Monoclonal Antibodies

Every plasma cell derived from a single B cell secretes antibodies against a specific antigen. These are called **monoclonal antibodies** because all of them are the same type. One method of producing monoclonal antibodies in vitro (outside the body in the laboratory) is depicted in Figure 33.12. B cells are removed from an animal (usually mice are used) and exposed to a particular antigen. 1 The resulting plasma cells are fused with myeloma cells (malignant plasma cells that live and divide indefinitely). The fused cells are called hybridomas—*hybrid-* because they result from the fusion of two different cells, and *-oma* because one of the cells is a cancer cell. 2 The hybridomas then secrete large amounts of the specified monoclonal antibody, which recognizes only a single antigen of interest.

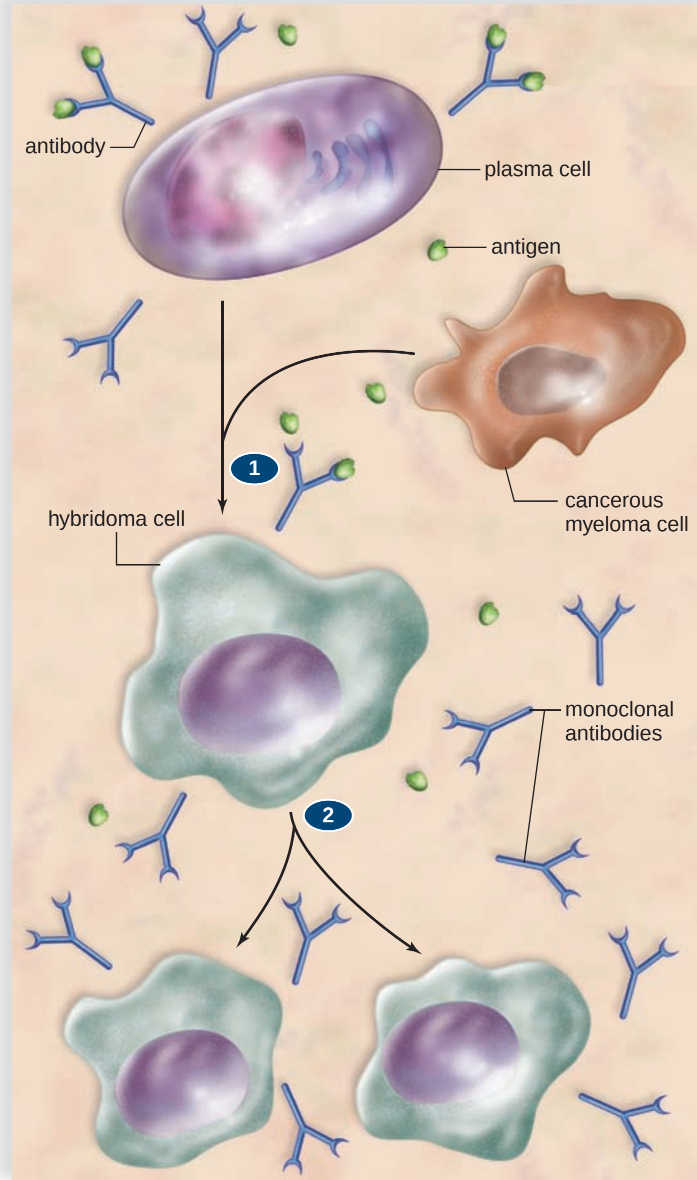


FIGURE 33.12 **Production of monoclonal antibodies.**

Plasma cells of the same type (derived from immunized mice) are fused with myeloma (cancerous) cells, producing hybridoma cells that are "immortal." Hybridoma cells divide and continue to produce the same type of antibody, called monoclonal antibodies.

Research Uses for Monoclonal Antibodies. The ability to quickly produce monoclonal antibodies in the laboratory has made them an important tool for academic research. Monoclonal antibodies are very useful because of their extreme specificity for only a particular molecule. A monoclonal antibody can be used to select out a specific molecule among many others, much like finding needles in a haystack. Now the molecule can be purified from all the others that are also present in a sample. In this way, monoclonal antibodies have simplified formerly tedious laboratory tasks, allowing investigators more time to focus on other priorities.

Medical Uses for Monoclonal Antibodies. Monoclonal antibodies also have many applications in medicine. For instance, they can now be used to make quick and certain diagnoses of various conditions. Today, a monoclonal antibody is used to signify pregnancy by detecting a particular hormone in the urine of a woman after she becomes pregnant. Thanks to this technology, pregnancy tests that once required a visit to a doctor's office and the use of expensive laboratory equipment can now be performed in the privacy and comfort of a woman's own home, at minimal expense.

Monoclonal antibodies can be used not only to diagnose infections and illnesses but also to fight them. Many bacteria and viruses possess unique proteins on their cell surfaces that make them easily recognized by an appropriate monoclonal antibody. When binding occurs with a certain monoclonal antibody but not another, a physician knows what type of infection is present. And because monoclonal antibodies can distinguish some cancer cells from normal tissue cells, they may also be used to identify cancers at very early stages when treatment can be most effective.

Finally, monoclonal antibodies have also shown promise as potential drugs to help fight disease. RSV, a common virus that causes serious respiratory tract infections in very young children, is now being successfully treated with a monoclonal antibody drug. The antibody recognizes a protein on the viral surface, and when it binds very tightly to the surface of the virus, the patient's own immune system can easily recognize the virus and destroy it before it has a chance to cause serious illness.

Other illnesses, such as cancer, are also being successfully treated with monoclonal antibodies. Since these antibodies are able to distinguish between cancerous and normal cells, they have been engineered to carry radioisotopes or toxic drugs to tumors so that cancer cells can be selectively destroyed without damaging other body cells. In short, monoclonal antibodies are helping scientists in their research and physicians in their attempts to diagnose and cure patients.

science focus

Antibody Diversity

In 1987, Susumu Tonegawa (Fig. 33A*a*) became the first Japanese scientist to win the Nobel Prize in Physiology or Medicine, after dedicating himself to finding the solution to an engrossing puzzle. Immunologists and geneticists knew that each B cell makes an antibody especially equipped to recognize the specific shape of a particular antigen. But they did not know how the human genome contained enough genetic information to permit the production of up to 2 million different antibody types needed to combat all of the pathogens we are likely to encounter during our lives.

The Puzzle

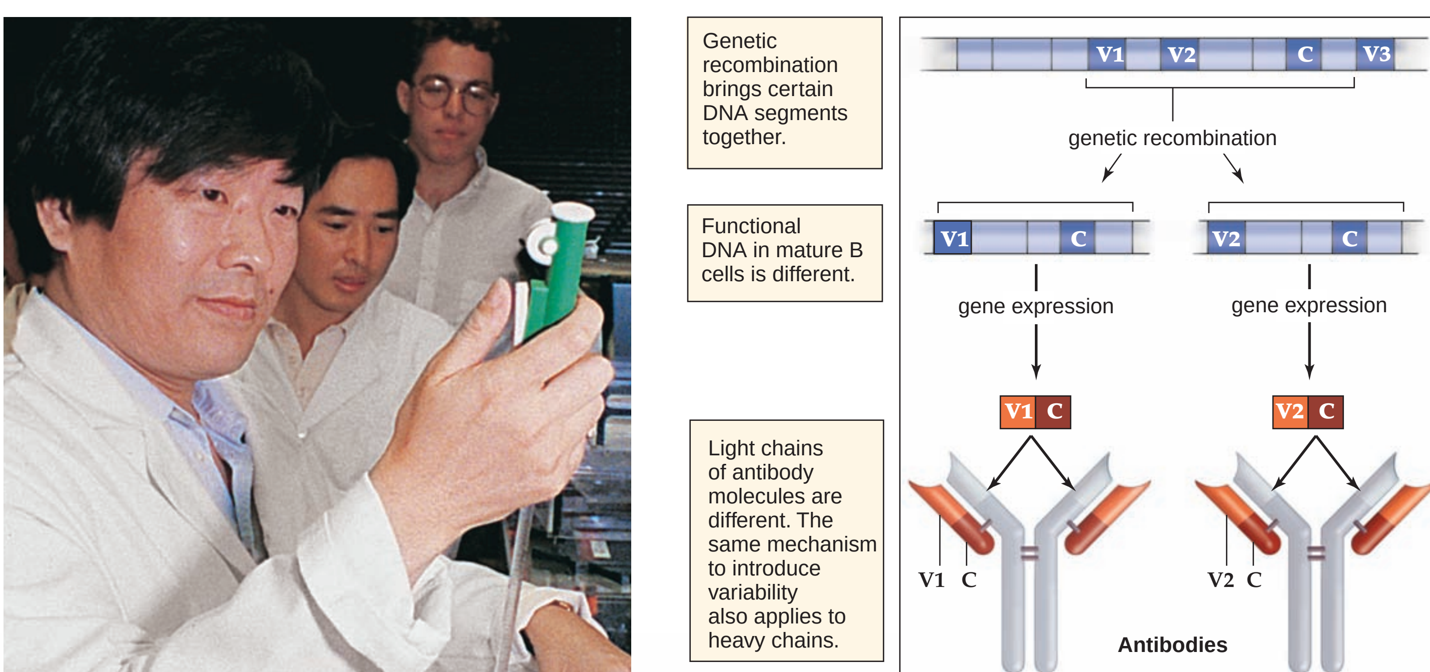
An antibody is composed of two light and two heavy polypeptide chains, which are divided into constant and variable regions. The constant region determines the antibody class, and the variable region determines the specificity of the antibody, because this is where an antigen binds to a specific antibody (see Fig. 33.11). Each B cell must have a genetic way to code for the variable regions of both the light and heavy chains.

The Experiment

Tonegawa's colleagues say that he is a creative genius who intuitively knows how to design experiments to answer specific questions. In this instance, he examined the DNA sequences of lymphoblasts (immature lymphocytes) and compared them to mature B cells. He found that the DNA segments coding for the variable and constant regions were scattered throughout the genome in lymphoblasts, and that only certain of these segments were present in each mature antibody-secreting B cell, where they randomly came together and coded for a specific variable region. Later, the variable and constant regions are joined to give a specific antibody (Fig. 33A*b*). As an analogy, consider that each person entering a supermarket chooses various items for purchase, and that the possible combination of items in any particular grocery bag is astronomical. Tonegawa also found that mutations occur as the variable segments are undergoing rearrangements. Such mutations are another source of antibody diversity.

A Prize Winner

Tonegawa received his BS in chemistry in 1963 at Kyoto University and earned his PhD in biology from the University of California at San Diego (UCSD) in 1969. After that, he worked as a research fellow at UCSD and the Salk Institute. In 1971, he moved to the Basel Institute for Immunology and began the experiments that eventually led to his Nobel Prize–winning discovery. Tonegawa also contributed to the effort to decipher the receptors of T cells. This was an even more challenging area of research than the diversity of antibodies produced by B cells. Since 1981, he has been a full professor at Massachusetts Institute of Technology (MIT), where he has a reputation for being an "aggressive, determined researcher" who often works late into the night.



a. Susumu Tonegawa in the laboratory

b. Antibody variable regions

FIGURE 33A Antibody diversity.
a. *Susumu Tonegawa received a Nobel Prize for his findings regarding antibody diversity.* ***b.*** *Different genes for the variable regions of heavy and light chains are brought together during the production of B lymphocytes so that the antigen receptors of each one can combine with only a particular antigen.*

T Cells and Cell-Mediated Immunity

T cells do not produce antibodies. Cell-mediated immunity is named for the action of cytotoxic T cells that directly attack diseased cells and cancer cells. Helper T cells, however, release cytokines that regulate both innate and acquired immunity and still other T cells are memory T cells that are ever ready to fight an infection.

Life History of T cells

T cells are formed in red bone marrow before they migrate to the thymus, a gland that secretes thymic hormones. These hormones stimulate T cells to develop *T-cell receptors* (*TCRs*). When a T cell leaves the thymus, it has a unique TCR, just as B cells have a BCR. Unlike B cells, however, T cells are unable to recognize an antigen without help. The antigen must be displayed to them by an antigen-presenting cell (APC), such as a dendritic cell or a macrophage. After phagocytizing a pathogen, APCs travel to a lymph node or the spleen, where T cells also congregate. In the meantime, the APC has broken the pathogen apart in a lysosome. A piece of the pathogen is then displayed in an **MHC (major histocompatibility complex) protein** on the cell's surface. MHC proteins are self-antigens because they mark cells as belonging to a particular individual and, therefore, make transplantation of organs difficult. MHC proteins differ by the sequence of their amino acids, and the immune system will attack as foreign any tissue that bears MHC antigens different from those of the individual.

In Figure 33.13, the different types of T cells have specific TCRs represented by their different shapes and colors. **1** A macrophage presents an antigen only to a T cell that has a TCR capable of combining with a particular antigen (colored green). **2** A major difference in recognition of an antigen by helper T cells and cytotoxic T cells is that helper T cells only recognize an antigen in combination with MHC class II molecules while cytotoxic T cells only recognize an antigen in combination with MHC class I molecules. In Figure 33.13 a cytotoxic T cell binds to an antigen displayed in combination with an MHC I and undergoes cloning during which many copies of the cytotoxic T cell are produced. **3** Some of the cloned cells become **memory T cells.**

4 As the illness disappears, the immune response wanes, and active T cells become susceptible to apoptosis, which is programmed cell death (see Fig. 9.2). As mentioned previously, apoptosis contributes to homeostasis by regulating the number of cells present in an organ, or in this case, in the immune system. When apoptosis does not occur as it should, T cell cancers (e.g., lymphomas and leukemias) can result. Also, in the thymus, any T cell that has the potential to destroy the body's own cells undergoes apoptosis.

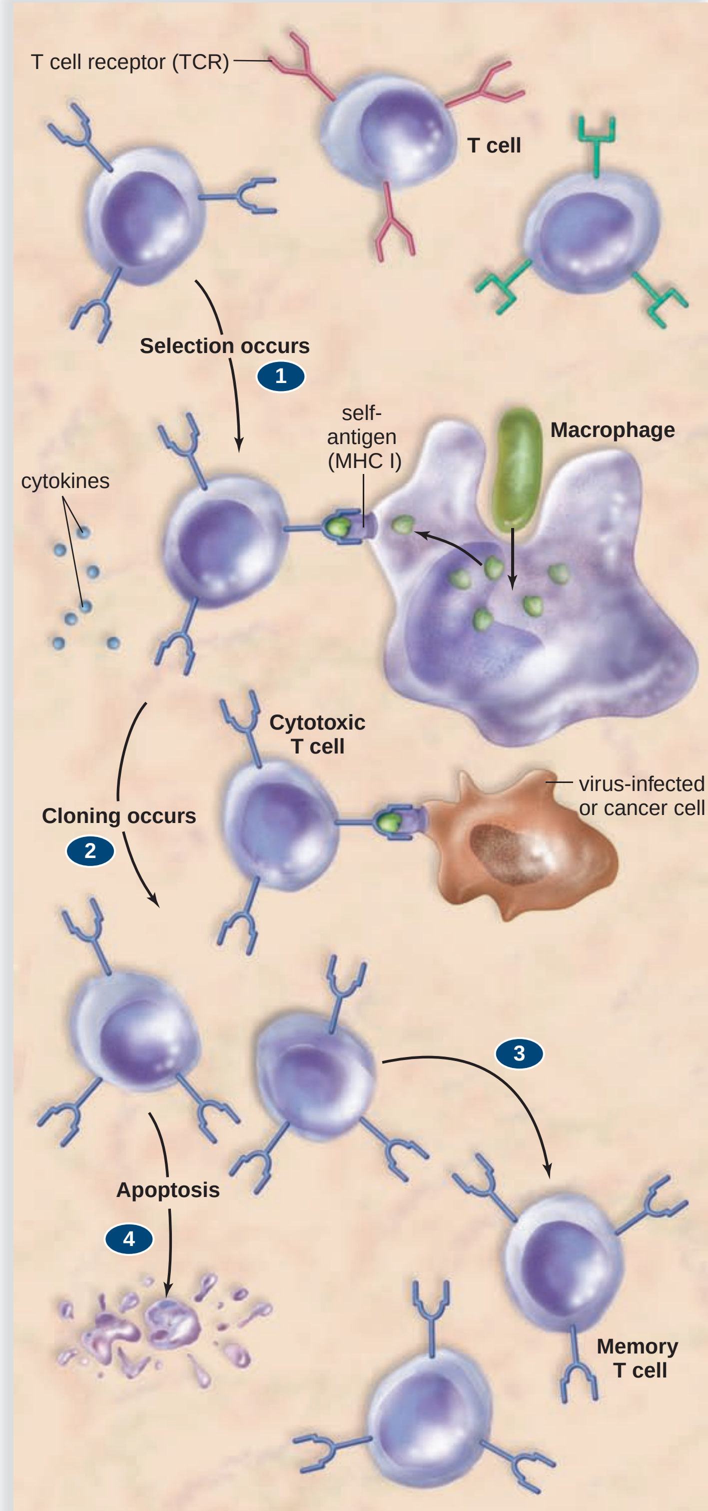
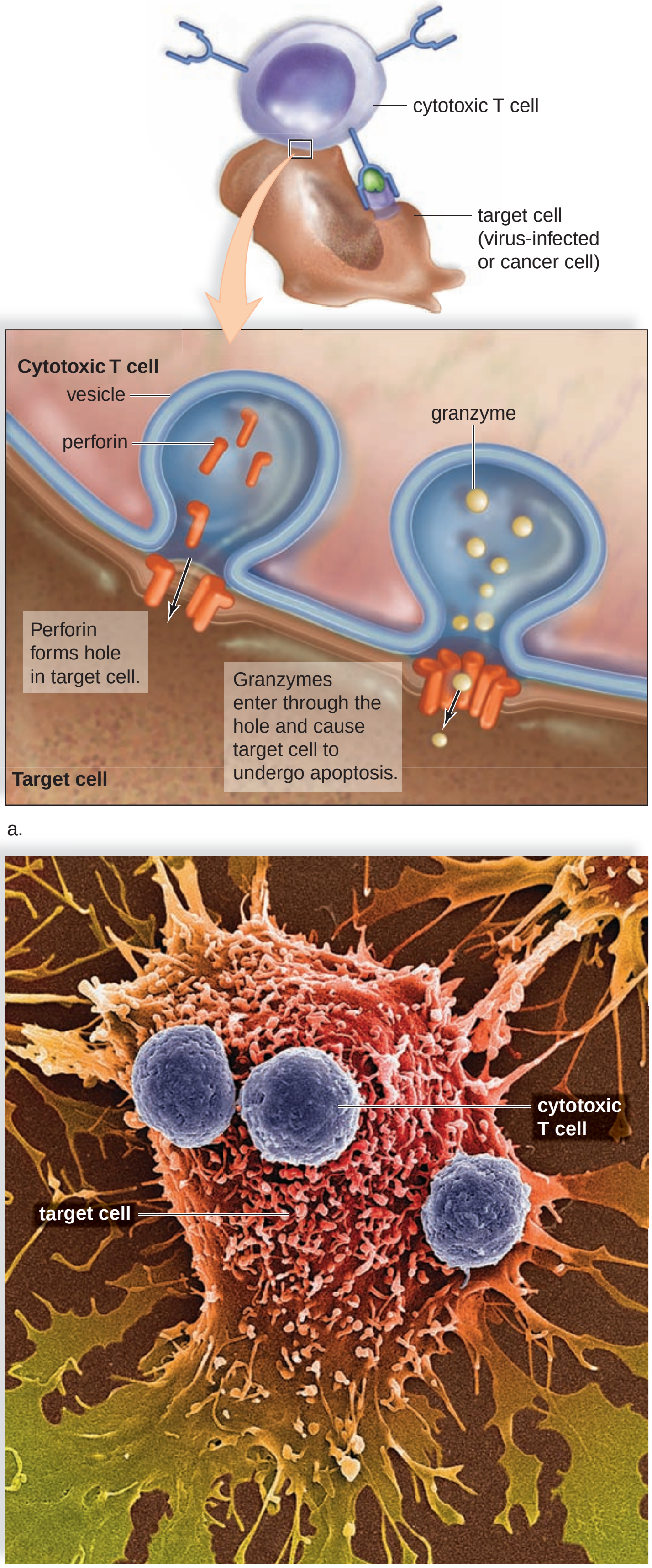


FIGURE 33.13 Clonal selection model as it applies to T cells. Each T cell has a T-cell receptor (TCR) designated by a shape and color that will combine only with a specific antigen. Activation of a T cell occurs when its TCR can combine with an antigen. A macrophage presents the antigen (colored green) in the groove of an MHC I. Thereafter, the T cell undergoes clonal expansion, and many copies of the same type T cell are produced. After the immune response has been successful, the majority of T cells undergo apoptosis, but a small number are memory T cells. Memory T cells provide protection should the same antigen enter the body again at a future time.

Functions of Cytotoxic T Cells and Helper T Cells

Cytotoxic T cells specialize in cell to cell combat. They have storage vacuoles containing perforins and storage vacuoles



SEM 1,250×

FIGURE 33.14 Cell-mediated immunity.

a. How a T cell destroys a virus-infected cell or cancer cell. **b.** The scanning electron micrograph shows cytotoxic T cells attacking and destroying a cancer cell (target cell).

containing enzymes called granzymes (Fig. 33.14). After a cytotoxic T cell is activated, it binds to a virus-infected cell or cancer cell, it releases perforin molecules, which perforate the plasma membrane, forming a pore. Cytotoxic T cells then deliver granzymes into the pore, and these cause the cell to undergo apoptosis and die. Once cytotoxic T cells have released the perforins and granzymes, they move on to the next target cell. Cytotoxic T cells are responsible for so-called cell-mediated immunity.

Helper T cells play a critical role in coordinating nonspecific defenses (innate immunity) and specific defenses (acquired immunity), including both cell-mediated immunity and also antibody-mediated immunity. How do helper T cells perform this function? After a helper T cell is activated, it secretes cytokines. Cytokines are chemical mediators that attract neutrophils, natural killer cells, and macrophages to where they are needed. Cytokines stimulate phagocytosis of pathogens, and they stimulate the clonal expansion of T and B cells. Cytokines are used for immunotherapy purposes also, as we shall discuss in the next section.

Because more and more immune cells are recruited by helper T cells, the number of pathogens eventually begins to wane. But by now the body is fully prepared to deal with this pathogen again. Therefore, it is said that the immune system possesses memory—it can often remember former antigens. Memory T cells, like memory B cells, are long-lived, and their number is far greater than the original number of T cells that could recognize a specific antigen. Therefore, when the same antigen enters the body later on, the immune response may occur so rapidly that no detectable illness occurs.

HIV Infections

The primary host for an HIV (human immunodeficiency virus) is a helper T cell, but macrophages are also under attack. After HIV enters a host cell, it reproduces as described in Figure 20.4, and many progeny bud from the cell. In other words, the host helper T cell produces viruses that go on to destroy more helper T cells. Figure 33B in the Health Focus on page 626 describes the progression of an HIV infection over time. At first an individual is able to stay ahead of the virus by producing enough helper T cells to keep their number within the normal range. But gradually, as the HIV count rises, the helper T cell count drops to way below normal. Then the person comes down with what are called opportunistic infections—infections that would be unable to take hold in a person with a healthy immune system. Now the individual has AIDS (acquired immunodeficiency syndrome). An HIV infection is presently a treatable disease, but the regimen of medicines is very difficult to maintain, and viral resistance to these medications is becoming apparent. Therefore, it is much wiser for individuals to prevent becoming infected by following the recommendations given on page 613.

health focus

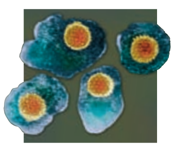
Opportunistic Infections and HIV

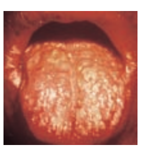
AIDS (acquired immunodeficiency syndrome) is caused by the destruction of the immune system, following an HIV (human immunodeficiency virus) infection. An HIV infection leads to the eventual destruction of immune system cells, known as helper T lymphocytes or, simply, helper T cells. Then, the individual succumbs to many unusual types of infections that would not cause disease in a person with a healthy immune system. Such infections are known as "opportunistic infections" (OIs).

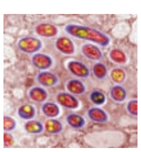

AIDS victim: Kaposi sarcoma is evident

HIV not only kills helper T cells by directly infecting them; it also causes many uninfected T cells to die by a variety of mechanisms, including apoptosis (programmed cell death or "cell suicide"). Many helper T cells are also killed by the person's own immune system as it tries to overcome the HIV infection. After initial infection with HIV, it may take up to ten years for an individual's helper T cells to become so depleted that the immune system can no longer organize a specific response to OIs (Fig. 33B). In a healthy individual, the number of helper T cells typically ranges from 800–1,000 cells per mm^3 of blood. The appearance of specific OIs can be associated with the helper T-cell count.

- Shingles. Painful infection with varicella-zoster (chickenpox) virus. Helper T-cell count of less than $500/mm^3$.
- Candidiasis. Fungal infection of the mouth, throat, or vagina. Helper T-cell count of about $350/mm^3$.
- *Pneumocystis* pneumonia. Fungal infection causing the lungs to become useless as they fill with fluid and debris. Helper T-cell count of less than $200/mm^3$.


Chickenpox virus


Candidiasis


Pneumocystic pneumonia

- Kaposi's sarcoma. Cancer of blood vessels due to human herpesvirus 8 gives rise to reddish purple, coin-sized spots and lesions on the skin. Helper T-cell count of less than $200/mm^3$.
- Toxoplasmic encephalitis. Protozoan infection characterized by severe headaches, fever, seizures, and coma. Helper T-cell count of less than $100/mm^3$.
- *Mycobacterium avium* complex (MAC). Bacterial infection resulting in persistent fever, night sweats, fatigue, weight loss, and anemia. Helper T-cell count of less than $75/mm^3$.
- Cytomegalovirus. Viral infection that leads to blindness; inflammation of the brain, throat ulcerations. Helper T-cell count of less than $50/mm^3$.

Due to development of powerful drug therapies that slow the progression of AIDS, people infected with HIV in the United States are suffering lower incidence of OIs than in the 1980s and 1990s. It is hoped that a vaccine will be developed for AIDS one day.

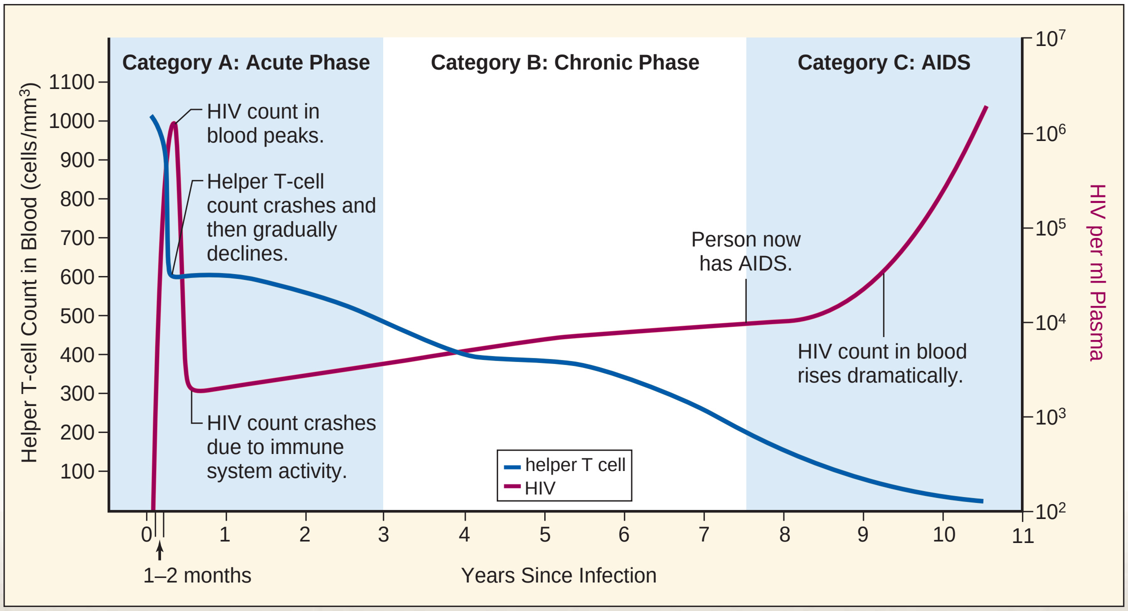


FIGURE 33B Progression of HIV infection during its three stages, called categories A, B, and C. *In category A, the individual may have no symptoms or very mild symptoms associated with the infection. By category B, opportunistic infections have begun to occur, such as candidiasis, shingles, and diarrhea. Category C is characterized by more severe opportunistic infections and is clinically described as AIDS.*

Cytokines and Cancer Therapy

The term cytokine simply means a soluble protein that acts as a signaling molecule. Because cytokines stimulate white blood cells, they have been studied as a possible adjunct therapy for cancer. We have already mentioned that interferons are cytokines. Interferons are produced by virus-infected cells, and they signal other cells of the need to prevent infection. Interferon has been investigated as a possible cancer drug, but so far it has proven to be effective only in certain patients, and the exact reasons for this, as yet, cannot be discerned. Also, interferon has a number of side effects that limit its use.

Cytokines called interleukins are produced by white blood cells, and they act to stimulate other white blood cells. Scientists actively engaged in interleukin research believe that interleukins will soon be used in addition to vaccines, for the treatment of chronic infectious diseases, and perhaps for the treatment of cancer. Interleukin antagonists may also prove helpful in preventing skin and organ rejection, autoimmune diseases, and allergies.

Because cancer cells carry an altered protein on their cell surface, they should be attacked and destroyed by cytotoxic T cells. Whenever cancer does develop, it is hypothesized that the cytotoxic T cells have not been activated. In that case, cytokines such as interleukins might awaken the immune system and lead to the destruction of the cancer. In one technique being investigated, researchers bioengineer APC cells withdrawn from the patient and activate the cells by culturing them in the presence of an interleukin. The engineered cells are then reinjected into the patient, who is given doses of interleukin to maintain the activity of the APC cells (Fig. 33.15).

