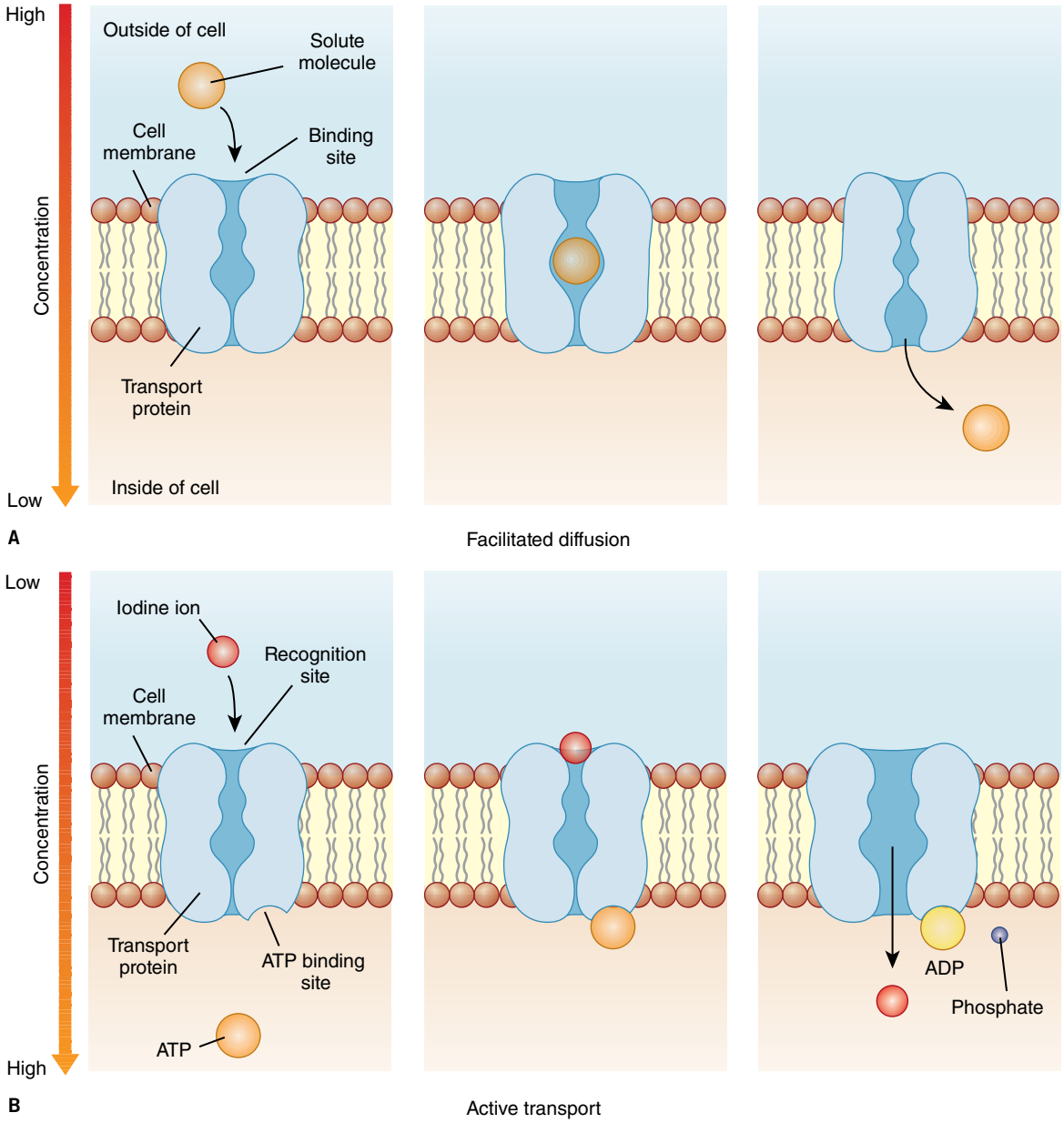


FIGURE 1-7 Facilitated diffusion and active transport. **(A)** Water-soluble molecules can also diffuse through membranes with the assistance of proteins in facilitated diffusion. **(B)** Other proteins use energy from ATP to move against concentration gradients in a process called active transport.

not to the solute (dissolved particles). The movement of the solvent usually continues until concentrations of the solute equalize on both sides of the membrane. **Osmotic pressure** refers to the tendency of water to move by osmosis—in other words, the solute's ability to attract water. This ability depends on the concentration of the solute. If too much water enters the cell membrane, the cell will swell and burst (**lysis**). If too much water moves out of the cell, the cell will shrink (**crenation**). Osmosis helps regulate fluid balance in the body; an example can be found in the functioning of the kidneys. In addition to osmotic pressure, hydrostatic and colloid osmotic pressures cause the movement of water (see the *Fluid, Electrolyte, and Acid–Base Homeostasis* chapter).

Active transport is the movement of a substance from an area of lower concentration to an area of higher concentration, against a concentration gradient (Figure 1-7). This movement requires a carrier molecule and energy (usually adenosine triphosphate [ATP]) because of the effort necessary to go against the gradient. The sodium–potassium (Na^+-K^+) pump is an example of active transport.

Endocytosis is the process of bringing a substance into the cell (FIGURE 1-8). The cell membrane surrounds the entering particles, engulfing them. **Phagocytosis**, or cell eating, occurs when this process involves solid particles. **Pinocytosis**, or cell drinking, takes place when this process involves a liquid. Components of the immune system use endocytosis,

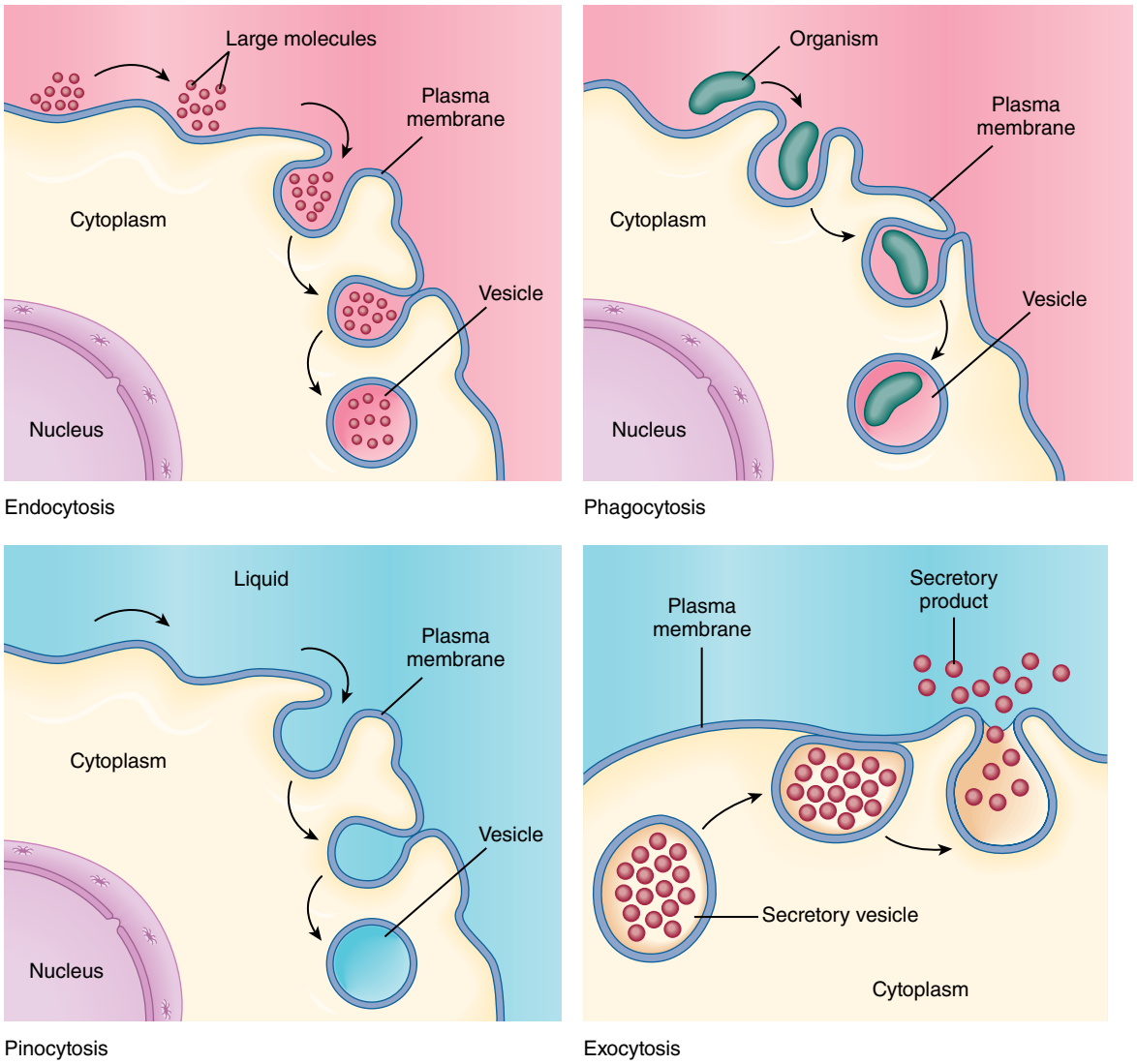


FIGURE 1-8 **(A)** Cells can engulf large particles, cell fragments, liquids, and even entire cells. **(B)** Cells can also get rid of large particles.

and particularly phagocytosis, to consume and destroy bacteria and other foreign material. **Exocytosis** is the release of materials from the cell, usually with the assistance of a vesicle (a membrane-bound sac) (Figure 1-8). Often glands secrete hormones using exocytosis.

Learning Points

Active Transport

To understand active transport, consider the overfilled elevator again. If the door opens and someone from outside the elevator attempts to get in, it will require a great deal of effort (energy) to enter the already full elevator. The sodium–potassium pump is an example of active transport in the body. Energy is required both to move sodium out of a cell, where the concentrations are high, and to move potassium into a cell, where the concentrations are high.

Energy Production

Cellular energy can be a mystery to many of us. To understand this energy, first we must understand that it comes in many forms (FIGURE 1-9). Cells can obtain energy from two main sources: the breakdown of glucose (a type of carbohydrate) and the breakdown of triglycerides (a type of fat). When these sources are not readily available, cells can turn to protein for energy.

The energy production process begins when food enters the gastrointestinal tract, where it is broken down into sugars, amino acids, and fatty acids. These substances are then either converted to larger molecules (e.g., glucose to glycogen, amino acids to proteins, and fatty acids to triglycerides and fats), stored until needed, or metabolized to make ATP. When used to make ATP, all three sources of energy must first be converted to acetyl coenzyme A (acetyl CoA). Through glycolysis, glucose is converted to pyruvate in the cytoplasm; the pyruvate is then converted to acetyl CoA. Amino acid catabolism also produces acetyl CoA, and fatty acids are oxidized to be converted to acetyl CoA as well. The acetyl CoA from all of these sources enters the Krebs cycle (i.e., the citric acid cycle), a high-electron-producing process that occurs inside the mitochondria. During the Krebs cycle, these molecules go through a complex series of reactions that consume oxygen, produce carbon dioxide and water as waste products, and convert adenosine diphosphate (ADP) to ATP.

