



Cells

Understanding Words

cyt-, cell: *cytoplasm*—fluid between the cell membrane and nuclear envelope.

endo-, within: *endoplasmic reticulum*—complex of membranous structures in the cytoplasm.

hyper-, above: *hypertonic*—solution that has a greater osmotic pressure than the cytosol.

hypo-, below: *hypotonic*—solution that has a lesser osmotic pressure than the cytosol.

inter-, between: *interphase*—stage between mitotic divisions of a cell.

iso-, equal: *isotonic*—solution that has an osmotic pressure equal to that of the cytosol.

lys-, to break up: *lysosome*—organelle containing enzymes that break down molecules of protein, carbohydrate, or nucleic acid.

mit-, thread: *mitosis*—stage of cell division when chromosomes condense and become visible.

phag-, to eat: *phagocytosis*—process by which a cell takes in solid particles.

pino-, to drink: *pinocytosis*—process by which a cell takes in tiny droplets of liquid.

pro-, before: *prophase*—first stage of mitosis.

som, body: *ribosome*—tiny, spherical organelle composed of protein and RNA.

vesic-, bladder: *vesicle*—small, saclike organelle that contains various substances to be transported or secreted.

Chapter Objectives

After you have studied this chapter, you should be able to

1. Explain how cells differ from one another.
2. Describe the general characteristics of a composite cell.
3. Explain how the components of a cell's membrane provide its functions.
4. Describe each kind of cytoplasmic organelle and explain its function.
5. Describe the cell nucleus and its parts.
6. Explain how substances move into and out of cells.
7. Describe the cell cycle.
8. Explain how a cell divides.
9. Describe several controls of cell division.

Certain people are naturally resistant to HIV, the virus that causes AIDS. For example, a woman received a blood transfusion in 1980 that was later found to be contaminated with HIV, but she never became infected. Some intravenous drug users share needles with people who later develop AIDS, and some prostitutes exposed to many HIV-positive men never themselves become infected.

We usually think of avoiding AIDS by avoiding activities that spread the virus, and this is without doubt the best course. But what protects these people, all of whom have been exposed to HIV? A lucky few individuals cannot contract AIDS because of an abnormality in their cells.

When HIV enters a human body, it approaches certain white blood cells, called CD4 helper T cells, that control the immune system. The virus binds first to receptors called CD4—the receptors are proteins that extend from the cell surface. Once bound, HIV moves down the

CD4 receptor and binds another receptor, called CCR5. Only then can the virus enter the cell, and start the chain reaction of viral replication that ultimately topples immunity.

Thanks to heredity, one percent of Caucasians in the United States, and far fewer Asians, African Americans, and Native Americans, have cell surfaces that lack the crucial CCR5 HIV docking sites. These lucky few individuals cannot get AIDS, because HIV cannot enter their cells. Another 20% of the Caucasian population (less for others) have half the normal number of CCR5 receptors. These people can become infected, but remain healthy longer than is usual.

Researchers are now applying this knowledge of how AIDS begins at the cellular level to develop vaccines and new treatments. Understanding how HIV interacts with cells, the units of life, has revealed what might finally prove to be HIV's Achilles heel—a protein portal called CCR5.

An adult human body consists of about 75 trillion **cells**, the basic units of an organism. All cells have much in common, yet those in different tissues are distinctive in a number of ways.

Cells vary considerably in size. We measure cell sizes in units called *micrometers* (mi'kro-me'terz). A micrometer equals one thousandth of a millimeter and is symbolized μm . A human egg cell is about 140 μm in diameter and is just barely visible to an unaided eye. This is large when compared to a red blood cell, which is about 7.5 μm in diameter, or the most common types of white blood cells, which vary from 10 to 12 μm in diameter. On the other hand, smooth muscle cells can be between 20 and 500 μm long (fig. 3.1).

Cells also vary in shape, and typically their shapes make possible their functions (fig. 3.2). For instance, nerve cells often have long, threadlike extensions many centimeters long that transmit nerve impulses from one part of the body to another. Epithelial cells that line the inside of the mouth are thin, flattened, and tightly packed, somewhat like floor tiles. They form a barrier that shields underlying tissue. Muscle cells, which contract and pull structures closer together, are slender and rodlike, with their ends attached to the parts they move. Muscle cells are filled with contractile proteins. An adipose cell is little more than a blob of fat; a B lymphocyte is an antibody factory. The human body is a conglomeration of many types of cells.

a thin membrane called the nuclear envelope. The cytoplasm is a mass of fluid that surrounds the nucleus and is itself encircled by the even-thinner cell membrane (also called a plasma membrane). Within the cytoplasm are specialized structures called **cytoplasmic organelles** that perform specific functions. The nucleus directs the overall activities of the cell by functioning as the hereditary headquarters, housing the genetic material (DNA).

Cells with nuclei, such as those of the human body, are termed *eukaryotic*, meaning "true nucleus." In contrast are the *prokaryotic* ("before nucleus") cells of bacteria. Although bacterial cells lack nuclei and other membrane-bound organelles and are thus simpler than eukaryotic cells, the bacteria are nevertheless quite a successful life form—they are literally everywhere, and have been for much longer than eukaryotic cells. A third type of cell, termed *archaea*, lack nuclei but have many features like those of eukaryotic cells.

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

A Composite Cell

It is not possible to describe a typical cell, because cells vary so greatly in size, shape, content, and function. We can, however, consider a hypothetical composite cell that includes many known cell structures (fig. 3.3).

A cell consists of three major parts—the **nucleus** (nu'kle-us), the **cytoplasm** (si'to-plazm), and the **cell membrane**. The nucleus is innermost and is enclosed by

Cell Membrane

The cell membrane is the outermost limit of a cell, but it is more than a simple boundary surrounding the cellular contents. It is an actively functioning part of the living material, and many important metabolic reactions take place on its surfaces.

General Characteristics

The cell membrane is extremely thin—visible only with the aid of an electron microscope (fig. 3.4)—but it is

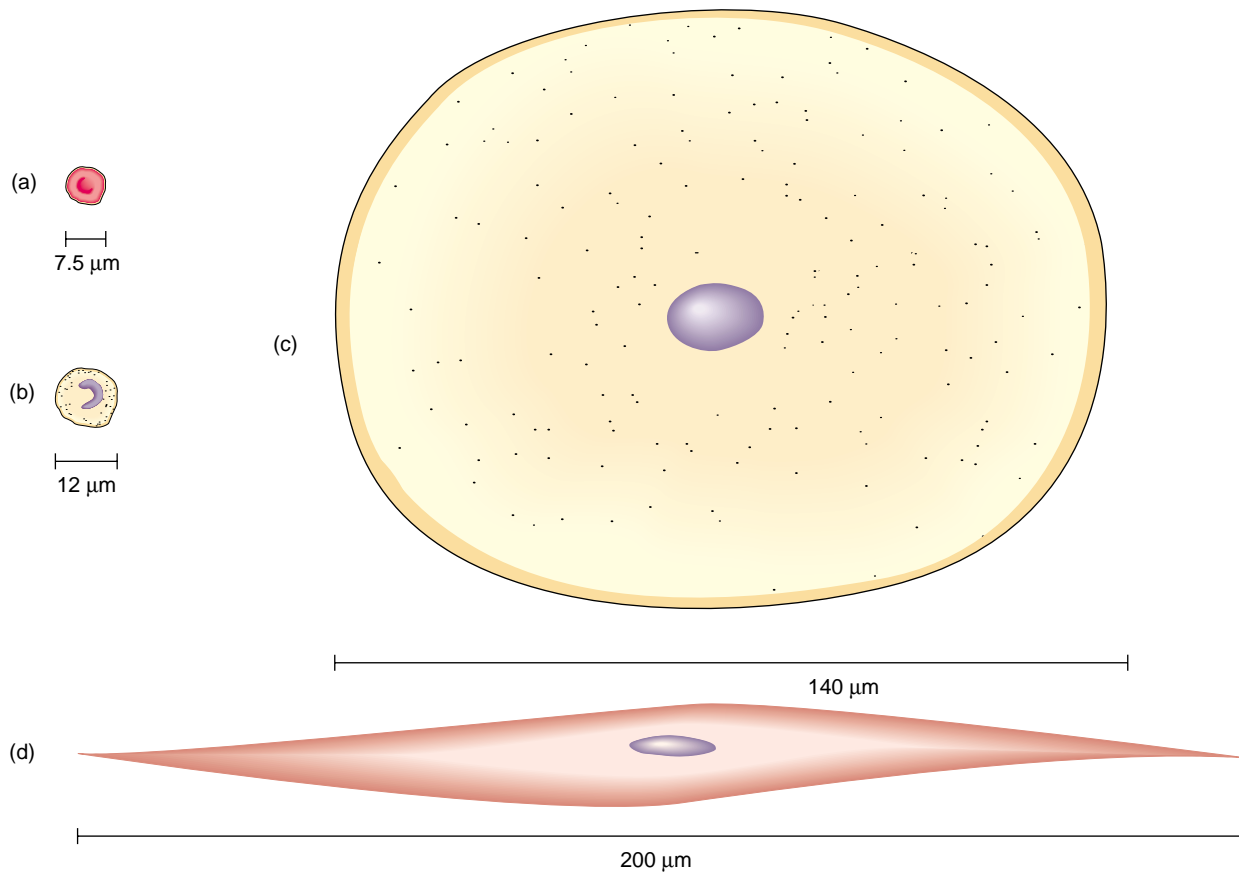


Figure 3.1

Cells vary considerably in size. This illustration shows the relative sizes of four types of cells. (a) Red blood cell, 7.5 μm in diameter; (b) white blood cell, 10–12 μm in diameter; (c) human egg cell, 140 μm in diameter; (d) smooth muscle cell, 20–500 μm in length.

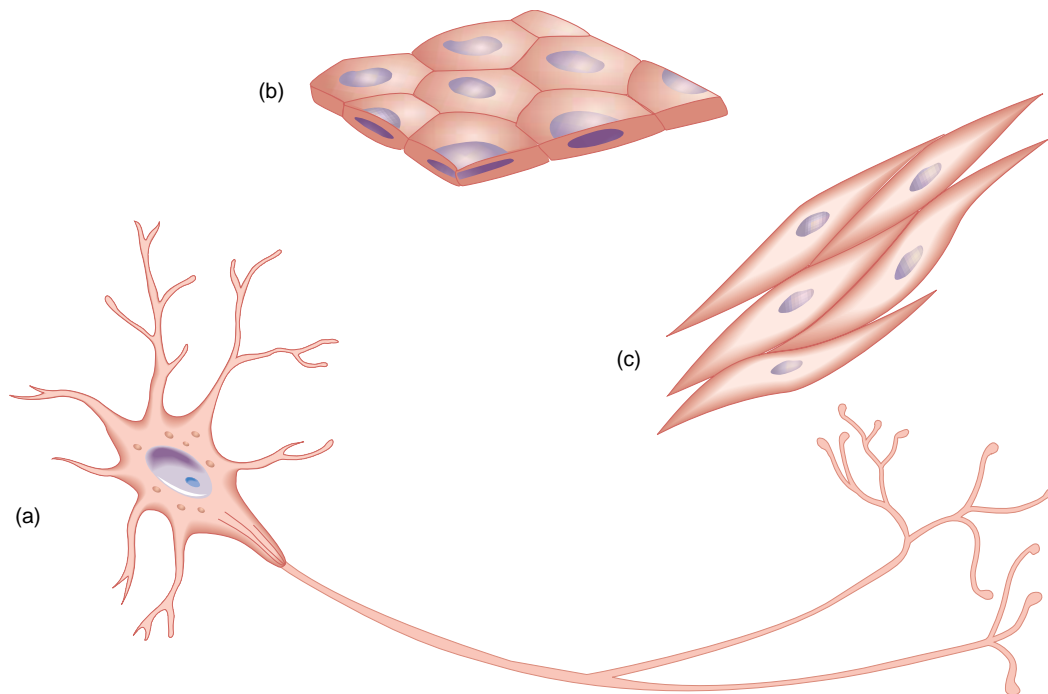


Figure 3.2

Cells vary in shape and function. (a) A nerve cell transmits impulses from one body part to another. (b) Epithelial cells protect underlying cells. (c) Muscle cells pull structures closer.

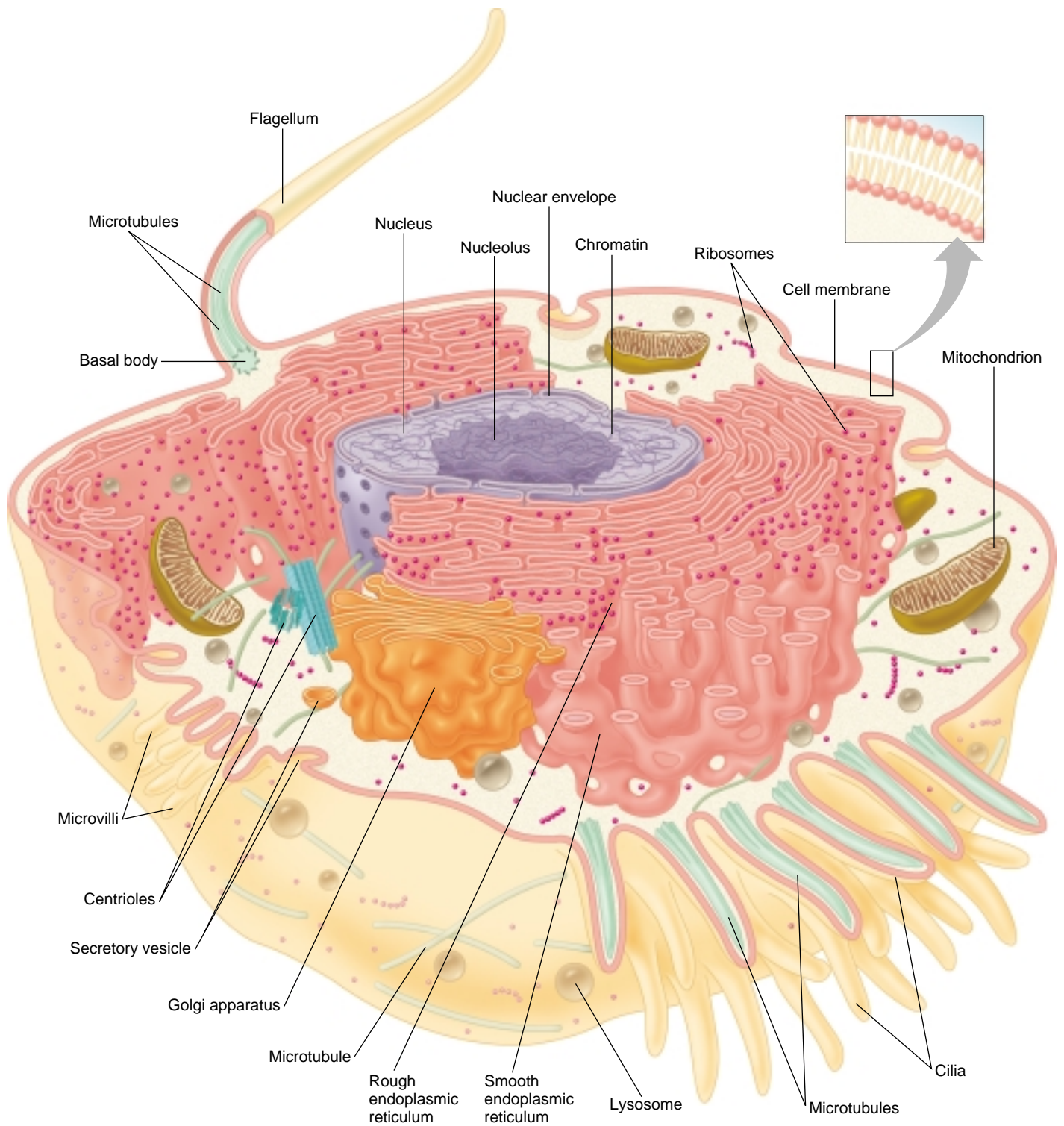


Figure 3.3

A composite cell. Organelles are not drawn to scale.



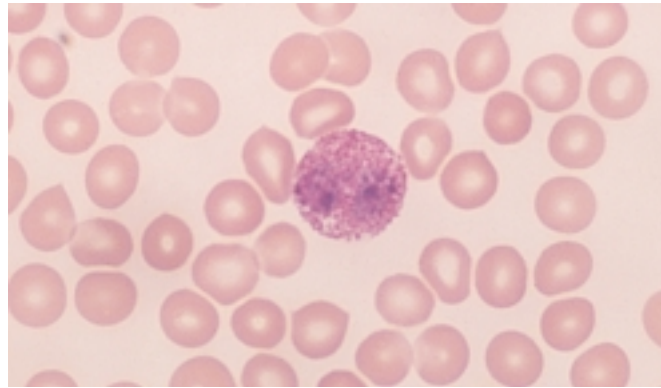
Figure 3.4

A transmission electron microscope.

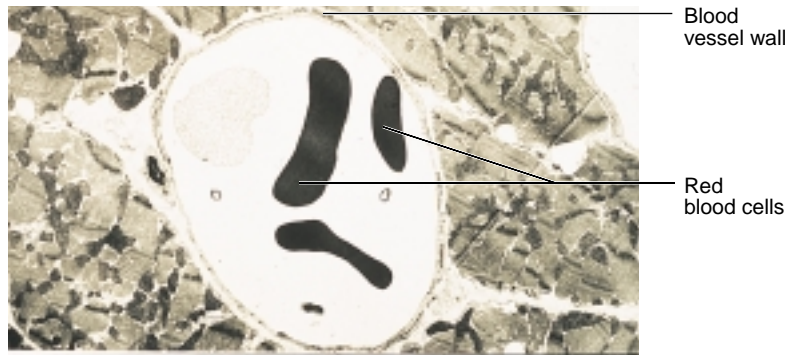
flexible and somewhat elastic. It typically has complex surface features with many outpouchings and infoldings that increase surface area. The cell membrane quickly seals tiny breaks, but if it is extensively damaged, cell contents escape, and the cell dies.

The maximum effective magnification possible using a light microscope is about 1,200 \times . A transmission electron microscope (TEM) provides an effective magnification of nearly 1,000,000 \times , whereas a scanning electron microscope (SEM), can provide about 50,000 \times . Photographs of microscopic objects (micrographs) produced using the light microscope and the transmission electron microscope are typically two-dimensional, but those obtained with the scanning electron microscope have a three-dimensional quality (fig. 3.5).

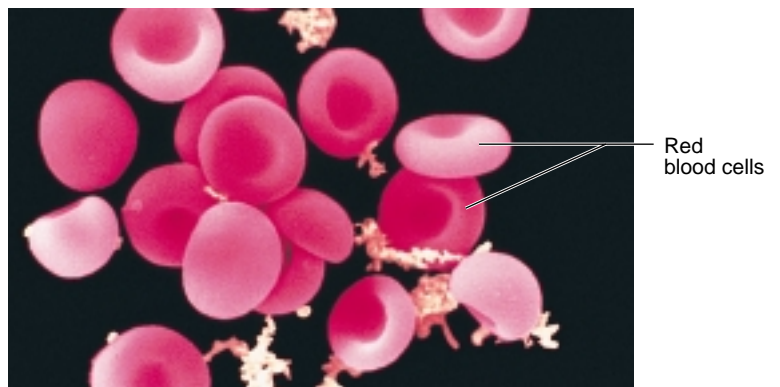
In addition to maintaining the integrity of the cell, the membrane controls the entrance and exit of substances, allowing some in while excluding others. A membrane that functions in this manner is *selectively permeable* (per'me-ah-bl). The cell membrane is crucial because it is a conduit between the cell and the extracellular fluids in the body's internal environment. It even allows the cell to receive and respond to incoming messages, a process called **signal transduction**. (Signal transduction is described in more detail in chapter 13, page 000.)



(a)



(b)



(c)

Figure 3.5

Human red blood cells as viewed using (a) a light microscope (1,200 \times), (b) a transmission electron microscope (2,500 \times), and (c) a scanning electron microscope (1,900 \times).

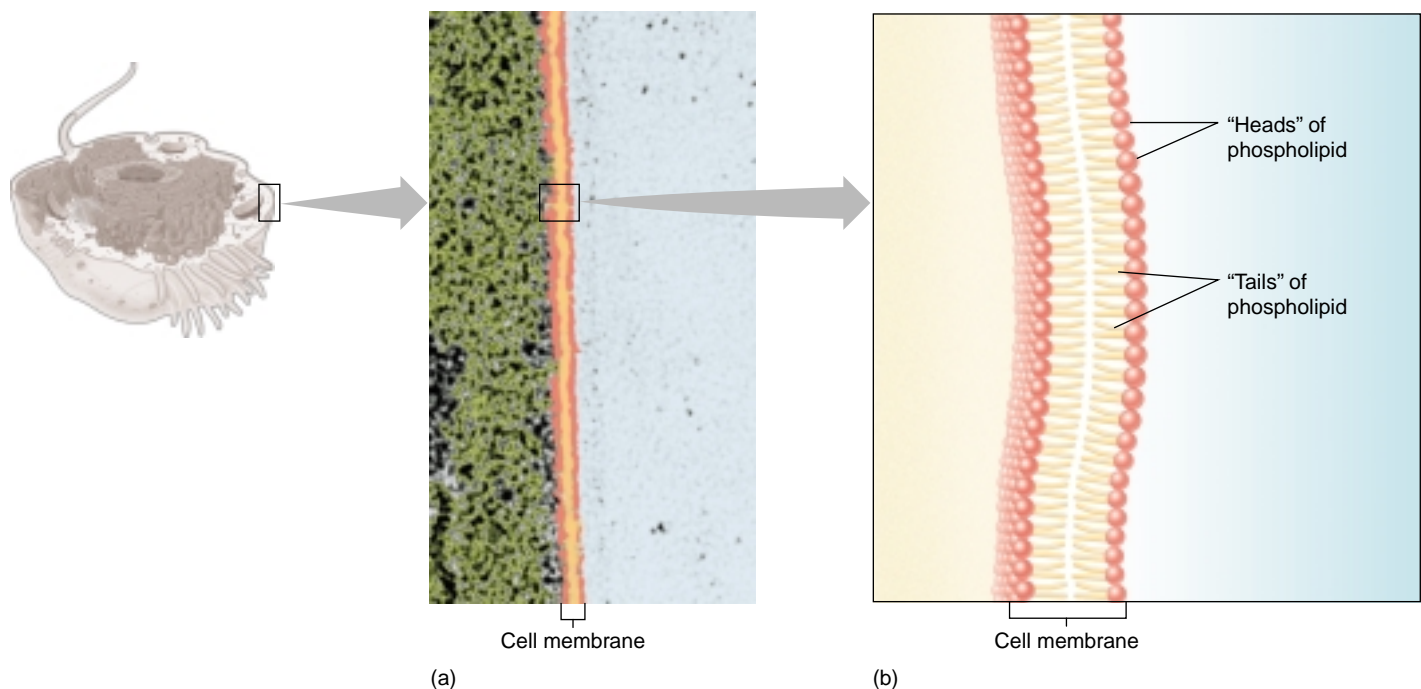


Figure 3.6

(a) A transmission electron micrograph of a cell membrane (250,000× micrograph enlarged to 600,000×); (b) the framework of the membrane consists of a double layer of phospholipid molecules.

Membrane Structure

Chemically, the cell membrane is mainly composed of lipids and proteins, with some carbohydrate. Its basic framework is a double layer (bilayer) of phospholipid molecules (see chapter 2 and fig. 2.14b) that self-assemble so that their water-soluble (hydrophilic or “water-loving”) “heads,” containing phosphate groups, form the surfaces of the membrane, and their water-insoluble (hydrophobic or “water-fearing”) “tails,” consisting of fatty acid chains, make up the interior of the membrane (see figs. 3.3 and 3.6). The lipid molecules can move sideways within the plane of the membrane, and collectively they form a thin, but stable fluid film.

∞ Reconnect to Polar Molecules, page 44.

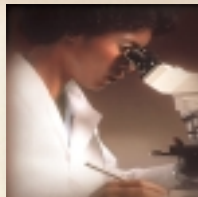
Because the interior of the cell membrane consists largely of the fatty acid portions of the phospholipid molecules, it is oily. Molecules that are soluble in lipids, such as oxygen, carbon dioxide, and steroid hormones, can pass through this layer easily; however, the layer is impermeable to water-soluble molecules, such as amino acids, sugars, proteins, nucleic acids, and various ions. Many cholesterol molecules embedded in the interior of the membrane also help make it impermeable to water-soluble substances. In addition, the relatively rigid structure of the cholesterol molecules helps stabilize the cell membrane.

A cell membrane includes only a few types of lipid molecules but many kinds of proteins (fig. 3.7), which provide the specialized functions of the membrane. The

membrane proteins can be classified according to their shapes. One group of proteins, for example, consists of tightly coiled, rodlike molecules embedded in the phospholipid bilayer. Some such fibrous proteins completely span the membrane; that is, they extend outward from its surface on one end, while their opposite ends communicate with the cell’s interior. These proteins often function as *receptors* that are specialized to combine with specific kinds of molecules, such as hormones (see chapter 13, p. 000).

