chapter 3

Cells

CLONING AND STEM CELLS. On February 7, 1997, a sheep appeared on the cover of *Nature* magazine and changed the world. Dolly was a cloned sheep—one whose development began, not as a sperm meeting an egg, but as a packet of genes from a cell in the breast of an adult sheep placed into an egg cell whose own packet of genes had been removed. The transferred genes took over, and Dolly developed, much as any sheep would, in a surrogate sheep mother. The rest, as they say, is history.

Dolly's existence evoked visions of someday farming human clones for spare parts, and a flurry of legislation bloomed to prevent this fate. Meanwhile, receiving far less attention was another technology that may make it possible to grow human cells into tissues and organs in laboratory culture—made-to-order replacement parts.

Stem cell technology begins not with a fertilized egg or an engineered first cell, but with a normal cell that naturally retains the ability to specialize as any, or nearly any, cell type. Such cells from embryos of pigs, cows, rabbits, sheep, and monkeys have been nurtured into various tissues. In humans, stem cells taken from blood in the umbilical cords of newborns are used to generate new bone marrow in people suffering from various blood disorders, with greater success than bone marrow transplants. Tissues in adults harbor stem cells too, which one day may be used to fashion needed parts. Neural stem cells, for example, are being studied for their use as implants to treat degenerative disorders such as Parkinson disease and multiple sclerosis, and heal spinal cord injuries.

Photo:
Dolly the cloned sheep made headlines in the late 1990s, but stem cell technology is much more likely to lead to new medical treatments than cloning.

Chapter Objectives

After studying this chapter, you should be able to do the following:

3.1 Introduction

1. Explain how cells differ from one another. (p. 49)

3.2 Composite Cell

2. Describe the characteristics of a composite cell. (p. 49)
3. Explain how the structure of a cell membrane makes possible its functions. (p. 51)
4. Describe each type of cytoplasmic organelle, and explain its function. (p. 52)
5. Describe the parts of the cell nucleus and its function. (p. 56)

3.3 Movements Through Cell Membranes

6. Explain how substances move through cell membranes. (p. 58)

3.4 The Cell Cycle

7. Describe the cell cycle. (p. 64)
8. Explain how a cell divides. (p. 65)
9. Discuss what happens when a cell specializes. (p. 67)
10. Describe how cell death is a normal part of development. (p. 68)

Aids to Understanding Words

cyt- [cell] *cyt*oplasm: Fluid (cytosol) and organelles that occupy the space between the cell membrane and nuclear envelope.

endo- [within] *endo*plasmic reticulum: Complex of membranous structures within the cytoplasm.

hyper- [above] *hyper*tonic: Solution that has a greater osmotic pressure than body fluids.

hypo- [below] *hypo*tonic: Solution that has a lesser osmotic pressure than body fluids.

inter- [between] *inter*phase: Stage that occurs between mitotic divisions of a cell.

iso- [equal] *iso*tonic: Solution that has the same osmotic pressure as body fluids.

mit- [thread] *mit*osis: Process of cell division when threadlike chromosomes become visible within a cell.

phag- [to eat] *phag*ocytosis: Process by which a cell takes in solid particles.

pino- [to drink] *pino*cytosis: Process by which a cell takes in tiny droplets of liquid.

-som [body] ribo*som*e: Tiny, spherical structure that consists of protein and RNA.

Key Terms

active transport (ak´tiv trans´port)
apoptosis (ap´´o-to´-sis)
cell membrane (sel mem´-brayn)
centrosome (sent´tro-sōm)
chromosome (kro´mo-sōm)
cytoplasm (si´to-plazm)
cytoskeleton (si-to-skel´-e-tun)
differentiation (dif´´er-en´´she-a´shun)
diffusion (dĭ-fu´zhun)
endocytosis (en´´do-si-to´sis)
endoplasmic reticulum (en´do-plaz´mik rĕ-tik´u-lum)
equilibrium (e´´kwĭ-lib´re-um)
exocytosis (ex-o-si-to´sis)
facilitated diffusion (fah-sil´´ĭ-tāt´ed dĭ-fu´zhun)
filtration (fil-tra´shun)
Golgi apparatus (gol´je ap´´ah-ra´tus)
lysosome (li´so-sōm)
mitochondrion (mi´´to-kon´dre-un); plural: mitochondria (mi´´to-kon´dre-ah)
mitosis (mi-to´sis)
nucleolus (nu-kle´o-lus)
nucleus (nu´kle-us)
organelle (or-gan-el´)
osmosis (oz-mo´sis)
phagocytosis (fag´´o-si-to´sis)
pinocytosis (pi´´no-si-to´sis)
ribosome (ri´bo-sōm)
selectively permeable (se-lek´tiv-le per´me-ah-bl)
vesicle (ves´ĭ-k'l)

3.1 Introduction

Recipe for a human being: cells, their products, and fluids. A cell, as the unit of life, is a world unto itself. To build a human, trillions of cells connect and interact, forming dynamic tissues, organs, and organ systems.

The estimated 75 trillion cells that make up an adult human body have much in common. Yet, cells in different tissues vary considerably in size and shape, and typically, their shapes make possible their functions. For instance, nerve cells often have long, threadlike extensions that transmit electrical impulses from one part of the body to another. Epithelial cells that line the inside of the mouth are thin, flattened, and tightly packed, an arrangement that enables them to protect underlying cells. Muscle cells, which pull structures closer together, are slender and rodlike, with their ends attached to the structures they move (fig. 3.1).

3.2 Composite Cell

Because cells vary so greatly in size, shape, content, and function, describing a "typical" cell is impossible. The cell shown in figure 3.2 and described in this chapter is a composite cell that includes many known cell structures. In reality, cells have most, but not all, of these structures.

Under the light microscope, with a properly applied stain to make structures visible, the **nucleus** (nu´kle-us), **cytoplasm** (si´to-plazm), and **cell membrane** (sel mem´-brayn) are easily seen. The nucleus is often centrally located in the cell and is surrounded by a thin nuclear envelope. The cytoplasm surrounds the nucleus and is itself encircled by an even thinner cell membrane (also called the plasma membrane).

Within the cytoplasm are specialized structures called **organelles** (or-gan-elz´), which can be seen clearly only under the higher magnification of electron microscopes. Organelles, suspended in a liquid called *cytosol,* perform specific functions, in a sense dividing the labor of the cell. The nucleus, on the other hand, directs overall cell activities by housing the genetic material. The cell membrane determines which substances enter and leave the cell, and oversees how cells interact.

CHECK YOUR RECALL

1. Give two examples to illustrate how the shape of a cell makes possible its function.
2. Name the three major parts of a cell.
3. What are the general functions of the cytoplasm, nucleus, and cell membrane?
4. What are organelles?

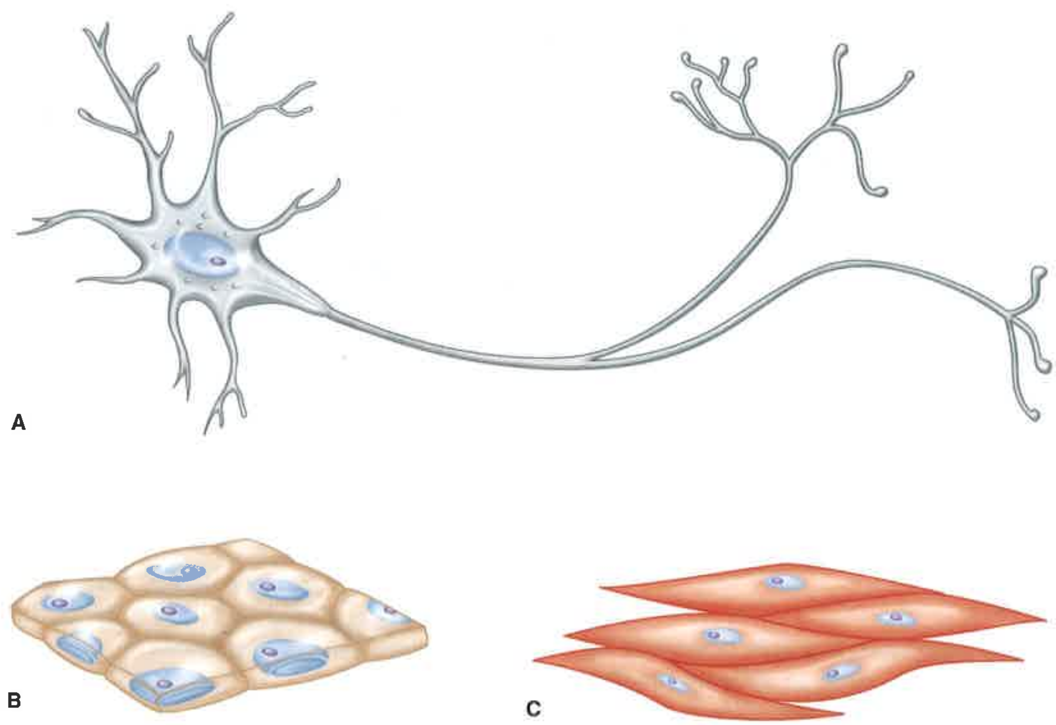

Figure 3.1
Cells vary in structure and function. (*A*) A nerve cell transmits impulses from one body part to another. (*B*) Epithelial cells protect underlying cells. (*C*) Muscle cells contract, pulling structures closer together.

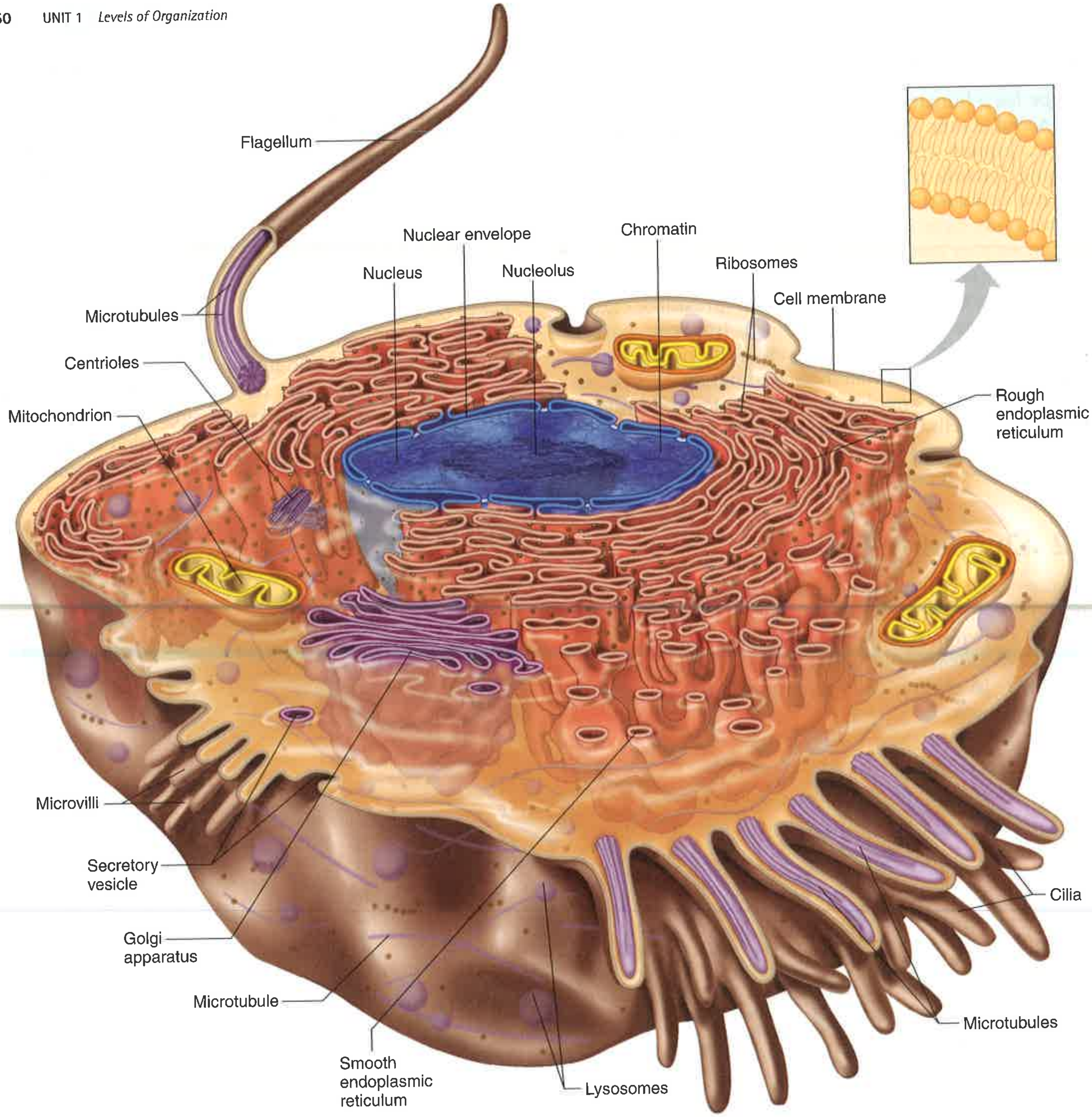

Figure 3.2
A composite cell. Organelles are not drawn to scale.

Cell Membrane

The cell membrane is more than a simple boundary surrounding the cellular contents. It is an actively functioning part of the living material. The cell membrane regulates movement of substances in and out of the cell and is the site of much biological activity. Molecules that are part of the cell membrane receive stimulation from outside the cell and transmit it into the cell, a process called *signal transduction*. The cell membrane also helps cells adhere to certain other cells, which is important in forming tissues.

General Characteristics

The cell membrane is extremely thin—visible only with the aid of an electron microscope—but it is flexible and somewhat elastic. It typically has complex surface features with many outpouchings and infoldings that increase surface area (fig. 3.2).

In addition to maintaining cell integrity, the cell membrane controls which substances exit and enter. A membrane that functions in this way is called **selectively permeable** (se-lek´tiv-le per´me-ah-bl) (also known as *semipermeable* or *differentially permeable*).

Cell Membrane Structure

A cell membrane is composed mainly of lipids, proteins, and a small quantity of carbohydrates. Its basic framework is a double layer, or *bilayer*, of phospholipid molecules. Each phospholipid molecule includes a phosphate group and two fatty acids bound to a glycerol molecule (see chapter 2, p. 40). The water-soluble phosphate "heads" form the surfaces of the membrane, and the water-insoluble fatty acid "tails" make up the interior of the membrane. The lipid molecules can move sideways within the plane of the membrane. Together they form a soft and flexible, but stable, fluid film.

Because the membrane's interior consists largely of the fatty acid portions of the phospholipid molecules (fig. 3.3), it is oily. Molecules such as oxygen and carbon dioxide, which are soluble in lipids, can pass through this bilayer easily. However, the bilayer is impermeable to water-soluble molecules, such as amino acids, sugars, proteins, nucleic acids, and various ions. Many cholesterol molecules embedded in the cell membrane's interior also help make the membrane less permeable to water-soluble substances. In addition, the relatively rigid structure of the cholesterol molecules helps stabilize the membrane.