This process works best when oxygen is readily available (i.e., aerobic respiration), but energy can be produced less efficiently when

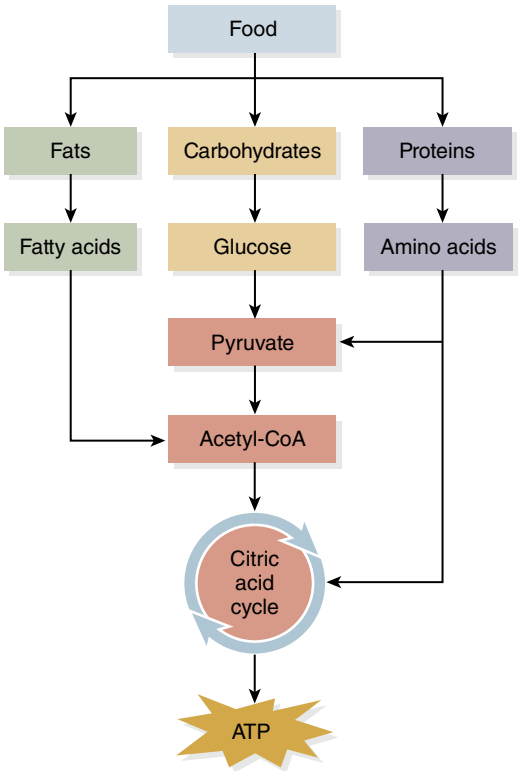


FIGURE 1-9 Energy production.

oxygen is not readily available (e.g., tissue hypoxia and exercise) through anaerobic respiration. Glycolysis does not need oxygen, but the pyruvate produced in the anaerobic process will be converted to lactic acid instead of acetyl CoA without it. Lactic acid excess can cause muscle pain and fatigue, metabolic acidosis, kidney failure, respiratory failure, and death.

Replication and Differentiation

A cell's basic requirement for life is ensuring that it can reproduce. Many cells divide numerous times throughout the life span, whereas others die and are replaced with new cells. **Proliferation** is the regulated process by which cells divide and reproduce. Genes (e.g., proto-oncogenes) and growth factor proteins (e.g., cytokines and erythropoietin) regulate this process, by either stimulating it or suppressing it. Environmental factors (e.g., temperature, chemical exposure, nutrition, and infections) at any stage of life can influence proliferation either positively or negatively.

The most common form of cell division, in which the cell divides into two separate cells, is **mitosis** (FIGURE 1-10). In mitosis, the division of one cell results in two genetically identical and equal daughter cells (i.e., diploid cells). This process involves four steps: prophase,

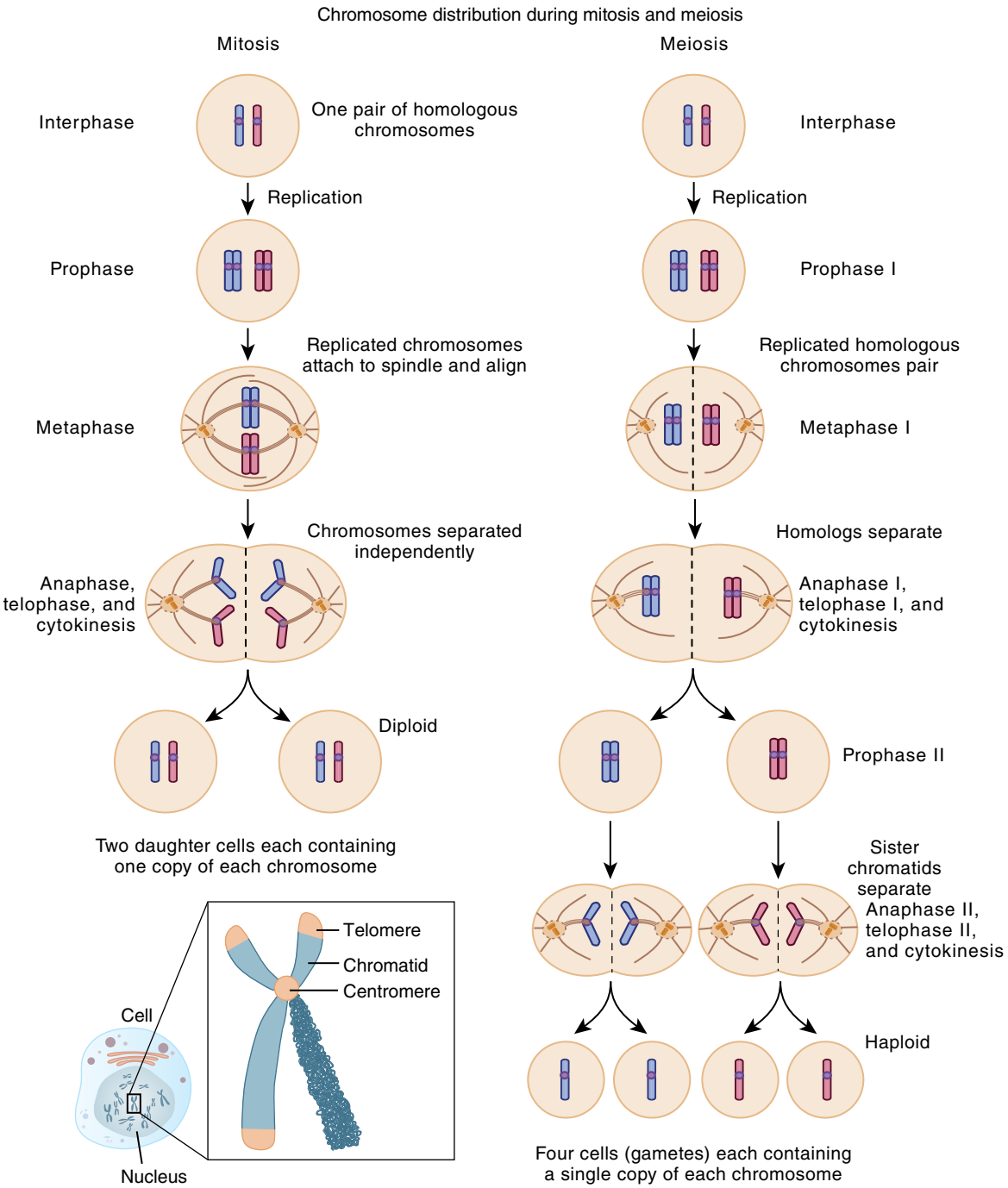


FIGURE 1-10 Mitosis and meiosis.

metaphase, anaphase, and telophase. In **prophase**, the chromosomes condense, and the nuclear membrane disintegrates. In **metaphase**, the spindle fibers attach to centromeres, and the chromosomes align. The chromosomes separate and move to opposite poles in **anaphase**. Finally, the chromosomes arrive at each pole, and new membranes are formed in **telophase**.

The average cell will divide 50 to 70 times before it dies. As the cell divides, the telomere on the end of the chromosome gets smaller—a mechanism of cell aging, according to the Hayflick limit theory. The telomere shortens with each division until it is no longer present, causing the cell to be broken down by programmed cell death.

Interphase refers to the period of the cycle between each mitosis phase. A typical cell spends most of its life in interphase. During this period, the cell is growing and preparing for mitosis—that is, organelles double in number,

DNA replicates, protein is synthesized, and the environment is assessed and primed.

Meiosis is a form of cell division that occurs only in mature sperm and ova (Figure 1-10). Meiosis also has four phases (prophase, metaphase, anaphase, and telophase) and is separated by an interphase. In males, testicles continuously produce sperm, and then the sperm travels to the epididymis to mature (i.e., spermatogenesis) and be stored until released during ejaculation. In females, a set number of ova are present at birth and mature in the ovaries (oogenesis). One or more eggs are released once a month during ovulation, approximately 2 weeks before menstruation starts. In the ovaries, the ova remain in the prophase for up to 45 years.

As the woman and her ova age, the risk of abnormal meiosis resulting in chromosomal defects increases. Normally, human cells contain 46 chromosomes, but sperm and ova contain 23 chromosomes each (i.e., haploid cells). One of the chromosomes determines sex. When a sperm and ovum join, the resulting organism (i.e., zygote) has 46 chromosomes (23 pairs). The zygote gets one sex chromosome from the ovum and one from the sperm. If the resulting pair is XX (homologous), the resulting fetus will be female. If the resulting pair is XY (heterologous), the resulting fetus will be male.

Differentiation is the process by which cells become specialized in terms of their type, function, structure, and cell cycle (FIGURE 1-11). Through this process, the primitive stem cells of the embryo (i.e., pluripotent) develop into more than 200 highly specialized cells found in the human body (e.g., cardiac cells and nerve cells). In the first 24 hours after fertilization, the zygote rapidly grows, producing cells as it does so (i.e., cleavage). Over the next few weeks, cells start developing into two groups. The outer layer forms tissue that supports the embryo (e.g., placenta),

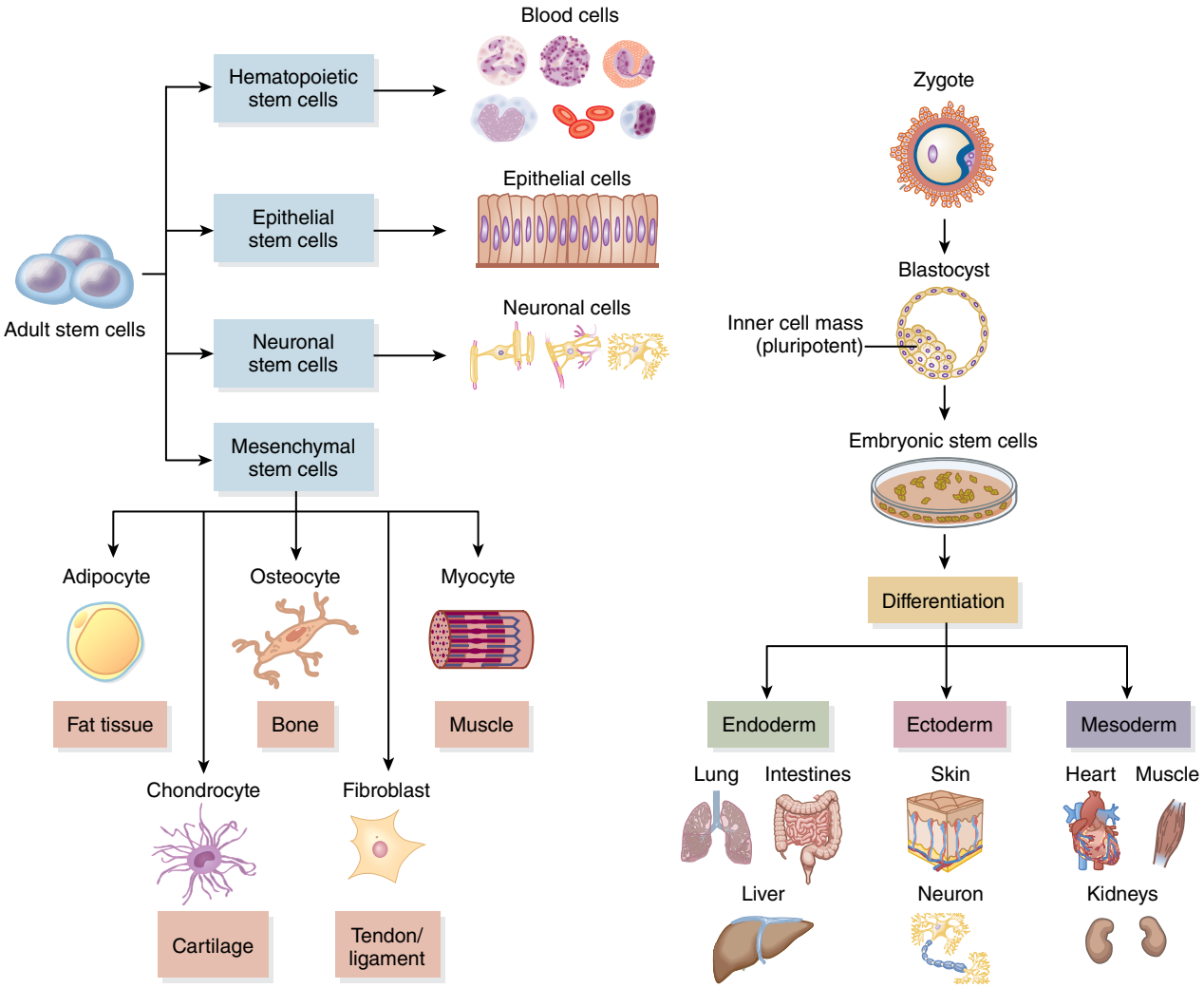


FIGURE 1-11 Differentiation.

and the inner core forms the different tissues and organs. The inner core divides into three germ layers—ectoderm, mesoderm, and endoderm. The ectoderm (outer layer) differentiates into the epidermis, hair, nails, brain, spinal cord, and peripheral nervous system. The mesoderm (middle layer) differentiates into the muscle, bone, connective tissue, kidneys, gonads, and circulatory system. The endoderm (inner layer) differentiates into the gastrointestinal tract, colon, liver, bladder, and lungs.

