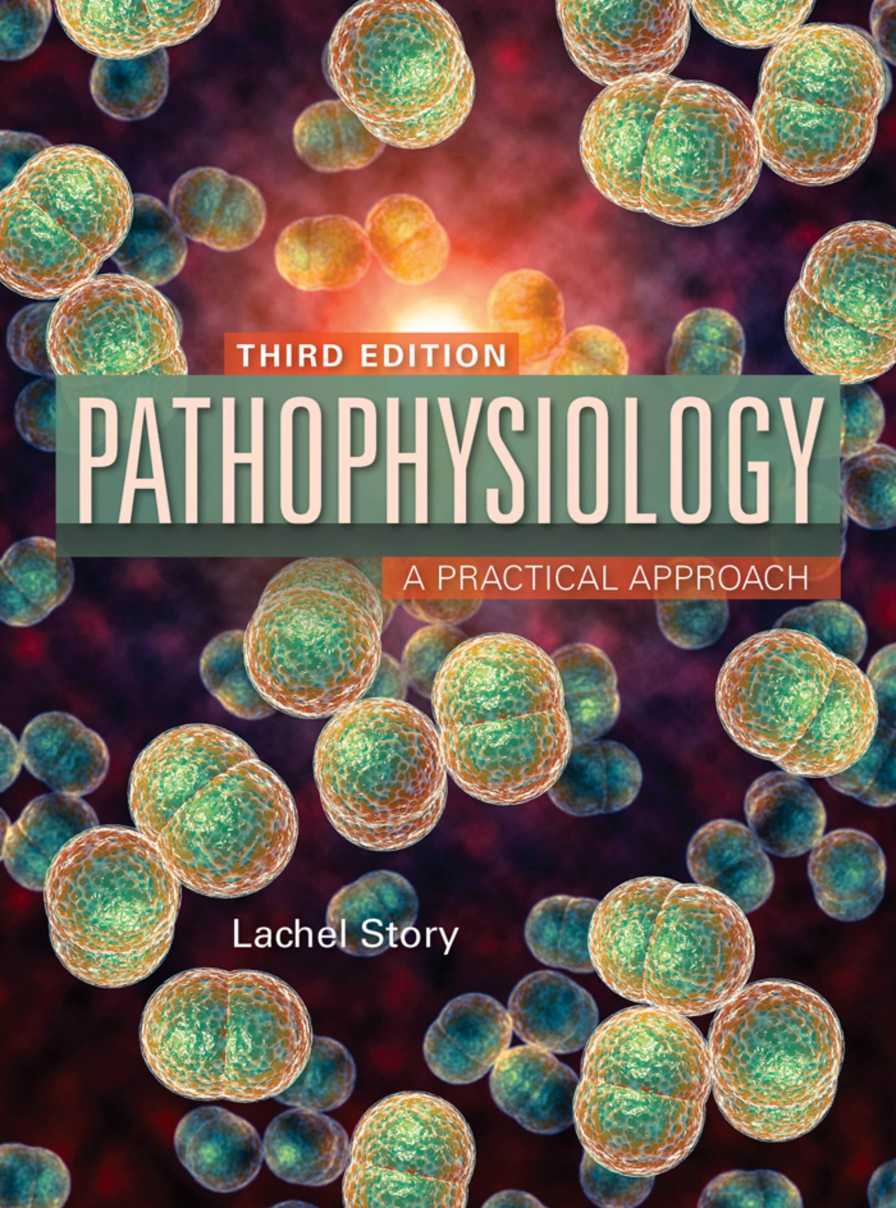

THIRD EDITION

# PATHOPHYSIOLOGY

## A PRACTICAL APPROACH

Lachel Story

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## A PRACTICAL APPROACH


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# Contents

# Preface

While teaching pathophysiology for more than 13 years and nursing for more than 21 years, I noticed a lack of pathophysiology books that students could relate to, and high student frustration in learning the convoluted material. Pathophysiology—while being the foundation of much of nursing education, from medical–surgical to pharmacology—is often an insurmountable barrier for students. They are faced with a copious amount of complicated information to weed through. 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 a student-friendly, understandable 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 ground-breaking 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 third 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. An increased focus on pediatric content and considerations has been threaded throughout. New and updated case studies add to students' understanding and ability to apply their learning on a practical level. Instructor resources have been expanded to 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 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, first the definition of health must 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 becomes 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 exist in a vacuum. 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 causing temporary stress to causing life-changing complications. Health and disease may be considered as two ends 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 (e.g., 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 are those that 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 are referred to as **metabolic** diseases (e.g., diabetes mellitus). **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 brain stem and controls vital functions such as blood pressure, temperature, and pulse. The reticular

