Insect hormones control molting and metamorphosis

Most invertebrate groups produce hormones as well; these control reproduction, growth, and color change. A dramatic action of hormones in insects is similar to the role of thyroid hormones in amphibian metamorphosis.

As insects grow during postembryonic development, their hardened exoskeletons do not expand. To overcome this problem, insects undergo a series of molts wherein they shed their old exoskeleton (figure 46.16) and secrete a new, larger one. In some insects, a juvenile insect, or larva, undergoes a radical transformation to the adult form during a single molt. This process is called metamorphosis.

Hormonal secretions influence both molting and metamorphosis in insects. Prior to molting, neurosecretory cells on the surface of the brain secrete a small peptide, **prothoracicotropic hormone (PTTH),** which in turn stimulates a gland in the thorax called the prothoracic gland to produce **molting hormone,** or **ecdysone** (see figure 46.16). High levels of ecdysone bring about the biochemical and behavioral changes that cause molting to occur.

Another pair of endocrine glands near the brain, called the *corpora allata*, produce a hormone called **juvenile hormone.** High levels of juvenile hormone prevent the transformation to the adult and result in a larval-to-larval molt. If the level of juvenile hormone is low, however, the molt will result in metamorphosis (figure 46.17).

Cancer cells may alter hormone production or have altered hormonal responses

Hormones and paracrine secretions actively regulate growth and cell division. Normally, hormone production is kept under precise control, but malfunctions in signaling systems can sometimes occur. Unregulated hormone stimulation can then lead to serious physical consequences.

Tumors that develop in endocrine glands, such as the anterior pituitary or the thyroid, can produce excessive amounts of hormones, causing conditions such as gigantism or hyperthyroidism. Spontaneous mutations can damage receptors or intracellular signaling proteins, with the result that target cell responses are activated even in the absence of hormone stimulation. Mutations in growth factor receptors, for example, can activate excessive cell division, resulting in tumor formation. Some tumors that develop in steroid-responsive tissues, such as the breast and prostate, remain sensitive to hormone stimulation. Blocking steroid hormone production can therefore diminish tumor growth.

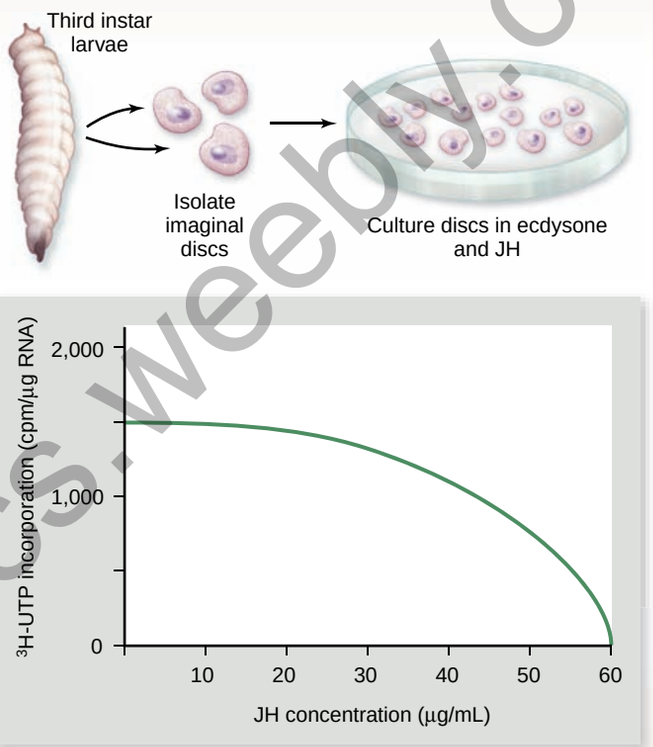
The important effects of hormones on development and differentiation are illustrated by the case of diethystilbestrol (DES). DES is a synthetic estrogen that was given to pregnant women from 1940 to 1970 to prevent miscarriage. It was subsequently discovered that daughters who had been exposed to DES as fetuses had an elevated probability of developing a rare form of cervical cancer later in life. Developmental alterations elicited by hormone treatment may thus take many years to become apparent.

SCIENTIFIC THINKING

Hypothesis: *Juvenile hormone blocks or inhibits the stimulation of gene expression by ecdysone.*

Prediction: *Treatment of isolated imaginal discs with ecdysone plus increasing amounts of JH should show a decrease in ecdysone stimulated transcription.*

Test: *Discs dissected from late third instar* Drosophila *larvae are incubated in the presence of ecdysone, with and without JH. Incorporation of ^{3}H-UTP into RNA was used as a measure of gene expression.*



Result: *The graph shows a relatively high incorporation of ^{3}H-UTP in the presence of ecdysone alone. The addition of JH causes dose-dependent reduction of RNA synthesis.*

Conclusion: *JH inhibits the ecdysone-stimulated synthesis of RNA in imaginal discs.*

Further Experiments: *How else can this system with isolated imaginal discs be used to analyze metamorphosis?*

Figure 46.17 **Effect of ecdysone and juvenile hormone on RNA synthesis in isolated *Drosophila* imaginal discs.**

Learning Outcomes Review 46.5

Testosterone causes an embryo to develop as a male; testosterone and estrogen produced at puberty are responsible for secondary sex characteristics. The female menstrual cycle is regulated by sex hormone balance. The thymus, the right atrium of the heart, and the kidneys secrete hormones although it is not their main function. In insects, molting hormone elicits molting, and low levels of juvenile hormone cause metamorphosis.

- ***Atrial natriuretic hormone reduces blood volume; would this affect blood pressure?***

Chapter Review

46.1 Regulation of Body Processes by Chemical Messengers

Hormones are signaling molecules carried by the blood and may have distant targets. Paracrine regulators act locally, and pheromones released into the environment communicate between individuals of the same species.

Some molecules act as both circulating hormones and neurotransmitters.

Norepinephrine is a neurotransmitter in the sympathetic nervous system and also is a hormone that is released into the blood by the adrenal glands.

Endocrine glands produce three chemical classes of hormones.

The three classes of endocrine hormones are peptides and proteins, such as TSH; amino acid derivatives, such as thyroxine; and steroids, such as estrogen and testosterone (see table 46.1).

Hormones can be categorized as lipophilic or hydrophilic.

Lipophilic hormones are fat-soluble and can cross the cell membrane; hydrophilic hormones are water-soluble and cannot cross membranes.

Paracrine regulators exert powerful effects within tissues.

Paracrine regulation occurs in most organs and among immune-system cells. Prostaglandins are involved in inflammation, and they are the target of NSAIDs.

46.2 Actions of Lipophilic Versus Hydrophilic Hormones

Lipophilic hormones activate intracellular receptors.

Circulating lipophilic hormones are carried in the blood bound to transport proteins (see figure 46.3). They pass through the plasma membrane and activate intracellular receptors. The hormone-receptor complex can bind to specific gene promoter regions termed hormone response elements to activate transcription.

Hydrophilic hormones activate receptors on target cell membranes.

Hydrophilic hormones bind to a membrane receptor to initiate a signal transduction pathway (see figure 46.6). Many receptors are kinases that phosphorylate proteins directly. Others are G protein–coupled receptors that activate a second-messenger system. Hydrophilic hormones tend to be short-lived, but lipophilic hormones tend to have effects of longer duration.

46.3 The Pituitary and Hypothalamus: The Body's Control Centers

The pituitary is a compound endocrine gland.

The anterior pituitary (adenohypophysis) is composed of glandular tissue derived from epithelial tissue; the posterior pituitary (neurohypophysis) is fibrous and is derived from neural tissue.

The posterior pituitary stores and releases two neurohormones.

The posterior pituitary contains axons from the hypothalamus that release neurohormones. One of these is ADH, involved in water reabsorption; the other is oxytocin.

The anterior pituitary produces seven hormones.

The hormones produced by the anterior pituitary include peptide, protein and glycoprotein hormones. These hormones tend to stimulate growth, and many are tropic hormones that stimulate other endocrine glands (see table 46.1).

Hypothalamic neurohormones regulate the anterior pituitary.

Releasing and inhibiting hormones produced in the hypothalamus pass to the anterior pituitary through a portal system and regulate the anterior pituitary's hormone production (see figure 46.8).

Feedback from peripheral endocrine glands regulates anterior-pituitary hormones.

The activity of the anterior pituitary is also regulated by negative feedback; for example, thyroxine, produced by the thyroid in response to TSH, inhibits further secretion of TSH (see figure 46.9).

Hormones of the anterior pituitary work directly and indirectly.

Three of the seven hormones, GH, prolactin, and MSH, work directly on nonendocrine tissues; the other four, ACTH, TSH, LH, and FSH, are tropic hormones that have endocrine glands as their targets. Defects in GH production can lead to either pituitary dwarfism (low), or gigantism (high).

46.4 The Major Peripheral Endocrine Glands

Some endocrine glands are controlled by tropic hormones of the pituitary, others are independent of pituitary control.

The thyroid gland regulates basal metabolism and development.

The thyroid hormones thyroxine and triiodothyronine regulate basal metabolism in vertebrates and trigger metamorphosis in amphibians (see figure 46.12).

Calcium homeostasis is regulated by several hormones.

Blood calcium is regulated by calcitonin, which lowers blood calcium levels, and parathyroid hormone, which raises blood calcium levels (see figure 46.13).

The adrenal gland releases both catecholamine and steroid hormones.

Catecholamines, epinephrine and norepinephrine, trigger "alarm" responses (see figure 46.14). Corticosteroids maintain glucose homeostasis and modulate some aspects of the immune response.

Pancreatic hormones are primary regulators of carbohydrate metabolism.

Blood glucose is controlled by antagonistic hormones. The pancreas secretes insulin, which reduces blood glucose, and glucagon, which raises blood glucose (see figure 46.15). Type I diabetes arises from loss of insulin-producing cells, and type II is a result of insulin insensitivity.

46.5 Other Hormones and Their Effects

Sex steroids regulate reproductive development.

Sex steroids regulate sexual development and reproduction. The ovaries primarily produce estrogen and progesterone, which are responsible for the menstrual cycle. The testes produce testosterone.

Melatonin is crucial to circadian cycles.

The pineal gland produces melatonin, which can control the dispersion of pigment granules and the daily wake–sleep cycles.

Some hormones are not produced by endocrine glands.

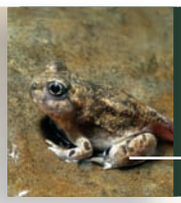
The thymus secretes hormones that regulate the immune system. The right atrium of the heart secretes atrial natriuretic hormone, which acts antagonistically to aldosterone. The skin manufactures and secretes vitamin D.

Insect hormones control molting and metamorphosis.

In insects the hormone ecdysone stimulates molting, and juvenile hormone levels control the nature of the molt. Metamorphosis requires high ecdysone and low juvenile hormone.

Cancer cells may alter hormone production or have altered hormonal responses.

Cancer developing from cells targeted by hormones, such as in the breast and prostate, may still be stimulated by those hormones.



Review Questions

UNDERSTAND

1. Which of the following best describes hormones?
   a. Hormones are relatively unstable and work only in the area adjacent to the gland that produced them.
   b. Hormones are long-lasting chemicals released from glands.
   c. All hormones are lipid-soluble.
   d. Hormones are chemical messengers that are released into the environment.
2. Steroid hormones
   a. can diffuse through the membrane without a carrier.
   b. have a direct effect on gene expression.
   c. bind to membrane receptors.
   d. both a and b
3. Second messengers are activated in response to
   a. steroid hormones.
   b. thyroxine.
   c. hydrophilic hormones.
   d. all of these.
4. Which of the following is true about lipophilic hormones?
   a. They are freely soluble in the blood.
   b. They require a transport protein in the bloodstream.
   c. They cannot enter their target cells.
   d. They are rapidly deactivated after binding to their receptors.
5. An organ is classified as part of the endocrine system if it
   a. produces cholesterol.
   b. is capable of converting amino acids into hormones.
   c. has intracellular receptors for hormones.
   d. secretes hormones into the circulatory system.
6. Hormones released from the pituitary gland have two different sources. Those that are produced by the neurons of the hypothalamus are released through the _____, and those produced within the pituitary are released through the _____.
   a. thalamus; hippocampus
   b. neurohypophysis; adenohypophysis
   c. right pituitary; left pituitary
   d. cortex; medulla
7. Which of the following conditions is unrelated to the production of growth hormone?
   a. Control of blood calcium
   b. Pituitary dwarfism
   c. Increased milk production in cows
   d. Acromegaly

APPLY

1. You think one of your teammates is using anabolic steroids to build muscle. You know that continued use of steroids can cause profound changes in cell function. This is due in part to the fact that these hormones act
   a. to regulate gene expression.
   b. by activating second messengers.
   c. as protein kinases.
   d. via G protein–coupled receptors.
2. Your Uncle Sal likes to party. When he goes out drinking, he complains that he needs to urinate more often. You explain to him that this is because alcohol suppresses the release of the hormone
   a. thyroxine, which increases water reabsorption from the kidney.
   b. thyroxine, which decreases water reabsorption from the kidney.
   c. ADH, which decreases water reabsorption from the kidney.
   d. ADH, which increases water reabsorption from the kidney.
3. Your new research project is to design a pesticide that will disrupt the endocrine systems of arthropods without harming humans and other mammals. Which of the following substances should be the target of your investigations?
   a. Insulin
   b. ADH
   c. Juvenile hormone
   d. Cortisol
4. Coat color in mammals is controlled by a hormone receptor called the melanocortin receptor. When this receptor is bound by the hormone MSH, pigment cells produce dark eumelanin. When the receptor is bound by an MSH antagonist that prevents MSH binding, pigment cells make yellow/red pheomelanin. In the Irish Setter, the overall red coat color could be due to a mutation in the
   a. receptor that prevents the antagonist from binding.
   b. receptor that prevents MSH from binding.
   c. MSH protein such that it binds the receptor more efficiently.
   d. antagonist such that it no longer binds to the receptor.
5. Tumors that affect the pituitary can lead to decreases in some, but not all, hormones released by the pituitary. A patient with such a tumor exhibits fatigue, weight loss, and low blood sugar. This is probably due to lack of production of
   a. GH, which leads to loss of muscle mass.
   b. ACTH, which leads to loss of production of glucocorticoids.

c. TSH, which leads to loss of production of thyroxin.
d. ADH, which leads to excess urine production.

6. You experience a longer period than normal between meals. Your body's response to this will be to produce
   a. insulin to raise your blood sugar.
   b. glucagon to raise your blood sugar.
   c. insulin to lower your blood sugar.
   d. glucagon to lower your blood sugar.
7. Mild vitamin D deficiency can lead to osteoporosis, or reduced bone mineral density. This is thought to be due to an association with increased levels of
   a. calcitonin, which leads to an increase in serum Ca^{2+} and bone loss.
   b. PTH, which leads to an increase in serum Ca^{2+} and bone loss.
   c. ADH, which reduces blood pressure and leads to bone loss.
   d. insulin, which leads to a decrease in blood glucose and bone loss.

SYNTHESIZE

1. How can blocking hormone production decrease cancerous tumor growth?
2. Suppose that two different organs, such as the liver and heart, are sensitive to a particular hormone (such as epinephrine). The cells in both organs have identical receptors for the hormone, and hormone-receptor binding produces the same intracellular second messenger in both organs. However, the hormone produces different effects in the two organs. Explain how this can happen.
3. Many physiological parameters, such as blood Ca^{2+} concentration and blood glucose levels, are controlled by two hormones that have opposite effects. What is the advantage of achieving regulation in this manner instead of by using a single hormone that changes the parameters in one direction only?

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Chapter 47

The Musculoskeletal System

Chapter Outline

Introduction

The ability to move is so much a part of our daily lives that we tend to take it for granted. It is made possible by the combination of a semirigid skeletal system, joints that act as hinges, and a muscular system that can pull on this skeleton. Animal locomotion can be thought of as muscular action that produces a change in body shape, which places a force on the outside environment. When a race horse runs down the track, its legs move forward and backward. As its feet contact the ground, the force they exert move its body forward at a considerable speed. In a similar way, when a bird takes off into flight, its wings exert force on the air; a swimming fish's movements push against the water. In this chapter, we will examine the nature of the muscular and skeletal systems that allow animal movement.

47.1 Types of Skeletal Systems

Learning Outcomes

1. *Compare hydrostatic skeletons, exoskeletons, and endoskeletons.*
2. *Explain how animals with hydrostatic skeletons move.*

Muscles have to pull against something to produce the changes that cause movement. This necessary form of supporting structure is called a skeletal system. Zoologists commonly recognize three types of skeletal systems in animals: **hydrostatic skeletons, exoskeletons,** and **endoskeletons.**

Hydrostatic skeletons use water pressure inside a body wall

Hydrostatic skeletons are found primarily in soft-bodied terrestrial invertebrates, such as earthworms and slugs, and soft-bodied aquatic invertebrates, such as jellyfish, and squids.

Musculoskeletal action in earthworms

In these animals a fluid-filled central cavity is encompassed by two sets of muscles in the body wall: circular muscles that are repeated in segments and run the length of the body, and longitudinal muscles that oppose the action of the circular muscles.

Muscles act on the fluid in the body's central space, which represents the hydrostatic skeleton. As locomotion begins (figure 47.1) the anterior circular muscles contract, pressing on the inner fluid, and forcing the front of the body to become thin as the body wall in this region extends forward.

On the underside of a worm's body are short, bristle-like structures called chaetae. When circular muscles act, the chaetae of that region are pulled up close to the body and lose contact with the ground. Circular-muscle activity is passed backward, segment by segment, to create a backward wave of contraction.

As this wave continues, the anterior circular muscles now relax, and the longitudinal muscles take over, thickening the front end of the worm and allowing the chaetae to protrude and regain contact with the ground. The chaetae now prevent that body section from slipping backward. This locomotion process proceeds as waves of circular muscle contraction are followed by waves of longitudinal muscle effects.

Exoskeletons consist of a rigid outer covering

Exoskeletons are a rigid, hard case that surrounds the body. Arthropods, such as crustaceans and insects, have exoskeletons made of the polysaccharide *chitin* (figure 47.2*a*). As you learned in earlier chapters, chitin is found in the cell walls of fungi and some protists as well as in the exoskeletons of arthropods.

A chitinous exoskeleton resists bending and thus acts as the skeletal framework of the body; it also protects the internal organs and provides attachment sites for the muscles, which lie inside the exoskeletal casing. But in order to grow, the animal must periodically molt, shedding the exoskeleton (see chapter 34). The animal is vulnerable to predation until the new (slightly larger) exoskeleton forms. Molting crabs and lobsters often hide until the process is completed.