A cell membrane includes a few types of lipid molecules, but many kinds of proteins, which provide special functions. Membrane proteins are classified according to their positions. For example, membrane-spanning (transmembrane) proteins extend through the lipid bilayer and may protrude from one or both faces. In contrast, peripheral membrane proteins are associated with one side of the bilayer. Membrane proteins also vary in shape—some may be globular, others rodlike.

Membrane proteins have a variety of functions. Some form receptors on the cell surface that bind incoming hormones or growth factors, starting signal transduction. The cell then responds. Other proteins transport ions or molecules across the cell membrane. Still other membrane proteins form selective channels that allow only particular ions to enter or leave. In nerve cells, for example, such selective channels control movement of sodium and potassium ions (see chapter 9, p. 212). The Genetics Connection (p. 52) discusses some inherited disorders that result from abnormal ion channels in cell membranes.

Proteins that extend from the inner face of the cell membrane anchor it to the rods and tubules that support the cell from within. Proteins that extend from the outer surface, where carbohydrate molecules may attach to them, mark the cell as part of a particular tissue or organ in a particular person. This identification is important for

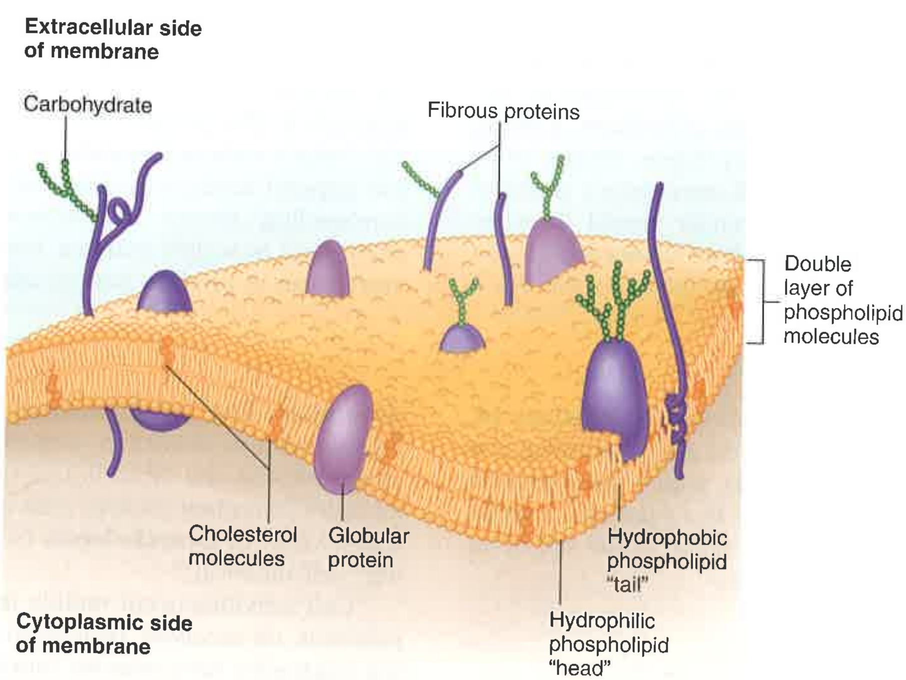

Figure 3.3
The cell membrane is composed primarily of phospholipids (and some cholesterol), with proteins scattered throughout the lipid bilayer and associated with its surfaces.

Genetics Connection

FAULTY ION CHANNELS CAUSE INHERITED DISEASE

What do collapsing horses, irregular heartbeats, and cystic fibrosis have in common? All result from abnormal ion channels in cell membranes.

Ion channels are protein-lined tunnels in the phospholipid bilayer of a biological membrane. These passageways permit electrical signals to pass in and out of membranes in the form of ions (charged particles). Many ion channels open or close like a gate in response to specific ions under specific conditions, such as a change in electrical forces across the membrane, binding of a molecule, or receiving biochemical messages from inside or outside the cell.

Ion channels are specific for calcium (Ca^{+2}), sodium (Na^{+}), potassium (K^{+}), or chloride (Cl^{-}). A cell membrane may have a few thousand ion channels specific for each of these ions. Ten million ions can pass through an ion channel in one second! Drugs may act by affecting ion channels, and abnormal ion channels cause certain disorders, including the following:

Hyperkalemic Periodic Paralysis and Sodium Channels

The quarter horse was originally bred in the 1600s to run the quarter mile, but one of the four very fast stallions used to establish much of today's population of 3 million animals inherited hyperkalemic periodic paralysis (HPP). The horse, otherwise a champion, sometimes collapsed from sudden attacks of weakness and paralysis.

HPP results from abnormal sodium channels in the cell membranes of muscle cells. But the trigger for the temporary paralysis is another ion: potassium. A rising blood potassium level, which may follow intense exercise, slightly alters the muscle cell membrane's electrical charge. Normally, this slight change would have no effect, but in horses with HPP, sodium channels open too widely, allowing too much sodium into the cell. For a short time, the muscle cell cannot respond to nervous stimulation. Although the effect is brief, it's long enough for the racehorse to fall.

People can inherit HPP too. In one family, several members collapsed suddenly after eating bananas! These fruits are very high in potassium, which caused the symptoms.

Long-QT Syndrome and Potassium Channels

Four children in a Norwegian family were born deaf, and three of them died at ages four, five, and nine. All of the children had inherited from unaffected "carrier" parents "long-QT syndrome associated with deafness." They had abnormal potassium channels in the heart muscle and in the inner ear. In the heart, the malfunctioning channels disrupted electrical activity, causing a fatal disturbance to the heart rhythm. In the inner ear, the abnormal channels caused an increase in the extracellular concentration of potassium ions, impairing hearing.

Cystic Fibrosis and Chloride Channels

A seventeenth-century English saying, "A child that is salty to taste will die shortly after birth," described the consequence of abnormal chloride channels in the inherited illness cystic fibrosis (CF). The disorder is inherited from carrier parents. The major symptoms—difficulty breathing, frequent severe respiratory infections, and a clogged pancreas that disrupts digestion—all result from buildup of extremely thick mucous secretions.

Abnormal chloride channels in cells lining the lung passageways and ducts of the pancreas cause the symptoms of CF. The primary defect in the chloride channels also causes sodium channels to malfunction. The result: Salt trapped inside cells draws moisture in and thickens surrounding mucus. Experimental gene therapy is attempting to supply patients' lung-lining cells with the instructions to produce normal chloride channels.

the functioning of the immune system (see chapter 14, p. 375). Another type of protein on a cell's surface is a cellular adhesion molecule (CAM), which determines a cell's interactions with other cells. For example, a series of CAMs helps a white blood cell move to the site of an injury, such as a splinter in the skin.

Cytoplasm

When viewed through a light microscope, cytoplasm usually appears as a clear jelly with specks scattered throughout. However, an electron microscope, which produces much greater magnification and the ability to distinguish fine detail (resolution), reveals that cytoplasm contains networks of membranes and organelles suspended in the clear liquid *cytosol*. Cytoplasm also includes abundant protein rods and tubules that form a framework, or **cytoskeleton** (si-to-skel´-e-tun), meaning "cell skeleton."

Cell activities occur mainly in the cytoplasm, where nutrients are received, processed, and used. The following organelles have specific functions:

1. **Endoplasmic reticulum** (en´do-plaz´mik rĕ-tik´u-lum) The endoplasmic reticulum (ER) is a complex organelle composed of membrane-bounded,

flattened sacs, elongated canals, and fluid-filled, bubblelike sacs called *vesicles.* These membranous parts are interconnected and communicate with the cell membrane, the nuclear envelope, and other organelles. The ER provides a vast tubular network that transports molecules from one cell part to another.

The endoplasmic reticulum participates in the synthesis of protein and lipid molecules. These molecules may leave the cell as secretions or be used within the cell for such functions as producing new ER or cell membrane as the cell grows.

In many places, the ER's outer membrane is studded with many tiny, spherical structures called *ribosomes,* which give the ER a textured appearance when viewed with an electron microscope (fig. 3.4*A, B*). These parts of the ER are called rough ER. The ribosomes are sites of protein synthesis and exist independently in the cytoplasm as well as associated with ER. Proteins being synthesized then move through ER tubules to another organelle, the Golgi apparatus, for further processing.

ER that lacks ribosomes is called *smooth ER* (fig. 3.4*C*). Smooth ER contains enzymes important in lipid synthesis, absorption of fats from the digestive tract, and the metabolism of drugs. Cells that break down drugs and alcohol, such as liver cells, have extensive networks of smooth ER.

2. **Ribosomes** (ri´bo-sōmz) Ribosomes are the sites of protein synthesis. Many ribosomes are attached to ER membranes; others are scattered throughout the cytoplasm. All ribosomes are composed of protein and RNA molecules. Ribosomes provide enzymes as well as a structural support for the RNA molecules that come together as the cell synthesizes proteins from amino acids. Chapter 4 (pp. 81–85) describes protein synthesis.

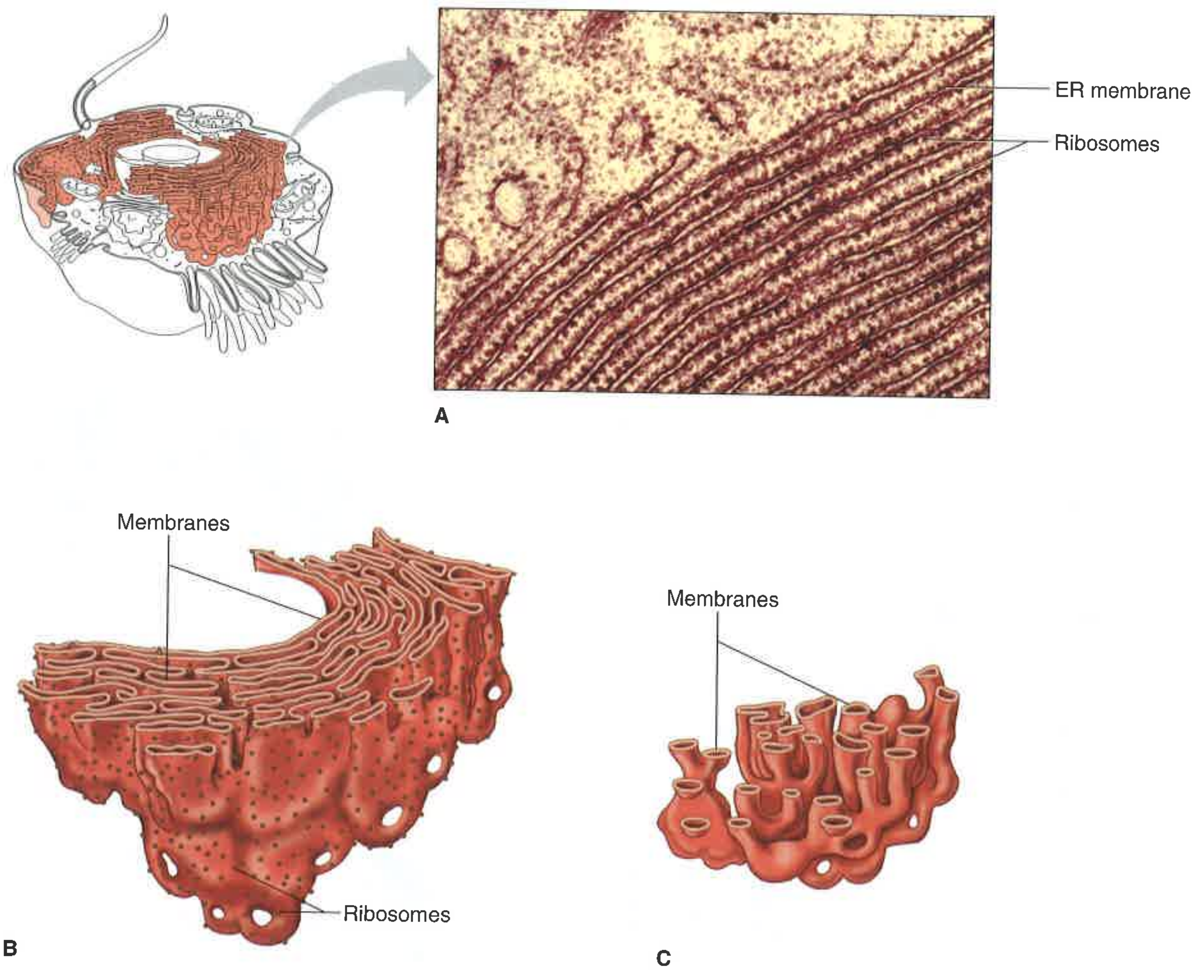

Figure 3.4
The endoplasmic reticulum. (*A*) A transmission electron micrograph of rough endoplasmic reticulum (ER) (28,500×). (*B*) Rough ER is dotted with ribosomes, whereas (*C*) smooth ER lacks ribosomes.

3. **Golgi apparatus** (gol´je ap´´ah-ra´tus) The Golgi apparatus is composed of a stack of about six flattened, membranous sacs. This organelle refines, packages, and delivers proteins synthesized on ribosomes associated with the ER. Proteins arrive at the Golgi apparatus enclosed in vesicles composed of the ER membrane. These vesicles fuse with the membrane at the innermost end of the Golgi apparatus, which is specialized to receive glycoproteins (sugars bound to proteins).

   As the glycoproteins pass from layer to layer through the stacks of Golgi membrane, they are modified chemically. For example, sugar molecules may be added or removed. When the altered glycoproteins reach the outermost layer, they are packaged in bits of Golgi membrane, which bud off and form bubblelike structures called transport vesicles. Such a vesicle may then move to and fuse with the cell membrane, releasing its contents to the outside as a secretion (figs. 3.2 and 3.5). This process is called *exocytosis* (see page 62). Other vesicles, some of which bud off the cell membrane's inner face, may transport glycoproteins to organelles within the cell. The vesicles in a cell form a delivery service of sorts.

CHECK YOUR RECALL

1. What is a selectively permeable membrane?
2. Describe the chemical structure of a cell membrane.
3. What are the functions of the endoplasmic reticulum?
4. Describe the functions of the Golgi apparatus.

4. **Mitochondria** (mi´´to-kon´dre-ah; *sing.* mi´´to-kon´dre-un) Mitochondria are elongated, fluid-filled sacs that vary in size and shape. They can move slowly through the cytoplasm and reproduce by dividing. A mitochondrion has an outer and an inner layer (figs. 3.2 and 3.6). The inner layer folds extensively to form partitions called *cristae*. Connected to the cristae are enzymes that control some of the chemical reactions that release energy from certain nutrient molecules. Mitochondria are the major sites of chemical reactions that transform

Mitochondria may provide clues to the origin of life. According to the endosymbiont theory, mitochondria are the remnants of once free-living bacteria-like cells that were swallowed by more complex primitive cells. These bacterial passengers remain in our cells today, where they are crucial to extracting energy from nutrients. The bacterium that causes typhus, for example, is remarkably similar to a mitochondrion.