Gene expression and growth factor proteins (e.g., fibroblast growth factor and vascular endothelial growth factors) stimulate differentiation. This process does not begin until approximately 15 to 60 days after the sperm fertilizes the ovum. During this time, the embryo is highly susceptible to damage from environmental influences. However, environmental factors (e.g., temperature, chemical exposure, nutrition, and infections) at any stage of life can influence differentiation both positively and negatively.

The stem cells found in the embryo are also present in adulthood. These somatic cells maintain and repair tissue, but they are multipotent in adulthood—that is, they can only make cells from their same type. For example, blood stem cells can make any type of blood cell (e.g., erythrocyte, leukocyte, or platelets). All stem cells can proliferate into more undifferentiated stem cells and differentiate into more specialized cells. Embryonic stem cells have been used to test new drugs (e.g., antitumor drugs) and show promise as a treatment for macular degeneration, spinal cord injury, stroke, burns, heart disease, diabetes mellitus type 1, osteoarthritis, and rheumatoid arthritis. Adult stem cells found in cord and placental blood as well as bone marrow have been used to treat leukemias (National Institutes of Health [NIH], 2016).

Learning Points

Emerging Research: Precision Medicine

In 2016, the National Institutes of Health (NIH) was charged with making precision medicine a priority (Holst, 2015). Precision medicine is an approach to disease treatment and prevention strategies that takes into account the similarities and differences among individuals. The traditional approach to care is a standardized treatment for all. In contrast, the individual's genes, microbiome, environment, and lifestyle are considered when determining treatment strategies with precision medicine.

As a part of this initiative, NIH started the *All of Us* research program. This program is collecting information on participants' medical history, lifestyle, and physical measurements (e.g., blood pressure, height, weight), as well as blood and urine samples to be used to develop preventive care and treatments (NIH, 2019). Targeted molecular drugs or therapy, also called *precision drugs*, have already been developed for several diseases such as cystic fibrosis. In cancer, several types of targeted drug therapies are available, such as monoclonal antibodies (immunotherapy) and hormones. In comparison to traditional chemotherapy, these drugs are designed to attack only the cancer cells, while having less effect on normal cells.

Tissue

Many cells in the body are organized into tissues and work together to perform specific functions. Two or more tissues can combine to form organs that perform a specific function, and groups of organs working together form systems. Humans have four basic types of tissues: epithelial, connective, muscular, and nervous (**FIGURE 1-12**).

Epithelial Tissue

Epithelial tissue is made up of tightly packed sheets of cells, allowing them to act as a barrier (**TABLE 1-2**). These sheets of cells can be present as a single layer (i.e., simple epithelium) or as multiple layers (i.e., stratified epithelium). Epithelial tissue is made up of three types of cells—squamous, cuboidal, and columnar. This type of tissue lines exterior (e.g., skin) and interior (e.g., body cavities, gastrointestinal tract, and hollow organs) surfaces. In addition to serving as a barrier, epithelial tissue is involved in absorption (e.g., lungs and small intestines), secretion (e.g., mucus), excretion, and movement of substances.

Connective Tissue

Connective tissue consists of cells suspended in an extracellular matrix (**FIGURE 1-13**). This matrix is typically made up of protein (e.g., collagen and fibrin) in a solid, liquid, or semi-solid substance. Connective tissue supports and connects other tissues. Connective tissue may be either loose (most common) or dense. Loose connective tissue supports organs and blood vessels as well as connects epithelial tissue to muscle. Dense connective tissue is fibrous and found in the tendons and ligaments that connect muscles to bone and bones to each other. Other forms of connective tissue includes adipose tissue, bone, cartilage, and blood.

Muscle Tissue

Muscle tissue is made up of cell fibers (i.e., myocytes) that contain contractile proteins

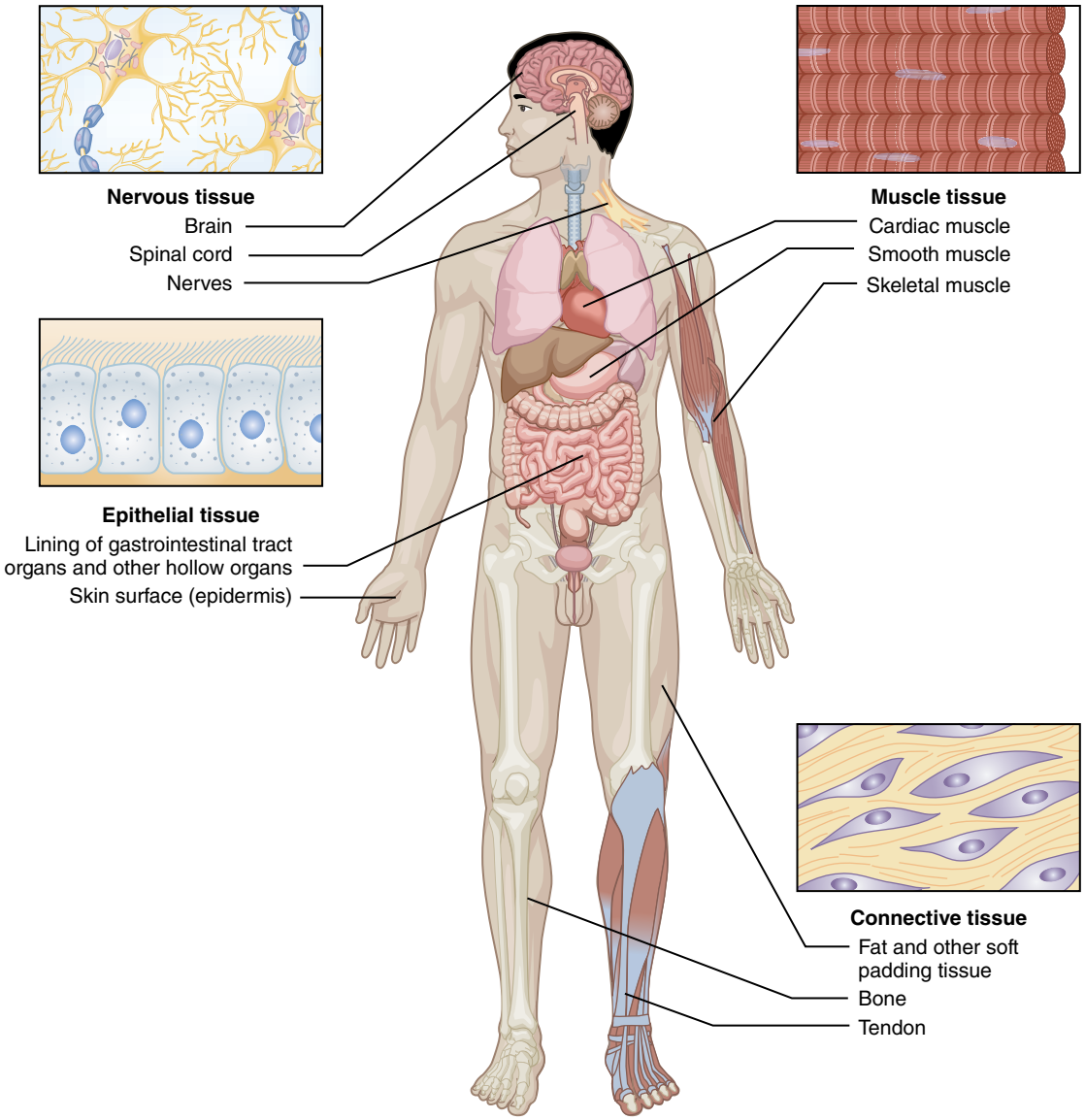
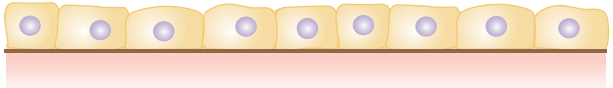


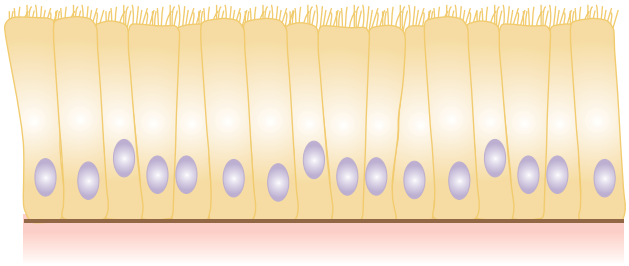
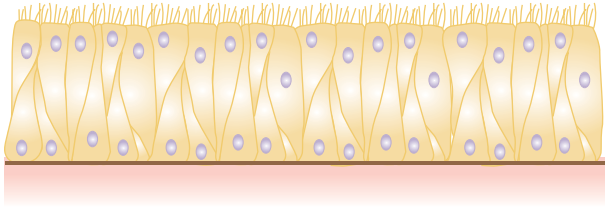
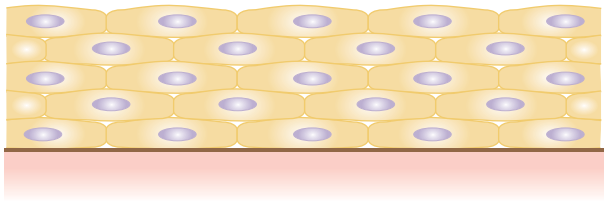
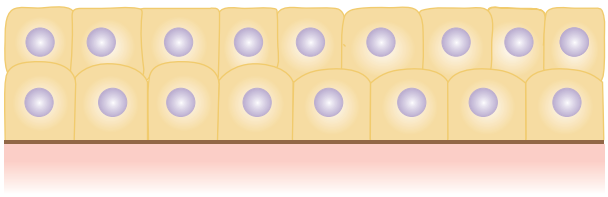
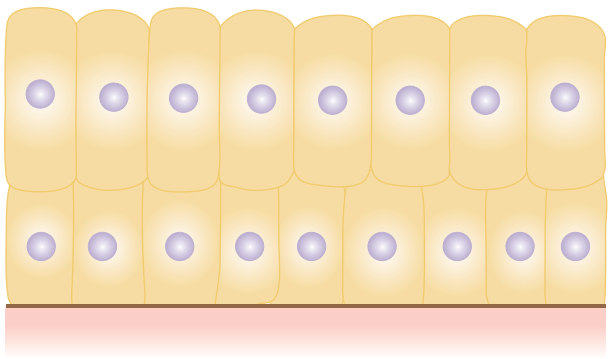
FIGURE 1-12 Types of tissue.