Another group of cell membrane proteins are more compact and globular. Some of these proteins, called *integral proteins*, are embedded in the interior of the phospholipid bilayer. Typically, they span the membrane and provide mechanisms by which small molecules and ions can cross the otherwise impermeable phospholipid bilayer. For example, some of these integral proteins form “pores” in the membrane that allow water molecules to pass through. Other integral proteins are highly selective and form channels that allow only particular ions to enter. In muscle and nerve cells, for example, selective channels control the movements of sodium and potassium ions, which are important in muscle contraction and nerve impulse conduction (see chapters 9, p. 000, and 10, p. 000). Clinical Application 3.1 discusses how abnormal ion channels can cause disease.

Yet other globular proteins, called *peripheral proteins*, associate with the surface of the cell membrane. These proteins function as enzymes (see chapter 4, p. 110), and many are part of signal transduction. Carbo-



Faulty Ion Channels Cause Disease

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

Ion channels are tunnels through the lipid bilayer of a biological membrane that consist of protein (see fig. 10.10). These passageways permit electrical signals to pass in and out of membranes in the form of ions. An ion channel functions as a gate, opening or closing to a specific ion in response to certain conditions. Ten million ions can pass through an ion channel in one second. Events that can trigger an ion channel to open or close include a change in voltage across the membrane, binding of a ligand (a molecule that binds specifically to a membrane receptor) to the cell membrane, or receiving biochemical messages from within the cell.

Abundant ion channels include those specific for calcium (Ca^{+2}), chloride (Cl^-), sodium (Na^+), or potassium (K^+). A cell may have a few thousand ion channels specific for each ion.

Many drugs act by affecting ion channels (table 3A). The distribution

of specific ion channels on particular cell types explains the symptoms of illnesses that result from abnormal channels. Following are descriptions of three illnesses caused by malfunctioning ion channels.

Hyperkalemic Periodic Paralysis and Sodium Channels

The quarter horse was originally bred to run the quarter mile in the 1600s. Four

particularly fast stallions were used to establish much of the current population of nearly 3 million animals. Unfortunately, one of the original stallions had an inherited condition called hyperkalemic periodic paralysis. The horse was indeed a champion, but the disease brought on symptoms undesirable in a racehorse—attacks of weakness and paralysis that caused sudden collapse.

Hyperkalemic periodic paralysis results from abnormal sodium channels in the cell membranes of muscle cells. But the trigger for the temporary paralysis is another ion: potassium. When the blood potassium level rises, as it may following

table 3A Drugs That Affect Ion Channels

| Target | Indication |
|--------------------|---|
| Calcium channels | Antihypertensives Antiangina (chest pain) |
| Sodium channels | Antiarrhythmias, diuretics Local anesthetics |
| Chloride channels | Anticonvulsants Muscle relaxants |
| Potassium channels | Antihypertensives, antidiabetics (noninsulin-dependent) |

hydrate groups associated with peripheral proteins form *glycoproteins* that help cells to recognize and bind to each other. This is important as cells aggregate to form tissues. Cell surface glycoproteins also mark the cells of an individual as “self.” The immune system can distinguish between “self” cell surfaces and “nonself” cell surfaces that may indicate a potential threat, such as the presence of infectious bacteria.

Intercellular Junctions

Some cells, such as blood cells, are separated from each other in fluid-filled spaces (intercellular (in“ter-sel“u-lar) spaces). Many other cell types, however, are tightly packed, with structures called **intercellular junctions** connecting their cell membranes.

In one type of intercellular junction, called a *tight junction*, the membranes of adjacent cells converge and fuse. The area of fusion surrounds the cell like a belt, and the junction closes the space between the cells. Cells that form sheetlike layers, such as those that line the inside of the digestive tract, often are joined by tight junctions. The linings of tiny blood vessels in the brain are extremely tight (Clinical Application 3.2).

Another type of intercellular junction, called a *desmosome*, rivets or “spot welds” adjacent skin cells, so they form a reinforced structural unit. The membranes of certain other cells, such as those in heart muscle and muscle of the digestive tract, are interconnected by tubular channels called *gap junctions*. These channels link the cytoplasm of adjacent cells and allow ions, nutrients

intense exercise, it slightly alters the muscle cell membrane's electrical potential. Normally, this slight change would have no effect. In affected horses, however, the change causes sodium channels to open too widely, and admit too much sodium into the cell. The influx of sodium renders the muscle cell unable to respond to nervous stimulation for a short time—but long enough for the racehorse to fall.

Humans can inherit this condition too. In one affected family, several members collapsed after eating bananas! Bananas are very high in potassium, which triggered the symptoms of hyperkalemic periodic paralysis.

Long-QT Syndrome and Potassium Channels

A Norwegian family had four children, all born deaf. Three of the children died at ages four, five, and nine; the fourth so far has been lucky. All of the children inherited from their unaffected “carrier” parents a condition called “long-QT syndrome associated with deafness.” They have abnormal potassium channels in the heart muscle and in the inner ear. In

the heart, the malfunctioning channels cause fatal arrhythmia. In the inner ear, the abnormal channels alter the concentration of potassium ions in a fluid, impairing hearing.

The inherited form of long-QT syndrome in the Norwegian family is extremely rare, but other forms of the condition are more common, causing 50,000 sudden deaths each year, often in apparently healthy children and young adults. Several cases were attributed to an interaction between the antihistamine Seldane (terfenadine) and either an antibiotic (erythromycin) or an antifungal drug (ketoconazole), before Seldane was removed from the market in 1997.

Diagnosing long-QT syndrome early is essential because the first symptom may be fatal. It is usually diagnosed following a sudden death of a relative or detected on a routine examination of the heart's electrical activity (an electrocardiogram, see fig. 15.21). Drugs, pacemakers, and surgery to remove certain nerves can treat the condition and possibly prevent sudden death.

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 affects 1 in 2,500 Caucasians, 1 in 14,000 blacks, and 1 in 90,000 Asians, and is inherited from two unaffected parents who are carriers. The major symptoms of impaired breathing, respiratory infections, and a clogged pancreas result from secretion of extremely thick mucus. Affected individuals undergo twice-daily exercise sessions to shake free the sticky mucus and take supplemental digestive enzymes to aid pancreatic function. Strong antibiotics are used to combat their frequent lung infections.

In 1989, researchers identified the microscopic defect that causes CF as abnormal chloride channels in cells lining the lung passageways and ducts in the pancreas. The primary defect in the chloride channels also causes sodium channels to malfunction. The result is salt trapped inside affected cells, which draws moisture in, thickening the surrounding mucus. Several experimental gene therapies attempt to correct affected cells' instructions for building chloride channel proteins. ■

(such as sugars, amino acids, and nucleotides), and other small molecules to move between them (fig. 3.8). Table 3.1 summarizes these intercellular junctions.

Cellular Adhesion Molecules

Often cells must interact dynamically and transiently, rather than form permanent attachments. Proteins called **cellular adhesion molecules**, or **CAMs** for short, guide cells on the move. Consider a white blood cell moving in the bloodstream to the site of an injury, where it is required to fight infection. Imagine that such a cell must reach a woody splinter embedded in a person's palm (fig. 3.9).

Once near the splinter, the white blood cell must slow down in the turbulence of the bloodstream. A type

of CAM called a *selectin* does this by coating the white blood cell and providing traction. The white blood cell slows to a roll and binds to carbohydrates on the inner capillary surface. Clotting blood, bacteria, and decaying tissue at the injury site release biochemicals (chemoattractants) that attract the white blood cell. Finally, a type of CAM called an *integrin* contacts an adhesion receptor protein protruding into the capillary space near the splinter and pushes up through the capillary cell membrane, grabbing the passing slowed white blood cell and directing it between the tilelike cells of the capillary wall. White blood cells collecting at an injury site produce inflammation and, with the dying bacteria, form pus. (The role of white blood cells in body defense is discussed further in chapter 16.)

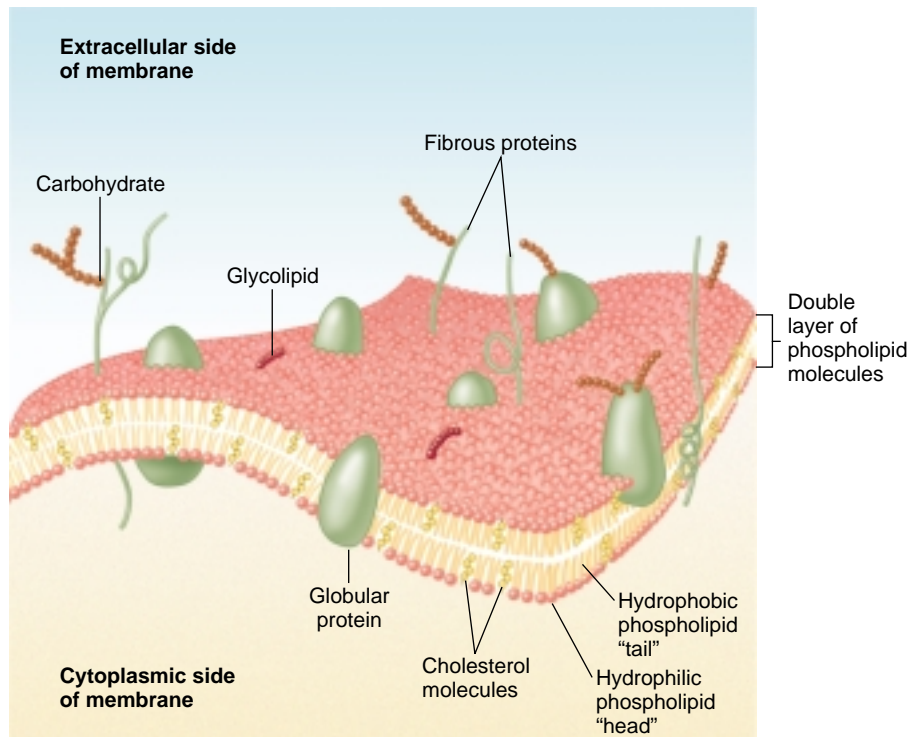


Figure 3.7

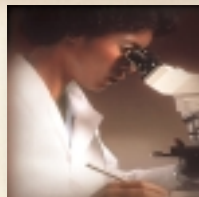
The cell membrane is composed primarily of phospholipids (and some cholesterol), with proteins scattered throughout the lipid bilayer and associated with its surfaces.

Brooke Blanton was born lacking the CAMs that enable white blood cells to adhere to blood vessel walls. As a result, her sores do not heal, never forming pus because white blood cells never reach injury sites. Brooke's earliest symptoms were teething sores that did not heal. Today, Brooke must be very careful to avoid injury or infection because her white blood cells, although plentiful and healthy, zip past her wounds.

Cytoplasm

When viewed through a light microscope, cytoplasm usually appears as clear jelly with specks scattered throughout. However, a transmission electron microscope (see fig. 3.4), which produces much greater magnification and ability to distinguish fine detail (resolution), reveals that cytoplasm contains networks of membranes and organelles suspended in a clear liquid called **cytosol**. Cytoplasm also contains abundant protein rods and tubules that form a supportive framework called the **cytoskeleton** (si'to-skel-i-tun).

| table 3.1 Types of Intercellular Junctions | | |
|--|---|---|
| Type | Function | Location |
| Tight junctions | Close space between cells by fusing cell membranes | Cells that line inside of the small intestine |
| Desmosomes | Bind cells by forming "spot welds" between cell membranes | Cells of the outer skin layer |
| Gap junctions | Form tubular channels between cells that allow substances to be exchanged | Muscle cells of the heart and digestive tract |



The Blood-Brain Barrier

Perhaps nowhere else in the body are cells attached as firmly and closely as they are in the 400-mile network of capillaries in the brain. The walls of these microscopic blood vessels are but a single cell thick. They form sheets that fold into minute tubules. A century ago, bacteriologist Paul Ehrlich showed the existence of the blood-brain barrier by injecting a dye intravenously. The brain failed to take up the dye, indicating that its blood vessels did not allow the molecules to leave and enter the brain's nervous tissue.

Studies in 1969 using the electron microscope revealed that in the brain, capillary cell membranes overlap to form a barrier of tight junctions. Unlike the cells forming capillary walls elsewhere in the body, which are pocked with vesicles and windowlike portals called clefts, the cells comprising this blood-brain barrier have few vesicles, and no clefts. Certain star-shaped brain cells called astrocytes contribute to this barrier as well.

The impenetrable barrier that the capillaries in the brain form shields delicate brain tissue from toxins in the bloodstream and from biochemical fluctuations that could be overwhelming if the brain had to con-

tinually respond to them. It also allows selective drug delivery to the periphery—for example some antihistamines do not cause drowsiness because they cannot breach the blood-brain barrier. But all this protection has a limitation—the brain cannot take up many therapeutic drugs that must penetrate to be effective. By studying the types of molecules embedded in the membranes of the cells forming the barrier, researchers are developing clever ways to sneak drugs into the brain. They can tag drugs to substances that can cross the barrier, design drugs to fit natural receptors in the barrier, or inject substances that temporarily relax the tight junctions forming the barrier. Drugs that can cross the

blood-brain barrier could be used to treat Alzheimer's disease, Parkinson's disease, brain tumors, and AIDS-related brain infections.

A malfunctioning blood-brain barrier can threaten health. During the Persian Gulf War in 1991, response of the barrier to stress in soldiers caused illness. Many troops were given a drug to protect against the effects of nerve gas on peripheral nerves—those outside the brain and spinal cord. The drug, based on its chemistry, was not expected to cross the blood-brain barrier. However, 213 Israeli soldiers treated with the drug developed brain-based symptoms, including nervousness, insomnia, headaches, drowsiness, and inability to pay attention and to do simple calculations. Further reports from soldiers, and experiments on mice, revealed that under stressful conditions, the blood-brain barrier can temporarily loosen, admitting a drug that it would normally keep out. The barrier, then, is not a fixed boundary, but rather a dynamic structure that can alter in response to a changing environment. ■

The activities of a cell occur largely in its cytoplasm, where nutrient molecules are received, processed, and used in various metabolic reactions. Within the cytoplasm, the following organelles have specific functions:

1. **Endoplasmic reticulum.** The endoplasmic reticulum (en'do-plaz'mik re-tik'u-lum (ER) is a complex organelle composed of membrane-bound flattened sacs, elongated canals, and fluid-filled vesicles. These membranous parts are interconnected, and they communicate with the cell membrane, the nuclear envelope, and certain cytoplasmic organelles. ER is widely distributed through the cytoplasm, providing a tubular transport system for molecules throughout the cell.

The endoplasmic reticulum also participates in the synthesis of protein and lipid molecules, some of which may be assembled into new membranes. Commonly, the outer membranous surface of the ER is studded with many tiny, spherical organelles called *ribosomes* (ri'bo-sōmz) that give the ER a textured appearance when viewed with an electron microscope. Such endoplasmic reticulum is termed *rough ER*. Endoplasmic reticulum that lacks ribosomes is called *smooth ER* (fig. 3.10).

The ribosomes of rough ER are sites of protein synthesis. The proteins may then move through the canals of the endoplasmic reticulum to the Golgi apparatus for further processing. Smooth ER, on the other hand, contains enzymes important in lipid synthesis.

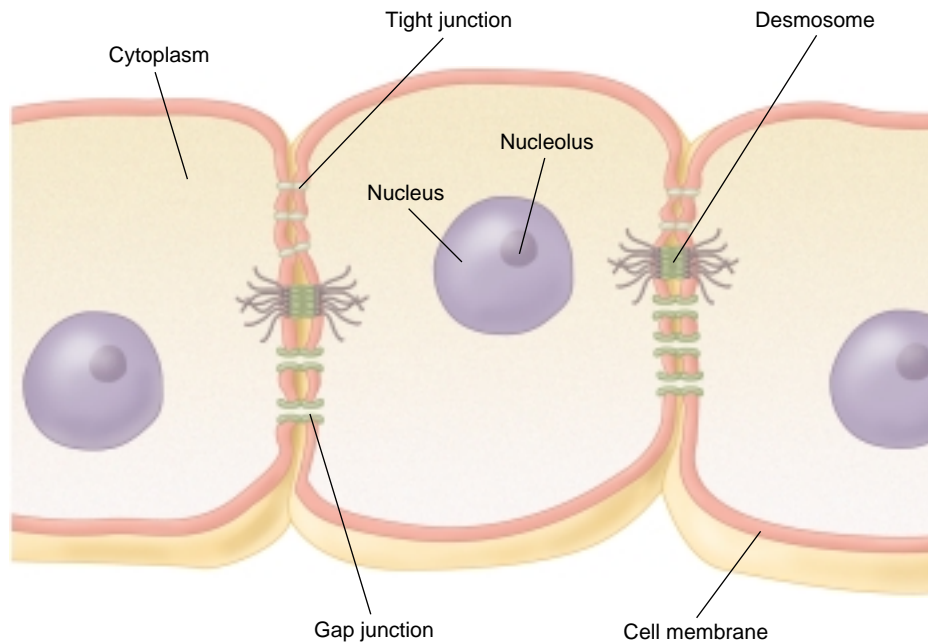


Figure 3.8

Some cells are joined by intercellular junctions, such as tight junctions that fuse neighboring membranes, desmosomes that serve as “spot welds,” or gap junctions that allow small molecules to move between the cytoplasm of adjacent cells.

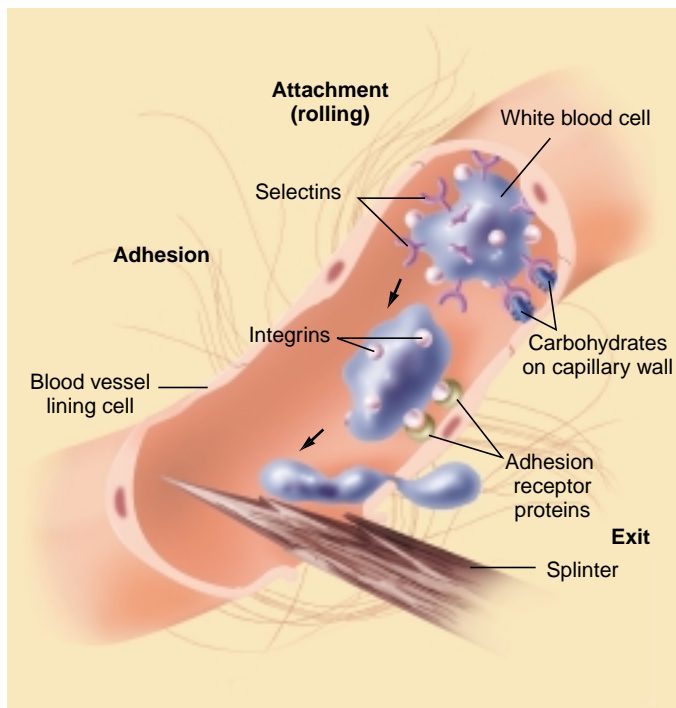


Figure 3.9

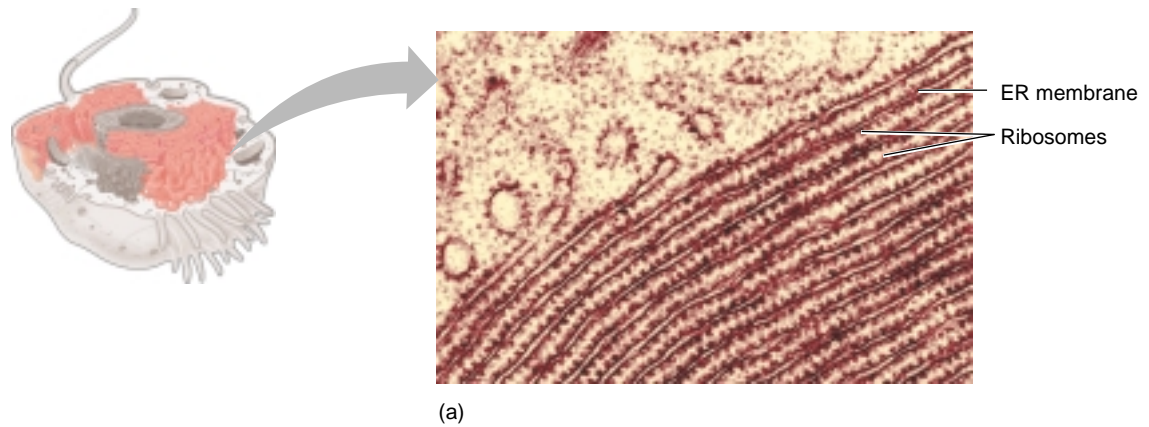
Cellular adhesion molecules (CAMs) direct white blood cells to injury sites, such as this splinter. Selectin proteins latch onto a rolling white blood cell and bind carbohydrates on the inner blood vessel wall at the same time, slowing the cell from moving at 2,500 micrometers per second to a more leisurely 50 micrometers per second. Chemoattractants are secreted. Then integrin proteins anchor the white blood cell to the blood vessel wall. Finally, the white blood cell squeezes between lining cells at the injury site and exits the bloodstream.

2. Ribosomes. Besides being found on the endoplasmic reticulum, some ribosomes are scattered freely throughout the cytoplasm. All ribosomes are composed of protein and RNA and provide a structural support and enzymes required to link amino acids to form proteins (see chapter 4, p. 127).

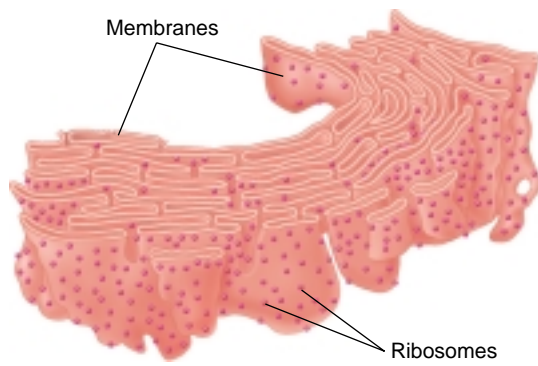
3. Golgi apparatus. The Golgi apparatus (gol’je ap’ah-ra’tus) is composed of a stack of half a dozen or so flattened, membranous sacs called *cisternae*. This organelle refines, packages, and delivers proteins synthesized by the ribosomes associated with the ER (fig. 3.11).

Proteins arrive at the Golgi apparatus enclosed in tiny vesicles composed of membrane from the endoplasmic reticulum. These sacs fuse to the membrane at the beginning or innermost end of the Golgi apparatus, which is specialized to receive proteins. Previously, these protein molecules were combined with sugar molecules as glycoproteins.

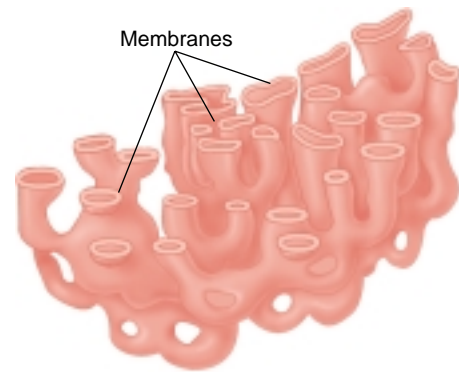
As the glycoproteins pass from layer to layer through the Golgi stacks, they are modified chemically. For example, sugar molecules may be added or removed from them. When the altered glycoproteins reach the outermost layer, they are packaged in bits of Golgi apparatus membrane that bud off and form transport vesicles. Such a vesicle may then move to the cell membrane, where it fuses and releases its contents to the outside of the cell as a secretion. Other vesicles may transport



(a)



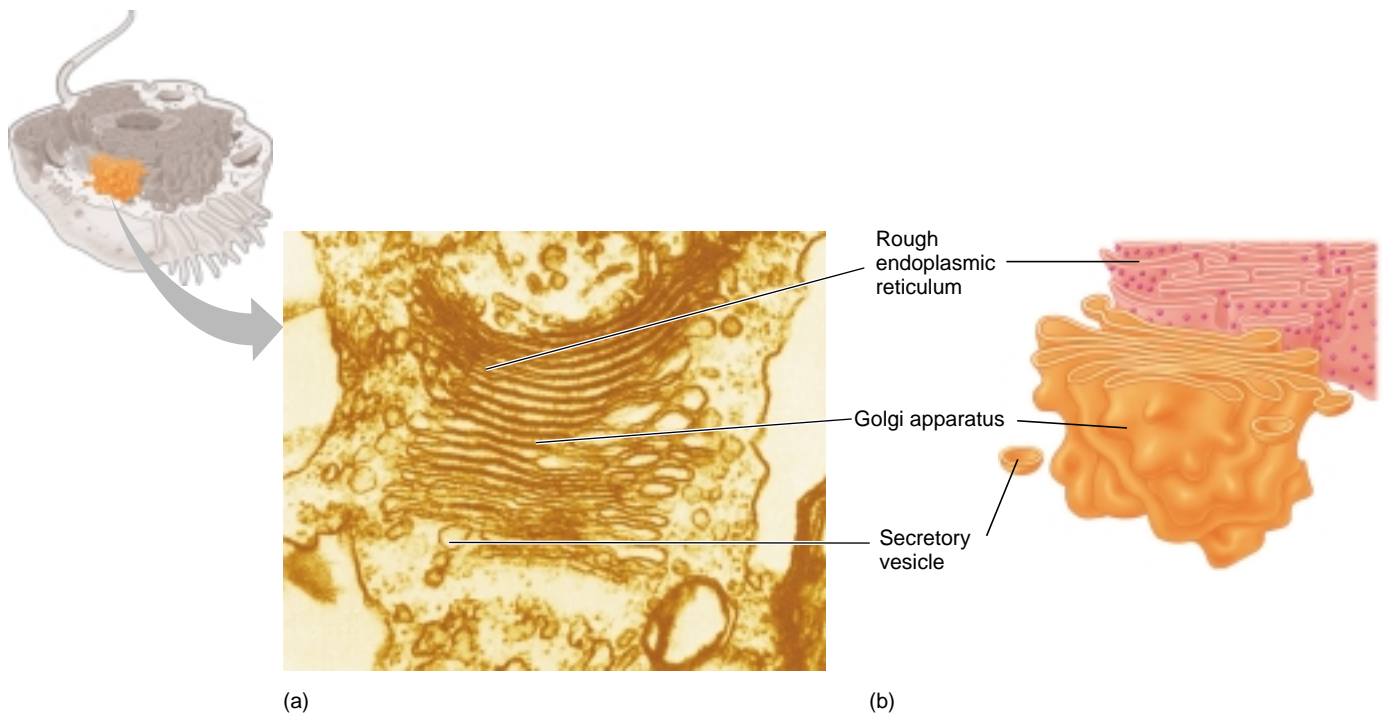
(b)



(c)

Figure 3.10

(a) A transmission electron micrograph of rough endoplasmic reticulum (ER) (28,000 \times). (b) Rough ER is dotted with ribosomes, whereas (c) smooth ER lacks ribosomes.