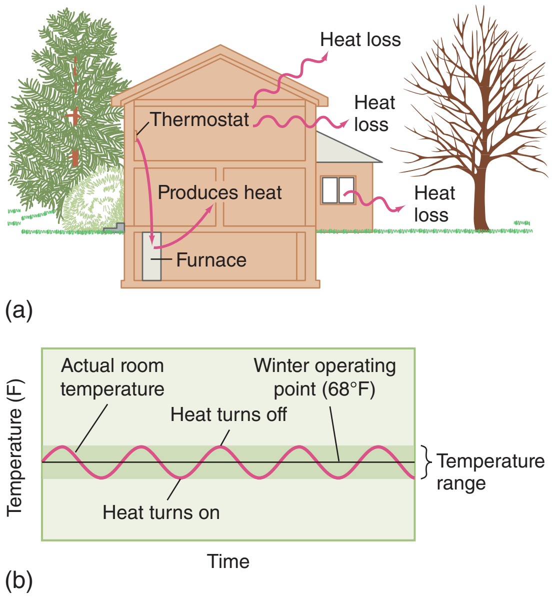


**FIGURE I-1** Homeostasis is like a house. (a) Heat is maintained in a house by a furnace, which compensates for heat loss. (b) A hypothetical temperature graph.

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. The body attempts to limit the damage from diseases by activating compensatory mechanisms. **Compensatory mechanisms** are 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.

The onset of the disease may be sudden or acute. Acute onset of a disease may include pronounced indicators such as pain or vomiting, whereas 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 less notable signs and occurs over a longer period. Chronic diseases may not ever resolve but may sometimes become 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**, or identification. 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 be specific to the cause of the disease or used to alleviate the disease's clinical manifestations. For example, an antibiotic may be used 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 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 factors affecting the health and disease of 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 occurrence, incidence, prevalence, transmission, and distribution of a disease. **Morbidity** refers to disease rates within a group. **Epidemics** occur when there are increasing numbers of people with 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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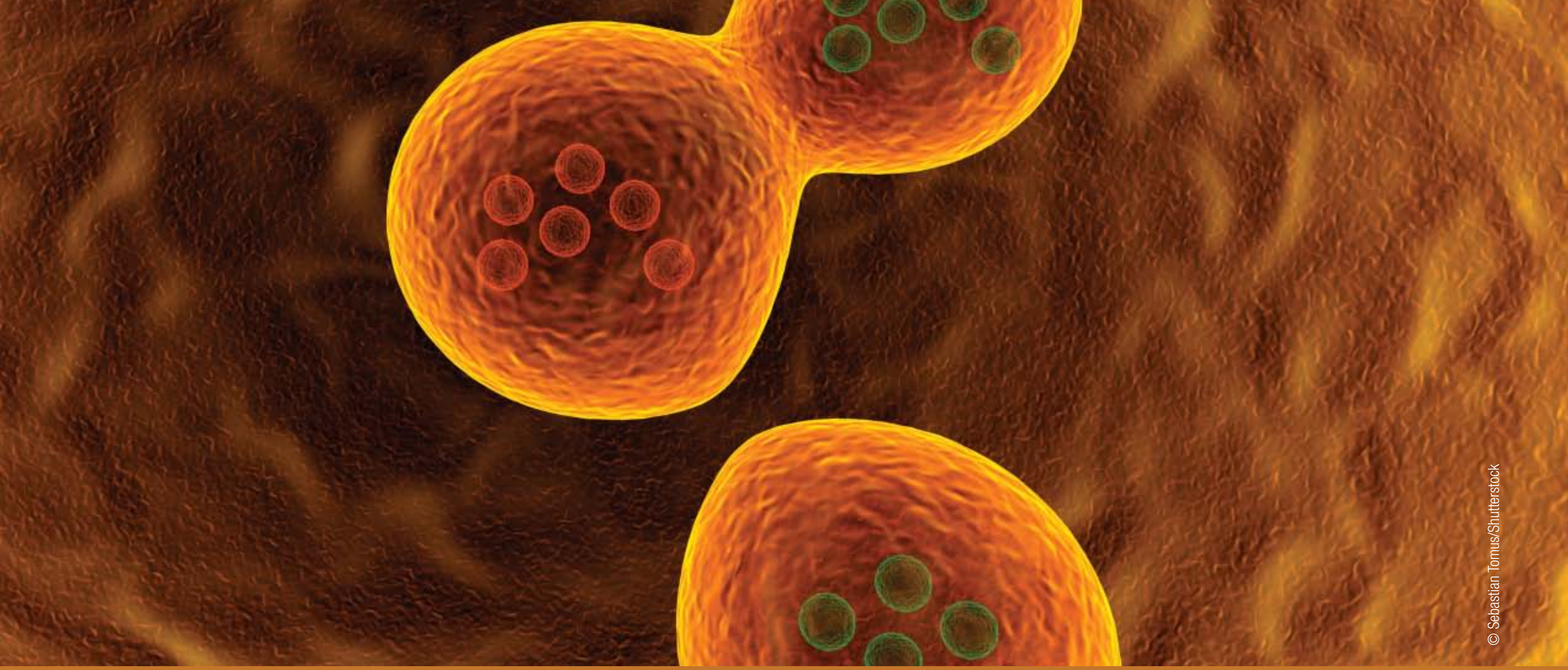