Tumor necrosis factor (TNF) is a cytokine produced by macrophages that has the ability to promote the inflammatory response and to cause the death of cancer cells. Like the interferons and interleukins, TNF stimulates the body's immune cells to fight cancer. TNF also directly affects tumor cells, damaging them and the blood vessels within the tumor. Without an adequate blood supply, a cancerous tumor cannot thrive. However, researchers are still uncertain about exactly how TNF destroys tumors. Researchers have found that TNF therapy is most effective and least toxic when directed at a specific tumor site, rather than used as a general medicine. Clinical trials are under way.

Check Your Progress 33.3

1. What steps accomplish a specific defense?
2. What are some examples of the immune system's use of a specific defense?
3. Which blood cells are mainly responsible for specific defense, and how do they function?

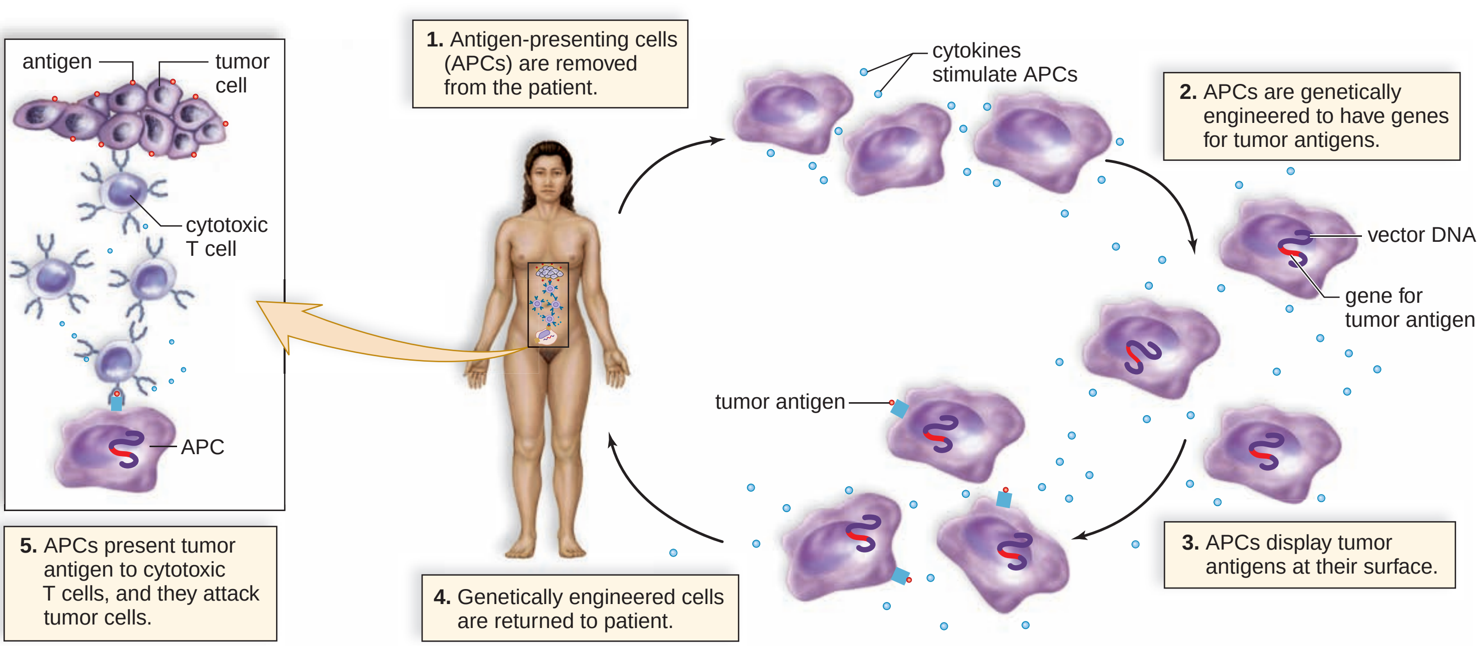


FIGURE 33.15 Immunotherapy.

1. Antigen-presenting cells (APCs) are removed and (2) are genetically engineered to (3) display tumor antigens. 4. After APCs are returned to the patient, (5) they present the antigen to cytotoxic T cells, which then kill tumor cells.

33.4 Immunity Side Effects

In certain instances, immunity works against the best interests of the body, as when it makes it more difficult to transplant organs from a donor to a recipient, causes autoimmune disorders, or leads to allergic reactions.

Tissue Rejection

Certain organs, such as skin, the heart, and the kidneys, could be transplanted easily from one person to another if the body did not attempt to reject them. Rejection occurs because antibodies and cytotoxic T cells bring about the destruction of foreign tissues in the body. When rejection occurs, the immune system is correctly distinguishing between self and nonself.

Organ rejection can be controlled by carefully selecting the organ to be transplanted and administering immunosuppressive drugs. It is best if the transplanted organ has the same type of MHC antigens as those of the recipient, because cytotoxic T cells recognize foreign MHC antigens. Two well-known immunosuppressive drugs, cyclosporine and tacrolimus, both act by inhibiting the production of certain cytokines that stimulate cytotoxic T cells.

Xenotransplantation, the transplantation of animal tissues and organs into human beings, is another way to solve the problem of rejection. Genetic engineering can make pig organs less antigenic by removing the MHC antigens. The ultimate goal is to make pig organs as widely accepted as blood type O. Other researchers hope that tissue engineering, including the production of human organs by using stem cells, will one day do away with the problem of rejection. Scientists have recently grown new heart valves in the laboratory using stem cells gathered from amniotic fluid following amniocentesis.

Disorders of the Immune System

We will discuss disorders in which the immune system mistakenly attacks the body's own cells as if they bear foreign antigens and other disorders in which immunity is lacking and infections are common.

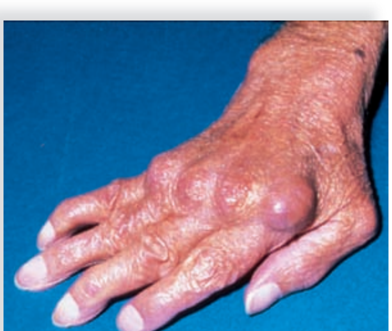


FIGURE 33.16 Rheumatoid arthritis.

Rheumatoid arthritis is due to recurring inflammation in skeletal joints, due to immune system attack.

Autoimmune diseases can be characterized by the failure of the immune system to distinguish between foreign antigens and the self-antigens that mark the body's own tissues. In an autoimmune disease, chronic inflammation occurs, and cytotoxic T cells or antibodies mistakenly attack the body's own cells.

The exact events that trigger an autoimmune disorder are not known. Some autoimmune disorders set in following a noticeable infection; for example, the heart damage following rheumatic fever is thought to be due to an autoimmune disorder triggered by the illness. Otherwise, most autoimmune disorders probably start after an undetected inflammatory response. However, the tendency to develop autoimmune disorders is known to be inherited in some cases, so there may be genetic causes as well.

FIGURE 33.17 Systemic lupus.

A butterfly-shaped rash appears on the face.

Since little is known about the origin of autoimmune disorders, no cures are currently available. Regardless, most of these conditions can be managed over the long term with immunosuppressive drugs that control the various symptoms.

Rheumatoid arthritis is a common autoimmune disorder that causes recurring inflammation in synovial joints (Fig. 33.16). Complement proteins, T cells, and B cells all participate in deterioration of the joints, which eventually become immobile. This chronic inflammation gradually causes destruction of the delicate membrane and cartilage within the joint.

In myasthenia gravis, a well-understood autoimmune disease, antibodies attach to and interfere with the functioning of neuromuscular junctions, causing muscular weakness.

Systemic lupus erythematosus (lupus) is a chronic autoimmune disorder characterized by the presence of antibodies to the nuclei of the body's cells. Unlike rheumatoid arthritis or myasthenia gravis, lupus affects multiple tissues and organs, and is still very poorly understood. The symptoms vary somewhat, but most patients experience a characteristic skin rash (Fig. 33.17), joint pain, and kidney damage. Lupus typically progresses to include many life-threatening complications.

When a person has an immune deficiency, the immune system is unable to protect the body against disease. Acquired immunodeficiency syndrome (AIDS) is an example of an acquired immune deficiency. As a result of a weakened immune system, AIDS patients show a greater susceptibility to infections and also have a higher risk of cancer (see page 626). Infrequently, a child may be born with an impaired immune system, caused by a defect in lymphocyte development. In severe combined immunodeficiency disease (SCID), both antibody- and cell-mediated immunity are lacking or inadequate. Without treatment, even common infections can be fatal. Gene therapy has been successful in SCID patients.

Allergies

Allergies are hypersensitivities to substances, such as pollen, food, or animal hair, that ordinarily would do no harm to the body. The response to these antigens, called allergens, usually includes some degree of tissue damage.

An **immediate allergic response** can occur within seconds of contact with the antigen. The response is caused by antibodies known as IgE (Table 33.1). IgE antibody receptors have mast cells in the tissues. When an allergen attaches to the IgE antibodies and the antibodies attach to their receptors on mast cells, the cells release histamine and other substances that bring about the allergic symptoms (Fig. 33.18). If the allergen is pollen, histamine stimulates the mucous membranes of the nose and eyes to release fluid, causing the runny nose and watery eyes typical of **hay fever.** If a person has **asthma,** the airways leading to the lungs constrict; labored breathing is accompanied by wheezing. Nausea, vomiting, and diarrhea typically occur when food contains an allergen.

Drugs called antihistamines are used to treat allergies. These drugs compete for the same receptors on the nose, eyes, airways, and lining of the digestive tract cells that ordinarily combine with histamine. In this way, histamine is prevented from binding and causing its unpleasant symptoms. However, antihistamines are only partially effective because mast cells release other molecules, in addition to histamine, that cause allergic symptoms.

Anaphylactic shock is an immediate allergic response that occurs after an allergen has entered the bloodstream. Bee stings and penicillin shots are known to cause this reaction in some individuals because both inject the allergen into the blood. Anaphylactic shock is characterized by a sudden and life-threatening drop in blood pressure, due to increased permeability of the capillaries by histamine.

People with allergies produce ten times more IgE than people without allergies. A new treatment using injections of monoclonal IgG antibodies for IgEs is currently being tested in individuals with severe food allergies. More routinely, injections of the allergen are given so that the body will build up high quantities of IgG antibodies. The hope is that these will combine with allergens received from the environment before they have a chance to combine with the IgE antibodies.

A **delayed allergic response** is initiated by memory T cells at the site of allergen contact in the body. The allergic response is regulated by the cytokines secreted by both T cells and macrophages. A classic example of a delayed allergic response is the skin test for tuberculosis (TB). When the test result is positive, the tissue where the antigen was injected becomes red and hardened. This indicates prior exposure to tubercle bacilli, the cause of TB. Contact dermatitis, which occurs when a person is allergic to poison ivy, jewelry, cosmetics, and many other substances that touch the skin, is another example of a delayed allergic response.

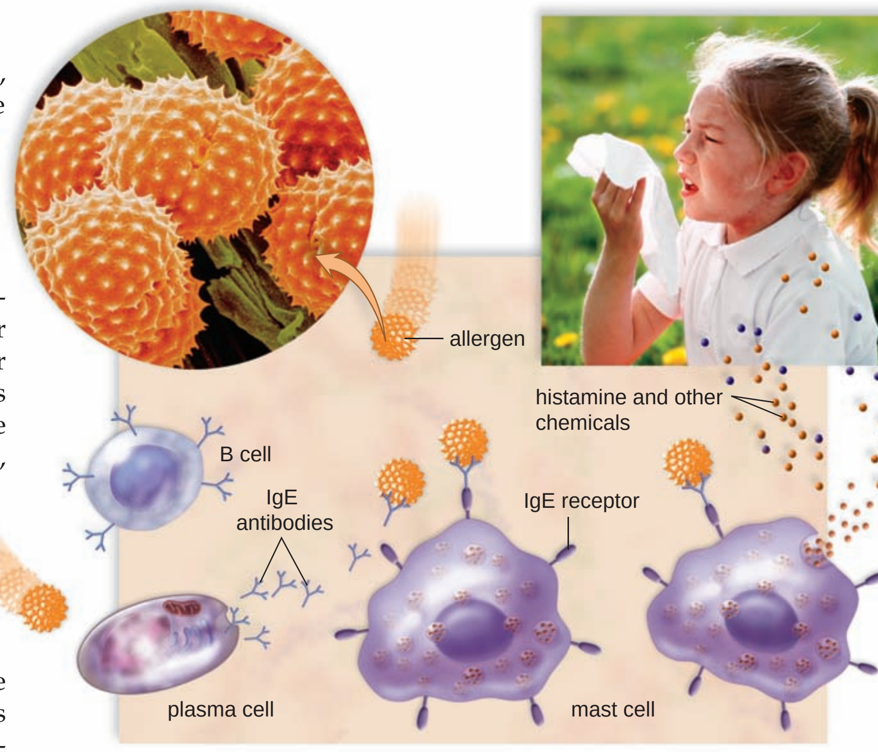


FIGURE 33.18 An allergic reaction.

An allergen attaches to IgE antibodies, which then cause mast cells to release histamine and other chemicals that are responsible for the allergic reaction.

Check Your Progress 33.4

1. What types of complications and disorders are associated with the functioning of the immune system? Explain each of these.

TABLE 33.1
Comparison of Immediate and Delayed Allergic Responses

	Immediate Response	*Delayed Response*
Onset of Symptoms	Takes several minutes	Takes 1 to 3 days
Lymphocytes Involved	B cells	T cells
Immune Reaction	IgE antibodies	Cell-mediated immunity
Type of Symptoms	Hay fever, asthma, and many other allergic responses	Contact dermatitis (e.g., poison ivy)
Therapy	Antihistamine and adrenaline	Cortisone

Connecting the Concepts

The role of the lymphatic system in homeostasis cannot be overemphasized. Excess tissue fluid, which is collected within lymphatic vessels, is called lymph. Because this fluid is returned to the cardiovascular system, blood volume and pressure are maintained. The lymphatic system is also intimately involved in immunity.

Levels of defense against invasion of the body by pathogens can be compared to how we protect our homes. Homes usually have external defenses such as a fence, a dog, or locked doors. Similarly, the body has barriers, such as the skin and mucous membranes, that prevent pathogens from entering the blood and lymph. Like a home alarm system, if invasion does occur, a signal goes off. First, nonspecific defense mechanisms such as the complement system and phagocytosis by white blood cells come into play. Finally, specific defense, which is dependent on the activities of B and T cells, occurs.

A strong connection exists between the immune, endocrine, and nervous systems. The thymus gland produces hormones that influence the immune response. Cortisone has the ability to mollify the inflammatory response. Cytokines help the body recover from disease in part by affecting the brain's temperature control center. A fever is thought to create an unfavorable environment for foreign invaders. Also, cytokines bring about a feeling of sluggishness, sleepiness, and loss of appetite. These behaviors tend to make us take care of ourselves until we feel better.

We continue our discussion of homeostasis in the next chapter, which considers the structure and function of the digestive system in both invertebrates and vertebrates.

summary

33.1 The Lymphatic System

The lymphatic system consists of lymphatic vessels and organs. The lymphatic vessels (1) receive glycerol and fatty acids packaged as lipoproteins at intestinal villi; (2) receive excess tissue fluid collected by lymphatic capillaries; and (3) carry these to the bloodstream.

Lymphocytes are produced and accumulated in the lymphatic organs (lymph nodes, tonsils, spleen, thymus gland, and red bone marrow). Lymph is cleansed of pathogens in lymph nodes, and blood is cleansed of pathogens in the spleen. T lymphocytes mature in the thymus, while B lymphocytes mature in the red bone marrow where all blood cells are produced. White blood cells such as these lymphocytes are necessary for nonspecific and specific defenses.

33.2 Nonspecific Defense Against Disease

Immunity involves nonspecific and specific defenses. Nonspecific defenses (also called innate immunity) include barriers to entry, the inflammatory response, phagocytes and natural killer cells, and protective proteins.

33.3 Specific Defense Against Disease

Specific defenses (also called acquired immunity) require B lymphocytes and T lymphocytes, also called B cells and T cells. B cells undergo clonal selection with production of plasma cells and memory B cells after their B-cell receptor combines with a specific antigen. Plasma cells secrete antibodies and are responsible for antibody-mediated immunity. Some progeny of activated B cells become memory B cells, which remain in the body and produce antibodies if the same antigen enters the body at a later date. Active (long-lived) immunity occurs as a response to an illness or the administration of vaccines when a person is well and in no immediate danger of contracting an infectious disease. Passive immunity is needed when an individual is in immediate danger of succumbing to an infectious disease. Passive immunity is short-lived because the antibodies are administered to and not made by the individual.

An antibody is usually a Y-shaped molecule that has two binding sites for a specific antigen. Monoclonal antibodies, which are produced by the same plasma cell, have various functions, from detecting infections to treating cancer.

T cells have T-cell receptors and are responsible for cell-mediated immunity. The two main types of T cells are cytotoxic T cells and helper T cells. Cytotoxic T cells kill virus-infected or cancer cells on contact. Helper T cells produce cytokines and regulate both nonspecific defenses (innate immunity) and specific defenses (acquired immunity). Cytokines, including interferon, are used in attempts to treat AIDS and to promote the body's ability to recover from cancer.

For a T cell to recognize an antigen, the antigen must be presented by an antigen-presenting cell (APC), a dendritic cell, or a macrophage, along with an MHC (major histocompatibility complex) protein. Thereafter, the activated T cell undergoes clonal expansion until the illness has been stemmed. Then, most of the activated T cells undergo apoptosis. A few cells remain, however, as memory T cells.

33.4 Immunity Side Effects

Immune side effects also include tissue rejection and autoimmune diseases. Allergic responses occur when the immune system reacts vigorously to substances not normally recognized as foreign. Immediate allergic responses, usually consisting of coldlike symptoms, are due to the activity of antibodies. Delayed allergic responses, such as contact dermatitis, are due to the activity of T cells.

understanding the terms

Peyer patches 615
plasma cell 619
red bone marrow 614
self-antigen 619
spleen 615
T cell 615
T-cell receptor (TCR) 619
thymus gland 615
tonsils 615

Match the terms to these definitions:

a. ______________ Antigens prepared in such a way that they can promote active immunity without causing disease.
b. ______________ Fluid, derived from tissue fluid, that is carried in lymphatic vessels.
c. ______________ Foreign substance, usually a protein or a polysaccharide, that stimulates the immune system to react, such as by producing antibodies.
d. ______________ Process of programmed cell death involving a cascade of specific cellular events leading to the death and destruction of the cell.
e. ______________ Lymphocyte that matures in the thymus and exists in three varieties, one of which kills antigen-bearing cells outright.

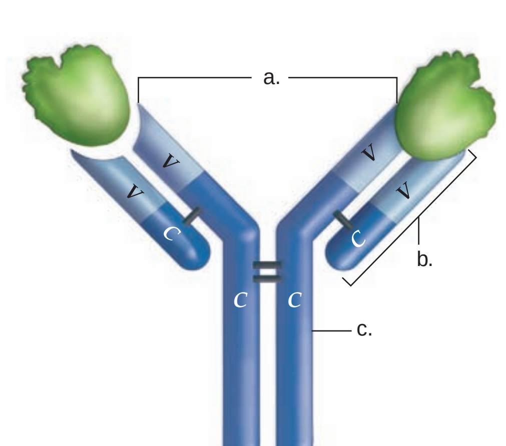
reviewing this chapter

1. Which functions of the lymphatic system are not assisted by another system? Explain. 614
2. Describe the microscopic structure and the function of lymph nodes, the spleen, the thymus gland, and red bone marrow. 614–15
3. Discuss the body's nonspecific defense mechanisms. 616–18
4. Describe the inflammatory response, and give a role for each type of cell and molecule that participates in the response. 616–18
5. Describe the clonal selection model as it applies to B cells. B cells are responsible for which type of immunity? 620
6. How is active immunity artificially achieved? How is passive immunity achieved? 620–21
7. Describe the structure of an antibody, and define the terms variable regions and constant regions. 621
8. How are monoclonal antibodies produced, and what are their applications? 622
9. Discuss the clonal selection model as it applies to T cells. 624
10. Name the two main types of T cells, and state their functions. 619, 624–25
11. What are cytokines, and how are they used in immunotherapy? 627
12. Discuss autoimmune diseases and allergies as they relate to the immune system. 628–29

testing yourself

Choose the best answer for each question.

1. Both veins and lymphatic vessels
   a. have thick walls of smooth muscle.
   b. contain valves for one-way flow of fluids.
   c. empty directly into the heart.
   d. are fed fluids from arterioles.
2. Complement
   a. is a nonspecific defense mechanism.
   b. is involved in the inflammatory response.
   c. is a series of proteins present in the plasma.
   d. plays a role in destroying bacteria.
   e. All of these are correct.
3. Which of these pertain(s) to T cells?
   a. have specific receptors
   b. are more than one type
   c. are responsible for cell-mediated immunity
   d. stimulate antibody production by B cells
   e. All of these are correct.
4. Which one of these does not pertain to B cells?
   a. have passed through the thymus
   b. have specific receptors
   c. are responsible for antibody-mediated immunity
   d. become plasma cells that synthesize and liberate antibodies
5. The clonal selection model says that
   a. an antigen selects certain B cells and suppresses them.
   b. an antigen stimulates the multiplication of B cells that produce antibodies against it.
   c. T cells select those B cells that should produce antibodies, regardless of antigens present.
   d. T cells suppress all B cells except the ones that should multiply and divide.
   e. Both b and c are correct.
6. Plasma cells are
   a. the same as memory cells.
   b. formed from blood plasma.
   c. B cells that are actively secreting antibody.
   d. inactive T cells carried in the plasma.
   e. a type of red blood cell.
7. Which of these pairs is incorrectly matched?
   a. cytotoxic T cells—help complement react
   b. cytotoxic T cells—active in tissue rejection
   c. macrophages—activate T cells
   d. memory T cells—long-living T cells
   e. T cells—mature in thymus
8. Vaccines are
   a. the same as monoclonal antibodies.
   b. treated bacteria or viruses, or one of their proteins.
   c. short-lived.
   d. MHC proteins.
   e. All of these are correct.
9. The inflammatory process involves
   a. complement, lymphocytes, and antigens.
   b. increased blood flow, phagocytes, and blood clotting.
   c. barriers to entry, tonsils, and fever.
   d. passive immunity, MHC proteins, and interferon.
   e. All of these are correct.
10. Label a–c on this IgG molecule using these terms: antigen-binding sites, light chain, heavy chain.



    d. What do *V* and *C* stand for in the diagram?

11. The lymphatic system does not
    a. transport tissue fluid back to the blood.
    b. transport absorbed lipoproteins from the small intestine to the blood.
    c. play a role in immunological defense.
    d. filter metabolic wastes, such as urea.
12. Which is a nonspecific defense against a pathogen?
    a. skin
    b. gastric juice
    c. complement
    d. interferons
    e. All of these are correct.
13. Which cell does not phagocytize?
    a. neutrophil
    b. lymphocyte
    c. monocyte
    d. macrophage
14. B cells mature within
    a. the lymph nodes.
    b. the spleen.
    c. the thymus.
    d. the bone marrow.
15. Plasma cells secrete
    a. antibodies.
    b. perforins.
    c. lysosomal enzymes.
    d. histamine.
    e. lymphokines.
16. Mast cell secretion occurs after an allergen combines with
    a. IgG antibodies.
    b. IgE antibodies.
    c. IgM antibodies.
    d. IgA antibodies.
17. After a second exposure to a vaccine,
    a. antibodies are made quickly and in greater amounts.
    b. immunity lasts longer than after the first exposure.
    c. antibodies of the IgG class are produced.
    d. plasma cells are active.
    e. All of these are correct.
18. Active immunity may be produced by
    a. having a disease.
    b. receiving a vaccine.
    c. receiving gamma globulin injections.
    d. Both a and b are correct.
    e. Both b and c are correct.
19. T cells do not
    a. promote the activity of B cells.
    b. undergo apoptosis.
    c. secrete cytokines.
    d. produce antibodies.
20. MHC proteins
    a. are present only on the surface of certain cells.
    b. help present the antigen to T cells.
    c. are unnecessary to the immune response.
    d. Both b and c are correct.
21. Lymph nodes
    a. block the flow of lymph.
    b. contain B cells and T cells.
    c. decrease in size during an illness.
    d. filter blood.
22. Which of the following is a function of the spleen?
    a. produces T cells
    b. removes worn-out red blood cells
    c. produces immunoglobulins
    d. produces macrophages
    e. regulates the immune system

thinking scientifically

1. The transplantation of organs from one person to another was impossible until the discovery of immunosuppressant drugs. Now, with the use of drugs such as cyclosporine, organs can be transplanted without rejection. Transplant patients must take immunosuppressant drugs for the remainder of their lives. How can a person do this and not eventually succumb to disease?
2. Laboratory mice are immunized with a measles vaccine. When the mice are challenged with measles virus to test the strength of their immunity, the memory cells do not completely prevent replication of the measles virus. The virus undergoes a few rounds of replication before the immune response is observed. You have developed a strain of mice with a much faster response to a viral challenge, but these mice often develop an autoimmune disease. Speculate on the connection between speed of response and an autoimmune disease.

bioethical issue

Cost of Drugs to Treat AIDS

Over 36 million people worldwide are living with AIDS. This disease is deadly without proper medical care but a chronic disease if treated. Drug companies typically charge a high price for AIDS medications because Americans and their insurance companies can afford them. However, these drugs are out of reach in many countries, such as those in Africa, where AIDS is a widespread problem. Some people argue that drug companies should use the profits from other drugs (such as those for heart disease, depression, and impotence) to make AIDS drugs affordable to those who need them. This has not happened yet. In some countries, governments have allowed companies to infringe on foreign patents held by major drug companies so that they can produce affordable AIDS drugs. Do drug companies have a moral obligation to provide low-cost AIDS drugs, even if they have to do so at a loss of revenue? Is it right for governments to ignore patent laws in order to provide their citizens with affordable drugs?

Biology website

The companion website for *Biology* provides a wealth of information organized and integrated by chapter. You will find practice tests, animations, videos, and much more that will complement your learning and understanding of general biology.

http://www.mhhe.com/maderbiology10

34

Digestive Systems and Nutrition

a great blue heron stands at the water's edge with its long neck cocked in the familiar S shape. To feed, its swordlike bill is launched forward to grasp a fish. Most birds, like the heron, are discontinuous feeders and feed periodically. Some birds, like a hummingbird, are continuous feeders and feed almost every waking moment. In keeping with feeding discontinuously, the esophagus of a great blue heron has a crop, a storage area that allows the bird to delay digestion of the meal. The bird's stomach has a gizzard that crushes hard materials with its muscular walls and abrades them with sand swallowed sometime in the past. Similar to humans, the bulk of enzymatic digestion and also absorption occur in the small intestine.

In this chapter, we will compare the digestive system of various animals before examining how the organs of the human digestive system function. This is the first step toward an appreciation of dietary concerns, which are also discussed.

This great blue heron has caught a fish. Digestion will produce nutrient molecules small enough to enter the bloodstream.

concepts

34.1 Digestive Tracts

Not all animals have a digestive tract. Consider, for example, that in sponges, digestion occurs in food vacuoles, as it does in protozoa. Digestion in hydras, which are cnidarians, begins in their gastrovascular cavity, but is finished in food vacuoles.

The majority of animals have some sort of gut, or digestive tract, where food is digested into small nutrient molecules that can cross plasma membranes. Digestion contributes to homeostasis by providing the body with the nutrients needed to sustain the life of cells. A digestive tract (1) ingests food, (2) breaks food down into small molecules that can cross plasma membranes, (3) absorbs these nutrient molecules, and (4) eliminates undigestible remains.

Incomplete Versus Complete Tracts

An **incomplete digestive tract** has a single opening, usually called a mouth. However, the single opening is used both as an entrance for food and an exit for wastes. Planarians, which are flatworms, have an incomplete tract (Fig. 34.1). It begins with a mouth and muscular pharynx and then the tract, a gastrovascular cavity, branches throughout the body. Planarians are primarily carnivorous and feed largely on smaller aquatic animals, as well as bits of organic debris. When a planarian is feeding, the pharynx actually extends beyond the mouth. The body is wrapped about the prey and the pharynx sucks up minute quantities at a time. Digestive enzymes present in the tract allow some extracellular digestion to occur. Digestion is finished intracellularly by the cells that line the tract. No cell in the body is far from the digestive tract; therefore, diffusion alone is sufficient to distribute nutrient molecules.

The digestive tract of a planarian is notable for its lack of specialized parts. It is saclike because the pharynx serves not only as an entrance for food but also as an exit for undigestible material. Specialization of parts does not occur under these circumstances.

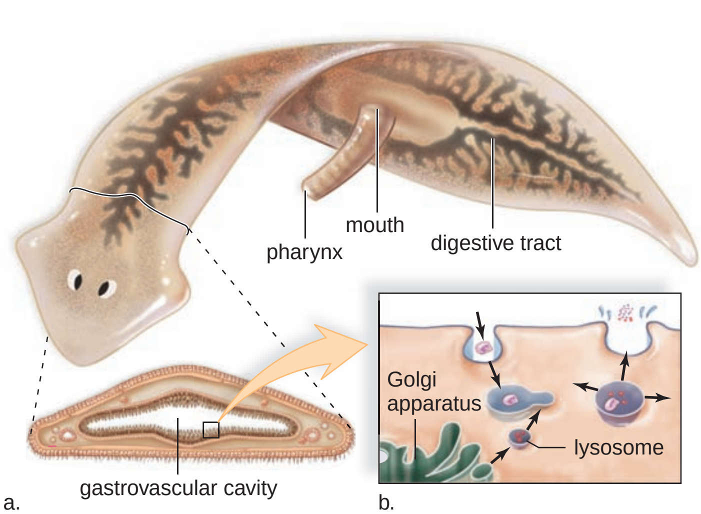


FIGURE 34.1 Incomplete digestive tract of a planarian.

a. Planarians, which are flatworms, have a gastrovascular cavity with a single opening that acts as both an entrance and an exit. Like hydra, planarians rely on intracellular digestion to complete the digestive process. **b.** Phagocytosis produces a vacuole, which joins with an enzyme-containing lysosome. The digested products pass from the vacuole into the cytoplasm before any undigestible material is eliminated at the plasma membrane.