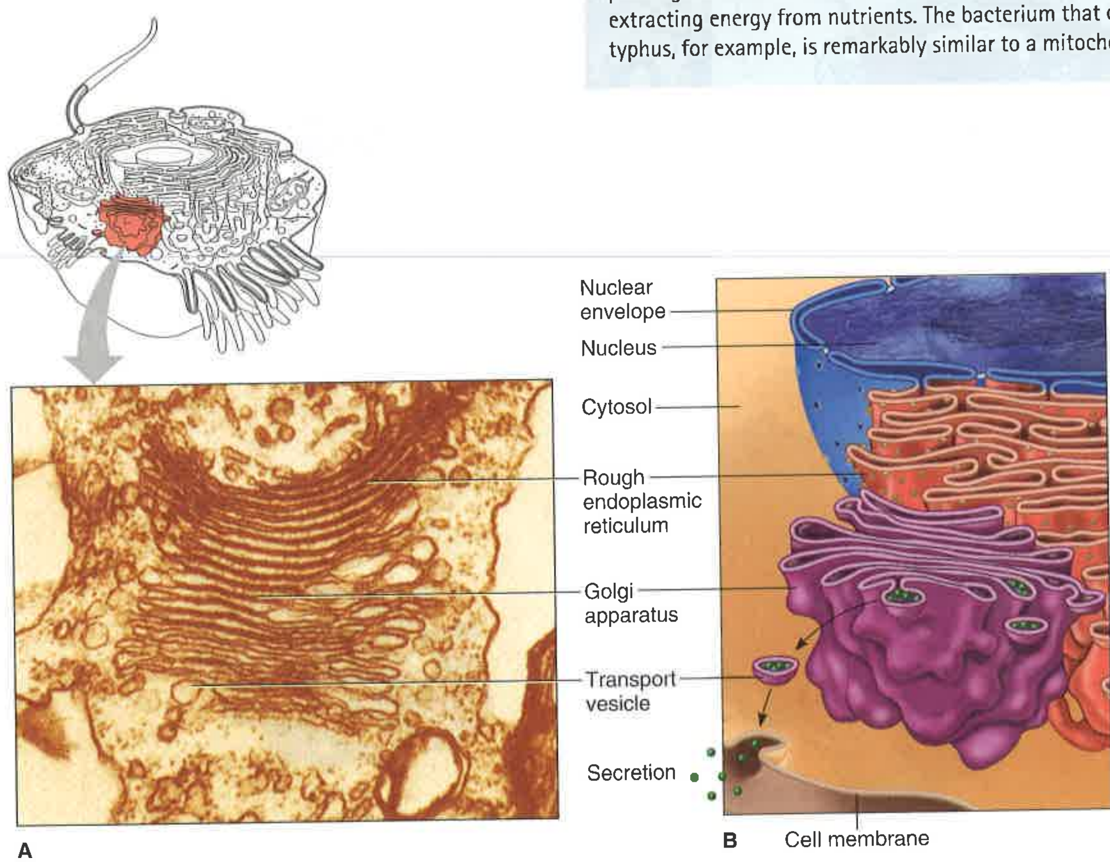

Figure 3.5
The Golgi apparatus. (*A*) A transmission electron micrograph of a Golgi apparatus (48,500×). (*B*) The Golgi apparatus consists of membranous sacs that continually receive vesicles from the endoplasmic reticulum and produce vesicles that enclose secretions.

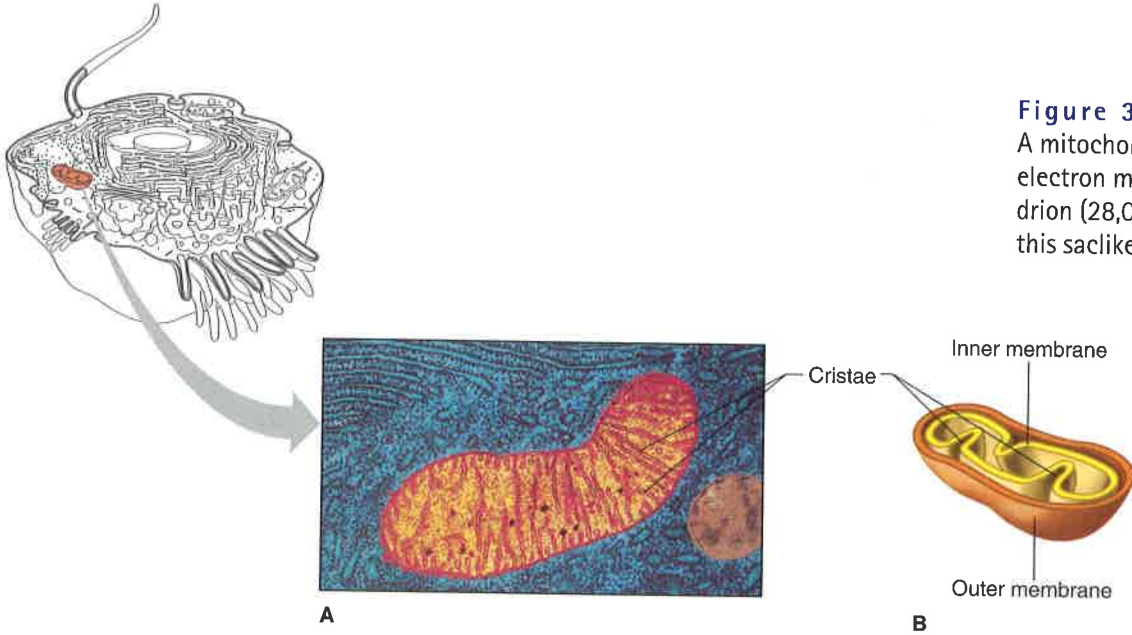

Figure 3.6
A mitochondrion. (*A*) A transmission electron micrograph of a mitochondrion (28,000×). (*B*) Cristae partition this saclike organelle.

this energy into adenosine triphosphate (ATP), a chemical form the cell can use. Very active cells, such as muscle cells, contain many thousands of mitochondria. (Chapter 4 p. 78 describes this energy-releasing function in more detail.) Mitochondria resemble bacterial cells and even contain a small amount of their own DNA.

5. **Lysosomes** (li´so-sōmz) Lysosomes, the "garbage disposals of the cell," are tiny membranous sacs (see fig. 3.2). They contain powerful enzymes that break down nutrient molecules or foreign particles. Certain white blood cells, for example, can engulf bacteria, which are then digested by the lysosomal enzymes. This is one way that white blood cells fight bacterial infections. Lysosomes also destroy worn cellular parts.
6. **Peroxisomes** (pĕ-roks´ĭ-sōmz) These membranous sacs are abundant in liver and kidney cells. They house enzymes that catalyze (speed) a variety of biochemical reactions, including synthesis of bile acids (used to digest fats); detoxification of hydrogen peroxide, a by-product of metabolism; breakdown of certain lipids and rare biochemicals; and detoxification of alcohol.
7. **Microfilaments and microtubules** Microfilaments and microtubules are two types of thin, threadlike strands within the cytoplasm. They form the cytoskeleton and are also part of structures that have specialized activities.

   Microfilaments are tiny rods of actin protein that form meshworks or bundles. They provide cell motility (movement). In muscle cells, for example, microfilaments aggregate to form *myofibrils*, which help these cells contract (see chapter 8, p. 173).

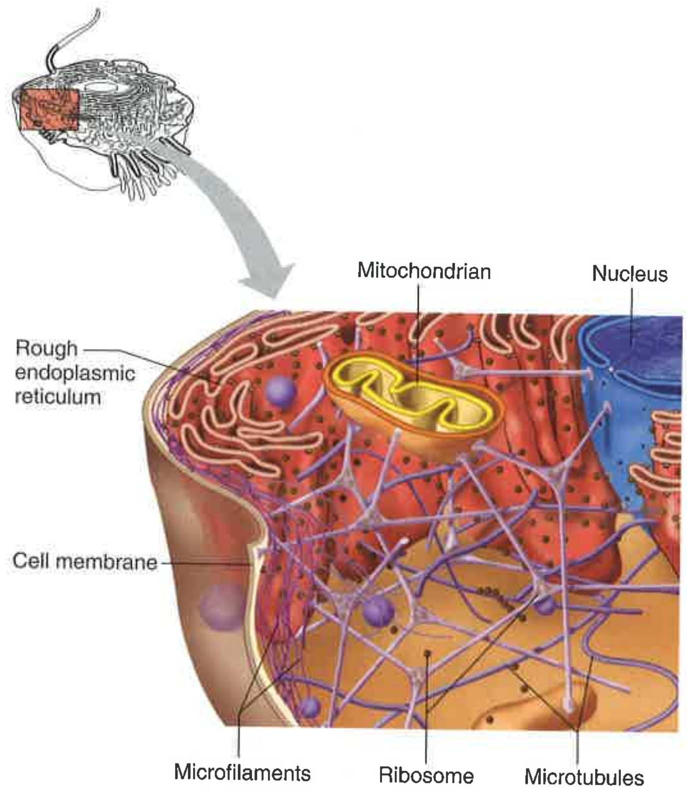

Figure 3.7
Microtubules built of tubulin and microfilaments built of actin help maintain the shape of a cell by forming a cytoskeleton within the cytoplasm.

Microtubules are long, slender tubes with diameters two or three times that of microfilaments. Microtubules are composed of globular tubulin proteins that are typically arrayed in a characteristic "9 + 2" pattern, in which nine outside tubules form a ring around two inner ones (fig. 3.7).

8. **Centrosome** (sent´tro-sōm) The centrosome is a structure near the Golgi apparatus and nucleus. It is nonmembranous and consists of two hollow cylinders, called *centrioles,* which are composed of microtubules (figs. 3.2 and 3.8). The centrioles lie at right angles to each other. During mitosis, they distribute chromosomes to newly forming cells.

9. **Cilia and flagella** Cilia and flagella, motile extensions from the surfaces of certain cells, are also composed of microtubules in a "9 + 2" array. They are similar structures that differ mainly in length and abundance.

   Cilia fringe the free surfaces of some epithelial (lining) cells. Each cilium is a tiny, hairlike structure that is attached beneath the cell membrane (see fig. 3.2). Cilia form in precise patterns, and they move in a "to-and-fro" manner, coordinated so that rows of cilia beat in succession, producing a wave of motion that sweeps over the ciliated surface. This wave moves fluids, such as mucus, over the surface of certain tissues, including those that form the inner linings of the respiratory tubes (fig. 3.9*A*).

   Flagella are considerably longer than cilia, and usually a cell has only a single flagellum. Flagella have an undulating wavelike motion, which begins at their base. The tail of a sperm cell is a flagellum that enables this motile cell to "swim" and is the only example of a flagellum in humans (fig. 3.9*B*).

10. **Vesicles** (ves´ĭ-k'lz) Vesicles (vacuoles) are membranous sacs formed by part of the cell membrane folding inward and pinching off. As a result, a tiny, bubblelike vesicle, containing some liquid or solid material formerly outside the cell, appears in the cytoplasm. The Golgi apparatus and ER also form vesicles that play a role in secretion (see fig. 3.2).

CHECK YOUR RECALL

1. Describe a mitochondrion.
2. What is the function of a lysosome?
3. How do microfilaments and microtubules differ?
4. What are some structures that consist of microtubules?

Cell Nucleus

The nucleus houses the genetic material (DNA), which directs all cell activities (figs. 3.2 and 3.10). It is a large, spherical structure enclosed in a double-layered **nuclear envelope,** which consists of inner and outer lipid bilayer membranes. The nuclear envelope has protein-lined channels called nuclear pores that allow certain molecules to exit the nucleus. A nuclear pore is not just a hole, but a complex opening formed from 100 or so types of proteins.

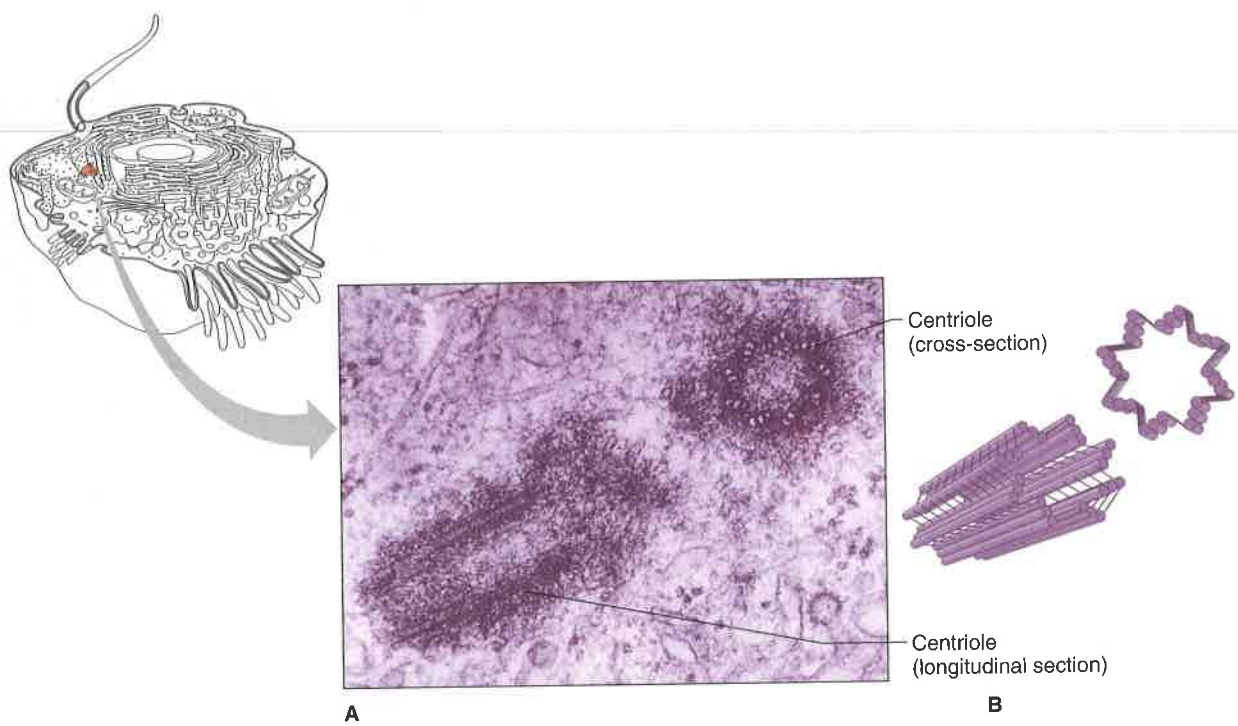

Figure 3.8
Centrioles. (*A*) Transmission electron micrograph of the two centrioles in a centrosome (120,000×). (*B*) The centrioles lie at right angles to one another.