CHAPTER 1

# Cellular Function

## LEARNING OBJECTIVES

- Describe basic cellular structures and function.
- 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
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phenotype
pinocytosis
plasma membrane
programmed cell death
prognosis
progression
proliferation
promotion
prophase
prophylactic
protoplasm
recessive
remission
selectively permeable
sex-linked
telophase
teratogens
TNM staging
tumor
wet gangrene

Pathophysiology inquiry 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, these diseases can be reduced to their 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 miniorganisms resulting from millions of years of evolution. Cells can arise only from a preexisting cell. 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, nucleus, 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 is the control center of the cell, contains all the genetic information (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. The exterior surface of the bilayer is charged and is less fatty than the interior surface. 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 process, 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 dissolved in water. Passage across the cell membrane is accomplished through several mechanisms, including diffusion, osmosis, facilitated diffusion, active transport, endocytosis, and exocytosis.

**Diffusion** is the movement of solutes—that is, particles dissolved in a solvent—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 concentrations of substances on either side of the membrane. Smaller particles diffuse more easily than larger ones, and less viscous solutions diffuse more rapidly than thicker solutions. Many substances, such as oxygen, enter the cell through diffusion.

**Learning Points**

To illustrate 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 with no 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**

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 (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, osmosis allows the cells to remain hydrated.

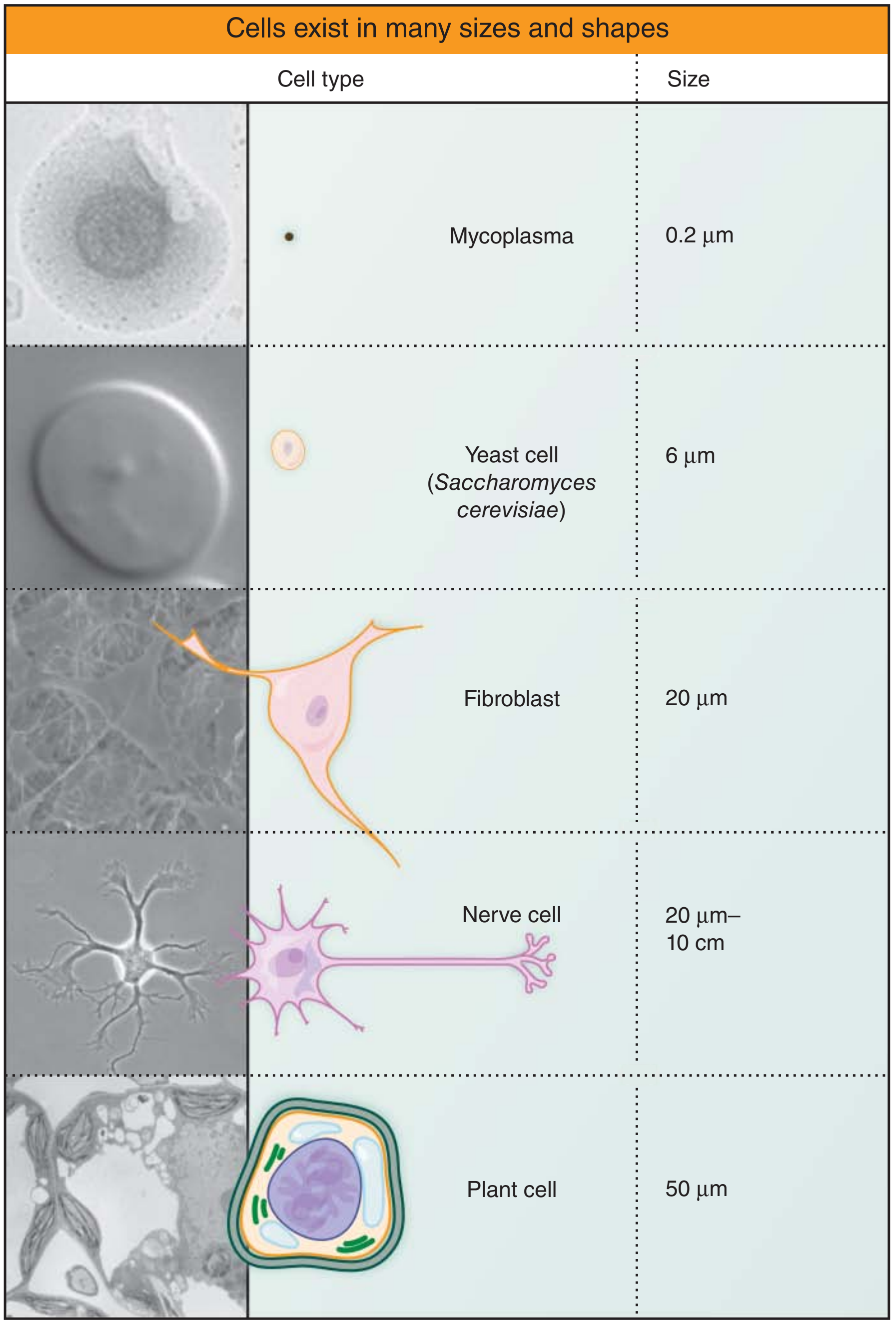


**FIGURE 1-1** Cells vary greatly in size and shape. Some cells are spherical, while others are long extensions.

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 Unversity

Courtesy of Ming H. Chen, University of Alberta

**Osmosis** is the 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 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. 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.