Exoskeletons have other limitations. The chitinous framework is not as strong as a bony, internal one. This fact by itself would set a limit for insect size, but there is a more important factor: Insects breathe through openings in their body that lead into tiny tubes, and as insect size increases beyond a certain limit, the ratio between the inside surface area of the tubes and the volume of the body overwhelms this sort of respiratory system. Finally, when muscles are confined within an

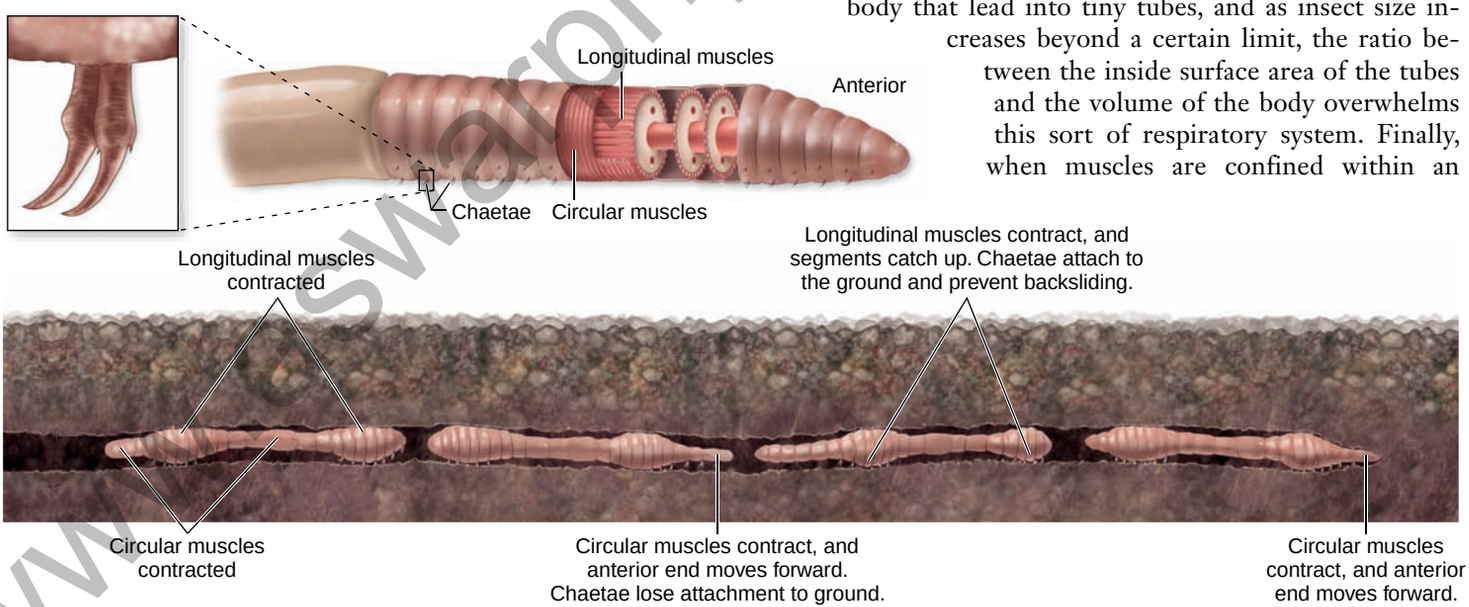
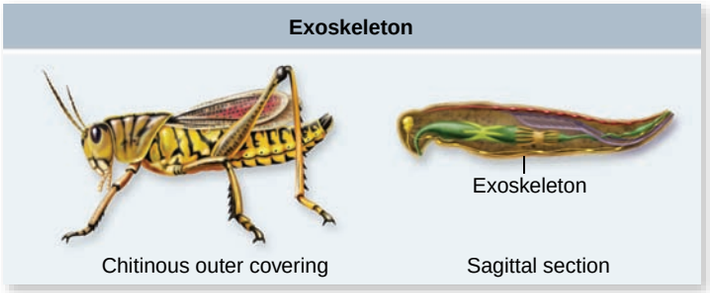
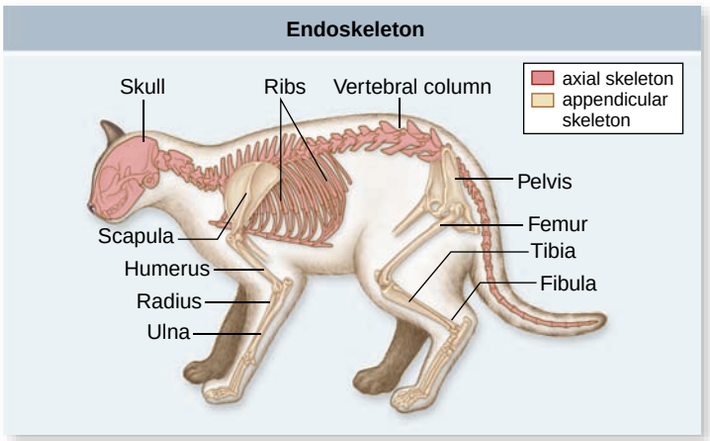


Figure 47.1 Locomotion in earthworms. The hydrostatic skeleton of the earthworm uses muscles to move fluid within the segmented body cavity, changing the shape of the animal. When circular muscles contract the pressure in the fluid rises. At the same time the longitudinal muscles relax, and the body becomes longer and thinner. When the longitudinal muscles contract and the circular muscles relax, the chaetae of the worm's lower surface extend to prevent backsliding. A wave of circular followed by longitudinal muscle contractions down the body produces forward movement.



a.



b.

Figure 47.2 Exoskeleton and endoskeleton.
a. The hard, tough outer covering of an arthropod, such as this grasshopper, is its exoskeleton and is composed of chitin.
b. Vertebrates, such as this cat, have endoskeletons formed of bone and cartilage. Some of the major bony features are labeled.

exoskeleton, they cannot enlarge in size and power with increased use, as they can in animals with endoskeletons.

Endoskeletons are composed of hard, internal structures

Endoskeletons, found in vertebrates and echinoderms, are rigid internal skeletons that form the body's framework and offer surfaces for muscle attachment. Echinoderms, such as sea urchins and sand dollars, have skeletons made of calcite, a crystalline form of calcium carbonate. This calcium compound is different from that in bone, which is based on calcium phosphate.

Vertebrate skeletal tissues

The vertebrate endoskeleton (figure 47.2b) includes fibrous dense connective tissue along with the more rigid special connective tissues, cartilage or bone (see chapter 43). Cartilage is strong and slightly flexible, a characteristic important in such functions as padding the ends of bones where they come together in a joint. Although some large, active animals such as sharks have totally cartilaginous skeletons, bone is the main component in vertebrate skeletons. Bone is much stronger than cartilage and much less flexible.

Unlike chitin, both cartilage and bone are living tissues. Bone, particularly, can have high metabolic activity, especially if bone cells are present throughout the matrix, a common condition. Bone, and to some extent cartilage, can change and remodel itself in response to injury or to physical stresses.

Learning Outcomes Review 47.1

With a hydrostatic skeleton, muscle contraction puts pressure on the fluid inside the body, forcing the body to extend. Opposing muscles then shorten the body to draw the animal forward. Invertebrate exoskeletons consist of hard chitin; they must be shed and renewed (molting) for the animal to grow. Endoskeletons are composed of fibrous dense connective tissue along with cartilage or mineralized bone.

- ***What limitations does an exoskeleton impose on terrestrial invertebrates?***

47.2 A Closer Look at Bone

Learning Outcomes

1. ***Compare intramembranous and endochondral development.***
2. ***Describe how growth occurs in epiphyses.***
3. ***Explain how bone remodeling occurs.***

Bone is a hard but resilient tissue that is unique to vertebrate animals. This connective tissue first appeared over 520 MYA and is now found in all vertebrates except cartilaginous fishes (see chapter 35).

Bones can be classified by two modes of development

Bone tissue itself can be of several types classified in a few different ways. The most common system is based on the way in which bone develops.

Intramembranous development

In intramembranous development, bones form within a layer of connective tissue. Many of the flat bones that make up the exterior of the skull and jaw are intramembranous.

Typically, the site of the intramembranous bone-to-be begins in a designated region in the dermis of the skin. During embryonic development, the dermis is formed largely of **mesenchyme**—a loose tissue consisting of undifferentiated mesenchyme cells and other cells that have arisen from them—along with collagen fibers. Some of the undifferentiated mesenchyme cells differentiate to become specialized cells called **osteoblasts** (figure 47.3). These osteoblasts arrange themselves along the collagenous fibers and begin to secrete the enzyme alkaline phosphatase, which causes calcium phosphate salts to form in a crystalline configuration called *hydroxyapatite*. The crystals merge along the fibers to encase them.

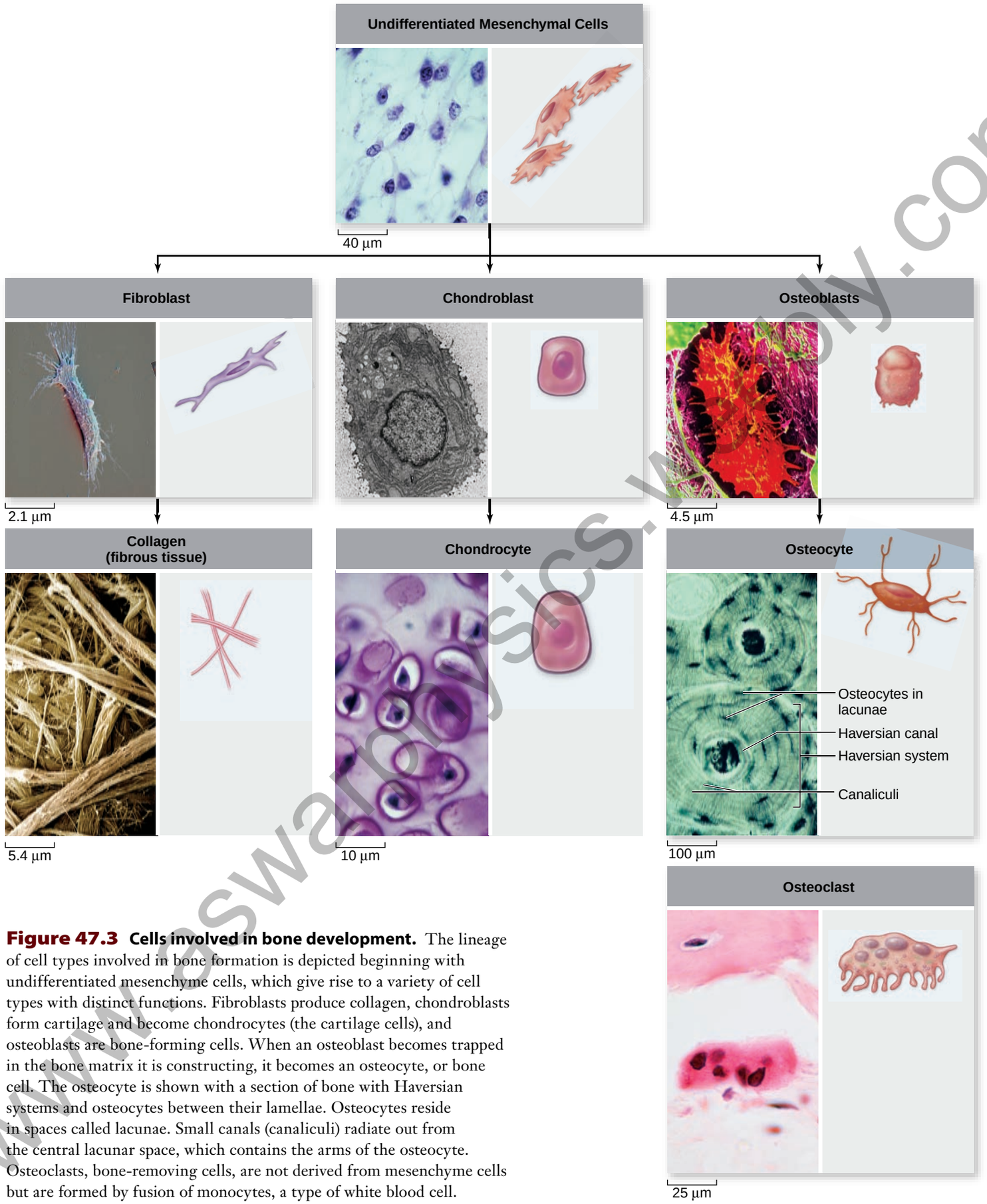


Figure 47.3 Cells involved in bone development. The lineage of cell types involved in bone formation is depicted beginning with undifferentiated mesenchyme cells, which give rise to a variety of cell types with distinct functions. Fibroblasts produce collagen, chondroblasts form cartilage and become chondrocytes (the cartilage cells), and osteoblasts are bone-forming cells. When an osteoblast becomes trapped in the bone matrix it is constructing, it becomes an osteocyte, or bone cell. The osteocyte is shown with a section of bone with Haversian systems and osteocytes between their lamellae. Osteocytes reside in spaces called lacunae. Small canals (canaliculi) radiate out from the central lacunar space, which contains the arms of the osteocyte. Osteoclasts, bone-removing cells, are not derived from mesenchyme cells but are formed by fusion of monocytes, a type of white blood cell.

The crystals give the bone its hardness, but without the resilience afforded by collagen's stretching ability, bone would be rigid but dangerously brittle. Typical bones have roughly equal volumes of collagen and hydroxyapatite, but hydroxyapatite contributes about 65% to the bone's weight.

As the osteoblasts continue to make bone crystals, some become trapped in the bone matrix and undergo dramatic changes in shape and function, now becoming cells called osteocytes (see figure 47.3). They lie in tight spaces within the bone matrix called lacunae. Little canals extending from the lacunae, called **canaliculi,** permit contact of the starburst-like extensions of each osteocyte with those of its neighbors (see figure 47.3). In this way, many cells within bones can participate in intercellular communication.

As an intramembranous bone grows, it requires alterations of shape. Imagine that you were modeling with clay, and you wanted to take a tiny clay bowl and make it larger. Simply putting more clay on the outside would not work; you would need to remove clay from the inside to increase the bowl's capacity as well. As bone grows, it must also undergo a remodeling process, with matrix being added in some regions and removed in others. This is where osteoclasts come in. These unusual cells are formed from the fusion of monocytes, a type of white blood cell, to form large multinucleate cells. Their function is to break down the bone matrix.

Endochondral development

Bones that form through endochondral development are typically those that are deeper in the body and form its architectural framework. Examples include vertebrae, ribs, bones of the shoulder and pelvis, long bones of the limbs, and the most internal of the skull bones. Endochondral bones begin as tiny, cartilaginous models that have the rough shape of the bones that eventually will be formed. Bone development of this kind consists of adding bone to the outside of the cartilaginous model, while replacing the interior cartilage with bone.

Bone added to the outside of the model is produced in the fibrous sheath that envelopes the cartilage. This sheath is tough and made of collagen fibers, but it also contains undifferentiated mesenchyme cells. Osteoblasts arise and sort themselves out along the fibers in the deepest part of the sheath. Bone is then formed between the sheath and the cartilaginous matrix. This process is somewhat similar to what occurs in the dermis in the production of intramembranous bone.

As the outer bone is formed, the interior cartilage begins to calcify. The calcium source for this process seems to be the cartilage cells themselves. As calcification continues, the inner cartilaginous tissue breaks down into pieces of debris. Blood vessels from the sheath, now called the periosteum, force their way through the outer bony jacket, thus entering the interior of the cartilaginous model, and cart off the debris. Again, trapped osteoblasts transform into osteocytes, and osteoclasts for bone remodeling arise from cell fusions in the same manner as occurs in intramembranous bone. Growth in bone thickness occurs by adding additional bone layers just beneath the periosteum.

Endochondral bones increase in length in a different way, unlike growth in intramembranous development. As an example, consider a long bone such as a mammalian humerus (in humans, the upper arm bone). Like many limb bones, it is formed of a slender shaft with widened ends, called **epiphyses** (figure 47.4).

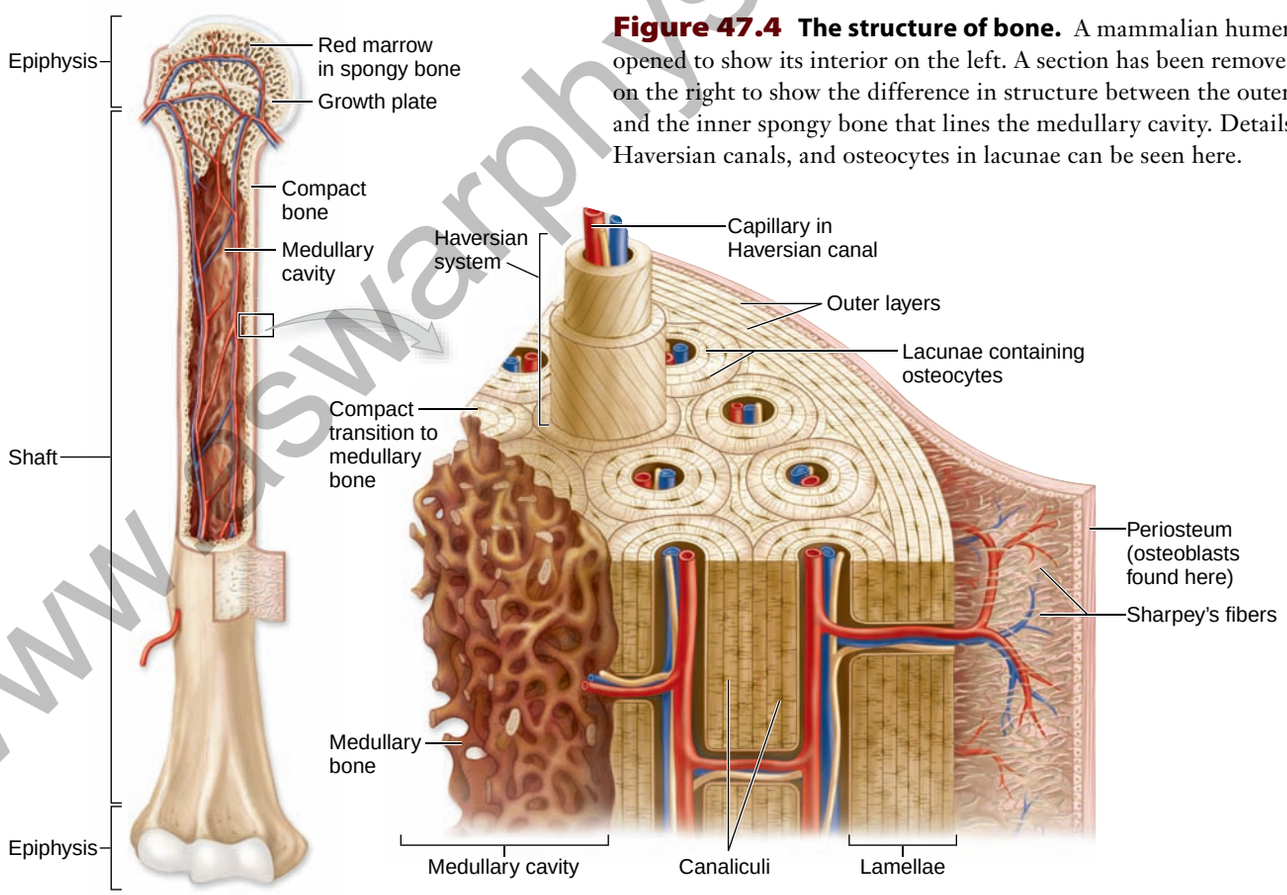


Figure 47.4 The structure of bone. A mammalian humerus is partly opened to show its interior on the left. A section has been removed and magnified on the right to show the difference in structure between the outer compact bone and the inner spongy bone that lines the medullary cavity. Details of basic layers, Haversian canals, and osteocytes in lacunae can be seen here.

Within the epiphyses are the *epiphyseal growth plates* that separate the epiphyses from the shaft itself. As long as the bone is growing in length, these growth plates are composed of cartilage (see figure 47.4). The actual events taking place in the plates are not simple, but they can be simply summarized.

1. During growth of a long bone, the cartilage of the growth plates is actively growing in the lengthwise direction to thicken the plate.
2. This growth pushes the epiphysis farther away from the slender shaft portion, which effectively increases the length of the bone.
3. At the same time, from the shaft's side, a process of cartilage calcification encroaches on the cartilaginous growth plate, so that the bony portion of the shaft elongates.

As long as the rate of new cartilage thickening stays ahead of the creeping calcification, the bone continues to grow in length. Eventually the cartilaginous expansion slows and is overtaken by the calcification, which obliterates this region of growth.

Growth in length usually ceases in humans by late adolescence. Although growth of the bone length is curtailed at this time, growth in width is not. The diameter of the shaft can be enhanced by bone addition just beneath the periosteum throughout an individual's life.

Bone structure may include blood vessels and nerves

Developing bone often has an internal blood supply, which is especially evident in endochondral bones. The internal blood routes, however, do not necessarily remain after the bones have completed development. In most mammals the endochondral bones retain internal blood vessels and are called **vascular bones.** Vascular bone is also found in many reptiles and a few amphibians. *Cellular bones* contain osteocytes, and many such bones are also vascular. This bone remains metabolically active (see figure 47.4).

In fishes and birds, bones are **avascular.** Typically avascular bone does not contain osteocytes and is termed *acellular bone*. This type of bone is fairly inert except for its surface, where the periosteum with its mesenchyme cells is capable of repairing the bone.

Many bones, particularly the endochondral long bones, contain a central cavity termed the *medullary cavity.* In many vertebrates, the medullary cavity houses the bone marrow, important in the manufacture of red and white blood cells. In such cases this cavity is termed the **marrow cavity.** Not all medullary cavities contain marrow, however. Light-boned birds, for example, have huge interior cavities, but they are empty of marrow. Birds depend on stem cells in other body locations to produce red blood cells.

Bone lining the medullary cavities differs from the smooth, dense bone found closer to the outer surface. Based on density and texture, bone falls into three categories: the outer dense **compact bone,** the **medullary bone** that lines the internal cavity, and **spongy bone** that has a honeycomb structure and typically forms the epiphyses inside a thick shell of compact bone. Both compact and spongy bone contribute to a bone's strength. Medullary cavities are lined with thin tissues called the **endosteum,** which contains no collagenous fibers but does possess other constituents including mesenchyme cells.

Vascular bone usually has a special internal organization called the **Haversian system.** Beneath the outer basic layers, endochondral bone is constructed of concentric layers called *Haversian lamellae*. These concentric tubes are laid down around narrow channels called *Haversian canals* that run parallel to the length of the bone. Haversian canals may contain nerve fibers but always contain blood vessels that keep the osteocytes alive even though they are entombed in the bony matrix.

The small vessels within the canals include both arterioles and venules or capillaries, and they connect to larger vessels that extend internally from both the periosteum and endosteum and that run in canals perpendicular to the Haversian canals.

Bone remodeling allows bone to respond to use or disuse

It is easy to think of bones as being inert, especially since we rarely encounter them except as the skeletons of dead animals. But just as muscles, skin, and other body tissues may change depending on the stresses of the environment, bone also is a dynamic tissue that can change with demands made on it.