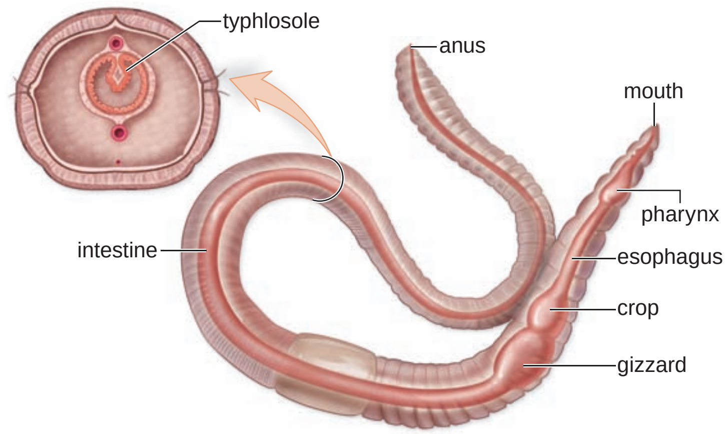


FIGURE 34.2 Complete digestive tract of an earthworm.

Complete digestive tracts have both a mouth and an anus and can have many specialized parts, such as those labeled in this drawing. Also in earthworms, which are annelids, the absorptive surface of the intestine is increased by an internal fold called the typhlosole.

Planarians have some modified parasitic relatives. Tapeworms, which are parasitic flatworms, lack a digestive system. Nutrient molecules are absorbed by the tapeworm from the intestinal juices of the host, which surround the tapeworm's body. The integument and body wall of the tapeworm are highly modified for this purpose. They have millions of microscopic, fingerlike projections that increase the surface area for absorption.

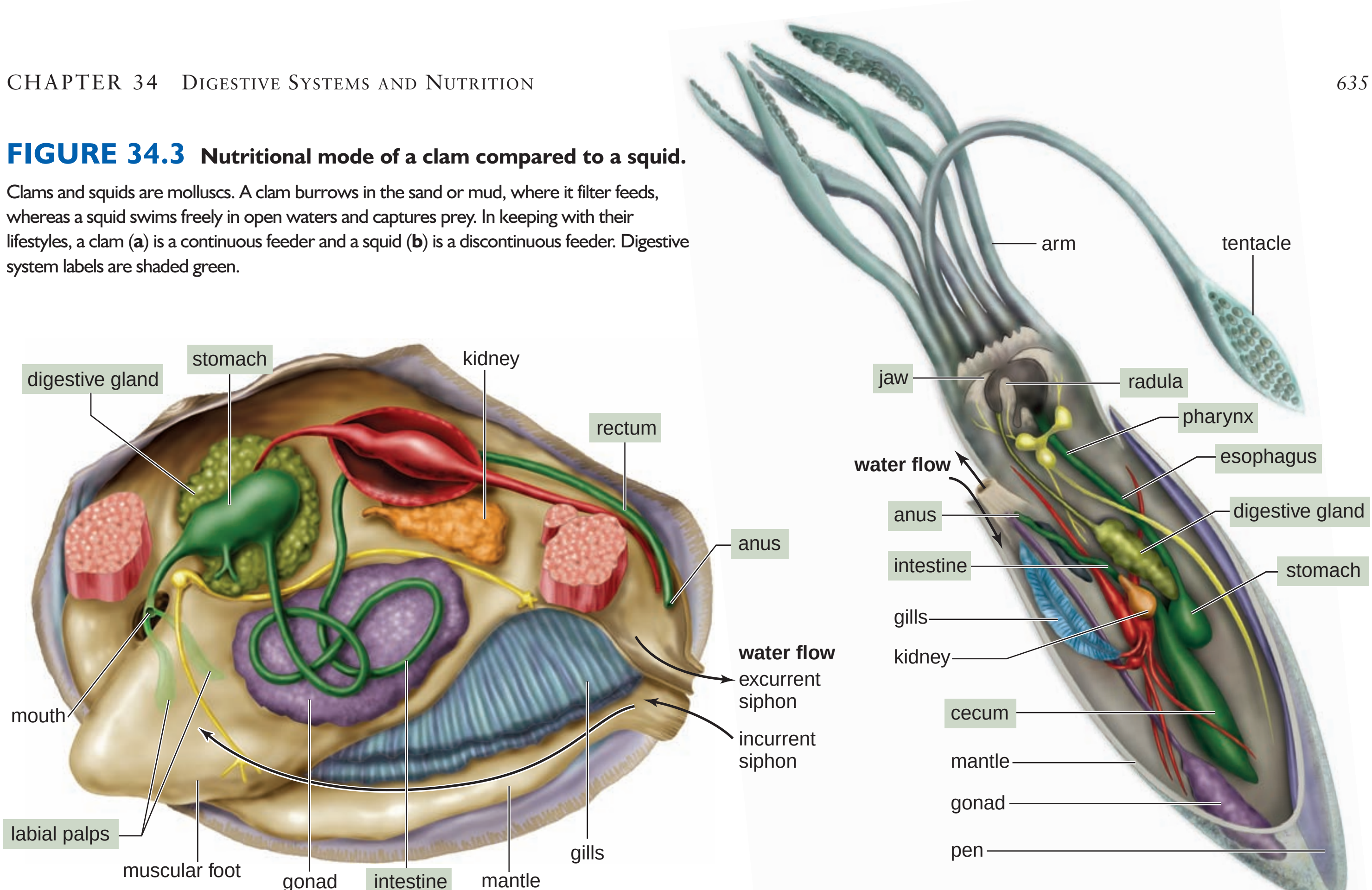
In contrast to planarians, earthworms, which are annelids, have a **complete digestive tract,** meaning that the tract has a mouth and an anus (Fig. 34.2). Earthworms feed mainly on decayed organic matter in soil. The muscular pharynx draws in food with a sucking action. Food then enters the crop, which is a storage area with thin, expansive walls. From there, food goes to the gizzard, where thick, muscular walls crush and sand grinds the food. Digestion is extracellular within an intestine. The surface area of digestive tracts is often increased for absorption of nutrient molecules, and in earthworms, this is accomplished by an intestinal fold called the **typhlosole.** Undigested remains pass out of the body at the anus. Specialization of parts is obvious in the earthworm because the pharynx, the crop, the gizzard, and the intestine each has a particular function in the digestive process.

Continuous Versus Discontinuous Feeders

Clams, which are molluscs, are continuous feeders, called filter feeders (Fig. 34.3*a*). Water is always moving into the mantle cavity by way of the incurrent siphon (slitlike opening) and depositing particles, including algae, protozoans, and minute invertebrates, on the gills. The size of the incurrent siphon permits the entrance of only small particles, which adhere to the gills. Ciliary action moves suitably sized particles to the labial palps, which force them through the mouth into the stomach. Digestive enzymes are secreted by a large digestive gland, but amoeboid cells present throughout the tract are believed to complete the digestive process by intracellular digestion.

FIGURE 34.3 Nutritional mode of a clam compared to a squid.

Clams and squids are molluscs. A clam burrows in the sand or mud, where it filter feeds, whereas a squid swims freely in open waters and captures prey. In keeping with their lifestyles, a clam (**a**) is a continuous feeder and a squid (**b**) is a discontinuous feeder. Digestive system labels are shaded green.



a. Digestive system (green) of clam

b. Digestive system (green) of squid

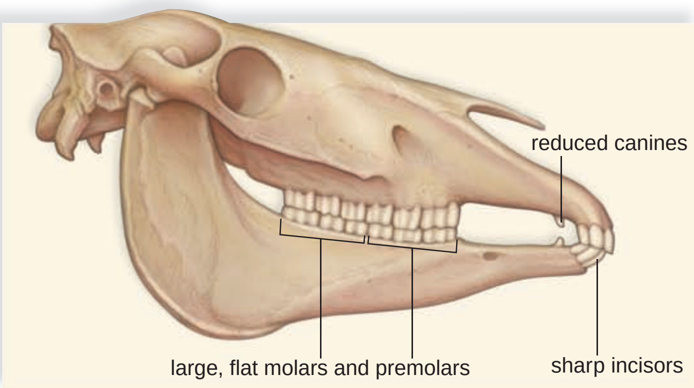
Marine fanworms, which are annelids, are continuous filter feeders. The ciliated appendages of these worms are specialized for gathering fine particles and microscopic plankton from the water. They allow only small particles to enter the mouth. Larger particles are rejected. A baleen whale, such as a blue whale, is an active filter feeder. Baleen, a keratinized curtainlike fringe, hangs from the roof of the mouth and filters small shrimp called krill from the water. A baleen whale filters up to a ton of krill every few minutes.

Squids, which are molluscs, are discontinuous feeders (Fig. 34.3*b*). The body of a squid is streamlined, and the animal moves rapidly through the water using jet propulsion (forceful expulsion of water from a tubular funnel). The head of a squid is surrounded by ten arms, two of which have developed into long, slender tentacles whose suckers have toothed, horny rings. These tentacles seize prey (fishes, shrimps, and worms) and bring it to the squid's beaklike jaws, which bite off pieces pulled into the mouth by the action of a **radula,** a tonguelike structure. An esophagus leads to a stomach and a cecum (blind sac), where digestion occurs. The stomach, supplemented by the cecum, retains food until digestion is complete. Discontinuous feeders, whether they are carnivores, like blue herons, or herbivores, like elephants, require a storage area for food, which can be a crop, where no digestion occurs, or a stomach, where digestion begins.

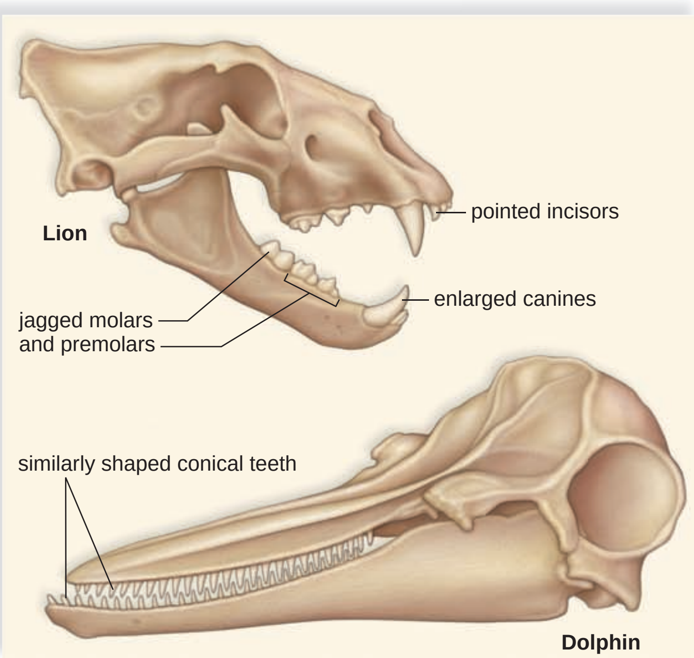
Adaptation to Diet

Some animals are omnivores; they eat both plants and animals. Others are herbivores; they feed only on plants. Still others are carnivores; they eat only other animals. Among invertebrates, filter feeders such as clams and tube worms are omnivores. Land snails, which are terrestrial molluscs, and some insects, such as grasshoppers and locusts, are herbivores. Spiders (arthropods) are carnivores, as are sea stars (echinoderms), which feed on clams. A sea star positions itself above a clam and uses its tube feet to pull the valves of the shell apart (see Fig. 28.27). Then, it everts a part of its stomach to start the digestive process, even while the clam is trying to close its shell. Some invertebrates are cannibalistic. A female praying mantis (an insect), if starved, will feed on her mate as the reproductive act is taking place!

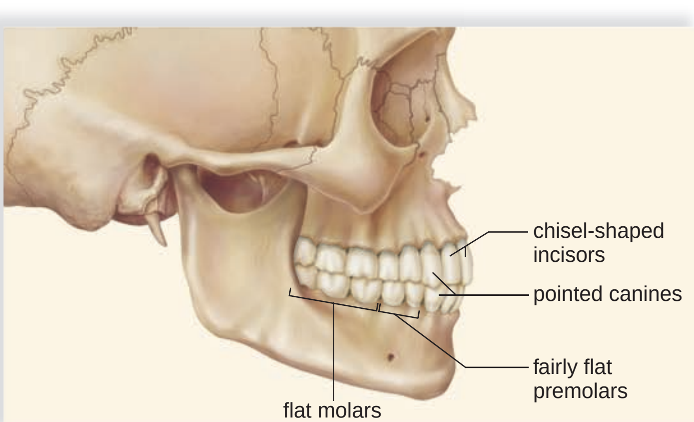
Among mammals, the dentition differs according to mode of nutrition. Among herbivores, the koala of Australia is famous for its diet of only eucalyptus leaves, and likewise many other mammals are browsers, feeding off bushes and trees. Grazers, like the horse, feed off grasses. The horse has sharp, even incisors for neatly clipping off blades of grass and large, flat premolars and molars for grinding and crushing the grass (Fig. 34.4*a*). Extensive grinding and crushing disrupts plant cell walls, allowing bacteria located in a part of the digestive tract called the cecum to digest cellulose. Other mammalian grazers, such as cattle, sheep, and deer, are ruminants with a large, four-chambered stomach. In contrast to horses, they graze quickly and swallow partially chewed grasses into a special part of the stomach called a **rumen.** Here, microorganisms start the digestive process, and the result, called cud, is regurgitated at a later time when the animal is no longer feeding. The cud is chewed again before being swallowed for complete digestion.



a. Horses are herbivores.



b. Lions and dolphins are carnivores.



c. Humans are omnivores.

FIGURE 34.4 Dentition among mammals.

a. Horses are herbivores and have teeth suitable to clipping and chewing grass. **b.** Lions and dolphins are carnivores. Dentition in a lion is suitable for killing large animals such as zebras and wildebeests and tearing apart their flesh. Dentition in a dolphin is suitable to grasping small animals like fishes, which are swallowed whole. **c.** Humans are omnivores and have teeth suitable to a mixed diet of vegetables and meat.

Many mammals, including dogs, lions, toothed whales, and dolphins, are carnivores. Lions use pointed canine teeth for killing, short incisors for scraping bones, and pointed molars for slicing flesh (Fig. 34.4*b*, *top*). Dolphins and toothed whales swallow food whole without chewing it first; they are equipped with many identical, conical teeth that are used to catch and grasp their slippery prey before swallowing (Fig. 34.4*b*, *bottom*). Meat is rich in protein and fat and is easier to digest than plant material. The intestine of a rabbit, a herbivore, is much longer than that of a similarly sized cat, a carnivore.

Humans, as well as raccoons, rats, and brown bears, are omnivores. Therefore, the dentition has a variety of specializations to accommodate both a vegetable diet and a meat diet. An adult human has 32 teeth. One-half of each jaw has teeth of four different types: two chisel-shaped incisors for shearing; one pointed canine for tearing; two fairly flat premolars for grinding; and three molars, well flattened for crushing (Fig. 34.4*c*).

Check Your Progress 34.1

1. A complete digestive tract can have many specialized parts. Explain.
2. Discontinuous feeders, but not continuous feeders, tend to have a storage area for food. Explain.
3. Compare the teeth of carnivores to those of herbivores.

34.2 Human Digestive Tract

Humans have a tube-within-a-tube body plan and a complete digestive tract, which begins with a mouth and ends in an anus. The major structures of the human digestive tract are illustrated in Figure 34.5. The pancreas, liver, and gallbladder are accessory organs of digestion, and they produce secretions that aid digestion.

The digestion of food in humans is an extracellular event. Digestion requires a cooperative effort between different parts of the body. Digestion consists of two major stages: mechanical digestion and chemical digestion. Mechanical digestion involves the physical breakdown of food into smaller particles. This is accomplished through the chewing of food in the mouth and the physical churning and mixing of food in the stomach and small intestine. Chemical digestion requires enzymes that are secreted by the digestive tract or by accessory glands that lie nearby. Specific enzymes break down particular macromolecules into smaller molecules that can be absorbed.

Mouth

The **mouth,** or oral cavity, serves as the beginning of the digestive tract. The palate, or roof of the mouth, separates the oral cavity from the nasal cavity. It consists of the anterior hard palate and the posterior soft palate. The fleshy uvula is the posterior extension of the soft palate (see Fig. 34.6). The cheeks and lips retain food while it is chewed by the teeth and mixed with saliva.

There are three major pairs of **salivary glands** that send their juices by way of ducts to the mouth. Saliva contains

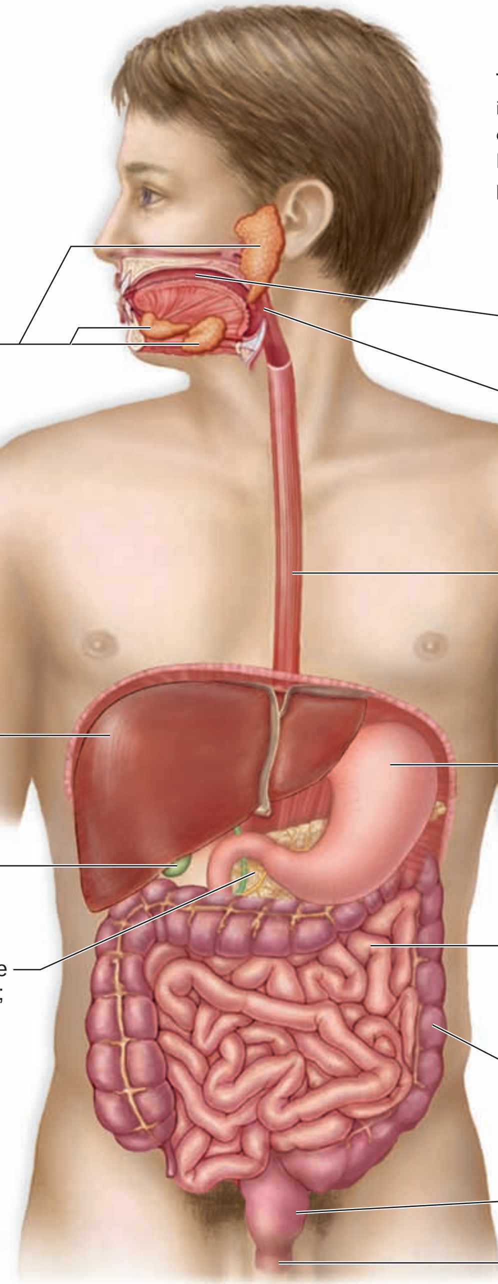


FIGURE 34.5 The human digestive tract.

Trace the path of food from the mouth to the anus. The large intestine consists of the cecum, the colon (ascending, transverse, descending, and sigmoid colons), the rectum, and the anus. Note also the location of the accessory organs of digestion: the pancreas, the liver, and the gallbladder.

the enzyme **salivary amylase,** which begins the process of starch digestion. The disaccharide maltose is a typical end product of salivary amylase digestion.

$$\text{starch} + H_2O \xrightarrow{\text{salivary amylase}} \text{maltose}$$

While in the mouth, food is manipulated by a muscular tongue, which has touch and pressure receptors similar to those in the skin. Taste buds, sensory receptors that are stimulated by the chemical composition of food, are also found primarily on the tongue as well as on the surface of the mouth. The tongue, which is composed of striated muscle and an outer layer of mucous membrane, mixes the chewed food with saliva. It then forms this mixture into a mass called a bolus in preparation for swallowing.

The Pharynx and the Esophagus

The digestive and respiratory passages come together in the **pharynx** and then separate. The **esophagus** [Gk. *eso,* within, and *phagein,* eat] is a tubular structure, of about 25 cm in length, that takes food to the stomach. Sphincters are muscles that encircle tubes and act as valves; tubes close when sphincters contract, and they open when sphincters relax. The lower gastroesophageal sphincter is located where the esophagus enters the stomach. When food enters the stomach, the sphincter relaxes for a few seconds and then it closes again. Heartburn occurs due to acid reflux, when some of the stomach's contents escape into the esophagus. When vomiting occurs, the abdominal muscles and the diaphragm, a muscle that separates the thoracic and abdominal cavities, contract.

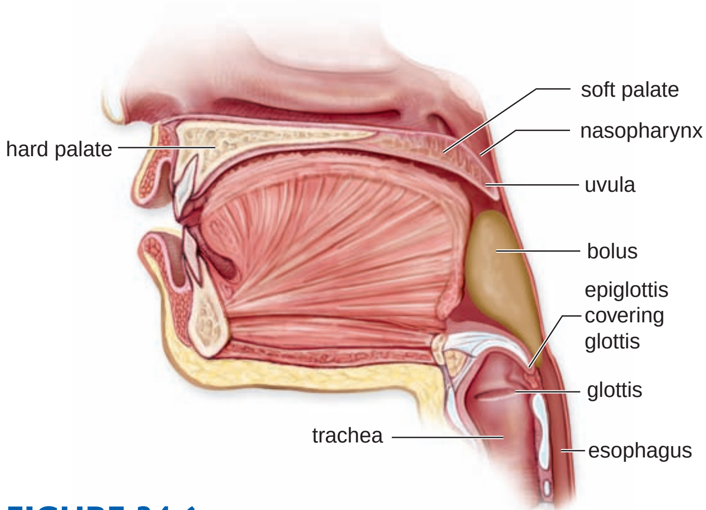


FIGURE 34.6 **Swallowing.**

Respiratory and digestive passages converge and diverge in the pharynx. When food is swallowed, the soft palate closes off the nasopharynx, and the epiglottis covers the glottis, forcing the bolus to pass down the esophagus. Therefore, a person does not breathe when swallowing.

When food is swallowed, the soft palate, the rear portion of the mouth's roof, moves back to close off the nasopharynx. A flap of tissue called the epiglottis covers the glottis, an opening into the trachea. Now the bolus must move through the pharynx into the esophagus because the air passages are blocked (Fig. 34.6). When food enters the esophagus, peristalsis begins. **Peristalsis** [Gk. *peri,* around, and *stalsis,* compression] is a rhythmical contraction that serves to move the contents along in tubular organs, such as the digestive tract (Fig. 34.7).

Stomach

The **stomach** is a thick-walled, J-shaped organ that lies on the left side of the body beneath the diaphragm. The wall of the stomach has deep folds (rugae) that disappear as the stomach fills to an approximate capacity of 1 liter. Therefore, humans can periodically eat relatively large meals and spend the rest of their time at other activities.

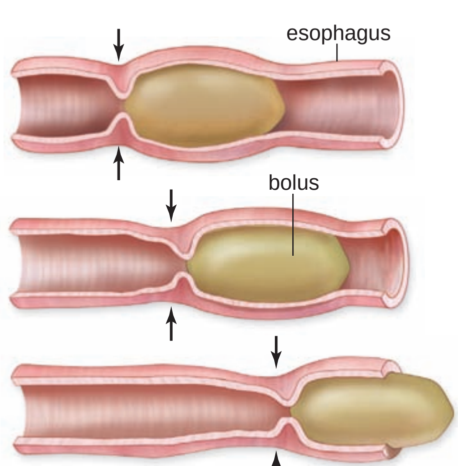


FIGURE 34.7 **Peristalsis in the digestive tract.**

These three drawings show how a peristaltic wave moves through a single section of the esophagus over time. The arrows point to areas of contraction.

The stomach (Fig. 34.8) is much more than a storage organ, as was discovered by William Beaumont in the mid-nineteenth century. Beaumont, an American doctor, had a French Canadian patient, Alexis St. Martin. St. Martin had been shot in the stomach, and when the wound healed, he was left with a fistula, or opening, that allowed Beaumont to look inside the stomach and to collect gastric (stomach) juices produced by gastric glands. Beaumont was able to determine that the muscular walls of the stomach contract vigorously and mix food with juices that are secreted whenever food enters the stomach. He found that gastric juice contains hydrochloric acid (HCl) and a substance, now called pepsin, that is active in digestion. He also found that the gastric juices are produced independently of the protective mucous secretions of the stomach. Beaumont's work, which was carefully and painstakingly done, pioneered the study of digestive physiology.

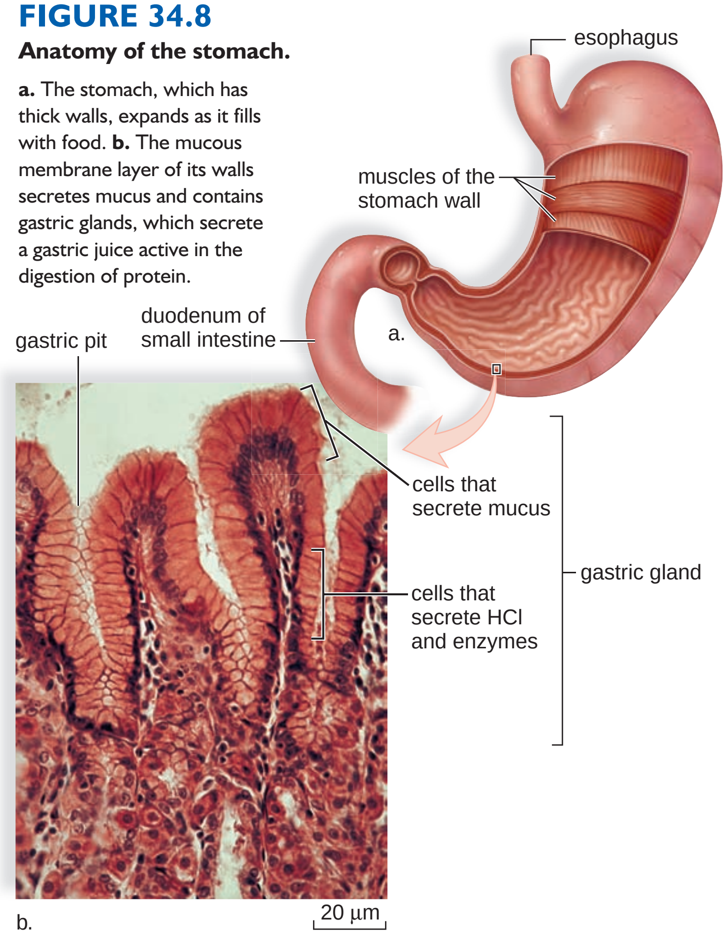
The epithelial lining of the stomach has millions of gastric pits, which lead into gastric glands. The gastric glands produce gastric juice. So much hydrochloric acid is secreted by the gastric glands that the stomach routinely has a pH of about 2. Such a high acidity usually is sufficient to kill bacteria and other microorganisms that might be in food. This low pH also stops the activity of salivary amylase, which functions optimally at the near-neutral pH of saliva.

As with the rest of the digestive tract, a thick layer of mucus protects the wall of the stomach from enzymatic action. Still, an ulcer, which is an open sore in the wall caused by the gradual destruction of tissues, does occur in some

FIGURE 34.8

Anatomy of the stomach.

a. The stomach, which has thick walls, expands as it fills with food. **b.** The mucous membrane layer of its walls secretes mucus and contains gastric glands, which secrete a gastric juice active in the digestion of protein.



individuals. Ulcers can be caused by an infection by an acid-resistant bacterium, *Helicobacter pylori,* which is able to attach to the epithelial lining. Wherever the bacterium attaches, the lining stops producing mucus, and the area becomes exposed to digestive action. As a result, an ulcer develops.

Eventually, food mixing with gastric juice in the stomach contents become **chyme,** which has a thick, creamy consistency. At the base of the stomach is a narrow opening controlled by a sphincter. A sphincter is a muscle that surrounds a tube and closes or opens the tube by contracting and relaxing. Whenever the sphincter relaxes, a small quantity of chyme passes through the opening into the small intestine. When chyme enters the small intestine, it sets off a neural reflex that causes the muscles of the sphincter to contract vigorously and to close the opening temporarily. Then the sphincter relaxes again and allows more chyme to enter. The slow manner in which chyme enters the small intestine allows for thorough digestion.

The Small Intestine

The **small intestine** is named for its small diameter (compared to that of the large intestine), but perhaps it should be called the long intestine. The small intestine averages about 6 m in length, compared to the large intestine, which is about 1.5 m in length.

The first 25 cm of the small intestine is called the **duodenum.** A duct brings bile from the liver and gallbladder, and pancreatic juice from the pancreas, into the small intestine (see Fig. 34.11*a*). **Bile** emulsifies fat—emulsification causes fat droplets to disperse in water. The intestine has a slightly basic pH because pancreatic juice contains sodium bicarbonate ($NaHCO_3$), which neutralizes chyme. The enzymes in pancreatic juice and enzymes produced by the intestinal wall complete the process of food digestion.

It has been suggested that the surface area of the small intestine is approximately that of a tennis court. What factors contribute to increasing its surface area? The wall of the small intestine contains fingerlike projections called villi (sing., **villus**), which give the intestinal wall a soft, velvety appearance (Fig. 34.9). A villus has an outer layer of columnar epithelial cells, and each of these cells has thousands of microscopic extensions called microvilli. Collectively, in electron micrographs, microvilli give the villi a fuzzy border, known as a "brush border." Since the microvilli bear the intestinal enzymes, these enzymes are called brush-border enzymes. The microvilli greatly increase the surface area of the villus for the absorption of nutrients.

Nutrients are absorbed into the vessels of a villus, which contains blood capillaries and a lymphatic capillary, called a **lacteal.** Sugars (digested from carbohydrates) and amino acids (digested from proteins) enter the blood capillaries of a villus. Glycerol and fatty acids (digested from fats) enter the epithelial cells of the villi, and within these cells they are joined and packaged as lipoprotein droplets, which enter a lacteal. After nutrients are absorbed, they are eventually carried to all the cells of the body by the bloodstream.