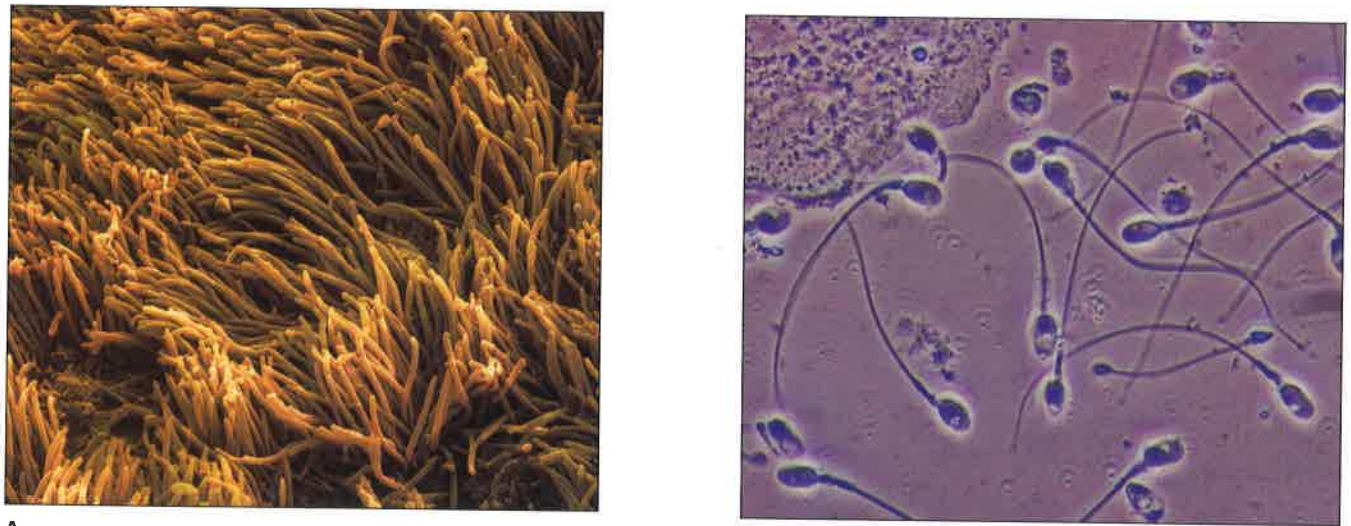

Figure 3.9
Cilia and flagella. (*A*) Cilia are common on the surfaces of certain cells, including those that form the inner lining of the respiratory tubes (5,800×). (*B*) Flagella form the tails of these human sperm cells (840×).

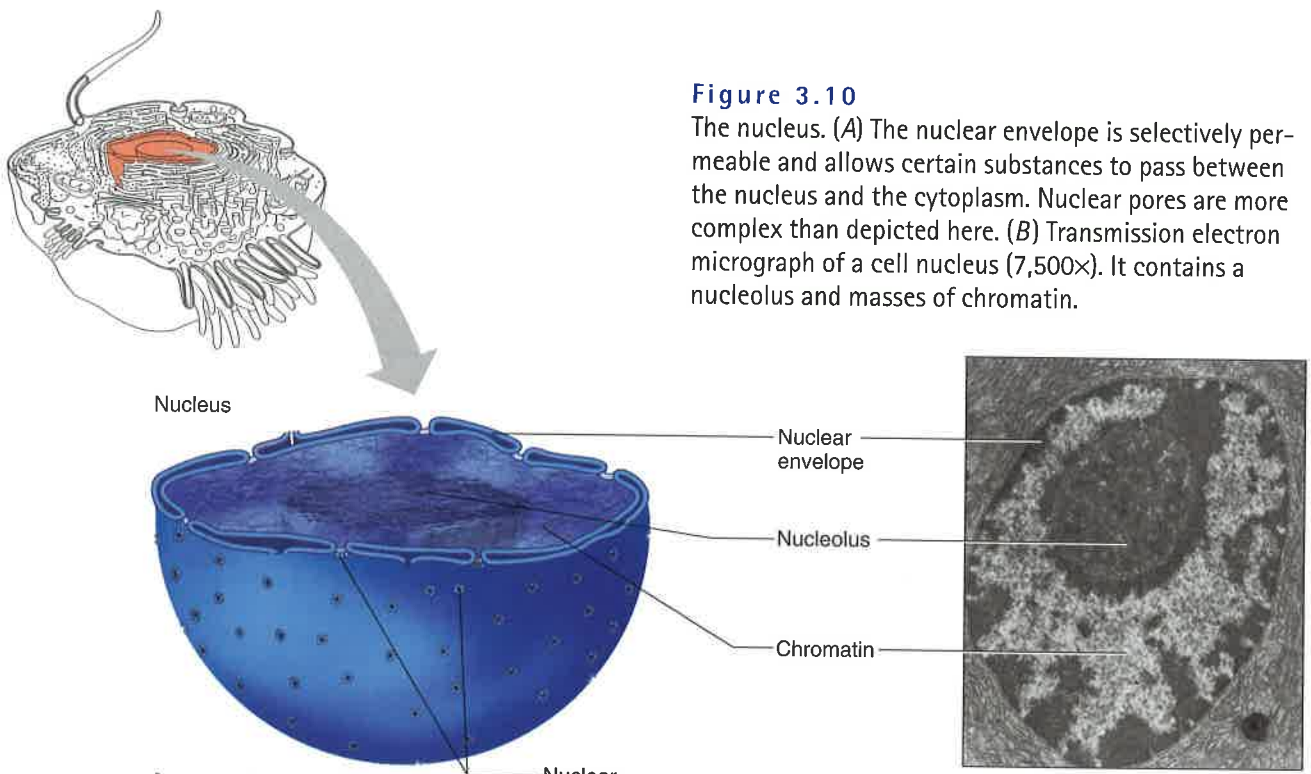

Figure 3.10
The nucleus. (*A*) The nuclear envelope is selectively permeable and allows certain substances to pass between the nucleus and the cytoplasm. Nuclear pores are more complex than depicted here. (*B*) Transmission electron micrograph of a cell nucleus (7,500×). It contains a nucleolus and masses of chromatin.

The nucleus contains a fluid in which the following structures are suspended:

1. **Nucleolus** (nu-kle´o-lus) A nucleolus ("little nucleus") is a small, dense body composed largely of RNA and protein. It has no surrounding membrane and forms in specialized regions of certain chromosomes. Ribosomes form in the nucleolus, then migrate through nuclear pores to the cytoplasm.
2. **Chromatin** Chromatin consists of loosely coiled fibers of DNA and protein called **chromosomes** (kro´mo-sōmz). The DNA contains the information for protein synthesis. When the cell begins to divide, chromatin fibers coil tightly and individual chromosomes become visible.

Table 3.1 summarizes the structures and functions of organelles.

CHECK YOUR RECALL

1. What structure separates the nuclear contents from the cytoplasm?
2. What is produced in the nucleolus?
3. What is chromatin?

3.3 Movements Through Cell Membranes

The cell membrane is a selective barrier that controls which substances enter and leave the cell. These movements include passive mechanisms that do not require cellular energy (diffusion, facilitated diffusion, osmosis, and filtration) and active mechanisms that use cellular energy (active transport, endocytosis, and exocytosis).

Passive Mechanisms

Diffusion

Diffusion (dĭ-fu´zhun) (also called *simple diffusion*) is the process by which molecules or ions scatter or spread spontaneously from regions where they are in higher concentrations toward regions where they are in lower concentrations. This difference in concentration is called a *concentration gradient*. Atoms, molecules, and ions are said to diffuse down their concentration gradients.

Under natural conditions, molecules and ions constantly move at high speeds. Each particle travels in a separate path along a straight line until it collides and bounces off some other particle, changing direction, colliding again, and changing direction once more. Such random motion mixes molecules. At body temperature, small molecules such as water move more than a thousand miles per hour. However, the internal environment is crowded, from a molecule's point of view. A single molecule may collide with other molecules a million times each second.

Consider sugar (a solute). When first put into a glass of water (a solvent), the sugar remains highly concentrated at the bottom of the glass (fig. 3.11). As a result of diffusion, the sugar molecules move away from the area of high concentration and spread into solution among the moving water molecules. Eventually the sugar molecules become uniformly distributed in the water, a state called **equilibrium** (e´´kwĭ-lib´re-um). Molecules continue to move after equilibrium occurs, but their concentrations no longer change.

Diffusion of a substance into or out of the cell can occur only if (1) the cell membrane is permeable to that substance, and (2) a concentration gradient exists such that the substance is at a higher concentration either out-

TABLE 3.1 STRUCTURES AND FUNCTIONS OF CYTOPLASMIC ORGANELLES

ORGANELLE(S)	STRUCTURE	FUNCTION
Cell membrane	Membrane composed of protein and lipid molecules	Maintains integrity of cell and controls passage of materials into and out of cell
Endoplasmic reticulum	Complex of interconnected membrane-bounded sacs and canals	Transports materials within cell, provides attachment for ribosomes, and synthesizes lipids
Ribosomes	Particles composed of protein and RNA molecules	Synthesize proteins
Golgi apparatus	Group of flattened, membranous sacs	Packages protein molecules for transport and secretion
Mitochondria	Membranous sacs with inner partitions	Release energy from nutrient molecules and transform energy into usable form
Lysosomes	Membranous sacs	Digest worn cellular parts or substances that enter cells
Peroxisomes	Membranous sacs	House enzymes that catalyze diverse reactions, including bile acid synthesis, lipid breakdown, and alcohol detoxification
Microfilaments and microtubules	Thin rods and tubules	Support the cytoplasm and help move substances and organelles within the cytoplasm
Centrosome	Nonmembranous structure composed of two rodlike centrioles	Helps distribute chromosomes to new cells during cell division
Cilia and flagella	Motile projections attached beneath the cell membrane	Cilia propel fluid over cellular surfaces, and a flagellum enables a sperm cell to move
Vesicles	Membranous sacs	Contain and transport various substances
Nuclear envelope	Double membrane that separates the nuclear contents from the cytoplasm	Maintains integrity of nucleus and controls passage of materials between nucleus and cytoplasm
Nucleolus	Dense, nonmembranous body composed of protein and RNA	Site of ribosome synthesis
Chromatin	Fibers composed of protein and DNA	Contains information for synthesizing proteins

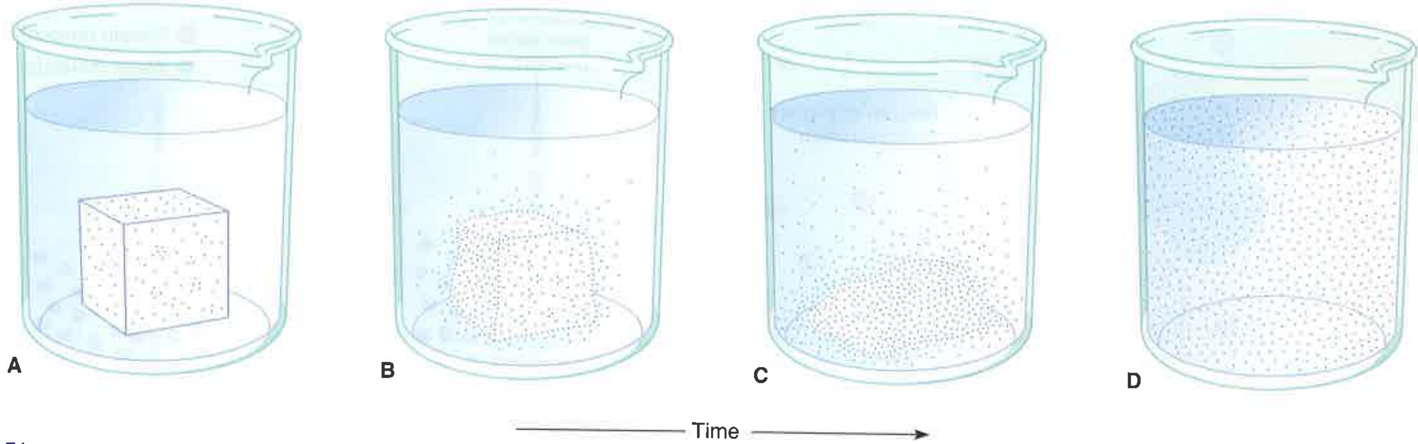

Figure 3.11
An example of diffusion. (*A, B,* and *C*) A sugar cube placed in water slowly disappears as the sugar molecules dissolve and then diffuse from regions where they are more concentrated toward regions where they are less concentrated. (*D*) Eventually, the sugar molecules are distributed evenly throughout the water.

side or inside the cell. Consider oxygen and carbon dioxide, two substances to which cell membranes are permeable. In the body, diffusion is the process whereby oxygen enters cells and carbon dioxide leaves cells, but equilibrium is never reached. Intracellular oxygen is always low because oxygen is constantly used up in metabolic reactions. Extracellular oxygen is maintained at a high level by homeostatic mechanisms in the respiratory and cardiovascular systems. Thus, a concentration gradient always allows oxygen to diffuse into the body's cells.

The level of carbon dioxide, produced as a waste product of metabolism, is always high inside cells. Homeostasis maintains a lower extracellular carbon dioxide level, so a concentration gradient always favors carbon dioxide diffusing out of cells (fig. 3.12).

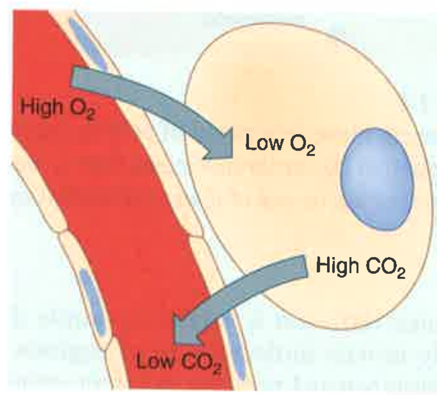

Figure 3.12
Diffusion is the process whereby oxygen enters the cells and carbon dioxide leaves the cells.

Dialysis is a chemical technique that uses diffusion to separate small molecules from larger ones in a liquid. The artificial kidney uses a variant of this process—*hemodialysis*—to treat patients suffering from kidney damage or failure. An artificial kidney (dialyzer) passes blood from a patient through a long, coiled tubing composed of porous cellophane. The size of the pores allows smaller molecules carried in the blood, such as the waste material urea, to exit through the tubing, while larger molecules, such as those of blood proteins, remain inside the tubing. The tubing is submerged in a tank of dialyzing fluid (wash solution), which contains varying concentrations of different chemicals. The fluid has low concentrations of substances that should leave the blood and higher concentrations of those that should remain in the blood.

Altering the concentrations of molecules in the dialyzing fluid can control which molecules diffuse out of blood and which remain in it. For example, to remove blood urea, the dialyzing fluid must have a lower urea concentration than the blood; to maintain blood glucose concentration, glucose concentration in the dialyzing fluid must be at least equal to that of the blood.