Mechanical stresses such as compression at joints, the forces of muscles on certain portions and features of a bone, and similar effects may all be remodeling factors that not only shape the bone during its embryonic development, but after birth as well. Depending on the directions and magnitudes of forces impinging on a bone, it may thicken; the size and shape of surface features to which muscles, tendons, or ligaments attach may change in size and shape; even the direction of the tiny bony struts that make up spongy bone may be altered.

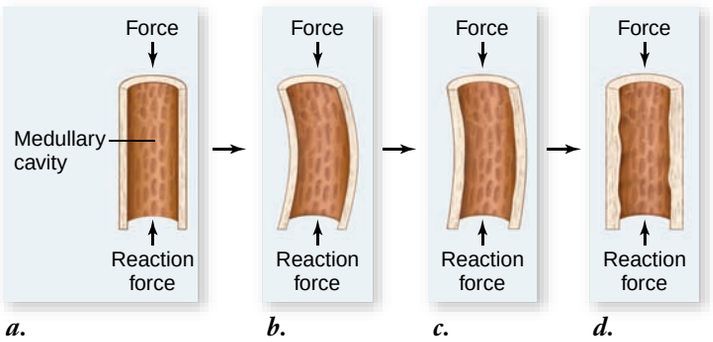


Figure 47.5 Model of stress and remodeling in a long bone. This figure shows a diagrammatic section of a long bone, such as a leg bone. The section is placed under a load or force, which causes a reaction force from the ground the leg is standing upon. ***a.*** Under a mild compressive load the bone does not bend. ***b.*** If the load is large enough, and the bone is not sufficiently thick, the bone will bend (the bending shown is exaggerated for clarity). ***c.*** Osteoblasts are signaled by the stresses in the bending section to produce additional bone. As the bone becomes thicker, the degree of bending is reduced. ***d.*** When sufficient bone is added to prevent significant bending, the production of new osteoblasts stops and no more bone is added.

Exercise and frequent use of muscles for a particular task change more than just the muscles; blood vessels and fibrous connective tissue increase, and the skeletal frame becomes more robust through bone thickening and enhancement.

The phenomenon of remodeling is known for all bones, but it is easiest to demonstrate in a long bone. Small forces may not have much of an effect on the bone, but larger ones—if frequent enough—can initiate remodeling (figure 47.5). In the example shown, larger compressive forces may tend to bend a bone, even if the bend is imperceptible to the eye. This bending stress promotes bone formation that thickens the bone. As the bone becomes thicker the amount of bending is reduced (figure 47.5*c*). Further bone addition produces sufficient bone thickness to entirely prevent significant bending (figure 47.5*d*). Once this point has been attained, the bone addition stops. This is another example of a negative-feedback system.

The effect of remodeling can be seen by examining bone thickness in rodents forced to exercise. The continual stresses placed on the limb bones cause additional bone to be deposited, leading to thicker and stronger bone (figure 47.6).

This phenomenon also has important medical implications. Osteoporosis, which is characterized by a loss of bone mineral density, is a debilitating and potentially life-threatening ailment that afflicts more than 25 million people in the United States, affecting primarily postmenopausal women, but also those suffering from malnutrition and a number of diseases. One treatment is a regimen of weight-lifting to stimulate bone deposition and thus counter the effects of osteoporosis.

SCIENTIFIC THINKING

Hypothesis: *Bone remodeling strengthens bones in response to external pressures.*

Prediction: *Bones that are used in more strenuous activities will deposit more bone and become stronger.*

Test: *Provide laboratory mice with an exercise wheel and make sure they run for several hours a day; keep a control group without a wheel.*

Mouse with exercise wheel | Mouse without exercise wheel

Result: *After 10 weeks, the running mice developed thicker limb bones.*

Further Experiments: *Modern microelectronics allow the development of stress sensors small enough to implant on the limb bone of a mouse. With such sensors, experiments can quantify how much stress different activities place on a bone and can more accurately investigate the relationship between the direction and magnitude of forces placed on a bone and the extent to which the bone remodels.*

Figure 47.6 The effect of exercise on bone remodeling.

Learning Outcomes Review 47.2

Intramembranous bone forms within a layer of connective tissue; endochondral bone originates with a cartilaginous model that is then replaced with bone tissue. Epiphyses are cartilaginous growth plates of endochondral bones. As the epiphyseal cartilage becomes calcified, bone growth ceases. Bone remodeling occurs in response to repeated stresses on bones from weight or muscle use, allowing bones to adapt.

- ***Why is vitamin D especially important for children and the elderly?***

47.3 *Joints and Skeletal Movement*

Learning Outcomes

1. ***Define the different types of joints.***
2. ***Explain how muscles produce movement at joints.***
3. ***Describe how antagonistic muscles work at a joint.***

Movements of the endoskeleton are powered by the skeletal musculature. The skeletal movements that respond to muscle action occur at **joints,** or articulations, where one bone meets another.

Moveable joints have different ranges of motion, depending on type

Each movable joint within the skeleton has a characteristic range of motion. Four basic joint movement patterns can be distinguished: *ball-and-socket*, *hinge*, *gliding*, and *combination*.

Ball-and-socket joints are like those of the hip, where the upper leg bone forms a ball fitting into a socket in the pelvis. This type of joint can perform universal movement in all directions, plus twisting of the ball (figure 47.7*a*).

The simplest type of joint is the **hinge joint,** such as the knee, where movement of the lower leg is restricted to rotate forward or backward, but not side to side (figure 47.7*b*).

Gliding joints can be found in the skulls of a number of nonmammalian vertebrates, but are also present between the lateral vertebral projections in many of them and in mammals as well (figure 47.7*c*). The vertebral projections are paired and extend from the front and back of each vertebra. The projections in front are a little lower, and each can slip along the undersurface of the posterior projection from the vertebra just ahead of it. This sliding joint gives stability to the vertebral column while allowing some flexibility of movement between vertebrae.

Combination joints are, as you might suppose, those that have movement characteristics of two or more joint types. The typical mammalian jaw joint is a good example.

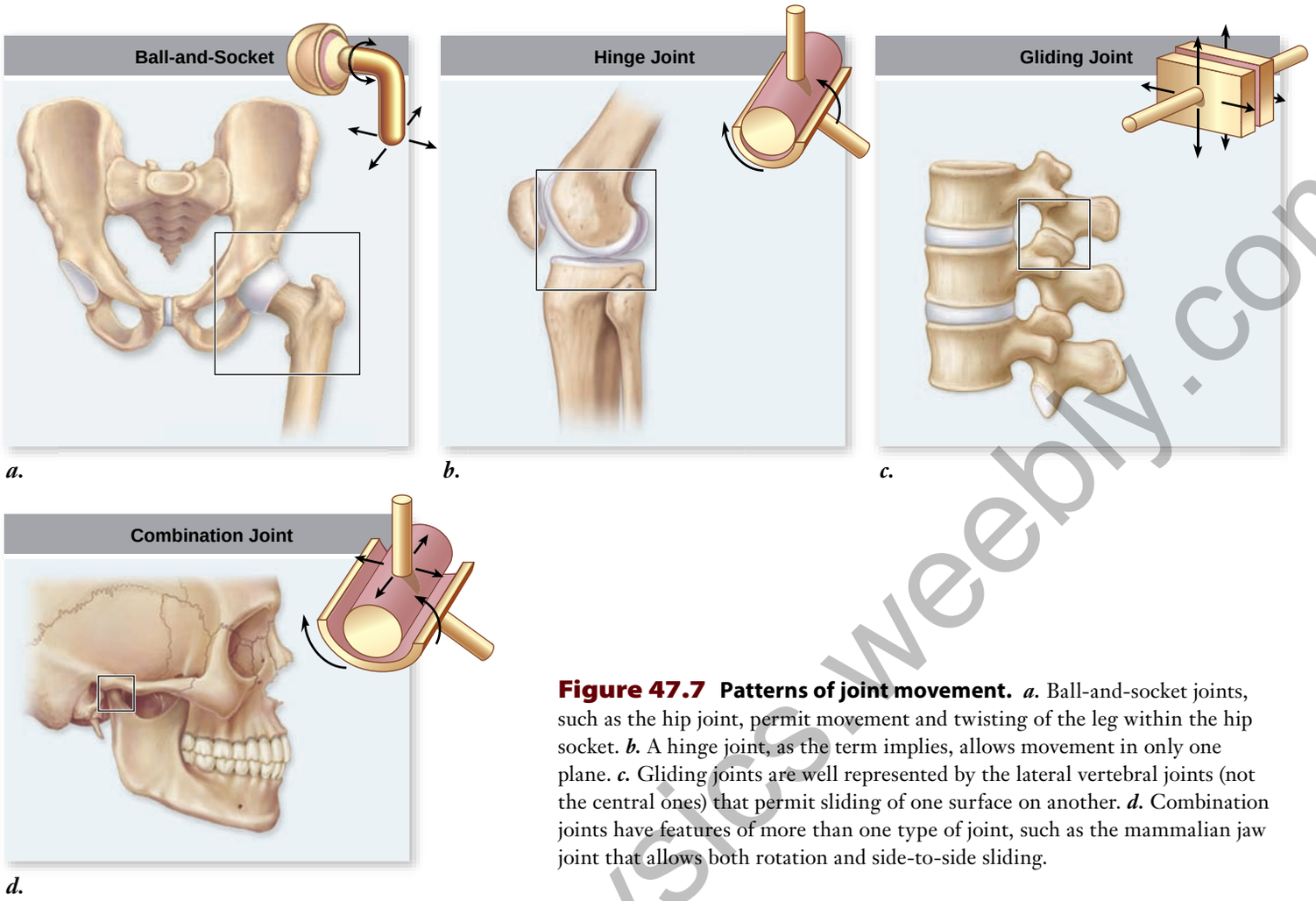


Figure 47.7 Patterns of joint movement. ***a.*** Ball-and-socket joints, such as the hip joint, permit movement and twisting of the leg within the hip socket. ***b.*** A hinge joint, as the term implies, allows movement in only one plane. ***c.*** Gliding joints are well represented by the lateral vertebral joints (not the central ones) that permit sliding of one surface on another. ***d.*** Combination joints have features of more than one type of joint, such as the mammalian jaw joint that allows both rotation and side-to-side sliding.

Most mammals chew food into small pieces. To chew food well, the lower jaw needs to move from side to side to get the best contact between upper and lower teeth. The lower jaw can also slip forward and backward to some extent. At the same time, the jaw joint must be shaped to allow the hinge-like opening and closing of the mouth. The mammalian joint conformation thus combines features from hinge and gliding joints (figure 47.7*d*).

Skeletal muscles pull on bones to produce movement at joints

Skeletal muscles produce movement of the skeleton when they contract. Usually, the two ends of a skeletal muscle are attached to different bones, although some may be attached to other structures, such as skin. There are two means of bone attachment: Muscle fibers may connect directly to the periosteum, the bone's fibrous covering, or sheets of muscle may be connected to bone by a dense connective tissue strap or cord, called a *tendon* that attaches to the periosteum (figure 47.8).

One attachment of the muscle, the origin, remains relatively stationary during a contraction. The other end, the insertion, is attached to a bone that moves when the muscle contracts. For example, contraction of the quadriceps muscles of the leg causes the lower leg to rotate forward relative to the upper leg section.

Typically, muscles are arranged so that any movement produced by one muscle can be reversed by another. The leg flexor muscles, called hamstrings (see figure 47.8), draw the lower leg back and upward, bending the knee. Its movement is countered by the quadriceps muscles. The important concept is that two muscles or muscle groups can be mutually antagonistic, with the action of one countered by the action of the other.

Learning Outcomes Review 47.3

Types of joints include ball-and-socket, hinge, gliding, and combination joints. Muscles, positioned across joints, cause movement of bones relative to each other by contracting and exerting pulling force. Antagonistic muscles oppose each other, a key feature since muscles can only contract and cannot push.

- ***In what ways does a bony endoskeleton overcome the limitations of an exoskeleton for terrestrial life forms?***

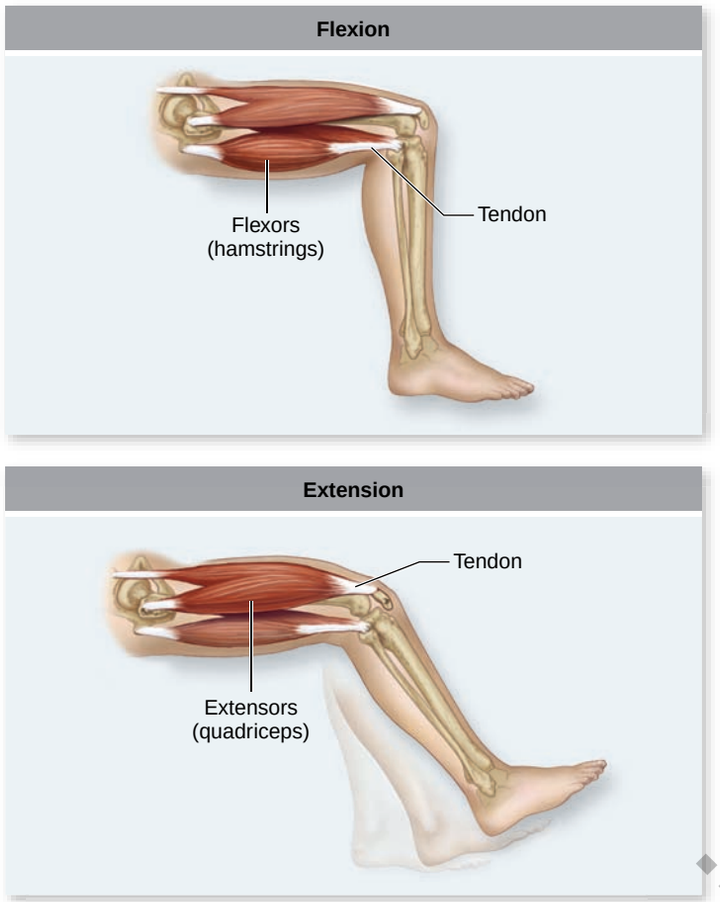


Figure 47.8 Flexor and extensor muscles of the leg.
Antagonistic muscles act in opposite ways. In humans, the hamstrings, a group of three muscles, cause the lower leg to move backward relative to the upper leg, whereas the quadriceps, a group of four muscles, pull the lower leg forward.

Inquiry question

Would the antagonistic muscles work in the same way in the legs of an animal with an exoskeleton, such as the grasshopper in figure 47.2?

47.4 *Muscle Contraction*

Learning Outcomes

1. ***Explain the sliding filament mechanism of muscle contraction.***
2. ***Describe the role of calcium in muscle contraction.***
3. ***Differentiate between slow-twitch and fast-twitch muscle fibers.***

This section concentrates on the skeletal muscle of vertebrates. Vertebrate muscle has enjoyed the most attention and is thus the best understood of animal muscular function. Each skeletal muscle contains numerous muscle fibers, as described in chapter 43. Each muscle fiber encloses a bundle of 4 to 20 elongated structures called **myofibrils.** Each myofibril, in turn, is composed of thick and thin **myofilaments** (figure 47.9).

Under a microscope, the myofibrils have alternating dark and light bands, which give skeletal muscle fiber its striped appearance. The thick myofilaments are stacked together to produce the dark bands, called *A bands;* the thin filaments alone are found in the light bands, or *I bands.*

Each I band in a myofibril is divided in half by a disk of protein called a *Z line* because of its appearance in electron micrographs. The thin filaments are anchored to these disks. In an electron micrograph of a myofibril (figure 47.10), the structure of the myofibril can be seen to repeat from Z line to Z line. This repeating structure, called a **sarcomere,** is the smallest subunit of muscle contraction.

Muscle fibers contract as overlapping filaments slide together

The thin filaments overlap with thick filaments on each side of an A band, but in a resting muscle, they do not project all the way to the center of the A band. As a result, the center of an A band (called an *H band*) is lighter than the areas on each side, which have interdigitating thick and thin filaments. This appearance of the sarcomeres changes when the muscle contracts.

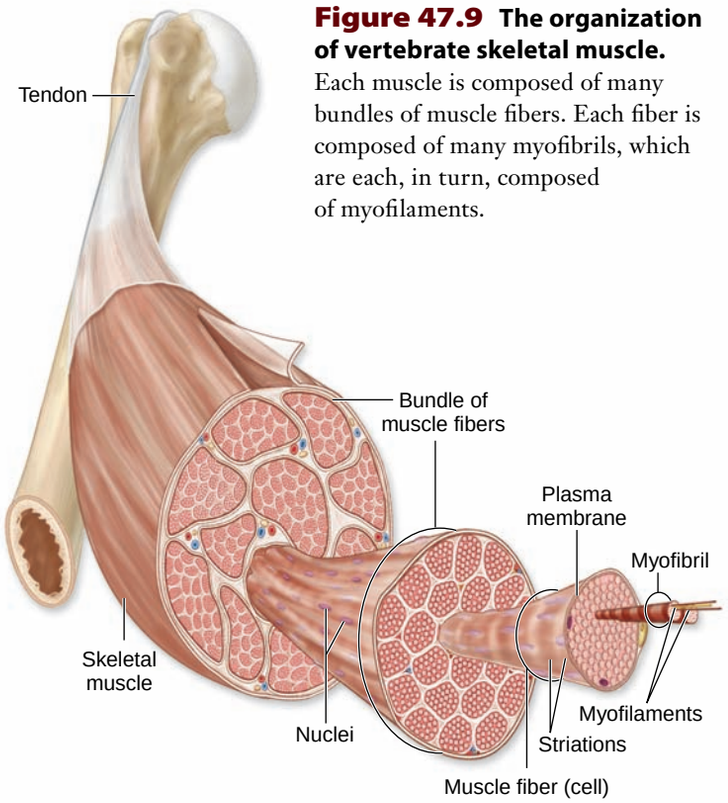


Figure 47.9 The organization of vertebrate skeletal muscle.
Each muscle is composed of many bundles of muscle fibers. Each fiber is composed of many myofibrils, which are each, in turn, composed of myofilaments.

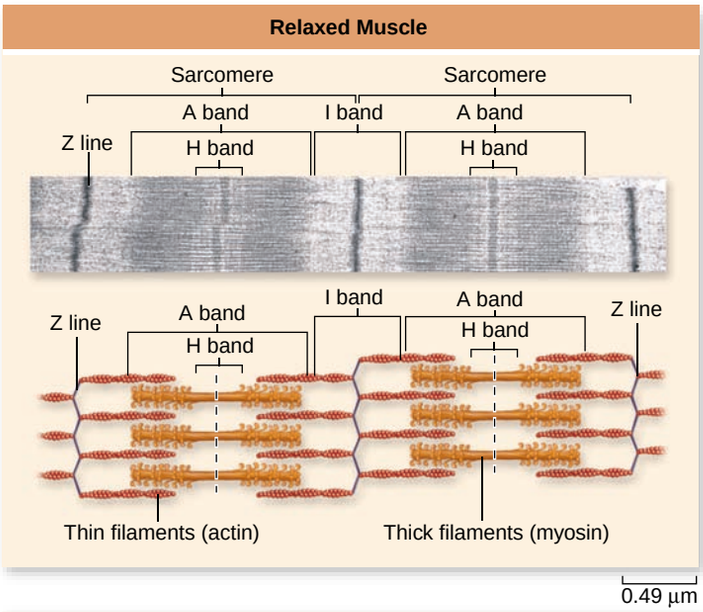


Figure 47.10 The structure of sarcomeres in relaxed and contracted muscles. Two sarcomeres are shown in micrographs and as drawings of thick and thin filaments. The Z lines form the borders of each sarcomere and the A bands represent thick filaments. The thin filaments are within the I bands and extend into the A bands interdigitated with thick filaments. The H band is the lighter-appearing central region of the A band containing only thick filaments. The muscle on the top is shown relaxed. In the contracted muscle in the bottom, the Z lines have moved closer together, with the I bands and H bands becoming shorter. The A band does not change in size as it contains the thick filaments, which do not change in length.