(a)

(b)

Figure 3.11

(a) A transmission electron micrograph of a Golgi apparatus (48,000 \times). (b) The Golgi apparatus consists of membranous sacs that continually receive vesicles from the endoplasmic reticulum and produce vesicles that enclose secretions.

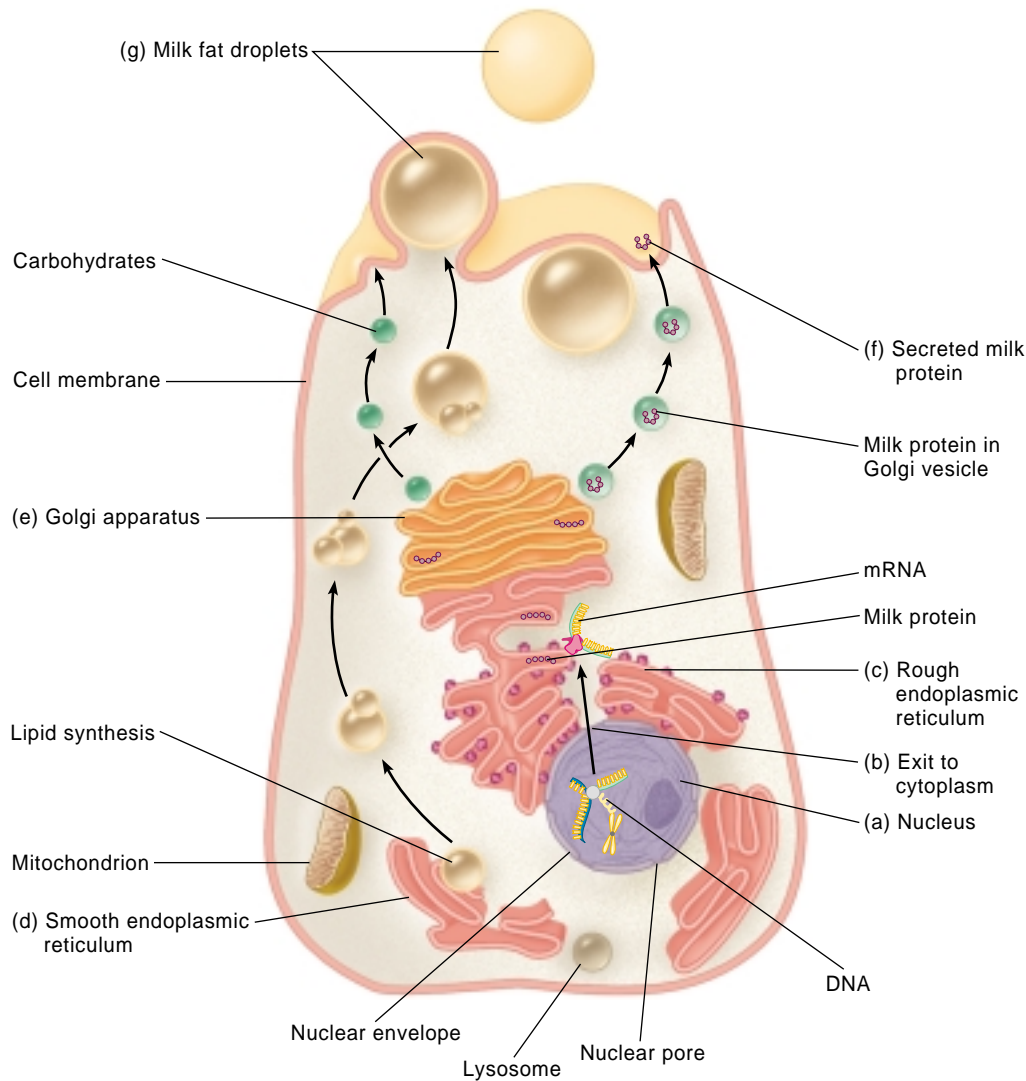


Figure 3.12

Milk secretion illustrates how organelles interact to synthesize, transport, store, and export biochemicals. Secretion begins in the nucleus (a), where messenger RNA molecules bearing genetic instructions for production of milk proteins exit through nuclear pores to the cytoplasm (b). Most proteins are synthesized on membranes of the rough endoplasmic reticulum (ER) (c), using amino acids in the cytoplasm. Lipids are synthesized in the smooth ER (d), and sugars are synthesized, assembled, and stored in the Golgi apparatus (e). An active mammary gland cell releases milk proteins from vesicles that bud off of the Golgi apparatus (f). Fat droplets pick up a layer of lipid from the cell membrane as they exit the cell (g). When the baby suckles, he or she receives a chemically complex secretion—milk.

glycoproteins to organelles within the cell (fig. 3.12). Movement of substances within cells by way of vesicles is called *vesicle trafficking*.

Some cells, including certain liver cells and white blood cells (lymphocytes), secrete glycoprotein molecules as rapidly as they are synthesized. However, certain other cells, such as those that manufacture protein hormones, release vesicles containing newly synthesized molecules only when the cells are stimulated. Otherwise, the loaded vesicles remain in the cytoplasm. (Chapter 13 discusses hormone secretion.)

Secretory vesicles that originate in the ER not only release substances outside the cell, but also provide new cell membrane. This is especially important during cell growth.

- 1 What is a selectively permeable membrane?
- 2 Describe the chemical structure of a cell membrane.
- 3 What are the different types of intercellular junctions?
- 4 What are some of the events of cellular adhesion?
- 5 What are the functions of the endoplasmic reticulum?
- 6 Describe how the Golgi apparatus functions.

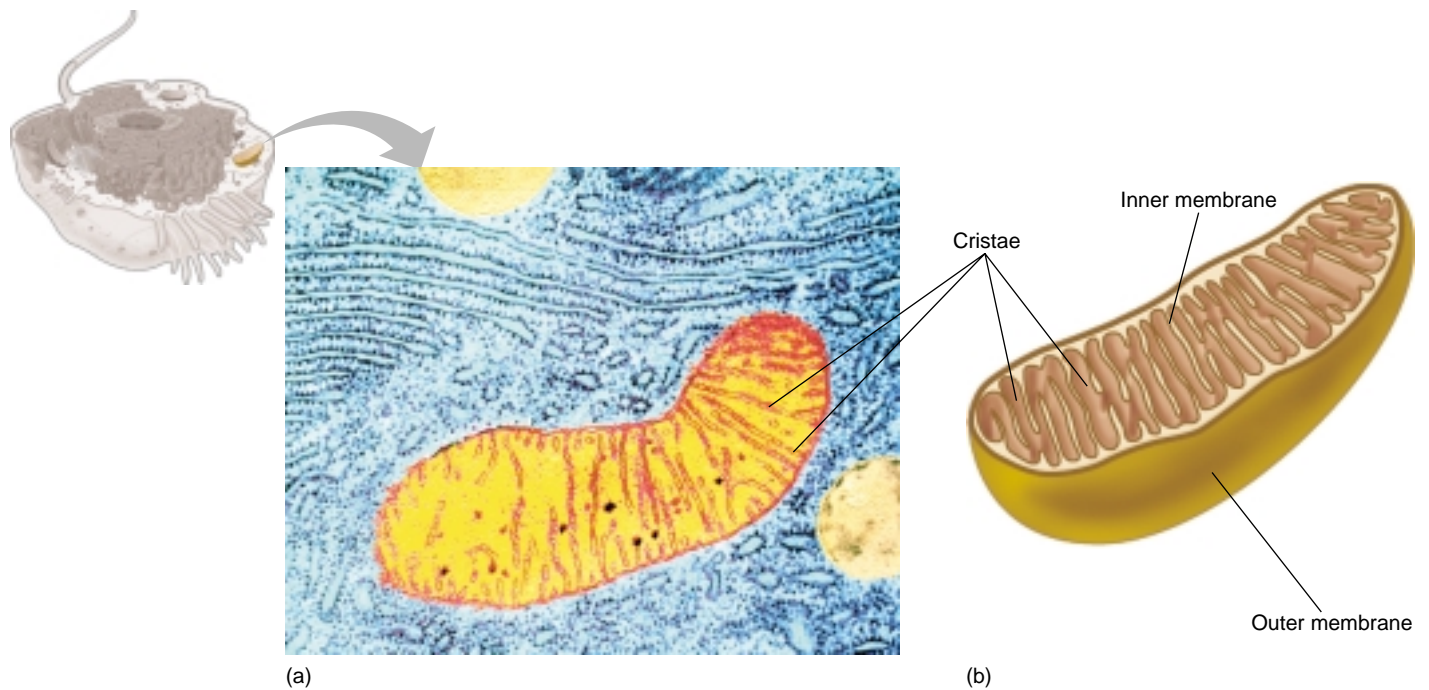


Figure 3.13

(a) A transmission electron micrograph of a mitochondrion (40,000 \times). (b) Cristae partition this saclike organelle.

- 4. Mitochondria.** Mitochondria (mi"to-kon'dre-ah) are elongated, fluid-filled sacs 2–5 μm long. They often move about slowly in the cytoplasm and can divide. A mitochondrion contains a small amount of DNA that encodes information for making a few kinds of proteins and specialized RNA. However, most proteins used in mitochondrial functions are encoded in the DNA of the nucleus. These proteins are synthesized elsewhere in the cell and then enter the mitochondria.

A mitochondrion (mi"to-kon'dre-on) has two layers—an outer membrane and an inner membrane. The inner membrane is folded extensively to form shelflike partitions called *cristae*. Small, stalked particles that contain enzymes are connected to the cristae. These enzymes and others dissolved in the fluid within the mitochondrion control many of the chemical reactions that release energy from glucose and other organic nutrients. The mitochondrion captures and transforms this newly released energy into a chemical form, the molecule **adenosine triphosphate** (ATP), that cells can readily use (fig. 3.13 and chapter 4, p. 114). For this reason the mitochondrion is sometimes called the "powerhouse" of the cell.

A typical cell has about 1,700 mitochondria, but cells with very high energy requirements, such as muscle, have many thousands of mitochondria. This is why a common symptom of illnesses

affecting mitochondria is muscle weakness. Symptoms of these "mitochondrial myopathies" include exercise intolerance and weak and flaccid muscles.

Mitochondria are particularly fascinating to biologists because they provide glimpses into the past. Mitochondria are passed to offspring from mothers only, because these organelles are excluded from the part of a sperm that enters an egg cell. Evolutionary biologists study the DNA sequences of genes in mitochondria to trace human origins, back to a long-ago group of ancestors metaphorically called "mitochondrial Eve."

Mitochondria may provide clues to a past far more remote than the beginnings of humankind. According to the widely accepted endosymbiont theory, mitochondria are the remnants of once free-living bacteria-like cells that were swallowed by primitive eukaryotic cells. These bacterial passengers remain in our cells today, where they participate in energy reactions.

- 5. Lysosomes.** Lysosomes (li'so-sōmz) are the "garbage disposals" of the cell, whose function is to dismantle debris. They are sometimes difficult to identify because their shapes vary so greatly. However, they commonly appear as tiny, membranous sacs (fig. 3.14). These sacs contain powerful enzymes that break down proteins, carbohydrates, and nucleic

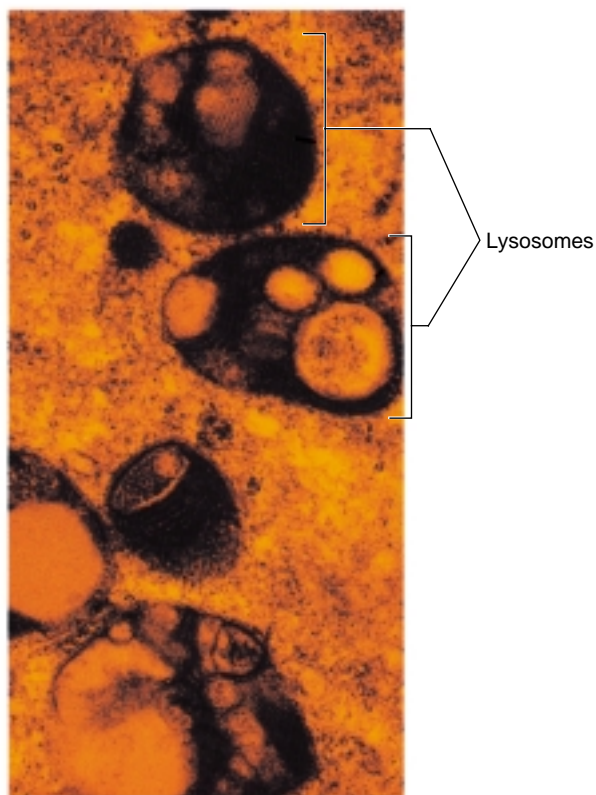


Figure 3.14

In this falsely colored transmission electron micrograph, lysosomes appear as membranous sacs (14,100 \times).

acids, including foreign particles composed of these substances. Certain white blood cells, for example, engulf bacteria that are then digested by the lysosomal enzymes. This is one way that white blood cells help stop bacterial infections.

Lysosomes also destroy worn cellular parts. In fact, lysosomes in certain scavenger cells may engulf and digest entire body cells that have been injured. How the lysosomal membrane is able to withstand being digested itself is not well understood, but this organelle sequesters enzymes that can function only under very acidic conditions, preventing them from destroying the cellular contents around them. Human lysosomes contain forty or so different types of enzymes. An abnormality in just one type of lysosomal enzyme can be devastating to health (Clinical Application 3.3).

- 6. Peroxisomes** (pě-roks'ĩ-somz). Peroxisomes are membranous sacs that resemble lysosomes in size and shape. Although present in all human cells, peroxisomes are most abundant in the liver and kidneys. Peroxisomes contain enzymes, called peroxidases, that catalyze metabolic reactions that

release hydrogen peroxide (H_2O_2) as a by-product. Peroxisomes also contain an enzyme called catalase, which decomposes hydrogen peroxide, which is toxic to cells.

The outer membrane of a peroxisome contains some forty types of enzymes, which catalyze a variety of biochemical reactions, including

- synthesis of bile acids, which are used in fat digestion
- breakdown of lipids called very long chain fatty acids
- degradation of rare biochemicals
- detoxification of alcohol

Abnormal peroxisomal enzymes can drastically affect health.

- 7. Centrosome.** A centrosome (sen'tro-sōm) (central body) is a structure located in the cytoplasm near the nucleus. It is nonmembranous and consists of two hollow cylinders called *centrioles* built of tubelike proteins called microtubules. The centrioles usually lie at right angles to each other. During cell division the centrioles move away from one another to either side of the nucleus, where they form spindle fibers that pull on and distribute *chromosomes*, (kro'mo-sōmz) which carry DNA information, to the newly forming cells (fig. 3.15).

Centrioles also form parts of hairlike cellular projections called cilia and flagella.

- 8. Cilia and flagella.** Cilia and flagella are motile extensions of certain cells. They are structurally similar and differ mainly in their length and the number present. Both consist of a constant number of microtubules organized in a distinct cylindrical pattern.

Cilia are abundant on the free surfaces of some epithelial cells. Each cilium is a tiny, hairlike structure about 10 μm long, which attaches just beneath the cell membrane to a modified centriole called a *basal body*.

Cilia occur in precise patterns. They have a “to-and-fro” type of movement that is coordinated so that rows of cilia beat one after the other, producing a wave that sweeps across the ciliated surface. For example, this action propels mucus over the surface of tissues that form the lining of the respiratory tract (fig. 3.16). Chemicals in cigarette smoke destroy cilia, which impairs the respiratory tract’s ability to expel bacteria. Infection may result.

A cell usually has only one flagellum, which is much longer than a cilium. A flagellum begins its characteristic undulating, wavelike motion at its

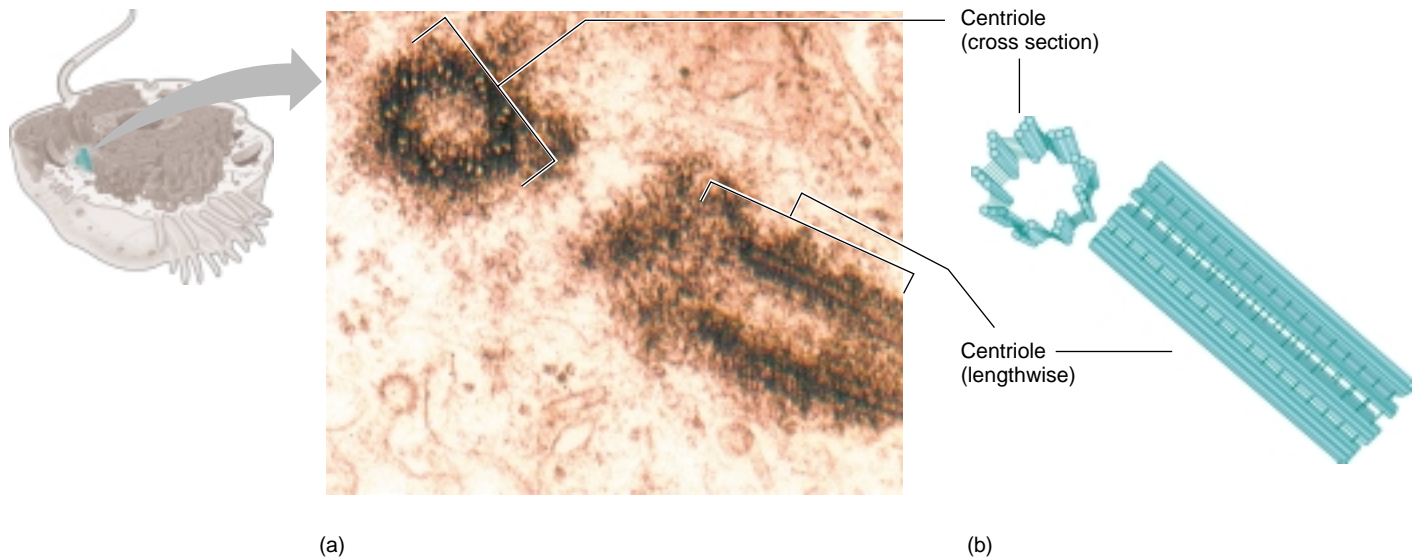


Figure 3.15

(a) A transmission electron micrograph of the two centrioles in a centrosome (142,000 \times). (b) Note that the centrioles lie at right angles to one another.

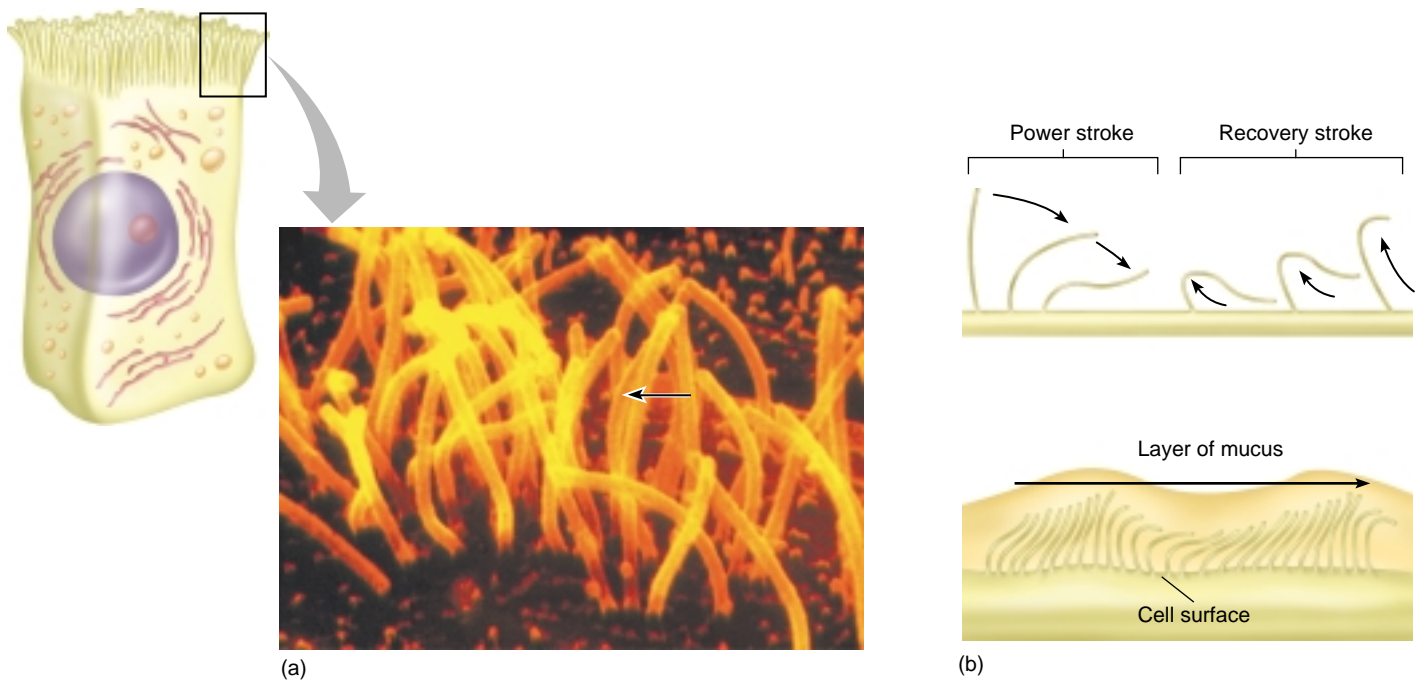


Figure 3.16

(a) Cilia, such as these (arrow), are common on the surfaces of certain cells that form the inner lining of the respiratory tract (10,000 \times). (b) Cilia have a power stroke and a recovery stroke that create a “to-and-fro” movement that sweeps fluids across the tissue surface.

base. The tail of a sperm cell, for example, is a flagellum that causes the sperm’s swimming movements (fig. 3.17 and chapter 22, p. 000).

9. Vesicles. Vesicles (ves’i’k’lz) (vacuoles) are membranous sacs that vary in size and contents.

They may form when a portion of the cell membrane folds inward and pinches off. As a result, a tiny, bubblelike vesicle, containing some liquid or solid material that was formerly outside the cell, enters the cytoplasm. The Golgi



Disease at the Organelle Level

German physiologist Rudolph Virchow first hypothesized cellular pathology—disease at the cellular level—in the 1850s.

Today, new treatments for many disorders are a direct result of understanding a disease process at the cellular level. Here, we examine how three abnormalities—in mitochondria, in peroxisomes, and in lysosomes—cause whole-body symptoms.

MELAS and Mitochondria

Sharon had always been small for her age, easily fatigued, slightly developmentally delayed, and had difficulty with schoolwork. She also had seizures. At age eleven, she suffered a stroke. An astute physician who observed Sharon's mother, Lillian, suspected that the girl's symptoms were all related, and the result of abnormal mitochondria, the organelles that house the biochemical reactions that extract energy from nutrients.