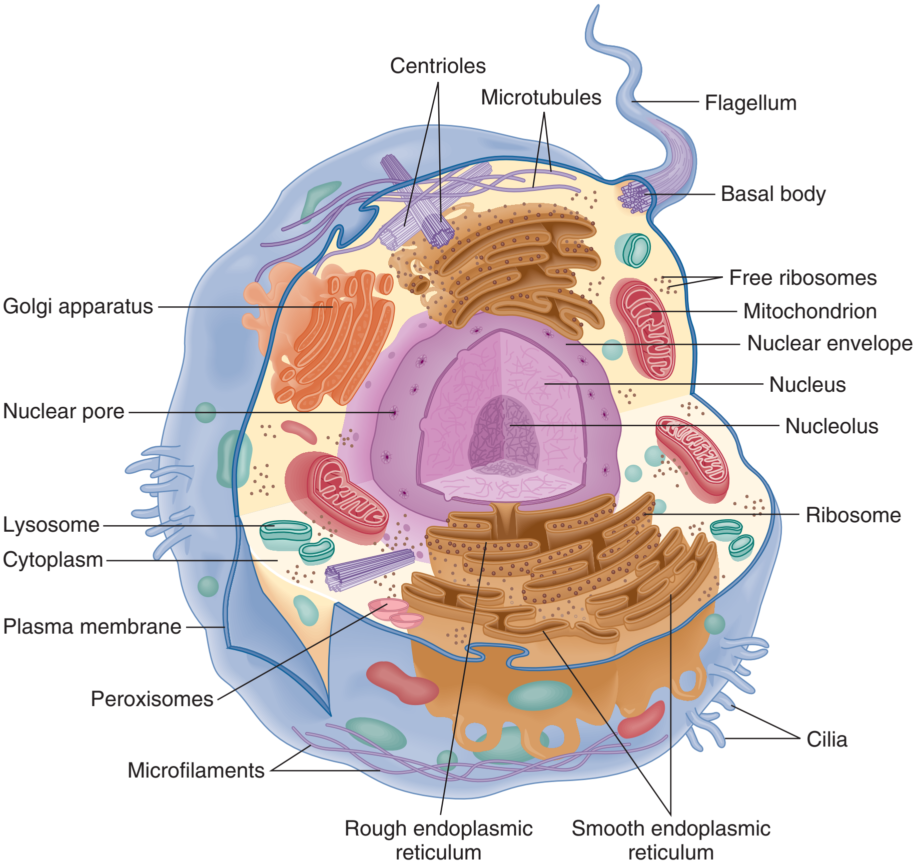


**FIGURE 1-2** The cytoplasm contains several organelles.

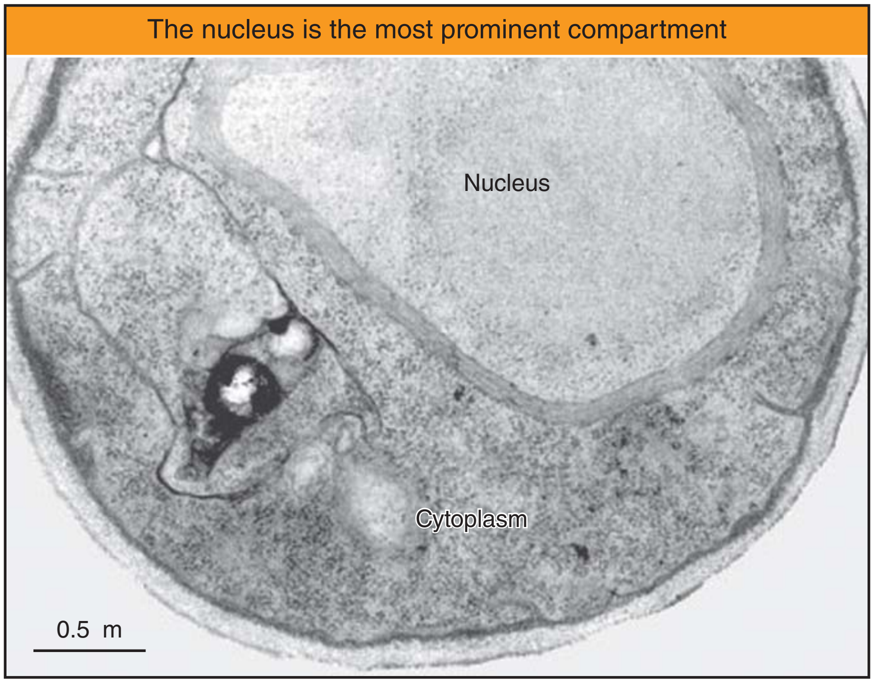


**FIGURE 1-3** Although the proportion of the cell that is taken up by the nucleus varies according to cell type, the nucleus is usually the largest and most prominent cellular compartment.