A muscle contracts and shortens because its myofibrils contract and shorten. When this occurs, the myofilaments do *not* shorten; instead, the thick and thin myofilaments slide relative to each other (see figure 47.10). The thin filaments slide deeper into the A bands, making the H bands narrower until, at maximal shortening, they disappear entirely. This also makes

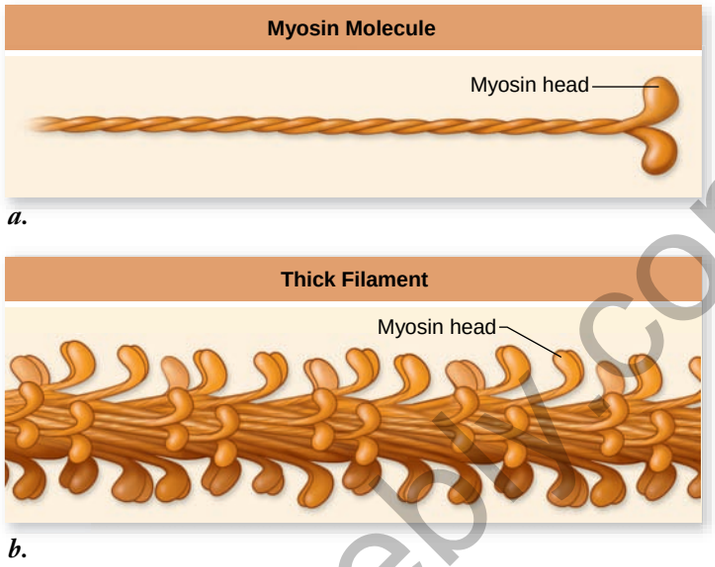


Figure 47.11 Thick filaments are composed of myosin. ***a.*** Each myosin molecule consists of two polypeptide chains shaped like golf clubs and wrapped around each other; at the end of each chain is a globular region referred to as the "head." ***b.*** Thick filaments consist of myosin molecules combined into bundles from which the heads protrude at regular intervals.

the I bands narrower, as the Z lines are brought closer together. This is the sliding filament mechanism of contraction.

The sliding filament mechanism

Electron micrographs reveal cross-bridges that extend from the thick to the thin filaments, suggesting a mechanism that might cause the filaments to slide. To understand how this is accomplished requires examining the thick and thin filaments at a molecular level. Biochemical studies show that each thick filament is composed of many subunits of the protein myosin packed together. The myosin protein consists of two subunits, each shaped like a golf club with a head region that protrudes from a long filament, with the filaments twisted together. Thick filaments are composed of many copies of myosin arranged with heads protruding from along the length of the fiber (figure 47.11). The myosin heads form the cross-bridges seen in electron micrographs.

Each thin filament consists primarily of many globular actin proteins arranged into two fibers twisted into a double helix (figure 47.12). If we were able to see a sarcomere at the molecular level, it would have the structure depicted in figure 47.13.

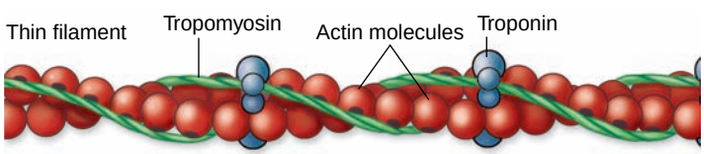
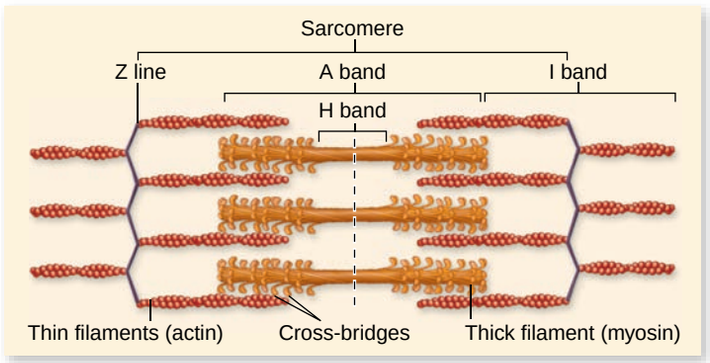
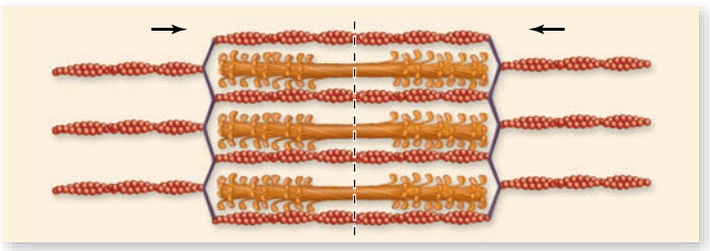


Figure 47.12 Thin filaments are composed of globular actin proteins. Two rows of actin proteins are twisted together in a helix to produce the thin filaments. Other proteins, tropomyosin and troponin, associate with the strands of actin and are involved in muscle contraction. These other proteins are discussed later in the chapter.



a.

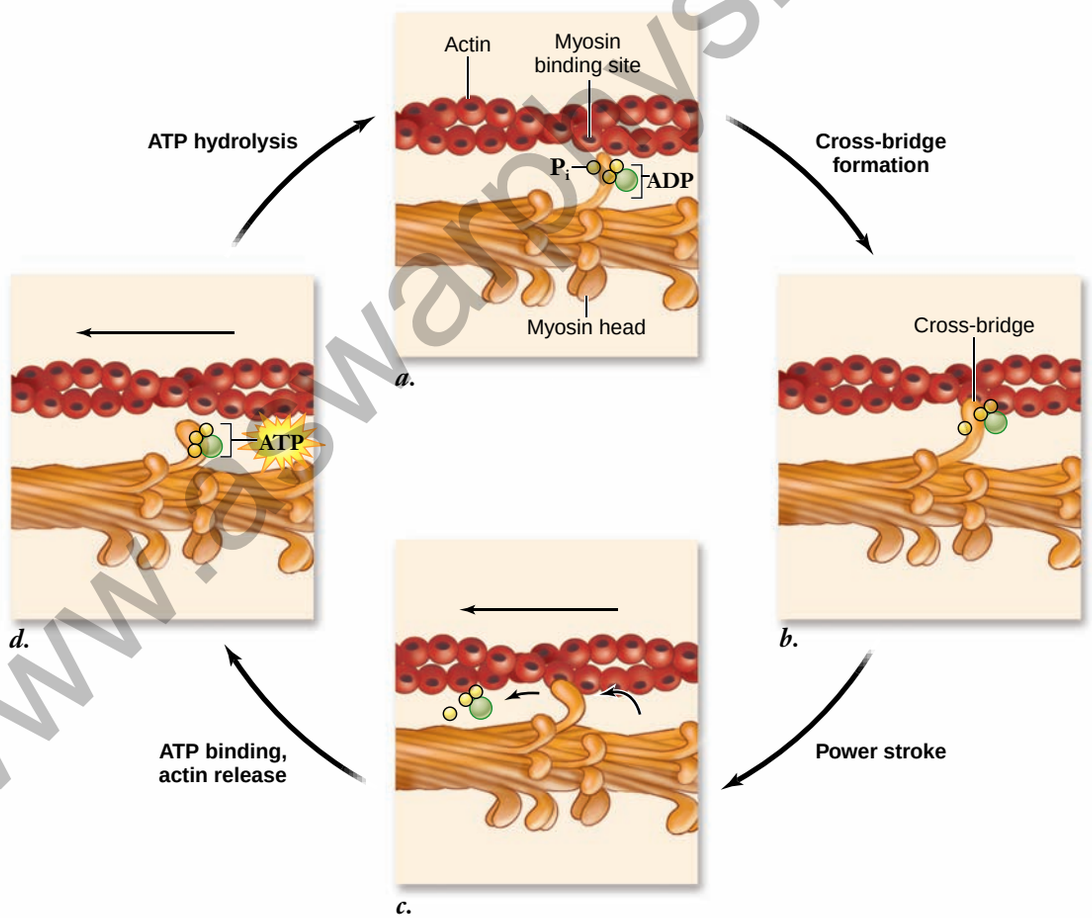


b.

Figure 47.13 The interaction of thick and thin filaments in striated muscle sarcomeres. ***a.*** The heads on the two ends of the thick filaments are oriented in opposite directions so that the cross-bridges pull the thin filaments and the Z lines on each side of the sarcomere toward the center. ***b.*** This sliding of the filaments produces muscle contraction.

Myosin is a member of the class of protein called *motor proteins* that are able to convert the chemical energy in ATP into mechanical energy (see chapter 4). This occurs by a series of events called the cross-bridge cycle (figure 47.14). When the myosin heads hydrolyze ATP into ADP and P_i, the conformation of myosin is changed, activating it for the later power stroke. The ADP and P_i both remain attached to the myosin head, keeping it in this activated conformation. The analogy to a mousetrap, set and ready to spring, is often made to describe this action. In this set position, the myosin head can bind to actin, forming cross-bridges. When a myosin head binds to actin, it releases the P_i and undergoes another conformational change, pulling the thin filament toward the center of the sarcomere in the *power stroke*, at which point it loses the ADP (see figures 47.13*b*, 47.14). At the end of the power stroke, the myosin head binds to a new molecule of ATP, which displaces it from actin. This cross-bridge cycle repeats as long as the muscle is stimulated to contract. This sequence of events can be thought of like pulling a rope hand-over-hand. The myosin heads are the hands and the actin fibers the rope.

In death, the cell can no longer produce ATP, and therefore the cross-bridges cannot be broken—causing the muscle stiffness of death called *rigor mortis*. A living cell, however, always has enough ATP to allow the myosin heads to detach from actin. How, then, is the cross-bridge cycle arrested so that the muscle can relax? We discuss the regulation of contraction and relaxation next.



a. *b.* *c.* *d.*

Figure 47.14 The cross-bridge cycle in muscle contraction. ***a.*** Hydrolysis of ATP by myosin causes a conformational change that moves the head into an energized state. The ADP and P_i remain bound to the myosin head, which can bind to actin. ***b.*** Myosin binds to actin forming a cross-bridge. ***c.*** During the power stroke, myosin returns to its original conformation, releasing ADP and P_i. ***d.*** ATP binds to the myosin head breaking the cross-bridge. ATP hydrolysis returns the myosin head to its energized conformation, allowing the cycle to begin again.

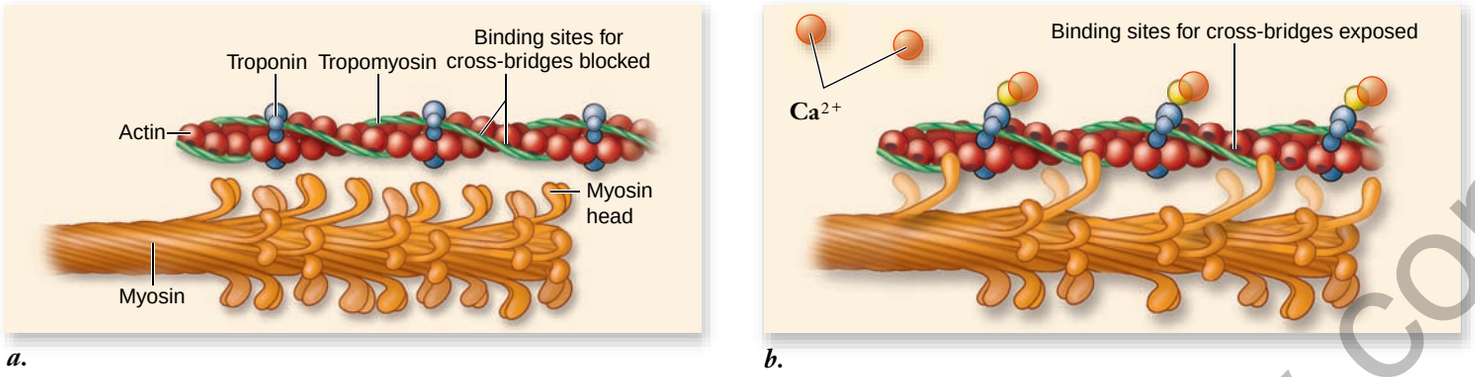


Figure 47.15 How calcium controls striated muscle contraction. ***a.*** When the muscle is at rest, a long filament of the protein tropomyosin blocks the myosin-binding sites on the actin molecule. Because myosin is unable to form cross-bridges with actin at these sites, muscle contraction cannot occur. ***b.*** When Ca^{2+} binds to another protein, troponin, the Ca^{2+}–troponin complex displaces tropomyosin and exposes the myosin-binding sites on actin, permitting cross-bridges to form and contraction to occur.

Contraction depends on calcium ion release following a nerve impulse

When a muscle is relaxed, its myosin heads are in the activated conformation bound to ADP and P_i, but they are unable to bind to actin. In the relaxed state, the attachment sites for the myosin heads on the actin are physically blocked by another protein, known as **tropomyosin,** in the thin filaments. Cross-bridges therefore cannot form and the filaments cannot slide.

For contraction to occur, the tropomyosin must be moved out of the way so that the myosin heads can bind to the uncovered actin-binding sites. This requires the action of **troponin,** a regulatory protein complex that holds tropomyosin and actin together. The regulatory interactions between troponin and tropomyosin are controlled by the calcium ion (Ca^{2+}) concentration of the muscle fiber cytoplasm.

When the Ca^{2+} concentration of the cytoplasm is low, tropomyosin inhibits cross-bridge formation (figure 47.15*a*). When the Ca^{2+} concentration is raised, Ca^{2+} binds to troponin, altering its conformation and shifting the troponin–tropomyosin complex. This shift in conformation exposes the myosin-binding sites on the actin. Cross-bridges can thus form, undergo power strokes, and produce muscle contraction (figure 47.15*b*).

Muscles need a reliable supply of Ca^{2+}. Muscle fibers store Ca^{2+} in a modified endoplasmic reticulum called a **sarcoplasmic reticulum (SR)** (figure 47.16). When a muscle fiber is stimulated to contract, the membrane of the muscle fiber becomes depolarized. This is transmitted deep into the muscle fiber by invaginations of the cell membrane called the **transverse tubules (T tubules).** Depolarization of the T tubules causes Ca^{2+} channels in the SR to open, releasing Ca^{2+} into the cytosol. Ca^{2+} then diffuses into the myofibrils, where it binds to troponin, altering its conformation and allowing contraction. The involvement of Ca^{2+} in muscle contraction is called **excitation–contraction coupling** because it is the release of Ca^{2+} that links the excitation of the muscle fiber by the motor neuron to the contraction of the muscle.

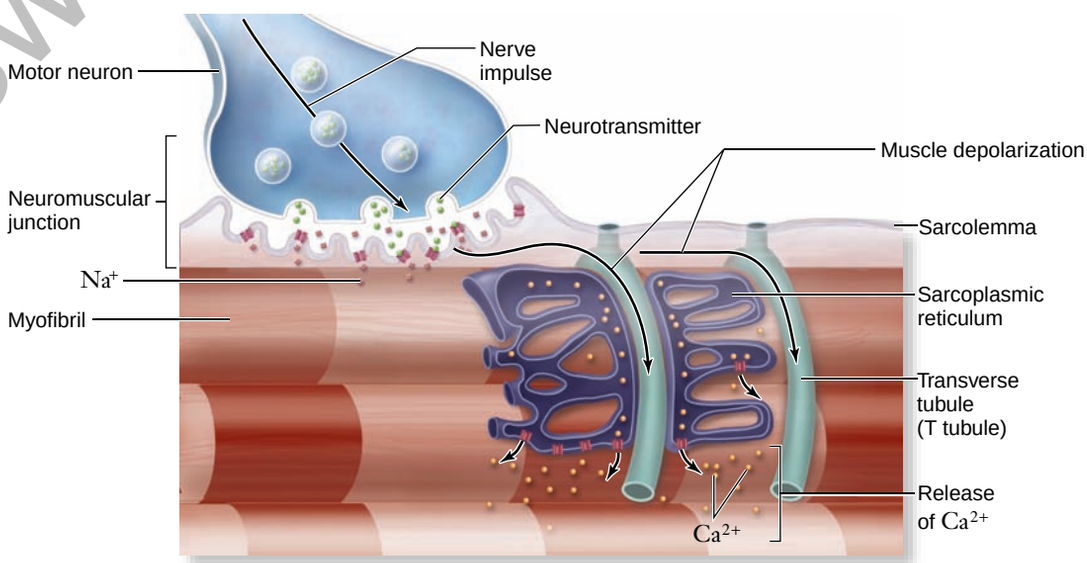


Figure 47.16 Relationship between the myofibrils, transverse tubules, and sarcoplasmic reticulum. Neurotransmitter released at a neuromuscular junction binds chemically gated Na^+ channels, causing the muscle cell membrane to depolarize. This depolarization is conducted along the muscle cell membrane and down the transverse tubules to stimulate the release of Ca^{2+} from the sarcoplasmic reticulum. Ca^{2+} diffuses through the cytoplasm to myofibrils, causing contraction.

Nerve impulses from motor neurons

Muscles are stimulated to contract by motor neurons. The motor neurons that stimulate skeletal muscles are called *somatic motor neurons.* The axon of a somatic motor neuron extends from the neuron cell body and branches to make synapses with a number of muscle fibers. These synapses between neurons and muscle cells are called *neuromuscular junctions* (see figure 47.16). One axon can stimulate many muscle fibers, and in some animals, a muscle fiber may be innervated by more than one motor neuron. However, in humans, each muscle fiber has only a single synapse with a branch of one axon.

When a somatic motor neuron delivers electrochemical impulses, it stimulates contraction of the muscle fibers it innervates (makes synapses with) through the following events:

1. The motor neuron, at the neuromuscular junction, releases the neurotransmitter acetylcholine (ACh). ACh binds to receptors in the muscle cell membrane to open Na^+ channels. The influx of Na^+ ions depolarizes the muscle cell membrane.
2. The impulses spread along the membrane of the muscle fiber and are carried into the muscle fibers through the T tubules.
3. The T tubules conduct the impulses toward the sarcoplasmic reticulum, opening Ca^{2+} channels and releasing Ca^{2+}. The Ca^{2+} binds to troponin, exposing the myosin-binding sites on the actin myofilaments and stimulating muscle contraction.

When impulses from the motor neuron cease, it stops releasing ACh, in turn stopping the production of impulses in the muscle fiber. Another membrane protein in the SR then uses energy from ATP hydrolysis to pump Ca^{2+} back into the SR by active transport. Troponin is no longer bound to Ca^{2+}, so tropomyosin returns to its inhibitory position, allowing the muscle to relax.

Motor units and recruitment

A single muscle fiber can produce variable tension depending on the frequency of stimulation. The response of an entire muscle depends on the number of individual fibers involved and their degree of tension. The set of muscle fibers innervated by all the axonal branches of a motor neuron, plus the motor neuron itself, is defined as a **motor unit** (figure 47.17).

Every time the motor neuron produces impulses, all muscle fibers in that motor unit contract together. The division of the muscle into motor units allows the muscle's strength of contraction to be finely graded, a requirement for coordinated movements. Muscles that require a finer degree of control, such as those that move the eyes, have smaller motor units (fewer muscle fibers per neuron). Muscles that require less precise control but must exert more force, such as the large muscles of the legs, have more fibers per motor neuron.

Most muscles contain motor units in a variety of sizes, and these can be selectively activated by the nervous system. The weakest contractions of a muscle involve activation of a few small motor units. If a slightly stronger contraction is necessary, additional small motor units are also activated. The initial increments of increased force are therefore relatively small. As ever greater forces are required, more units and larger units are brought into action, and the force increments become larger.

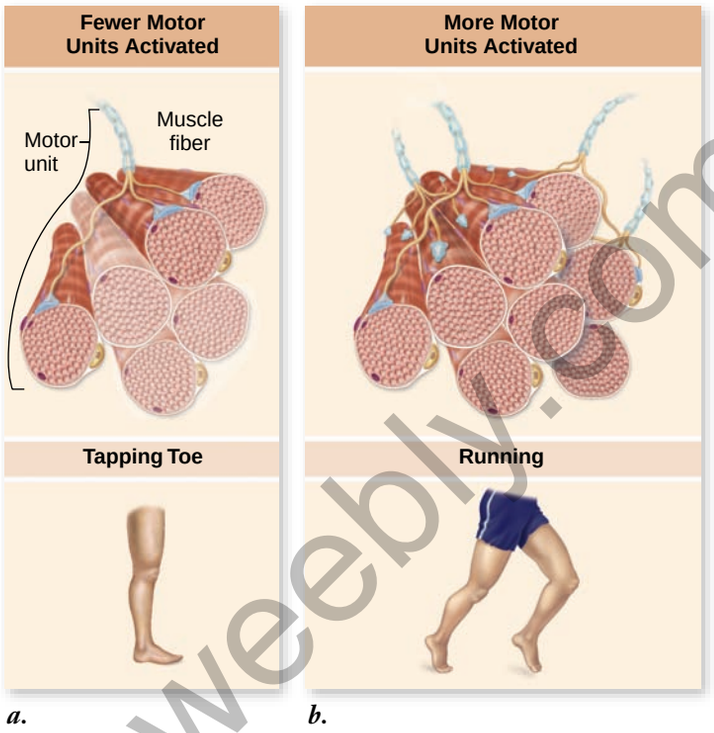


Figure 47.17 The number and size of motor units.
A motor unit consists of a motor neuron and all of the muscle fibers it innervates. ***a.*** Precise muscle contractions require smaller motor units. ***b.*** Large muscle movements require larger motor units. The more motor units activated, the stronger the contraction.