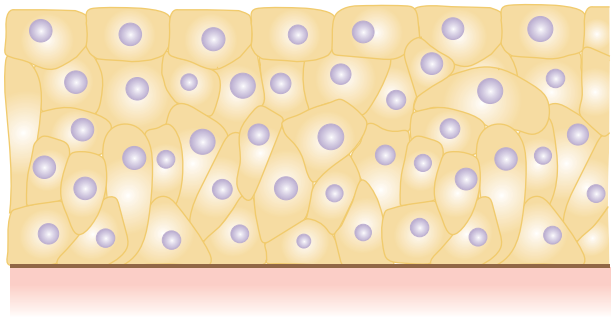
TABLE 1-2 Epithelial Tissue Cells

Cells	Locations	Function
Simple squamous epithelium 	Alveoli in the lungs and the lining of the heart, blood vessels, and lymphatic vessels	Permits materials to exchange through diffusion and filtration and secretes lubricating substances
Simple cuboidal epithelium 	Ducts and secretory portions of small glands as well as the kidney tubules	Secretes and absorbs

(*continues*)

TABLE 1-2 Epithelial Tissue Cells (*Continued*)

Cells	Locations	Function
Simple columnar epithelium 	Ciliated tissues including the bronchi, uterine tubes, and uterus; smooth (nonciliated) tissues are found in the digestive tract bladder	Absorbs; secretes mucus and enzymes
Pseudostratified columnar epithelium 	Ciliated tissue lines the trachea and a majority of the upper respiratory tract	Secretes mucus; ciliated tissue shifts mucus
Stratified squamous epithelium 	Lines the esophagus, mouth, and vagina	Prevents abrasion
Stratified cuboidal epithelium 	Sweat, salivary, and mammary glands	Protects
Stratified columnar epithelium 	The male urethra and the ducts of some glands	Secretes and protects

Cells	Locations	Function
Transitional epithelium 	Lines the bladder, urethra, and ureters	Allows for expansion of the urinary organs

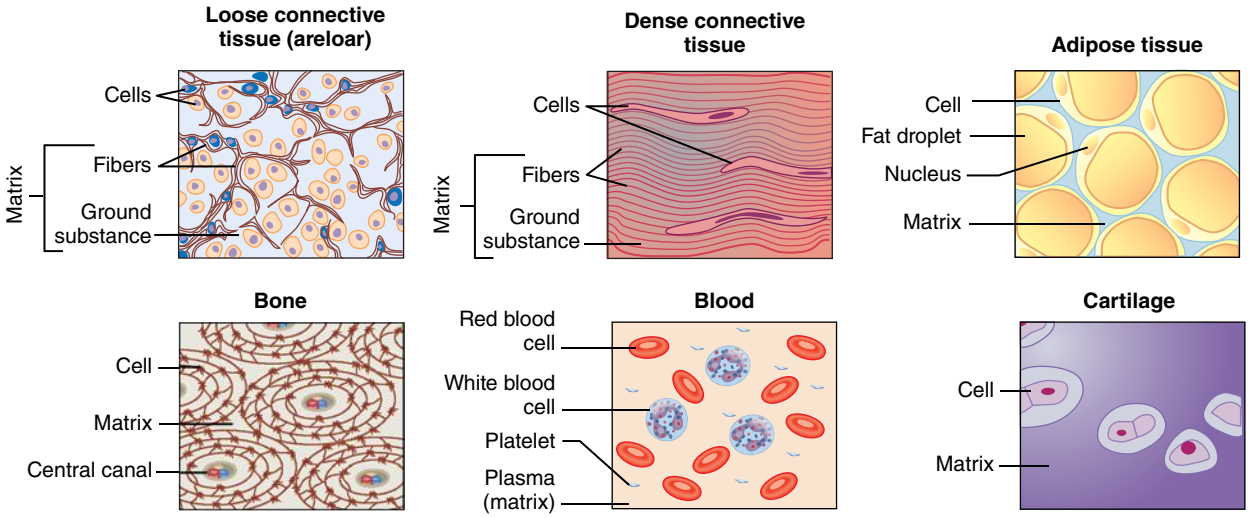


FIGURE 1-13 Types of connective tissues.

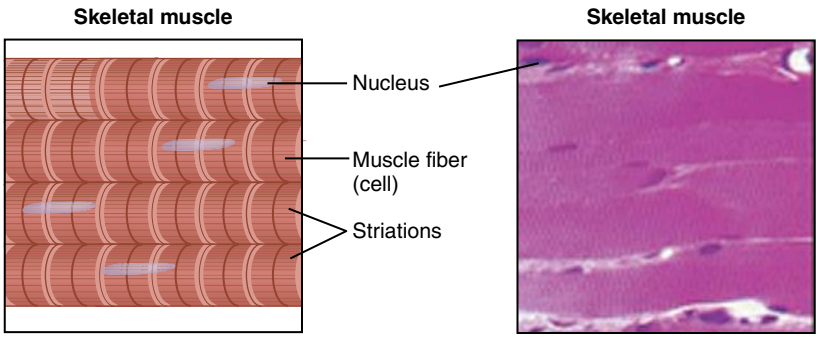
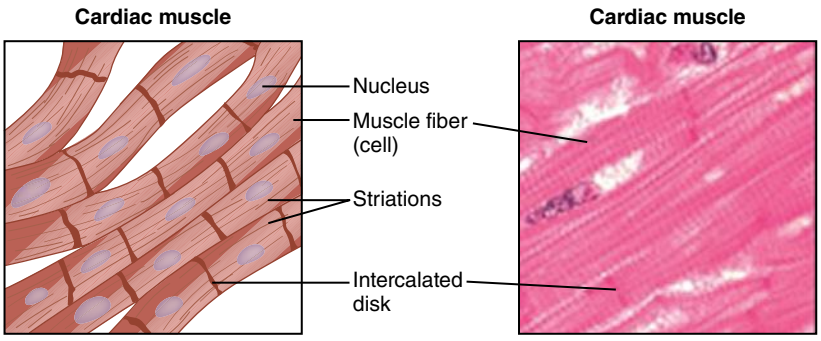
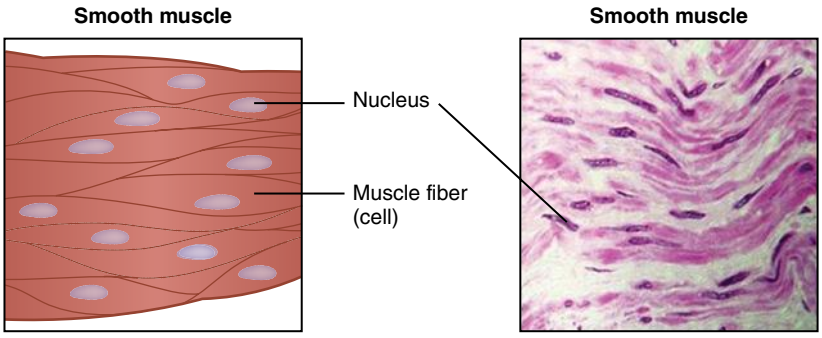
(i.e., actin and myosin) (**TABLE 1-3**). Muscle fibers contract when myosin pulls the actin filaments, causing them to slide over themselves. The myosin attaches to the actin when calcium is released from smooth endoplasmic reticulum (ER) inside the muscle fibers. Impulses from nerve cells (i.e., motor neurons) and neurotransmitters (i.e., acetylcholine) trigger this release of calcium from the muscle fiber. Once the calcium causes the head of the myosin to attach to the actin filament, ATP in the muscle provides the energy needed to pull the actin filament inward. To meet the muscle fibers' high energy needs, ATP is recycled repeatedly in rapid succession. During vigorous activity, ATP stores become depleted, oxygen levels drop sharply, glucose production ceases, and lactic acid accumulates.

Muscle tissue allows the body to maintain an upright stance and to move, and it helps substances such as blood and food move through the body. Muscles may be under voluntary or involuntary control. Three main types of muscles are distinguished: skeletal, cardiac, and smooth. Skeletal muscle tissue is striated or striped. This tissue attaches bone to tendons and allows for voluntary movement. Cardiac muscle is found in the walls of the heart and is also striated, but it is not under voluntary control. Cardiac muscle fibers are connected by intercalated disks that allow them to contract in coordination. Smooth muscle tissue is found in the walls of blood vessels, gastrointestinal tract, uterus, urinary bladder, and other internal structures. This tissue is not striated, and it is under involuntary control.

Nervous Tissue

Nervous tissue senses, processes, and responds to internal and external stimuli. It consists of two basic types of cells: neurons and neuroglia

TABLE 1-3 Muscle Tissue

Characteristics	
• Long and cylindrical • Multinucleated • Striated • Voluntary	
• Shorter and branched • Uninucleated • Striated • Involuntary • Intercalated disks	
• Spindle-shaped • Uninucleated • Nonstriated • Involuntary	

Images in column 3 are Courtesy of the Centers for Disease Control and Prevention.

(FIGURE 1-14). Neurons, the basic functional units of nervous tissue, generate and transmit nerve impulses. These cells can occur in several sizes and shapes, but they all share similar characteristics. Neurons do not have the ability to divide, and they require a constant supply of oxygen and glucose. Neurons contain projections called axons that transmit impulses away from the cell body, as well as dendrites that make connections with nearby cells and transmit impulses toward the cell body. Neuroglia cells scaffold neural tissue (e.g., astrocytes and ependymal cells), isolate and protect neurons, speed up nerve transmission (e.g., Schwann cells), regulate interstitial fluid, defend neurons against pathogens, and assist with neural repair.

Cellular Adaptation and Damage

Cellular Adaptation

Cells are constantly exposed to a variety of environmental factors that can cause damage. Cells attempt to prevent their own death from environmental changes through **adaptation**. That is, they may modify their size, numbers, or types in an attempt to manage these

changes and maintain homeostasis. Adaptation may involve one or a combination of these modifications. These modifications may be considered normal or abnormal depending on whether they were mediated through standard pathways. They may also be permanent or reversible. Once the stimulus is removed, however, adaptation ceases. Specific types of adaptive changes include atrophy, hypertrophy, hyperplasia, metaplasia, and dysplasia (FIGURE 1-15).

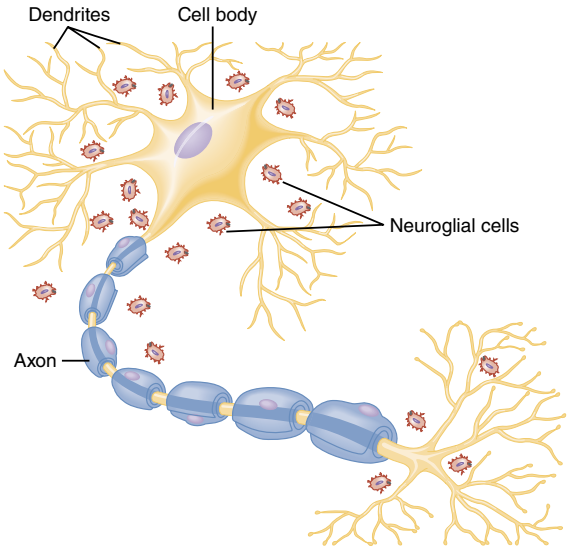


FIGURE 1-14 Nervous tissue cells.