**TABLE 1-1 Overview of Cell Organelles**

| Organelle | Structure | Function |
|---|---|---|
| Nucleus | Round or oval body; surrounded by nuclear envelope. | Contains the genetic information necessary for control of cell structure and function; DNA contains hereditary information. |
| Nucleolus | Round or oval body in the nucleus consisting of DNA and RNA. | Produces ribosomal RNA. |
| Endoplasmic reticulum (ER) | Network of membranous tubules in the cytoplasm of the cell. Smooth endoplasmic reticulum (SER) contains no ribosomes. Rough endoplasmic reticulum (RER) is studded with ribosomes. | SER is involved in the production of phospholipids and has many different functions depending on the cells; RER is the site of the synthesis of lysosomal enzymes and proteins for extracellular use. |
| Ribosomes | Small particles found in the cytoplasm; made of RNA and protein. | Aid in protein production on the RER and polysomes. |
| Golgi complex | Series of flattened sacs usually located near the nucleus. | Sorts, chemically modifies, and packages proteins produced on the RER. |
| 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 for release. |
| Food vacuole | Membrane-bound vesicle containing material engulfed by the cell. | Stores ingested material and combines with lysosomes. |
| Lysosome | Round, membrane-bound structure containing digestive enzymes. | Combines with food vacuoles and digests materials engulfed by cells. |
| Peroximomes | Small structures containing enzymes. | Break down various potentially toxic intracellular molecules. |
| Mitochondria | Round, oval, or elongated structures with a double membrane. The inner membrane is shaped into folds. | Complete the breakdown of glucose, producing nicotine adenine dinucleotide (NADH) and adenosine triphosphate (ATP). |
| 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, not plants. | Help organize spindle apparatus necessary for cell division. |

**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. **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 because of the effort necessary to go against the gradient. This energy is usually in the form of adenosine triphosphate (ATP).

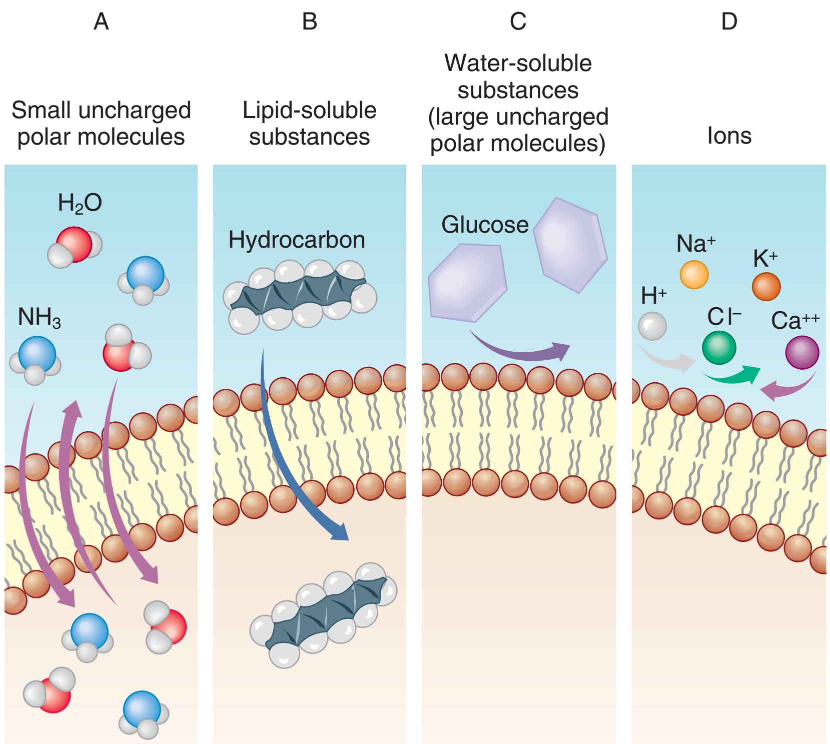


**FIGURE 1-4** A selectively permeable membrane maintains homeostasis by allowing some molecules to pass through, while others may not.

**Endocytosis** is the process of bringing a substance into the cell (**FIGURE 1-8**). The cell membrane surrounds the 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, 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

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 full elevator. The sodium–potassium pump is an example of active transport in the body. Energy is required to move sodium out of the cell where the concentrations are high and move potassium into the cell where the concentrations are high.