The doctor noticed that Lillian was uncoordinated and had numb hands. When she asked if Lillian ever had migraine headaches, she said that she suffered from them nearly

daily, as did her two sisters and one brother. Lillian and her siblings also had diabetes mellitus and muscle weakness. Based on this information, the doctor ordered several blood tests for mother and daughter, which revealed that both had elevated levels of biochemicals (pyruvic acid and lactic acid) that indicated that they were unable to extract the maximal energy from nutrients. Muscle biopsies then showed the source of the problem—abnormal mitochondria. Accumulation of these mitochondria in smooth muscle cells in blood vessel walls in the brain caused Sharon's stroke and was probably also causing her seizures.

All of the affected family members were diagnosed with a disorder called MELAS, which stands for the major

symptoms—mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes. Their mitochondria cannot synthesize some of the proteins required to carry out the energy reactions. The responsible gene is part of the DNA in mitochondria, and Lillian's mother transmitted it to all of her children. But because mitochondria are usually inherited only from the mother, Sharon's uncle will not pass MELAS to his children.

Adrenoleukodystrophy (ALD) and Peroxisomes

For young Lorenzo Odone, the first sign of adrenoleukodystrophy was disruptive behavior in school. When he became lethargic, weak, and dizzy, his teachers and parents realized that his problem was not just temper tantrums. His skin darkened, blood sugar levels plummeted, heart rhythm altered, and the levels of electrolytes in his body fluids

apparatus and ER also form vesicles. Fleets of vesicles transport many substances into and out of cells in vesicle trafficking.

- 10. Microfilaments and microtubules.** Two types of threadlike structures in the cytoplasm are microfilaments and microtubules. Microfilaments are tiny rods of the protein actin that typically occur in meshworks or bundles. They cause various kinds of cellular movements. In muscle cells, for example, microfilaments constitute *myofibrils*, which cause these cells to shorten or contract. In other cells, microfilaments associated with the inner surface of the cell membrane aid cell motility (fig. 3.18).

Microtubules are long, slender tubes with diameters two or three times greater than those of microfilaments. They are composed of the globular protein tubulin. Microtubules are usually somewhat

rigid and form the cytoskeleton, which helps maintain the shape of the cell (fig. 3.19). In cilia and flagella, microtubules interact to provide movement (see figs. 3.16 and 3.17).

Microtubules also move organelles and structures within the cell. For instance, microtubules are assembled from tubulin subunits in the cytoplasm during cell division and help distribute chromosomes to the newly forming cells, a process described in more detail later in this chapter. Microtubules also provide conduits for organelles, like the tracks of a roller coaster.

- 11. Other structures.** In addition to organelles, cytoplasm contains lifeless chemicals called *inclusions*. These usually are in a cell temporarily. Inclusions include stored nutrients such as glycogen and lipids, and pigments such as melanin in the skin.

changed. He lost control over his limbs as his nervous system continued to deteriorate. Lorenzo's parents took him to many doctors. Finally, one of them tested the child's blood for an enzyme normally manufactured in peroxisomes.

Lorenzo's peroxisomes lacked the second most abundant protein in the outer membrane of this organelle. Normally, the missing protein transports an enzyme into the peroxisome. The enzyme controls breakdown of a type of very long chain fatty acid. Without the enzyme, the fatty acid builds up in cells in the brain and spinal cord, eventually stripping these cells of their fatty sheaths, made of a substance called myelin. Without the myelin sheaths, the nerve cells cannot transmit messages fast enough. Death comes in a few years.

For Lorenzo and many other sufferers of ALD, eating a type of triglyceride from rapeseed oil slows the buildup of the very long chain fatty acids for a few years, stalling symptoms. But the treatment eventually impairs blood clotting and other vital functions and fails to halt the progression of the illness.

The disappointment over the failure of "Lorenzo's oil" may be lessened by a drug that activates a different gene, whose protein product can replace the missing or abnormal one in ALD. In cells from children with ALD, the replacement protein stopped the buildup of very-long-chain fatty acids, and also increased the number of peroxisomes.

Tay-Sachs Disease and Lysosomes

Michael was a pleasant, happy infant who seemed to be developing normally until about six months of age. Able to roll over and sit for a few seconds, he suddenly seemed to lose those abilities. Soon, he no longer turned and smiled at his mother's voice, and he did not seem as interested in his mobile. Concerned about Michael's reversals in development, his anxious parents took him to the doctor. It took exams by several specialists to diagnose Michael's Tay-Sachs disease, because, thanks to screening programs in the population groups known to have this inherited illness, fewer than ten new cases appear each year. Michael's parents were not

among those ethnic groups and previously had no idea that they both were carriers of the gene that causes this very rare illness.

A neurologist clinched her suspicion of Tay-Sachs by looking into Michael's eyes, where she saw the telltale "cherry red spot" indicating the illness. A look at his cells provided further clues—the lysosomes, tiny enzyme-filled sacs, were swollen to huge proportions. Michael's lysosomes lacked one of the forty types of lysosomal enzymes, resulting in a "lysosomal storage disease" that built up fatty material on his nerve cells. His nervous system would continue to fail, and he would be paralyzed and unable to see or hear by the time he died, before the age of four years.

The cellular and molecular signs of Tay-Sachs disease—the swollen lysosomes and missing enzyme—had been present long before Michael began to lag developmentally. The next time his parents expected a child, they had her tested before birth for the enzyme deficiency. They learned, happily, that she would be a carrier like themselves, but not ill. ■

- 1 Why are mitochondria called the "powerhouses" of cells?
- 2 How do lysosomes function?
- 3 Describe the functions of microfilaments and microtubules.
- 4 Distinguish between organelles and inclusions.

Cell Nucleus

A nucleus is a relatively large, usually spherical structure that directs the activities of the cell. It is enclosed in a double-layered **nuclear envelope**, which consists of an inner and an outer lipid bilayer membrane. These two membranes have a narrow space between them but are joined at places that surround relatively large openings called **nuclear pores**. These pores are not mere perforations, but channels consisting of more than 100 different

types of proteins. Nuclear pores allow certain dissolved substances to move between the nucleus and the cytoplasm (fig. 3.20), most notably molecules of messenger RNA that carry genetic information.

The nucleus contains a fluid (nucleoplasm) in which other structures float. These structures include the following:

1. **Nucleolus.** A nucleolus (nu-kle'o-lus) ("little nucleus") is a small, dense body largely composed of RNA and protein. It has no surrounding membrane and is formed in specialized regions of certain chromosomes. It is the site of ribosome production. Once ribosomes form, they migrate through the nuclear pores to the cytoplasm. A cell may have more than one nucleolus. The nuclei of cells that synthesize large amounts of protein, such as those of glands, may contain especially large nucleoli.

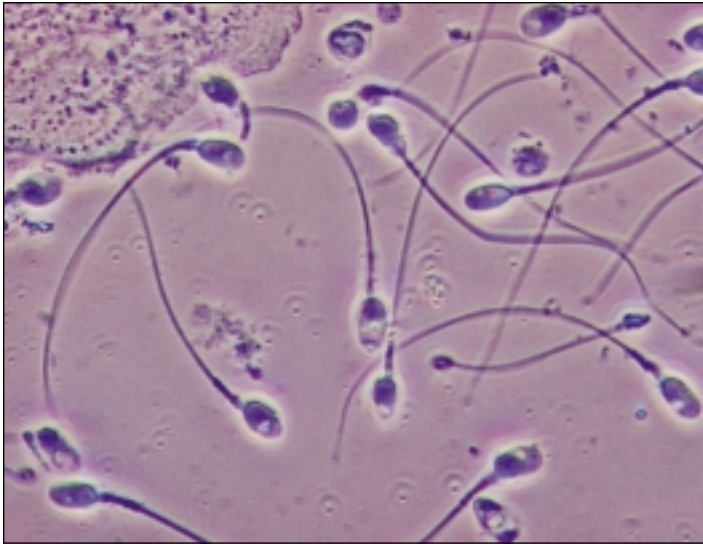


Figure 3.17

Light micrograph of human sperm cells (1,000 \times). Flagella form the tails of these cells.

2. **Chromatin.** Chromatin consists of loosely coiled fibers in the nuclear fluid. When cell division begins, these fibers become more tightly coiled to form rodlike chromosomes. Chromatin fibers are composed of continuous DNA molecules wrapped around clusters of eight molecules of proteins called histones, giving the appearance of beads on a string. The DNA molecules contain the information for synthesis of proteins.

Table 3.2 summarizes the structures and functions of organelles.

- 1 How are the nuclear contents separated from the cytoplasm?
- 2 What is the function of the nucleolus?
- 3 What is chromatin?

Cells die in different ways. *Apoptosis* (ap"o-to'sus) is one form of cell death in which the cell manufactures an enzyme that cuts up DNA not protected by histones. This is an active process because a new substance is made. Apoptosis is important in shaping the embryo, in maintaining organ form during growth, and in developing the immune system and the brain.

Necrosis is a type of cell death that is a passive response to severe injury. Typically proteins lose their characteristic shapes, and the cell membrane deteriorates as the cell swells and bursts. Unlike apoptosis, necrosis causes great inflammation.

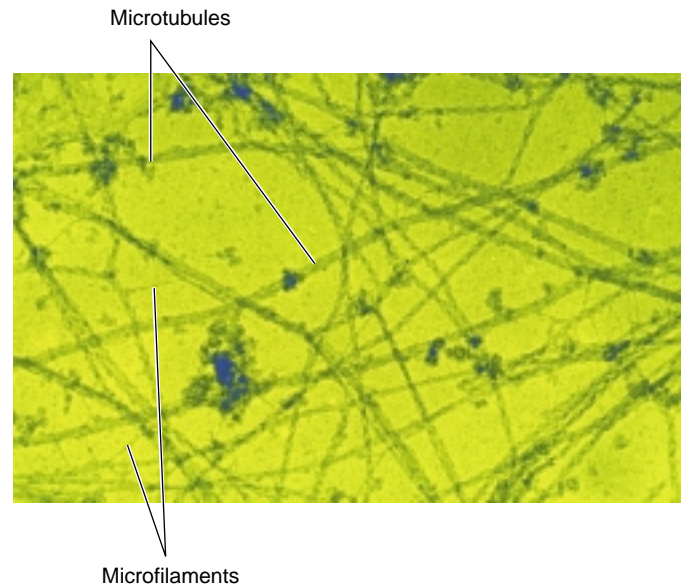


Figure 3.18

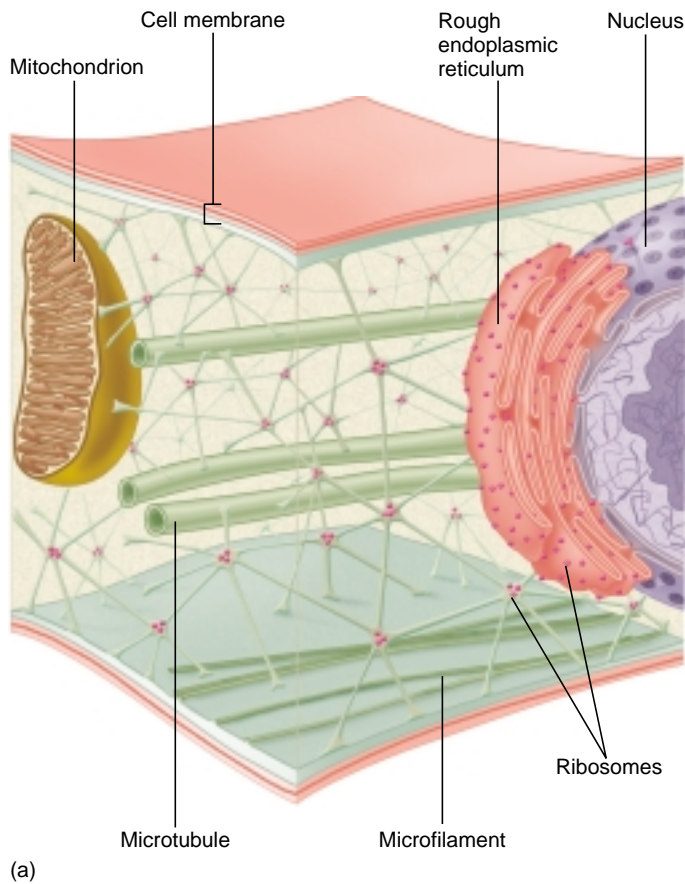
A transmission electron micrograph of microfilaments and microtubules within the cytoplasm (35,000 \times).

Movements into and out of the Cell

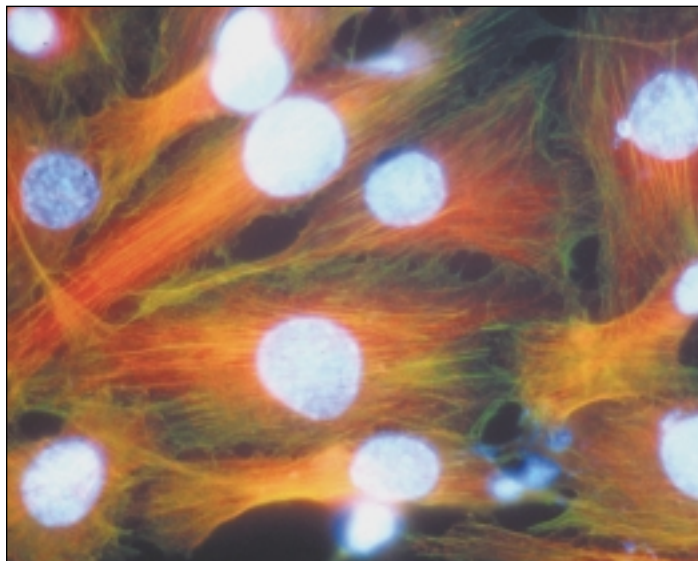
The cell membrane is a barrier that controls which substances enter and leave the cell. Oxygen and nutrient molecules enter through this membrane, whereas carbon dioxide and other wastes leave through it. These movements involve *physical* (or passive) processes such as diffusion, facilitated diffusion, osmosis, and filtration, and *physiological* (or active) mechanisms such as active transport, endocytosis, and exocytosis. The mechanisms by which substances cross the cell membrane are important for understanding many aspects of physiology.

Diffusion

Diffusion (di-fu'zhun) (also called simple diffusion) is the tendency of atoms, molecules, and ions in a liquid or air solution to move from areas of higher concentration to areas of lower concentration, thus becoming more evenly distributed, or more *diffuse*. Diffusion occurs because atoms, molecules, and ions are in constant motion. Each particle travels in a separate path along a straight line until it collides with some other particle and bounces off. Then it moves in its new direction until it collides again and changes direction once more. Because collisions are less likely if there are fewer particles, there is a net movement of particles from an area of higher concentration to an area of lower concentration. This difference in concentrations is called a *concentration gradient*, and atoms, molecules, and ions are said to diffuse down a concentration gradient. With time, the concentration of a given substance becomes uniform throughout a solution.



(a)



(b)

Figure 3.19

(a) Microtubules help maintain the shape of a cell by forming an internal “scaffolding,” or cytoskeleton, beneath the cell membrane and within the cytoplasm. (b) A falsely colored electron micrograph of cells showing the cytoskeleton (250× micrograph enlarged to 750×).

This is the condition of *diffusional equilibrium* (dī-fū'zhun-ul e'kwi-lib're-um). At diffusional equilibrium, although random movements continue, there is no further net movement, and the concentration of a substance will be uniform throughout the solution.

Random molecular movement that causes diffusion results from heat energy in the environment. The warmer the conditions and the smaller the molecules, the faster they move. At body temperature, small molecules like water move over a thousand miles per hour. However, the internal environment is a crowded place from a molecule's point of view. A single molecule may collide with other molecules a million times each second. So even at these high speeds, diffusion occurs relatively slowly. However, the small size of cells enables molecules and ions to diffuse in or out in a fraction of a second.

Consider sugar (a solute) put into a glass of water (a solvent), as illustrated in figure 3.21. The sugar at first remains in high concentration at the bottom of the glass. As the sugar molecules move about, they may collide with each other or miss each other completely. Since they are less likely to collide with each other in areas where there are fewer sugar molecules, sugar molecules gradually diffuse from areas of high concentration to areas of lower concentration (*down* the concentration gradient), and eventually the sugar molecules evenly distribute in the water.

To better understand how diffusion accounts for the movement of molecules through a cell membrane, imagine a container of water that is separated into two compartments by a completely permeable membrane (fig. 3.22). This membrane has many pores that are large enough for water and sugar molecules to pass through. The sugar molecules are placed in one compartment (A) but not in the other (B). Although the sugar molecules move in all directions, more move from compartment A (where they are in greater concentration) through the pores in the membrane and into compartment B (where they are in lesser concentration) than move in the other direction. Thus, sugar diffuses from compartment A to compartment B. At the same time, the water molecules diffuse from compartment B (where they are in greater concentration) through the pores into compartment A (where they are in lesser concentration). Eventually, equilibrium is achieved with equal concentrations of water and sugar in each compartment.

Diffusional equilibrium does not normally occur in living systems. Rather, the term *physiological steady state*, where concentrations of diffusing substances are unequal but stable, is more appropriate. For example, intracellular (in'trah-sel'u-lar) oxygen is always low

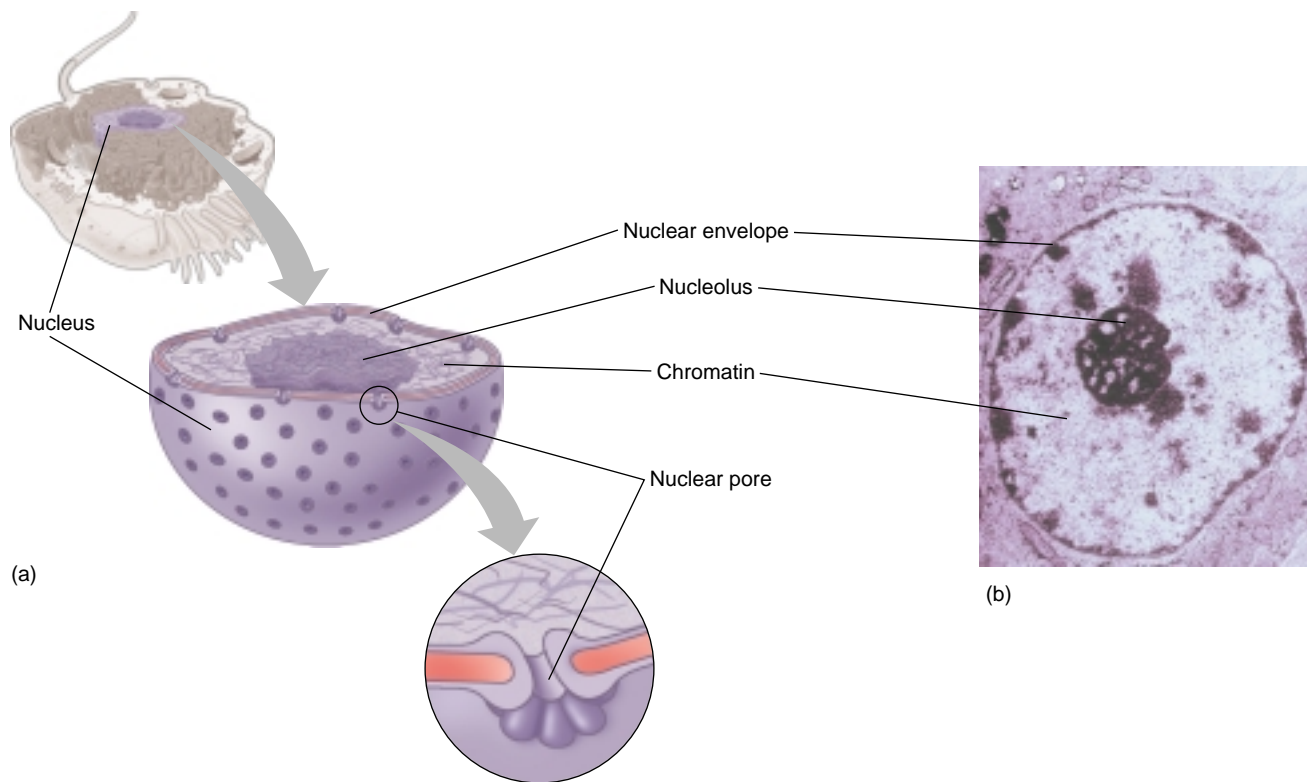


Figure 3.20

(a) The pores in the nuclear envelope allow certain substances to pass between the nucleus and the cytoplasm. (b) A transmission electron micrograph of a cell nucleus (8,000 \times). It contains a nucleolus and masses of chromatin.

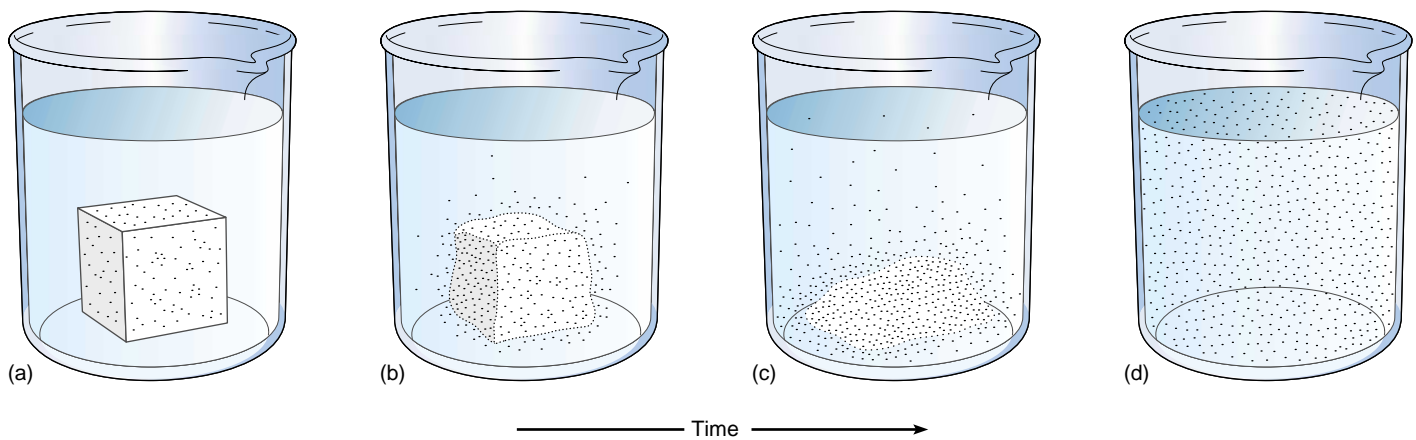


Figure 3.21

An example of diffusion (a, b, and c). A sugar cube placed in water slowly disappears as the sugar molecules diffuse from regions where they are more concentrated toward regions where they are less concentrated. (d) Eventually, the sugar molecules distribute evenly throughout the water.

| Organelle | Structure | Function |
|---------------------------------|---|---|
| Cell membrane | Membrane mainly composed of protein and lipid molecules | Maintains integrity of the cell, controls the passage of materials into and out of the cell, and provides for signal transduction |
| Endoplasmic reticulum | Complex of connected, membrane-bound sacs, canals, and vesicles | Transports materials within the 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 and modifies protein molecules for transport and secretion |
| Mitochondria | Membranous sacs with inner partitions | Release energy from food molecules and transform energy into usable form |
| Lysosomes | Membranous sacs | Contain enzymes capable of digesting worn cellular parts or substances that enter cells |
| Peroxisomes | Membranous vesicles | Contain enzymes called peroxidases, important in the breakdown of many organic molecules |
| Centrosome | Nonmembranous structure composed of two rodlike centrioles | Helps distribute chromosomes to new cells during cell division and initiates formation of cilia |
| Cilia | Motile projections attached to basal bodies beneath the cell membrane | Propel fluids over cellular surface |
| Flagella | Motile projections attached to basal bodies beneath the cell membrane | Enable sperm cells to move |
| Vesicles | Membranous sacs | Contain substances that recently entered the cell and store and transport newly synthesized molecules |
| Microfilaments and microtubules | Thin rods and tubules | Support cytoplasm and help move substances and organelles within the cytoplasm |
| Nuclear envelope | Porous double membrane that separates the nuclear contents from the cytoplasm | Maintains the integrity of the nucleus and controls the passage of materials between the nucleus and cytoplasm |
| Nucleolus | Dense, nonmembranous body composed of protein and RNA molecules | Site of ribosome formation |
| Chromatin | Fibers composed of protein and DNA molecules | Contains cellular information for synthesizing proteins |

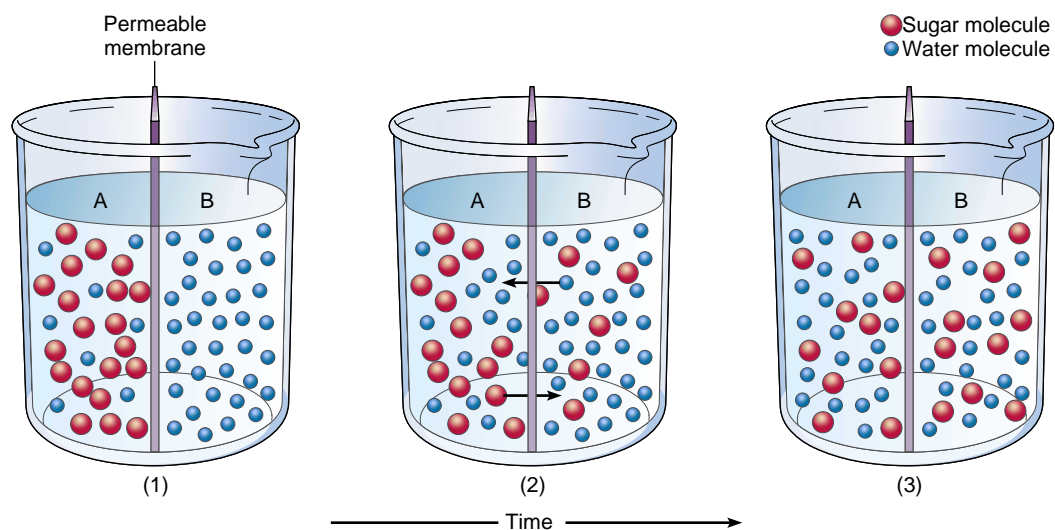


Figure 3.22

(1) A membrane permeable to water and sugar molecules separates a container into two compartments. Compartment *A* contains both types of molecules, while compartment *B* contains only water molecules. (2) As a result of molecular motions, sugar molecules tend to diffuse from compartment *A* into compartment *B*. Water molecules tend to diffuse from compartment *B* into compartment *A*. (3) Eventually, equilibrium is reached.