Facilitated Diffusion

Substances that are not able to pass through the lipid bilayer need the help of membrane proteins to get across, a process known as **facilitated diffusion** (fah-sil´´ĭ-tāt´ed dĭ-fu´zhun) (fig. 3.13). One form involves the ion channels and pores described earlier. Molecules like glucose and amino acids are not lipid soluble, yet are too large to pass through membrane channels. They enter cells by another form of facilitated diffusion. In this process, which occurs in most cells, the glucose molecule combines with a special protein carrier molecule at the surface of the cell membrane. This union of the glucose and carrier molecules changes the shape of the carrier, enabling it to move glucose to the other side of the membrane. The carrier releases the glucose and then returns to its original shape and picks up another glucose molecule. The hormone *insulin,* discussed in chapter 11 (p. 296), promotes facilitated diffusion of glucose through the membranes of certain cells.

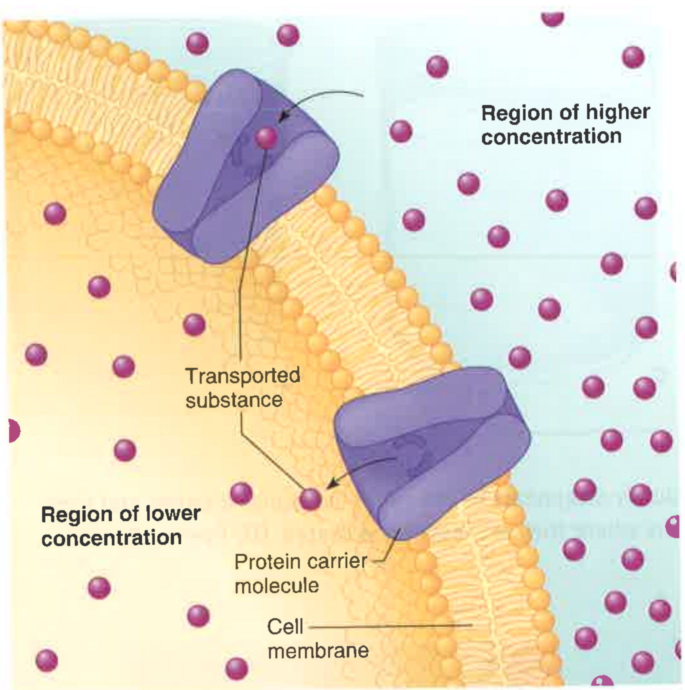

Figure 3.13
Some substances move into or out of cells by facilitated diffusion, transported by carrier molecules from a region of higher concentration to one of lower concentration.

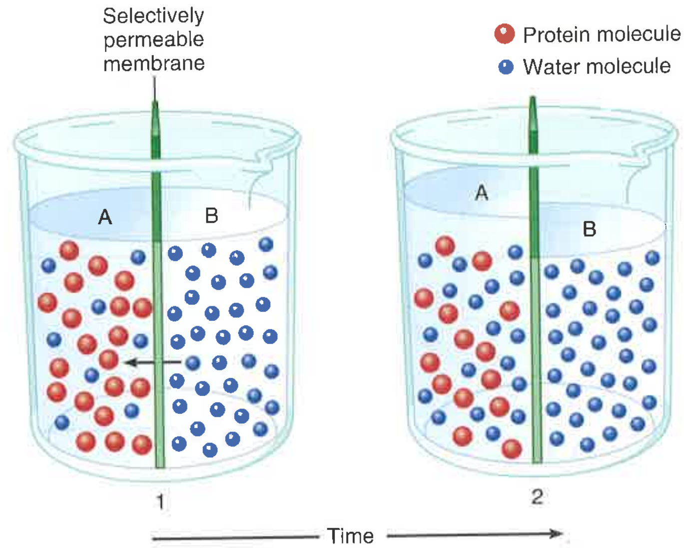

Figure 3.14
Osmosis. (*1*) A selectively permeable membrane separates the container into two compartments. At first, compartment *A* contains water and protein molecules, while compartment *B* contains only water. As a result of molecular motion, water diffuses by osmosis from compartment *B* into compartment *A*. Protein molecules remain in compartment *A* because they are too large to pass through the pores of the membrane. (*2*) Also, because more water is entering compartment *A* than is leaving it, water accumulates in this compartment. The level of liquid rises on this side.

Facilitated diffusion is similar to simple diffusion in that it only moves molecules from regions of higher concentration toward regions of lower concentration. The number of carrier molecules in the cell membrane limits the rate of facilitated diffusion.

Osmosis

Osmosis (oz-mo´sis) is a special case of diffusion. It occurs whenever water molecules diffuse from a region of higher water concentration to a region of lower water concentration across a selectively permeable membrane, such as a cell membrane. In the example that follows, assume that the selectively permeable membrane is permeable to water molecules (the solvent), but impermeable to protein molecules (the solute).

In solutions, a higher concentration of solute (protein in this case) means a lower concentration of water; a lower concentration of solute means a higher concentration of water. This is because solute molecules take up space that water molecules would otherwise occupy.

Just like molecules of other substances, molecules of water diffuse from areas of higher concentration to areas of lower concentration. In figure 3.14, the presence of protein in compartment *A* means that the water concentration there is less than the concentration of pure water in compartment *B*. Therefore, water diffuses from compartment *B* across the selectively permeable membrane and into compartment *A*. In other words, water moves from compartment *B* into compartment *A* by osmosis. Protein, on the other hand, cannot diffuse out of compartment *A* because the selectively permeable membrane is impermeable to it.

Note in figure 3.14 that, as osmosis occurs, the water level on side *A* rises. This ability of osmosis to generate enough pressure to lift a volume of water is called *osmotic pressure*. The greater the concentration of nonpermeable solute particles (protein in this case) in a solution, the *lower* the water concentration of that solution and the *greater* the osmotic pressure. Water always tends to diffuse toward solutions of greater osmotic pressure.

Since cell membranes are generally permeable to water, water equilibrates by osmosis throughout the body, and the concentration of water and solutes everywhere in the intracellular and extracellular fluids is essentially the same. Therefore, the osmotic pressure of the intracellular and extracellular fluids is the same. Any solution that has the same osmotic pressure as body fluids is called **isotonic.**

Solutions with a higher osmotic pressure than body fluids are called **hypertonic.** If cells are put into a hypertonic solution, there is a net movement of water by osmosis out of the cells into the surrounding solution, and the cells shrink. Conversely, cells put into a **hypotonic** solution, which has a lower osmotic pressure than body fluids, tend to gain water by osmosis and swell (fig. 3.15).

The concentration of solute in solutions that are infused into body tissues or blood must be controlled. Otherwise, osmosis may cause cells to swell or shrink, impairing their function. For instance, if red blood cells are placed in distilled water (which is hypotonic to them), water diffuses into the cells, and they burst (hemolyze). On the other hand, red blood cells exposed to 0.9% NaCl solution (normal saline) do not change in shape because this solution is isotonic to human cells. A red blood cell placed in a hypertonic solution shrinks.

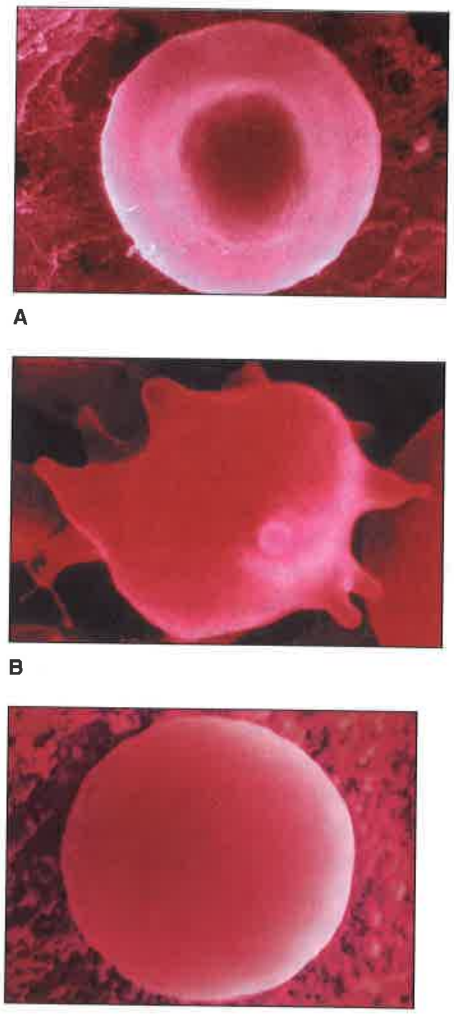

Figure 3.15
Red blood cells placed (*A*) in an isotonic solution, equal volumes of water enter and leave cells, size and shape remain unchanged. (*B*) In a hypertonic solution, more water leaves than enters, and cells shrink. (*C*) In a hypotonic solution, more water enters than leaves, cells swell and may burst (5,000×).

Filtration

Molecules pass through membranes by diffusion or osmosis because of random movements. In other instances, the process of **filtration** (fil-tra´shun) forces molecules through membranes.

Filtration is commonly used to separate solids from water. One method is to pour a mixture of solids and water onto filter paper in a funnel. The paper is a porous membrane through which the small water molecules can pass, leaving behind the larger solid particles. Hydrostatic pressure, which is created by the weight of water on the paper due to gravity, forces the water molecules through to the other side. A familiar example of filtration is making coffee by the drip method.

In the body, tissue fluid forms when water and small dissolved substances are forced out through the thin, porous walls of blood capillaries, but larger particles, such as blood protein molecules, are left inside (fig. 3.16). The force for this movement comes from blood pressure, generated mostly by heart action, which is greater within the vessel than outside it. However, the impermeable proteins tend to hold water in blood vessels by osmosis, thus preventing the formation of excess tissue fluid, a condition called **edema.**

CHECK YOUR RECALL

1. What kinds of substances diffuse most readily through a cell membrane?
2. Explain the differences between diffusion and osmosis.
3. Distinguish among hypertonic, hypotonic, and isotonic solutions.
4. Explain how filtration occurs within the body.

Active Mechanisms

When molecules or ions pass through cell membranes by diffusion, facilitated diffusion, or osmosis, their net movements are from regions of higher concentration toward regions of lower concentration. Sometimes, how-

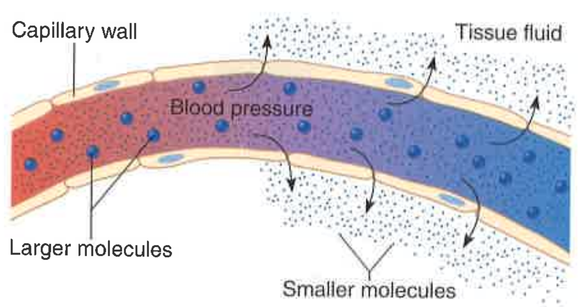

Figure 3.16
In this example of filtration, blood pressure forces smaller molecules through tiny openings in the capillary wall. The larger molecules remain inside.

ever, particles move from a region of lower concentration to one of higher concentration. This requires energy, which comes from cellular metabolism and, specifically, from a molecule called adenosine triphosphate (ATP).

Active Transport

Active transport (ak´tiv trans´port) is a process that moves particles through membranes from a region of lower concentration to a region of higher concentration. Sodium ions, for example, can diffuse passively into cells through protein channels in cell membranes, but their concentration typically remains much greater outside cells than inside. This occurs because active transport continually moves sodium ions through cell membranes from regions of lower concentration (inside) to regions of higher concentration (outside). Equilibrium is never reached.

Active transport is similar to facilitated diffusion in that it uses specific carrier molecules in cell membranes (fig. 3.17). It differs from facilitated diffusion in that particles move from areas of low concentration to areas of high concentration, and energy from ATP is required. Up to 40% of a cell's energy supply may be used to actively transport particles through cell membranes.

The carrier molecules in active transport are proteins with binding sites that combine with the particles being transported. Such a union triggers release of energy, and this alters the shape of the carrier protein. As a result, the "passenger" particles move through the membrane. Once on the other side, the transported particles are released, and the carriers can accept other passenger molecules at that binding site. Because these carrier proteins transport substances from regions of low concentration to regions of high concentration, they are sometimes called "pumps."

Particles that are actively transported across cell membranes include sugars and amino acids as well as sodium, potassium, calcium, and hydrogen ions. Active transport also absorbs nutrient molecules into cells that line intestinal walls.

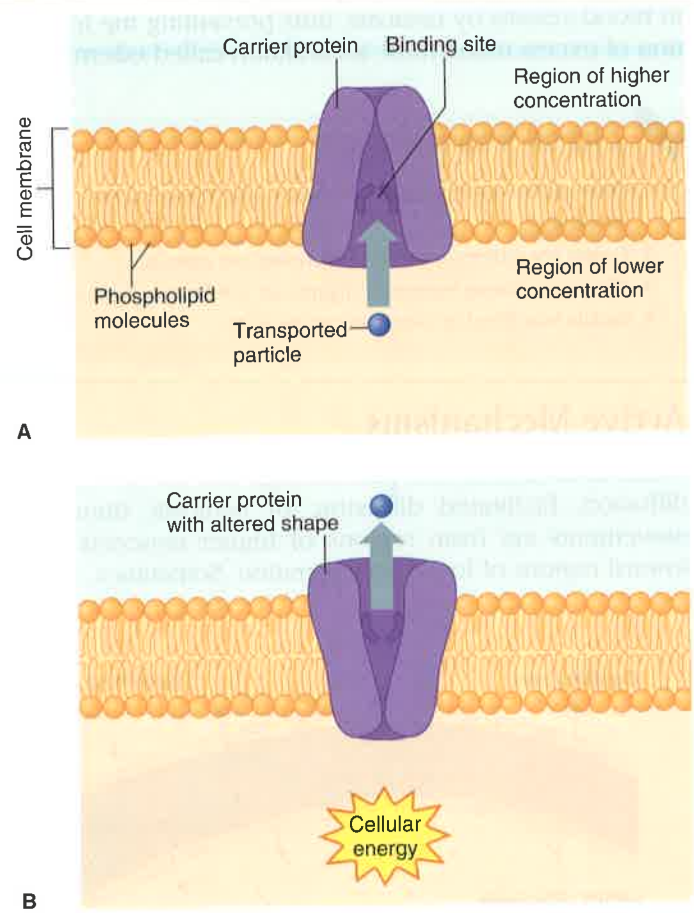

Figure 3.17
Active transport. (*A*) During active transport, a molecule or an ion combines with a carrier protein, whose shape changes as a result. (*B*) This process, which requires cellular energy, transports the particle across the cell membrane.

Endocytosis and Exocytosis

Two processes use cellular energy to move substances into or out of a cell without actually crossing the cell membrane. In **endocytosis** (en´´do-si-to´sis), molecules or other particles that are too large to enter a cell by diffusion, facilitated diffusion, or active transport are conveyed within a vesicle formed from a section of the cell membrane. In **exocytosis** (ex-o-si-to´sis), the reverse process secretes a substance stored in a vesicle from the cell. Nerve cells use exocytosis to release the neurotransmitter chemicals that signal other nerve cells, muscle cells, or glands.