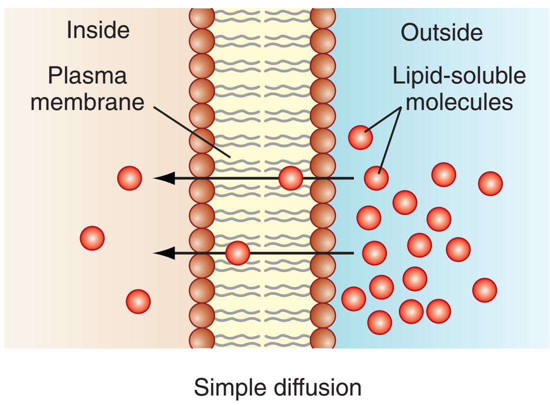


**FIGURE 1-5** Lipid-soluble substances pass through the membrane directly via simple diffusion.

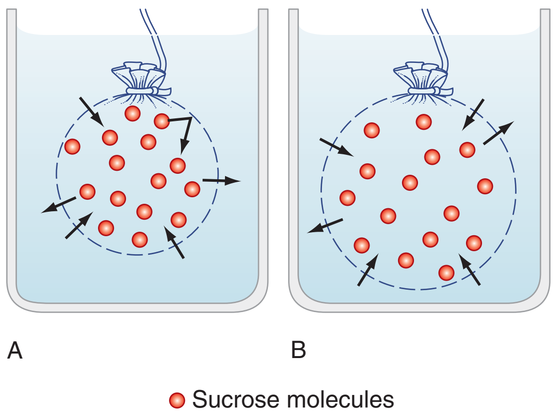


**FIGURE 1-6** (a) When a bag of sugar water is immersed in a solution of pure water, (b) water will diffuse into the bag toward the lower concentrations of water, causing the bag to swell.

## Energy Production

Energy can be a mystery to many of us. To understand energy, first we must understand that it comes in many forms. 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). Food enters the gastrointestinal tract, where it is broken down into sugars, amino acids, and fatty acids. These substances then are 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). Acetyl CoA enters the Krebs cycle, a high-electron-producing process, of the mitochondria. During the Krebs cycle, these molecules go through a complex series of reactions that result in the production of large amounts of ATP.