This cumulative increase of numbers and sizes of motor units to produce a stronger contraction is termed **recruitment.**

The two main types of muscle fibers are slow-twitch and fast-twitch

An isolated skeletal muscle can be studied by stimulating it artificially with electric shocks. A muscle stimulated with a single electric shock quickly contracts and relaxes in a response called a twitch. Increasing the stimulus voltage increases the strength of the twitch up to a maximum. If a second electric shock is delivered immediately after the first, it produces a second twitch that may partially "ride piggyback" on the first. This cumulative response is called summation (figure 47.18).

An increasing frequency of electric shocks shortens the relaxation time between successive twitches as the strength of contraction increases. Finally, at a particular frequency of stimulation, no visible relaxation occurs between successive twitches. Contraction is smooth and sustained, as it is during normal muscle contraction in the body. This sustained contraction is called **tetanus.** (The disease known as tetanus gets its name because the muscles of its victims go into an agonizing state of contraction.)

Skeletal muscle fibers can be divided on the basis of their contraction speed into *slow-twitch*, or *type I*, *fibers* and *fast-twitch*, or *type II*, *fibers*. The muscles that move the eyes, for example, have a high proportion of fast-twitch fibers and reach maximum tension in about 7.3 milliseconds (msec); the soleus muscle in the leg, by contrast, has a high proportion

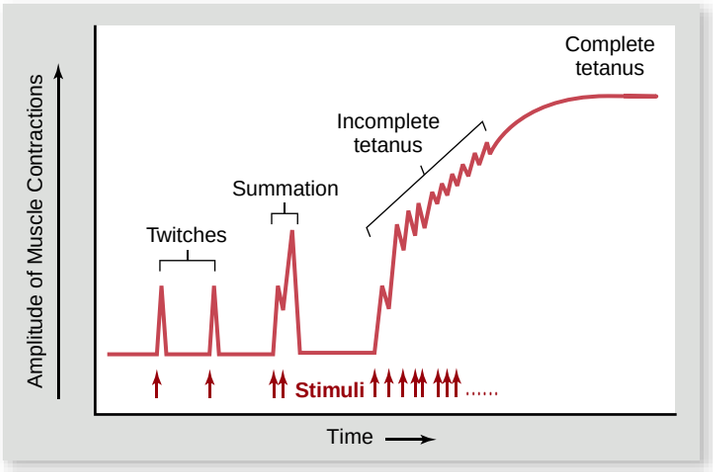


Figure 47.18 Summation. Muscle twitches summate to produce a sustained, tetanic contraction. This pattern is produced when the muscle is stimulated electrically or naturally by neurons. Tetanus, a smooth, sustained contraction, is the normal type of muscle contraction in the body.

Inquiry question

What determines the maximum amplitude of a summated muscle contraction?

of slow-twitch fibers and requires about 100 msec to reach maximum tension (figure 47.19).

Slow-twitch fibers

Slow-twitch fibers have a rich capillary supply, numerous mitochondria and aerobic respiratory enzymes, and a high concentration of **myoglobin** pigment. Myoglobin is a red pigment similar to the hemoglobin in red blood cells, but its higher affinity for oxygen improves the delivery of oxygen to the slow-twitch fibers. Because of their high myoglobin content, slow-twitch fibers are also called *red fibers*. These fibers can sustain action for a long period of time without fatigue.

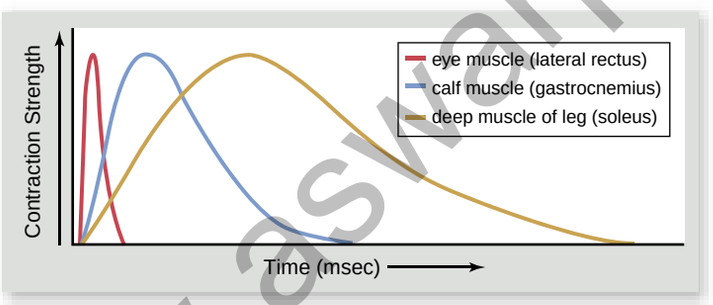


Figure 47.19 Skeletal muscles have different proportions of fast-twitch and slow-twitch fibers. The muscles that move the eye contain mostly fast-twitch fibers, whereas the deep muscle of the leg (the soleus) contains mostly slow-twitch fibers. The calf muscle (gastrocnemius) is intermediate in its composition.

Inquiry question

How would you determine if the calf muscle contains a mix of fast-twitch and slow-twitch fibers, or instead is composed of an intermediate form of fiber?

Fast-twitch fibers

The thicker **fast-twitch fibers** have fewer capillaries and mitochondria than slow-twitch fibers and not as much myoglobin; hence, these fibers are also called *white fibers*. Fast-twitch fibers can respire anaerobically by using a large store of glycogen and high concentrations of glycolytic enzymes. The "dark meat" and "white meat" found in chicken and turkey consists of muscles with primarily red and white fibers, respectively. Fast-twitch fibers are adapted for the rapid generation of power and can grow thicker and stronger in response to weight training; however, they lack the endurance characteristics of slow-twitch fibers.

In addition to the type I and type II fibers, human muscles have an intermediate form of fibers that are fast-twitch, but they also have a high oxidative capacity and so are more resistant to fatigue. Endurance training increases the proportion of these fibers in muscles.

In general, human sprinters tend to have more fast-twitch fibers, whereas long-distance runners have more slow-twitch fibers. These differences are paralleled in the animal world. Comparisons of closely related species that differ in their lifestyles show that species that rely on short, high-speed movements to capture prey or evade predators tend to have more fast-twitch fibers, whereas closely related species that move more slowly, but for longer periods of time, have more slow-twitch fibers.

Muscle metabolism changes with the demands made on it

Skeletal muscles at rest obtain most of their energy from the aerobic respiration of fatty acids (see chapter 7). During use of the muscle, such as during exercise, muscle stores of glycogen and glucose delivered by the blood are also used as energy sources. The energy obtained by cellular respiration is used to make ATP, which is needed for the movement of the cross-bridges during muscle contraction and the pumping of Ca^{2+} back into the sarcoplasmic reticulum during muscle relaxation.

Skeletal muscles respire anaerobically for the first 45 to 90 sec of moderate-to-heavy exercise because the cardiopulmonary system requires this amount of time to increase the oxygen supply to the muscles. If exercise is not overly strenuous, aerobic respiration then contributes the major portion of the skeletal muscle energy requirements following the first 2 min of exercise. However, more vigorous exercise may require more ATP than can be provided by aerobic respiration, in which case anaerobic respiration continues to provide ATP as well.

Whether exercise is light, moderate, or intense for a particular individual depends on that person's maximal capacity for aerobic exercise. The maximum rate of oxygen consumption in the body is called the *aerobic capacity*. In general, individuals in better condition have greater aerobic capacity and thus can sustain higher levels of aerobic exercise for longer periods without having to also use anaerobic respiration.

Physical training increases aerobic capacity and muscle strength

Muscle fatigue refers to the use-dependent decrease in the ability of a muscle to generate force. Fatigue is highly variable and can arise from a number of causes. The intensity of contraction as well as duration of contraction are involved. In addition, fatigue is affected by cellular metabolism: aerobic or anaerobic. In the case of short-duration maximal exertion, fatigue was long thought to be caused by a buildup of lactic acid (from anaerobic metabolism). More recent data also implicate a buildup in inorganic phosphate (P_i) from the breakdown of creatine phosphate, which also occurs during anaerobic metabolism. In longer term, lower intensity exertion, fatigue appears to result from depletion of glycogen.

Because the depletion of muscle glycogen places a limit on exercise, any adaptation that spares muscle glycogen will improve physical endurance. Trained athletes have an increased proportion of energy derived from the aerobic respiration of fatty acids, resulting in a slower depletion of their muscle glycogen reserve. Athletes also have greater muscle vascularization, which facilitates both oxygen delivery and lactic acid removal. Because the aerobic capacity of endurance-trained athletes is higher than that of untrained people, athletes can perform for longer and put forth more effort before muscle fatigue occurs.

Endurance training does not increase muscle size. Muscle enlargement is produced only by frequent periods of high-intensity exercise in which muscles work against high resistance, as in weight lifting. Resistance training increases the thickness of type II (fast-twitch) muscle fibers, causing skeletal muscles to grow by hypertrophy (increased cell size) rather than by cell division and an increased number of cells.

Learning Outcomes Review 47.4

Sliding of myofilaments within muscle myofibrils is responsible for contraction; it involves the motor protein myosin, which forms cross-bridges on actin fibers. The process of shortening is controlled by Ca^{2+} ions released from the sarcoplasmic reticulum. The Ca^{2+} binds to troponin, making myosin-binding sites in actin available. Slow-twitch fibers can sustain activity for a longer period of time; fast-twitch fibers use glycogen for rapid generation of power.

- ***What advantages do increased myoglobin and mitochondria confer on slow-twitch fibers?***

47.5 Modes of Animal Locomotion

Learning Outcomes

1. *Describe how friction and gravity affect locomotion.*
2. *Discuss how lift is created by wings.*
3. *Explain how evolution has shaped structures used for locomotion.*

Animals are unique among multicellular organisms in their ability to move actively from one place to another. Locomotion requires both a propulsive mechanism and a control mechanism. There are a wide variety of propulsive mechanisms, most involving contracting muscles to generate the necessary force. Ultimately, it is the nervous system that activates and coordinates the muscles used in locomotion. In large animals, active locomotion is almost always produced by appendages that oscillate—*appendicular locomotion*—or by bodies that undulate, pulse, or undergo peristaltic waves—*axial locomotion.*

Although animal locomotion occurs in many different forms, the general principles remain much the same in all groups. The physical constraints to movement—gravity and friction—are the same in every environment, differing only in degree.

Swimmers must contend with friction when moving through water

For swimming animals, the buoyancy of water reduces the effect of gravity. As a result, the primary force retarding forward movement is frictional drag, so body shape is important in reducing the force needed to push through the water.

Some marine invertebrates move about using hydraulic propulsion. For example, scallops clap the two sides of their shells together forcefully, and squids and octopuses squirt water like a marine jet, as described in chapter 34.

In contrast, many invertebrates and all aquatic vertebrates swim. Swimming involves pushing against the water with some part of the body. At one extreme, eels and sea snakes swim by sinuous undulations of the entire body (figure 47.20*a*). The undulating body waves of eel-like swimming are created by waves of muscle contraction alternating between the left and right axial musculature. As each body segment in turn pushes against the water, the moving wave forces the eel forward.

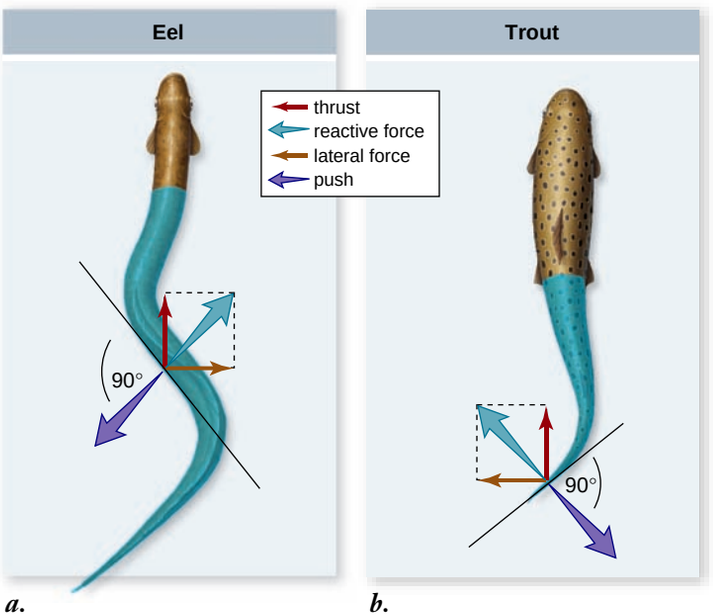


Figure 47.20 Movements of swimming fishes. *a.* An eel pushes against the water with its whole body, whereas (*b*) a trout pushes only with its posterior half.

Other types of fish use similar mechanics as the eel but generate most of their propulsion from the posterior part of the body using the caudal (rear) fin (figure 47.20*b*). This also allows considerable specialization in the front end of the body without sacrificing propulsive force. Reptiles, such as alligators, swim in the same manner using undulations of the tail.

Whales and other marine mammals such as sea lions have evolutionarily returned to an aquatic lifestyle (see figure 21.12) and have convergently evolved a similar form of locomotion. Like fish, marine mammals also swim using undulating body waves. However, unlike any of the fishes, the waves pass from top to bottom and not from side to side. This difference illustrates how past evolutionary history can shape subsequent evolutionary change. The mammalian vertebral column is structured differently from that of fish in a way that stiffens the spine and allows little side-to-side flexibility. For this reason, when the ancestor of whales reentered aquatic habitats, they evolved adaptations for swimming that used dorsoventral (top-to-bottom) flexing.

Many terrestrial tetrapod vertebrates are able to swim, usually through movement of their limbs. Most birds that swim, such as ducks and geese, propel themselves through the water by pushing against it with their hind legs, which typically have webbed feet. Frogs and most aquatic mammals also swim with their hind legs and have webbed feet. Tetrapod vertebrates that swim with their forelegs usually have these limbs modified as flippers and "fly" through the water using motions very similar to those used by aerial fliers; examples include sea turtles, penguins, and fur seals.

Terrestrial locomotion must deal primarily with gravity

Air is a much less dense medium than water, and thus the frictional forces countering movement on land are much less than those in water. Instead, countering the force of gravity is the biggest challenge for nonaquatic organisms, which either must move on land or fly through the air.

The three great groups of terrestrial animals—mollusks, arthropods, and vertebrates—each move over land in different ways.

Mollusk locomotion is much slower than that of the other groups. Snails, slugs, and other terrestrial mollusks secrete a path of mucus that they glide along, pushing with a muscular foot.

Only vertebrates and arthropods (insects, spiders, and crustaceans) have developed a means of rapid surface locomotion. In both groups, the body is raised above the ground and moved forward by pushing against the ground with a series of jointed appendages, the legs.

Although animals may walk on only two legs or more than 100, the same general principles guide terrestrial locomotion. Because legs must provide support as well as propulsion, it is important that the sequence of their movements not shove the body's center of gravity outside the legs' zone of support, unless the duration of such imbalance is short. Otherwise, the animal will fall. The need to maintain stability determines the sequence of leg movements, which are similar in vertebrates and arthropods.

The apparent differences in the walking gaits of these two groups reflect the differences in leg number. Vertebrates walk on two or four legs; all arthropods have six or more limbs. Although the many legs of arthropods increase stability during locomotion, they also appear to reduce the maximum speed that can be attained.

The basic walking pattern of quadrupeds, from salamanders to most mammals, is left hind leg, right foreleg, right hind leg, left foreleg. The highest running speeds of quadruped mammals, such as the gallop of a horse, may involve the animal being supported by only one leg, or even none at all. This is because mammals have evolved changes in the structure of both their axial and appendicular skeleton that permit running by a series of leaps.

Vertebrates such as kangaroos, rabbits, and frogs are effective leapers (figure 47.21). However, insects are the true Olympians of the leaping world. Many insects, such as grasshoppers, have enormous leg muscles, and some small insects can jump to heights more than 100 times the length of their body!

Flying uses air for support

The evolution of flight is a classic example of convergent evolution, having occurred independently four times, once in insects and three times among vertebrates (figure 47.22*a*). All three vertebrate fliers modified the forelimb into a wing structure, but they did so in different ways, illustrating how natural selection can sometimes build similar structures through different evolutionary pathways (figure 47.22*b*). In both birds and pterosaurs (an extinct group of reptiles that flourished alongside

Figure 47.21 Animals that hop or leap use their rear legs to propel themselves through the air. The powerful leg muscles of this frog allow it to explode from a crouched position to a takeoff in about 100 msec.

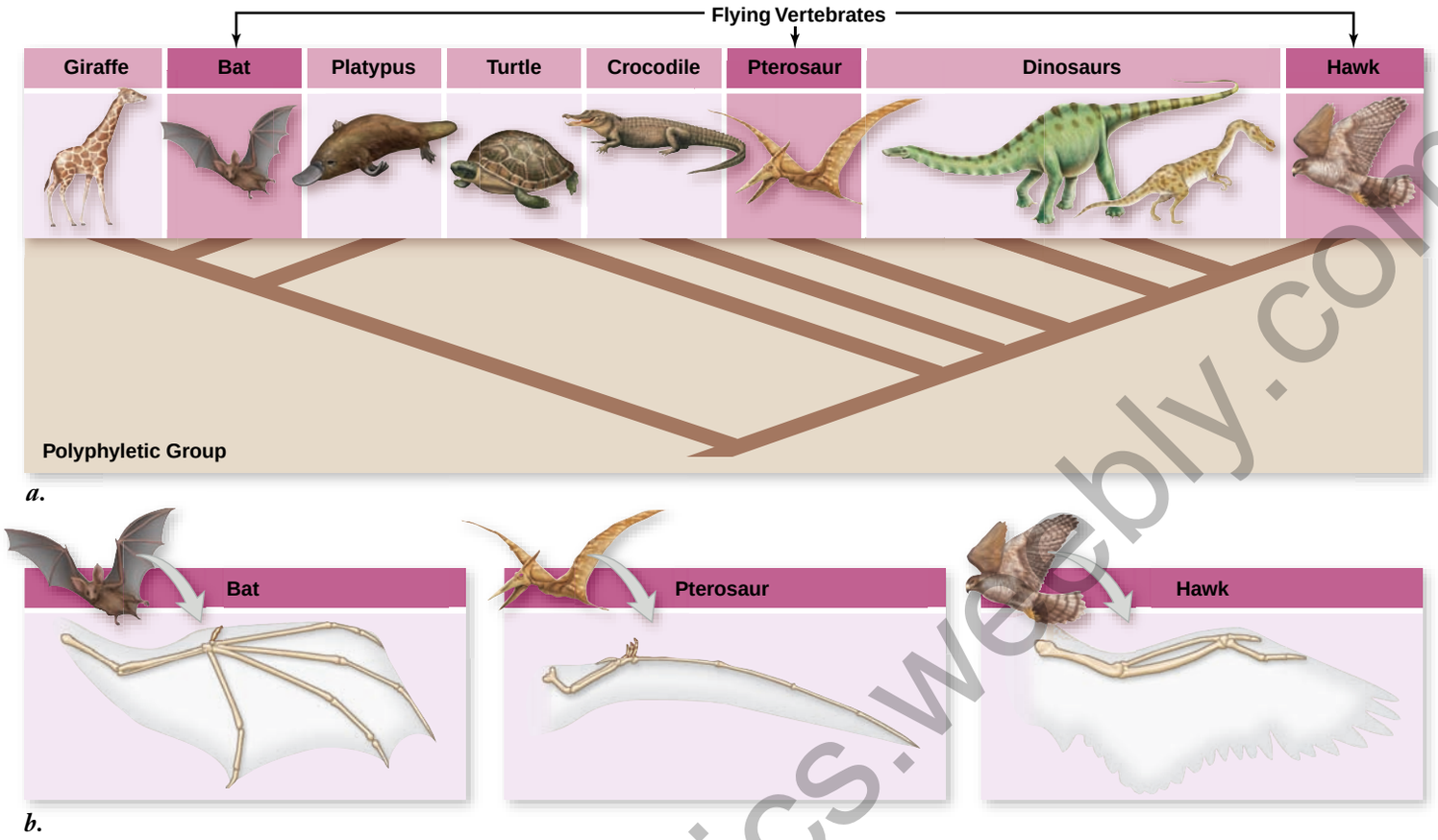


Figure 47.22 Convergent evolution of wings in vertebrates. Wings evolved independently in birds, bats and pterosaurs, in each case by elongation of different elements of the forelimb.

the dinosaurs), the wing is built on a single support, but in birds it is elongation of the radius, ulna, and wrist bones, whereas in pterosaurs it is an elongation of the fourth finger bone. By contrast, in bats the wing is supported by multiple bones, each of which is an elongated finger bone. A second difference is that the wings of pterosaurs and bats are composed of a membrane formed from skin, whereas birds use feathers, which are modified from reptile scales.

In all groups, active flying takes place in much the same way. Propulsion is achieved by pushing down against the air with wings. This alone provides enough lift to keep insects in the air. Vertebrates, being larger, need greater lift, obtaining it with wings whose upper surface is more convex (in cross section) than the lower. Because air travels farther over the top surface, it moves faster. A fluid, like air, decreases its internal pressure the faster it moves. Thus, there is a lower pressure on top of the wing and higher pressure on the bottom of the wing. This is the same principle used by airplane wings.

In birds and most insects, the raising and lowering of the wings is achieved by the alternate contraction of extensor muscles (elevators) and flexor muscles (depressors). Four insect orders (including those containing flies, mosquitoes, wasps, bees, and beetles) beat their wings at frequencies ranging from 100 to more than 1000 times per second, faster than nerves can carry successive impulses!