Large Intestine

The **large intestine,** which includes the cecum, the colon, the rectum, and the anus, is larger in diameter (6.5 cm) but shorter in length (1.5 m) than the small intestine. The large intestine absorbs water, salts, and some vitamins. It also stores undigestible material until it is eliminated at the anus. No digestion takes place in the large intestine.

The cecum, which lies below the junction with the small intestine, is the blind end of the large intestine. The cecum has a small projection called the vermiform **appendix** [L. *verm,* worm, and *form,* shape, and *append,* an addition] (Fig. 34.10). In humans, the appendix may play a role in fighting infections. In the case of appendicitis, the appendix becomes infected and so filled with fluid that it may burst. If an infected appendix bursts before it can be removed, it can lead to a serious, generalized infection of the abdominal lining, called peritonitis.

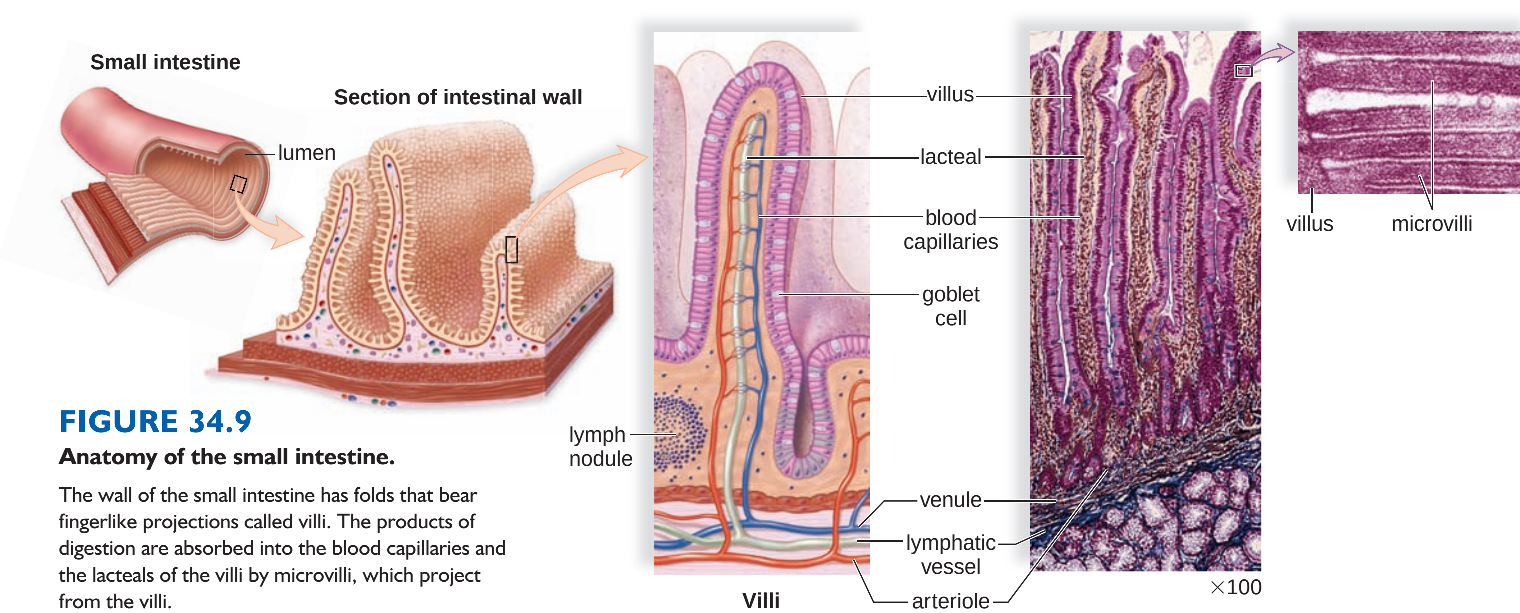


FIGURE 34.9
Anatomy of the small intestine.
The wall of the small intestine has folds that bear fingerlike projections called villi. The products of digestion are absorbed into the blood capillaries and the lacteals of the villi by microvilli, which project from the villi.

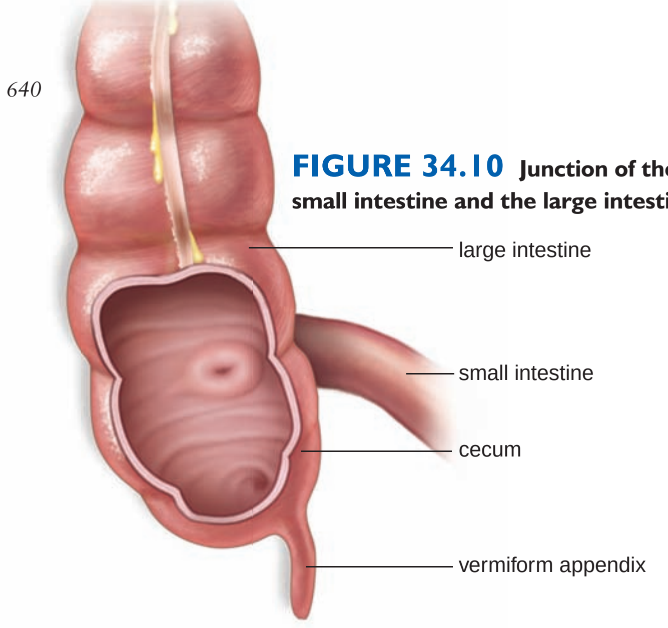


FIGURE 34.10 **Junction of the small intestine and the large intestine.**

The colon joins the rectum, the last 20 cm of the large intestine. About 1.5 liters of water enters the digestive tract daily as a result of eating and drinking. An additional 8.5 liters enter the digestive tract each day carrying the various substances secreted by the digestive glands. About 95% of this water is absorbed by the small intestine, and much of the remaining portion is absorbed by the colon. If this water is not reabsorbed, **diarrhea** can lead to serious dehydration and ion loss, especially in children.

The large intestine has a large population of bacteria, notably *Escherichia coli.* The bacteria break down undigestible material, and they also produce some vitamins, such as vitamin K. Vitamin K is necessary to blood clotting. Digestive wastes (feces) eventually leave the body through the **anus,** the opening of the anal canal. Feces are about 75% water and 25% solid matter. Almost one-third of this solid matter is made up of intestinal bacteria. The remainder is undigested plant material, fats, waste products (such as bile pigments), inorganic material, mucus, and dead cells from the intestinal lining. The color of feces is the result of bilirubin breakdown and the presence of oxidized iron. The foul odor is the result of bacterial action.

The colon is subject to the development of **polyps,** which are small growths arising from the mucosa. Polyps, whether they are benign or cancerous, can be removed surgically. Some investigators believe that dietary fat increases the likelihood of colon cancer. Dietary fat causes an increase in bile secretion, and it could be that intestinal bacteria convert bile salts to substances that promote the development of colon cancer. Dietary fibers absorb water and add bulk, thereby diluting the concentration of bile salts and facilitating the movement of substances through the intestine. Regular elimination reduces the time that the colon wall is exposed to any cancer-promoting agents in feces.

Check Your Progress 34.2A

1. Trace the path of food from the mouth to the large intestine.
2. What are the functions of the small intestine, and how is the wall of the small intestine modified to perform these functions?

Three Accessory Organs

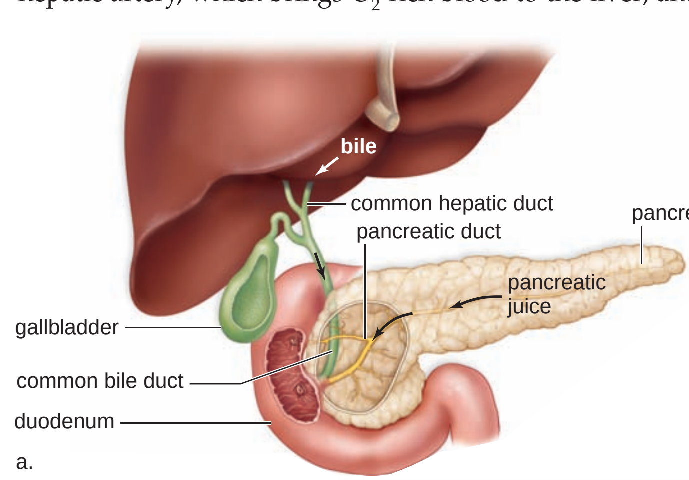
The pancreas, liver, and gallbladder are accessory digestive organs. Figure 34.11*a* shows how the pancreatic duct from the pancreas and the common bile duct from the liver and gallbladder enter the duodenum.

The Pancreas

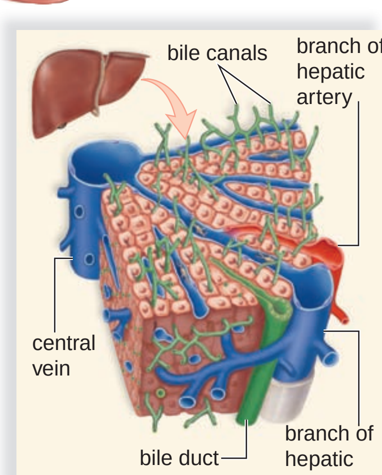
The **pancreas** lies deep in the abdominal cavity, resting on the posterior abdominal wall. It is an elongated and somewhat flattened organ that has both an endocrine and an exocrine function. As an endocrine gland, it secretes insulin and glucagon, hormones that help keep the blood glucose level within normal limits. In this chapter, however, we are interested in its exocrine function. Most pancreatic cells produce pancreatic juice, which contains sodium bicarbonate ($NaHCO_3$) and digestive enzymes for all types of food. Sodium bicarbonate neutralizes acid chyme from the stomach. Pancreatic amylase digests starch, trypsin digests protein, and lipase digests fat.

The Liver

The **liver,** which is the largest gland in the body, lies mainly in the upper right section of the abdominal cavity, under the diaphragm (see Fig. 34.5). The liver contains approximately 100,000 lobules that serve as its structural and functional units (Fig. 34.11*b*). Triads, located between the lobules, consist of a bile duct, which takes bile away from the liver; a branch of the hepatic artery, which brings O_2-rich blood to the liver; and a



a.



b.

FIGURE 34.11 **Liver, gallbladder, and pancreas.**

a. The liver makes bile, which is stored in the gallbladder and sent (black arrow) to the small intestine by way of the common bile duct. The pancreas produces digestive enzymes that are sent (black arrows) to the small intestine by way of the pancreatic duct. **b.** The liver contains over 100,000 lobules. Each lobule contains many cells that perform the various functions of the liver. They remove and add materials to the blood and deposit bile in a duct.

health focus

Wall of the Digestive Tract

We can compare the human digestive tract to a garden hose that has a beginning (mouth) and an end (anus). The so-called **lumen** is the central space where food is digested. The wall of the digestive tract has four layers (Fig. 34A), and we will associate each layer with a particular disorder.

The first layer of the wall next to the lumen is called the **mucosa.** The mucosa is more familiarly called a mucous membrane and, of course, it produces mucus, which protects the wall from the digestive enzymes inside the lumen. In the mouth, stomach, and small intestine, the mucosa either contains glands that secrete and/or receive digestive enzymes from glands that secrete digestive enzymes.

Diverticulosis is a condition in which portions of the mucosa literally have pushed through the other layers and formed pouches, where food can collect. The pouches can be likened to an inner tube that pokes through weak places in a tire. When the pouches become infected or inflamed, the condition is called *diverticulitis.* This happens in 10–25% of people with diverticulosis.

The second layer in the digestive wall is called the **submucosa.** The submucosal layer is a broad band of loose connective tissue that contains blood vessels, lymphatic vessels, and nerves. These are the vessels that will carry the nutrients absorbed by the mucosa. Lymph nodules, called Peyer's patches, are also in the submucosa. Like the tonsils, they help protect us from disease. Because the submucosa contains blood vessels, it can be the site of an inflammatory response that leads to *inflammatory bowel disease (IBD),* characterized by chronic diarrhea, abdominal pain, fever, and weight loss.

The third layer is termed the **muscularis,** and it contains two layers of smooth muscle. The inner, circular layer encircles the tract; the outer, longitudinal layer lies in the same direction as the tract. The contraction of these muscles, which are under nervous control, accounts for movement of digested food from the esophagus to the anus. The muscularis can be associated with *irritable bowel syndrome (IBS),* in which contractions of the wall cause abdominal pain, constipation, and/or diarrhea. The underlying cause of IBS is not known, although some suggest stress as an underlying cause.

The fourth layer of the tract is the **serosa** (serous membrane layer), which secretes a serous fluid. The serosa is a part of the peritoneum, the internal lining of the abdominal cavity. The appendix is a worm-shaped blind tube projecting from the first part of the large intestine on the right side of the abdomen. An inflamed appendix (*appendicitis*) has to be removed because, should the appendix burst, the result can be *peritonitis,* a life-threatening infection of the peritoneum.

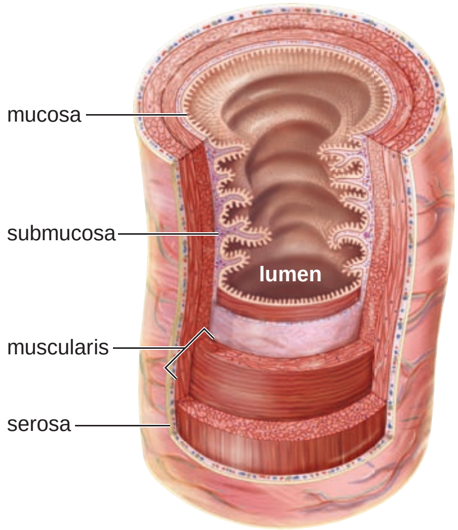


FIGURE 34A Wall of the digestive tract. *The wall of the digestive tract contains the four layers noted.*

branch of the hepatic portal vein, which transports nutrients from the intestines (see Fig. 32.10). The central veins of lobules enter a hepatic vein. Blood moves from the intestines to the liver via the hepatic portal vein and from the liver to the inferior vena cava via the hepatic veins.

In some ways, the liver acts as the gatekeeper to the blood (Table 34.1). As blood in the hepatic portal vein passes through the liver, it removes poisonous substances and detoxifies them. The liver also removes and stores iron and the vitamins A, B_{12}, D, E, and K. The liver makes the plasma proteins and helps regulate the quantity of cholesterol in the blood.

The liver maintains the blood glucose level at about 100 mg/100 ml (0.1%), even though a person eats intermittently. When insulin is present, any excess glucose present in blood is removed and stored by the liver as glycogen. Between meals, glycogen is broken down to glucose, which enters the hepatic veins, and in this way, the blood glucose level remains constant.

If the supply of glycogen is depleted, the liver converts glycerol (from fats) and amino acids to glucose molecules. The conversion of amino acids to glucose necessitates deamination, the removal of amino groups. By a complex metabolic pathway, the liver then combines ammonia with carbon dioxide to form urea. Urea is the usual nitrogenous waste product from amino acid breakdown in humans.

The liver produces bile, which is stored in the gallbladder. Bile has a yellowish green color because it contains the bile pigment *bilirubin,* derived from the breakdown of hemoglobin, the red pigment of red blood cells. Bile also contains bile salts.

TABLE 34.1

Functions of the Liver

1. Detoxifies blood by removing and metabolizing poisonous substances
2. Stores iron and the vitamins A, B_{12}, D, E, and K
3. Makes plasma proteins, such as albumins and fibrinogen, from amino acids
4. Stores glucose as glycogen after a meal, and breaks down glycogen to glucose to maintain the glucose level of blood between eating periods
5. Produces urea after breaking down amino acids
6. Removes bilirubin, a breakdown product of hemoglobin from the blood, and excretes it in bile, a liver product
7. Helps regulate blood cholesterol level, converting some to bile salts

Bile salts are derived from cholesterol, and they emulsify fat in the small intestine. When fat is emulsified, it breaks up into droplets, providing a much larger surface area, which can be acted upon by a digestive enzyme from the pancreas.

Liver Disorders. Hepatitis and cirrhosis are two serious diseases that affect the entire liver and hinder its ability to repair itself. Therefore, they are life-threatening diseases. When a person has a liver ailment, jaundice may occur. **Jaundice** is present when the skin and the whites of the eyes have a yellowish tinge. Jaundice occurs because bilirubin is deposited in the skin, due to an abnormally large amount in the blood. Jaundice can also result from **hepatitis,** inflammation of the liver. Viral hepatitis occurs in several forms. Hepatitis A is usually acquired from sewage-contaminated drinking water. Hepatitis B, which is usually spread by sexual contact, can also be spread by blood transfusions or contaminated needles. The hepatitis B virus is more contagious than the AIDS virus, which is spread in the same way. Thankfully, however, a vaccine is now available for hepatitis B. Hepatitis C, which is usually acquired by contact with infected blood and for which there is no vaccine, can lead to chronic hepatitis, liver cancer, and death.

Cirrhosis is another chronic disease of the liver. First, the organ becomes fatty, and then liver tissue is replaced by inactive fibrous scar tissue. Cirrhosis of the liver is often seen in alcoholics, due to malnutrition and to the excessive amounts of alcohol (a toxin) the liver is forced to break down.

The liver has amazing regenerative powers and can recover if the rate of regeneration exceeds the rate of damage. During liver failure, however, there may not be enough time to let the liver heal itself. Liver transplantation is usually the preferred treatment for liver failure, but artificial livers have been developed and tried in a few cases. One type is a cartridge that contains liver cells. The patient's blood passes through the cellulose acetate tubing of the cartridge and is serviced in the same manner as with a normal liver.

The Gallbladder

The **gallbladder** is a pear-shaped, muscular sac attached to the surface of the liver (see Fig. 34.5). About 1,000 ml of bile are produced by the liver each day, and any excess is stored in the gallbladder. Water is reabsorbed by the gallbladder so that bile becomes a thick, mucuslike material. When needed, bile leaves the gallbladder and proceeds to the duodenum via the common bile duct.

The cholesterol content of bile can come out of solution and form crystals. If the crystals grow in size, they form gallstones. The passage of the stones from the gallbladder may block the common bile duct and cause obstructive jaundice. Then, the gallbladder must be removed.

Check Your Progress 34.2B

1. What are the three main accessory organs that assist with the digestive process?
2. How does each accessory organ contribute to the digestion of food?

34.3 Digestive Enzymes

The various digestive enzymes present in the digestive juices, mentioned previously, help break down carbohydrates, proteins, nucleic acids, and fats, the major components of food. Starch is a polysaccharide, and its digestion begins in the mouth. Saliva from the salivary glands has a neutral pH and contains **salivary amylase,** the first enzyme to act on starch.

$$\text{starch} + H_2O \xrightarrow{\text{salivary amylase}} \text{maltose}$$

Maltose molecules cannot be absorbed by the intestine; additional digestive action in the small intestine converts maltose to glucose, which can be absorbed.

Protein digestion begins in the stomach. Gastric juice secreted by gastric glands has a very low pH—about 2—because it contains hydrochloric acid (HCl). Pepsinogen, a precursor that is converted to **pepsin** when exposed to HCl, is also present in gastric juice. Pepsin acts on protein to produce peptides.

$$\text{protein} + H_2O \xrightarrow{\text{pepsin}} \text{peptides}$$

Peptides are usually too large to be absorbed by the intestinal lining, but later they are broken down to amino acids in the small intestine.

Starch, proteins, nucleic acids, and fats are all enzymatically broken down in the small intestine. Pancreatic juice, which enters the duodenum, has a basic pH because it contains sodium bicarbonate ($NaHCO_3$). One pancreatic enzyme, **pancreatic amylase,** digests starch (Fig. 34.12*a*).

$$\text{starch} + H_2O \xrightarrow{\text{pancreatic amylase}} \text{maltose}$$

Another pancreatic enzyme, **trypsin,** digests protein (Fig. 34.12*b*).

$$\text{protein} + H_2O \xrightarrow{\text{trypsin}} \text{peptides}$$

Trypsin is secreted as trypsinogen, which is converted to trypsin in the duodenum.

Maltase and peptidases, enzymes produced by the small intestine, complete the digestion of starch to glucose and protein to amino acids, respectively. Glucose and amino acids are small molecules that cross into the cells of the villi and enter the blood (Fig. 34.12*a*, *b*).

Maltose, a disaccharide that results from the first step in starch digestion, is digested to glucose by **maltase.**

$$\text{maltose} + H_2O \xrightarrow{\text{maltase}} \text{glucose} + \text{glucose}$$

Other disaccharides have their own enzyme and are digested in the small intestine. The absence of any one of these enzymes can cause illness.

Peptides, which result from the first step in protein digestion, are digested to amino acids by **peptidases.**

$$\text{peptides} + H_2O \xrightarrow{\text{peptidases}} \text{amino acids}$$

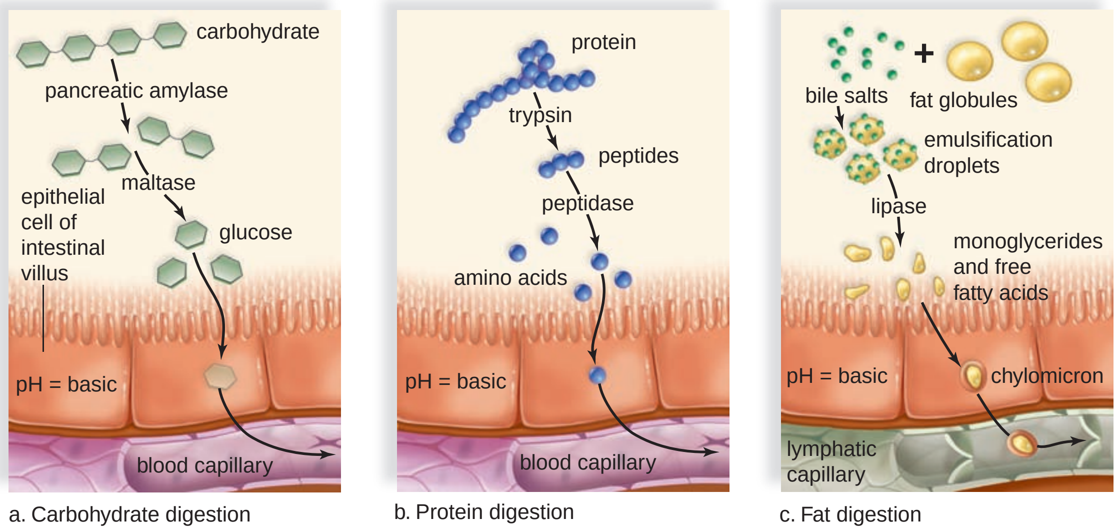


FIGURE 34.12 Digestion and absorption of nutrients.

a. Starch is digested to glucose, which is actively transported into the epithelial cells of intestinal villi. From there, glucose moves into the bloodstream. **b.** Proteins are digested to amino acids, which are actively transported into the epithelial cells of intestinal villi. From there, amino acids move into the bloodstream. **c.** Fats are emulsified by bile and digested to monoglycerides and fatty acids. These diffuse into epithelial cells, where they recombine and join with proteins to form lipoproteins, called chylomicrons. Chylomicrons enter a lacteal.

Lipase, a third pancreatic enzyme, digests fat molecules in fat droplets after they have been emulsified by bile salts.

$$\text{fat} \xrightarrow{\text{bile salts}} \text{fat droplets}$$

$$\text{fat droplets} + H_2O \xrightarrow{\text{lipase}} \text{glycerol} + 3 \text{ fatty acids}$$

Specifically, the end products of lipase digestion are monoglycerides (glycerol + one fatty acid) and fatty acids. These enter the cells of the villi, and within these cells, they are rejoined and packaged as lipoprotein droplets, called chylomicrons. Chylomicrons enter the lacteals (Fig. 34.12*c*).

Check Your Progress 34.3

1. Describe the breakdown and absorption of starch and protein.

34.4 Nutrition

This part of the chapter discusses the benefits of a balanced diet, which should include all necessary minerals and vitamins.

Carbohydrates

Carbohydrates are present in food in the form of sugars, starch, and fiber. Fruits, vegetables, milk, and honey are natural sources of sugars. Glucose and fructose are monosaccharide sugars, and lactose (milk sugar) and sucrose (table sugar) are disaccharides. After being absorbed from the digestive tract into the bloodstream, all sugars are converted to glucose for transport in the blood and use by cells. Glucose is the preferred direct energy source in cells.

Plants store glucose as starch, and animals store glucose as glycogen. Good sources of starch are beans, peas, cereal grains, and potatoes. Starch is digested to glucose in the digestive tract, and any excess glucose is stored as glycogen. Although other animals likewise store glucose as glycogen in liver or muscle tissue (meat), little is left by the time an animal is eaten for food. Except for honey and milk, which contain sugars, animal foods do not contain carbohydrates.

Fiber includes various undigestible carbohydrates derived from plants. Food sources rich in fiber include beans, peas, nuts, fruits, and vegetables. Whole-grain products are also a good source of fiber, and are therefore more nutritious than food products made from refined grains. During *refinement*, fiber and also vitamins and minerals are removed from grains, so that primarily starch remains. For example, a slice of bread made from whole-wheat flour contains 3 g of fiber; a slice of bread made from refined wheat flour contains less than 1 g of fiber.

Technically, fiber is not a nutrient for humans because it cannot be digested to small molecules that enter the bloodstream. Insoluble fiber, however, adds bulk to fecal material, which stimulates movement in the large intestine, preventing constipation. Soluble fiber combines with bile acids and cholesterol in the small intestine and prevents them from being absorbed. In this way, high-fiber diets may protect against heart disease. The typical American consumes only about 15 g of fiber each day; the recommended daily intake of fiber is 25 g for women and 38 g for men. To increase your fiber intake, eat whole-grain foods, snack on fresh fruits and raw vegetables, and include nuts and beans in your diet (Fig. 34.13).

If you, or someone you know, has lost weight by following the Atkins or South Beach diet, you may think "carbs" are unhealthy and should be avoided. According to nutritionists, however, carbohydrates should supply a large portion of your energy needs. Evidence suggests that Americans are not eating the right kind of carbohydrates. In some countries, the traditional diet is 60–70% high-fiber carbohydrates, and these people have a low incidence of the diseases that plague Americans.

Some nutritionists hypothesize that the high intake of foods that are rich in refined carbohydrates and fructose sweeteners processed from cornstarch may be responsible

FIGURE 34.13 **Fiber-rich foods.**

Plants provide a good source of carbohydrates. They also provide a good source of vitamins, minerals, and fiber when they are not processed (refined).

for the prevalence of obesity in the United States. Because certain foods, such as donuts, cakes, pies, and cookies, are high in both refined carbohydrates and fat, it is difficult to determine which dietary component is responsible for the current epidemic of obesity among Americans. In any case, they are empty-calorie foods that provide sugars but no vitamins or minerals. Nutritionists also point out that consuming too much energy from any source contributes to body fat, which increases a person's risk of obesity and associated illnesses.

Lipids

Like carbohydrates, **triglycerides** (fats and oils) supply energy for cells, but **fat** is stored for the long term in the body. Nutritionists generally recommend that people include unsaturated, rather than saturated, fats in their diets. Two unsaturated fatty acids (alpha-linolenic and linoleic acids) are *essential* in the diet. They can be supplied by eating fatty fish and by including plant oils, such as canola and soybean oils, in the diet. Delayed growth and skin problems can develop in people whose diets lack these essential unsaturated *fatty* acids.

Animal-derived foods, such as butter, meat, whole milk, and cheeses, contain saturated fatty acids. Plant oils contain unsaturated fatty acids; each type of oil has a particular percentage of monounsaturated and polyunsaturated fatty acids.

Cholesterol, a lipid, can be synthesized by the body. Cells use cholesterol to make various compounds, including bile, steroid hormones, and vitamin D. Plant foods do not contain cholesterol; only animal foods such as cheese, egg yolks, liver, and certain shellfish (shrimp and lobster) are rich in cholesterol. Elevated blood cholesterol levels are associated with an increased risk of cardiovascular disease, the number-one killer of Americans. A diet rich in cholesterol and saturated fats increases the risk of cardiovascular disease.

Statistical studies suggest that trans-fatty acids (trans-fats) are even more harmful than saturated fatty acids. Trans-fatty acids arise when unsaturated oils are hydrogenated to produce a solid fat, as in shortening and some margarines. Trans-fatty acids may reduce the function of the plasma membrane receptors that clear cholesterol from the bloodstream. Trans-fatty acids are found in commercially packaged foods, such as cookies and crackers; in commercially fried foods, such as french fries; and in packaged snacks (Fig. 34.14).

Proteins

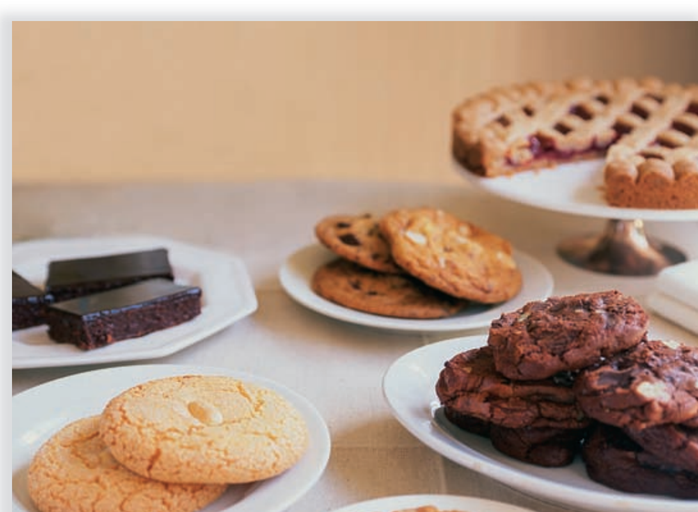
Dietary **proteins** are digested to amino acids, which cells use to synthesize hundreds of cellular proteins. Of the 20 different amino acids, nine are *essential amino acids* that must be present in the diet. Children will not grow if their diets lack the essential amino acids. Eggs, milk products, meat, poultry, and most other foods derived from animals contain all nine essential amino acids and are considered "complete" or "high-quality" protein sources.