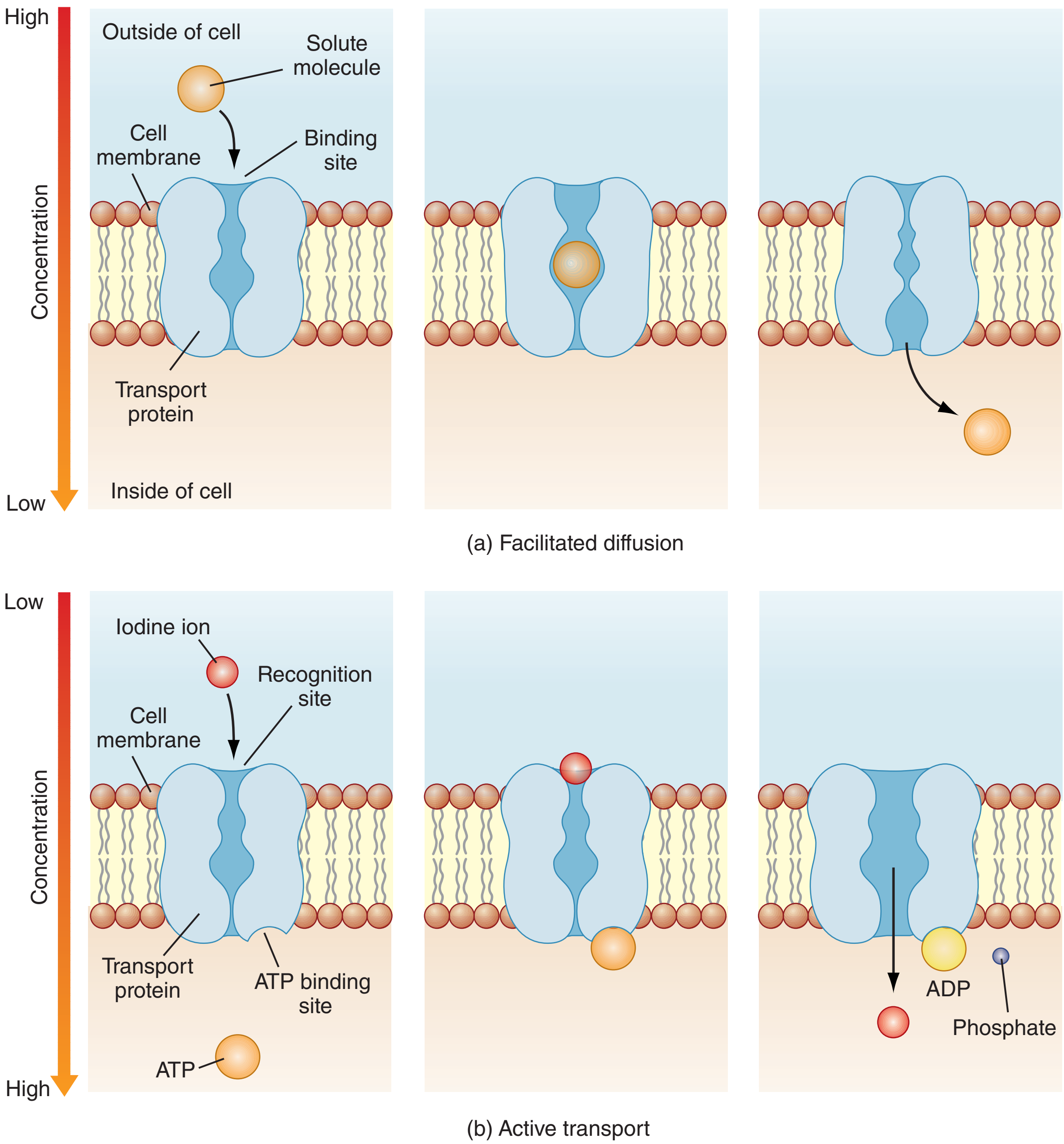


**FIGURE 1-7** Facilitated diffusion and active transport. (a) Water-soluble molecules can also diffuse through membranes with the assistance of proteins in facilitated diffusion. (b) Other proteins use energy from ATP to move against concentration gradients in a process called active transport.

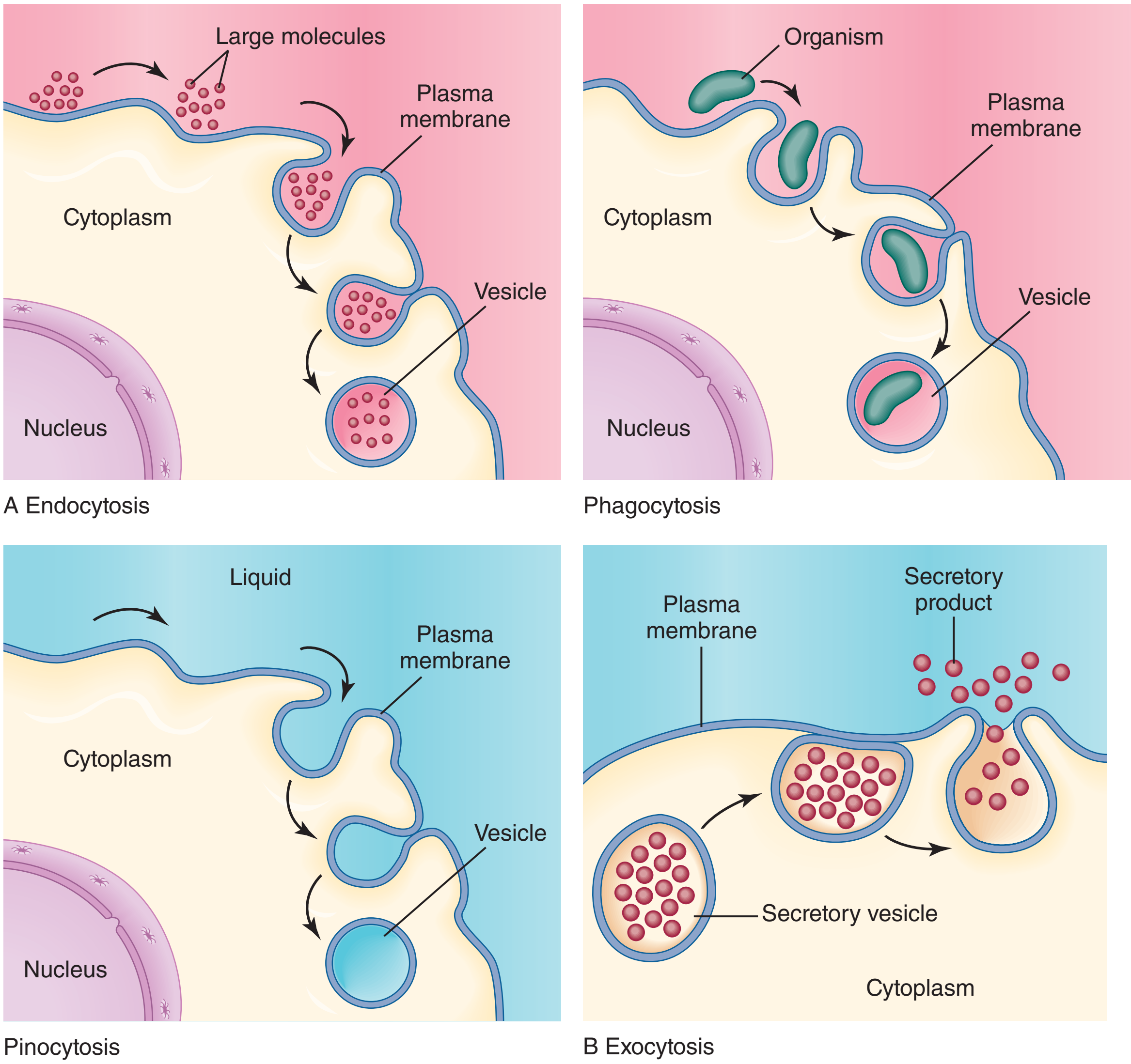


**FIGURE 1-8** (a) Cells can engulf large particles, cell fragments, liquids, and even entire cells. (b) Cells can also get rid of large particles.