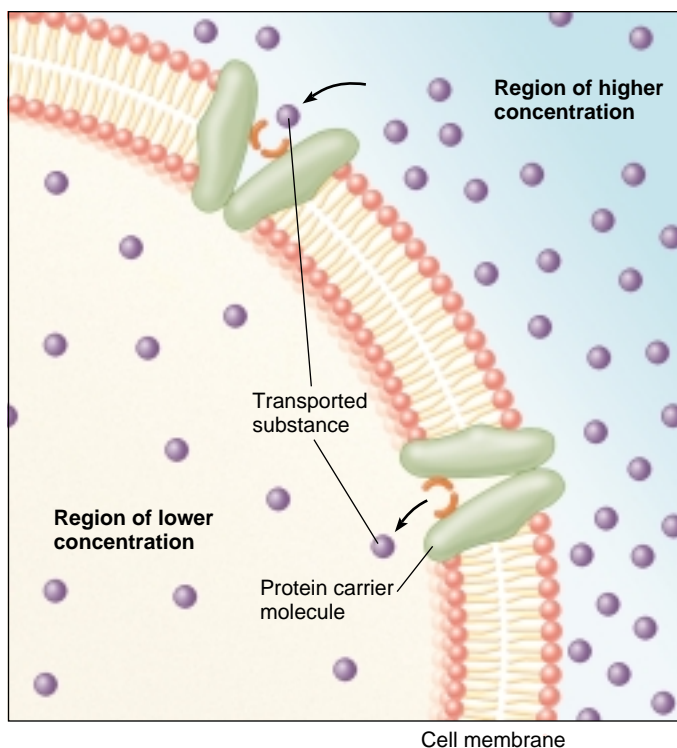


Figure 3.23

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.

because oxygen is used up in metabolic reactions. Extracellular (eks"trah-sel"u-lar) oxygen is maintained high by the respiratory and cardiovascular systems, thus providing a gradient for oxygen to diffuse continuously into body cells.

In general, diffusion of substances into or out of cells can occur if (1) the cell membrane is permeable to that substance and (2) if a concentration gradient for that substance exists, such that it is at a higher concentration either outside or inside of the cell.

Some of the previous examples considered imaginary membranes with specific permeabilities. For the cell membrane, the issue of permeability is somewhat more complex because of its selective nature. Lipid-soluble substances, such as oxygen, carbon dioxide, steroids, and general anesthetics, freely cross the cell membrane by simple diffusion. Small solutes that are not lipid-soluble, such as ions of sodium, potassium and chloride, may diffuse through protein channels in the membrane, described earlier. (Water molecules may also diffuse through similar channels, called pores.) Because this type of movement uses membrane proteins as "helpers," it is considered to be a form of another type of diffusion, called **facilitated diffusion** (fah-sil"i-tat'ed di-fu'zhun). Facilitated diffusion is very important not only for ions, but for larger water-soluble molecules, such as glucose and amino acids.

A number of factors influence the diffusion rate, but those most important in the body are distance, the concentration gradient, and temperature. In general, diffusion is more rapid over shorter distances, larger concentration gradients, and at higher temperatures. Homeostasis maintains all three of these factors at optimum levels.

Facilitated Diffusion

Most sugars and amino acids are insoluble in lipids, and they are too large to pass through cell membrane pores. Facilitated diffusion includes not only protein channels, but also certain proteins that function as "carriers" to bring such molecules across the cell membrane. In the facilitated diffusion of glucose, for example, glucose combines with a protein carrier molecule at the surface of the membrane. This union of glucose and carrier molecule changes the shape of the carrier that moves glucose to the inner face of the membrane. The glucose portion is released, and the carrier molecule can return to its original shape to pick up another glucose molecule. The hormone *insulin*, discussed in chapter 13 (p. 000), promotes facilitated diffusion of glucose through the membranes of certain cells.

Facilitated diffusion is similar to simple diffusion in that it can move molecules only from regions of higher concentration toward regions of lower concentration. However, unlike simple diffusion, the number of carrier molecules in the cell membrane limits the rate of facilitated diffusion (fig. 3.23).

Osmosis

Osmosis (oz-mo'sis) is the diffusion of water molecules 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 following example, assume that the selectively permeable membrane is permeable to water molecules (the solvent) but impermeable to sucrose molecules (the solute).

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

Just like molecules of other substances, molecules of water will diffuse from areas of higher concentration to areas of lower concentration. In figure 3.24, the presence of sucrose 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. Sucrose, on the other hand, cannot diffuse out of compartment A because the selectively permeable membrane is impermeable to it.

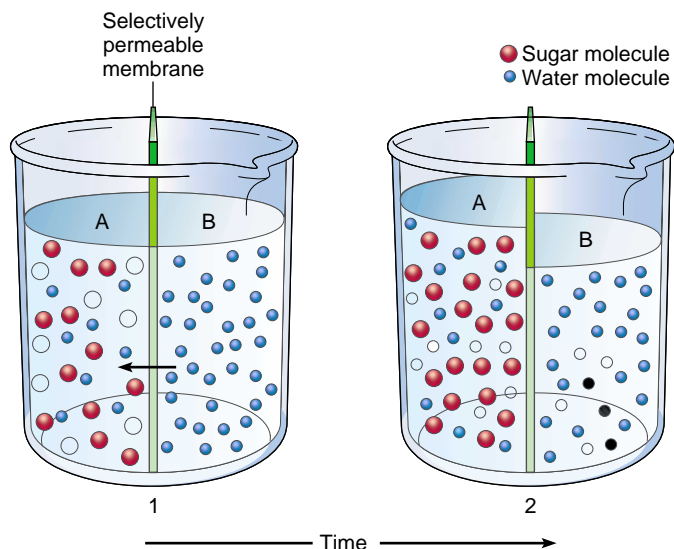


Figure 3.24

Osmosis. (1) A selectively permeable membrane separates the container into two compartments. At first, compartment A contains water and sugar molecules, whereas compartment B contains only water. As a result of molecular motions, water diffuses by osmosis from compartment B into compartment A. Sugar 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.

Note in figure 3.24 that as osmosis occurs, the level of water 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 (sucrose 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 that have a higher osmotic pressure than body fluids are called **hypertonic**. If cells are put into a hypertonic solution, there will be 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. Although cell membranes are somewhat elastic, the cells may swell so much that they burst. Figure 3.25 illustrates the effects of the three types of solutions on red blood cells.

It is important to control the concentration of solute in solutions that are infused into body tissues or blood. 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 will diffuse into the cells, and they will burst (hemolyze). On the other hand, if red blood cells are exposed to 0.9% NaCl solution (normal saline), the cells will remain unchanged because this solution is isotonic to human cells. Similarly, a 5% solution of glucose is isotonic to human cells. (The lower percentage is needed with NaCl to produce an isotonic solution, in part because NaCl ionizes in solution more completely and produces more solute particles than does glucose.)

Filtration

Molecules move through membranes by diffusion or osmosis because of their random movements. In other instances, molecules are forced through membranes by the process of **filtration** (fil-tra'shun).

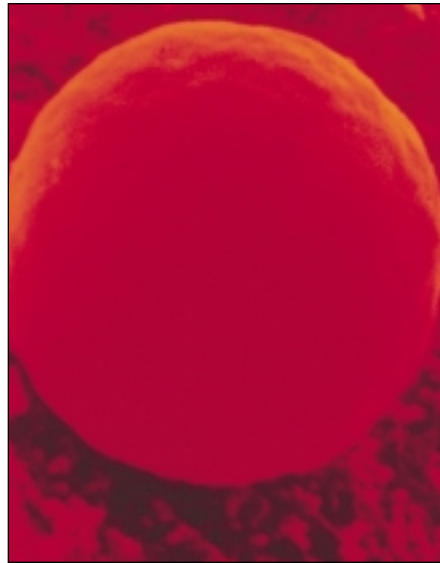
Filtration is commonly used to separate solids from water. One method is to pour a mixture of solids and water onto filter paper in a funnel (fig. 3.26). The paper serves as a porous membrane through which the small water molecules can pass, leaving the larger solid particles behind. Hydrostatic pressure, which is created by the weight of water due to gravity, forces the water molecules through to the other side. An example of this is making coffee by the drip method.

In the body, tissue fluid forms when water and 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. 3.27). The force for this movement comes from blood pressure, generated largely by heart action, which is greater within the vessel than outside it. (Although heart action is an active body process, filtration is still considered passive because it can occur due to the pressure caused by gravity alone.) Filtration is discussed further in chapters 15 (p. 000) and 20 (p. 000).

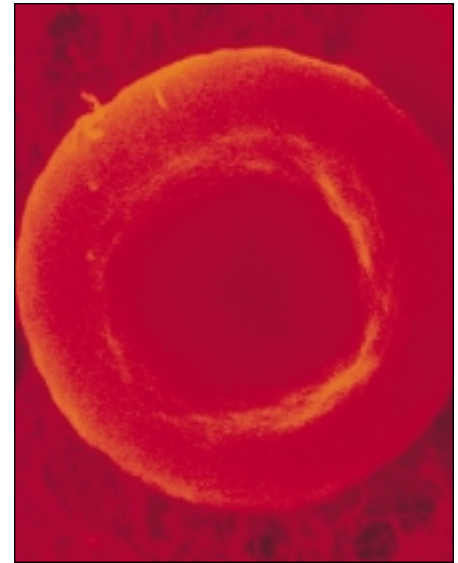
- 1 What kinds of substances most readily diffuse through a cell membrane?
- 2 Explain the differences among diffusion, facilitated diffusion, and osmosis.
- 3 Distinguish among hypertonic, hypotonic, and isotonic solutions.
- 4 Explain how filtration occurs in the body.



(a) Cell in hypertonic solution



(b) Cell in hypotonic solution



(c) Cell in isotonic solution

Figure 3.25

(a) If red blood cells are placed in a hypertonic solution, more water leaves than enters, and the cells shrink (8,200 \times). (b) In a hypotonic solution, more water enters than leaves, and the cells swell, become spherical, and may burst (8,200 \times). (c) In an isotonic solution, equal volumes of water enter and leave the cells, and their sizes and shapes remain unchanged (8,200 \times).

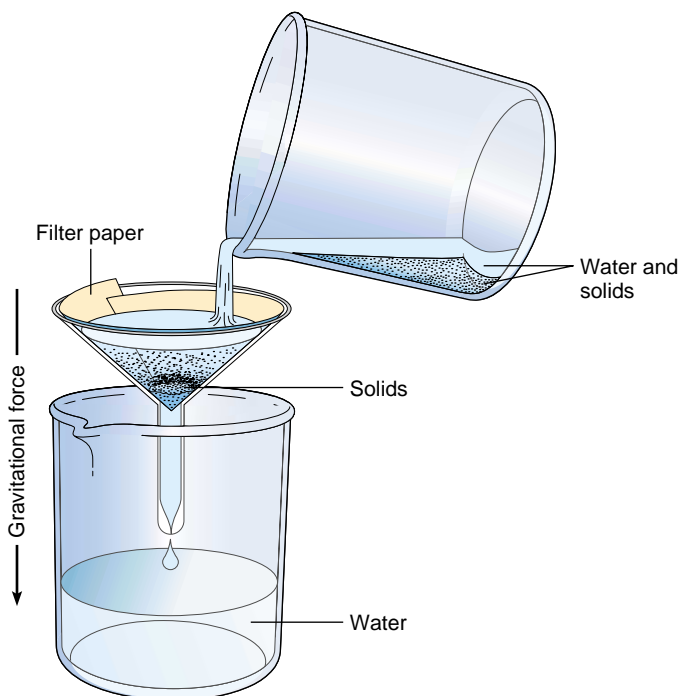


Figure 3.26

In this example of filtration, gravity provides the force that pulls water through filter paper, while tiny openings in the paper retain the solids. This process is similar to the drip method of preparing coffee.

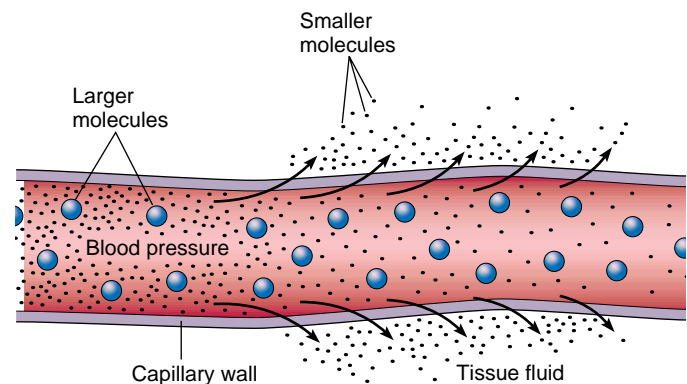


Figure 3.27

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

Active Transport

When molecules or ions pass through cell membranes by diffusion, facilitated diffusion, or osmosis, their net movement is from regions of higher concentration to regions of lower concentration. Sometimes, however, the net movement of particles passing through membranes is in the opposite direction, from a region of lower concentration to one of higher concentration.

Sodium ions, for example, can diffuse slowly through cell membranes. Yet, the concentration of these ions typically remains many times greater on the outside

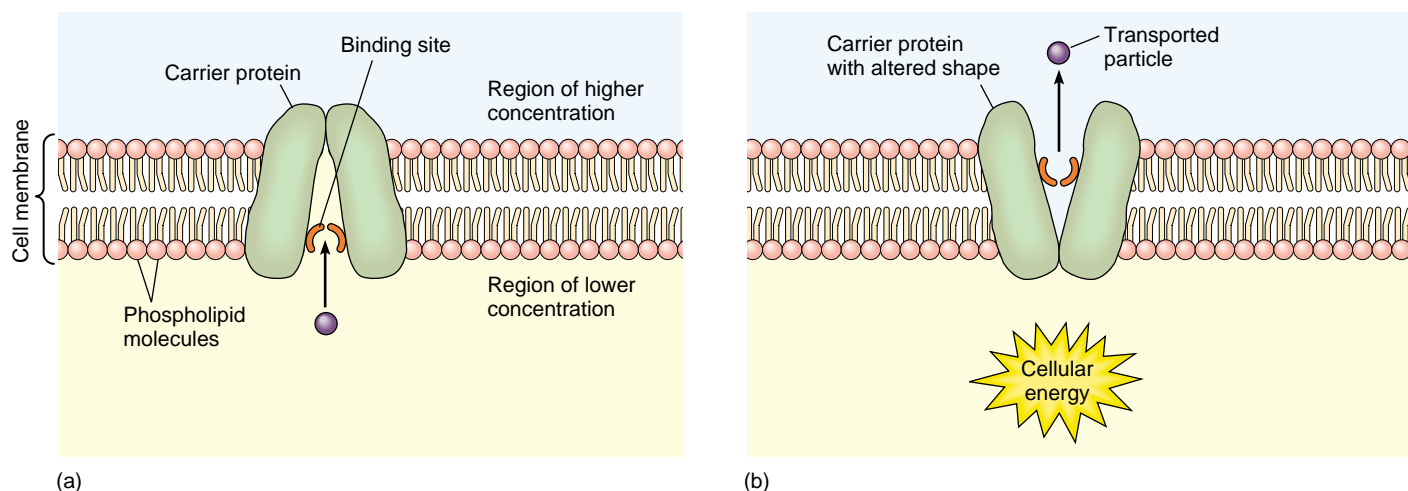


Figure 3.28

(a) During active transport, a molecule or ion combines with a carrier protein, whose shape is altered as a result. (b) This process, which requires energy, transports the particle through the cell membrane from an area of low concentration to an area of high concentration. Different substances move into or out of cells by this process.

cells (in the extracellular fluid) than inside cells (in the intracellular fluid). This is because sodium ions are continually moved through the cell membrane from regions of lower concentration (inside) to regions of higher concentration (outside). Movement against a concentration gradient is called **active transport** (ak'tiv trans'port) and requires energy derived from cellular metabolism. Up to 40% of a cell's energy supply may be used for active transport of particles through its membranes.

Active transport is similar to facilitated diffusion in that it uses carrier molecules within cell membranes. As figure 3.28 shows, these carrier molecules are proteins that have binding sites that combine with the specific particles being transported. Such a union triggers release of cellular energy, and this energy alters the shape of the carrier protein. As a result, the "passenger" molecules move through the membrane. Once on the other side, the transported particles are released, and the carrier molecules can accept other passenger molecules at their binding sites. Because they transport substances from regions of low concentration to regions of higher concentration, these carrier proteins are sometimes called "pumps." A sodium/potassium pump, for example, transports sodium ions out of cells and potassium ions into cells.

Particles that are moved across cell membranes by active transport include sugars, amino acids, and sodium, potassium, calcium, and hydrogen ions. Some of these substances are actively transported into cells, and others are transported out. Movements of this type are important to cell survival, particularly maintenance of homeostasis. Some of these movements are described in subsequent chapters as they apply to specific organ systems.

Endocytosis

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 or active transport are conveyed within a vesicle that forms 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.

The three forms of endocytosis are pinocytosis, phagocytosis, and receptor-mediated endocytosis. In **pinocytosis**, (pi'-no-si-to'sis) cells take in tiny droplets of liquid from their surroundings (fig. 3.29). When this happens, a small portion of cell membrane indents (invaginates). The open end of the tubelike part thus formed seals off and produces a small vesicle about 0.1 μm in diameter. This tiny sac detaches from the surface and moves into the cytoplasm.

For a time, the vesicular membrane, which was part of the cell membrane, separates its contents from the rest of the cell; however, the membrane eventually breaks down and the liquid inside becomes part of the cytoplasm. In this way, a cell is able to 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) is similar to pinocytosis, but the cell takes in solids rather than liquid. Certain kinds of cells, including some white blood cells, are called **phagocytes** because they can take in solid particles such as bacteria and cellular debris. When a phagocyte first encounters such a particle, the particle attaches to the 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

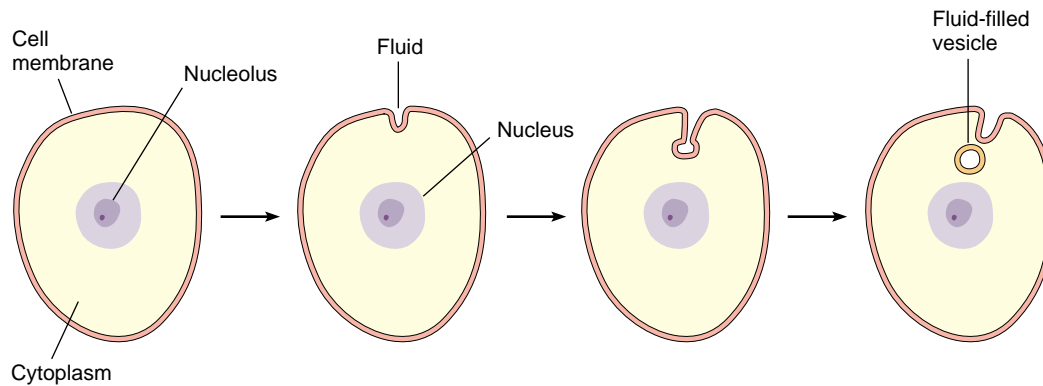


Figure 3.29

A cell may take in a tiny droplet of fluid from its surroundings by pinocytosis.

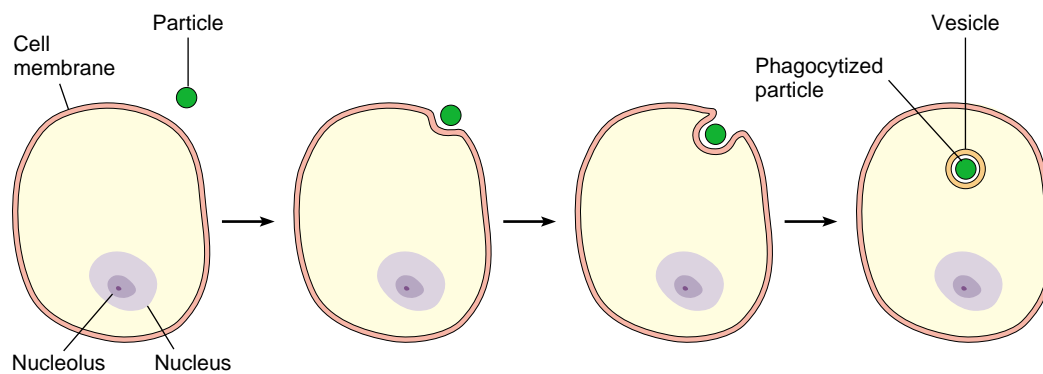


Figure 3.30

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

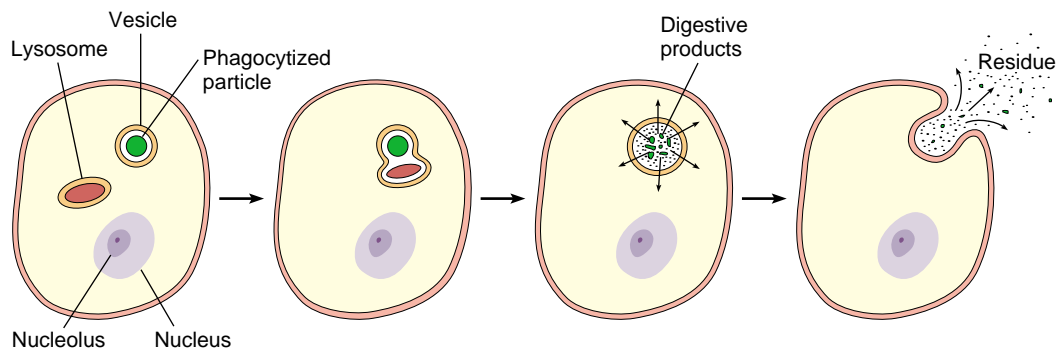


Figure 3.31

When a lysosome combines with a vesicle that contains a phagocytized particle, its digestive enzymes may destroy the particle. The products of this intracellular digestion diffuse into the cytoplasm. Any residue may be expelled from the cell by exocytosis.

membrane surrounding the solid detaches from the cell's surface, forming a vesicle containing the particle (fig. 3.30). Such a vesicle may be several micrometers in diameter.

Usually, a lysosome soon combines with such a newly formed vesicle, and lysosomal digestive enzymes decompose the contents (fig. 3.31). The products of this

decomposition may then diffuse out of the lysosome and into the cytoplasm, where they may be used as raw materials in metabolic processes. Exocytosis may expel any remaining residue. In this way, phagocytic cells dispose of foreign objects, such as dust particles, remove damaged cells or cell parts that are no longer functional, or destroy bacteria that might otherwise cause infections.