Foods derived from plants generally do not have as much protein per serving as those derived from animals, and each type of plant food generally lacks one or more of the essential amino acids. Therefore, most plant foods are "incomplete" or "low-quality" protein sources. Vegetarians, however, do not have to rely on animal sources of protein. To meet their protein needs, total vegetarians (vegans) can eat grains, beans, and nuts in various combinations. Also, tofu, soymilk, and other foods made from processed soybeans are complete protein sources. A balanced vegetarian diet is quite possible with a little planning.

According to nutritionists, protein should not supply the bulk of dietary calories. The average American eats about twice as much protein as he or she needs, and some people may be on a diet that encourages the intake of proteins, instead of carbohydrates, as an energy source. Also, bodybuilders should realize that excess amino acids are not always converted into muscle tissue. When amino acids are broken down, the liver removes the nitrogen portion (*deamination*) and uses it to form urea, which is excreted in urine.

FIGURE 34.14 **Food high in trans-fats.**

Most people enjoy sweets, but cookies and cakes are apt to contain saturated fats and trans-fats.



The water needed for excretion of urea can cause dehydration when a person is exercising and losing water by sweating. High-protein diets can also increase calcium loss in the urine and encourage the formation of kidney stones. Furthermore, high-protein foods often contain a high amount of fat.

Diet and Obesity

Nutritionists point out that consuming too many Calories from any source contributes to body fat, which increases a person's risk of obesity and associated illnesses. (Obesity is defined as weighing 30% more than the ideal body weight for your height and body build.) Still, foods such as donuts, cakes, pies, cookies, and white bread, which are high in refined carbohydrates (starches and sugars), and fried foods, which are high in fat, may very well be responsible for the current epidemic of obesity among Americans. Also implicated is the lack of exercise because of a sedentary lifestyle. Type 2 diabetes and cardiovascular disease are often seen in people who are obese.

Type 2 Diabetes

Diabetes mellitus is indicated by the presence of glucose in the urine. Glucose has spilled over into the urine because there is too high a level of glucose in the blood. Diabetes occurs in two forms. Type 1 diabetes is not associated with obesity. When a person has type 1 diabetes, the pancreas does not produce insulin, and the patient must have daily insulin injections. In contrast, children, and more often adults, with type 2 diabetes are usually obese and display impaired insulin production and insulin resistance. In a person with insulin resistance, the body's cells fail to take up glucose, even when insulin is present. Therefore, the blood glucose level exceeds the normal level, and glucose appears in the urine.

Type 2 diabetes is increasing rapidly in most industrialized countries of the world. A healthy diet, increased physical activity, and weight loss have been seen to improve the ability of insulin to function properly in type 2 diabetics (Fig. 34.15). It is well worth the effort to control type 2 diabetes because all diabetics, whether type 1 or type 2, are at risk for blindness, kidney disease, as well as cardiovascular disease.

FIGURE 34.15 **Exercising for good health.** Regular exercise helps prevent and control type 2 diabetes.

Cardiovascular Disease

In the United States, cardiovascular disease, which includes hypertension, heart attack, and stroke, is among the leading causes of death. Cardiovascular disease is often due to arteries blocked by plaque, which contains saturated fats and cholesterol. Cholesterol is carried in the blood by two types of lipoproteins: low-density lipoprotein (LDL) and high-density lipoprotein (HDL). LDL molecules are considered "bad" because they are like delivery trucks that carry cholesterol from the liver to the cells and to the arterial walls. HDL molecules are considered "good" because they are like garbage trucks that dispose of cholesterol. HDL transports cholesterol from the cells to the liver, which converts it to bile salts that enter the small intestine.

Consuming saturated fats, including trans-fats, tends to raise LDL cholesterol levels, while eating unsaturated fats lowers LDL cholesterol levels. Beef, dairy foods, and coconut oil are rich sources of saturated fat. Foods containing partially hydrogenated oils (e.g., vegetable shortening and stick margarine) are sources of trans-fats. Unsaturated fatty acids in olive and canola oils, most nuts, and coldwater fish tend to lower LDL cholesterol levels. Furthermore, coldwater fish (e.g., herring, sardines, tuna, and salmon) contain polyunsaturated fatty acids and especially *omega-3 unsaturated fatty acids,* which are believed to reduce the risk of cardiovascular disease. However, taking fish oil supplements to obtain omega-3s is not recommended without a physician's approval, because too much of these fatty acids can interfere with normal blood clotting.

The American Heart Association recommends limiting total cholesterol intake to 300 mg per day. This requires careful selection of the foods we include in our daily diets. For example, an egg yolk contains about 210 mg of cholesterol, which would be two-thirds of the recommended daily intake. Still, this doesn't mean eggs should be eliminated from a healthy diet, since the proteins in them are very nutritious; in fact, most healthy people can eat a couple of whole eggs each week without experiencing an increase in their blood cholesterol levels.

A physician can determine whether patients' blood lipid levels are normal. If a person's cholesterol and triglyceride levels are elevated, modifying the fat content of the diet, losing excess body fat, and exercising regularly can reduce them. If lifestyle changes do not lower blood lipid levels enough to reduce the risk of cardiovascular disease, a physician may prescribe special medications.

Vitamins and Minerals

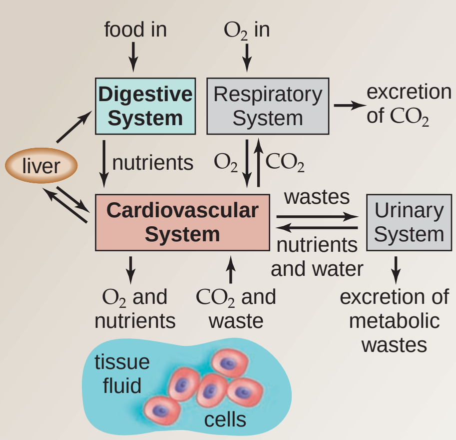
Vitamins are organic compounds (other than carbohydrates, fats, and proteins) that regulate various metabolic activities and must be present in the diet. Many vitamins are part of coenzymes; for example, niacin is the name for a portion of the coenzyme NAD^+, and riboflavin is a part of FAD. Coenzymes are needed in small amounts because they are used over and over again in cells. Not all vitamins are coenzymes; vitamin A, for example, is a precursor for the pigment that prevents night blindness. It has been known for some time that the absence of a vitamin can be associated with a particular disorder. Vitamins are especially abundant in fruits and vegetables, and so it is suggested that we eat about 4 1/2 cups of fruits and vegetables per day. Although many foods are now enriched or fortified with vitamins, some individuals are still at risk for vitamin deficiencies, generally as a result of poor food choices.

The body also needs about 20 elements called **minerals** for various physiological functions, including regulation of biochemical reactions, maintenance of fluid balance, and incorporation into certain structures and compounds. Occasionally individuals (especially women) do not receive enough iron, calcium, magnesium, or zinc in their diets. Adult females need more iron in the diet than males (18 mg compared to 10 mg) if they are menstruating each month. Many people take calcium supplements, as directed by a physician, to counteract osteoporosis, a degenerative bone disease that especially affects older men and women. Many people consume too much sodium, even double the amount needed. Excess sodium can cause water retention and contribute to hypertension.

Check Your Progress 34.4

1. Why is a diet that includes plentiful vegetables better for you than a diet that includes excess protein?
2. How can you decrease your chances of acquiring type 2 diabetes and cardiovascular disease?

Connecting the Concepts



The digestive system consists of the digestive tract with the mouth at one end and the anus at the other end. Food enters the mouth and is digested to small nutrient molecules, which enter the bloodstream at the small intestine. Undigestible residue (feces) exits at the anus.

Digestive juices enter the tract from the salivary glands and the pancreas. The gallbladder also sends bile to the tract for emulsification of fats. Bile is made in the liver, which makes a significant contribution to homeostasis by helping to keep the composition of the blood constant. For example, after eating and under the influence of insulin, the liver stores glucose from the digestive tract as glycogen and releases glucose to the blood in between eating. The liver also removes nitrogenous and other types of injurious molecules from the blood and metabolizes them to excretory products that the bloodstream takes to the kidneys.

Nutrient molecules, such as amino acids, glucose, and vitamins, are absorbed from the small intestine into the blood. Fatty acids and glycerol enter the lacteals, a part of the lymphatic system. Body cells receive these molecules from blood and then build the body's own proteins and carbohydrates. In Chapter 35, we consider the contribution of the respiratory system to homeostasis.

summary

34.1 Digestive Tracts

Some animals (e.g., planarians) have an incomplete digestive tract, so called because there is only one opening. An incomplete tract has little specialization of parts. Other animals (e.g., earthworms) have a complete digestive tract, so called because the tract has both a mouth and an anus. A complete tract tends to have specialization of parts.

Some animals are continuous feeders (e.g., clams, which are filter feeders); others are discontinuous feeders (e.g., squid). Discontinuous feeders need a storage area for food.

Most mammals have teeth. Herbivores need teeth that can clip off plant material and grind it up. Also, the herbivore's stomach contains bacteria that can digest cellulose.

Carnivores need teeth that can tear and rip meat into pieces. Meat is easier to digest than plant material, so the digestive system of carnivores has fewer specialized regions and the intestine is shorter than that of herbivores.

34.2 Human Digestive Tract

In the human digestive tract, food is chewed and manipulated in the mouth, where salivary glands secrete saliva. Saliva contains salivary amylase, which begins carbohydrate digestion.

Food then passes to the pharynx and down the esophagus by peristalsis to the stomach. The stomach stores and mixes food with mucus and gastric juices to produce chyme. Pepsin begins protein digestion in the stomach.

The duodenum of the small intestine receives bile from the liver and pancreatic juice from the pancreas. Bile emulsifies fat and readies it for digestion by an enzyme produced by the pancreas. The pancreas also produces enzymes that digest starch and protein. The intestinal enzymes finish the process of chemical digestion.

The walls of the small intestine have fingerlike projections called villi where small nutrient molecules are absorbed. Amino acids and glucose enter the blood vessels of a villus. Glycerol and fatty acids are joined and packaged as lipoproteins before entering lymphatic vessels called lacteals in a villus.

The large intestine consists of the cecum, the colon, and the rectum, which ends at the anus. The large intestine does not produce digestive enzymes; it does absorb water, salts, and some vitamins. Reduced water absorption results in diarrhea. The intake of water and fiber help prevent constipation.

Three accessory organs of digestion—the pancreas, liver, and gallbladder—send secretions to the duodenum via ducts. The pancreas produces pancreatic juice, which contains digestive enzymes for carbohydrates, protein, and fat.

The liver produces bile, which is stored in the gallbladder. The liver receives blood from the small intestine by way of the hepatic portal vein. It has numerous important functions, and any malfunction of the liver is a matter of considerable concern.

34.3 Digestive Enzymes

Digestive enzymes are present in digestive juices and break down food into the nutrient molecules glucose, amino acids, fatty acids, and glycerol. Salivary amylase and pancreatic amylase begin the digestion of starch. Pepsin and trypsin digest protein to peptides. Following emulsification by bile, lipase digests fat to glycerol and fatty acids. Intestinal enzymes finish the digestion of starch and protein.

Each digestive enzyme is present in a particular part of the digestive tract. Salivary amylase functions in the mouth; pepsin functions in the stomach; trypsin, lipase, and pancreatic amylase occur in the intestine along with the various enzymes that digest disaccharides and peptides.

34.4 Nutrition

The nutrients released by the digestive process should provide us with an adequate amount of energy, essential amino acids and fatty acids, and all necessary vitamins and minerals.

Carbohydrates are necessary in the diet, simple sugars and refined starches are not helpful because they provide calories but no fiber, vitamins, or minerals. Proteins supply us with essential amino acids, but it is wise to avoid meats that are fatty because fats from animal sources are saturated. While unsaturated fatty acids, particularly the omega-3 fatty acids, are protective against cardiovascular disease, the saturated fatty acids lead to plaque, which blocks blood vessels. Obesity is to be avoided particularly because obesity is now known to be associated with the development of type 2 diabetes and cardiovascular disease.

understanding the terms

anus 640
appendix 639
bile 639
carbohydrate 643
cholesterol 644
chyme 639
cirrhosis 642
complete digestive tract 634
diarrhea 640
duodenum 639
esophagus 637
fat 644
fiber 643
gallbladder 642
hepatitis 642
incomplete digestive tract 634
jaundice 642
lacteal 639
large intestine 639
lipase 643
liver 640
lumen 641
maltase 642
mineral 646
mouth 636
mucosa 641
muscularis 641
pancreas 640
pancreatic amylase 642
pepsin 642
peptidase 642
peristalsis 638
pharynx 637
polyp 640
protein 644
radula 635
rumen 635
salivary amylase 637, 642
salivary gland 636
serosa 641
small intestine 639
stomach 638
submucosa 641
triglyceride 644
trypsin 642
typhlosole 634
villus 639
vitamin 646

Match the terms to these definitions:

a. ______________ Essential requirement in the diet, needed in small amounts. They are often part of coenzymes.
b. ______________ Fat-digesting enzyme secreted by the pancreas.
c. ______________ Lymphatic vessel in an intestinal villus; it aids in the absorption of fats.
d. ______________ Muscular tube for moving swallowed food from the pharynx to the stomach.
e. ______________ Organ attached to the liver that serves to store and concentrate bile.

reviewing this chapter

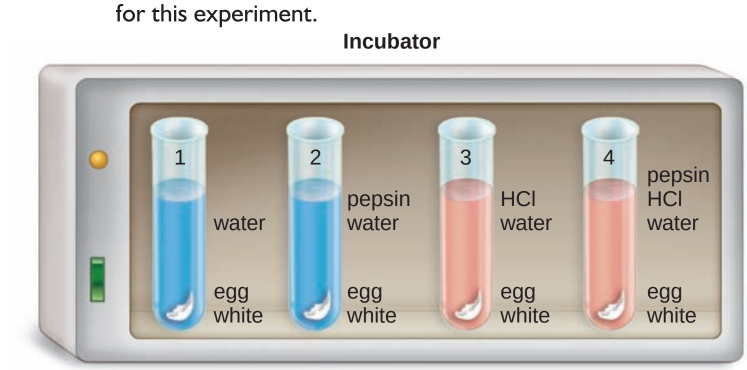
1. Contrast the incomplete digestive tract with the complete digestive tract, using the planarian and earthworm as examples. 634
2. Contrast a continuous feeder with a discontinuous feeder, using the clam and squid as examples. 634–35
3. Contrast the dentition of the mammalian herbivore with that of the mammalian carnivore, using the horse and lion as examples. 635–36
4. List the parts of the human digestive tract, anatomically describe them, and state the contribution of each to the digestive process. 636–40
5. Discuss the absorption of the products of digestion into the lymphatic and cardiovascular systems. 639
6. Describe the structure and function of the large intestine. Name several medical conditions associated with the large intestine. 639–40
7. State the location and describe the functions of the pancreas, the liver, and the gallbladder. 640–42
8. Name and discuss three serious illnesses of the liver. 642
9. Assume that you have just eaten a ham sandwich. Discuss the digestion of the contents of the sandwich. Mention all the necessary enzymes. 642–43
10. Explain why good nutrition is important to human health. Explain why obesity can lead to type 2 diabetes and cardiovascular disease. 643–46

testing yourself

Choose the best answer for each question.

1. Animals that feed discontinuously
   a. have digestive tracts that permit storage.
   b. are always filter feeders.
   c. exhibit extremely rapid digestion.
   d. have a nonspecialized digestive tract.
   e. usually eat only meat.
2. In which of these types of animals would you expect the digestive tract to be more complex?
   a. those with a single opening for the entrance of food and exit of wastes
   b. those with two openings, one serving as an entrance and the other as an exit
   c. only those complex animals that also have a respiratory system
   d. those with two openings that use the digestive tract to help fight infections
   e. All but a are correct.

3. The typhlosole within the gut of an earthworm compares best to which of these organs in humans?
   a. teeth in the mouth
   b. esophagus in the thoracic cavity
   c. folds in the stomach
   d. villi in the small intestine
   e. the large intestine because it absorbs water
4. Which of these animals is a continuous feeder with a complete digestive tract?
   a. planarian
   b. clam
   c. squid
   d. lion
   e. human
5. Tracing the path of food in humans, which step is out of order first?
   a. mouth
   b. pharynx
   c. esophagus
   d. small intestine
   e. stomach
   f. large intestine
6. The products of digestion are
   a. large macromolecules needed by the body.
   b. enzymes needed to digest food.
   c. small nutrient molecules that can be absorbed.
   d. regulatory hormones of various kinds.
   e. the foods we eat.
7. Why can a person not swallow food and talk at the same time?
   a. To swallow, the epiglottis must close off the trachea.
   b. The brain cannot control two activities at once.
   c. To speak, air must come through the larynx to form sounds.
   d. A swallowing reflex is only initiated when the mouth is closed.
   e. Both a and c are correct.
8. Which of these could be absorbed directly without need of digestion?
   a. glucose
   b. fat
   c. protein
   d. nucleic acid
   e. All of these are correct.
9. Which association is incorrect?
   a. protein—trypsin
   b. fat—lipase
   c. maltose—pepsin
   d. starch—amylase
   e. protein—pepsin
10. Most of the absorption of the products of digestion takes place in humans across
    a. the squamous epithelium of the esophagus.
    b. the convoluted walls of the stomach.
    c. the fingerlike villi of the small intestine.
    d. the smooth wall of the large intestine.
    e. the lacteals of the lymphatic system.
11. The hepatic portal vein is located between
    a. the hepatic vein and the vena cava.
    b. two capillary beds.
    c. the pancreas and the small intestine.
    d. the small intestine and the liver.
    e. Both b and d are correct.
12. Bile in humans
    a. is an important enzyme for the digestion of fats.
    b. is made by the gallbladder.
    c. emulsifies fat.
    d. must be activated during the first few weeks of life.
    e. All of these are correct.
13. Which of these is not a function of the liver in adults?
    a. produces bile
    b. stores glucose
    c. produces urea
    d. makes red blood cells
    e. produces proteins needed for blood clotting
14. The large intestine in humans
    a. digests all types of food.
    b. is the longest part of the intestinal tract.
    c. absorbs water.
    d. is connected to the stomach.
    e. All of these are correct.
15. The appendix connects to the
    a. cecum.
    b. small intestine.
    c. esophagus.
    d. large intestine.
    e. liver.
    f. All of these are correct.
16. Which association is incorrect?
    a. mouth—starch digestion
    b. esophagus—protein digestion
    c. small intestine—starch, lipid, protein digestion
    d. stomach—food storage
    e. liver—production of bile
17. Predict and explain the expected digestive results per test tube for this experiment.



thinking scientifically

1. A drug for leukemia is not broken down in the stomach and is well absorbed by the intestine. However, the molecular form of the drug collected from the blood is not the same as the form that was swallowed by the patient. What explanation is most likely?
2. Snakes often swallow whole animals, a process that takes a long time. Then snakes spend some time digesting their food. What structural modifications would allow slow swallowing and storage of a whole animal to occur? What chemical modifications would be necessary to digest a whole animal?

Biology website

The companion website for *Biology* provides a wealth of information organized and integrated by chapter. You will find practice tests, animations, videos, and much more that will complement your learning and understanding of general biology.

http://www.mhhe.com/maderbiology10

35

Respiratory Systems

elephant seals can dive to a depth of 1,500 m and stay submerged for two hours, even though they breathe air like we do. Their secret includes these adaptations: aquatic mammals (seals, whales, dolphins) have more blood cells and more blood per body weight than we do; their muscles are chock full of myoglobin, a respiratory pigment that stores oxygen in the muscles; and they have a special diving response. The heart rate slows down, the peripheral blood vessels constrict, and the blood circulates to only the heart and lungs. Now the spleen releases its supply of fully-oxygenated red blood cells, keeping the heart and brain going for a while longer.

Humans sometimes free-dive—we can't store oxygen, but we can bring on the diving response. You can practice by submerging your face in cold water. If you hold your breath long enough, the spleen will discharge its red blood cells. Even so, free-diving is not recommended for humans; it can have disasterous results because humans are highly adapted to live on land. In this chapter, we will learn how animals in the water and on land ordinarily breathe and transport gases to and from their cells.

An elephant seal can free-dive and suspend breathing for two hours.

concepts

35.1 GAS EXCHANGE SURFACES

- Respiration comprises ventilation, external respiration, and internal respiration. 650
- Gas exchange surfaces vary according to the complexity of the animal and the environment. The gills of fish are suitable to an aquatic environment, and the tracheal system of insects and the lungs of humans are suitable to a land environment. 650–54

35.2 BREATHING AND TRANSPORT OF GASES

- All terrestrial animals, except birds, use tidal ventilation; birds use one-way ventilation. Inspiration and expiration occur during ventilation. 656–57
- The human breathing rate is regulated, and it increases when the blood concentration of H^+ and CO_2 rises. 657
- In humans, the respiratory pigment hemoglobin transports oxygen from the lungs to the tissues and aids the transport of carbon dioxide from the tissues to the lungs. 658–59

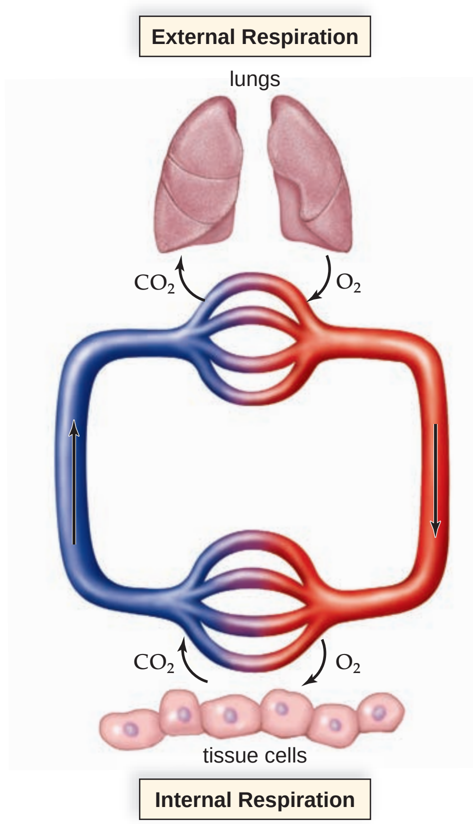
35.3 RESPIRATION AND HEALTH

- The respiratory tract is especially subject to infections. 660
- Cigarette smoking contributes to two major lung disorders—emphysema and cancer. 661

35.1 Gas Exchange Surfaces

Respiration is the sequence of events that results in gas exchange between the body's cells and the environment. In terrestrial vertebrates, respiration includes these steps:

- **Ventilation** (i.e., breathing) includes inspiration (entrance of air into the lungs) and expiration (exit of air from the lungs).
- **External respiration** is gas exchange between the air and the blood within the lungs. Blood then transports oxygen from the lungs to the tissues.
- **Internal respiration** is gas exchange between the blood and the tissue fluid. (The body's cells exchange gases with the tissue fluid.) The blood then transports carbon dioxide to the lungs.



Gas exchange takes place by the physical process of diffusion. For external respiration to be effective, the gas-exchange region must be (1) moist, (2) thin, and (3) large in relation to the size of the body. Some animals, such as planarians, are small and shaped in a way that allows the surface of the animal to be the gas-exchange surface. Most complex animals have specialized external respiration surfaces, such as gills in aquatic animals and lungs in terrestrial animals. The effectiveness of diffusion is enhanced by vascularization (the presence of many capillaries), and delivery of oxygen to the cells is promoted when the blood contains a respiratory pigment, such as hemoglobin.

Regardless of the particular external respiration surface and the manner in which gases are delivered to the cells, in the end, oxygen enters mitochondria, where cellular respiration takes place. Without internal respiration, ATP production does not take place, and life ceases.

External Gas-Exchange Surfaces

It is more difficult for animals to obtain oxygen from water than from air. Water fully saturated with air contains only a fraction of the amount of oxygen that would be present in the same volume of air. Also, water is more dense than air. Therefore, aquatic animals expend more energy carrying out gas exchange than do terrestrial animals. Fishes use as much as 25% of their energy output to respire, while terrestrial mammals use only 1–2% of their energy output for that purpose.

Hydras, which are cnidarians, and planarians, which are flatworms, have a large surface area in comparison to their size. This makes it possible for most of their cells to exchange gases directly with the environment. In hydras, the outer layer of cells is in contact with the external environment, and the inner layer can exchange gases with the water in the gastrovascular cavity (Fig. 35.1). In planarians, the flattened body permits cells to exchange gases with the external environment.

The tubular shape of annelids (segmented worms) also provides a surface area adequate for external respiration. The earthworm, an annelid, is an example of a terrestrial invertebrate that is able to use its body surface for respiration because the capillaries come close to the surface (Fig. 35.2).

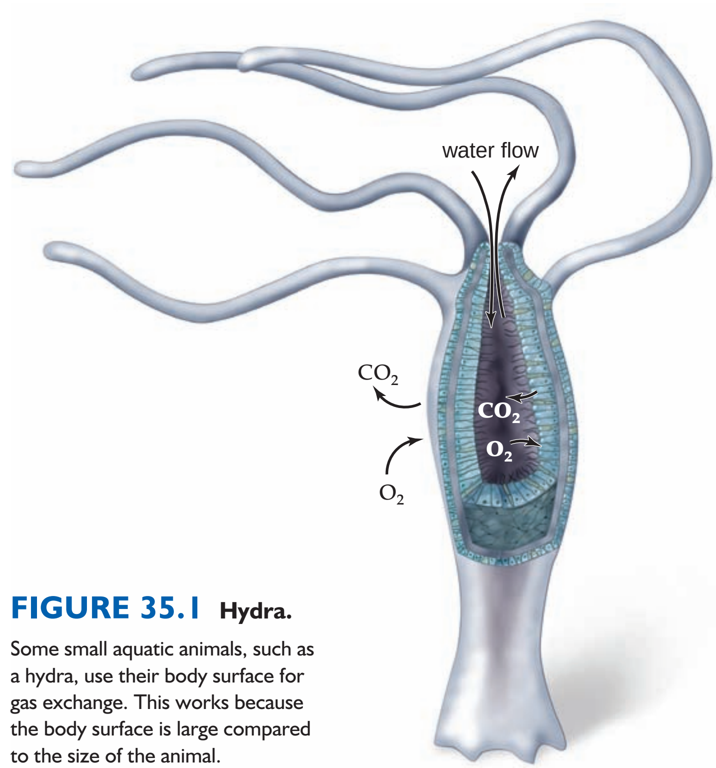


FIGURE 35.1 Hydra.
Some small aquatic animals, such as a hydra, use their body surface for gas exchange. This works because the body surface is large compared to the size of the animal.

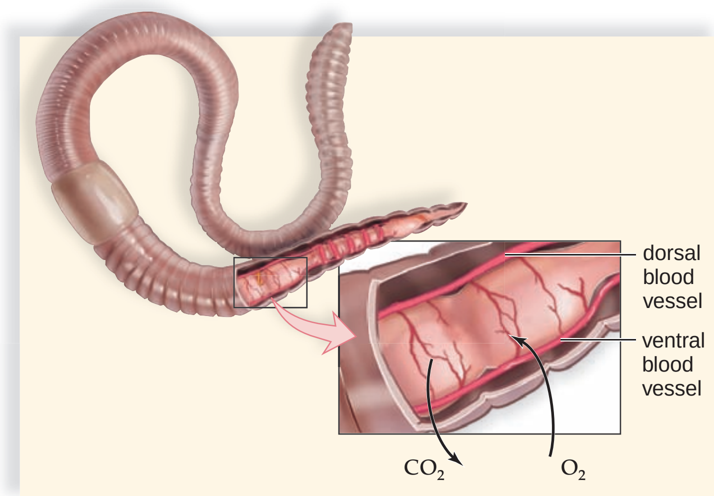


FIGURE 35.2 Earthworm.

An earthworm's entire external surface functions in external respiration.

An earthworm keeps its body surface moist by secreting mucus and by releasing fluids from excretory pores. Further, the worm is behaviorally adapted to remain in damp soil during the day, when the air is driest. In addition to a tubular shape, aquatic polychaete worms have extensions of the body wall called parapodia, which are vascularized and used for gas exchange.

Aquatic invertebrates (e.g., clams and crayfish) and aquatic vertebrates (e.g., fish and tadpoles) have gills that extract oxygen from a watery environment. **Gills** are finely divided, vascularized outgrowths of the body surface or the pharynx (Fig. 35.3*a*). Various mechanisms are used to pump water across the gills, depending on the organism.

Insects have a system of air tubes called tracheae through which oxygen is delivered directly to the cells without entering the blood (Fig. 35.3*b*). Tracheole fluid occurs at the end of the tracheae. Air sacs located near the wings, legs, and abdomen act as bellows to help move the air into the tubes through external openings.

Terrestrial vertebrates usually have **lungs,** which are vascularized outgrowths from the lower pharyngeal region. The tadpoles of frogs live in the water and have gills as external respiratory organs, but adult amphibians possess simple, saclike lungs. Most amphibians respire to some extent through the skin, and some salamanders depend entirely on the skin, which is kept moist by mucus produced by numerous glands on the surface of the body.

The lungs of birds and mammals are elaborately subdivided into small passageways and spaces, respectively (Fig. 35.3*c*). It has been estimated that human lungs have a total surface area that is at least 50 times the skin's surface area. Air is a rich source of oxygen compared to water; however, it does have a drying effect on external respiratory surfaces. A human loses about 350 ml of water per day when the air has a relative humidity of only 50%. To keep the lungs from drying out, air is moistened as it moves through the passageways leading to the lungs.