Endocytosis occurs in three forms: pinocytosis, phagocytosis, and receptor-mediated endocytosis. In **pinocytosis** (pi´´no-si-to´sis), meaning "cell drinking," cells take in tiny droplets of liquid from their surroundings, as a small portion of the cell membrane indents. The open end of the tubelike part that forms seals off and produces a small vesicle, which detaches from the surface and moves into the cytoplasm. Eventually, the vesicular membrane breaks down, and the liquid inside becomes part of the cytoplasm. In this way, a cell can take in water and the particles dissolved in it, such as proteins, that otherwise might be too large to enter.

Phagocytosis (fag´´o-si-to´sis), meaning "cell eating," is similar to pinocytosis, but the cell takes in solids rather than liquids. Certain kinds of white blood cells are called *phagocytes* because they can take in solid particles such as bacteria and cellular debris. When a phagocyte first encounters a particle, the particle attaches to the phagocyte's cell membrane. This stimulates a portion of the membrane to project outward, surround the particle, and slowly draw it inside the cell. The part of the membrane surrounding the particle detaches from the cell's surface, forming a vesicle that contains the particle (fig. 3.18).

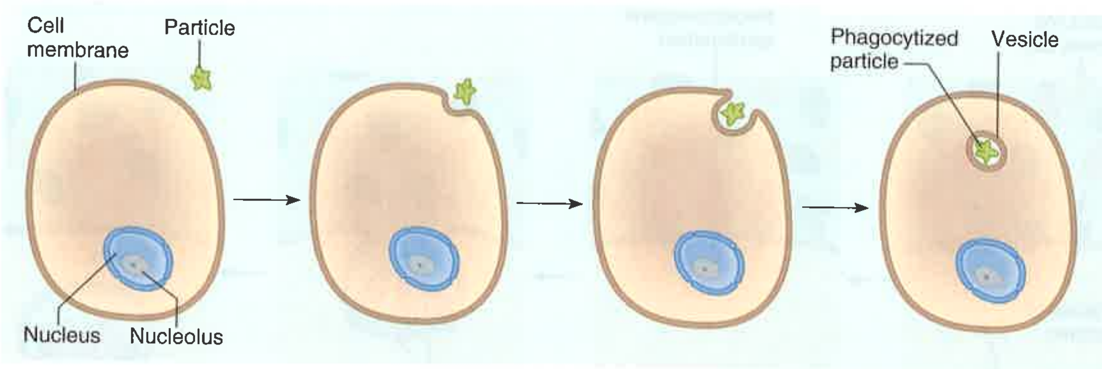

Figure 3.18
A cell may take in a solid particle from its surroundings by phagocytosis.

TABLE 3.2 MOVEMENTS THROUGH CELL MEMBRANES

PROCESS	CHARACTERISTICS	SOURCE OF ENERGY	EXAMPLE
Passive mechanisms			
Diffusion	Molecules or ions move from regions of higher concentration toward regions of lower concentration.	Molecular motion	Exchange of oxygen and carbon dioxide in lungs
Facilitated diffusion	Carrier molecules move molecules through a membrane from a region of higher concentration to one of lower concentration.	Molecular motion	Movement of glucose through cell membrane
Osmosis	Water molecules move from regions of higher concentration toward regions of lower concentration through a selectively permeable membrane.	Molecular motion	Distilled water entering a cell
Filtration	Molecules are forced from regions of higher pressure to regions of lower pressure.	Hydrostatic pressure	Water molecules leaving blood capillaries
Active mechanisms			
Active transport	Carrier molecules move molecules or ions through membranes from regions of lower concentration toward regions of higher concentration.	Cellular energy (ATP)	Movement of various ions, sugars, and amino acids through membranes
Endocytosis			
Pinocytosis	Membrane engulfs droplets of liquid from surroundings.	Cellular energy	Membrane forming vesicles containing liquid and dissolved particles
Phagocytosis	Membrane engulfs particles from surroundings.	Cellular energy	White blood cell engulfing bacterial cell
Receptor-mediated endocytosis	Receptors bind specific ligands, and they are drawn into the cell.	Cellular energy	Cholesterol molecules entering cells
Exocytosis	Vesicle fuses with membrane to expel substances from cell.	Cellular energy	Secretion of certain hormones

Commonly, a lysosome then combines with such a newly formed vesicle, and the lysosomal digestive enzymes decompose the contents. The products of this decomposition may diffuse out of the lysosome and into the cytoplasm. Exocytosis usually expels remaining residue from the cell.

Pinocytosis and phagocytosis engulf any molecules in the vicinity of the cell membrane. In contrast, **receptor-mediated endocytosis** moves very specific kinds of particles into the cell (fig. 3.19) by binding them first. In this process, protein molecules extend through a portion of the cell membrane to the outer surface, where they serve as receptors to which only specific substances (ligands) from outside the cell can bind. Cholesterol molecules enter cells by this mechanism. Table 3.2 summarizes the types of movements into and out of cells.

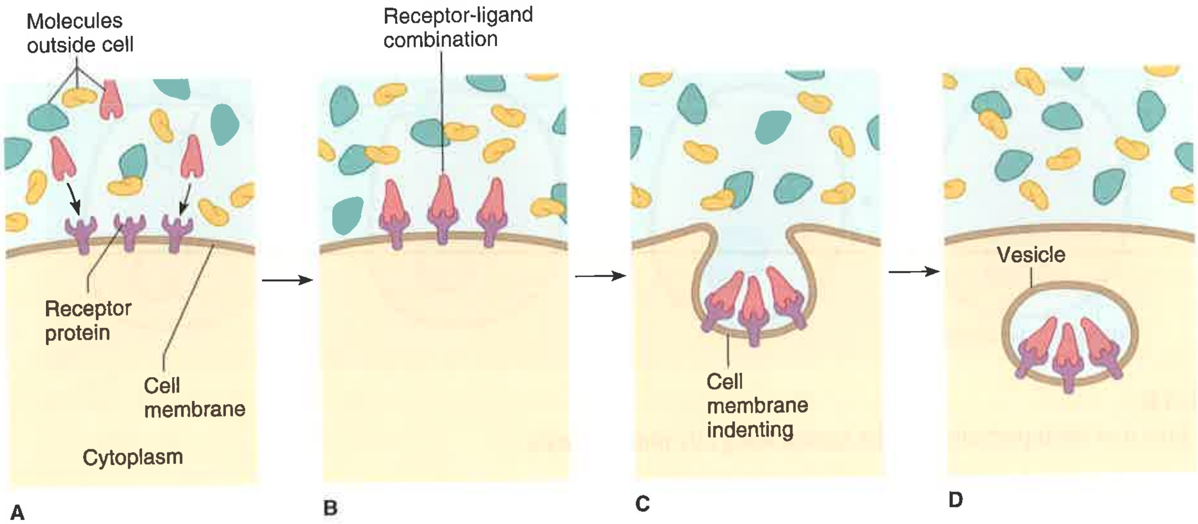

Figure 3.19
Receptor-mediated endocytosis. (*A*) A specific substance binds to a receptor site protein. (*B, C*) The combination of the substance with the receptor site protein stimulates the cell membrane to indent. (*D*) The resulting vesicle transports the substance into the cytoplasm.

CHECK YOUR RECALL

1. What type of mechanism maintains unequal concentrations of ions on opposite sides of a cell membrane?
2. How are facilitated diffusion and active transport similar? How are they different?
3. What is the difference between endocytosis and exocytosis?
4. How is receptor-mediated endocytosis more specific than pinocytosis or phagocytosis?

3.4 The Cell Cycle

The series of changes that a cell undergoes from the time it forms until it divides is called the *cell cycle* (fig. 3.20). Superficially, this cycle seems rather simple: A newly formed cell grows for a time and then divides to form two new cells, which in turn may grow and divide. Yet, the stages of the cycle are quite complex and include interphase, mitosis, cytoplasmic division (cytokinesis), and differentiation. Several events called *checkpoints* control the cell cycle. Of particular importance is the restriction checkpoint that determines a cell's fate—whether it will continue in the cell cycle and divide, move into a nondividing stage as a specialized cell, or die.

The cell cycle is very highly regulated. Stimulation, such as from a hormone, may trigger cell division. This occurs, for example, when the breasts develop into milk-producing glands during pregnancy.

Cells do not normally divide continually. Most types of human cells, if grown in the laboratory, divide only

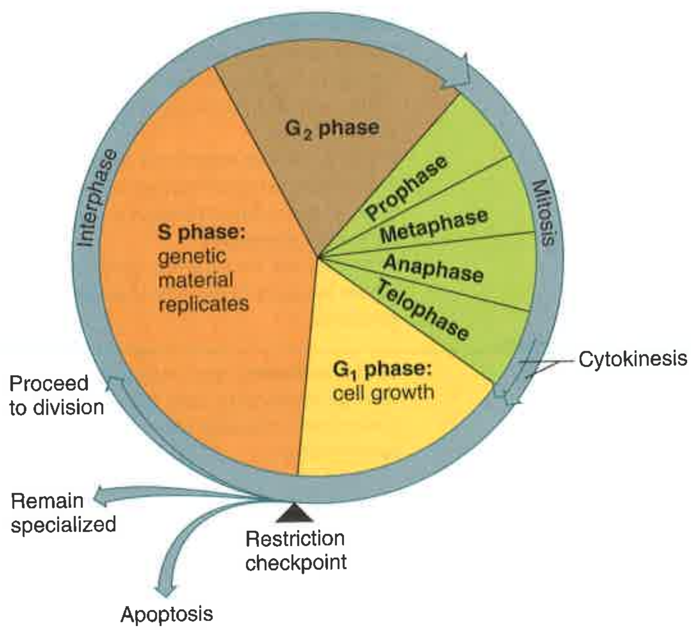

Figure 3.20
The cell cycle is divided into interphase, when cellular components duplicate, and cell division (mitosis and cytokinesis), when the cell splits in two, distributing its contents into two cells. Interphase is divided into two gap phases (G_1 and G_2), when specific molecules and structures duplicate, and a synthesis phase (S), when the genetic material replicates. Mitosis can be described as consisting of stages—prophase, metaphase, anaphase, and telophase.

forty to sixty times. Presumably, such limits operate in the body too. Some cells may divide the maximum number of times, such as cells that line the small intestine. Others normally do not divide, such as nerve cells. A cell "knows" when to stop dividing because of a built-in "clock" in the form of the chromosome tips. These structures, called *telomeres,* shorten with each mitosis. When they shorten to a certain length, the cell ceases dividing.

Interphase

Before a cell actively divides, it must grow and duplicate much of its contents, so that two cells can form from one. This period of preparedness is called **interphase.**

Once thought to be a time of rest, interphase is actually a time of great synthetic activity. During interphase, the cell obtains nutrients, utilizes them to manufacture new living material, and maintains routine "housekeeping" functions. The cell duplicates membranes, ribosomes, lysosomes, and mitochondria. Perhaps most importantly, the cell in interphase takes on the tremendous task of replicating its genetic material. This is important so that each of the two new cells will have a complete set of genetic instructions.

Interphase is considered in phases. DNA is replicated during the S, or synthesis phase, which is bracketed by two gap or growth periods, called G_1 and G_2, when other structures are duplicated.

Mitosis

A cell can divide in two ways. The first process, called *meiosis,* is part of *gametogenesis,* the formation of egg cells (in the female) and sperm cells (in the male). Since an egg fertilized by a sperm must have the normal complement of 46 chromosomes, both the egg and the sperm must first halve their normal chromosome number to 23 chromosomes. Meiosis, through a process called reduction division, accomplishes this. Chapter 19 (p. 500) describes meiosis in detail.

The second form of cell division increases cell number, which is necessary for growth and development and for wound healing. It consists of two separate processes: (1) division of the nucleus, called **mitosis** (mi-to´sis), and (2) division of the cytoplasm, called **cytokinesis** (si´´to-ki-ne´sis).

Division of the nucleus must be very precise because it contains the DNA. Each new cell resulting from mitosis must have a complete and accurate copy of this information to survive. DNA replicates during interphase, but is equally distributed into two new cells in mitosis.

Although mitosis is often described in terms of stages, the process is continuous, without marked changes between one step and the next (fig. 3.21). Stages, however, indicate the sequence of major events. They include:

1. **Prophase** One of the first indications that a cell is going to divide is that the chromosomes become visible in the nucleus. Because the cell has gone through S phase each prophase chromosome is composed of two identical portions (chromatids), which are temporarily attached at a region on each called the *centromere.*

   The centrioles of the centrosome replicate just before mitosis begins. During prophase, the two newly formed centriole pairs move to opposite ends of the cell. Soon, the nuclear envelope and the nucleolus break up, disperse, and are no longer visible. Microtubules are assembled from tubulin proteins in the cytoplasm and associate with the centrioles and chromosomes. A spindle-shaped array of microtubules (spindle fibers) forms between the centrioles as they move apart.
2. **Metaphase** The chromosomes line up about midway between the centrioles, as a result of microtubule activity. Spindle fibers attach to the centromeres of each chromosome so that a fiber from one pair of centrioles contacts one centromere, and a fiber from the other pair of centrioles attaches to the other centromere.
3. **Anaphase** Soon the centromeres are pulled apart. As the chromatids separate, they become individual chromosomes. The separated chromosomes now move in opposite directions, once again guided by microtubule activity. The spindle fibers shorten and pull their attached chromosomes toward the centrioles at opposite ends of the cell.
4. **Telophase** The final stage of mitosis begins when the chromosomes complete their migration toward the centrioles. It is much like prophase, but in reverse. As the chromosomes approach the centrioles, they begin to elongate and unwind from rodlike into the threadlike fibers of chromatin. A nuclear envelope forms around each chromosome set, and nucleoli appear within the newly formed nuclei. Finally, the microtubules disassemble into free tubulin molecules.