In these insects, the flight muscles are not attached to the wings at all, but rather to the stiff wall of the thorax, which is distorted in and out by their contraction. The reason these muscles can contract so fast is that the contraction of one muscle set stretches the other set, triggering its contraction in turn without waiting for the arrival of a nerve impulse.

In addition to active flight, many species have evolved adaptations—primarily flaps of skin that increase surface area and thus slow down the rate of descent—to enhance their ability to glide long distances. Gliders have done this in many ways, including flaps of skin along the body in flying squirrels, snakes, and lizards; webbing between the toes in frogs; and the evolution in some lizards of ribs that extend beyond the body wall and that are connected by skin that can be spread out to form a large gliding surface.

Learning Outcomes Review 47.5

Locomotion involves friction and pressure created by body parts, often appendages, against water, air, or ground. Walking, running, and flying require supporting the body against gravity's pull. Flight is achieved when a pressure difference between air flowing over the top and bottom of a wing creates lift. Solutions to locomotion have evolved convergently many times, in both homologous and nonhomologous structures.

- ***In what ways would locomotion by a series of leaps be more advantageous than by alternation of legs?***

Chapter Review

47.1 Types of Skeletal Systems

Hydrostatic skeletons use water pressure inside a body wall.

By muscular contractions, earthworms press fluid into different parts of the body, causing them to move (see figure 47.1).

Exoskeletons consist of a rigid outer covering.

The exoskeleton, composed of hard chitin, must be shed for the organism to grow (see figure 47.2*a*).

Endoskeletons are composed of hard, internal structures.

Endoskeletons of vertebrates are living connective tissues that may be mineralized with calcium phosphate (see figure 47.2*b*).

47.2 A Closer Look at Bone

Bones can be classified by two modes of development.

In intramembranous development, bone forms within a layer of connective tissue (see figure 47.3). In endochondral development, bone fills in a cartilaginous model.

Osteoblasts initiate bone development; osteocytes form from osteoblasts; and osteoclasts break down and resorb bone.

Bones grow by lengthening and widening. Cartilage remaining after development of the epiphyses serves as a pad between bone surfaces (see figure 47.4).

Bone structure may include blood vessels and nerves.

In birds and fishes, bone is avascular and basically acellular. In other vertebrates, bone contains bone cells, blood capillaries, and nerves collected in Haversian systems.

Bone remodeling allows bone to respond to use or disuse.

Bone structure may thicken or thin depending on use and on forces impinging on the bone (see figure 47.5).

47.3 Joints and Skeletal Movement

Moveable joints have different ranges of motion, depending on type.

Ball-and-socket joints can perform movement in all directions; hinge joints have restricted movement; gliding joints slide, providing stability and flexibility; and combination joints allow rotation and sliding (see figure 47.7).

Skeletal muscles pull on bones to produce movement at joints.

Muscles attach to the periosteum directly or through a tendon. Skeletal muscles occur in antagonistic pairs that oppose each other's movement (see figure 47.8).

47.4 Muscle Contraction

Muscle fibers contract as overlapping filaments slide together.

The different myofibril bands seen microscopically result from the degree of overlap of actin and myosin filaments (see figure 47.10). Muscle contraction occurs when actin and myosin filaments form cross-bridges and slide relative to each other.

The globular head of myosin forms a cross-bridge with actin when ATP is hydrolyzed to ADP and P_i. Upon bridging, it pulls the thin filament toward the center of the sarcomere. The head then binds to a new ATP, releasing from actin (see figure 47.14).

Contraction depends on calcium ion release following a nerve impulse.

Tropomyosin, attached to actin by troponin, blocks formation of a cross-bridge. Nerve stimulation releases calcium from the sarcoplasmic reticulum into the cytosol, and formation of a troponin–calcium complex displaces tropomyosin, allowing cross-bridges to form (see figures 47.15, 47.16).

Motor units are composed of a single motor neuron and all the muscle fibers innervated by its branches (see figure 47.17).

The two main types of muscle fibers are slow-twitch and fast-twitch.

A twitch is the interval between contraction and relaxation of a single muscle stimulation. Summation occurs when a second twitch "piggybacks" on the first twitch. Tetanus is the state when no relaxation occurs between twitches (see figure 47.18).

The two major types of skeletal muscle fibers are slow-twitch fibers (endurance), and fast-twitch fibers (power bursts).

Muscle metabolism changes with the demands made on it.

At rest skeletal muscles obtain energy by metabolism of fatty acids. When active, energy comes from glucose and glycogen.

Muscle fatigue is a use-dependent decrease in the ability of the muscle to generate force.

Endurance training does not increase muscle size; high-intensity exercise with resistance increases the size of the muscle (hypertrophy).

47.5 Modes of Animal Locomotion

Swimmers must contend with friction when moving through water.

Among vertebrates, aquatic locomotion occurs by pushing some or all of the body against the water. Many vertebrates undulate the body or tail for propulsion, but others use their limbs (see figure 47.20).

Terrestrial locomotion must deal primarily with gravity.

Most terrestrial animals move by lifting their bodies off the ground and pushing against the ground with appendages. Terrestrial animals that walk or run use fundamentally the same mechanisms during locomotion.

Flying uses air for support.

Propulsion is accomplished as wings push down against the air. Lift in larger organisms is created by a pressure difference as air flows above and below a convex wing.

In both flying and gliding, convergent evolution has produced the same outcome through different evolutionary pathways.

Review Questions

UNDERSTAND

1. Exoskeletons and endoskeletons differ in that
   a. an exoskeleton is rigid, and an endoskeleton is flexible.
   b. endoskeletons are found only in vertebrates.
   c. exoskeletons are composed of calcium, and endoskeletons are built from chitin.
   d. exoskeletons are external to the soft tissues, and endoskeletons are internal.
2. Worms use a hydrostatic skeleton to generate movement. How do they do this?
   a. Their bones are filled with water, which provides the weight of the skeleton.
   b. The change in body structure is caused by contraction of muscles compressing the watery body fluid.
   c. The muscles contain water vacuoles, which, when filled, provide a rigid internal structure.
   d. The term *hydrostatic* simply refers to moist environment. They generate movement just as arthropods do.
3. You take X-rays of two individuals. Ray has been a weight lifter and body builder for 30 years; Ben has led a mostly sedentary life. What differences would you expect in their X-rays?
   a. No difference, they would both have thicker bones than a younger person due to natural thickening with age.
   b. No difference, lifestyle does not affect bone density.
   c. Ray would have thicker bones due to reshaping as a result of physical stress.
   d. Ben would have thicker bones because bone accumulates like fat tissue from a sedentary lifestyle.
4. Which of the following statements best describes the sliding filament mechanism of muscle contraction?
   a. Actin and myosin filaments do not shorten, but rather, slide past each other.
   b. Actin and myosin filaments shorten and slide past each other.
   c. As they slide past each other, actin filaments shorten, but myosin filaments do not shorten.
   d. As they slide past each other, myosin filaments shorten, but actin filaments do not shorten.
5. Motor neurons stimulate muscle contraction via the release of
   a. Ca^{2+}.
   b. ATP.
   c. acetylcholine.
   d. hormones.
6. Which of the following statements about muscle metabolism is false?
   a. Skeletal muscles at rest obtain most of their energy from muscle glycogen and blood glucose.
   b. ATP can be quickly obtained by combining ADP with phosphate derived from creatine phosphate.
   c. Exercise intensity is related to the maximum rate of oxygen consumption.
   d. ATP is required for the pumping of the Ca^{2+} back into the sarcoplasmic reticulum.
7. If you wanted to study the use of ATP during a single contraction cycle within a muscle cell, which of the following processes would you use?
   a. Summation
   b. Twitch
   c. Treppe
   d. Tetanus
8. Place the following events in the correct order.
   1. Sarcoplasmic reticulum releases Ca^{2+}.
   2. Myosin binds to actin.
   3. Action potential arrives from neuron.
   4. Ca^{2+} binds to troponin.

   a. 1, 2, 3, 4
   b. 3, 1, 2, 4
   c. 2, 4, 3, 1
   d. 3, 1, 4, 2

APPLY

1. Bone develops by one of two mechanisms depending on the underlying scaffold. Which pairing correctly describes these mechanisms?
   a. Intramembranous and extramembranous
   b. Endochondral and exochondral
   c. Extramembranous and exochondral
   d. Endochondral and intramembranous
2. You have identified a calcium storage disease in rats. How would this inability to store Ca^{2+} affect muscle contraction?
   a. Ca^{2+} would be unable to bind to tropomyosin, which enables troponin to move and reveal binding sites for cross-bridges.
   b. Ca^{2+} would be unable to bind to troponin, which enables tropomyosin to move and reveal binding sites for cross-bridges.
   c. Ca^{2+} would be unable to bind to tropomyosin, which enables troponin to release ATP.
   d. Ca^{2+} would be unable to bind to troponin, which enables tropomyosin to release ATP.
3. How do the muscles move your hand through space?
   a. By contraction
   b. By attaching to two bones across a joint
   c. By lengthening
   d. Both a and b are correct
4. How can osteocytes remain alive within bone?
   a. Bones are composed of only dead or dormant cells.
   b. Haversian canals are bone structures that contain blood vessels that provide materials for the osteocytes.
   c. Osteocytes have membrane extensions that protrude from bone and allow them to exchange materials with the surrounding fluids.
   d. Bones are hollow in the middle and the low pressure there draws fluid from the blood that nourishes the osteocytes.

5. Swimming underwater using forelimbs for propulsion is similar to flying through the air because
   a. birds are the only class of vertebrates that have species that do both.
   b. both involve coordinating movements of the forelimbs and hindlimbs.
   c. both must counter strong forces caused by friction.
   d. both involve generating lift by pushing down on the air or water to counter gravity.
6. If a drug inhibits the release of ACh, what will happen?
   a. Somatic motor neurons will fail to activate.
   b. Somatic motor neuron impulses will not lead to muscle fiber contraction.
   c. Myosin molecules will fail to release ADP.
   d. An influx of sodium ions will lead to muscle cell membrane depolarization.

SYNTHESIZE

1. You are designing a space-exploration vehicle to use on a planet with a gravity greater than Earth. Given a choice between a hydrostatic or an exoskeleton, which would you choose? Why?
2. You start running as fast as you can. Then, you settle into a jog that you can easily maintain. How do energy sources utilized by your skeletal muscles change during the switch? Why?
3. The nerve gas methylphosphonofluoridic acid (sarin) inhibits the enzyme acetylcholinesterase, required to break down acetylcholine. Based on this information, what are the likely effects of this nerve gas on muscle function?
4. If natural selection favors the evolution of wings in different types of vertebrates, why didn't it produce structures that were built in the same way?

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Chapter 48

The Digestive System

Chapter Outline

Introduction

Plants and other photosynthetic organisms can produce the organic molecules they need from inorganic components. Therefore, they are autotrophs, or self-sustaining. Animals, such as the chipmunk shown, are heterotrophs: They must consume organic molecules present in other organisms. The molecules heterotrophs eat must be digested into smaller molecules in order to be absorbed into the animal's body. Once these products of digestion enter the body, the animal can use them for energy in cellular respiration or for the construction of the larger molecules that make up its tissues. The process of animal digestion is the focus of this chapter.

48.1 Types of Digestive Systems

Learning Outcomes

1. *Distinguish between incomplete and complete digestive systems.*
2. *List the components of the vertebrate digestive tract.*
3. *Describe the tissue layers of the gastrointestinal tract.*

Heterotrophs are divided into three groups on the basis of their food sources. Animals that eat plants exclusively are classified as **herbivores;** common examples include algae-eating snails, sapsucking insects, and vertebrates such as cattle, horses, rabbits, and sparrows. Animals that eat other animals, such as crabs, squid, many insects, cats, eagles, trout, and frogs, are **carnivores.** Animals that eat both plants and other animals are **omnivores.** Humans are omnivores, as are pigs, bears, and crows.

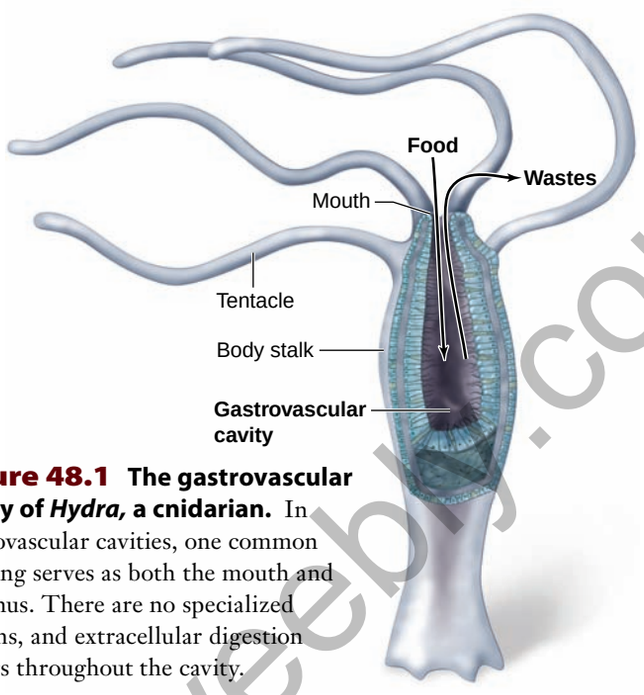


Figure 48.1 The gastrovascular cavity of *Hydra,* a cnidarian. In gastrovascular cavities, one common opening serves as both the mouth and the anus. There are no specialized regions, and extracellular digestion occurs throughout the cavity.

Invertebrate digestive systems are bags or tubes

Single-celled organisms as well as sponges digest their food intracellularly. Other multicellular animals digest their food extracellularly, within a digestive cavity. In this case, the digestive enzymes are released into a cavity that is continuous with the animal's external environment. In cnidarians and in flatworms such as planarians, the digestive cavity has only one opening that serves as both mouth and anus (see chapter 33). There is no specialization within this type of digestive system, called a *gastrovascular cavity*, because every cell is exposed to all stages of food digestion (figure 48.1).

Specialization occurs when the digestive tract, or alimentary canal, has a separate mouth and anus, so that transport of food is one-way. The most primitive digestive tract is seen in nematodes (phylum Nematoda), where it is simply a tubular *gut* lined by an epithelial membrane. Earthworms (phylum Annelida) have a digestive tract specialized in different regions for the ingestion, storage, fragmentation, digestion, and absorption of food. All more complex animal groups, including all vertebrates, show similar specializations (figure 48.2).

The ingested food may be stored in a specialized region of the digestive tract or it may first be subjected to physical fragmentation. This fragmentation may occur through the chewing action of teeth (in the mouth of many vertebrates) or the grinding action of pebbles (in the gizzard of earthworms and birds). Chemical digestion then occurs, breaking down the larger food molecules of polysaccharides and disaccharides, fats, and proteins into their smallest subunits.

Chemical digestion involves hydrolysis reactions that liberate the subunit molecules—primarily monosaccharides, amino acids, and fatty acids—from the food. These products of chemical digestion pass through the epithelial lining of the gut into the blood, in a process known as *absorption*. Any molecules in the food that are not absorbed cannot be used by the animal. These waste products are excreted, or defecated, from the anus.

Vertebrate digestive systems include highly specialized structures molded by diet

In humans and other vertebrates, the digestive system consists of a tubular gastrointestinal tract and accessory digestive organs (figure 48.3).

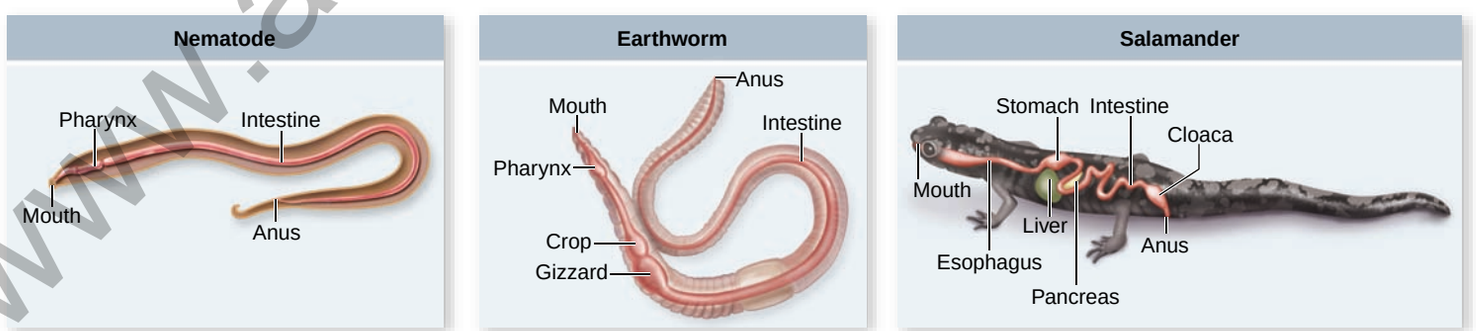


Figure 48.2 The one-way digestive tract of nematodes, earthworms, and vertebrates. One-way movement through the digestive tract allows different regions of the digestive system to become specialized for different functions.

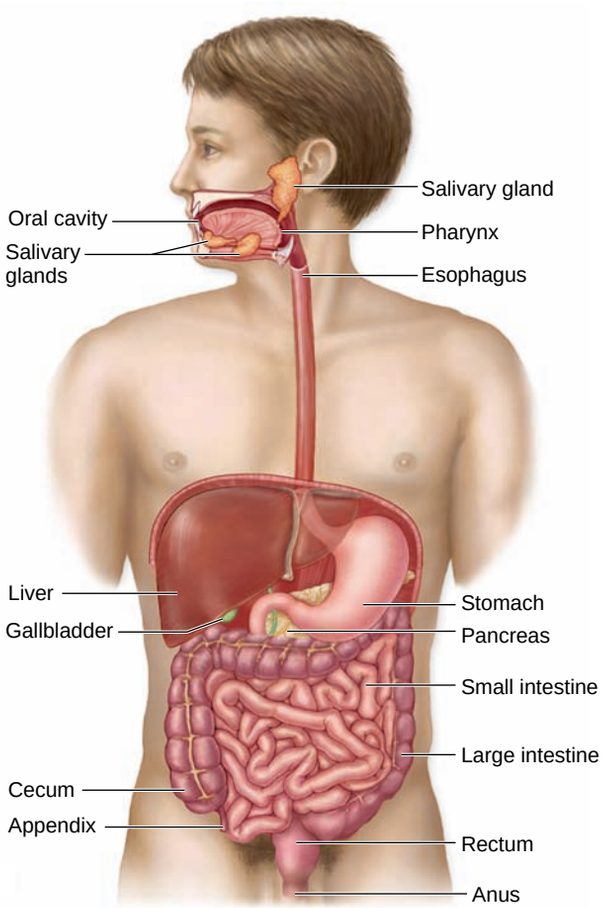


Figure 48.3 The human digestive system. The human digestive system consists of the oral cavity, esophagus, stomach, small intestine, large intestine, rectum, and anus; and is aided by accessory organs.

Overview of the digestive tract

The initial components of the gastrointestinal tract are the mouth and the pharynx, which is the common passage of the oral and nasal cavities. The pharynx leads to the esophagus, a muscular tube that delivers food to the stomach, where some preliminary digestion occurs.

From the stomach, food passes to the small intestine, where a battery of digestive enzymes continues the digestive process. The products of digestion, together with minerals and water, are absorbed across the wall of the small intestine into the bloodstream. What remains is emptied into the large intestine, where some of the remaining water and minerals are absorbed.

In most vertebrates other than mammals, the waste products emerge from the large intestine into a cavity called the cloaca (see figure 48.2), which also receives the products of the urinary and reproductive systems. In mammals, the urogenital products are separated from the fecal material in the large intestine; the fecal material enters the rectum and is expelled through the anus.

The accessory digestive organs include the liver, which produces *bile* (a green solution that emulsifies fat), the gallbladder, which stores and concentrates the bile, and the pancreas. The pancreas produces *pancreatic juice*, which contains digestive enzymes and bicarbonate buffer. Both bile and pancreatic juice

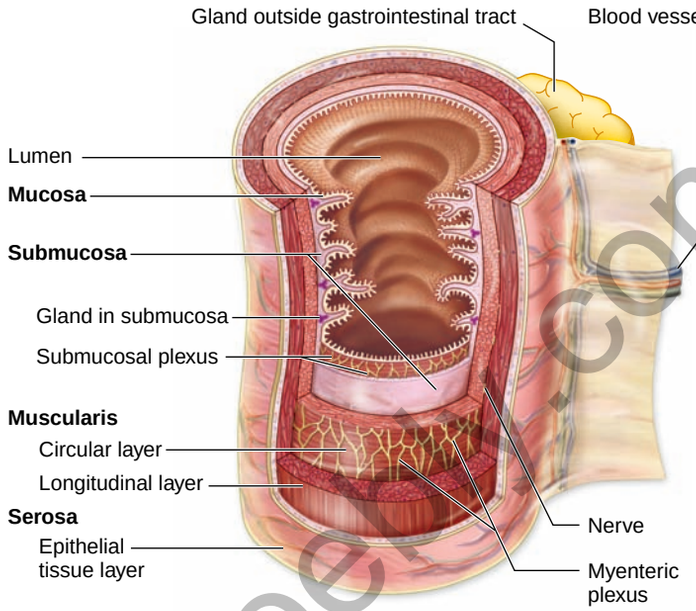


Figure 48.4 The layers of the gastrointestinal tract. The mucosa contains an epithelial lining; the submucosa is composed of connective tissue; and the muscularis consists of smooth muscles. Glands secrete substances via ducts into specific regions of the tract.

are secreted into the first region of the small intestine, the duodenum, where they aid digestion.