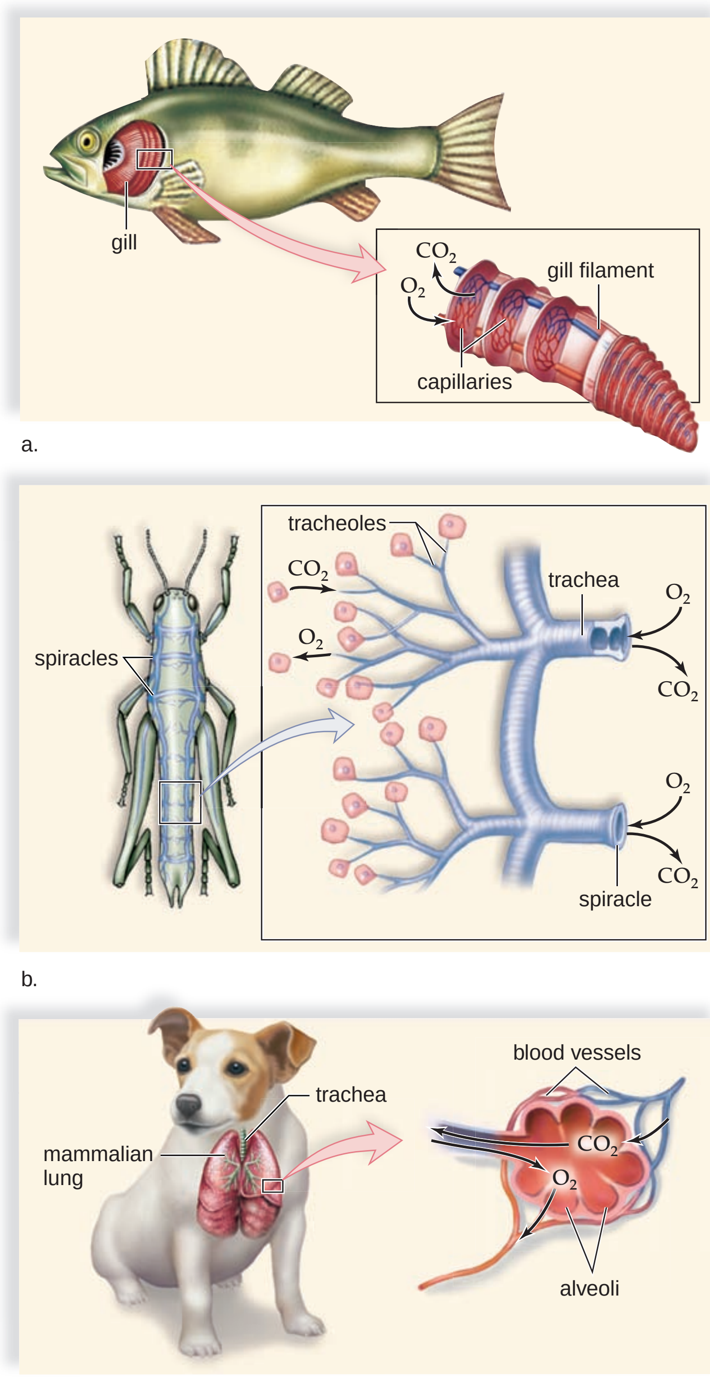


FIGURE 35.3 Respiratory organs.

a. Fish have gills to assist external respiration. **b.** Insects have a tracheal system that delivers oxygen directly to their cells. **c.** Vertebrates have lungs with a large total external respiration surface.

The Gills of a Fish

Animals with gills use various means of ventilation. Among molluscs, such as a clam or a squid, water is drawn into the mantle cavity, where it passes through the gills. In crustaceans, such as crabs and shrimps, which are arthropods, the gills are located in thoracic chambers covered by the exoskeleton. The action of specialized appendages located near the mouth keeps the water moving. In fish, ventilation is brought about by the combined action of the mouth and gill covers, or opercula (sing., operculum). When the mouth is open, the opercula are closed and water is drawn in. Then the mouth closes, and the opercula open, drawing the water from the pharynx through the gill slits located between the gill arches.

As mentioned, the gills of bony fishes are outward extensions of the pharynx (Fig. 35.4). On the outside of the gill arches, the gills are composed of filaments that are folded into platelike lamellae. Fish use **countercurrent exchange** to transfer oxygen from the surrounding water into their blood. *Con*current flow would mean that O_2-rich water passing over the gills would flow in the same direction as O_2-poor blood in the blood vessels. This arrangement would result in an equilibrium point, at which only half the oxygen in the water would be captured. *Counter*current flow means that the two fluids flow in opposite directions. With countercurrent flow, as blood gains oxygen, it always encounters water having an even higher oxygen content. A countercurrent mechanism prevents an equilibrium point from being reached, and about 80–90% of the initial dissolved oxygen in water is extracted.

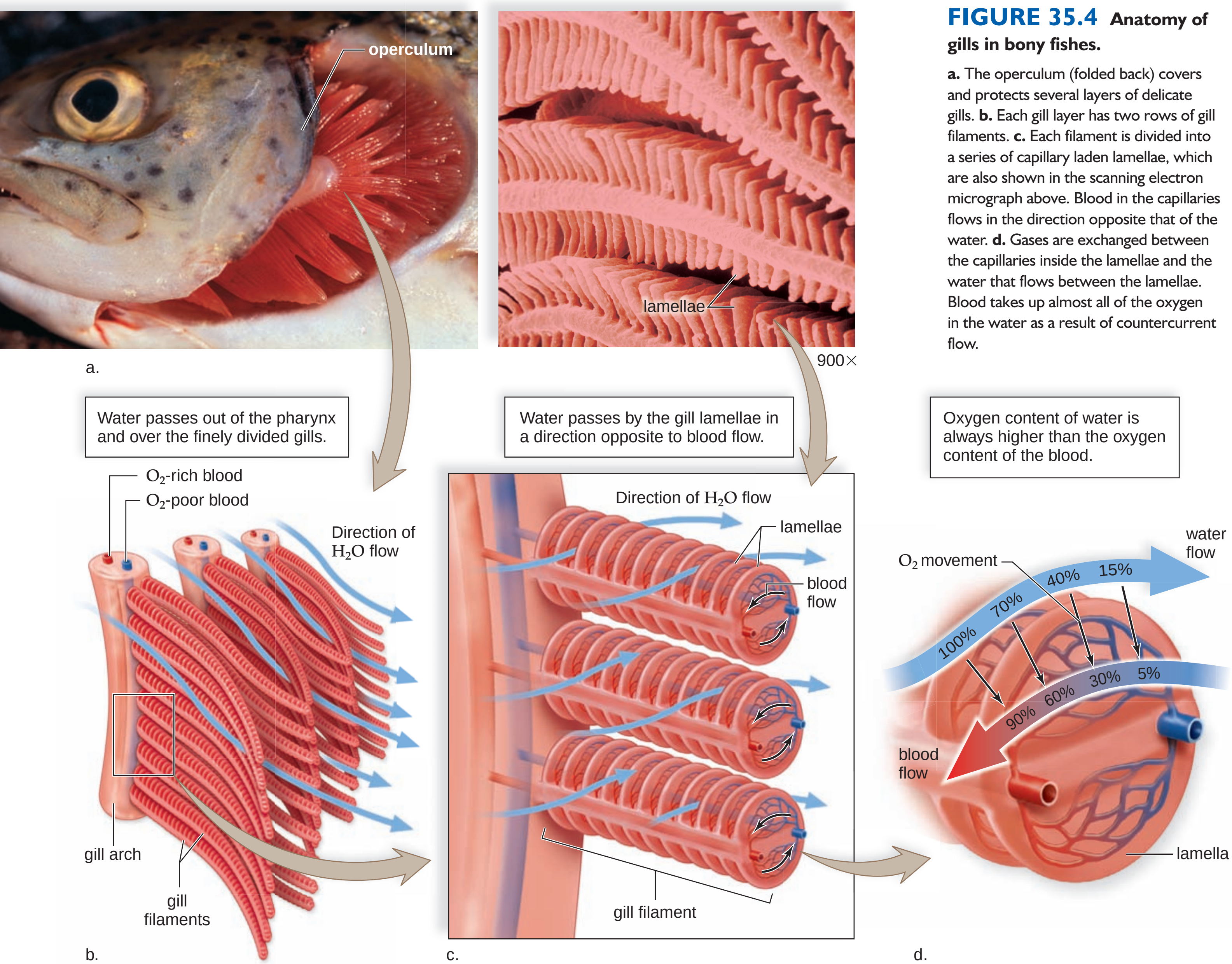


FIGURE 35.4 **Anatomy of gills in bony fishes.**

a. The operculum (folded back) covers and protects several layers of delicate gills. **b.** Each gill layer has two rows of gill filaments. **c.** Each filament is divided into a series of capillary laden lamellae, which are also shown in the scanning electron micrograph above. Blood in the capillaries flows in the direction opposite that of the water. **d.** Gases are exchanged between the capillaries inside the lamellae and the water that flows between the lamellae. Blood takes up almost all of the oxygen in the water as a result of countercurrent flow.

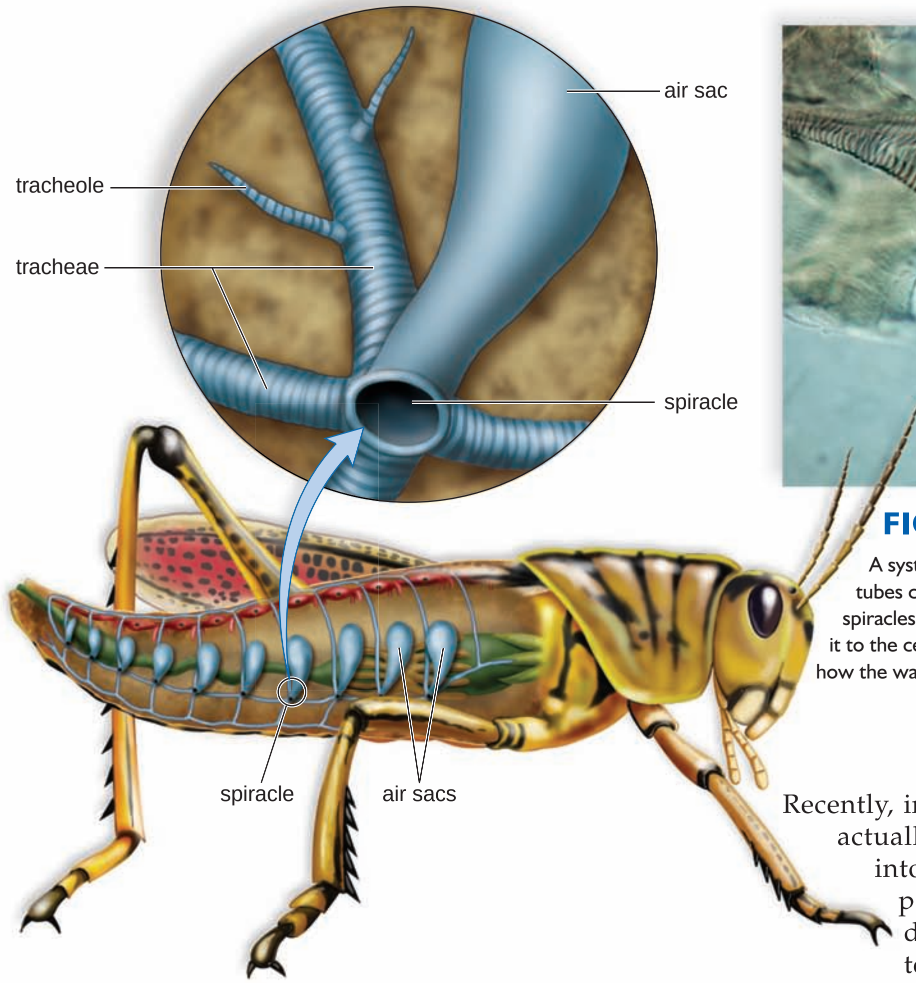


FIGURE 35.5 **Tracheae of insects.**

A system of air tubes extends throughout the body of an insect, and the tubes carry oxygen to the cells. Air enters the tracheae at openings called spiracles. From here, the air moves to the smaller tracheoles, which take it to the cells, where gas exchange takes place. The photomicrograph shows how the walls of the trachea are stiffened with bands of chitin.

The Tracheal System of Insects

Arthropods are coelomate animals, but the coelom is reduced and the internal organs lie within a cavity called the hemocoel because it contains hemolymph, a mixture of blood and lymph. Hemolymph flows freely through the hemocoel, making circulation in arthropods inefficient. Many insects are adapted for flight, and their flight muscles require a steady supply of oxygen. Insects overcome the inefficiency of their blood flow by having a respiratory system that consists of **tracheae,** tiny air tubes that take oxygen directly to the cells (Fig. 35.5). Tracheae have a single layer of cells supported by spiral thickenings of chitin. The tracheae branch into even smaller tubules called tracheoles, which also branch and rebranch until finally the air tubes are only about 0.1 μm in diameter. There are so many fine tracheoles that almost every cell is near one. Also, the tracheoles indent the plasma membrane so that they terminate close to mitochondria. Therefore, O_2 can flow more directly from a tracheole to mitochondria, where cellular respiration occurs. The tracheae also dispose of CO_2.

The tracheoles are fluid-filled, but the larger tracheae contain air and open to the outside by way of spiracles (Fig. 35.5). Usually, the spiracle has some sort of closing device that reduces water loss, and this may be why insects have no trouble inhabiting drier climates. Recently, investigators presented evidence that tracheae actually expand and contract, thereby drawing air into and out of the system. This method is comparable to the way the human lungs expand to draw air into them. Otherwise, a tracheal system consisting of an expansive network of thin-walled tubes seems to be an entirely different mechanism of respiration from those used by other animals.

It's been suggested that a tracheal system that has no efficient method to improve flow is sufficient only in small insects. Larger insects have still another mechanism to ventilate—keep the air moving in and out—tracheae. Many larger insects have air sacs, which are thin-walled and flexible, located near major muscles. Contraction of these muscles causes the air sacs to empty, and relaxation causes the air sacs to expand and draw in air. Even so, insects still lack the efficient circulatory system of birds and mammals that is able to pump O_2-rich blood through arteries to all the cells of the body. This may be why insects remain small, despite the attempts of movies to make us think otherwise.

A tracheal system is an adaptation to breathing air, and yet, some insect larval stages and even some adult insects live in the water. In these instances, the tracheae do not receive air by way of spiracles. Instead, diffusion of oxygen across the body wall supplies the tracheae with oxygen. Mayfly and stonefly nymphs have thin extensions of the body wall called tracheal gills—the tracheae are particularly numerous in this area. This is an interesting adaptation because it dramatizes that tracheae function to deliver oxygen in the same manner as vertebrate blood vessels.

The Lungs of Humans

The human respiratory system includes all of the structures that conduct air in a continuous pathway to and from the lungs (Fig. 35.6*a*). The lungs lie deep within the thoracic cavity, where they are protected from drying out. As air moves through the nose, the pharynx, the trachea, and the bronchi to the lungs, it is filtered so that it is free of debris, warmed, and humidified. By the time the air reaches the lungs, it is at body temperature and saturated with water. In the nose, hairs and cilia act as a screening device. In the trachea and the bronchi, cilia beat upward, carrying mucus, dust, and occasional small bits of food that "went down the wrong way" into the throat, where the accumulation may be swallowed or expectorated (Fig. 35.6*b*).

The hard and soft palates separate the nasal cavities from the mouth, but the air and food passages cross in the **pharynx.** This may seem inefficient, and there is danger of choking if food accidentally enters the trachea; however, this arrangement does have the advantage of letting you breathe through your mouth in case your nose is plugged up. In addition, it permits greater intake of air during heavy exercise, when greater gas exchange is required.

Air passes from the pharynx through the **glottis,** an opening into the **larynx,** or voice box. At the edges of the glottis, embedded in mucous membrane, are the **vocal cords.** These flexible and pliable bands of connective tissue vibrate and produce sound when air is expelled past them through the glottis from the larynx.

The larynx and the trachea remain open to receive air at all times. The larynx is held open by a complex of nine cartilages, among them the Adam's apple. Easily seen in many men, the Adam's apple resembles a small, rounded apple just under the skin in the front of the neck. The **trachea** is held open by a series of C-shaped, cartilaginous rings that do not completely meet in the rear. When food is being swallowed, the larynx rises, and the glottis is closed by a flap of tissue called the **epiglottis.** A backward movement of the soft palate covers the entrance of the nasal passages into the pharynx. The food then enters the esophagus, which lies behind the larynx.

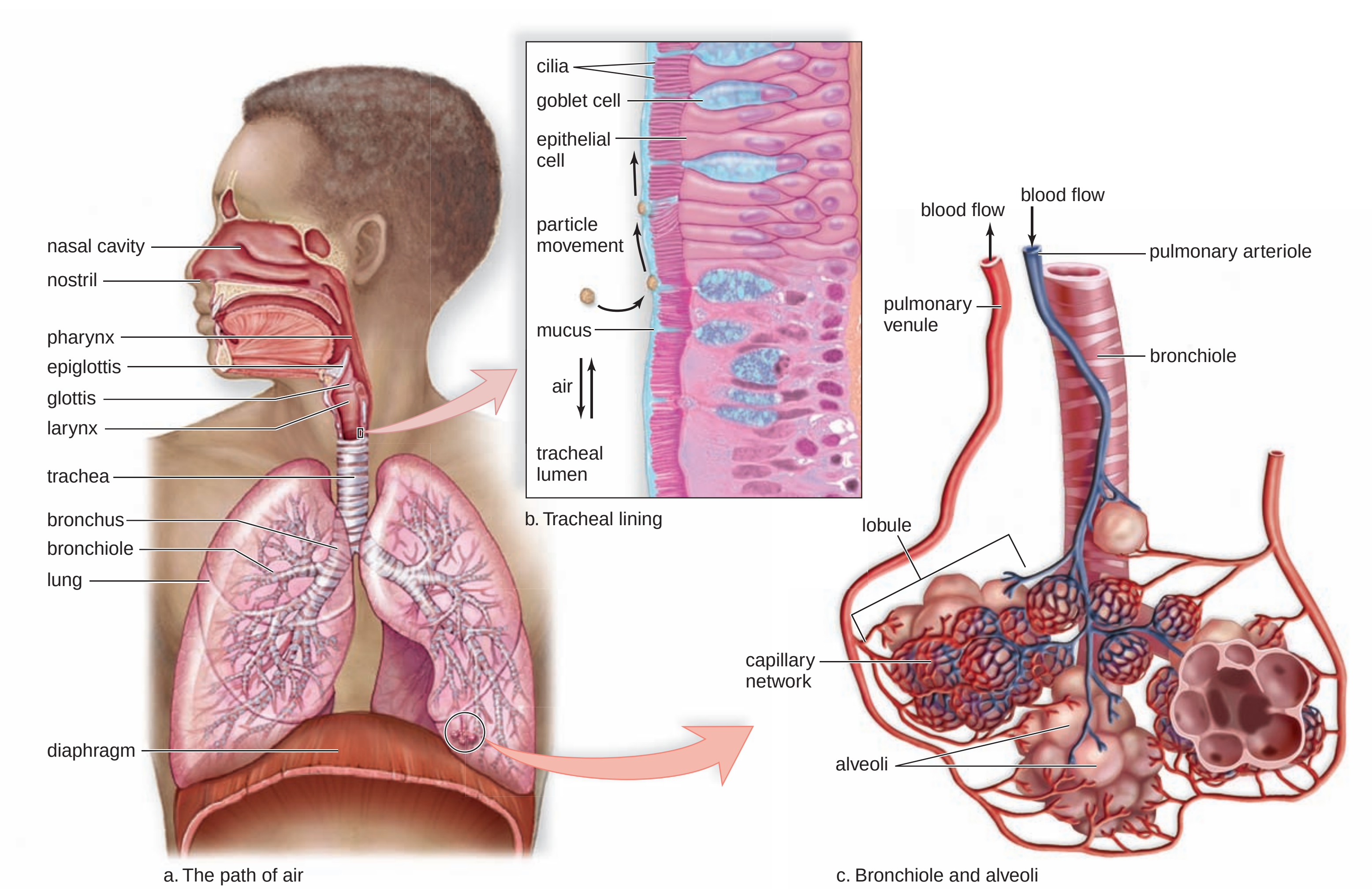


FIGURE 35.6 The human respiratory tract.

a. The respiratory tract extends from the nose to the lungs, which are composed of air sacs called alveoli. **b.** The lining of the trachea is a ciliated epithelium (art above, micrograph below) with mucus-producing goblet cells. The lining prevents inhaled particles from reaching the lungs: the mucus traps the particles, and the cilia help move the mucus toward the throat, where it can be swallowed. **c.** Gas exchange occurs between air in the alveoli and blood within a capillary network that surrounds the alveoli.

science focus

Questions About Tobacco, Smoking, and Health

Is there a safe way to smoke? No. All cigarettes can damage the human body. Any amount of smoke is dangerous.

Is cigarette smoking really addictive? Yes. The nicotine in cigarette smoke causes addiction to smoking. Nicotine is an addictive drug (just like heroin and cocaine) for three main reasons: Small amounts make the smoker want to smoke more; smokers usually suffer withdrawal symptoms when they stop; and nicotine can affect the mood and nature of the smoker.

Does smoking cause cancer? Yes. Tobacco use accounts for about one-third of all cancer deaths in the United States. Smoking causes almost 90% of lung cancers. Smoking also causes cancers of the larynx (voice box), oral cavity, pharynx (throat), and esophagus, and contributes to the development of cancers of the bladder, pancreas, cervix, kidney, and stomach.

How does cigarette smoke affect the lungs? Cigarette smoking causes several lung diseases that can be just as dangerous as lung cancer: chronic bronchitis, in which the airways produce excess mucus, forcing the smoker to cough more; emphysema, a disease that slowly destroys a person's ability to breathe; and chronic obstructive pulmonary disease, a name that encompasses both chronic bronchitis and emphysema.

Why do smokers have "smoker's cough"? Cigarette smoke contains chemicals that irritate the air passages and lungs. When a smoker inhales these substances, the body tries to protect itself by producing mucus and stimulating coughing. Normally, cilia (tiny, hairlike formations that line the airways) beat outward and "sweep" harmful material out of the lungs. Smoke, however, decreases this sweeping action, so some of the poisons in the smoke remain in the lungs.

If you smoke but do not inhale, is there any danger? Yes. Even if smokers don't inhale, they are breathing the smoke secondhand and are still at risk for lung cancer. Pipe and cigar smokers, who often do not inhale, are at increased risk for lip, mouth, tongue, and several other cancers.

Does cigarette smoking affect the heart? Yes. Smoking increases the risk of heart disease, which is the number-one cause of death in the United States. Smoking is a risk factor for heart disease, but cigarette smoking is the biggest risk factor for sudden heart death. Smokers are more likely to die from a heart attack within an hour of the attack than nonsmokers. Cigarette smoke can cause harm to the heart at very low levels, much lower than the amount that causes lung disease.

How does smoking affect pregnant women and their babies? Smoking during pregnancy is linked to a greater chance of miscarriage, premature delivery, stillbirth, infant death, low birth weight, and sudden infant death syndrome (SIDS). When a pregnant woman smokes, she is really smoking for two because the nicotine, carbon monoxide, and other dangerous chemicals in smoke enter her bloodstream and then pass into the baby's body, preventing the baby from getting essential nutrients and oxygen for growth.

What are some of the short-term and long-term effects of smoking cigarettes? Short-term effects include shortness of breath and a nagging cough, diminished ability to smell and taste, premature aging of the skin, and increased risk of sexual impotence in men. Long-term effects include many types of cancer, heart disease, aneurysms, bronchitis, emphysema, and stroke. Smoking contributes to the severity of pneumonia and asthma.

What are the dangers of environmental tobacco smoke (ETS)? In nonsmokers, ETS causes about 3,000 lung cancer deaths and about 35,000 to 40,000 deaths from heart disease each year. Children whose parents smoke are more likely to suffer from asthma, pneumonia or bronchitis, ear infections, coughing, wheezing, and increased mucus production in the first two years of life than children who come from smoke-free households.

Are chewing tobacco and snuff safe alternatives to cigarette smoking? No. The juice from smokeless tobacco is absorbed directly through the lining of the mouth. This creates sores and white patches that often lead to cancer of the mouth. Smokeless tobacco users also greatly increase their risk of other cancers, including those of the pharynx (throat). Other effects of smokeless tobacco include harm to teeth and gums.

The trachea divides into two primary **bronchi,** which enter the right and left lungs. Branching continues, eventually forming a great number of smaller passages called **bronchioles.** The two bronchi resemble the trachea in structure, but as the bronchial tubes divide and subdivide, their walls become thinner, and rings of cartilage are no longer present. Each bronchiole terminates in an elongated space enclosed by a multitude of air pockets, or sacs, called **alveoli,** which make up the lungs (Fig. 35.6*c*). Internal gas exchange occurs between the air in the alveoli and the blood in the capillaries.

Check Your Progress 35.1

1. Per unit volume, air contains more oxygen than water, but breathing air causes one problem easily preventable in the water. What is it?
2. One page 650, we said that respiration has three events, but this is not so in insects. Explain.
3. Name six illnesses associated with smoking cigarettes.

35.2 Breathing and Transport of Gases

During breathing, the lungs are ventilated. O_2 moves into the blood, and CO_2 moves out of the blood into the lungs. Blood transports O_2 to the body's cells and CO_2 from the cells to the lungs.

Breathing

Terrestrial vertebrates ventilate their lungs by moving air into and out of the respiratory tract. Amphibians use positive pressure to force air into the respiratory tract. With the mouth and nostrils firmly shut, the floor of the mouth rises and pushes the air into the lungs. Reptiles, birds, and mammals use negative pressure to move air into the lungs and positive pressure to move it out. **Inspiration** (or inhalation) is the act of moving air into the lungs, and **expiration** (or exhalation) is the act of moving air out of the lungs.

Reptiles have jointed ribs that can be raised to expand the lungs, but mammals have both a rib cage and a diaphragm. The **diaphragm** is a horizontal muscle that divides the thoracic cavity (above) from the abdominal cavity (below). During inspiration in mammals, the rib cage moves up and out, and the diaphragm contracts and moves down (Fig. 35.7). As the thoracic (chest) cavity expands and lung volume increases, air flows into the lungs due to decreased air pressure in the thoracic cavity and lungs. Also, inspiration is the active phase of breathing in reptiles and mammals.

During expiration in mammals, the rib cage moves down, and the diaphragm relaxes and moves up to its former position (Fig. 35.8). No muscle contraction is required and expiration is the inactive phase of breathing in reptiles and mammals. During expiration, air flows out as a result of increased pressure in the thoracic cavity and lungs.

We can liken ventilation in reptiles and mammals to the way a bellows, used to fan a fire, functions (Fig. 35.9). First, the handles of the bellows are pulled apart, decreasing the air pressure inside the bellows. This causes air to automatically flow into the bellows, just as air automatically enters the lungs because the rib cage moves up and out during inspiration. Then, when the handles of the bellows are pushed together, air automatically flows out because the air pressure increases inside the bellows. Similarly, air

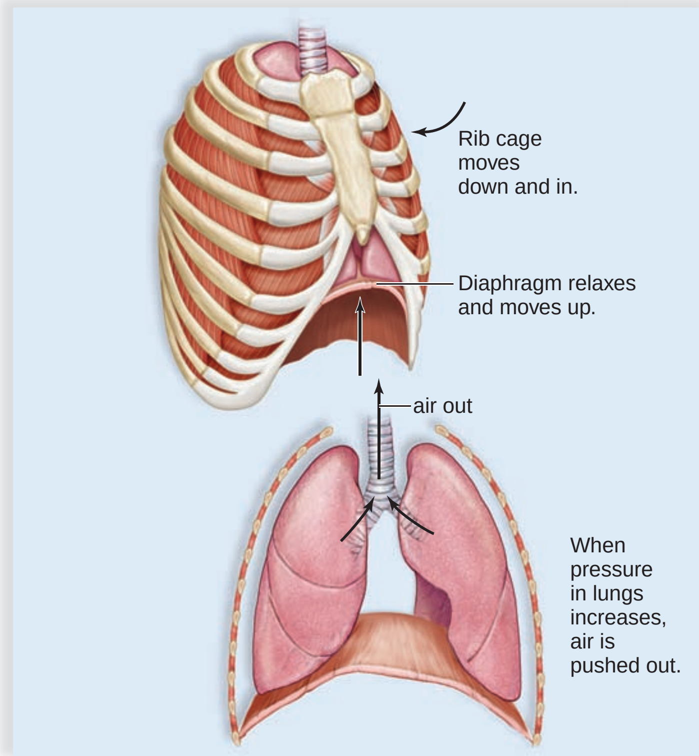


FIGURE 35.8 Expiration.

During expiration, the thoracic cavity and lungs resume their original positions and pressures. Now, air is forced out.

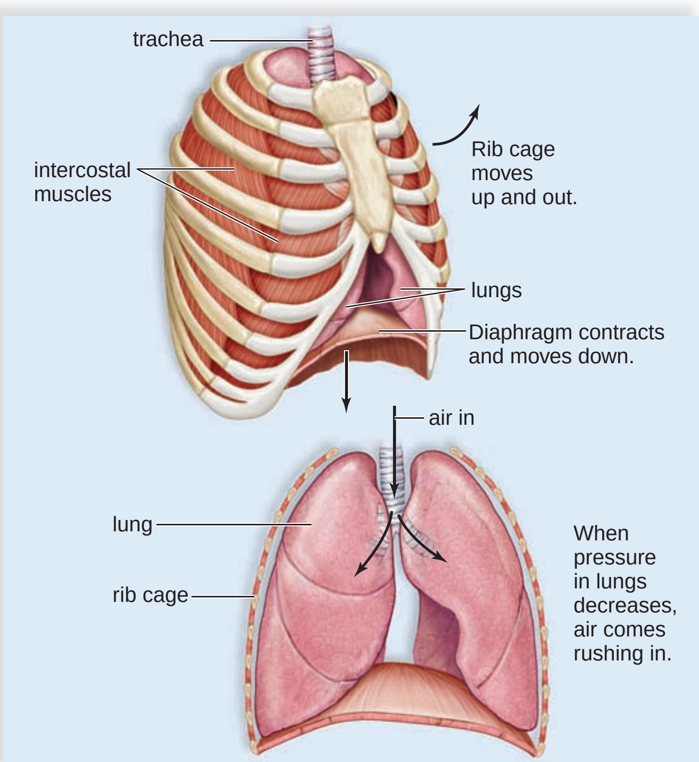


FIGURE 35.7 Inspiration.