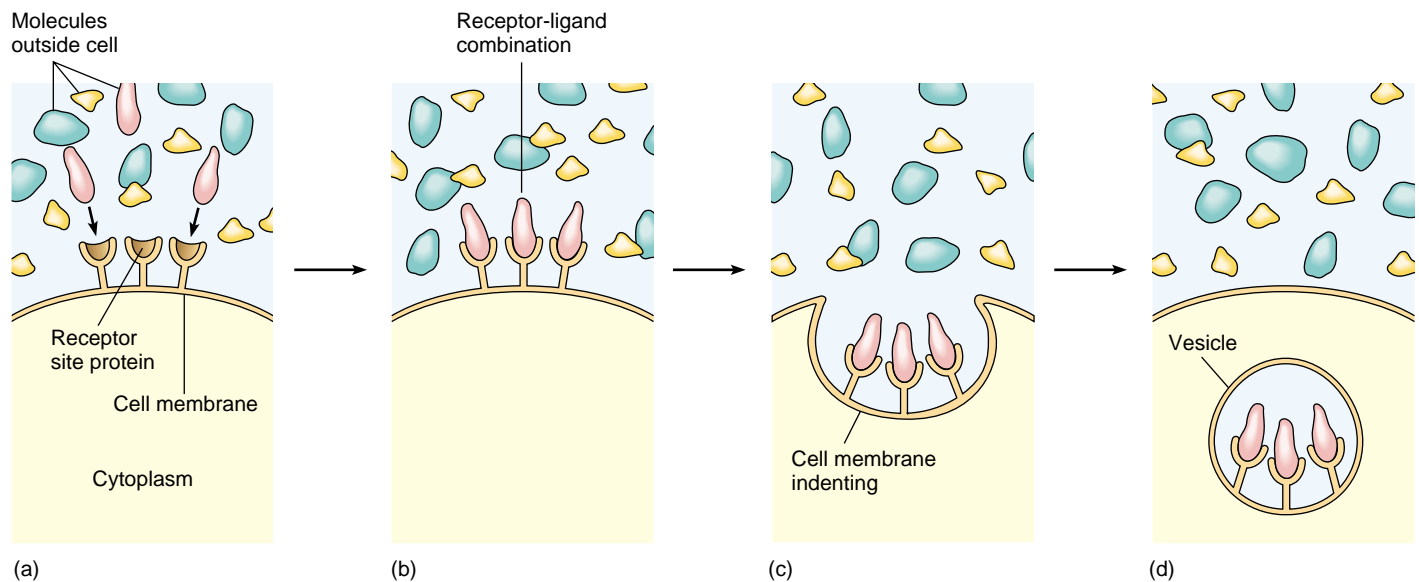


Figure 3.32

Receptor-mediated endocytosis. (a) A specific substance binds to a receptor site protein. (b and 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.

Phagocytosis is an important line of defense against invasion by disease-causing microorganisms.

Pinocytosis and phagocytosis engulf nonspecifically. In contrast is the more discriminating **receptor-mediated endocytosis**, which moves very specific kinds of particles into the cell. In this mechanism, protein molecules extend through the cell membrane and are exposed on its outer surface. These proteins are receptors to which specific substances from the fluid surroundings of the cell can bind. Molecules that can bind to the receptor sites selectively enter the cell; other kinds of molecules are left outside (fig. 3.32). (Molecules that bind specifically to receptors are called *ligands*.)

Entry of cholesterol molecules into cells illustrates receptor-mediated endocytosis. Cholesterol molecules synthesized in liver cells are packaged into large spherical particles called *low-density lipoproteins* (LDL). An LDL particle has a coating that contains a binding protein called *apoprotein-B*. The membranes of various body cells have receptors for apoprotein-B. When the liver releases LDL particles into the blood, cells with apoprotein-B receptors can recognize the LDL particles and bind them. Formation of such a receptor-ligand combination stimulates the cell membrane to indent and form a vesicle around the LDL particle. The vesicle carries the LDL particle to a lysosome, where enzymes digest it and release the cholesterol molecules for cellular use.

Receptor-mediated endocytosis is particularly important because it allows cells with the appropriate re-

ceptors to remove and process specific kinds of substances from their surroundings, even when these substances are present in very low concentrations. In short, this mechanism provides specificity.

As a toddler, Stormie Jones already had a blood serum cholesterol level six times normal. Before she died at age ten, she had suffered several heart attacks and had undergone two cardiac bypass surgeries, several heart valve replacements, and finally a heart-liver transplant. The transplant lowered her blood cholesterol to a near-normal level, but she died from the multiple traumas suffered over her short lifetime.

Stormie had the severe form of familial hypercholesterolemia (FH), meaning simply too much cholesterol in the blood. Her liver cells lacked LDL receptors. Blocked from entering cells, cholesterol accumulated in her bloodstream, forming the plaques that caused her heart disease.

Stormie Jones was one in a million. Far more common are the one in 500 people who have the milder form of FH, in which liver cells have half the normal number of LDL receptors. These individuals are prone to suffer heart attacks in early adulthood. However, they can delay symptom onset by taking precautions to avoid cholesterol buildup, such as exercising, eating a low-fat diet, and not smoking. (These precautions may also benefit individuals not suffering from FH.)

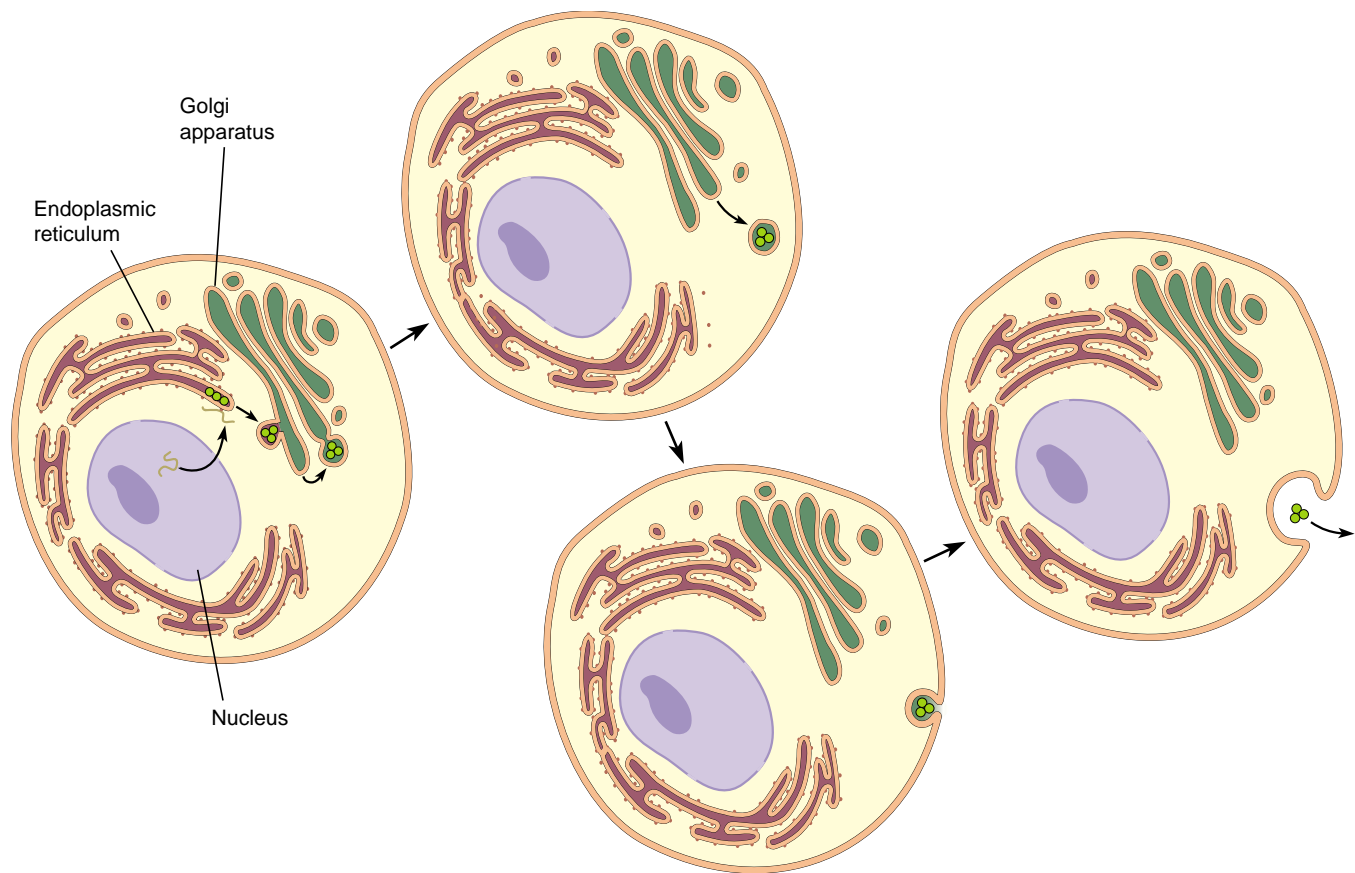


Figure 3.33

Exocytosis releases particles, such as newly synthesized proteins, from cells.

Exocytosis

Exocytosis is essentially the reverse of endocytosis. In exocytosis, substances made within the cell are packaged into a vesicle, which then fuses with the cell membrane, thereby releasing its contents outside the cell. Cells secrete some proteins by this process. Nerve cells use exocytosis to release the neurotransmitter chemicals that signal other nerve cells, muscle cells, or glands (fig. 3.33). The Golgi apparatus plays a role in this process, as described earlier in this chapter (page 74).

Transcytosis

Endocytosis brings a substance into a cell, and exocytosis transports a substance out of a cell. Another process, **transcytosis** (tranz-si-to'-sis), combines endocytosis and exocytosis (fig. 3.34). Transcytosis is the selective and rapid transport of a substance or particle from one end of a cell to the other. It enables substances to cross barriers formed by tightly connected cells.

HIV, the virus that causes AIDS, may initially infect a human body by using transcytosis to cross lining (epithelial) cells in the anus and female reproductive tract. Experiments using tissues growing in laboratory culture show that HIV enters white blood cells in mu-

cous secretions, and the secretions then carry the infected cells to an epithelial barrier. Near these lining cells, viruses rapidly exit the infected white blood cells and are quickly enveloped by the lining cell membranes in receptor-mediated endocytosis. HIV particles are ferried, in vesicles, through the lining cell, without actually infecting (taking over) the cell, to exit from the cell membrane at the other end of the cell—in as little as thirty minutes! After transcytosis, the HIV particles infect white blood cells beyond the epithelial barrier. Table 3.3 summarizes the types of movement into and out of the cell.

- 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 pinocytosis and phagocytosis?
- 4 Describe receptor-mediated endocytosis.
- 5 What does transcytosis accomplish?

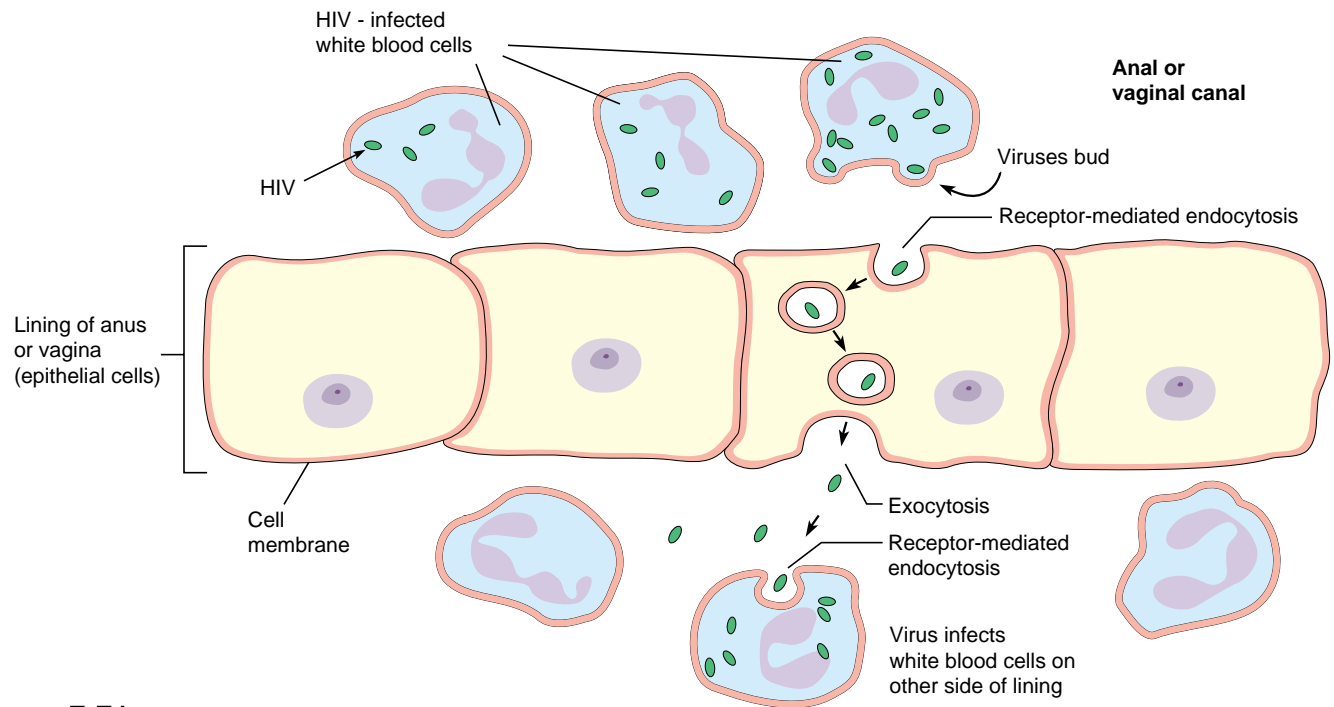


Figure 3.34
Transcytosis transports HIV across the lining of the anus or vagina.

| Process | Characteristics | Source of Energy | Example |
|---|--|----------------------|--|
| I. Passive (Physical) Processes | | | |
| A. Simple diffusion | Molecules or ions move from regions of higher concentration toward regions of lower concentration. | Molecular motion | Exchange of oxygen and carbon dioxide in the lungs |
| B. Facilitated diffusion | Molecules move across the membrane through channels or by carrier molecules from a region of higher concentration to one of lower concentration. | Molecular motion | Movement of glucose through a cell membrane |
| C. 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 |
| D. Filtration | Smaller molecules are forced through porous membranes from regions of higher pressure to regions of lower pressure. | Hydrostatic pressure | Molecules leaving blood capillaries |
| II. Active (Physiological) Processes | | | |
| A. Active transport | Carrier molecules transport molecules or ions through membranes from regions of lower concentration toward regions of higher concentration. | Cellular energy | Movement of various ions and amino acids through membranes |
| B. Endocytosis | | | |
| 1. Pinocytosis | Membrane engulfs droplets of liquid from surroundings. | Cellular energy | Membrane-forming vesicles containing large particles dissolved in water |
| 2. Phagocytosis | Membrane engulfs solid particles from surroundings. | Cellular energy | White blood cell membrane engulfing bacterial cell |
| 3. Receptor-mediated endocytosis | Membrane engulfs selected molecules combined with receptor proteins. | Cellular energy | Cell removing cholesterol-containing LDL particles from its surroundings |
| C. Exocytosis | Vesicles fuse with membrane and release contents outside of the cell. | Cellular energy | Protein secretion, neurotransmitter release |
| D. Transcytosis | Combines receptor-mediated endocytosis and exocytosis to ferry particles through a cell | Cellular energy | HIV crossing a cell layer |

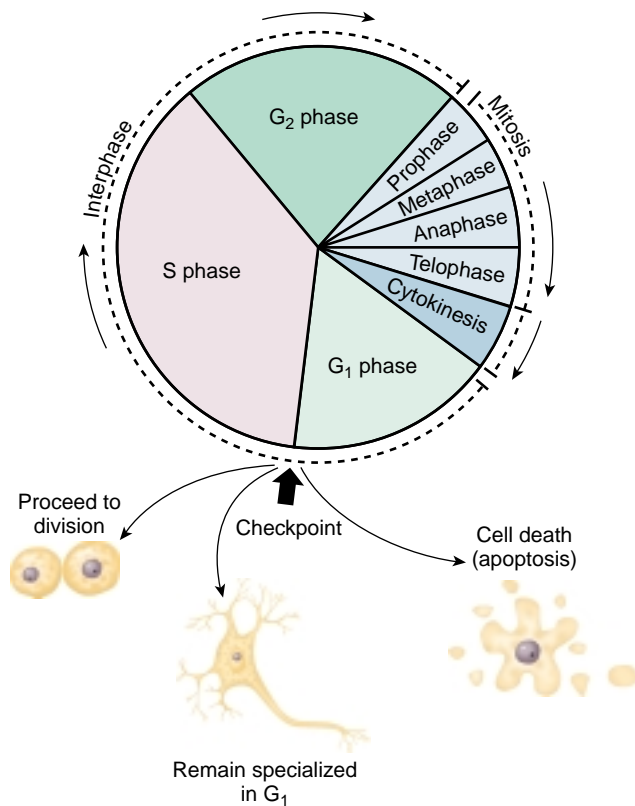


Figure 3.35

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 (G₁ and G₂), when specific molecules and structures duplicate, and a synthesis phase (S), when the genetic material replicates.

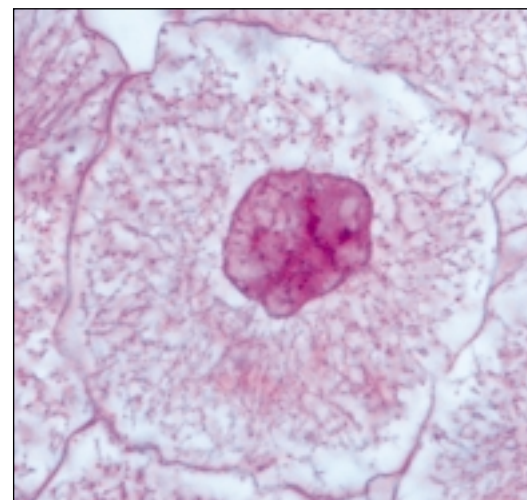
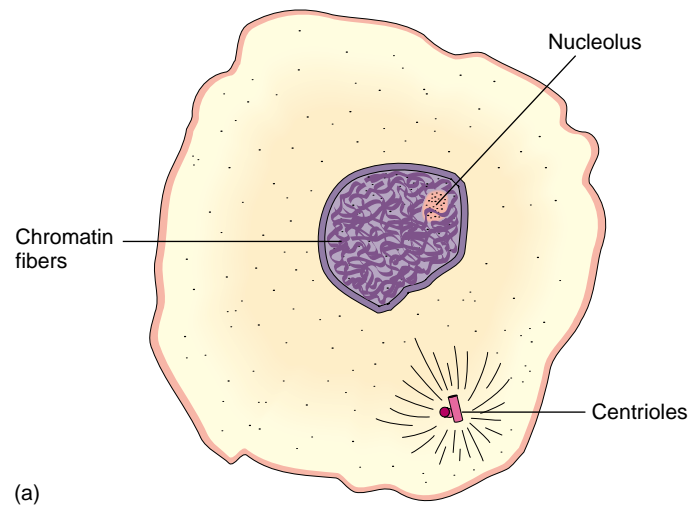
The Cell Cycle

The series of changes that a cell undergoes, from the time it forms until it divides, is called the **cell cycle** (fig. 3.35). Superficially, this cycle seems rather simple—a newly formed cell grows for a time, and then divides in half to form two new cells, which in turn may grow and divide. Yet the specific events of the cycle are quite complex. For ease of study, the cell cycle can be considered to consist of distinct stages, which include interphase, mitosis, cytoplasmic division, and differentiation.

The actions of several types of proteins form “checkpoints” that control the cell cycle. One particularly important checkpoint determines a cell’s fate—that is, whether it will continue in the cell cycle and divide, stay specialized yet alive, or die.

Interphase

Once thought to be a time of rest, interphase is actually a very active period. During interphase, the cell grows and maintains its routine functions as well as its contributions to the internal environment (fig. 3.36).



(b)

Figure 3.36

(a) Interphase lasts until a cell begins to undergo mitosis. (b) A micrograph of a cell in interphase (250× micrograph enlarged to 1,000×). Although present, centrioles and chromatin fibers are not clearly visible at this magnification.

If the cell is developmentally programmed to divide, it must amass important biochemicals and duplicate much of its contents so that two cells can form from one. For example, the cell must take on the tremendous task of replicating its genetic material. It must also synthesize or duplicate membranes, ribosomes, lysosomes, peroxisomes and mitochondria.

Interphase is divided into phases based on the sequence of activities. DNA is replicated during S phase (S stands for synthesis), and is bracketed by two G phases, G₁ and G₂ (G stands for gap or growth). Structures other than DNA are synthesized during the G phases, and cellular growth occurs then too (see fig. 3.35).

Mitosis

Mitosis is a form of cell division that occurs in somatic (nonsex) cells, and produces two new cells from an original cell (fig. 3.37). These new cells are genetically identical, each with the full complement of 46 (23 pairs) of chromosomes. In contrast is *meiosis*, another form of cell division that occurs only in sex cells (sperm and eggs). Meiosis halves the chromosome number, a mechanism that ensures that when sperm meets egg, the total number of 46 chromosomes is restored. Chapter 22 (p. 000) considers meiosis in detail.

Mitosis is sometimes called cellular reproduction, because it results in two cells from one—the cell reproduces. This may be confusing, because meiosis is the prelude to human sexual reproduction. Both mitosis and meiosis are forms of cell division, with similar steps but different outcomes, and occurring in different types of cells.

During mitosis, the nuclear contents divide, an event called karyokinesis, and then the cytoplasm is apportioned into the two cells, a process called cytokinesis. Mitosis must be very precise, because the nucleus contains the information, in the form of DNA molecules, that “tells” the cell how to function. Each new cell must have a complete copy of this information in order to survive. Although the chromosomes have already been copied in interphase, it is in mitosis that the chromosome sets are evenly distributed between the two forming cells.

Mitosis is a continuous process, but it is described in stages that indicate the sequence of major events, as follows:

1. **Prophase.** One of the first indications that a cell is going to divide is the appearance of *chromosomes*. These structures form as fibers of chromatin condense into tightly coiled rods. During interphase, the DNA molecules replicate so that each chromosome is composed of two identical structures, called chromatids, that are temporarily attached by a region on each called a *centromere*.
The centrioles of the centrosome replicate just before the onset of mitosis, and during prophase, the two newly formed pairs of centrioles move to opposite sides of the cell. Soon the nuclear envelope and the nucleolus disperse and are no longer visible. Microtubules are assembled from tubulin proteins in the cytoplasm, and these structures associate with the centrioles and chromosomes (figs. 3.38 and 3.39). A spindle-shaped array of microtubules (spindle fibers) forms between the centrioles as they move apart.

2. **Metaphase.** Spindle fibers attach to the centromeres of the chromosomes so that a fiber accompanying one chromatid attaches to one centromere and a fiber accompanying the other chromatid attaches to its centromere (fig. 3.40). The chromosomes move along the spindle fibers and align about midway between the centrioles as a result of microtubule activity.
3. **Anaphase.** Soon the centromeres of the chromatids separate, and these identical chromatids are now considered individual chromosomes. The separated chromosomes move in opposite directions, and once again the movement results from microtubule activity. The spindle fibers shorten and pull their attached chromosomes toward the centrioles at opposite sides of the cell (fig. 3.41).
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 identical sets of chromosomes approach their respective centrioles, they begin to elongate and unwind from rodlike structures to threadlike structures. A nuclear envelope forms around each chromosome set, and nucleoli become visible within the newly formed nuclei. Finally, the microtubules disassemble into free tubulin molecules (fig. 3.42).

Table 3.4 summarizes the stages of mitosis.

Cytoplasmic Division

Cytoplasmic division (cytokinesis) begins during anaphase when the cell membrane starts to constrict around the middle, which it continues to do through telophase. The musclelike contraction of a ring of actin microfilaments pinches off two cells from one. The microfilaments assemble in the cytoplasm and attach to the inner surface of the cell membrane. The contractile ring forms at right angles to the microtubules that pulled the chromosomes to opposite ends of the cell during mitosis. As the ring pinches, it separates the two newly formed nuclei and apportions about half of the organelles into each of the daughter cells. The newly formed cells may differ slightly in size and number of organelles and inclusions, but they have identical chromosomes and thus contain identical DNA information. (fig. 3.43).

Cellular Differentiation

Because all body cells (except egg and sperm) contain the same DNA information, they might be expected to look and function alike; obviously, they do not. The process by which cells develop different structures and specialized functions is called **differentiation** (dif“er-en“she-a“shun).