Atrophy occurs because of decreased work demands on the cell. Under all circumstances, the body attempts to work as efficiently as possible to conserve energy and resources. Thus, the cells decrease in size and number when cellular work demands decrease. These atrophied cells utilize less oxygen, and their organelles decrease in size and number. Causes of atrophy may include disuse, denervation, endocrine hypofunction, inadequate nutrition, and ischemia. An example of disuse atrophy can be seen when a muscle shrinks in an extremity with a fracture that has been in an immobilizing cast for an extended period. Denervation atrophy is closely associated with disuse; it can be seen when a muscle shrinks in a paralyzed extremity. Atrophy because of a loss of endocrine function occurs when the reproductive organs of postmenopausal women shrink. When these organs are not supplied with adequate nutrition and blood flow, cells shrink due to a lack of substances necessary for their

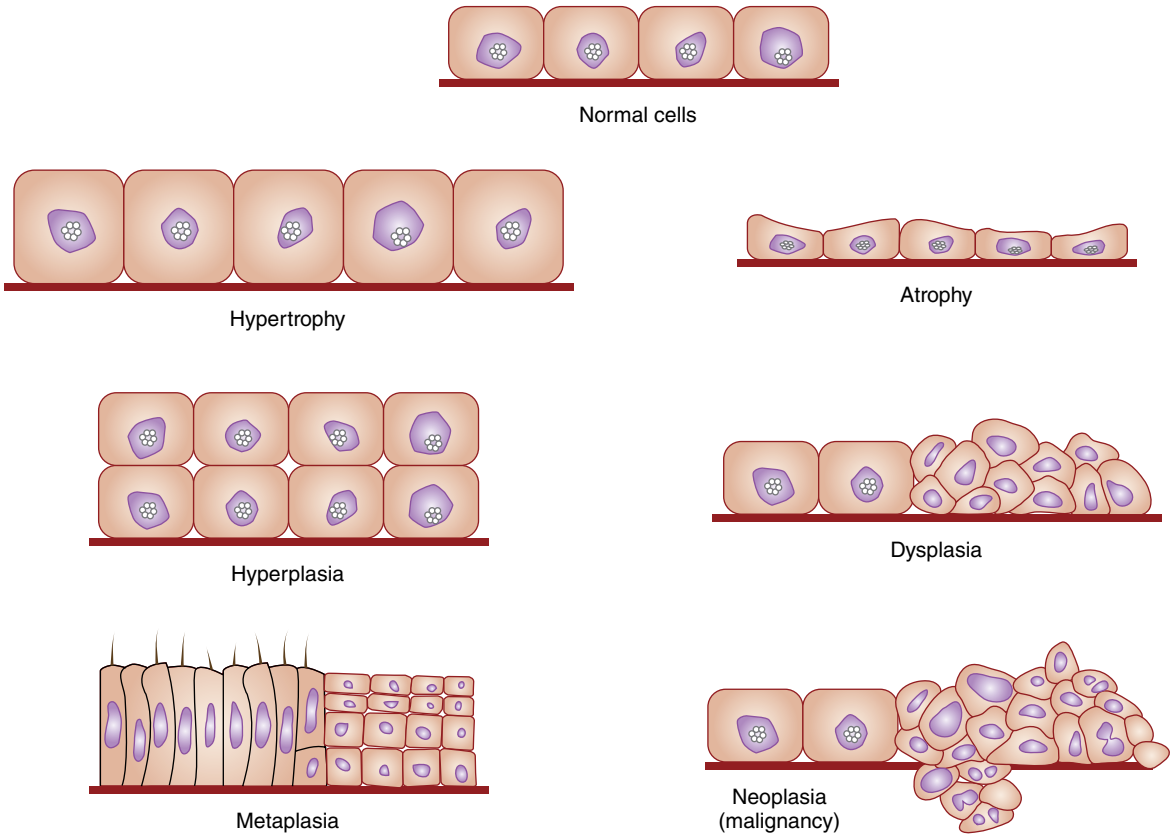


FIGURE 1-15 Cellular adaptation: abnormal cellular growth patterns.

survival—much like when water and fertilizer are withheld from a plant.

The opposite of atrophy is **hypertrophy**. Hypertrophy occurs when cells increase in size in an attempt to meet increased work demands. This size increase may result from either normal or abnormal changes. Such changes are commonly seen in cardiac and skeletal muscle. For example, consider what happens when a body builder diligently performs biceps curls with weights—the biceps gets larger. This type of hypertrophy is a normal change. An abnormal hypertrophic change can be seen with hypertension (high blood pressure). Just as the biceps muscle grows larger from increased work, so the cardiac muscle will thicken and enlarge when hypertension places an increased workload on it. The biceps muscle increases in strength and function when its workload is increased; in contrast, the heart loses the flexibility to fill with blood and pump the blood when the cardiac muscle increases in size. This abnormal hypertrophic change can lead to complications such as cardiomyopathy and heart failure (see the *Cardiovascular Function* chapter).

Hyperplasia refers to an increase in the number of cells in an organ or tissue. This increase occurs only in cells that have the ability to perform mitotic division, such as epithelial cells. Hyperplasia differs from hypertrophy, but these processes often occur together because they have similar triggers. The hyperplasia process is usually a result of normal stimuli. Examples of such normal hyperplasia include that seen in menstruation, liver regeneration, wound healing, and skin warts. Hyperplasia can also be abnormal, especially when caused by excessive hormone or growth factors. Examples of pathologic hyperplasia include endometrial hyperplasia that can result from an oversecretion of estrogen and a subsequent progesterone imbalance. Pathologic hyperplasia is not necessarily cancerous, but it can create a supportive environment for cancerous proliferation.

The process in which one adult cell is replaced by another cell type is called **metaplasia**. This change is usually initiated by chronic irritation and inflammation, such that a more virulent cell line emerges. The cell types do not cross over the overarching cell type. For instance, epithelial cells may be converted into another type of epithelial cell, but they will not be replaced with nerve cells. Examples of metaplastic changes are the ciliary changes that can occur in the respiratory tract because of chronic smoking or vitamin A deficiency. Metaplasia does not necessarily lead to cancerous changes; however, cancerous changes will likely occur if the stimulus is not removed.

The final cellular adaptation is **dysplasia**. In dysplasia, cells mutate into cells of a different size, shape, and appearance (i.e., atypical cells). Although dysplasia is abnormal, it is potentially reversible by removing the trigger. Dysplastic changes are often implicated as precancerous cells. The reproductive and respiratory tracts are common sites for this type of adaptation because of their increased exposure to carcinogens (e.g., human papillomavirus and cigarette smoke).

Cellular Injury and Death

Cellular injury can occur in many ways and is usually reversible up to a point. Whether the injury is reversible or irreversible usually depends on the severity of the injury and intrinsic factors (e.g., blood supply and nutritional status). Cell injury can occur because of (1) physical agents (e.g., mechanical forces and extreme temperature), (2) chemical injury (e.g., pollution, lead, and drugs), (3) radiation, (4) biological agents (e.g., viruses, bacteria, and parasites), (5) low oxygen levels (e.g., hypoxia or ischemia), and (6) nutritional imbalances. Such an injury often causes ATP depletion, cell membrane dysfunction, metabolic waste accumulation, or abnormal immune responses (e.g., phagocytizing and storing abnormal substances). The cell's resistance to and tolerance of the injury can influence its ability to survive. For example, nervous and cardiac cells can survive only a few minutes without oxygen, while connective tissue may be able to survive for a few days.

Death is a normal part of the human existence, and matters are no different at the cellular level. When cellular injury becomes irreversible, it usually results in cell death. The process of eliminating unwanted cells, called **programmed cell death**, usually occurs through the **apoptosis** mechanism (**FIGURE 1-16**). Programmed cell death occurs at a specific point in development; apoptosis specifically occurs because of morphologic (structure or form) changes. This mechanism of cell death is not limited to developmental causes but may also result from environmental triggers. Apoptosis is important in tissue development, immune defense, and cancer prevention. If unregulated, this mechanism can result in inappropriate destruction of cells. Such inappropriate activation of apoptosis can

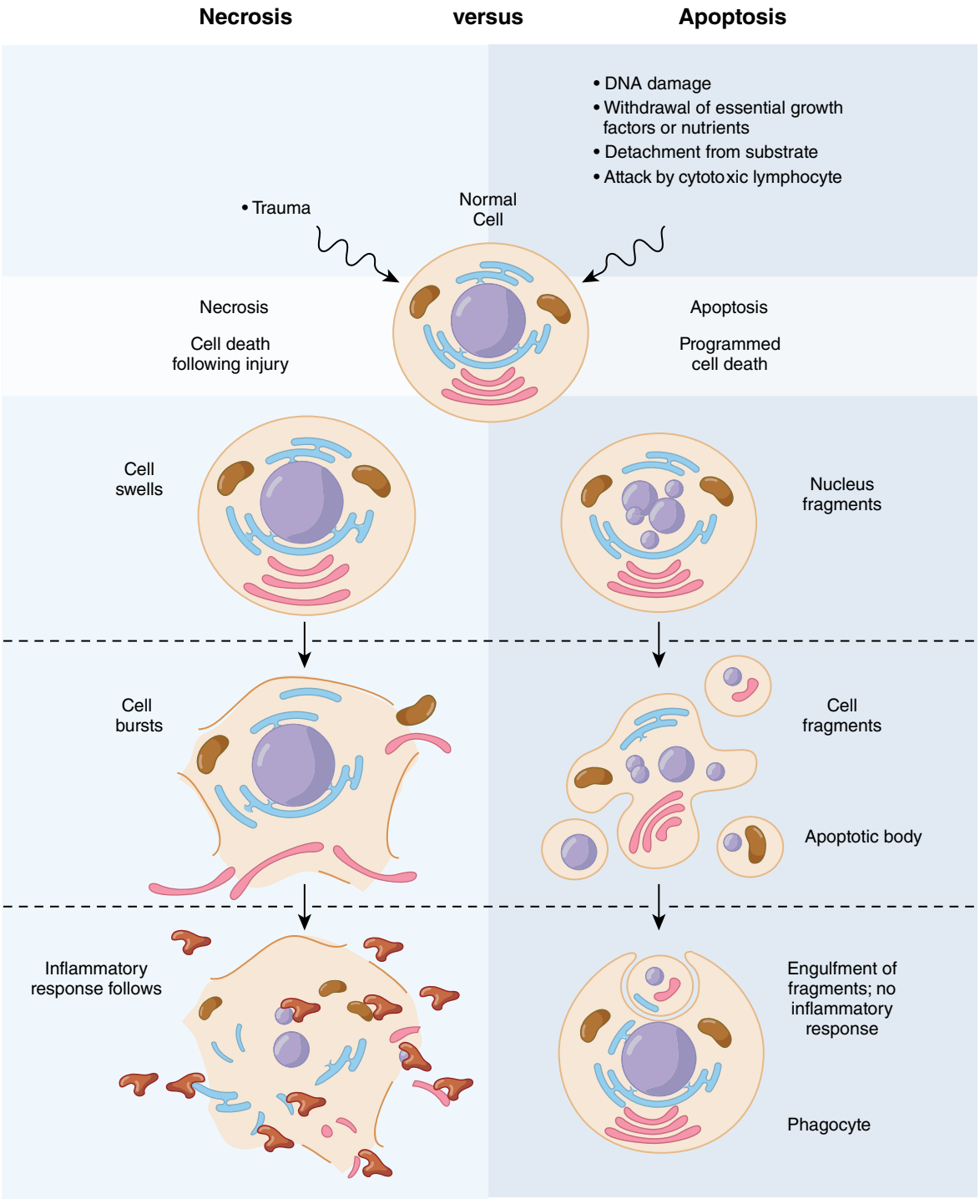


FIGURE 1-16 Cellular damage can result in necrosis, which has a different appearance from that of apoptosis, as organelles swell and the plasma membrane ruptures.

occur in degenerative neurologic diseases such as Alzheimer disease (see the *Neural Function* chapter).