During inspiration, the thoracic cavity and lungs expand so that air is drawn in.

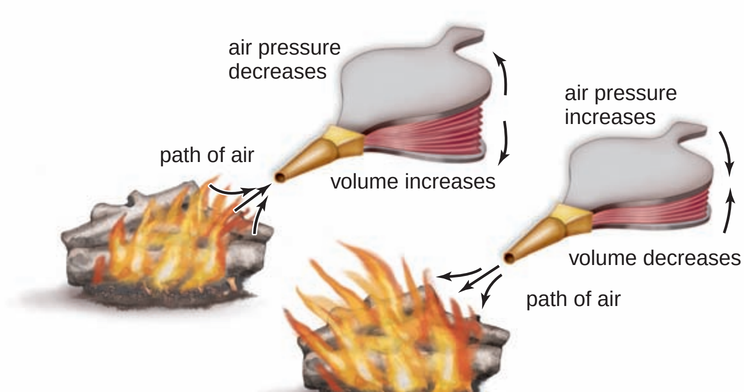
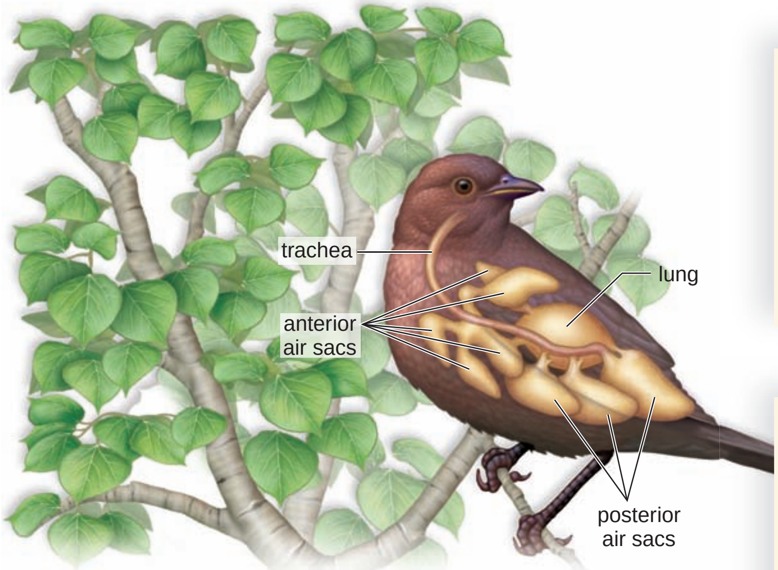


FIGURE 35.9 Bellows.

Lungs function much as bellows do.



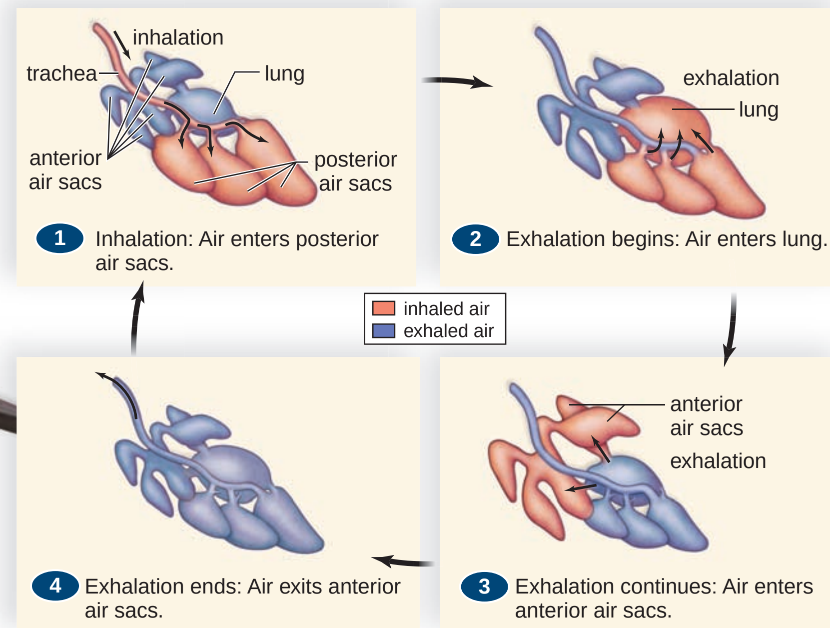


FIGURE 35.10 Respiratory system in birds.

Air sacs are attached to the lungs of birds. These allow birds to have a one-way mechanism of ventilating their lungs.

automatically exits the lungs when the rib cage moves down and in during expiration. The analogy is not exact, however, because no force is required for the rib cage to move down, and inspiration is the only active phase of breathing. Forced expiration can occur if we so desire, however.

All terrestrial vertebrates, except birds, use a *tidal ventilation mechanism,* so called because the air moves in and out by the same route. This means that the lungs of amphibians, reptiles, and mammals are not completely emptied and refilled during each breathing cycle. Because of this, the air entering mixes with used air remaining in the lungs. While this does help conserve water, it also decreases gas-exchange efficiency. In contrast, birds use a *one-way ventilation mechanism* (Fig. 35.10). Incoming air is carried past the lungs by a trachea, which takes it to a set of posterior air sacs. The air then passes forward through the lungs into a set of anterior air sacs. From here, it is finally expelled. Notice that fresh air never mixes with used air in the lungs of birds, thereby greatly improving gas-exchange efficiency.

Modifications of Breathing in Humans

Normally, adults have a breathing rate of 12 to 20 ventilations per minute. The rhythm of ventilation is controlled by a **respiratory center** in the medulla oblongata of the brain. The respiratory center automatically sends out impulses by way of a spinal nerve to the diaphragm (phrenic nerve) and intercostal nerves to the intercostal muscles of the rib cage (Fig. 35.11). Now inspiration occurs. When the respiratory center stops sending neuronal signals to the diaphragm and the rib cage, expiration occurs.

Although the respiratory center automatically controls the rate and depth of breathing, its activity can also be influenced by nervous input and chemical input. Following forced inhalation, stretch receptors in the alveolar walls initiate inhibitory nerve impulses that travel from the inflated lungs to the respiratory center. This stops the respiratory center from sending out nerve impulses.

The respiratory center is directly sensitive to the levels of hydrogen ions (H^+). However, when carbon dioxide (CO_2) enters the blood, it reacts with water and releases hydrogen ions. In this way, CO_2 participates in regulating the breathing rate. When hydrogen ions rise in the blood and the pH decreases, the respiratory center increases the rate and depth of breathing. The chemoreceptors in the **carotid bodies,** located in the carotid arteries, and in the **aortic bodies,** located in the aorta, will stimulate the respiratory center during intense exercise due to a reduction in pH and also if and when arterial oxygen decreases to 50% of normal.

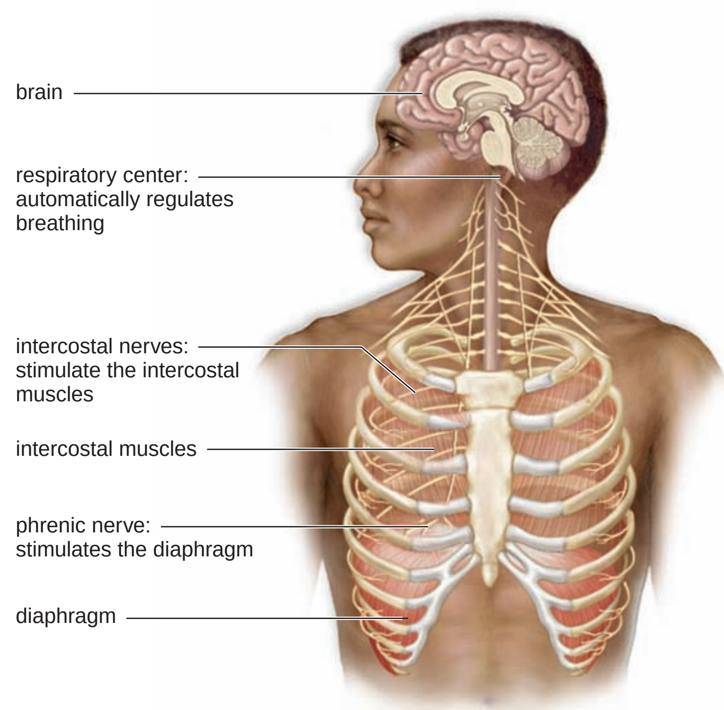


FIGURE 35.11 Nervous control of breathing.

The breathing rate can be modified by nervous stimulation of the intercostal muscles and diaphragm.

Gas Exchange and Transport

Respiration includes the exchange of gases in our lungs, called external respiration, as well as the exchange of gases in the tissues, called internal respiration (Fig. 35.12). The principles of diffusion largely govern the movement of gases into and out of blood vessels in the lungs and in the tissues. Gases exert pressure, and the amount of pressure each gas exerts is called the **partial pressure,** symbolized as P_{O_2} and P_{CO_2}. If the partial pressure of oxygen differs across a membrane, oxygen will diffuse from the higher to the lower pressure. Similarly, CO_2 diffuses from the higher to the lower partial pressure.

Ventilation causes the alveoli of the lungs to have a higher P_{O_2} and a lower P_{CO_2} than the blood in pulmonary capillaries, and this accounts for the exchange of gases in the lungs. When blood reaches the tissues, cellular respiration in cells causes the tissue fluid to have a lower P_{O_2} and a higher P_{CO_2} than the blood in the systemic capillaries and this accounts for the exchange of gases in the tissues.

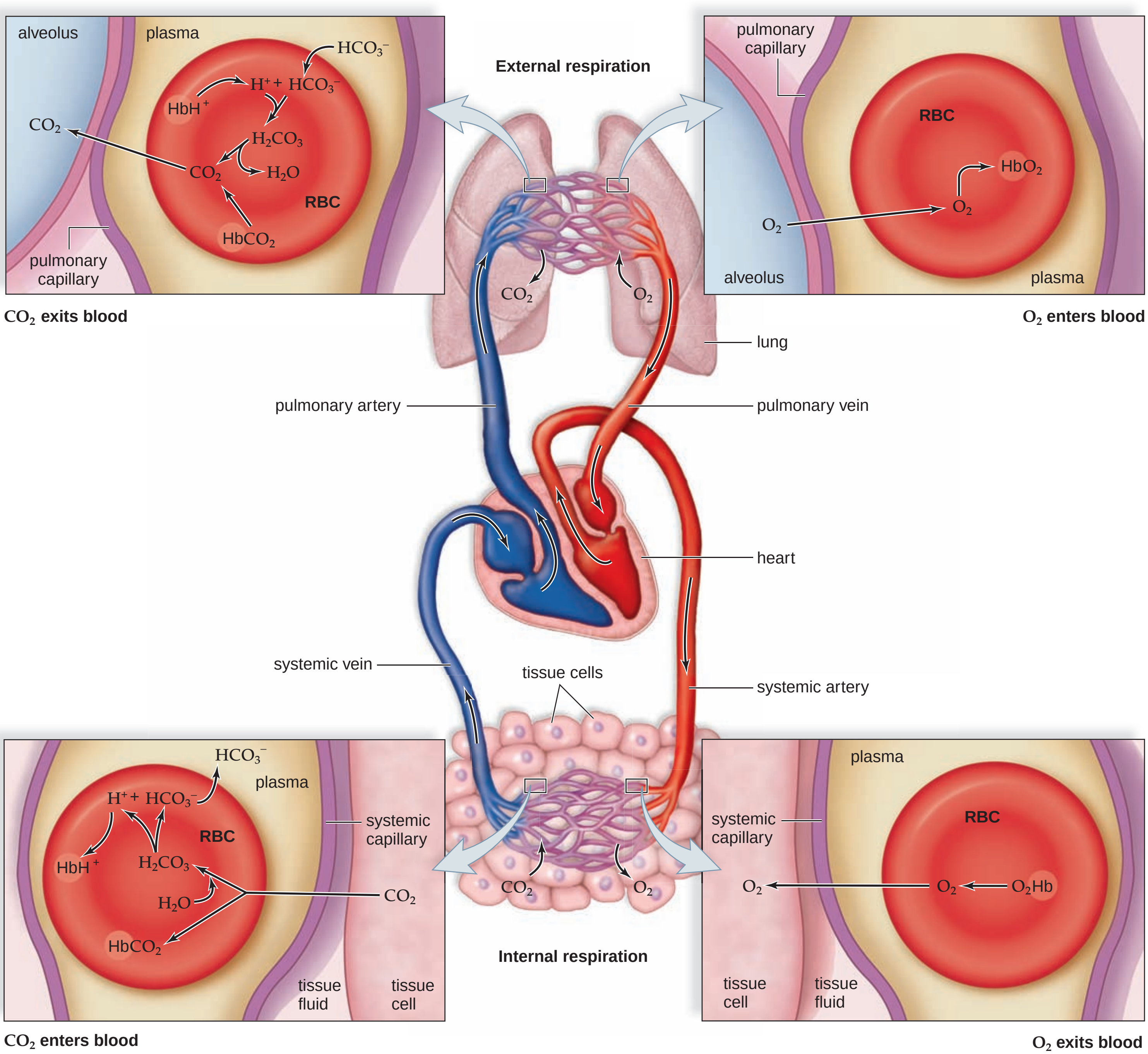


FIGURE 35.12 External and internal respiration.

During external respiration (*above*) in the lungs, carbon dioxide (CO_2) leaves blood, and oxygen (O_2) enters blood. During internal respiration (*below*) in the tissues, oxygen leaves blood, and carbon dioxide enters blood.

Transport of Oxygen and Carbon Dioxide

External Respiration. As blood enters the lungs, a small amount of CO_2 is being carried by hemoglobin with the formula $HbCO_2$. Also, some hemoglobin is carrying hydrogen ions with the formula HbH^+. Most of the CO_2 in the pulmonary capillaries is carried as bicarbonate ions (HCO_3^-) in the plasma. As the free CO_2 from the following equation begins to diffuse out, this reaction is driven to the right:

$$\underset{\text{hydrogen ion}}{H^+} + \underset{\text{bicarbonate ion}}{HCO_3^-} \longrightarrow \underset{\text{carbonic acid}}{H_2CO_3} \longrightarrow \underset{\text{water}}{H_2O} + \underset{\text{carbon dioxide}}{CO_2}$$

The reaction occurs in red blood cells, where the enzyme **carbonic anhydrase** speeds the breakdown of carbonic acid (see Fig. 35.12, *upper left*). Pushing this equation to the far right by breathing fast can cause you to stop breathing for a time; pushing this equation to the left by not breathing is even more temporary because breathing will soon resume due to the rise in H^+.

Most oxygen entering the pulmonary capillaries from the alveoli of the lungs combines with **hemoglobin (Hb)** in red blood cells (RBCs) to form **oxyhemoglobin** (Fig. 35.12, *upper right*):

$$\underset{\text{deoxyhemoglobin}}{Hb} + \underset{\text{oxygen}}{O_2} \longrightarrow \underset{\text{oxyhemoglobin}}{HbO_2}$$

At the normal P_{O_2} in the lungs, hemoglobin is practically saturated with oxygen. Each hemoglobin molecule contains four polypeptide chains, and each chain is folded around an iron-containing group called **heme** (Fig. 35.13). It is actually the iron that forms a loose association with oxygen. Since there are about 250 million hemoglobin molecules in each red blood cell, each red blood cell is capable of carrying at least one billion molecules of oxygen.

Unfortunately, carbon monoxide (CO) is an air pollutant that comes from the incomplete combustion of natural gas and gasoline. Because CO is a colorless, odorless gas, people can be unaware that they are breathing it. But once CO is in the bloodstream, it combines with the iron of hemoglobin 200 times more tightly than oxygen, and the result can be death. This is the reason that homes are equipped with CO detectors.

Internal Respiration. Blood entering the systemic capillaries is a bright red color because RBCs contain oxyhemoglobin. Because the temperature in the tissues is higher and the pH is lower than in the lungs, oxyhemoglobin has a tendency to give up oxygen:

$$HbO_2 \longrightarrow Hb + O_2$$

Oxygen diffuses out of the blood into the tissues because the P_{O_2} of tissue fluid is lower than that of blood (see Fig. 35.12, *lower right*). The lower P_{O_2} is due to cells continuously using up oxygen in cellular respiration. After oxyhemoglobin gives up O_2, O_2 leaves the blood and enters tissue fluid, where it is taken up by cells.

Carbon dioxide, on the other hand, enters blood from the tissues because the P_{CO_2} of tissue fluid is higher than that of blood. Carbon dioxide, produced continuously by cells, collects in tissue fluid. After CO_2 diffuses into the blood, it enters the red blood cells, where a small amount combines with the protein portion of hemoglobin to form **carbaminohemoglobin** ($HbCO_2$). Most of the CO_2, however, is transported in the form of the **bicarbonate ion** (HCO_3^-). First, CO_2 combines with water, forming carbonic acid, and then this dissociates to a hydrogen ion (H^+) and HCO_3^-:

$$\underset{\text{carbon dioxide}}{CO_2} + \underset{\text{water}}{H_2O} \longrightarrow \underset{\text{carbonic acid}}{H_2CO_3} \longrightarrow \underset{\text{hydrogen ion}}{H^+} + \underset{\text{bicarbonate ion}}{HCO_3^-}$$

Carbonic anhydrase also speeds this reaction. The HCO_3^- diffuses out of the red blood cells to be carried in the plasma (see Fig. 35.12, *lower left*).

The release of H^+ from this reaction could drastically change the pH of the blood, which is highly undesirable because cells require a normal pH in order to remain healthy. However, the H^+ is absorbed by the globin portions of hemoglobin. Hemoglobin that has combined with H^+ is called reduced hemoglobin and has the formula HbH^+. HbH^+ plays a vital role in maintaining the normal pH of the blood. Blood that leaves the systemic capillaries is a dark maroon color because red blood cells contain reduced hemoglobin.

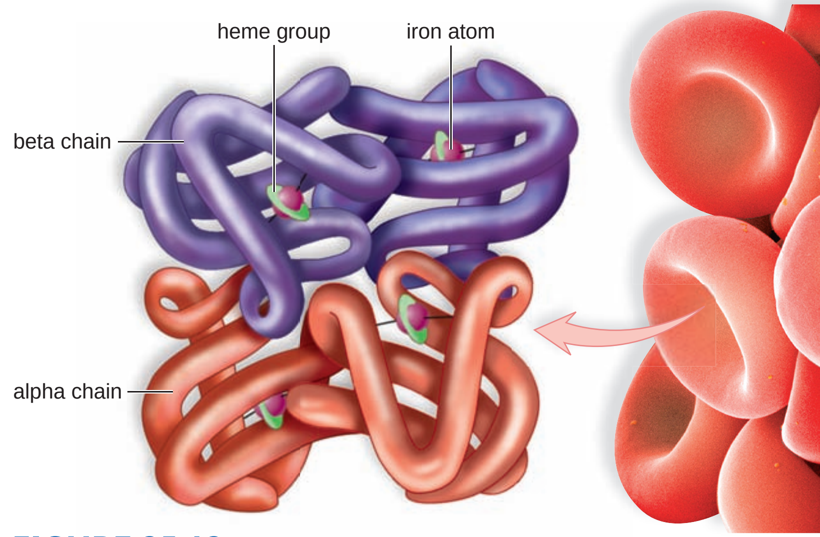


FIGURE 35.13 Hemoglobin.

Hemoglobin consists of four polypeptide chains (two alpha—red; two beta—purple), each associated with a heme group. Each heme group contains an iron atom, which can bind to O_2.

Check Your Progress 35.2

1. Explain the process of inspiration and expiration in humans.
2. Describe the functions of hemoglobin in the transport of O_2 and CO_2.

35.3 Respiration and Health

We have seen that the entire respiratory tract has a warm, wet, mucous membrane lining that is constantly exposed to environmental air. The quality of this air, determined by the pollutants and the pathogens therein, can affect our health.

Lower Respiratory Tract Disorders

Lower respiratory tract infections and disorders are shown in Figure 35.14.

Infections

Acute bronchitis is an infection of the primary and secondary bronchi. Usually it is preceded by a viral upper respiratory infection that has led to a secondary bacterial infection. Most likely, a nonproductive cough has become a deep cough that expectorates mucus and perhaps pus.

Pneumonia is a viral, bacterial, or fungal infection of the lungs in which bronchi and alveoli fill with a discharge, such as pus and fluid (Fig. 35.14). Most often it is preceded by influenza. Rather than being a generalized lung infection, pneumonia may be localized in specific lobules of the lungs. Obviously the more lobules involved, the more serious the infection. Pneumonia can be caused by a microbe that is usually held in check but has gained the upper hand due to stress and/or reduced immunity. AIDS patients are subject to a particularly rare form of pneumonia caused by a fungal-like organism called *Pneumocystis carinii*. Pneumonia of this type is almost never seen in individuals with a healthy immune system. High fever and chills with headache and chest pain are symptoms of pneumonia.

Pulmonary tuberculosis is caused by the tubercle bacillus, a type of bacterium. It is possible to tell if a person has ever been exposed to tuberculosis with a skin test in which a highly diluted extract of the bacillus is injected into the skin of the patient. A person who has never been in contact with the tubercle bacillus shows no reaction, but one who has developed immunity to the organism shows an area of inflammation that peaks in about 48 hours. When tubercle bacilli invade the lung tissue, the cells build a protective capsule about the organisms, isolating them from the rest of the body. This tiny capsule is called a tubercle. If the resistance of the body is high, the imprisoned organisms die, but if the resistance is low, the organisms eventually can be liberated. If a chest X ray detects active tubercles, the individual is put on appropriate drug therapy to ensure the localization of the disease and the eventual destruction of any live bacterial organisms.

Tuberculosis was a major killer in the United States before the middle of the twentieth century, after which antibiotic therapy brought it largely under control. In recent years, the incidence of tuberculosis has been on the rise, particularly among AIDS patients, the homeless, and the rural poor. Worse, the new strains are resistant to the usual antibiotic therapy.

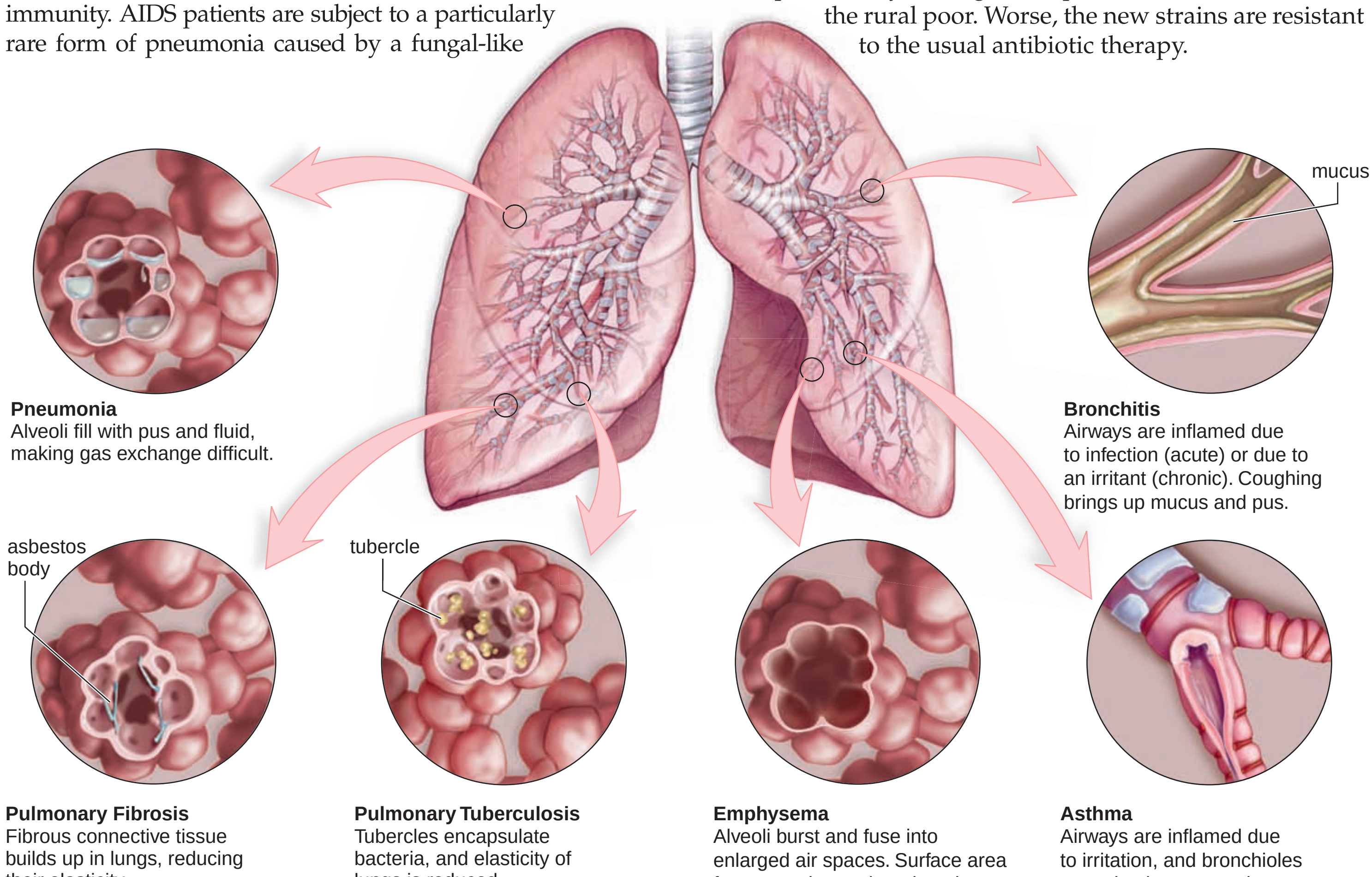
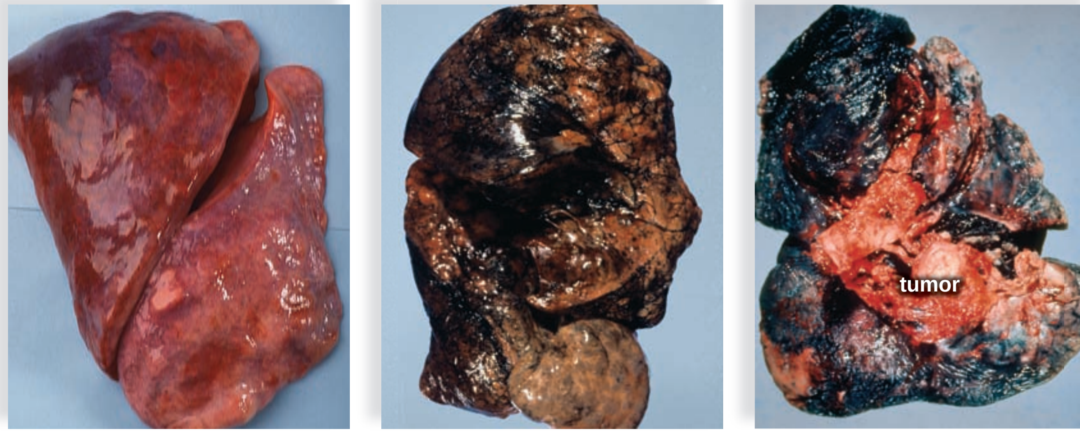


FIGURE 35.14 Common bronchial and pulmonary diseases.

Exposure to infectious pathogens and/or polluted air, including tobacco smoke, causes the diseases and disorders shown here.

FIGURE 35.15 Smoking and lung disorders.

Smoking causes almost 90% of all lung cancers and is also a major cause of emphysema. **a.** Normal lungs. **b.** The lungs of a person who died from emphysema are shrunken and blackened from trapped smoke. **c.** The lungs of a person who died from lung cancer are blackened from smoke except for the presence of the tumor, which is a mass of malformed soft tissue.



a. Normal lungs b. Emphysema c. Lung cancer

Disorders

Inhaling particles such as silica (sand), coal dust, asbestos, and, now it seems, fiberglass can lead to *pulmonary fibrosis*, a condition in which fibrous connective tissue builds up in the lungs. The lungs cannot inflate properly and are always tending toward deflation. Breathing asbestos is also associated with the development of cancer. Since asbestos has been used so widely as a fireproofing and insulating agent, unwarranted exposure has occurred.

In *chronic bronchitis,* the airways are inflamed and filled with mucus. A cough that brings up mucus is common. The bronchi have undergone degenerative changes, including the loss of cilia and their normal cleansing action. Under these conditions, an infection is more likely to occur. Smoking cigarettes and cigars and exposure to other pollutants, such as was experienced by workers and bystanders at Ground Zero after the September 11, 2001, attack, is the most frequent cause of chronic bronchitis.

Emphysema is a chronic and incurable lung disorder in which the alveoli are distended and their walls damaged so that the surface area available for gas exchange is reduced. Emphysema is often preceded by chronic bronchitis. Air trapped in the lungs leads to alveolar damage and a noticeable ballooning of the chest. The elastic recoil of the lungs is reduced, so not only are the airways narrowed, but the driving force behind expiration is also reduced. The patient is breathless and may have a cough. Because the surface area for gas exchange is reduced, oxygen reaching the heart and the brain is reduced. Even so, the heart works furiously to force more blood through the lungs, and an increased workload on the heart can result. Lack of oxygen to the brain can make the person feel depressed, sluggish, and irritable. Exercise, drug therapy, and supplemental oxygen, along with giving up smoking, may relieve the symptoms and possibly slow the progression of emphysema. Upon death, the lungs are decidedly abnormal (Fig. 35.15*b*).