Tissues of the digestive tract

The tubular gastrointestinal tract of a vertebrate has a characteristic layered structure (figure 48.4). The innermost layer is the **mucosa,** an epithelium that lines the interior, or lumen, of the tract. The next major tissue layer, made of connective tissue, is called the **submucosa.**

Just outside the submucosa is the **muscularis,** which consists of a double layer of smooth muscles. The muscles in the inner layer have a circular orientation and serve to constrict the gut, whereas those in the outer layer are arranged longitudinally and work to shorten it. Another epithelial tissue layer, the **serosa,** covers the external surface of the tract. Nerve networks, intertwined in *plexuses* between muscle layers, are located in the submucosa and help regulate the gastrointestinal activities.

In the rest of this chapter, we focus on the details of the vertebrate digestive system's structure and function. We close the chapter with discussion of nutrients that are essential to vertebrates.

Learning Outcomes Review 48.1

Incomplete digestive tracts have only one opening; complete digestive tracts are flow-through, with a mouth and an anus. The digestive system of vertebrates includes mouth and pharynx, esophagus, stomach, small and large intestines, cloaca or rectum, anus, and accessory organs. The layers of tissue that compose the tubular tract are the mucosa, the submucosa, the muscularis, and the serosa.

- ***What might be the advantages of a one-way digestive system?***

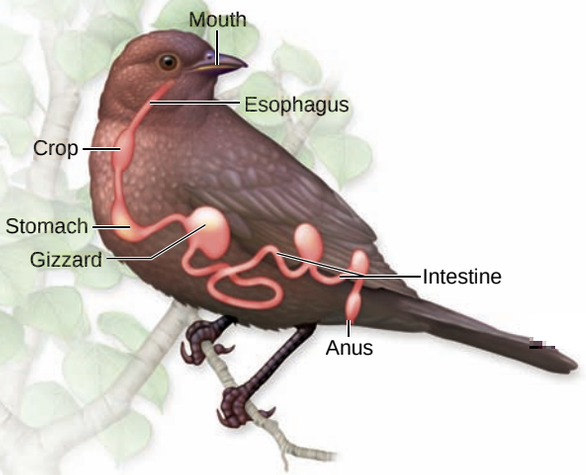


Figure 48.5 The digestive tract of birds. Birds lack teeth but have a muscular chamber called the gizzard that works to break down food. Birds swallow gritty objects or pebbles that lodge in the gizzard and pulverize food before it passes into the intestine. Food is stored in the crop.

48.2 *The Mouth and Teeth: Food Capture and Bulk Processing*

Learning Outcomes

1. *Identify adaptive variation in vertebrate tooth shape.*
2. *Understand the role of the mouth in the digestive process.*

Specializations of the digestive systems in different kinds of vertebrates reflect the way these animals live. Birds, which lack teeth, break up food in their two-chambered stomachs (figure 48.5). In one of these chambers, called the *gizzard*, small pebbles ingested by the bird are churned together with the food by muscular action. This churning grinds up the seeds and other hard plant material into smaller chunks that can be digested more easily.

Vertebrate teeth are adapted to different types of food items

Many vertebrates have teeth (figure 48.6), used for chewing, or *mastication*, that break up food into small particles and mix it with fluid secretions. Carnivorous mammals have pointed teeth that lack flat grinding surfaces. Such teeth are adapted for cutting and shearing. Carnivores often tear off pieces of their prey but have little need to chew them, because digestive enzymes can act directly on animal cells. By contrast, grass-eating herbivores must pulverize the cellulose cell walls of plant tissue before the bacteria in their rumens or cecae can digest them. These animals have large, flat teeth with complex ridges well suited to grinding.

Human teeth are specialized for eating both plant and animal food. Viewed simply, humans are carnivores in the front of the mouth and herbivores in the back (see figure 48.6). The four front teeth in the upper and lower jaws are sharp, chisel-shaped incisors used for biting. On each side of the incisors are sharp, pointed teeth called cuspids (sometimes referred to as "canine" teeth), which are used for tearing food. Behind the canines are two premolars and three molars, all with flattened, ridged surfaces for grinding and crushing food.

The mouth is a chamber for ingestion and initial processing

Inside the mouth, the tongue mixes food with a mucous solution, saliva. In humans, three pairs of salivary glands secrete saliva into the mouth through ducts in the mouth's mucosal lining. Saliva moistens and lubricates the food so that it is easier to swallow and does not abrade the tissue of the esophagus as it passes through.

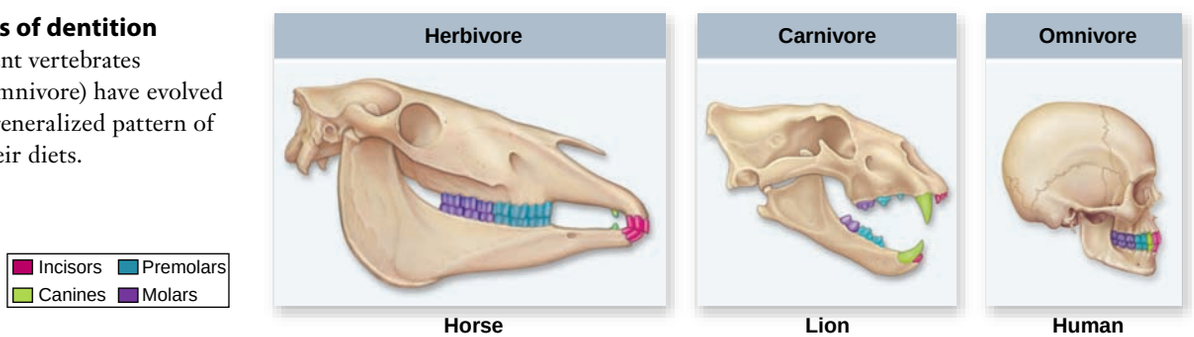
Saliva also contains the hydrolytic enzyme salivary amylase, which initiates the breakdown of the polysaccharide starch into the disaccharide maltose. This digestion is usually minimal in humans, however, because most people don't chew their food very long.

Stimulation of salivation

The secretions of the salivary glands are controlled by the nervous system, which in humans maintains a constant flow of about half a milliliter per minute when the mouth is empty of food. This continuous secretion keeps the mouth moist.

The presence of food in the mouth triggers an increased rate of secretion. Taste buds as well as olfactory (smell) neurons send impulses to the brain, which responds by stimulating the salivary glands (see chapter 46). The most potent stimuli are acidic solutions; lemon juice, for example, can increase the rate of salivation eightfold. The sight, sound, or smell of food can stimulate salivation markedly in many

Figure 48.6 Patterns of dentition depend on diet. Different vertebrates (herbivore, carnivore, or omnivore) have evolved specific variations from a generalized pattern of dentition depending on their diets.



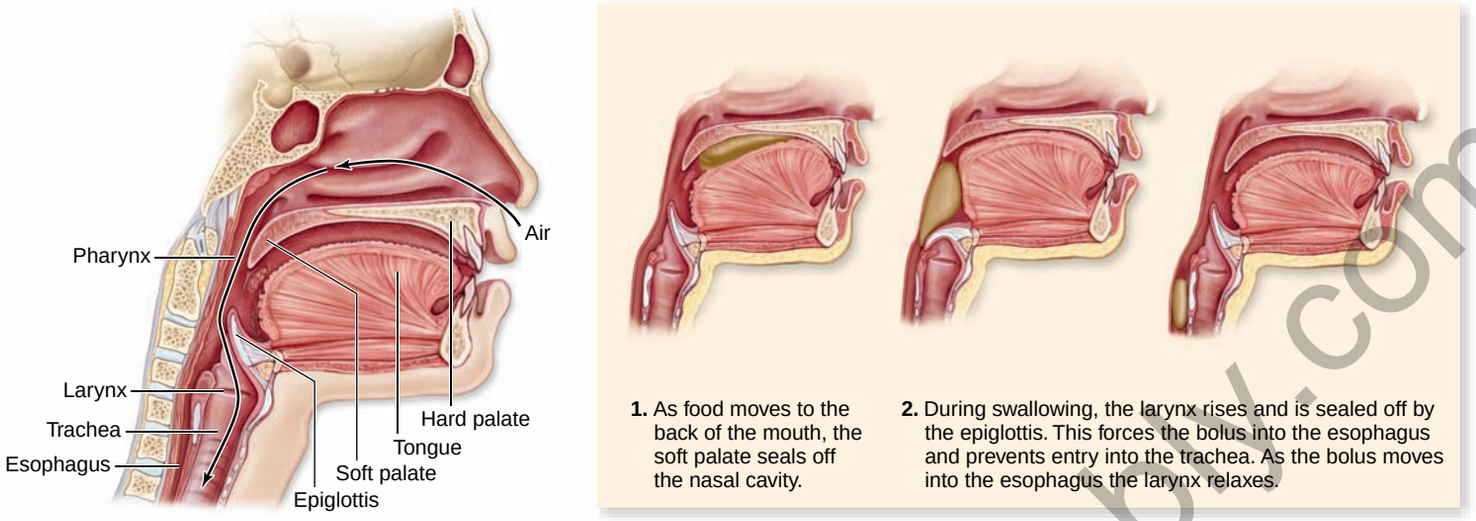


Figure 48.7 The mechanics of swallowing. Cross section through head and throat showing relevant structures (left). During swallowing (right) the tongue pushes the palate upward, and the soft palate seals off the nasal cavity. Elevation of the larynx causes the epiglottis to seal off the trachea, thus preventing food from entering the airway.

Inquiry question

What goes wrong to cause someone to choke?

animals; in humans, thinking or talking about food can also have this effect.

Swallowing

Swallowing is initiated by voluntary action, then is continued under involuntary control. When food is ready to be swallowed, the tongue moves it to the back of the mouth. In mammals, the process of swallowing begins when the soft palate elevates, pushing against the back wall of the pharynx (figure 48.7). Elevation of the soft palate seals off the nasal cavity and prevents food from entering it. Pressure against the pharynx triggers an automatic, involuntary response, the swallowing reflex. Because it is a reflex, swallowing cannot be stopped once it is initiated.

Neurons within the walls of the pharynx send impulses to the swallowing center in the brain. In response, electrical impulses in motor neurons stimulate muscles to contract and raise the **larynx** (voice box). This pushes the glottis, the opening from the larynx into the trachea (windpipe), against a flap of tissue called the **epiglottis.** These actions keep food out of the respiratory tract, directing it instead into the esophagus.

Learning Outcomes Review 48.2

In vertebrates with teeth, tooth shape exhibits adaptations to diet: herbivores have large, flat teeth for grinding, whereas carnivores have pointed teeth for tearing. The mouth serves as an initial processing center, tasting ingested food, breaking it down, and beginning digestion with saliva secretion prior to swallowing.

- ***Which parts of the food ingestion process are voluntary and which are involuntary?***

48.3 *The Esophagus and the Stomach: The Early Stages of Digestion*

Learning Outcomes

1. ***Describe how food moves through the esophagus.***
2. ***Explain what digestive processes take place in the stomach.***

Swallowed food enters a muscular tube called the esophagus, which connects the pharynx to the stomach. The esophagus actively moves a processed lump of food, called a **bolus,** through the action of muscles. Food from a meal is stored in the stomach where it undergoes early stages of digestion.

Muscular contractions of the esophagus move food to the stomach

In adult humans, the esophagus is about 25 cm long; the upper third is enveloped in skeletal muscle for voluntary control of swallowing, whereas the lower two-thirds is surrounded by involuntary smooth muscle. The swallowing center stimulates successive one-directional waves of contraction in these muscles that move food along the esophagus to the stomach. These rhythmic waves of muscular contraction are called

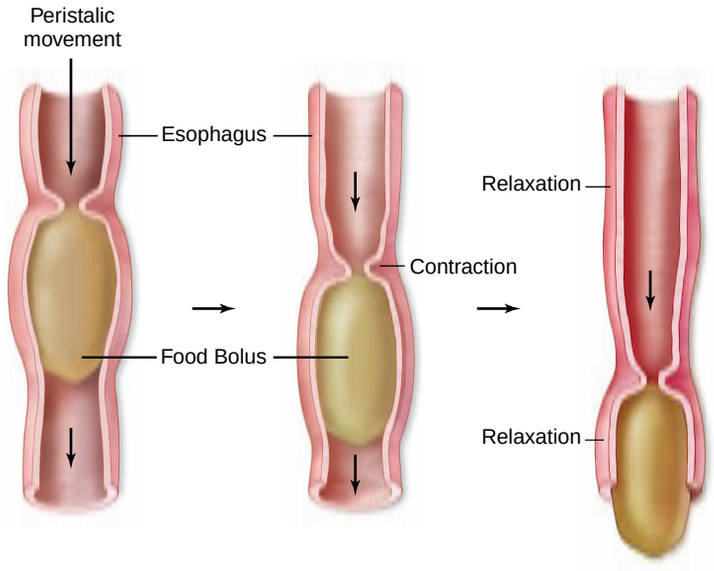


Figure 48.8 The esophagus and peristalsis. After food has entered the esophagus, rhythmic waves of muscular contraction, called peristalsis, move the food down to the stomach.

peristalsis (figure 48.8); they enable humans and other vertebrates to swallow even if they are upside down.

In many vertebrates, the movement of food from the esophagus into the stomach is controlled by a ring of circular smooth muscle, or a *sphincter*, that opens in response to the pressure exerted by the food. Contraction of this sphincter prevents food in the stomach from moving back into the esophagus. Rodents and horses have a true sphincter at this site, and as a result they cannot regurgitate; humans lack a true sphincter. Normally, the esophagus is closed off except during swallowing.

The stomach is a "holding station" involved in acidic breakdown of food

The **stomach** (figure 48.9) is a saclike portion of the digestive tract. Its inner surface is highly convoluted, enabling it to fold up when empty and open out like an expanding balloon as it fills with food. For example, the human stomach has a volume of only about 50 mL when empty, but, it may expand to contain 2 to 4 L of food when full. Carnivores that engage in sporadic gorging as an important survival strategy possess stomachs that are able to distend even more.

Secretory systems

The stomach contains a third layer of smooth muscle for churning food and mixing it with **gastric juice,** an acidic secretion of the tubular gastric glands of the mucosa (see figure 48.9). These exocrine glands contain three kinds of secretory cells: *mucus-secreting cells*, *parietal cells*, which secrete hydrochloric acid (HCl), and *chief cells*, which secrete **pepsinogen,** the inactive form of the protease (protein-digesting enzyme) **pepsin.**

Pepsinogen has 44 additional amino acids that block its active site. HCl causes pepsinogen to unfold, exposing the active site, which then acts to remove the 44 amino acids. This yields the active protease, pepsin. This process of secreting an inactive form that is then converted into an active enzyme outside the cell prevents the chief cells from digesting themselves. In the stomach, mucus produced by mucus-secreting cells serves

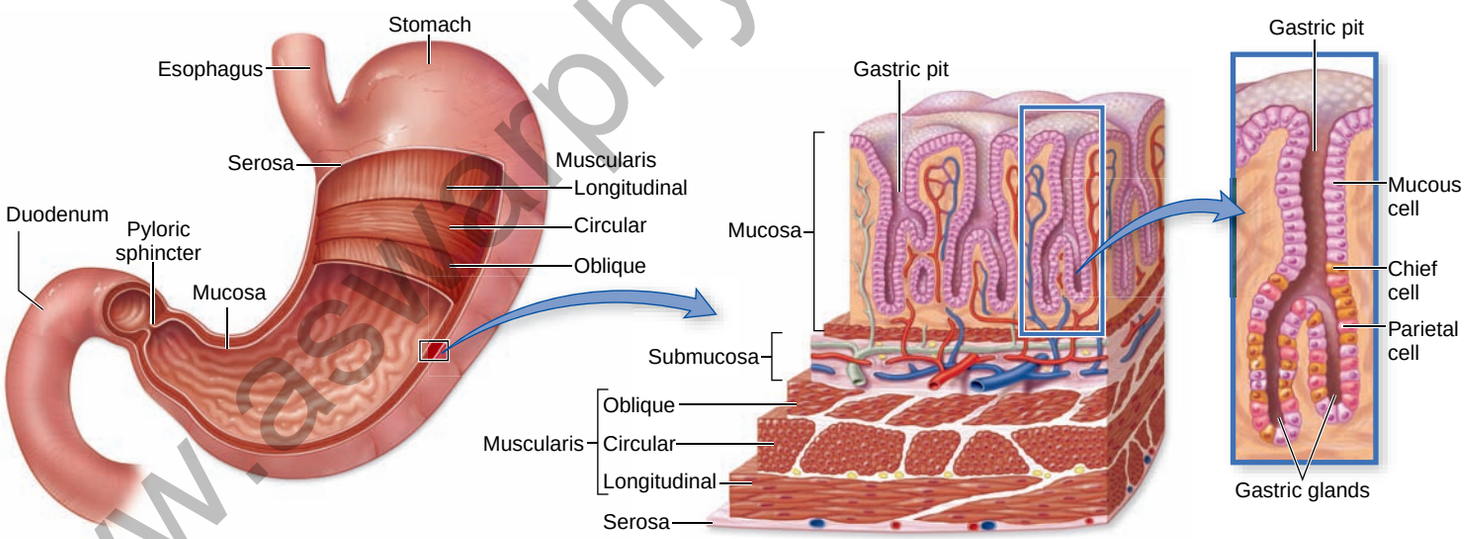


Figure 48.9 The stomach and duodenum. Food enters the stomach from the esophagus. A ring of smooth muscle called the pyloric sphincter controls the entrance to the duodenum, the upper part of the small intestine. The epithelial walls of the stomach are dotted with deep infoldings called gastric pits that contain gastric glands. The gastric glands consist of mucous cells, chief cells that secrete pepsinogen, and parietal cells that secrete HCl. Gastric pits are the openings of the gastric glands.

Inquiry question

How does the digestive system keep from being digested by the gastric secretions it produces?

the same purpose, covering the interior walls and preventing them from being digested.

In addition to producing HCl, the parietal cells of the stomach also secrete **intrinsic factor,** a polypeptide needed for the intestinal absorption of vitamin B_{12}. Because this vitamin is required for the production of red blood cells, people who lack sufficient intrinsic factor develop a type of anemia (low red blood cell count) called *pernicious anemia*.

Action of acid

The human stomach produces about 2 L of HCl and other gastric secretions every day, creating a very acidic solution. The concentration of HCl in this solution is about 10 millimolar (mM), equal to a pH of 2. Thus, gastric juice is about 250,000 times more acidic than blood, whose normal pH is 7.4.

The low pH in the stomach helps denature food proteins, making them easier to digest, and keeps pepsin maximally active. Active pepsin hydrolyzes food proteins into shorter chains of polypeptides that are not fully digested until the mixture enters the small intestine. The mixture of partially digested food and gastric juice is called **chyme.** In adult humans, only proteins are partially digested in the stomach—no significant digestion of carbohydrates or fats occurs there.

The acidic solution within the stomach also kills most of the bacteria that are ingested with the food. The few bacteria that survive the stomach and enter the intestine intact are able to grow and multiply there, particularly in the large intestine. In fact, vertebrates harbor thriving colonies of bacteria within their intestines, and bacteria are a major component of feces. As we discuss later, bacteria that live within the digestive tracts of ruminants play a key role in the ability of these mammals to digest cellulose.

Ulcers

Overproduction of gastric acid can occasionally eat a hole through the wall of the stomach or the duodenum, causing a peptic ulcer. Although we once blamed consumption of spicy food, the most common cause of peptic ulcers is now thought to be infection with the bacterium *Heliobacter pylori*.

H. pylori can grow on the lining of the human stomach, surviving the acid pH by secreting substances that buffer the pH of its immediate surroundings. Although infection with *H. pylori* is common in the United States (about 20% of people younger than 40 and 50% older than 60), most people are asymptomatic. However, in some cases, infection by *H. pylori* can reduce or weaken the mucosal layer in the stomach or duodenum, allowing acidic secretions to attack the underlying epithelium. Antibiotic treatment of the infection can reduce symptoms and often even cure the ulcer.