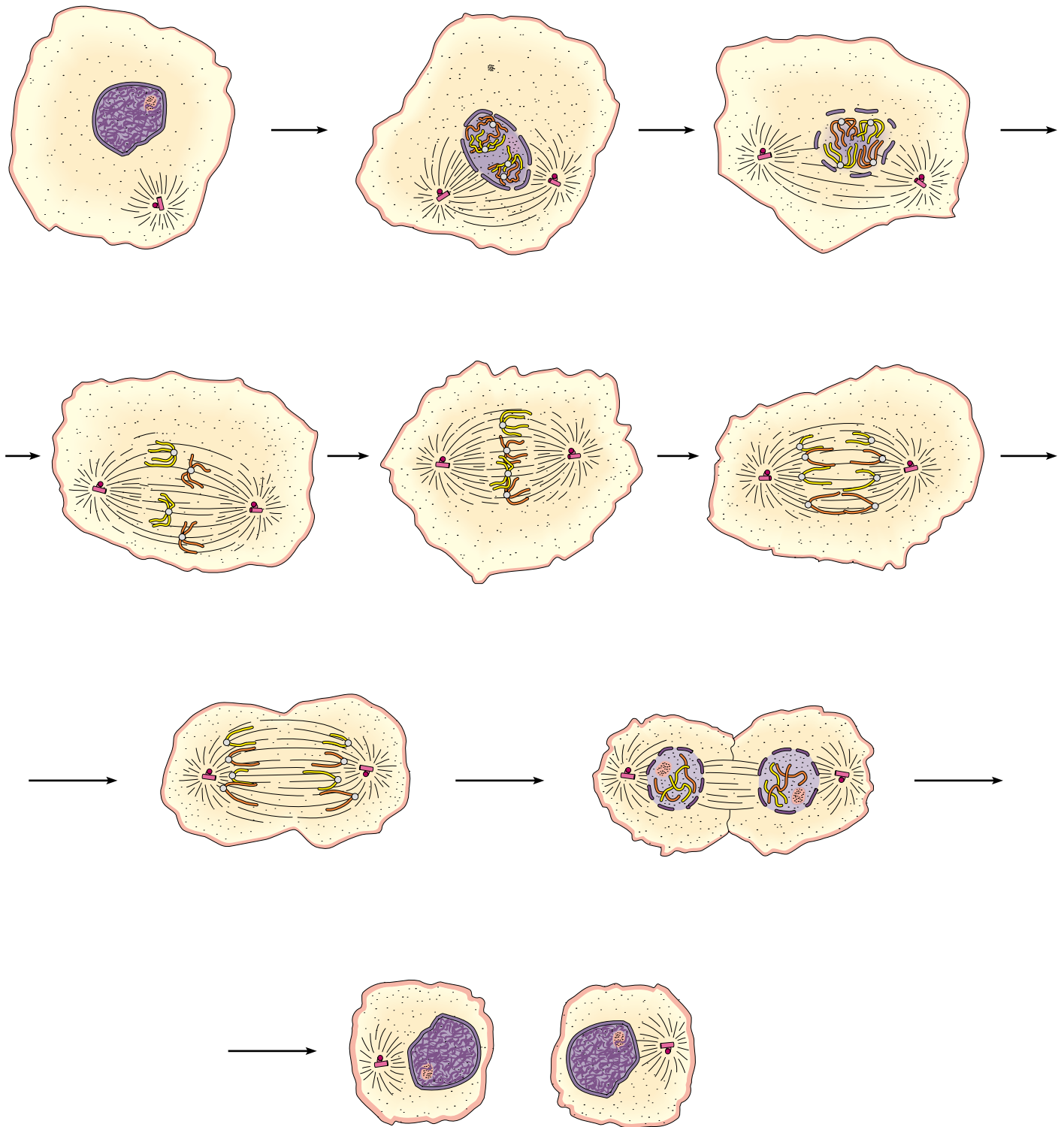


Figure 3.37

Mitosis is a continuous process during which the replicated genetic material is divided into two equal portions. After reading about mitosis, identify the phases of the process and the cell parts shown in this diagram.

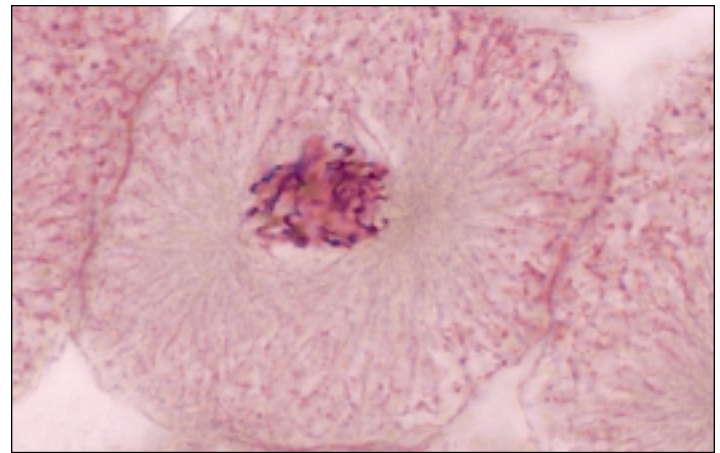
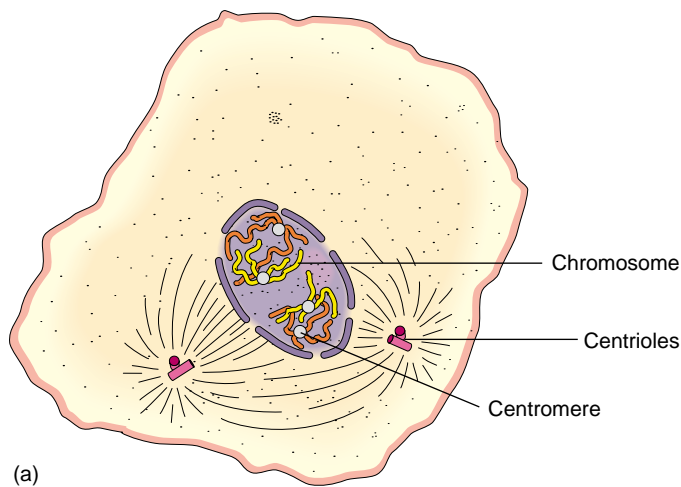


Figure 3.38

(a) In prophase, chromosomes form from chromatin in the nucleus, and the centrioles move to opposite sides of the cell. (b) A micrograph of a cell in prophase (250 \times micrograph enlarged to 1,000 \times).

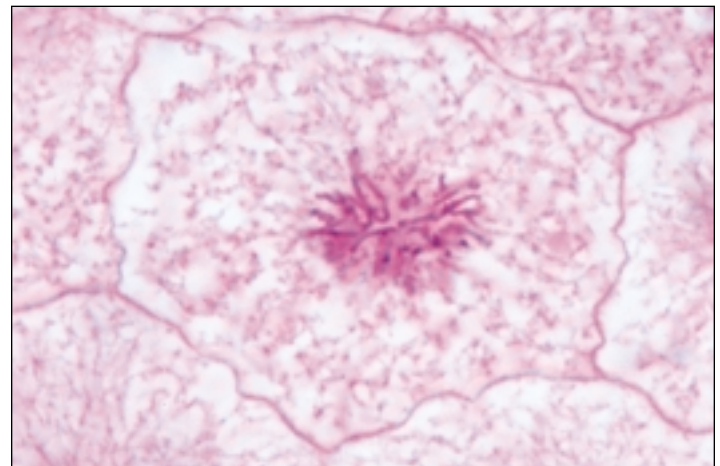
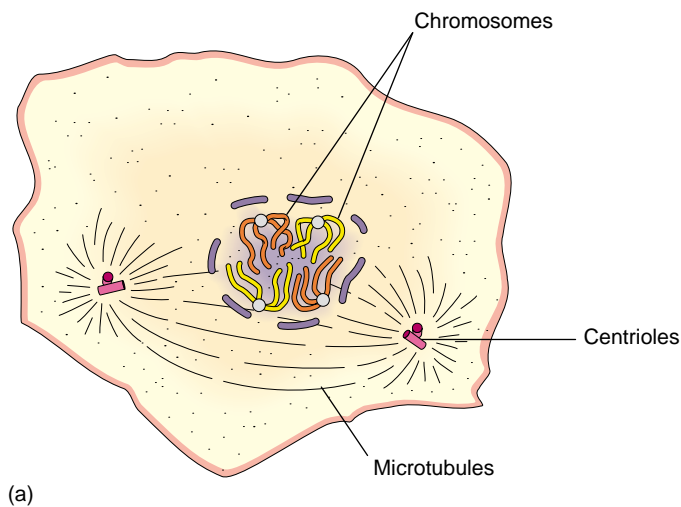


Figure 3.39

(a) Later in prophase, the nuclear envelope and nucleolus disappear. (b) A micrograph of a cell in late prophase (polar view) (280 \times micrograph enlarged to 1,000 \times).

At fertilization (conception), a single cell forms from two, an egg cell and a sperm cell. The fertilized egg cell divides to form two cells; they, in turn, divide into four cells; the four become eight; and so forth. Then, during the third to eighth weeks, the cells specialize, developing distinctive structures and beginning to function in different ways. Some become skin cells, others become bone cells, and still others become nerve cells (fig. 3.44). A newborn has more than 200 types of cells.

Cellular differentiation reflects genetic control. Special proteins activate some genes and repress others, controlling the amounts of different biochemicals in the cell, and therefore sculpting its characteristics. In a nerve cell,

the genes controlling neurotransmitter synthesis are activated; in a bone cell, these genes are silenced because it does not use neurotransmitters, but genes encoding the protein collagen, a major component of bone, are very active. A differentiated cell can be compared to a library. It contains a complete collection of information, but only some of that information is accessed. Different cell types interact to form the tissues, organs, and organ systems that make survival of the individual possible.

- 1** Why is precise division of nuclear materials during mitosis important?
- 2** Describe the events that occur during mitosis.

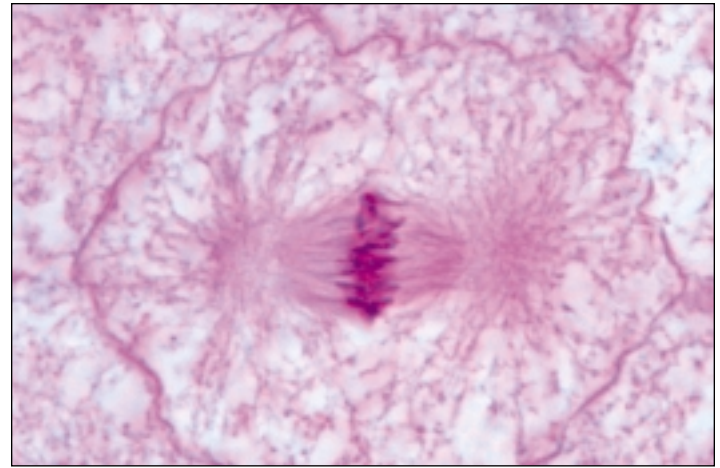
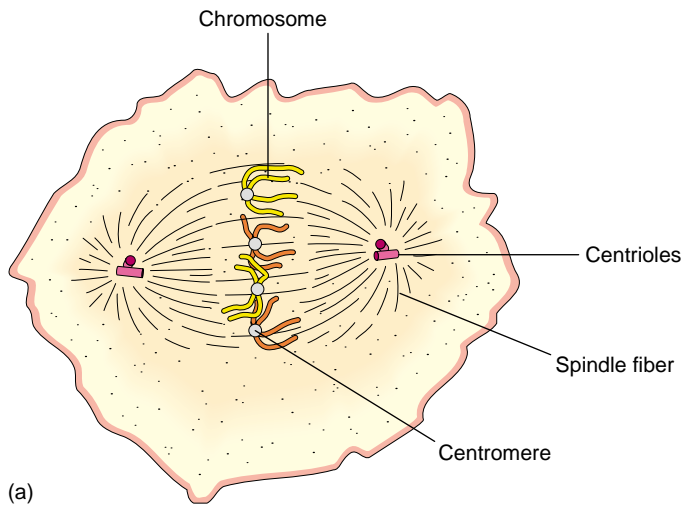


Figure 3.40

(a) In metaphase, chromosomes line up midway between the centrioles. (b) A micrograph of a cell in metaphase (280 \times micrograph enlarged to 1,000 \times). Although present, centrioles are not clearly visible at this magnification.

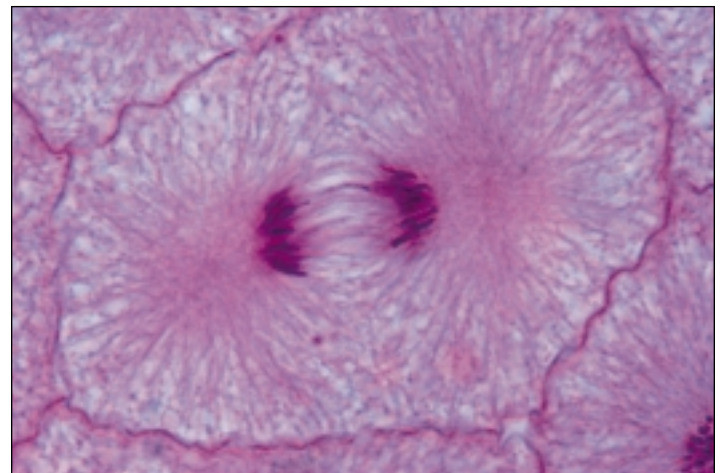
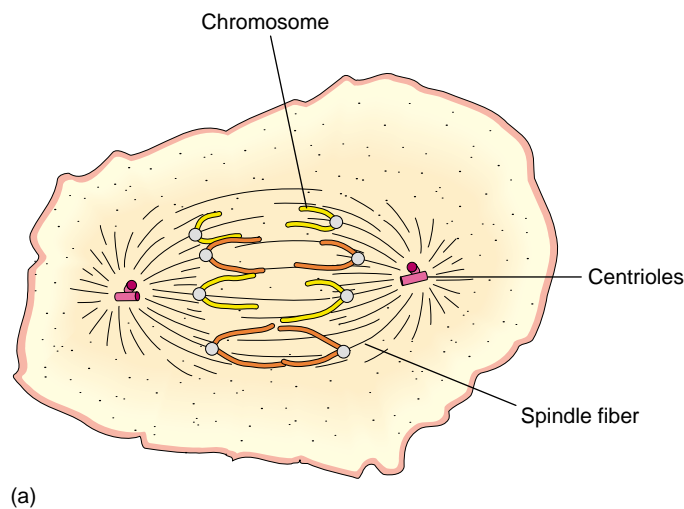


Figure 3.41

(a) In anaphase, centromeres divide, and the spindle fibers that have become attached to them pull the chromatids, now called chromosomes, toward the centrioles. (b) A micrograph of a cell in anaphase (280 \times micrograph enlarged to 1,100 \times).

3 Name the process by which some cells become muscle cells and others become nerve cells.

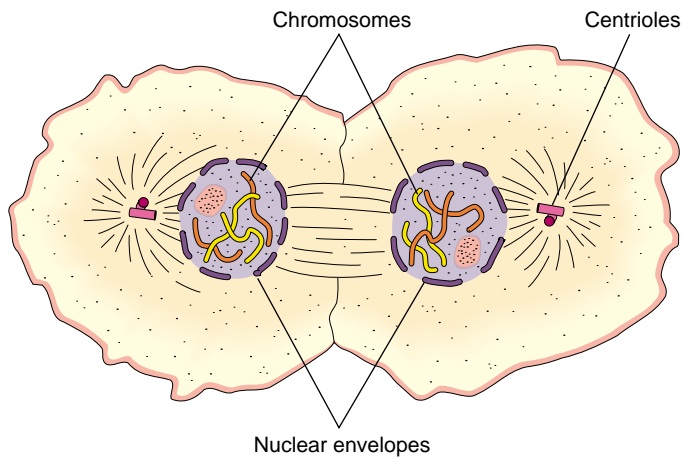
4 How does DNA control differentiation?

Control of Cell Division

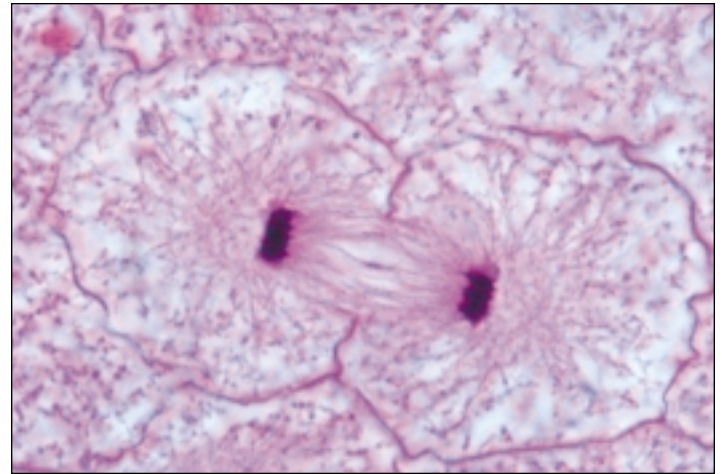
How often a cell divides is strictly controlled and varies with cell type. Skin cells, blood-forming cells, and cells that line the intestine, for example, divide often and continually. In contrast, cells of the liver divide a specific number of times and then cease—they are alive and specialized, but no longer divide. If, however, injury or sur-

gery removes some liver cells, the remaining cells may be stimulated to divide again, regenerating the organ. Some cells, such as certain nerve cells, lose their ability to divide as they differentiate; therefore, damage to these nerve cells usually permanently impairs nerve function. Most organs include cells, called **stem cells**, that retain the ability to divide into adulthood, giving the body a built-in repair mechanism of sorts. In the brain, for example, neural stem cells can produce new nerve cells. Researchers are just discovering the extent of the body's reserve of stem cells.

Clinical Application 3.4 considers cloning, a technique that places the nucleus of a differentiated cell into a



(a)



(b)

Figure 3.42

(a) In telophase, chromosomes elongate to become chromatin threads, and the cytoplasm begins to be distributed between the two newly forming cells. The replicated chromatids have separated to form the chromosomes of the two new cells. (b) A micrograph of a cell in telophase (280 \times micrograph enlarged to 1,100 \times).

| Stage | Major Events |
|-----------|---|
| Prophase | Chromatin condenses into chromosomes; centrioles move to opposite sides of cytoplasm; nuclear membrane and nucleolus disperse; microtubules appear and associate with centrioles and chromatids of chromosomes. |
| Metaphase | Spindle fibers from the centrioles attach to the centromeres of each chromosome; chromosomes align midway between the centrioles. |
| Anaphase | Centromeres separate, and chromatids of the chromosomes separate; spindle fibers shorten and pull these new individual chromosomes toward centrioles. |
| Telophase | Chromosomes elongate and form chromatin threads; nuclear membranes appear around each chromosome set; nucleoli appear; microtubules break down. |

fertilized egg cell lacking a nucleus and regenerates a new individual from the altered cell. The ability to clone indicates that even a nucleus in a highly differentiated cell can be stimulated to express genes that it normally represses.

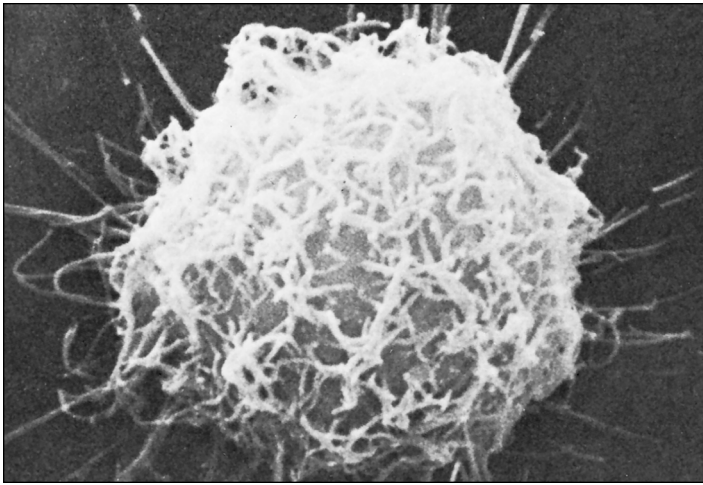
Most types of human cells divide up to about 50 times when grown in the laboratory. Adherence to this limit can be startling. A connective tissue cell from a human fetus divides 35 to 63 times, the average being about 50 times. However, a similar cell from an adult does so only 14 to 29 times, as if the cells “know” how many times they have divided.

A physical basis for this mitotic clock is the DNA at the tips of chromosomes (telomeres), where the same six-nucleotide sequence repeats many hundreds of times. Each mitosis removes up to 1,200 nucleotides. When the chromosome tips wear down to a certain point, this somehow signals the cell to cease dividing.

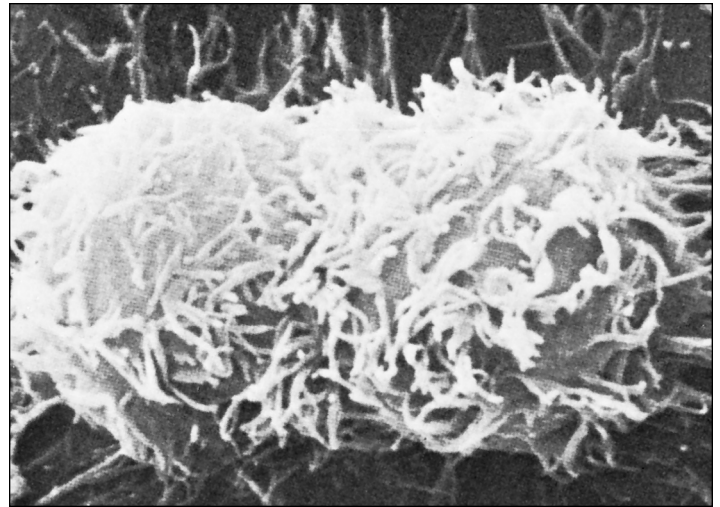
Other external and internal factors influence the timing and frequency of mitosis. Within cells, waxing and waning levels of proteins called kinases and cyclins control the cell cycle. Another internal influence is cell size, specifically the ratio between the surface area the cell membrane provides and the cell volume. The larger the cell, the more nutrients it requires to maintain the activities of life. However, a cell’s surface area limits the amount of nutrients that can enter. Because volume increases faster than does surface area, a cell can grow too large to efficiently obtain nutrients. A cell can solve this growth problem by dividing. The resulting daughter cells are smaller than the original cell and thus have a more favorable surface area-to-volume relationship.

External controls of cell division include hormones and growth factors. Hormones are biochemicals manufactured in a gland and transported in the bloodstream to a site where they exert an effect. Hormones signal mitosis in the lining of a woman’s uterus each month, building up the tissue to nurture a possible pregnancy. Similarly, a pregnant woman’s hormones stimulate mitosis in her breasts when their function as milk-producing glands will soon be required.

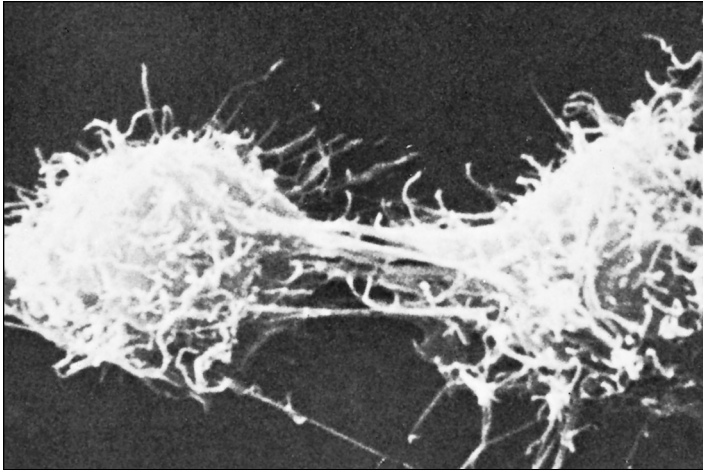
Growth factors are like hormones in function but act closer to their sites of synthesis. Epidermal growth factor, for example, stimulates growth of new skin beneath the scab on a skinned knee. Salivary glands also



(a)



(b)



(c)

Figure 3.43

Following mitosis, the cytoplasm of a cell divides in two, as seen in these scanning electron micrographs (a. 3,750 \times ; b. 3,750 \times ; c. 3,190 \times).

From *Scanning Electron Microscopy in Biology*, by R. G. Kessel and C. Y. Shih. © 1976 Springer-Verlag.

produce this growth factor. This is why an animal's licking a wound may speed healing.

Growth factors are used as drugs. Epidermal growth factor (EGF), for example, can hasten healing of a wounded or transplanted cornea, a one-cell-thick layer covering the eye. Normally these cells do not divide. However, cells of a damaged cornea treated with EGF undergo mitosis, restoring a complete cell layer. EGF is also used to help the body accept skin grafts and to stimulate healing of skin ulcers that occur as a complication of diabetes.

Space availability is another external factor that influences the timing and rate of cell division. Healthy cells

do not divide if they are surrounded by other cells, a phenomenon called contact (density dependent) inhibition.

- 1 How do cells vary in their rates of division?
- 2 Which factors control the number of times and the rate at which cells divide?

Health Consequences of Loss of Cell Division Control

Control of cell division is absolutely crucial to health. With too infrequent mitoses, an embryo could not develop, a child could not grow, and wounds would not heal. Too frequent mitoses produce an abnormal growth, or neoplasm, which may form a disorganized mass called a **tumor**.