Asthma is a disease of the bronchi and bronchioles that is marked by wheezing, breathlessness, and sometimes cough and expectoration of mucus. The airways are unusually sensitive to specific irritants, which can include a wide range of allergens such as pollen, animal dander, dust, cigarette smoke, and industrial fumes. Even cold air can be an irritant. When exposed to the irritant, the smooth muscle in the bronchioles undergoes spasms. It now appears that chemical mediators given off by immune cells in the bronchioles result in the spasms. Most asthma patients have some degree of bronchial inflammation that reduces the diameter of the airways and contributes to the seriousness of an attack. Asthma is not curable, but it is treatable. Special inhalers can control the inflammation and possibly prevent an attack, while other types of inhalers can stop the muscle spasms should an attack occur.

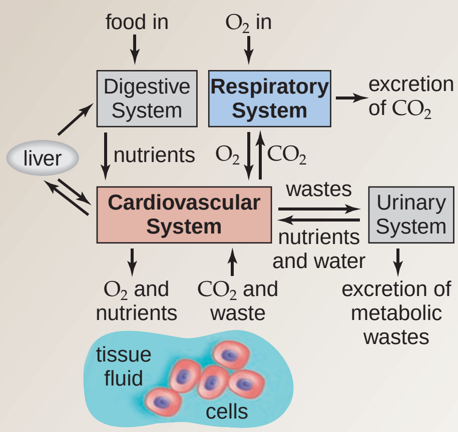
Lung Cancer

Lung cancer used to be more prevalent in men than in women, but recently it has surpassed breast cancer as a cause of death in women. This can be linked to an increase in the number of women who smoke today. Nearly 150,000 people in the United States die of lung cancer each year (Fig. 35.15*c*). The American Cancer Society links over 85% of these deaths to smoking. Autopsies on smokers have revealed the progressive steps by which the most common form of lung cancer develops. The first event appears to be thickening of the lining of the airways. Then there is a loss of cilia so that it is impossible to prevent dust and dirt from settling in the lungs. Following this, cells with atypical nuclei appear in the thickened lining. A tumor consisting of disordered cells with atypical nuclei is considered to be cancer in situ (at one location). A final step occurs when some of these cells break loose and penetrate other tissues, a process called metastasis. Now the cancer has spread. The original tumor may grow until a bronchus is blocked, cutting off the supply of air to that lung. The entire lung then collapses, the secretions trapped in the lung spaces become infected, and pneumonia or a lung abscess (localized area of pus) results. The only treatment that offers a possibility of cure is to remove a lobe or the whole lung before metastasis has had time to occur. This operation is called a *pneumonectomy***.**

Check Your Progress 35.3

1. Which of the lower respiratory tract disorders are largely due to infections and which are largely environmental in origin?

Connecting the Concepts



In mammals, the respiratory system consists of the respiratory tract with the nasal passages (or mouth) at one end and the lungs at the other end. Inspired air is 20% O_2 and 0.04% CO_2, while expired air is about 14% O_2 and 6% CO_2. Gas exchange in the lungs accounts for the difference in composition of inspired and expired air.

In the lungs, oxygen is absorbed into the bloodstream and from there it is transported by red blood cells to the capillaries, where it exits and enters tissue fluid. On the other hand, carbon dioxide enters capillaries at the tissues and is transported largely as the bicarbonate ion to the lungs, where it is converted to carbon dioxide and exits the body. Diffusion alone accounts for gas exchange in the lungs, called external respiration, and gas exchange in the tissues, called internal respiration. Energy is not needed, as gases follow their concentration gradients according to their partial pressures.

Internal gas exchange is extremely critical because cells use oxygen and release carbon dioxide as a result of cellular respiration, the process that generates ATP in cells. External gas exchange has the benefit of helping to keep the pH of the blood constant as required for homeostasis. When carbon dioxide exits, the blood pH returns to normal. In Chapter 36, we consider the contribution of the kidneys to homeostasis.

summary

35.1 Gas Exchange Surfaces

Some aquatic animals, such as hydras and planarians, use their entire body surface for gas exchange. Most animals have a specialized gas-exchange area. Large aquatic animals usually pass water through gills. In bony fishes, blood in the capillaries flows in the direction opposite that of the water. Blood takes up almost all of the oxygen in the water as a result of this countercurrent flow. On land, insects use tracheal systems, and vertebrates have lungs. In insects, air enters the tracheae at openings called spiracles. From there, the air moves to ever smaller tracheoles until gas exchange takes place at the cells themselves. Lungs are found inside the body, where water loss is reduced. To ventilate the lungs, some vertebrates use positive pressure, but most inhale, using muscular contraction to produce a negative pressure that causes air to rush into the lungs. When the breathing muscles relax, air is exhaled.

Birds have a series of air sacs attached to the lungs. When a bird inhales, air enters the posterior air sacs, and when a bird exhales, air moves through the lungs to the anterior air sacs before exiting the respiratory tract. The one-way flow of air through the lungs allows more fresh air to be present in the lungs with each breath, and this leads to greater uptake of oxygen from one breath of air.

35.2 Breathing and Transport of Gases

During inspiration, air enters the body at nasal cavities and then passes from the pharynx through the glottis, larynx, trachea, bronchi, and bronchioles to the alveoli of the lungs, where exchange occurs, and during expiration air passes in the opposite direction. Humans breathe by negative pressure, as do other mammals. During inspiration, the rib cage goes up and out, and the diaphragm lowers. The lungs expand and air comes rushing in. During expiration, the rib cage goes down and in, and the diaphragm rises. Therefore, air rushes out.

The rate of breathing increases when the amount of H^+ and carbon dioxide in the blood rises, as detected by chemoreceptors such as the aortic and carotid bodies.

Gas exchange in the lungs and tissues is brought about by diffusion. Hemoglobin transports oxygen in the blood; carbon dioxide is mainly transported in plasma as the bicarbonate ion. Excess hydrogen ions are transported by hemoglobin. The enzyme carbonic anhydrase found in red blood cells speeds the formation of the bicarbonate ion.

35.3 Respiration and Health

The respiratory tract is subject to infections such as pneumonia and pulmonary tuberculosis. New strains of tuberculosis are resistant to the usual antibiotic therapy.

Major lung disorders are usually due to cigarette smoking. In chronic bronchitis the air passages are inflamed, mucus is common, and the cilia that line the respiratory tract are gone. Emphysema and lung cancer are two of the most serious consequences of smoking cigarettes. When the lungs of these patients are removed upon death, they are blackened by smoke.

understanding the terms

alveolus (pl., alveoli) 654
aortic body 657
bicarbonate ion 659
bronchiole 655
bronchus (pl., bronchi) 655
carbaminohemoglobin 659
carbonic anhydrase 659
carotid body 657
countercurrent exchange 652
diaphragm 656
epiglottis 654
expiration 656
external respiration 650
gills 651
glottis 654
heme 659
hemoglobin (Hb) 659
inspiration 656
internal respiration 650
larynx 654
lungs 651
oxyhemoglobin 659
partial pressure 658
pharynx 654
respiration 650
respiratory center 657
trachea (pl., tracheae) 653, 654
ventilation 650
vocal cord 654

Match the terms to these definitions:

a. ______________ In terrestrial vertebrates, the mechanical act of moving air in and out of the lungs; breathing.

b. ______________ Dome-shaped muscularized sheet separating the thoracic cavity from the abdominal cavity in mammals.

c. ______________ Fold of tissue within the larynx; creates vocal sounds when it vibrates.

d. ______________ Respiratory organ in most aquatic animals; in fish, an outward extension of the pharynx.
e. ______________ Stage during breathing when air is pushed out of the lungs.

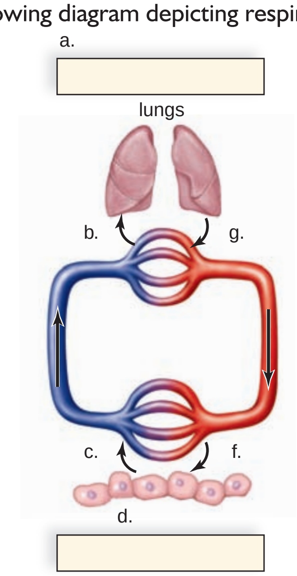
reviewing this chapter

1. Compare the respiratory organs of aquatic animals to those of terrestrial animals. 650–54
2. How does the countercurrent flow of blood within gill capillaries and water passing across the gills assist respiration in fishes? 652
3. Why is it beneficial for the body wall of earthworms to be moist? Why don't insects require circulatory system involvement in air transport? 653
4. Name the parts of the human respiratory system, and list a function for each part. How is air reaching the lungs cleansed? 654
5. Explain the phrase "breathing by using negative pressure." 656
6. Contrast the tidal ventilation mechanism in humans with the one-way ventilation mechanism in birds, and explain the benefits of the ventilation mechanism in birds. 656–57
7. The concentration of what substances in blood controls the breathing rate in humans? Explain. 658
8. How are oxygen and carbon dioxide transported in blood? What does carbonic anhydrase do? 659
9. Which conditions depicted in Figure 35.14 are due to infection? Which are due to behavioral or environmental factors? Explain. 660–61

testing yourself

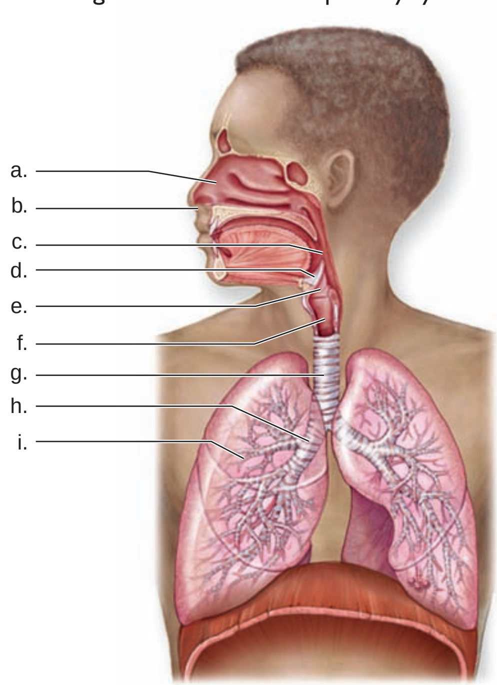
Choose the best answer for each question.

1. Label the following diagram depicting respiration.



2. One problem faced by terrestrial animals with lungs, but not by aquatic animals with gills, is that
   a. gas exchange involves water loss.
   b. breathing requires considerable energy.
   c. oxygen diffuses very slowly in air.
   d. the concentration of oxygen in water is greater than that in air.
   e. All of these are correct.
3. In which animal is the circulatory system not involved in gas transport?
   a. mouse
   b. dragonfly
   c. trout
   d. sparrow
   e. human
4. Birds have more efficient lungs than humans because the flow of air
   a. is the same during both inspiration and expiration.
   b. travels in only one direction through the lungs.
   c. never backs up as it does in human lungs.
   d. is not hindered by a larynx.
   e. enters their bones.
5. Which animal breathes by positive pressure?
   a. fish
   b. human
   c. bird
   d. frog
   e. planarian
6. Which of these is a true statement?
   a. In lung capillaries, carbon dioxide combines with water to produce carbonic acid.
   b. In tissue capillaries, carbonic acid breaks down to carbon dioxide and water.
   c. In lung capillaries, carbonic acid breaks down to carbon dioxide and water.
   d. In tissue capillaries, carbonic acid combines with hydrogen ions to form the carbonate ion.
   e. All of these statements are true.
7. Air enters the human lungs because
   a. atmospheric pressure is less than the pressure inside the lungs.
   b. atmospheric pressure is greater than the pressure inside the lungs.
   c. although the pressures are the same inside and outside, the partial pressure of oxygen is lower within the lungs.
   d. the residual air in the lungs causes the partial pressure of oxygen to be less than it is outside.
   e. the process of breathing pushes air into the lungs.
8. If the digestive and respiratory tracts were completely separate in humans, there would be no need for
   a. swallowing.
   b. a nose.
   c. an epiglottis.
   d. a diaphragm.
   e. All of these are correct.
9. In tracing the path of air in humans, you would list the trachea
   a. directly after the nose.
   b. directly before the bronchi.
   c. before the pharynx.
   d. directly before the lungs.
   e. Both a and c are correct.
10. In humans, the respiratory control center
    a. is stimulated by carbon dioxide.
    b. is located in the medulla oblongata.
    c. controls the rate of breathing.
    d. is stimulated by hydrogen ion concentration.
    e. All of these are correct.
11. Carbon dioxide is carried in the plasma
    a. in combination with hemoglobin.
    b. as the bicarbonate ion.
    c. combined with carbonic anhydrase.
    d. only as a part of tissue fluid.
    e. All of these are correct.
12. Which of these is anatomically incorrect?
    a. The nose has two nasal cavities.
    b. The pharynx connects the nasal and oral cavities to the larynx.
    c. The larynx contains the vocal cords.
    d. The trachea enters the lungs.
    e. The lungs contain many alveoli.

13. How is inhaled air modified before it reaches the lungs?
    a. It must be humidified.
    b. It must be warmed.
    c. It must be filtered and cleansed.
    d. All of these are correct.
14. Internal respiration refers to
    a. the exchange of gases between the air and the blood in the lungs.
    b. the movement of air into the lungs.
    c. the exchange of gases between the blood and tissue fluid.
    d. cellular respiration, resulting in the production of ATP.
15. The chemical reaction that converts carbon dioxide to a bicarbonate ion takes place in
    a. the blood plasma.
    b. red blood cells.
    c. the alveolus.
    d. the hemoglobin molecule.
16. Which of these would affect hemoglobin's O_2-binding capacity?
    a. pH
    b. partial pressure of oxygen
    c. blood pressure
    d. temperature
    e. All of these except c are correct.
17. The enzyme carbonic anhydrase
    a. causes the blood to be more basic in the tissues.
    b. speeds the conversion of carbonic acid to carbon dioxide and water.
    c. actively transports carbon dioxide out of capillaries.
    d. is active only at high altitudes.
    e. All of these are correct.
18. Which of these is incorrect concerning inspiration?
    a. Rib cage moves up and out.
    b. Diaphragm contracts and moves down.
    c. Pressure in lungs decreases, and air comes rushing in.
    d. The lungs expand because air comes rushing in.
19. Label this diagram of the human respiratory system.



thinking scientifically

1. You are a physician who witnessed Christopher Reeve's riding accident. Why might you immediately use mouth to mouth resuscitation until mechanical ventilation becomes available?
2. Fetal hemoglobin picks up oxygen from the maternal blood. If the oxygen-binding characteristics of hemoglobin in the fetus were identical to the hemoglobin of the mother, oxygen could never be transferred at the placenta to fetal circulation. What hypothesis about the oxygen-binding characteristics of fetal hemoglobin would explain how fetuses get the oxygen they need?

bioethical issue

Antibiotic Therapy

Antibiotics cure respiratory infections, but there are problems associated with antibiotic therapy. Aside from a possible allergic reaction, antibiotics not only kill off disease-causing bacteria, but they also reduce the number of beneficial bacteria in the intestinal tract and other locations. These beneficial bacteria hold in check the growth of other pathogens that now begin to flourish. Diarrhea can result, as can a vaginal yeast infection. The use of antibiotics can also prevent natural immunity from occurring, leading to the need for recurring antibiotic therapy. Especially alarming at this time is the occurrence of resistance. Resistance takes place when vulnerable bacteria are killed off by an antibiotic, and this allows resistant bacteria to become prevalent. The bacteria that cause ear, nose, and throat infections as well as scarlet fever and pneumonia are becoming widely resistant because we have not been using antibiotics properly. Tuberculosis is on the rise, and the new strains are resistant to the usual combined antibiotic therapy.

Every citizen needs to be aware of our present crisis situation. Stuart Levy, a Tufts University School of Medicine microbiologist, says that we should do what is ethical for society and ourselves. What is needed? Antibiotics kill bacteria, not viruses—therefore, we shouldn't take antibiotics unless we know for sure we have a bacterial infection. And we shouldn't take them prophylactically—that is, just in case we might need one. If antibiotics are taken in low dosages and intermittently, resistant strains are bound to take over. Animal and agricultural use should be pared down, and household disinfectants should no longer be spiked with antibacterial agents. Perhaps then, Levy says, vulnerable bacteria will begin to supplant the resistant ones in the population. Are you doing all you can to prevent bacteria from becoming resistant?

Biology website

The companion website for *Biology* provides a wealth of information organized and integrated by chapter. You will find practice tests, animations, videos, and much more that will complement your learning and understanding of general biology.

http://www.mhhe.com/maderbiology10

36

Body Fluid Regulation and Excretory Systems

If the salt concentration in body fluids is too high, cells shrink and die. If it is too low, cells explode and die. Yet animals are found in all sorts of environments, including marine environments that are too salty, freshwater environments that don't have enough salt, and even terrestrial environments that are simply too dry. Animals clearly spend a lot of energy regulating the composition of their body fluids, and chief among the organs that help are the kidneys of the urinary system. Sometimes animals, such as marine birds and reptiles, get a little help from accessory glands. Sea turtles have salt glands located above their eye that, true to their name, rid the body of salt. When the glands excrete a salty solution collected from body fluids, sea turtles appear to cry. We don't have salt glands and cannot survive after drinking salty water because the kidneys alone can't handle all the salt.

In this chapter, you will learn how animals excrete various metabolic wastes while maintaining their normal saltwater balance and their pH balance. The latter functions are of primary importance to homeostasis and continued good health.

Marine organisms rid the body of excess salt; fishes extrude salt at their gills, and turtles do so near their eyes.

concepts

36.1 Excretion and the Environment

The particular nitrogenous end product differs among animals according to the environment, but an excretory organ tends to be tubular, as we will see first among the invertebrates and then among the vertebrates.

Nitrogenous Waste Products

The breakdown of various molecules, including amino acids and nucleic acids, results in nitrogenous wastes. For simplicity's sake, we will limit our discussion to amino acid metabolism. When amino acids are broken down by the body to generate energy, or are converted to fats or carbohydrates, the amino groups ($—NH_2$) must be removed because they are not needed. Once the amino groups have been removed, they may be excreted from the body in the form of ammonia, urea, or uric acid, depending on the species. Removal of amino groups from amino acids requires a fairly set amount of energy. However, the amount of energy required to convert amino groups to ammonia, urea, or uric acid differs, as indicated in Figure 36.1.

Ammonia

Amino groups removed from amino acids immediately form **ammonia** (NH_3) by the addition of a third hydrogen ion. Little or no energy is required to convert an amino group to ammonia by adding a hydrogen ion. Ammonia is quite toxic and can be a nitrogenous excretory product if a good deal of water is available to wash it from the body. Ammonia is excreted by most fishes and other aquatic animals whose gills and skin surfaces are in direct contact with the water of the environment.

Urea

Production of urea requires the expenditure of energy because it is produced in the liver by a set of energy-requiring enzymatic reactions, known as the urea cycle. In this cycle, carrier molecules take up carbon dioxide and two molecules of ammonia, finally releasing urea. **Urea** is much less toxic than ammonia and can be excreted in a moderately concentrated solution. This allows body water to be conserved, an important advantage for terrestrial animals with limited access to water. Sharks, adult amphibians, and mammals usually excrete urea as their main nitrogenous waste.

Uric Acid

Uric acid is synthesized by a long, complex series of enzymatic reactions that requires expenditure of even more ATP than does urea synthesis. **Uric acid** is not very toxic, and it is poorly soluble in water. Poor solubility is an advantage if water conservation is needed, because uric acid can be concentrated even more readily than can urea. Uric acid is routinely excreted by insects, reptiles, and birds. In reptiles and birds, a dilute solution of uric acid passes from the kidneys to the *cloaca,* a common reservoir for the products of the digestive, urinary, and reproductive systems. The cloacal contents are refluxed into the large intestine, where water is reabsorbed. The white substance in bird feces is uric acid. Embryos of reptiles and birds develop inside completely enclosed shelled eggs. The production of insoluble, relatively nontoxic uric acid is advantageous for shelled embryos because all nitrogenous wastes are stored inside the shell until hatching takes place. Here again, the advantage of water conservation seems to counterbalance the disadvantage of energy expenditure for synthesis of an excretory molecule.

In general, it is possible to predict which metabolic waste product an animal excretes based on its anatomy and environment—but not always. For example, unlike most other birds, hummingbirds excrete more ammonia than uric acid. **Excretion** of ammonia, as stated, requires a lot of fluid to keep its toxicity under control. Recall that hummingbirds are fluid feeders, and as such, they have plenty of fluid available for excreting ammonia.

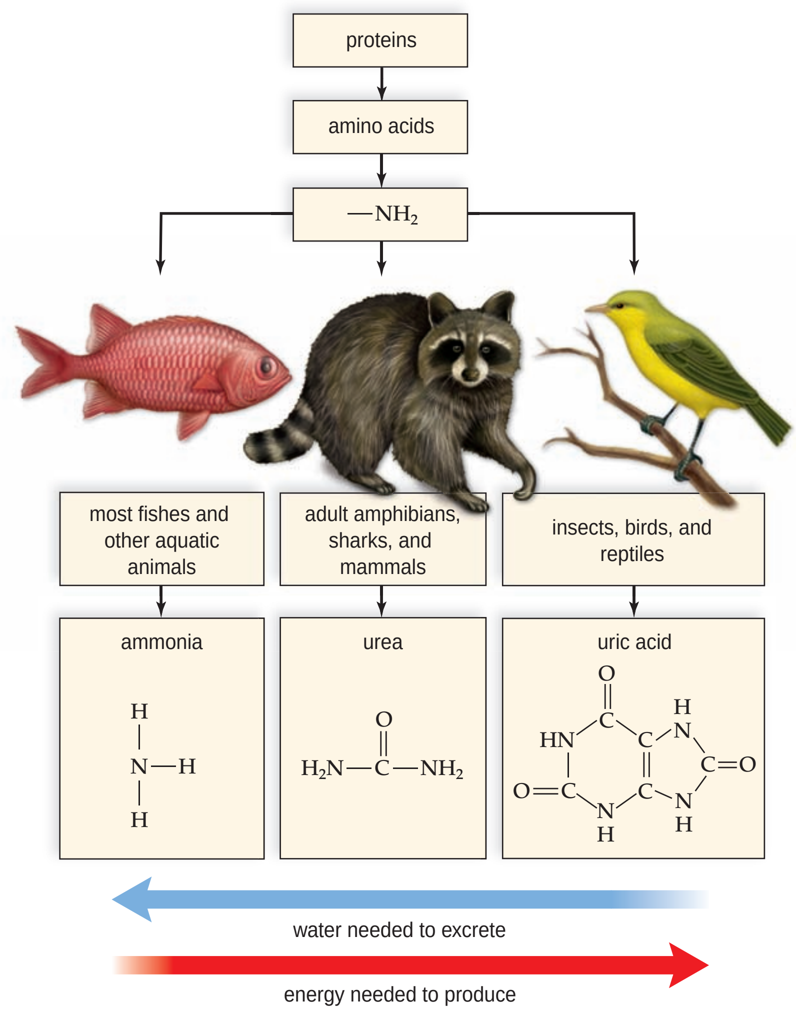


FIGURE 36.1 Nitrogenous wastes.

Proteins are hydrolyzed to amino acids, whose breakdown results in carbon chains and amino groups ($—NH_2$). The carbon chains can be used as an energy source, but the amino groups must be excreted as ammonia, urea, or uric acid.

Excretory Organs Among Invertebrates

Most animals have tubular excretory organs that regulate the water-salt balance of the body and excrete metabolic wastes into the environment. Here we give three examples among the invertebrates.

The planarians, which are flatworms living in fresh water, have two strands of branching excretory tubules that open to the outside of the body through excretory pores (Fig. 36.2*a*). Located along the tubules are bulblike **flame cells,** each of which contains a cluster of beating cilia that looks like a flickering flame under the microscope. The beating of flame-cell cilia propels fluid through the excretory tubules and out of the body. The system is believed to function in ridding the body of excess water and in excreting wastes.

The body of an earthworm is divided into segments, and nearly every body segment has a pair of excretory structures called **nephridia.** Each nephridium is a tubule with a ciliated opening and an excretory pore (Fig. 36.2*b*). As fluid from the coelom is propelled through the tubule by beating cilia, its composition is modified. For example, nutrient substances are reabsorbed and carried away by a network of capillaries surrounding the tubule. The urine of an earthworm contains metabolic wastes, salts, and water. Although the earthworm is considered a terrestrial animal, it excretes a very dilute urine. Each day, an earthworm may produce a volume of urine equal to 60% of its body weight. The excretion of ammonia is consistent with these data.

Insects have a unique excretory system consisting of long, thin tubules called **Malpighian tubules** attached to the gut. Uric acid is actively transported from the surrounding hemolymph into these tubules, and water follows a salt gradient established by active transport of K^+. Water and other useful substances are reabsorbed at the rectum, but the uric acid leaves the body at the anus. Insects that live in water, or eat large quantities of moist food, reabsorb little water. But insects in dry environments reabsorb most of the water and excrete a dry, semisolid mass of uric acid.

The excretory organs of other arthropods are given different names, although they function similarly. In crustaceans (e.g., crabs, crayfish), nitrogenous wastes are generally removed by diffusion across the gills—for those species that have gills. Even so, crustaceans possess excretory organs called *green glands* located in the ventral portion of the head region. Fluid collects within the tubules from the surrounding blood of the hemocoel, but this fluid is modified by the time it leaves the tubules. The secretion of salts into the tubule regulates the amount of urine excreted. In shrimp and pillbugs, the excretory organs are located in the maxillary segments and are called *maxillary glands.* Spiders, scorpions, and other arachnids possess *coxal glands,* which are located near one or more appendages and used for excretion. Coxal glands are spherical sacs resembling annelid nephridia. Wastes are collected from the surrounding blood of the hemocoel and discharged through pores at one to several pairs of appendages.

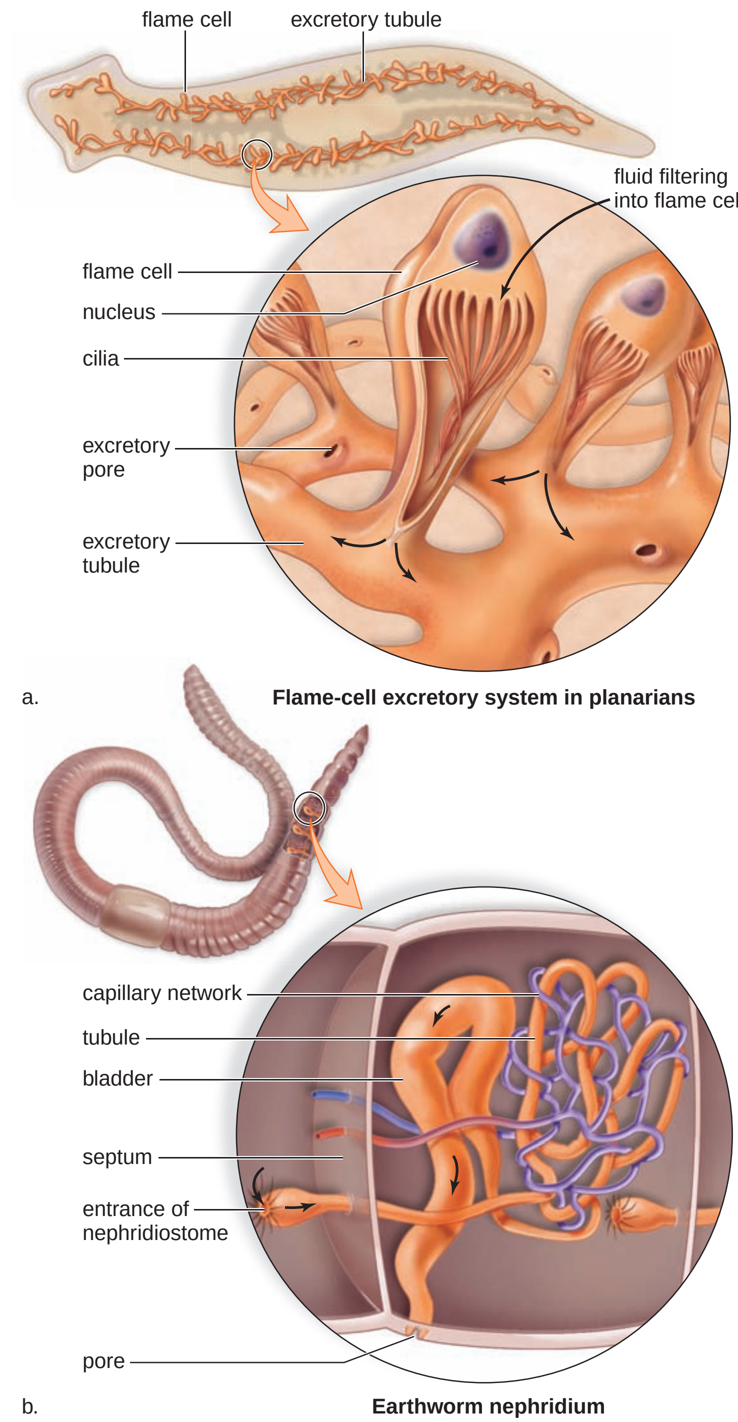


FIGURE 36.2 Excretory organs in animals.

a. Two or more tracts of branching tubules run the length of the body and open to the outside by pores. At the ends of side branches are small bulblike cells called flame cells. **b.** The nephridium has a ciliated opening, the nephridiostome, that leads to a coiled tubule surrounded by a capillary network. Urine can be temporarily stored in the bladder before being released to the outside via a pore termed a nephridiopore.

In conclusion, invertebrates utilize tubules to rid the body of wastes and maintain a water-salt balance. On occasion, excretion also involves other organs, such as the rectum in the earthworm and the gills in crayfish.