Not all cell death is apoptotic, however. Cell death can also occur because of ischemia or necrosis (Figure 1-16). **Ischemia** refers to inadequate blood flow to tissue or an organ. This lack of blood flow essentially strangles the tissue or organ by limiting the supply of necessary nutrients and oxygen. Ischemia can leave cells damaged to the extent that they cannot survive, a condition called **infarction**. **Necrosis** is another type of cell death, which can occur due to injury, disease, or ischemia.

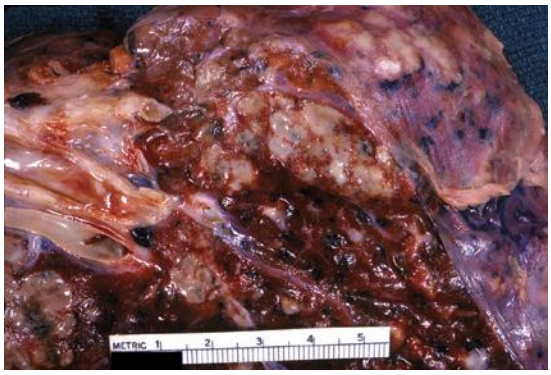


FIGURE 1-17 Liquefaction necrosis.

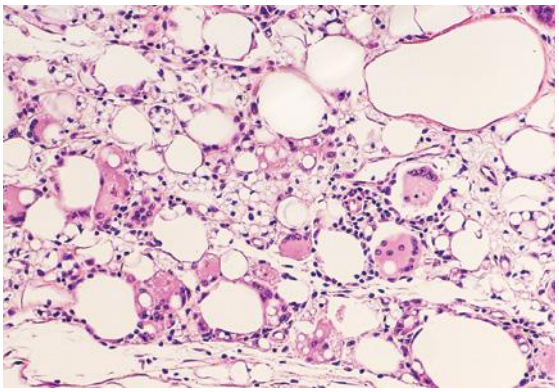


FIGURE 1-19 Fat necrosis.

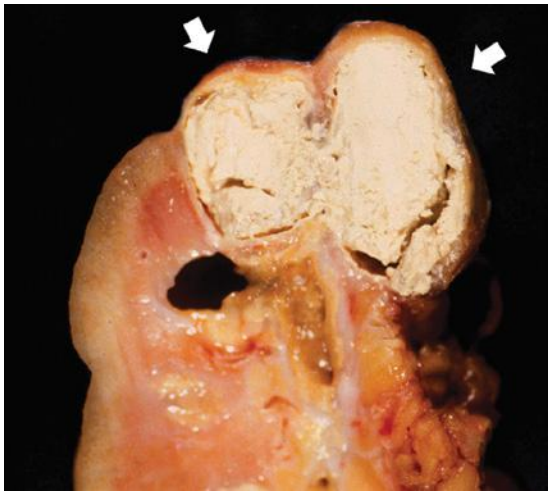


FIGURE 1-18 Caseous necrosis.

Reproduced from Gibson, M. S., Pucket, M. L., & Shelly, M. E. (2004). Renal tuberculosis. *Radiographics*, *24*(1), 251–256.

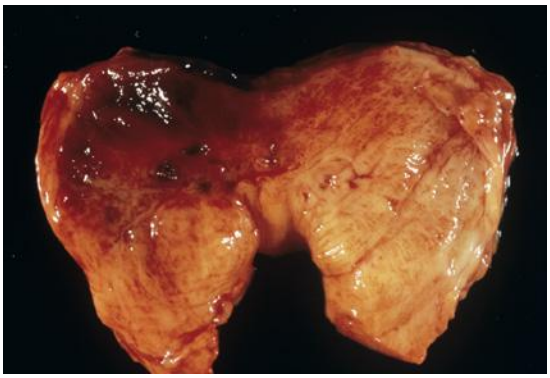


FIGURE 1-20 Coagulative necrosis.

The difference between apoptosis and necrosis lies mostly in the cell's morphologic changes. In apoptosis, the cells condense or shrink; in necrosis, the cells swell and burst.

Necrosis can take one of several pathways. **Liquefaction necrosis** (FIGURE 1-17) occurs when caustic enzymes dissolve and liquefy necrotic cells. The most common site of this type of necrosis is the brain, which contains a plentiful supply of these enzymes. **Caseous necrosis** (FIGURE 1-18) occurs when the necrotic cells disintegrate, but the cellular debris remains in the area for months or years. This type of necrosis, which has a cottage cheese–like appearance, is most commonly noted with pulmonary tuberculosis. **Fat necrosis** (FIGURE 1-19) occurs when lipase enzymes break down intracellular triglycerides into free fatty acids, which then combine with magnesium, sodium, and calcium to form soaps. These soaps give fat necrosis an opaque, chalky appearance. Fat necrosis is commonly associated with breast injury (e.g., surgery, radiation, or trauma) or acute pancreatitis. **Coagulative necrosis** (FIGURE 1-20) usually results from an interruption in blood flow. In such a case, the pH drops (acidosis), denaturing the cell's enzymes. This type of necrosis most often occurs in the kidneys, heart, and adrenal glands.

Gangrene is a form of coagulative necrosis that represents a combination of impaired blood flow and a bacterial invasion. Gangrene usually occurs in the legs because of arteriosclerosis (hardening of the arteries) or in the gastrointestinal tract. It most commonly takes one of three forms: dry, wet, or gas. **Dry gangrene** (FIGURE 1-21) occurs when bacterial presence is minimal, and the skin has a dry, dark brown, or black appearance. **Wet gangrene** (FIGURE 1-22) occurs with liquefaction necrosis. In this condition, extensive damage from bacteria and white blood cells produces a liquid wound. Wet gangrene can occur in the extremities as well as in internal organs. **Gas gangrene** (FIGURE 1-23)

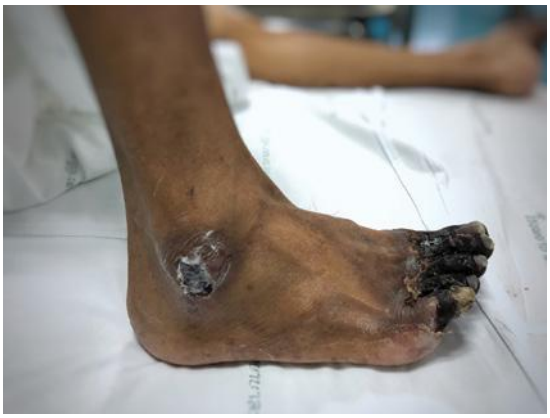


FIGURE 1-21 Dry gangrene.

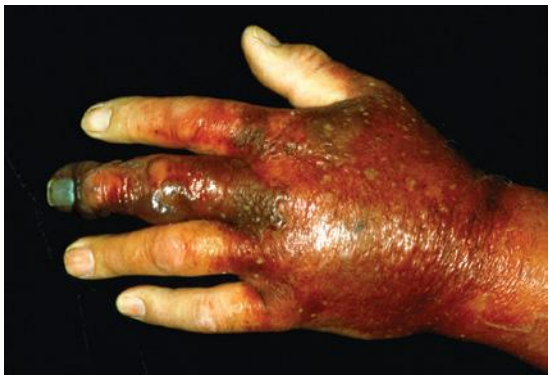


FIGURE 1-22 Wet gangrene.

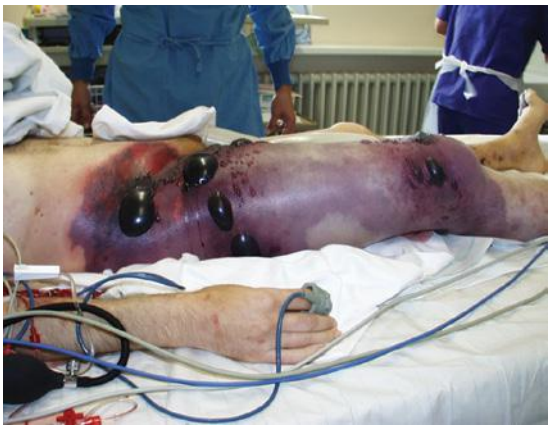


FIGURE 1-23 Gas gangrene.

Reproduced from Schröpfer, E., Rauthe, S., & Meyer, T. (2008). Diagnosis and misdiagnosis of necrotizing soft tissue infections: Three case reports. *Cases Journal*, *1*, 252.

develops because of the presence of *Clostridium*, an anaerobic bacterium. This type of gangrene is the most serious and has the greatest potential to be fatal. The bacterium releases toxins that destroy surrounding cells, so the infection spreads rapidly. The gas released from this process bubbles from the tissue, often underneath the skin. Other less common but often serious types of gangrene include necrotizing fasciitis (caused by group A *Streptococcus*), Fournier gangrene (affects the penis and genitalia), and Meleney synergistic gangrene (seen in patients after surgery; *Staphylococcus aureus* and *Streptococcus* organisms are present).

Another important mechanism of cellular injury is free radicals (e.g., reactive oxygen species). **Free radicals** are injurious, unstable agents that can cause cell death. A single unbalanced atom initiates this pathway, which can rapidly produce a wide range of damage. Such an atom has an unpaired electron, making it unstable. In an attempt to stabilize itself, the atom borrows an electron from a nearby atom, usually rendering it unstable. This newly unstable atom will then borrow an electron from its neighbor, creating a domino effect that continues until the atom giving the electron is stable without it. The extent of damage that this process causes depends on how long this chain of events continues. The immune system is equipped with agents to protect or limit the damage (see the *Immunity* chapter) that might occur because of this process, and certain dietary components can aid in this fight (e.g., antioxidants such as vitamins C and E and beta-carotene). Free radicals have been linked to cancer, aging, and a variety of other conditions (e.g., heart disease, diabetes mellitus, and hypertension).

Neoplasm

When the process of cellular proliferation or differentiation goes wrong, neoplasms can develop. A **neoplasm**, or **tumor**, is a group of cells whose growth is no longer responding to (i.e., constrained by) normal regulatory processes, usually because of a mutation. The disease state associated with this uncontrolled growth is termed **cancer**. Cancer's key features include rapid, uncontrolled proliferation and a loss of differentiation (i.e., **anaplasia**). To varying degrees, cancer cells differ from normal cells in size, shape, number, differentiation, purpose, and function. The less the cell resembles the original cell, the more anaplastic the cell is. Anaplastic cells may begin functioning as completely different cells, often producing hormones or hormone-like substances. This uncontrolled proliferation and changes in differentiation are a result of genetic, epigenetic (gene expression), and environmental

factors. Such changes result from a series of events or factors, not just one.