## 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. The most common form of cell division, in which the cell divides into two separate cells, is **mitosis** (**FIGURE 1-9**). In mitosis, the division of one cell results in two genetically identical and equal daughter cells. This process occurs in four steps—prophase, 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**. **Meiosis** is a form of cell division that occurs only in mature sperm and ova (Figure 1-9). Normally, human cells contain 46 chromosomes, but sperm and ova contain 23 chromosomes each. When the sperm and ova join, the resulting organism has 46 chromosomes.

**Differentiation** is a process by which cells become specialized in terms of cell type, function, structure, and cell cycle. This process does not begin until approximately 15–60 days after the sperm fertilizes the ova. During this time, the embryo is the most susceptible to damage from environmental influences. Differentiation is the process by which the primitive stem cells of the embryo develop into the highly specialized cells of the human (e.g., cardiac cells and nerve cells).

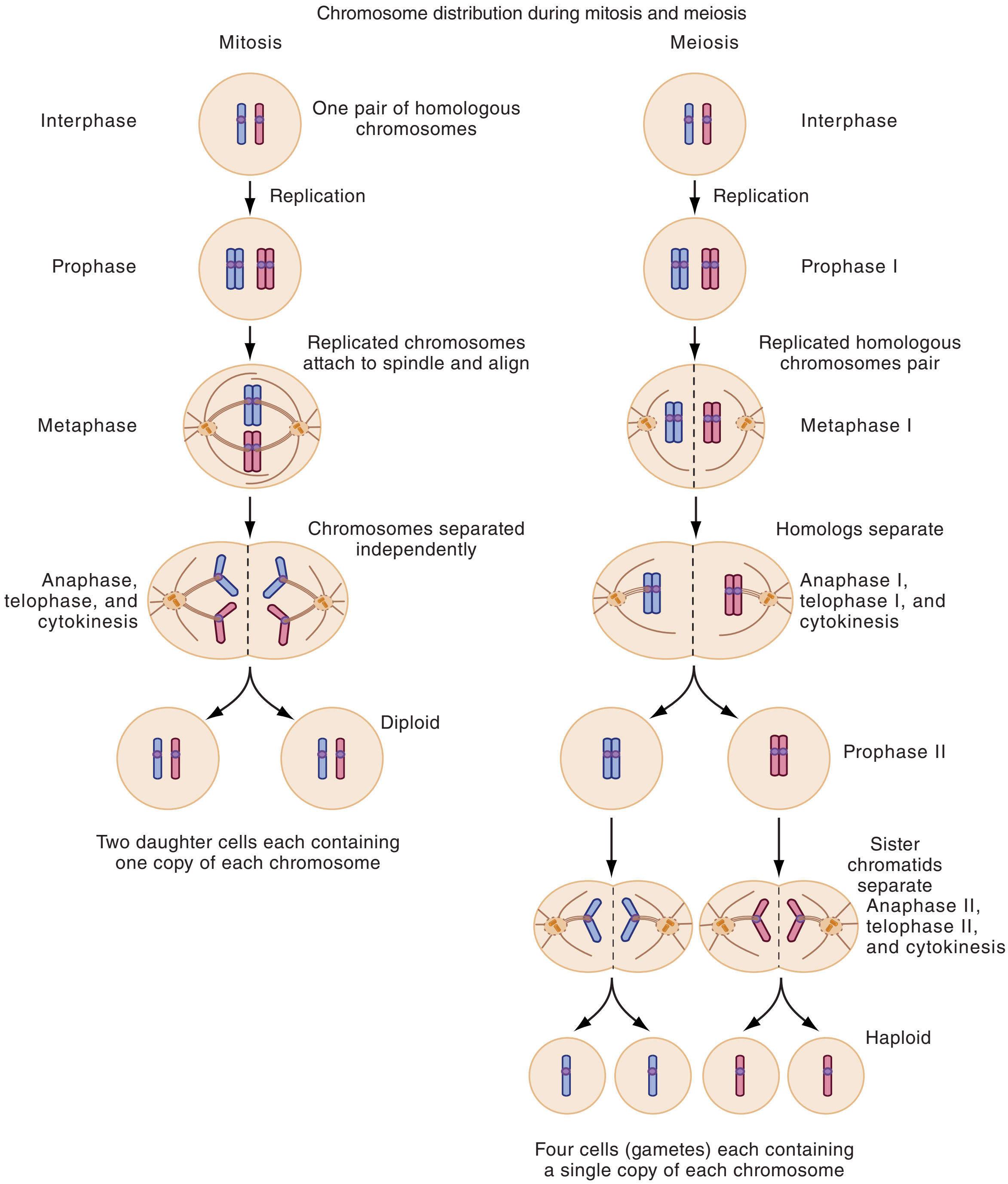


**FIGURE 1-9** Mitosis and meiosis.

# 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**. 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 normal or abnormal depending on whether they were mediated through standard pathways. They may also be permanent or reversible. Nevertheless, once the stimulus is removed, adaptation ceases. Specific types of adaptive changes include atrophy, hypertrophy, hyperplasia, metaplasia, and dysplasia (**FIGURE 1-10**).

**Atrophy** occurs because of decreased work demands on the cell. The body attempts to work