Cytoplasmic Division

Cytoplasmic division (cytokinesis) begins during anaphase, when the cell membrane starts to constrict down the middle of the cell. This constriction continues through telophase. Contraction of a ring of microfilaments, which assemble in the cytoplasm and attach to the inner surface of the cell membrane, divides the cytoplasm. The contractile ring lies at right angles to the microtubules that pulled the chromosomes to opposite sides of the cell. The ring pinches inward, separating the two newly formed nuclei and distributing about half

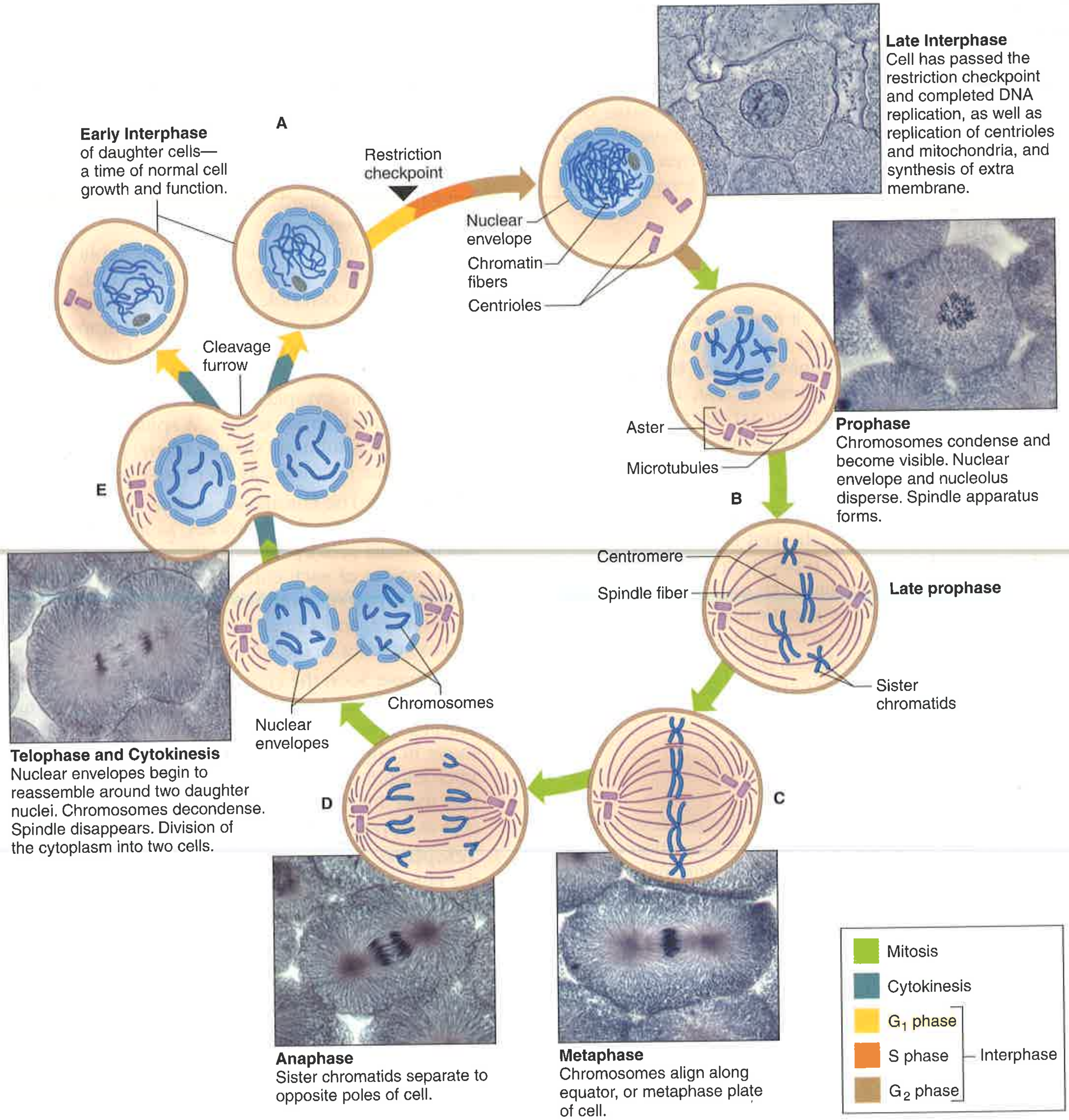

Figure 3.21
Mitosis and cytokinesis. (*A*) During interphase, before mitosis, chromosomes are visible only as chromatin fibers. A single pair of centrioles is present, but not visible at this magnification. (*B*) In prophase, as mitosis begins, chromosomes have condensed and are easily visible when stained. The centrioles have replicated, and each pair moves to an opposite end of the cell. The nuclear envelope and nucleolus disappear, and spindle fibers associate with the centrioles and the chromosomes. (*C*) In metaphase, the chromosomes line up midway between the centrioles. (*D*) In anaphase, the centromeres are pulled apart by the spindle fibers, and the chromatids, now individual chromosomes, move in opposite directions. (*E*) In telophase, chromosomes complete their migration and become chromatin, the nuclear envelope reforms, and microtubules disassemble. Cytokinesis, which actually began during anaphase, continues during telophase. Not all chromosomes are shown in these drawings. (Micrographs approximately 360×)

Topic of Interest

CANCER

Cancer is a group of closely related diseases that can occur in many different tissues. One in three of us will develop some form of cancer. These conditions result from changes in cells that alter the cell cycle. Cancers share the following characteristics:

1. **Hyperplasia** Hyperplasia is uncontrolled cell division. Normal cells divide a set number of times, signaled by the shortening of chromosome tips. Cancer cells activate an enzyme, called *telomerase,* that continually rebuilds chromosomes, so that cells are not signaled to stop dividing.
2. **Dedifferentiation** Cancer cells typically resemble undifferentiated cells, a state termed dedifferentiation. Cancer cells lose the specialized structures and functions of the normal type of cell from which they descend, and are therefore said to be dedifferentiated. Cancer cells also grow into disorganized masses, rather than forming orderly groups as normal cells do.
3. **Invasiveness** Cancer cells break through boundaries, called *basement membranes,* which separate cell types within some organs.
4. **Angiogenesis** Cancer cells induce the formation of blood vessels, which nourish them and remove wastes, enabling the cancer to persist, grow, and spread.
5. **Metastasis** Metastasis is a tendency to spread into other tissues. Normal cells usually aggregate in groups of similar kinds. Small numbers of cancer cells can detach from their original mass and move from their place of origin (fig. 3A), often into the bloodstream. They may establish new tumors elsewhere in the body.

Mutations in certain genes cause many cancers. A cancer-causing mutation may activate a cancer-causing oncogene (a gene that normally controls mitotic rate) or inactivate a protective gene called a tumor suppressor. Most often, a person inherits one abnormal cancer-causing gene. When the second copy of that gene changes (mutates), sometimes in response to an environmental trigger, cancer develops. Some cancers result from a series of genetic changes.

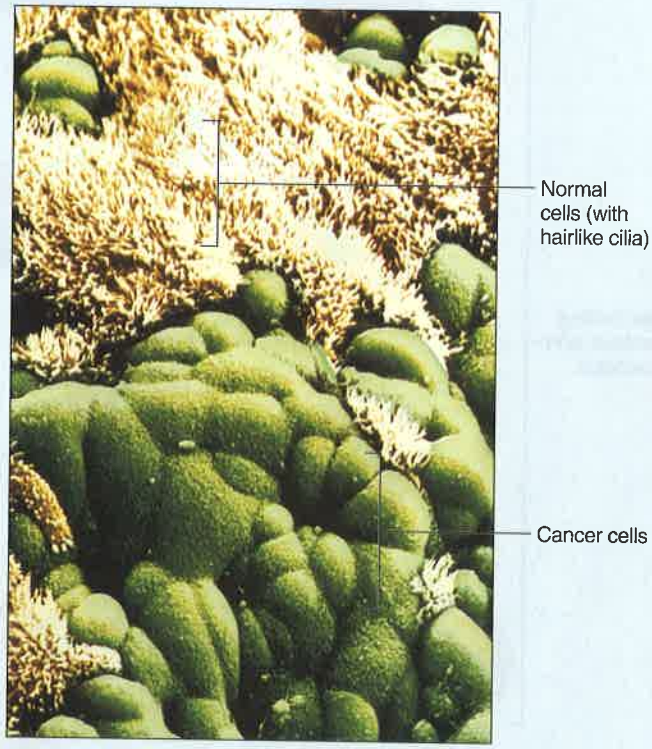

Figure 3A
The lack of cilia on these cancer cells is one sign of their dedifferentiation (2,250×).

of the organelles into each new cell. The new cells may differ slightly in size and number of organelles, but they contain identical genetic information.

Cell Differentiation

All body cells form by mitosis and contain the same DNA information, yet they do not look or function alike. A fertilized egg cell divides to form two new cells; they, in turn, divide into four cells, the four yield eight, and so forth. Then, sometime during development, the cells begin to *specialize* (fig. 3.22). That is, they develop special structures or begin to function in different ways. Some cells become muscle cells, others become bone cells, and still others become nerve cells.

The process by which cells develop different characteristics in structure and function is called **differentiation** (dif′′er-en′′she-a′shun). Cells differentiate by expressing some of the DNA information and repressing other DNA information. For example, the DNA information required for general cell activities is activated in both nerve and bone cells, but information important to specific bone cell functions is activated in bone cells, yet repressed in nerve cells. Similarly, the information necessary for specific nerve cell functions is repressed in bone cells. By birth, a human has more than 260 types of specialized cells. Throughout life, certain cells, called stem cells, remain relatively unspecialized. These cells retain the potential to produce new differentiated cells. Stem cells are important in growth and healing.

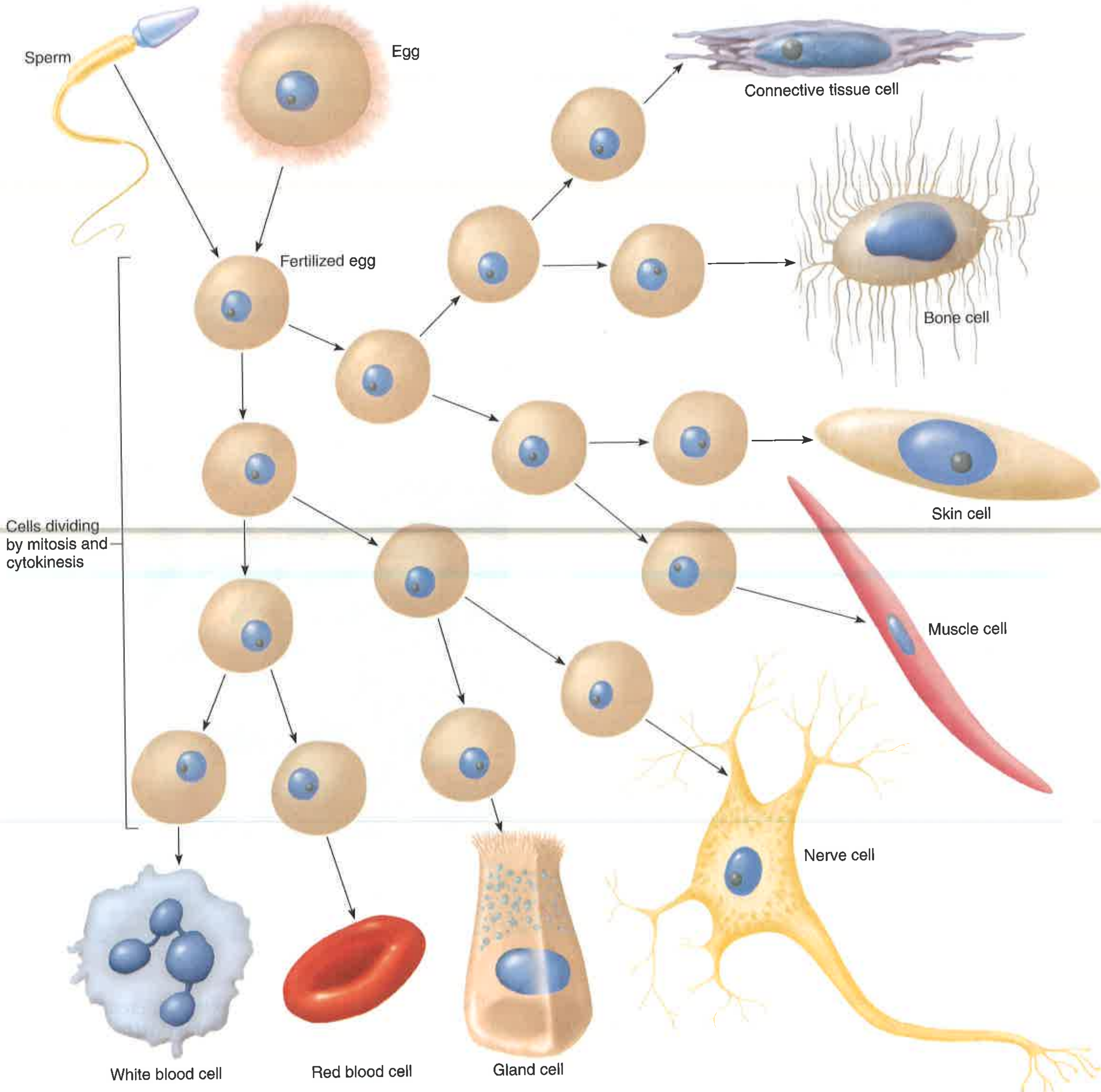

Figure 3.22
During development, many body cells are produced from a single fertilized egg cell by mitosis. As these cells differentiate, they become different kinds of cells with specialized functions. (Relative cell sizes are not to scale.)

Cell Death

A cell that does not divide or specialize has another option—it may die. **Apoptosis** (ap′′o-to′-sis) is a form of cell death that is actually a normal part of development, sculpting organs from overgrown tissues. In the fetus, apoptosis carves away webbing between developing fingers and toes, removes extra brain cells, and preserves only those immune system cells that recognize the body's cell surfaces. After birth, apoptosis follows a sunburn—it literally peels away cells so damaged that they might otherwise turn cancerous.

A cell in the throes of apoptosis goes through characteristic steps. It rounds up and bulges, the nuclear membrane breaks down, chromatin condenses, and enzymes chop the chromosomes into many equal-sized pieces. Finally, the cell shatters into membrane-enclosed fragments, and a scavenger cell mops it up.

CHECK YOUR RECALL

1. Why is it important that the division of nuclear materials during mitosis be precise?
2. Describe the events that occur during mitosis.
3. Name the process by which cells specialize.
4. How is cell death a normal part of development?

Clinical Connection

In certain highly specialized cell types, endocytosis and exocytosis meet in a process called, appropriately, transcytosis. A particle enters such a cell by endocytosis, journeys through the cytoplasm, then exits the cell by exocytosis from the other end.

Transcytosis occurs in the lining of the small intestine, where rare cells called M cells sample bits of food, transporting the captured molecules through themselves, then ejecting them by exocytosis to be met by a gathering of immune system cells just beneath the cell's basal surface. From here, if the transported particles are recognized as posing a threat, they may stimulate an immune response, and other cells flood the small intestinal lining with specific antibodies against the potentially dangerous substance. This transcytosis through the M cell portals of the small intestinal lining thus ensures that what is eaten is safe. The infectious prion proteins, discussed in the Clinical Connection in Chapter 2 (p. 44), can enter the body by evading the M cell barrier in the small intestine. Variant Creutzfeldt-Jakob disease may be transmitted this way from infected beef. Before the 1970s, cannibals in Papua New Guinea contracted a prion disorder called kuru by consuming their war heroes.

Another example of transcytosis occurs in the female genital tract and in the rectum. HIV (the virus that causes AIDS) uses this route to cross the epithelium, and reach the bloodstream.