Tumors are of two types. A *benign* tumor remains in place like a lump, eventually interfering with the

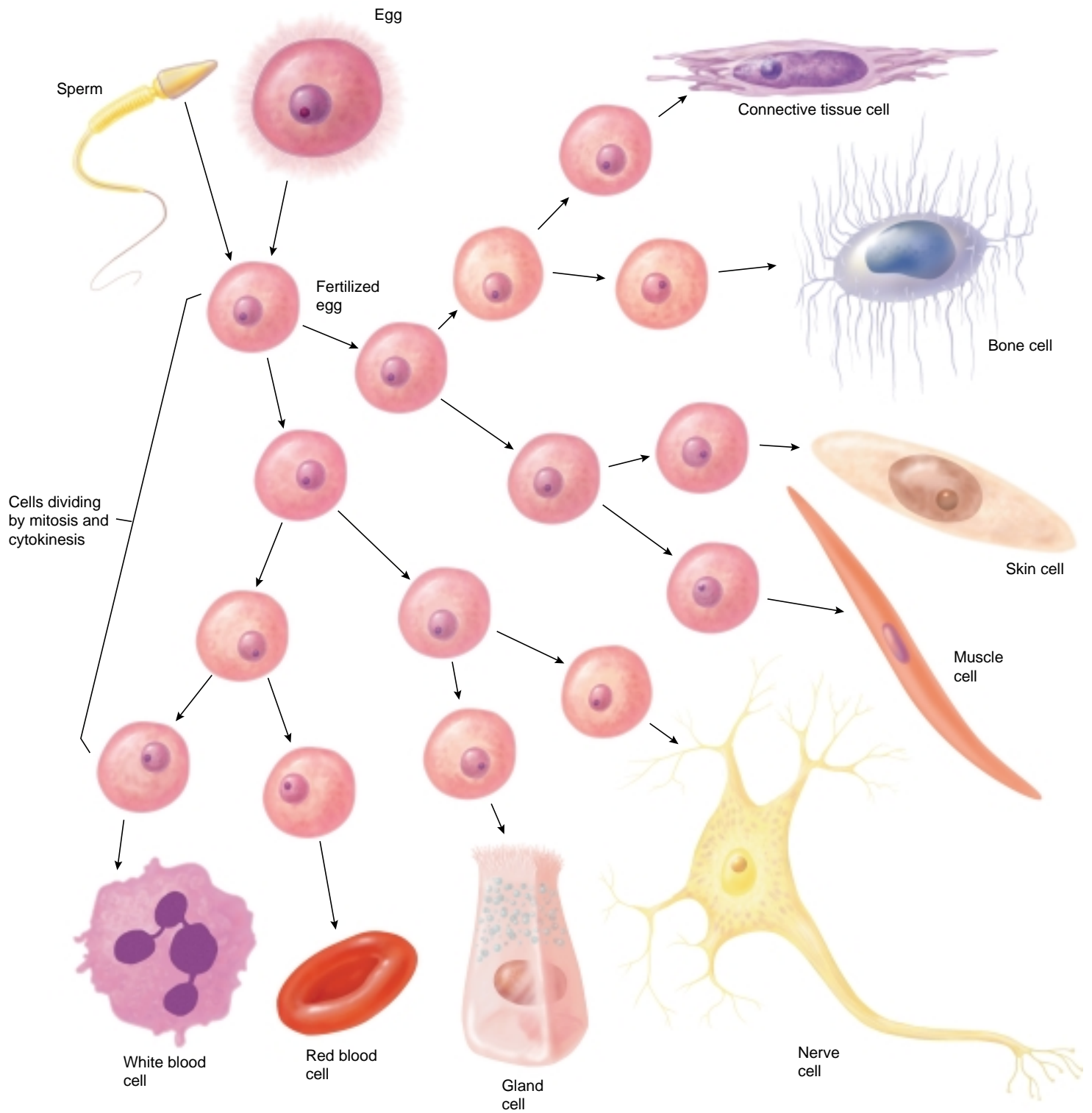
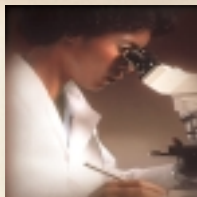


Figure 3.44

The trillions of cells in an adult human ultimately derive by mitosis from the original fertilized egg cell. As different genes are turned on or off in different cells, the characteristics of specific cell types emerge. (Relative cell sizes are not to scale.)



Cloning

The human body is built of more than 200 types of specialized, or differentiated, cell types. Once a cell activates certain subsets of the total genetic package present in all cells, there usually isn't any turning back. A nerve cell remains a nerve cell; an adipose cell stays an adipose cell. In contrast to a differentiated cell, a fertilized egg cell retains the potential to become any cell type—a little like a college student before declaring a major. Such a cell is called "pluripotent." Something about the cytoplasm of the cell keeps it in a state where it can follow any cell "fate."

What would happen if a nucleus from a differentiated cell was placed in a fertilized egg cell whose nucleus had been removed? Would the special egg cytoplasm literally turn back the developmental clock, returning the differentiated cell's nucleus to a pluripotent state, and possibly enabling it to specialize in a different way? In 1996, Scottish researchers did just that, in sheep. They took a cell from an adult sheep's breast and transferred its nucleus to a fertilized egg cell whose nucleus had been removed. The altered cell divided, and divided again, and when it was a ball of cells, it was implanted into an unrelated ewe. Development continued. On February 7, 1997, the result—a now-famous sheep named Dolly—graced the cover of *Nature* magazine and immediately triggered worldwide controversy (fig. 3A). Mice, pigs, and cows have since been cloned from the nuclei of adult cells. Cloning from fetal cell nuclei has been possible since the 1960s, mostly in amphibians.

Dolly is a clone of the sheep that donated the breast cell, which means that, except for the small amount of mitochondrial DNA, the two animals are genetically identical. Creating Dolly was quite a feat—it took 277 tries. Cloning other mammals has been equally challenging. Not only is it

technically difficult, but newborn clones do not often fare well. Something about starting from a body (somatic) cell nucleus, rather than from a fertilized egg cell's nucleus, harms health.

Despite the difficulty of the procedure, and the fact that it had not been performed on humans, public reaction in the months following Dolly's debut was largely negative, as talk centered on cloning humans. Politicians called for "no-clone zones," editorials envisioned scenarios of farming replicas to harvest their organs for spare parts, and films and cartoons sensationalizing or poking fun at cloning flourished (fig. 3B).

Lost in the fear of cloning was the fact that restoring developmental potential to a specialized cell can have

medical applications. Cloning would enable rapid mass production of cows genetically altered to produce proteins that are of use to humans as drugs—such cows, for example, already make the human versions of an anticlotting drug that saves lives following heart attacks and strokes. Pigs genetically altered to have cell surfaces compatible with humans are being considered as organ donors for humans—cloning would scale-up that technology.

Cloning humans raises a broader, more philosophical issue. To what extent do genes determine who we are? That is, how identical are individuals who have the same genes? That question has already been answered by naturally occurring human clones—identical twins. Extensive analysis of identical twins who were separated at birth demonstrates that although they are physically alike and share many health characteristics and even some peculiar quirks, they also differ in many ways. The environment exerts powerful effects on who we are, contributing to characteristics such as personality traits that are harder to define biochemically. ■



Figure 3A
Dolly, a most unusual ewe.

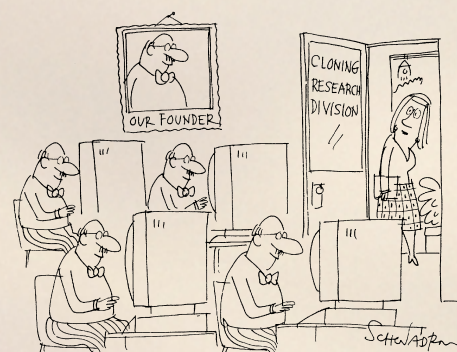


Figure 3B
A view of cloning.

function of healthy tissue. A *malignant*, or cancerous, tumor looks quite different—it is invasive, extending into surrounding tissue. A growing malignant tumor may roughly resemble a crab with outreaching claws, which is where the name “cancer” comes from. Cancer cells, if not stopped, eventually reach the circulation and spread, or metastasize, to other sites. Table 3.5 lists characteristics of cancer cells, and figure 3.45 illustrates how cancer cells infiltrate healthy tissue.

Cancer is a collection of disorders distinguished by their site of origin and the affected cell type. Many cancers are treatable with surgery, radiation, chemicals (chemotherapy), or immune system substances (biologicals) used as drugs. Experimental gene therapy fights cancer by giving tumor cells surface molecules that attract an attack by the immune system.

At least two types of genes cause cancer. **Oncogenes** activate other genes that increase cell division rate. **Tumor suppressor genes** normally hold mitosis in check. When tumor suppressor genes are removed or otherwise inactivated, this lifts control of the cell cycle, and uncontrolled cell division leading to cancer results (fig. 3.46). Environmental factors, such as exposure to toxic chemicals or radiation, may induce cancer by altering (mutating) oncogenes and tumor suppressor genes in body (somatic) cells. Cancer may also be the consequence of a failure of normal cell death, resulting in overgrowth.

Normal anatomy and physiology—in other words, health—ultimately depend upon both the quality and quantity of the cells that comprise the human body. Understanding the cellular bases of disease suggests new diagnosis and treatment methods.

- 1 How can too infrequent cell division affect health?
- 2 How can too frequent cell division affect health?
- 3 What is the difference between a benign and a cancerous tumor?
- 4 What are two ways that genes cause cancer?
- 5 How can factors in the environment cause cancer?

| table | 3.5 Characteristics of Cancer Cells |
|-------|--|
| | Loss of cell cycle control |
| | Heritability (a cancer cell divides to form more cancer cells) |
| | Transplantability (a cancer cell implanted into another individual will cause cancer to develop) |
| | Dedifferentiation (loss of specialized characteristics) |
| | Loss of contact inhibition |
| | Ability to induce local blood vessel formation (angiogenesis) |
| | Invasiveness |
| | Ability to metastasize (spread) |

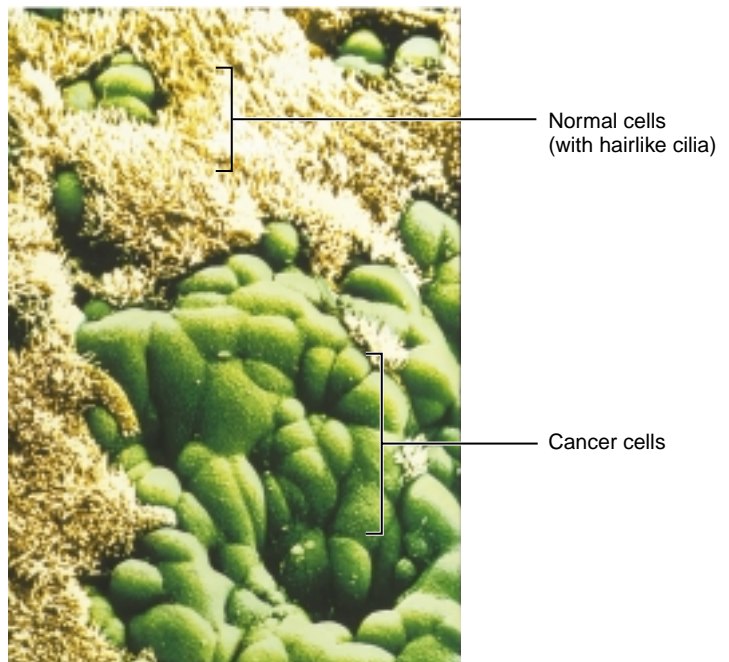


Figure 3.45

A cancer cell is rounder and less specialized than surrounding healthy cells. It secretes biochemicals that cut through nearby tissue and others that stimulate formation of blood vessels that nurture the tumor’s growth (2,200×).

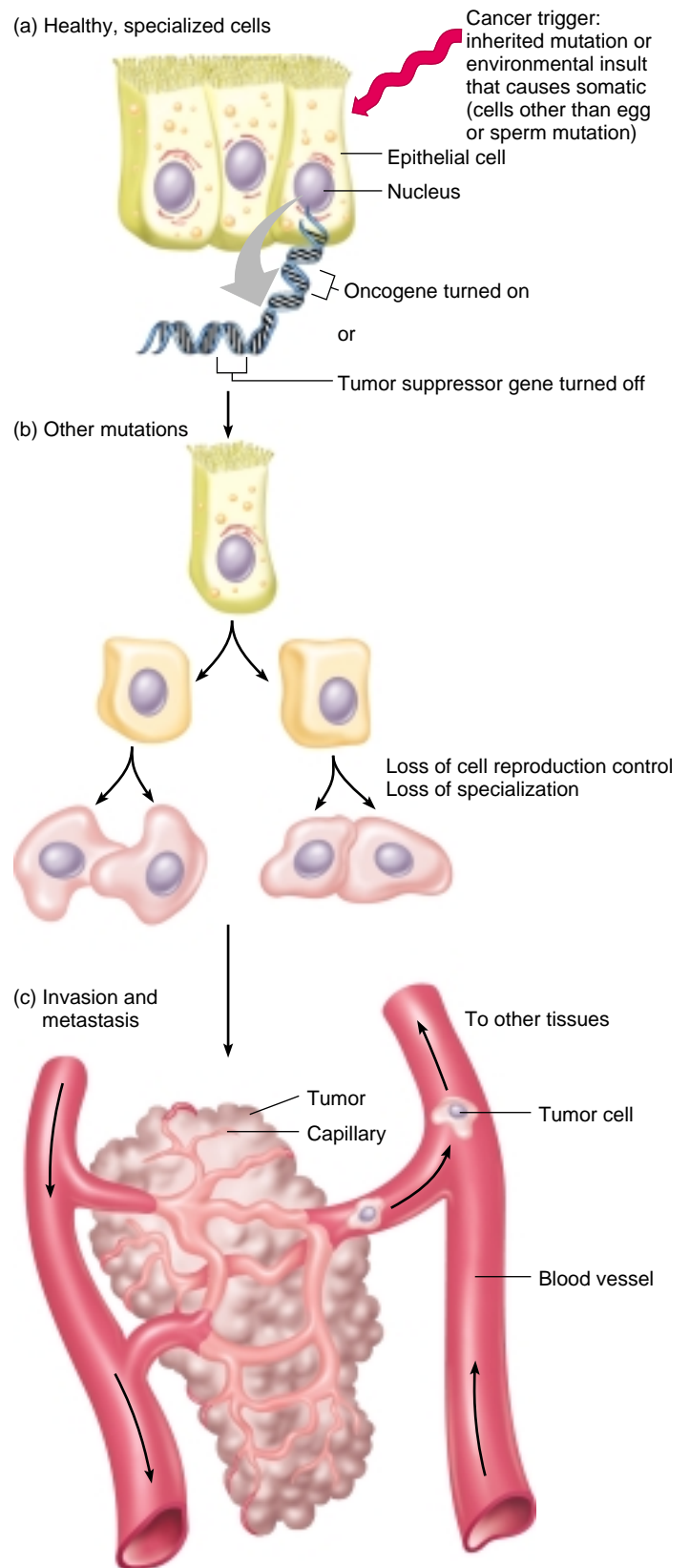


Figure 3.46

(a) In a healthy cell, oncogenes are not overexpressed, and tumor suppressor genes are expressed. As a result, cell division rate is under control. Cancer begins in a single cell when an oncogene is turned on or a tumor suppressor gene is turned off. This initial step may result from an inherited mutation, or from exposure to radiation, viruses, or chemicals that cause cancer in a somatic (nonsex) cell. (b) Malignancy often results from a series of genetic alterations (mutations). An affected cell divides more often than the cell type it descends from and eventually loses its specialized characteristics. (c) Cancers grow and spread by inducing formation of blood vessels to nourish them and then breaking away from their original location. The renegade cells often undergo further genetic change and surface characteristic alterations as they travel. This changeable nature is why many treatments eventually cease to work or a supposedly vanquished cancer shows up someplace in the body other than where it originated.

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Chapter 3: Cells

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Chapter Summary

Introduction (page 65)

Cells vary considerably in size, shape, and function. The shapes of cells are important in determining their functions.

A Composite Cell (page 65)

1. A cell includes a nucleus, cytoplasm, and a cell membrane.
2. Cytoplasmic organelles perform specific vital functions, but the nucleus controls the overall activities of the cell.
3. Cell membrane
 - a. The cell membrane forms the outermost limit of the living material.
 - b. It acts as a selectively permeable passageway that controls the movements of substances between the cell and its surroundings and thus is the site of signal transduction.
 - c. It includes protein, lipid, and carbohydrate molecules.
 - d. The cell membrane framework mainly consists of a double layer of phospholipid molecules.
 - e. Molecules that are soluble in lipids pass through the membrane easily, but water-soluble molecules do not.
 - f. Cholesterol molecules help stabilize the membrane.
 - g. Proteins provide the special functions of the membrane.
 - (1) Rodlike proteins form receptors on cell surfaces.
 - (2) Globular proteins form channels for passage of various ions and molecules.
 - h. Specialized intercellular junctions (tight junctions, desmosomes, and gap junctions) connect cells.
 - i. Cell adhesion molecules oversee some cell interactions and movements.
4. Cytoplasm
 - a. Cytoplasm contains networks of membranes and organelles suspended in fluid.
 - b. Endoplasmic reticulum is composed of connected membranous sacs, canals, and vesicles that provide a tubular communication system and an attachment for ribosomes; it also functions in the synthesis of proteins and lipids.
 - c. Ribosomes are particles of protein and RNA that function in protein synthesis.
 - d. The Golgi apparatus is a stack of flattened, membranous sacs that package glycoproteins for secretion.
 - e. Mitochondria are membranous sacs that contain enzymes that catalyze the reactions that release energy from nutrient molecules and transform it into a usable form.
 - f. Lysosomes are membranous sacs containing digestive enzymes that destroy debris and worn-out organelles.
 - g. Peroxisomes are membranous, enzyme-containing vesicles.
 - h. The centrosome is a nonmembranous structure consisting of two centrioles that aid in the distribution of chromosomes during cell division.
 - i. Cilia and flagella are motile extensions on some cell surfaces.
 - (1) Cilia are numerous tiny, hairlike structures that wave, moving fluids across cell surfaces.
 - (2) Flagella are longer extensions such as the tail of a sperm cell.

- j. Vesicles are membranous sacs containing substances that recently entered or were produced in the cell.
- k. Microfilaments and microtubules are threadlike structures that aid cellular movements and support and stabilize the cytoplasm.
- l. Cytoplasm may contain nonliving cellular products, such as nutrients and pigments, called inclusions.
5. Cell nucleus
 - a. The nucleus is enclosed in a double-layered nuclear envelope that has nuclear pores that control movement of substances between the nucleus and cytoplasm.
 - b. A nucleolus is a dense body of protein and RNA where ribosome synthesis occurs.
 - c. Chromatin is composed of loosely coiled fibers of protein and DNA that condense into chromosomes during cell division.

Movements into and out of the Cell (page 82)

Movement of substances into and out of the cell may use physical or physiological processes.

1. Diffusion
 - a. Diffusion is due to the random movement of molecules in air or liquid solution.
 - b. Diffusion is movement of molecules or ions from regions of higher concentration toward regions of lower concentration (down a concentration gradient).
 - c. It is responsible for exchanges of oxygen and carbon dioxide within the body.
 - d. The most important factors determining the rate of diffusion in the body include distance, the concentration gradient, and temperature.
2. Facilitated diffusion
 - a. Facilitated diffusion uses protein channels or carrier molecules in the cell membrane.
 - b. This process moves substances such as ions, sugars, and amino acids from regions of higher concentration to regions of lower concentration.
3. Osmosis
 - a. Osmosis is a special case of diffusion in which water molecules diffuse from regions of higher water concentration to lower water concentration through a selectively permeable membrane.
 - b. Osmotic pressure increases as the number of particles dissolved in a solution increases.
 - c. Cells lose water when placed in hypertonic solutions and gain water when placed in hypotonic solutions.
 - d. A solution is isotonic when it contains the same concentration of dissolved particles as the cell contents.
4. Filtration
 - a. In filtration, molecules move from regions of higher hydrostatic pressure toward regions of lower hydrostatic pressure.
 - b. Blood pressure filters water and dissolved substances through porous capillary walls.
5. Active transport
 - a. Active transport moves molecules or ions from regions of lower concentration to regions of higher concentration.

- b. It requires cellular energy and carrier molecules in the cell membrane.
- 6. Endocytosis
 - a. In pinocytosis, a cell membrane engulfs tiny droplets of liquid.
 - b. In phagocytosis, a cell membrane engulfs solid particles.
 - c. In receptor-mediated endocytosis, receptor proteins combine with specific molecules in the cell surroundings. The membrane engulfs the combinations.
- 7. Exocytosis
 - a. Exocytosis is the reverse of endocytosis.
 - b. In exocytosis, vesicles containing secretions fuse with the cell membrane, releasing the substances to the outside.
- 8. Transcytosis
 - a. Transcytosis combines endocytosis and exocytosis.
 - b. In transcytosis, a substance or particle crosses a cell.
 - c. Transcytosis is specific and rapid.

The Cell Cycle (page 94)

1. The cell cycle includes interphase, mitosis, cytoplasmic division, and differentiation.
2. Interphase
 - a. Interphase is the stage when a cell grows, DNA replicates, and new organelles form.

- b. It terminates when the cell begins mitosis.
- 3. Mitosis
 - a. Mitosis is the division and distribution of DNA to daughter cells.
 - b. The stages of mitosis include prophase, metaphase, anaphase, and telophase.
- 4. The cytoplasm divides into two portions following mitosis.
- 5. Cell differentiation is the specialization of cell structures and functions.

Control of Cell Division (page 98)

1. Cell division capacities vary greatly among cell types.
2. Chromosome tips that shorten with each mitosis provide a mitotic clock, usually limiting the number of divisions to 50.
3. Cell division is limited, and controlled by both internal and external factors.
4. As a cell grows, its surface area increases to a lesser degree than its volume, and eventually the area becomes inadequate for the requirements of the living material within the cell. When a cell divides the daughter cells have more favorable surface area-volume relationships.
5. Cancer is the consequence of a loss of cell cycle control.

Critical Thinking Questions

1. Which process—diffusion, osmosis, or filtration—accounts for the following situations?
 - a. Injection of a drug that is hypertonic to the tissues stimulates pain.
 - b. A person with extremely low blood pressure stops producing urine.
 - c. The concentration of urea in the dialyzing fluid of an artificial kidney is kept low.
2. Which characteristic of cell membranes may explain why fat-soluble substances such as chloroform and ether rapidly affect cells?
3. A person exposed to many X rays may lose white blood cells and become more susceptible to infection. How are these effects related?
4. Exposure to tobacco smoke causes cilia to cease moving and degenerate. Why might this explain why tobacco smokers have an increased incidence of respiratory infections?
5. How would you explain the function of phagocytic cells to a patient with a bacterial infection?
6. How is knowledge of how cell division is controlled important to an understanding of each of the following?
 - a. growth
 - b. wound healing
 - c. cancer
7. Why are enlarged lysosomes a sign of a serious illness?

Review Exercises

1. Use specific examples to illustrate how cells vary in size.
2. Describe how the shapes of nerve, epithelial, and muscle cells are well suited to their functions.
3. Name the major components of a cell, and describe how they interact.
4. Discuss the structure and functions of a cell membrane.
5. How do cilia, flagella, and cell adhesion molecules move cells?
6. Distinguish between organelles and inclusions.
7. Define *selectively permeable*.
8. Describe the chemical structure of a membrane.
9. Explain how the structure of a cell membrane determines which types of substances it admits.
10. Explain the function of membrane proteins.
11. Describe three kinds of intercellular junctions.
12. Describe the structures and functions of each of the following:
 - a. endoplasmic reticulum
 - b. ribosome
 - c. Golgi apparatus

- d. mitochondrion
 - e. lysosome
 - f. peroxisome
 - g. cilium
 - h. flagellum
 - i. centrosome
 - j. vesicle
 - k. microfilament
 - l. microtubule
13. Describe the structure of the nucleus and the functions of its contents.
 14. Distinguish between diffusion and facilitated diffusion.
 15. Name three factors that increase the rate of diffusion.
 16. Explain how diffusion aids gas exchange within the body.
 17. Define *osmosis*.
 18. Define *osmotic pressure*.
 19. Explain how the number of solute particles in a solution affects its osmotic pressure.
 20. Distinguish among solutions that are hypertonic, hypotonic, and isotonic.
 21. Define *filtration*.
 22. Explain how filtration moves substances through capillary walls.
 23. Explain why active transport is called a physiological process, whereas diffusion is called a physical process.
 24. Explain the function of carrier molecules in active transport.
 25. Distinguish between pinocytosis and phagocytosis.
 26. Describe *receptor-mediated endocytosis*. How might it be used to deliver drugs across the blood-brain barrier?
 27. Explain how transcytosis includes endocytosis and exocytosis.
 28. List the phases in the cell cycle. Why is interphase *not* a time of cellular rest?
 29. Name the two processes included in cell division.
 30. Describe the major events of mitosis.
 31. Explain how the cytoplasm is divided during cell division.
 32. Explain what happens during interphase.
 33. Define *differentiation*.
 34. Explain how differentiation may reflect repression of DNA information.
 35. How does loss of genetic control cause cancer?