A healthy body is equipped with the necessary defenses to shield it against cancer (see the *Immunity* chapter). When those defenses fail, however, cancer prevails. **Carcinogenesis**, the process by which cancer develops, occurs in three phases: initiation, promotion, and progression (FIGURE 1-24).

Initiation involves the exposure of the cell to a substance or event (e.g., chemicals, viruses, radiation, hormones, or other environmental agents) that causes DNA damage or mutation, especially affecting proto-oncogenes and tumor suppressor genes. Usually the body has enzymes that detect these events and repair the damage. If the event is overlooked, the mutation can become permanent and be passed on to future cellular generations, making it vulnerable if additional insults occur. Additionally, risk for DNA replication and repair errors and carcinogen exposure increases over time, resulting in higher rates of cancer with aging.

Promotion involves the mutated cells' exposure to factors (e.g., hormones, nitrates, or nicotine) that promote growth through epigenetic mechanisms (e.g., DNA methylation, histone modification, and microribonucleic acids). This phase may occur just after initiation or years later, and it can be reversible if the promoting factors are removed. Many new cancer therapies aim to reverse this phase.

In **progression**, the tumor invades, metastasizes (spreads), and becomes resistant to drug therapy. The microenvironment (e.g., available blood flow, nearby tissue or cells, or hormones present) surrounding the cancer cells influences its ability to proliferate, survive, invade, and metastasize. Additionally, this environment influences the cancer cell's response to treatment. Moreover, the immune system is impaired during stress states, which can affect its ability to find and respond to carcinogenesis. This final phase is permanent or irreversible.

More than 100 diseases are classified as a cancer, and most organs and tissues are vulnerable to this condition. Cancer prognosis depends on the type of cancer and the individual's health. Some cancers are aggressive (e.g., pancreatic cancer), whereas others are easy to treat (e.g., testicular cancers). In recent years, the survival rates for some cancers have significantly improved because of advancements in screening and treatment (e.g., breast cancer). Even though cancer deaths decreased by 26% between 1991 and 2015, cancer remains the second leading cause of death in the United States (Centers for Disease Control and Prevention, 2016; National Cancer Institute, 2018).

Benign and Malignant Tumors

The two major types of neoplasms are benign and malignant (TABLE 1-4; FIGURE 1-25). **Benign** tumors usually consist of differentiated (less anaplastic) cells that are reproducing more rapidly than normal cells. Because of their differentiation, benign tumors are more like normal cells and cause fewer problems. Benign

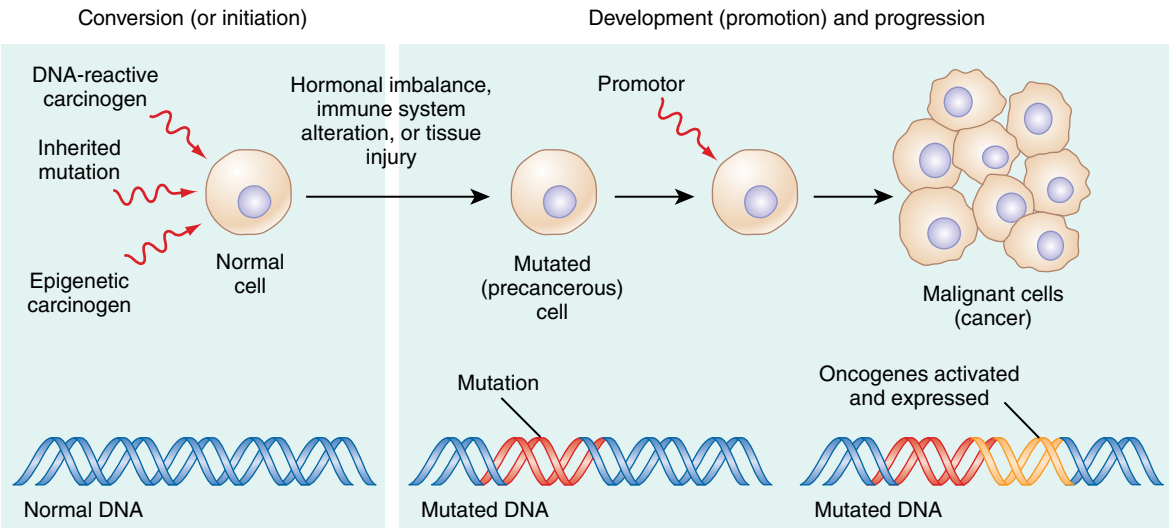


FIGURE 1-24 Carcinogenesis: the stages leading to cancer.

TABLE 1-4 Characteristics of Benign and Malignant Tumors

	Benign Tumors	Malignant Tumors
Cells	Similar to normal cells Differentiated Mitosis is fairly normal	Varied in size and shape Many undifferentiated Mitosis is increased and atypical
Growth	Relatively slow Expanding mass Frequently encapsulated	Rapid growth Cells are not adhesive, infiltrate tissue No capsule
Spread	Remains localized	Invades nearby tissue or metastasizes to distant sites through blood and lymph vessels
Systemic effects	Rare	Common
Life threatening	Only in certain locations (e.g., brain)	Yes, by tissue destruction and spread

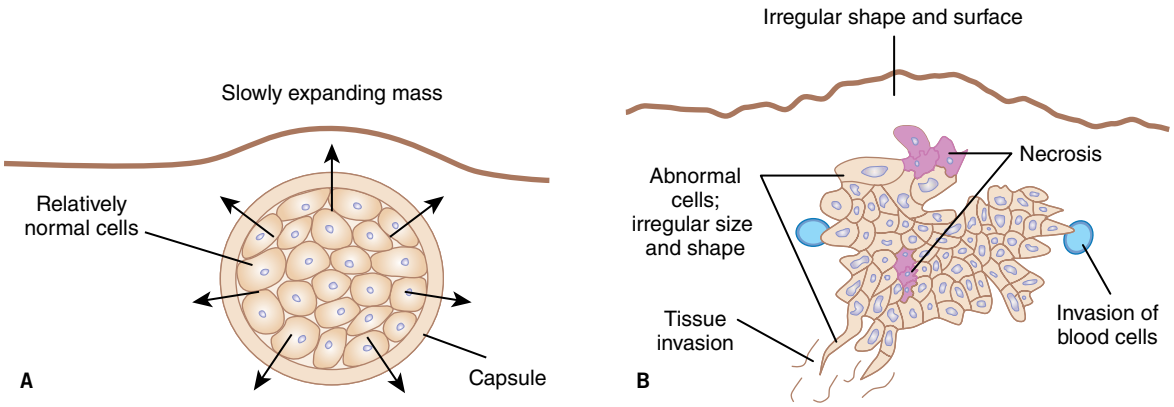


FIGURE 1-25 Characteristics of **(A)** benign and **(B)** malignant tumors.

cells are usually encapsulated and unable to **metastasize**. The tumor, however, can compress surrounding tissue as it grows. Benign tumors usually cause problems due to that compression. Regardless of its size, if the tumor arises in a sensitive area such as the brain or spinal cord, it can cause devastating problems.

Malignant tumors usually consist of undifferentiated (more anaplastic), nonfunctioning cells that are reproducing rapidly. Such tumors often penetrate surrounding tissue and spread to secondary sites. The tumor's ability to metastasize (**FIGURE 1-26**; **FIGURE 1-27**) depends on its ability to access and survive in the circulatory or lymphatic system. Most commonly, the tumor metastasizes to tissue or organs near the primary site, but some tumor cells may travel to distant sites (**TABLE 1-5**).

Regardless of the type of tumor, several factors are essential for the tumor's progression and survival. The tumor must have an adequate blood supply, and sometimes it will divert the blood supply from surrounding tissue to meet those needs. The tumor will grow only as large as what the blood supply will support. Location is critical because it determines the cytology of the tumor as well as the tumor's ability to survive and metastasize. Host factors including age, gender, health status, and immune function will also affect the tumor. Alterations in some of these host factors can create a prime environment for the tumor to grow and prosper.

Clinical Manifestations

In most cases, a patient's prognosis improves the earlier the cancer is detected and treated. Healthcare providers, patients, and family members detect many cases of cancer first through the recognition of manifestations. Heeding these

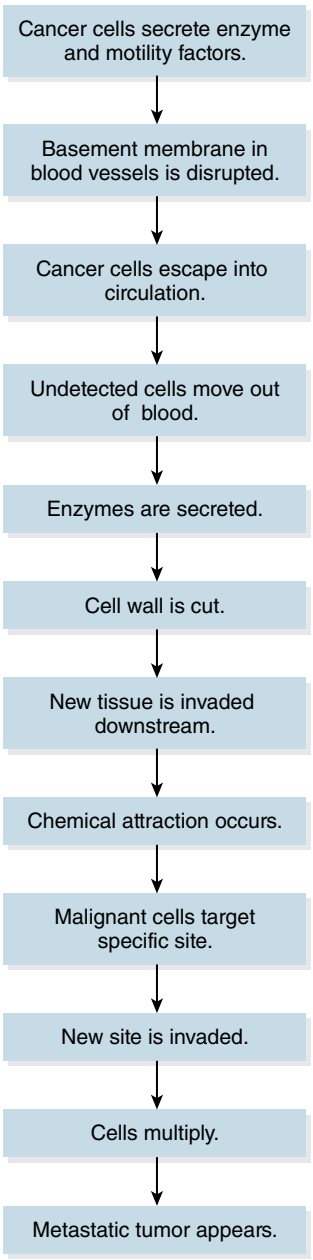


FIGURE 1-26 How cancer metastasizes.

warning signs is vital to initiating treatment early. Unfortunately, people often ignore or do not recognize the warning signs for a variety of reasons (e.g., denial and symptom ambiguity).

As the cancer progresses, the patient may present with manifestations of advancing disease, including anemia, cachexia, fatigue, infection, leukopenia, thrombocytopenia, and pain. Anemia—that is, decreased red blood cells—can be a result of the bloodborne cancers (e.g., leukemias), chronic bleeding, malnutrition, chemotherapy, or radiation. Cachexia, a generalized wasting syndrome in which the person appears

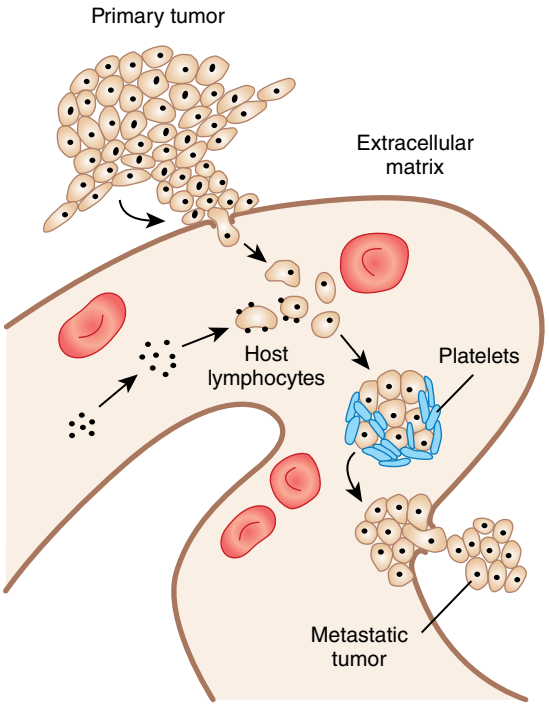


FIGURE 1-27 Pathogenesis of metastasis.