SUMMARY OUTLINE

3.1 Introduction (p. 49)

Cells vary considerably in size, shape, and function. The shapes of cells make possible their functions.

3.2 Composite Cell (p. 49)

A cell includes a nucleus, cytoplasm, and a cell membrane. Organelles perform specific functions; the nucleus controls overall cell activities because it contains DNA.

1. Cell membrane
   a. The cell membrane forms the outermost limit of the living material.
   b. It is a selectively permeable passageway that controls the entrance and exit of substances. Its molecules transmit signals.
   c. The cell membrane includes protein, lipid, and carbohydrate molecules.
   d. The cell membrane's framework is mainly a bilayer of phospholipid molecules.
   e. Molecules that are soluble in lipids pass through the cell membrane easily, but water-soluble molecules do not.
   f. Proteins function as receptors on membrane surfaces and form channels for the passage of ions and molecules. They can be classified by position.
   g. Carbohydrates associated with membrane proteins enable certain cells to recognize one another.
2. Cytoplasm
   a. Cytoplasm contains membranes, organelles, and the rods and tubules of the cytoskeleton, suspended in cytosol.
   b. The endoplasmic reticulum is a tubular communication system in the cytoplasm that transports lipids and proteins.
   c. Ribosomes function in protein synthesis.
   d. The Golgi apparatus packages glycoproteins for secretion.
   e. Mitochondria contain enzymes that catalyze reactions that release energy from nutrient molecules.
   f. Lysosomes contain digestive enzymes that decompose substances.
   g. Peroxisomes house enzymes that catalyze bile acid synthesis, hydrogen peroxide degradation, lipid breakdown, and detoxification of alcohol.
   h. Microfilaments (built of actin) and microtubules (built of tubulin) aid cellular movements and support and stabilize the cytoplasm and organelles. Together they form the cytoskeleton. Microtubules also form centrioles, cilia, and flagella.
   i. The centrosome contains centrioles that aid in distributing chromosomes during cell division.
   j. Cilia and flagella are motile extensions from cell surfaces.
   k. Vesicles contain substances that recently entered the cell or that are to be secreted from the cell.
3. Cell nucleus
   a. The nucleus is enclosed in a double-layered nuclear envelope.
   b. It contains a nucleolus, which is the site of ribosome production.
   c. It contains chromatin, which is composed of loosely coiled fibers of DNA and protein. As chromatin fibers condense, chromosomes become visible during cell division.

3.3 Movements Through Cell Membranes (p. 58)

The cell membrane is a barrier through which substances enter and leave a cell.

1. Passive mechanisms do not require cellular energy.
   a. Diffusion
      (1) Diffusion is the movement of molecules or ions from regions of higher concentration toward regions of lower concentration.
      (2) It exchanges oxygen and carbon dioxide.

b. Facilitated diffusion
   (1) In facilitated diffusion, special carrier molecules move substances through the cell membrane.
   (2) This process moves substances only from regions of higher concentration toward regions of lower concentration.

c. Osmosis
   (1) Osmosis is diffusion of water molecules from regions of higher water concentration toward regions of lower water concentration through a selectively permeable membrane.
   (2) Osmotic pressure increases as the number of impermeable particles dissolved in a solution increases.
   (3) A solution is isotonic to a cell when it has the same osmotic pressure as the cell.
   (4) Cells lose water when placed in hypertonic solutions and gain water when placed in hypotonic solutions.

d. Filtration
   (1) Filtration is the movement of molecules from regions of higher hydrostatic pressure toward regions of lower hydrostatic pressure.
   (2) Blood pressure causes filtration through porous capillary walls, forming tissue fluid.

2. Active mechanisms require cellular energy.
   a. Active transport
      (1) Active transport moves molecules or ions from regions of lower concentration toward regions of higher concentration.
      (2) It requires cellular energy from ATP and carrier molecules in the cell membrane.
   b. Endocytosis and exocytosis
      (1) Endocytosis may convey relatively large particles into a cell. Exocytosis is the reverse of endocytosis.
      (2) In pinocytosis, a cell membrane engulfs tiny droplets of liquid.
      (3) In phagocytosis, a cell membrane engulfs solid particles.
      (4) Receptor-mediated endocytosis moves specific types of particles into cells.

3.4 The Cell Cycle (p. 64)

The cell cycle includes interphase, mitosis, cytoplasmic division, and differentiation. It is highly regulated.

1. Interphase
   a. During interphase, a cell duplicates membranes, ribosomes, organelles, and DNA.
   b. Interphase terminates when mitosis begins.
2. Mitosis
   a. Meiosis is a form of cell division that forms sex cells.
   b. Mitosis is the division and distribution of genetic material, organelles, and other structures to new cells.
   c. The stages of mitosis are prophase, metaphase, anaphase, and telophase.
3. Cytoplasmic division distributes cytoplasm into two portions following mitosis.
4. Cell differentiation is the development of specialized structures and functions.
5. A cell that does not divide or differentiate may undergo apoptosis, a form of cell death that is a normal part of development.

REVIEW EXERCISES

1. Describe how the shapes of nerve and muscle cells are important for their functions. (p. 49)
2. Name the three major portions of a cell, and describe their relationships to one another. (p. 49)
3. Define *selectively permeable.* (p. 51)
4. Describe the chemical structure of a cell membrane. (p. 51)
5. Explain how the structure of a cell membrane determines which substances can pass through it. (p. 51)
6. Describe the structures and functions of each of the following (p. 52):
   a. Endoplasmic reticulum
   b. Ribosomes
   c. Golgi apparatus
   d. Mitochondria
   e. Lysosomes
   f. Peroxisomes
   g. Microfilaments
   h. Microtubules
   i. Centrosome
   j. Cilia and flagella
   k. Vesicles
7. Describe the structure and contents of the nucleus. (p. 56)
8. Define *diffusion.* (p. 58)
9. Explain how diffusion aids in the exchange of gases within the body. (p. 59)
10. Distinguish between diffusion and facilitated diffusion. (p. 59)
11. Define *osmosis.* (p. 60)
12. Define *osmotic pressure.* (p. 60)
13. Distinguish between solutions that are hypertonic, hypotonic, and isotonic. (p. 60)
14. Define *filtration.* (p. 61)
15. Explain how filtration moves substances through capillary walls. (p. 61)
16. Distinguish between facilitated diffusion and active transport. (p. 62)
17. Distinguish between pinocytosis and phagocytosis. (p. 62)
18. Identify the structures that make receptor-mediated endocytosis specific. (p. 63)
19. List the phases of the cell cycle. (p. 64)
20. Explain what happens during interphase. (p. 65)
21. Name the two types of cell division. (p. 65)
22. Describe the major events of mitosis. (p. 65)
23. Explain how the cytoplasm divides. (p. 65)
24. Define *differentiation.* (p. 67)
25. Describe apoptosis. (p. 68)

CRITICAL THINKING

1. Organelles compartmentalize a cell, much as a department store displays related items together. What advantage does such compartmentalization offer a large cell? Cite two examples of organelles and the activities they compartmentalize.
2. Liver cells are packed with glucose. What mechanism could be used to transport more glucose into a liver cell? Why would only this mode of transport work?
3. In an inherited condition called glycogen cardiomyopathy, teenagers develop muscle weakness, which affects the heart as well as other muscles. Samples of the affected muscle cells contain huge lysosomes, swollen with the carbohydrate glycogen. How might this condition arise?
4. Why does a muscle cell contain many mitochondria, and a white blood cell contain many lysosomes?

SUMMARY OUTLINE

2.1 Introduction (p. 31)

Chemistry describes the composition of substances and how chemicals react with each other.

2.2 Structure of Matter (p. 31)

1. Elements and atoms
   a. Naturally occurring matter on earth is composed of 92 elements.
   b. Some elements occur in pure form, but many are found combined with other elements.
   c. Elements are composed of atoms, which are the smallest complete units of elements.
   d. Atoms of different elements vary in size, weight, and ways of interacting.
2. Atomic structure
   a. An atom consists of one or more electrons surrounding a nucleus, which contains one or more protons and usually one or more neutrons.
   b. Electrons are negatively charged, protons are positively charged, and neutrons are uncharged.
   c. A complete atom is electrically neutral.
   d. An element's atomic number is equal to the number of protons in each atom. The atomic weight is equal to the number of protons plus the number of neutrons in each atom.
3. Bonding of atoms
   a. When atoms combine, they gain, lose, or share electrons.
   b. Electrons occupy shells around a nucleus.
   c. Atoms with completely filled outer shells are inert, but atoms with incompletely filled outer shells tend to gain, lose, or share electrons and thus achieve stable structures.
   d. Atoms that lose electrons become positively charged ions. Atoms that gain electrons become negatively charged ions.
   e. Ions with opposite electrical charges attract and form ionic bonds. Atoms that share electrons form covalent bonds.
4. Molecules and compounds
   a. Two or more atoms of the same element may bond to form a molecule of that element. Atoms of different elements may bond to form a molecule of a compound.
   b. Molecules contain definite kinds and numbers of atoms.
5. Formulas
   a. A molecular formula represents the numbers and types of atoms in a molecule.
   b. A structural formula depicts the arrangement of atoms within a molecule.
6. Chemical reactions
   a. A chemical reaction breaks or forms bonds between atoms, ions, or molecules.
   b. Three types of chemical reactions are: synthesis, in which larger molecules form from smaller particles; decomposition, in which larger molecules are broken down into smaller particles; and exchange reactions, in which the parts of two different molecules trade positions.
   c. Many reactions are reversible. The direction of a reaction depends on the proportions of reactants and end products, the energy available, and the presence of catalysts.
7. Acids and bases
   a. Compounds that release ions when they dissolve in water are electrolytes.
   b. Electrolytes that release hydrogen ions are acids, and those that release hydroxyl or other ions that react with hydrogen ions are bases.
   c. A value called pH represents a solution's concentration of hydrogen ions (H^+) and hydroxide ions (OH^-).
   d. A solution with equal numbers of H^+ and OH^- is neutral and has a pH of 7.0. A solution with more H^+ than OH^- is acidic and has a pH less than 7.0. A solution with fewer H^+ than OH^- is basic and has a pH greater than 7.0.
   e. Each whole number on the pH scale represents a tenfold difference in the hydrogen ion concentration.

2.3 Chemical Constituents of Cells (p. 37)

Molecules containing carbon and hydrogen atoms are organic and are usually nonelectrolytes. Other molecules are inorganic and are usually electrolytes.

1. Inorganic substances
   a. Water is the most abundant compound in cells and is a solvent in which chemical reactions occur. Water transports chemicals and heat.
   b. Oxygen releases energy from glucose and other nutrients. This energy drives metabolism.
   c. Carbon dioxide is produced when metabolism releases energy.
   d. Salts provide a variety of ions that metabolic processes require.
2. Organic substances
   a. Carbohydrates provide much of the energy that cells require and also contribute to cell structure. Their basic building blocks are simple sugar molecules.
   b. Lipids, such as fats, phospholipids, and steroids, supply energy and build cell parts. The basic building blocks of fats—the most common lipid—are molecules of glycerol and fatty acids.
   c. Proteins serve as structural materials, energy sources, hormones, cell surface receptors, and enzymes.
      (1) Enzymes speed chemical reactions without being consumed.
      (2) The building blocks of proteins are amino acids.
      (3) Proteins vary in the numbers and types of amino acids they contain and in the sequence of these amino acids.
      (4) The amino acid chain of a protein molecule folds into a complex shape that is maintained largely by hydrogen bonds.
      (5) Excessive heat, radiation, electricity, altered pH, or various chemicals can denature proteins.
   d. Nucleic acids are the genetic material and control cellular activities.
      (1) Nucleic acid molecules are composed of nucleotides.
      (2) The two types of nucleic acids are RNA and DNA.
      (3) DNA molecules store information that cell parts use to construct specific protein molecules. RNA molecules help synthesize proteins.

REVIEW EXERCISES

1. Define *chemistry.* (p. 31)
2. Define *matter.* (p. 31)
3. Explain the relationship between elements and atoms. (p. 31)
4. List the four most abundant elements in the human body. (p. 31)
5. Describe the major parts of an atom. (p. 31)
6. Explain why a complete atom is electrically neutral. (p. 31)
7. Define *atomic number* and *atomic weight.* (p. 32)
8. Explain how electrons are arranged within an atom. (p. 32)
9. Distinguish between an ionic bond and a covalent bond. (p. 34)
10. Explain the relationship between molecules and compounds. (p. 35)
11. Distinguish between a molecular formula and a structural formula. (p. 35)

12. Explain what the formula $C_6H_{12}O_6$ means. (p. 35)
13. Describe three major types of chemical reactions. (p. 36)
14. Explain what a reversible reaction is. (p. 36)
15. Define *catalyst.* (p. 36)
16. Define *acid* and *base.* (p. 37)
17. Explain what pH measures, and describe the pH scale. (p. 37)
18. Distinguish between electrolytes and nonelectrolytes. (p. 37)
19. Distinguish between inorganic and organic substances. (p. 37)
20. Describe the roles water and oxygen play in the human body. (p. 38)
21. List several of the ions found in body fluids. (p. 38)
22. Describe the general characteristics of carbohydrates. (p. 39)
23. Distinguish between simple and complex carbohydrates. (p. 39)
24. Describe the general characteristics of lipids. (p. 39)
25. Define *triglyceride.* (p. 40)
26. Distinguish between saturated and unsaturated fats. (p. 40)
27. Describe the general characteristics of proteins. (p. 41)
28. Define *enzyme.* (p. 41)
29. Explain how protein molecules may denature. (p. 43)
30. Describe the structure of nucleic acids. (p. 43)
31. Explain the major functions of nucleic acids. (p. 44)

CRITICAL THINKING

1. If a shampoo is labeled "nonalkaline," would it more likely have a pH of 3, 7, or 12?
2. A topping for ice cream contains fructose, hydrogenated soybean oil, salt, and cellulose. What types of chemicals are in it?
3. An advertisement for a supposedly healthful cookie claims that it contains an "organic carbohydrate." Why is this statement silly?
4. At a restaurant, a waiter recommends a sparkling carbonated beverage, claiming that it contains no carbohydrates. The product label lists water and fructose as ingredients. Is the waiter correct?
5. A Horta is a fictional animal (from "Star Trek") whose biochemistry is based on the element silicon. Consult a periodic table. Is silicon a likely substitute for carbon in a life-form? Cite a reason for your answer.
6. A man on a very low-fat diet proclaims to his friend, "I'm going to get my cholesterol down to zero!" Why is this an impossible (and undesirable) goal?
7. What acidic and basic substances do you encounter in your everyday activities? What acidic foods do you eat regularly? What basic foods do you eat?
8. How would you explain the dietary importance of amino acids and proteins to a person who is following a diet composed primarily of carbohydrates?
9. What clinical laboratory tests have you encountered that require a knowledge of chemistry to understand the significance of what they measure?

WEB CONNECTIONS

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