TABLE 1-5 Common Sites of Metastasis

Cancer Type	Main Sites of Metastasis*
Bladder	Bone, liver, lung
Breast	Bone, brain, liver, lung
Colorectal	Liver, lung, peritoneum
Kidney	Adrenal gland, bone, brain, liver, lung
Lung	Adrenal gland, bone, brain, liver, other lung
Melanoma	Bone, brain, liver, lung, skin/muscle
Ovary	Liver, lung, peritoneum
Pancreas	Liver, lung, peritoneum
Prostate	Adrenal gland, bone, liver, lung
Stomach	Liver, lung, peritoneum
Thyroid	Bone, liver, lung
Uterus	Bone, liver, lung, peritoneum, vagina

* In alphabetical order.

Reproduced from National Cancer Institute. (2017). Metastatic cancer. Retrieved from http://www.cancer.gov/about-cancer/what-is-cancer/metastatic-fact-sheet

Myth Busters

Myth 1: Cancer is a death sentence.

While cancer remains the second leading cause of death in the United States, cancer deaths have dropped 26% since 1990 due to improvements in screening, treatments, lifestyle choices, and education (National Cancer Institute, 2018). Additionally, new cases of cancer decreased 2.1% per year between 1999 and 2015, and patients with cancer are living longer. The overall 5-year cancer survival rate improved from 40% in 1975 to 69% in 2010.

Myth 2: Standing in front of a microwave oven while it is cooking food can increase your risk for cancer.

This myth may hold a grain of truth. An increased cancer risk has been linked to increased levels of ionizing radiation (e.g., X-rays) because such radiation detaches electrons from atoms. Microwaves use non-ionizing microwave radiation to heat food. Early microwave ovens emitted higher levels of this radiation, which may have increased users' cancer risk to a slight extent. Research has never been able to determine whether cancer risk increases with exposure to non-ionizing radiation. Currently, Food and Drug Administration guidelines limit the amount of the non-ionizing radiation microwave ovens can emit, further decreasing the cancer risk associated with these devices.

Myth 3: Using cell phones can increase your risk of cancer.

Cell phones use the same non-ionizing microwave radiation as microwave ovens do to emit a signal. Even though these devices may be in close proximity to your head while in use, evidence does not support the assertion that they increase your risk of brain cancer. Using a cell phone for an extended period at one time will heat your ear for the same reason that the microwave heats your food, but no clear evidence suggests that this extended use increases cancer risk.

Myth 4: Artificial sweeteners cause cancer.

Numerous studies have been focused on the safety of artificial sweeteners, and no evidence suggests that they cause cancer.

emaciated, often occurs due to malnutrition. Fatigue, or feeling of weakness, results from the parasitic nature of a tumor, anemia, malnutrition, stress, anxiety, and chemotherapy. Factors that can increase the risk for infection include bone marrow depression, chemotherapy, and stress. Leukopenia (low leukocyte levels) and thrombocytopenia (low platelet levels) are common side effects of chemotherapy and radiation due to bone marrow depression. Pain is often associated with cancer due to tissue pressure, obstructions, tissue invasion, visceral stretching, tissue destruction, and inflammation. Other manifestations depend on the type and location of the cancer (see the specific cancer discussions in their relevant chapters).

Diagnosis

Diagnosis of cancer is complex and is specific to the type of cancer suspected. This section provides a basic overview of cancer diagnostic procedures; more specifics are presented in other chapters as specific cancers are discussed. A set of diagnostic procedures usually follows a thorough history and physical examination. These procedures may vary depending on the type of cancer suspected. The intention of the diagnostic tests is to identify cancer cells, establish the cytology, and determine the primary site and any secondary sites; however, all these goals are not always accomplished. The healthcare provider will gather as much information as possible to paint the clearest and most complete picture possible of the patient so as to develop an appropriate treatment plan.

Some screening tests are used for early detection of cancer cells as well as for staging the cancer (**TABLE 1-6**). These screening tests include X-rays, radioactive isotope scanning, computed tomography scans, endoscopies, ultrasonography, magnetic resonance imaging, positron emission tomography scanning, biopsies, and blood tests. Some of the blood tests may include tumor markers—substances secreted by the cancer cells—for specific

TABLE 1-6 Cancer Screening Guidelines

Screening Area	Recommendations
Breast	
Mammogram	Every year at age 40 and older or every 2 years at ages 50–74; can discontinue after age 75 unless expected to live longer than 10 years
Clinical breast examination	Every year at age 40 and older; every 3 years at ages 20–39
Breast self-examination	Suggested monthly for age 20 and older
BRCA1 and *BRCA2* genetic testing	Only recommended for women with a family history
Ovary	
BRCA1 and *BRCA2* genetic testing	Only recommended for women with a family history
Cervix	
Papanicolaou (Pap) test	Every 3 years between the ages of 21 and 65
	Not necessary after age 65 unless serious cervical precancer or cancer present in the past 20 years
Human papillomavirus (HPV)	Every 5 years between the ages of 30 and 65
Endometrium	
Endometrial biopsy or pelvic ultrasound	Yearly beginning at age 35 for those women at risk for colon cancer
Prostate	
Prostate-specific antigen (PSA)	Frequency depends on risk factors; may begin as early as age 40
Digital rectal examination	Frequency depends on risk factors; may begin as early as age 40
Colon and Rectum	
Fecal occult blood test	Yearly at age 50 and older
Fecal immunochemical test	Yearly at age 50 and older
Stool DNA test	Every 3 years at age 50 and older
Flexible sigmoidoscopy	Every 5 years at age 50 and older
Barium enema	Every 5 years at age 50 and older
Colonoscopy	Every 10 years at age 50 and older
Virtual colonography	Every 5 years at age 50 and older

Data from American Cancer Society. (2018). American Cancer Society guidelines for the early detection of cancer. Retrieved from http://www.cancer.org/National Cancer Institute. www.cancer.gov; United States Preventive Services Task Force recommendations. https://www.uspreventiveservicestaskforce.org/BrowseRec/Index

cancers (TABLE 1-7). These tumor markers not only aid in cancer detection but also assist in tracking disease progression and treatment response.

Malignant cancer cells are classified based on the degree of differentiation (grading) and extent of disease (staging). The **grading** system determines the degree of differentiation on a scale of 1 to 4, in order of clinical severity. For instance, grade 1 cancers are well differentiated, meaning they are less likely to cause serious problems because they are more like the original tissue. By comparison, grade 4 cancers are undifferentiated, meaning they are highly likely to cause serious problems because they do not share any characteristics of the original tissue. The **TNM staging** system evaluates the tumor size, nodal involvement, and metastatic progress (FIGURE 1-28).

Treatment

Cancer treatment usually consists of a combination of chemotherapy, radiation, surgery, targeted therapy, hormone therapy, immunotherapy, hyperthermia, stem cell transplants, photodynamic therapy, and laser treatment. Additionally, other strategies may include watchful waiting and alternative therapies (e.g., herbs, diet, and acupuncture). The goal of treatment may be **curative** (eradicate the disease), **palliative** (treat symptoms to increase comfort), or **prophylactic** (prevent the disease).

TABLE 1-7 Common Tumor Cell Markers

Marker	Malignant Condition	Nonmalignant Condition
Alpha-fetoprotein	Liver cancer Ovarian germ cell cancer Testicular germ cell cancer	Ataxia telangiectasia Cirrhosis Hepatitis Pregnancy
Anaplastic lymphoma kinase (ALK)	Lung cancer Large-cell lymphoma	Unknown
BCR-ABL	Chronic myeloid leukemia Acute lymphocytic leukemia	Unknown
$Beta_2$ microglobulin (B2M)	Multiple myeloma Chronic lymphocytic leukemia Some lymphomas	Kidney disease
Carcinoembryonic antigen	Bladder cancer Breast cancer Cervical cancer Colorectal cancer Kidney cancer Liver cancer Lung cancer Lymphoma Melanoma Ovarian cancer Pancreatic cancer Stomach cancer Thyroid cancer	Inflammatory bowel disease Liver disease Pancreatitis Chronic obstructive pulmonary disease Rheumatoid arthritis Tobacco use
CA 15-3	Breast cancer Lung cancer Ovarian cancer Prostate cancer	Benign breast disease Endometriosis Hepatitis Lactation Benign ovarian disease Pelvic inflammatory disease Pregnancy
CA 19-9	Bile duct cancer Colorectal cancer Pancreatic cancer Stomach cancer	Thyroid disease Rheumatoid arthritis Cholecystitis Inflammatory bowel disease Cirrhosis Pancreatitis
CA 27-29	Breast cancer Colon cancer Kidney cancer Liver cancer Lung cancer Ovarian cancer Pancreatic cancer Stomach cancer Uterine cancer	Benign breast disease Endometriosis Kidney disease Liver disease Ovarian cysts Pregnancy (first trimester)

(*continues*)

TABLE 1-7 Common Tumor Cell Markers (*Continued*)

Marker	Malignant Condition	Nonmalignant Condition
CA 125	Colorectal cancer Gastric cancer Ovarian cancer Pancreatic cancer	Endometriosis Liver disease Menstruation Pancreatitis Pelvic inflammatory disease Peritonitis Pregnancy
Human chorionic gonadotropin	Choriocarcinoma Embryonic cell carcinoma Liver cancer Lung cancer Pancreatic cancer Stomach cancer Testicular cancer	Marijuana use Pregnancy
Lactate dehydrogenase	Almost all cancers Ewing sarcoma Leukemia Non-Hodgkin lymphoma Testicular cancer	Anemia Heart failure Hypothyroidism Liver disease Lung disease
Neuron-specific enolase	Kidney cancer Melanoma Neuroblastoma Pancreatic cancer Small-cell lung cancer Testicular cancer Thyroid cancer Wilms tumor	Unknown
Prostatic acid phosphatase	Prostate cancer	Benign prostate conditions
Prostate-specific antigen	Prostate cancer Multiple myeloma Lung cancer	Benign prostatic hyperplasia Prostatitis

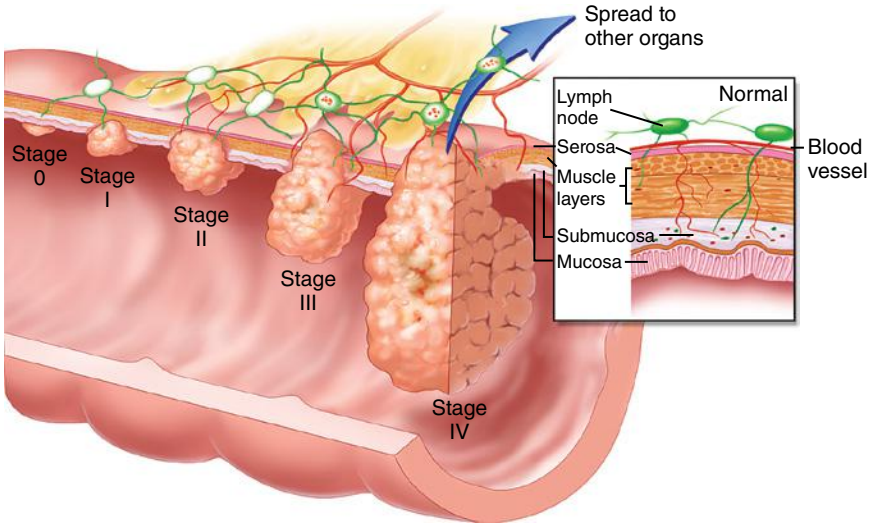


FIGURE 1-28 TNM staging system. The example shown is staging of colorectal cancer.