Leaving the stomach

Chyme leaves the stomach through the *pyloric sphincter* (see figure 48.9) to enter the small intestine. This is where all terminal digestion of carbohydrates, lipids, and proteins occurs and where the products of digestion—amino acids, glucose, and so on—are absorbed into the blood. Only some of the water in chyme and a few substances, such as aspirin and alcohol, are absorbed through the wall of the stomach.

Learning Outcomes Review 48.3

Peristaltic waves of contraction and relaxation of smooth muscle propel food along the esophagus to the stomach. Gastric juice contains strong hydrochloric acid and the enzyme pepsin, a protease that begins the breakdown of proteins into shorter polypeptides. The acidic chyme is then transferred through the pyloric sphincter into the small intestine.

- ***Suppose you ate a chicken sandwich (chicken breast on bread with mayonnaise). Which of these foods would begin its breakdown in the stomach?***

48.4 The Intestines: Breakdown, Absorption, and Elimination

Learning Outcomes

1. *Compare the structures of the small and large intestines.*
2. *Name the accessory organs and describe their roles.*
3. *Explain how absorbed nutrients move into the blood or lymph capillaries.*

The capacity of the small intestine is limited, and its digestive processes take time. Consequently, efficient digestion requires that only relatively small amounts of chyme be introduced from the stomach into the small intestine at any one time. Coordination between gastric and intestinal activities is regulated by neural and hormonal signals, which we will describe in section 48.6.

The structure of the small intestine is specialized for digestion and nutrient uptake

The small intestine is approximately 4.5 m long in a living person, but 6 m long at autopsy when all the muscles have relaxed. The first 25 cm is the **duodenum;** the remainder of the small intestine is divided into the **jejunum** and the **ileum.**

The duodenum receives acidic chyme from the stomach, digestive enzymes and bicarbonate from the pancreas, and bile from the liver and gallbladder. Enzymes in the pancreatic juice digest larger food molecules into smaller fragments. This digestion occurs primarily in the duodenum and jejunum.

The epithelial wall of the small intestine is covered with tiny, fingerlike projections called **villi** (singular, *villus;* figure 48.10). In turn, each epithelial cell lining the villi is covered on its apical surface (the side facing the lumen) by many foldings of the plasma membrane that form cytoplasmic extensions called **microvilli.** These are quite tiny and can be seen clearly only with an electron microscope. Under a light micrograph, the microvilli resemble the

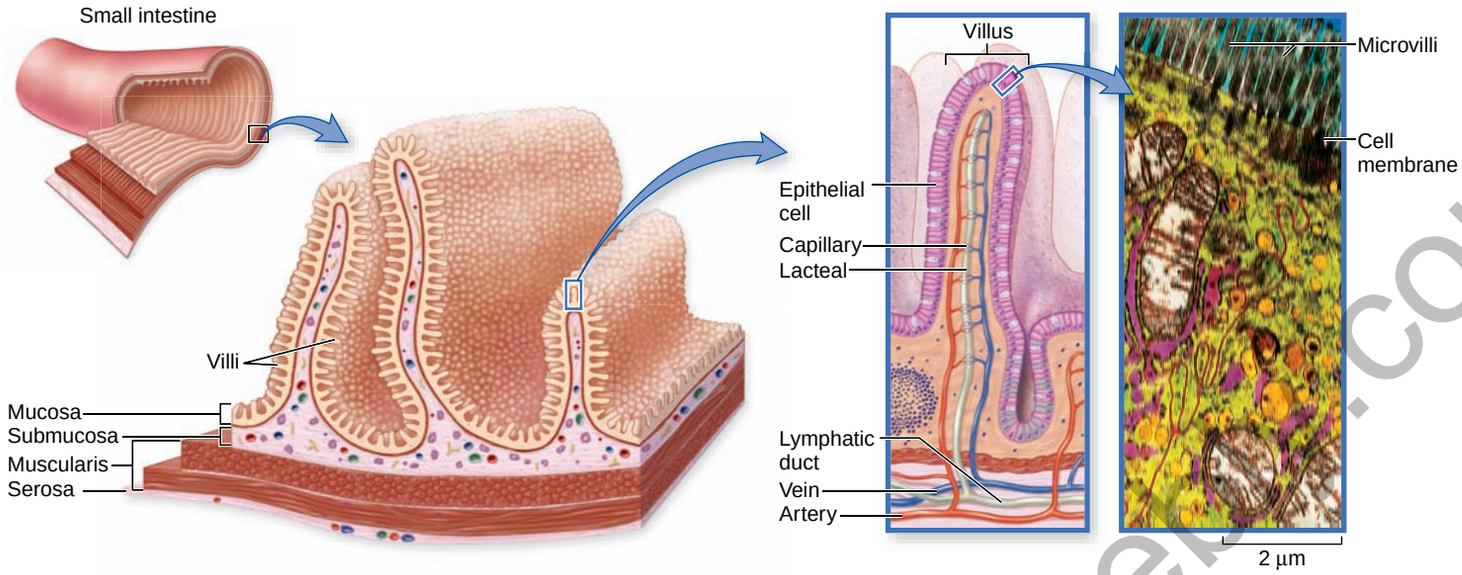


Figure 48.10 The small intestine. Successive enlargements show folded epithelium studded with villi that increase the surface area. The micrograph shows an epithelial cell with numerous microvilli.

bristles of a brush, and for that reason the epithelial wall of the small intestine is also called a *brush border*.

The villi and microvilli greatly increase the surface area of the small intestine; in humans, this surface area is 300 m^2—about 3200 square feet, larger than a tennis court! It is over this vast surface that the products of digestion are absorbed.

The microvilli also participate in digestion because a number of digestive enzymes are embedded within the epithelial cells' plasma membranes, with their active sites exposed to the chyme. These brush border enzymes include those that hydrolyze the disaccharides lactose and sucrose, among others. Many adult humans lose the ability to produce the brush border enzyme lactase and therefore cannot digest lactose (milk sugar), a rather common condition called *lactose intolerance*. The brush border enzymes complete the digestive process that started with the action of salivary amylase in the mouth.

Accessory organs secrete enzymes into the small intestine

The main organs that aid digestion are the pancreas, liver, and gallbladder. They empty their secretions, primarily enzymes, through ducts directly into the small intestine.

Secretions of the pancreas

The pancreas (figure 48.11), a large gland situated near the junction of the stomach and the small intestine, secretes pancreatic fluid into the duodenum through the *pancreatic duct;* thus, the pancreas functions as an exocrine gland. This fluid contains a host of enzymes, including **trypsin** and **chymotrypsin,** which digest proteins; **pancreatic amylase,** which digests starch; and **lipase,** which digests fat. Like pepsin in the stomach, these enzymes are released into the duodenum primarily as inactive enzymes and are then activated by trypsin, which is first activated by a brush border enzyme of the intestine.

Pancreatic enzymes digest proteins into smaller polypeptides, polysaccharides into shorter chains of sugars, and fats into free fatty acids and monoglycerides. Digestion of proteins and carbohydrates is then completed by the brush border enzymes. Pancreatic fluid also contains bicarbonate, which neutralizes the HCl from the stomach and gives the chyme in the duodenum a slightly alkaline pH. The digestive enzymes and

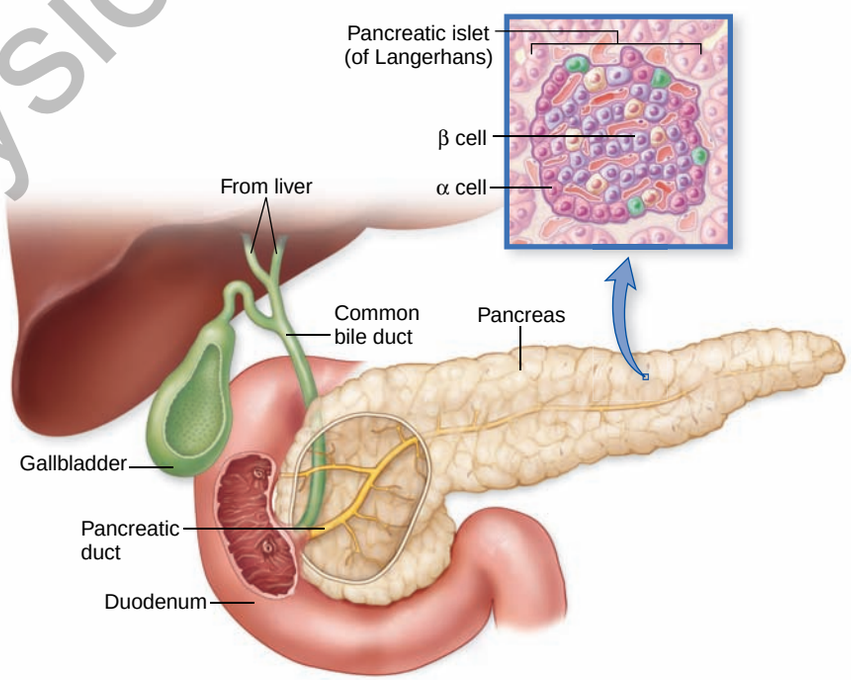


Figure 48.11 The pancreas. The pancreatic and bile ducts empty into the duodenum. The pancreas secretes pancreatic juice into the pancreatic duct. The pancreatic islets of Langerhans secrete hormones into the blood; α cells secrete glucagon, and β cells secrete insulin. The liver secretes bile, which consists of bile pigments (waste products from the liver) and bile salts. Bile salts play a role in the digestion of fats. Bile is concentrated and stored in the gallbladder until it is needed in the duodenum on the arrival of fatty food.

bicarbonate are produced by clusters of secretory cells known as **acini.**

In addition to its exocrine role in digestion, the pancreas also functions as an endocrine gland, secreting several hormones into the blood that control the blood levels of glucose and other nutrients. These hormones are produced in the **islets of Langerhans,** clusters of endocrine cells scattered throughout the pancreas. The two most important pancreatic hormones, insulin and glucagon, were described in chapter 46; their actions are also discussed later on.

Liver and gallbladder

The **liver** is the largest internal organ of the body (see figure 48.3). In an adult human, the liver weighs about 1.5 kg and is the size of a football. The main exocrine secretion of the liver is bile, a fluid mixture consisting of *bile pigments* and *bile salts* that is delivered into the duodenum during the digestion of a meal.

The bile pigments do not participate in digestion; they are waste products resulting from the liver's destruction of old red blood cells and are ultimately eliminated with the feces. If the excretion of bile pigments by the liver is blocked, the pigments can accumulate in the blood and cause a yellow staining of the tissues known as *jaundice.*

In contrast, the bile salts play a very important role in preparing fats for subsequent enzymatic digestion. Because fats are insoluble in water, they enter the intestine as drops within the watery chyme. The bile salts, which are partly lipid-soluble and partly water-soluble, work like detergents, dispersing the large drops of fat into a fine suspension of smaller droplets. This emulsification action produces a greater surface area of fat for the action of lipase enzymes, and thus allows the digestion of fat to proceed more rapidly.

After bile is produced in the liver, it is stored and concentrated in the gallbladder. The arrival of fatty food in the duodenum triggers a neural and endocrine reflex that stimulates the gallbladder to contract, causing bile to be transported through the common bile duct and injected into the duodenum (these reflexes are the topic of a later section). Gallstones are hardened precipitates of cholesterol that form in some individuals. If these stones block the bile duct, contraction of the gallbladder causes intense pain, often felt in the back. In severe cases of blockage, surgical removal of the gallbladder may be performed.

Absorbed nutrients move into blood or lymph capillaries

After their enzymatic breakdown, proteins and carbohydrates are absorbed as amino acids and monosaccharides, respectively. They are transported across the brush border into the epithelial cells that line the intestine by a combination of active transport and facilitated diffusion (figure 48.12*a*). Glucose is transported by coupled transport with Na^+ ions (also called secondary active transport). Fructose, found in most fruit, is transported by facilitated diffusion. Most amino acids are transported by active transport using a variety of different transporters. Some of these carrier proteins use cotransport with Na^+ ions; others transport only amino acids. Once they have entered epithelial cells across the apical membrane, these monosaccharides and amino acids move through the cytoplasm and are transported across the basolateral membrane and into the blood capillaries within the villi.

The blood carries these products of digestion from the intestine to the liver via the hepatic portal vein. A portal vein connects two beds of capillaries instead of returning to the heart. In

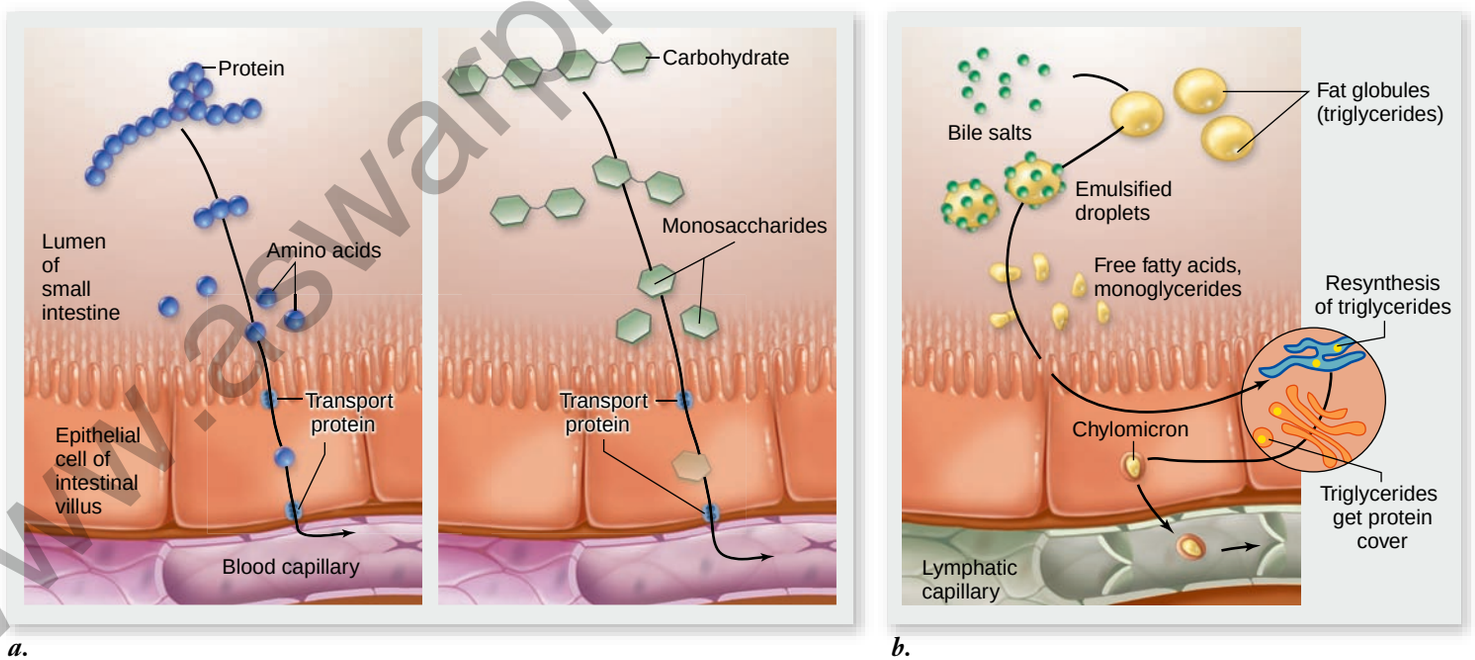


Figure 48.12 Absorption of the products of digestion. ***a.*** Monosaccharides and amino acids are transported into blood capillaries. ***b.*** Fatty acids and monoglycerides within the intestinal lumen are absorbed and converted within the intestinal epithelial cells into triglycerides. These are then coated with proteins to form structures called chylomicrons, which enter lymphatic capillaries.

this case, the intestine is connected to the liver by the hepatic portal vein, thus the liver receives blood-borne molecules from the intestine. Because of the hepatic portal vein, the liver is the first organ to receive most of the products of digestion, except for fat.

The products of fat digestion are absorbed by a different mechanism (figure 48.12*b*). Fats (triglycerides) are hydrolyzed into fatty acids and monoglycerides by digestion. These fatty acids and monoglycerides are nonpolar and can thus enter epithelial cells by simple diffusion. Once inside the intestinal epithelial cells they are reassembled into triglycerides. The triglycerides then combine with proteins to form small particles called **chylomicrons,** which are too bulky to enter blood capillaries in the intestine. Instead of entering the hepatic portal circulation, the chylomicrons are absorbed into lymphatic capillaries (see chapter 50), which empty their contents into the blood in veins near the neck. Chylomicrons can make the blood plasma appear cloudy if a sample of blood is drawn after a fatty meal.

The amount of fluid passing through the small intestine in a day is startlingly large: approximately 9 L. However, almost all of this fluid is absorbed into the body rather than eliminated in the feces: About 8.5 L is absorbed in the small intestine and an additional 350 mL in the large intestine. Only about 50 g of solid and 100 mL of liquid leaves the body as feces. The normal fluid absorption efficiency of the human digestive tract approaches 99%, which is very high indeed.

The large intestine eliminates waste material

The large intestine, or **colon,** is much shorter than the small intestine, occupying approximately the last meter of the digestive tract; it is called "large" because of its larger diameter, not its length. The small intestine empties directly into the large intestine at a junction where two vestigial structures, the **cecum** and the **appendix,** remain (figure 48.13). No digestion takes place within the large intestine, and only about 4% of the absorption of fluids by the intestine occurs there.

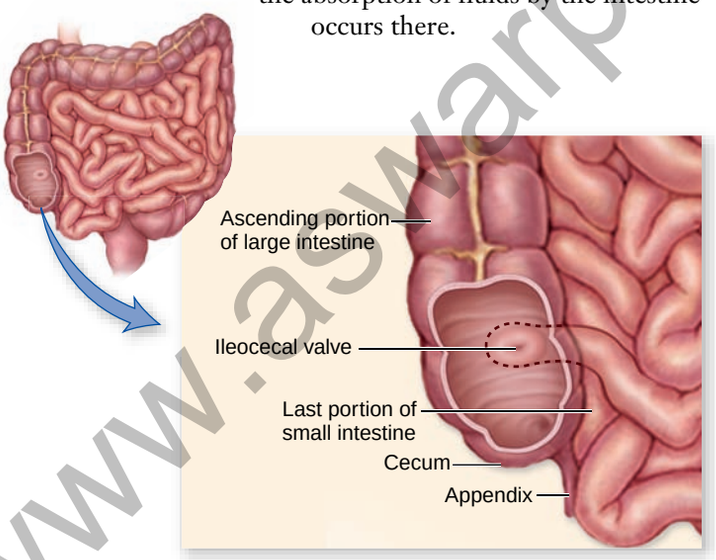


Figure 48.13 The junction of the small and large intestines in humans. The large intestine, or colon, starts with the cecum, which is relatively small in humans compared with that in other mammals. A vestigial structure called the appendix extends from the cecum.

The large intestine is not as convoluted as the small intestine, and its inner surface has no villi. Consequently, the large intestine has less than 1/30 the absorptive surface area of the small intestine. The function of the large intestine is to absorb water, remaining electrolytes, and products of bacterial metabolism (including vitamin K). The large intestine prepares waste material to be expelled from the body.

Many bacteria live and reproduce within the large intestine, and the excess bacteria are incorporated into the refuse material, called *feces.* Bacterial fermentation produces gas within the colon at a rate of about 500 mL per day. This rate increases greatly after the consumption of beans or other types of vegetables because the passage of undigested plant material (fiber) into the large intestine provides substrates for bacterial fermentation.

The human colon has evolved to process food with a relatively high fiber content. Diets that are low in fiber, which are common in the United States and other developed countries, result in a slower passage of food through the colon. Low dietary fiber content is thought to be associated with the level of colon cancer in the United States, which is among the highest in the world.

Compacted feces, driven by peristaltic contractions of the large intestine, pass from the large intestine into a short tube called the rectum. From the rectum, the feces exit the body through the anus. Two sphincters control passage through the anus. The first is composed of smooth muscle and opens involuntarily in response to pressure inside the rectum. The second, composed of striated muscle, can be controlled voluntarily by the brain, thus permitting a conscious decision to delay defecation.

Learning Outcomes Review 48.4

The small intestine is where most digestion takes place; its inner surface is covered with villi that increase its absorptive surface area. The large intestine absorbs water, electrolytes, and bacterial metabolites. Digestion is accomplished by a combination of enzymes from the pancreas and by bile salts released from the liver. Glucose and amino acids are absorbed by active transport and facilitated diffusion. Fat is absorbed by simple diffusion.

- ***Why does fat not require transport to cross the intestinal epithelium?***

48.5 *Variations in Vertebrate Digestive Systems*

Learning Outcomes

1. ***Explain how vertebrates digest cellulose.***
2. ***Describe how rumination works.***
3. ***Discuss convergent evolution at the molecular level in herbivores.***

Animals lack the enzymes necessary to digest cellulose, but the digestive tracts of some animals contain bacteria and

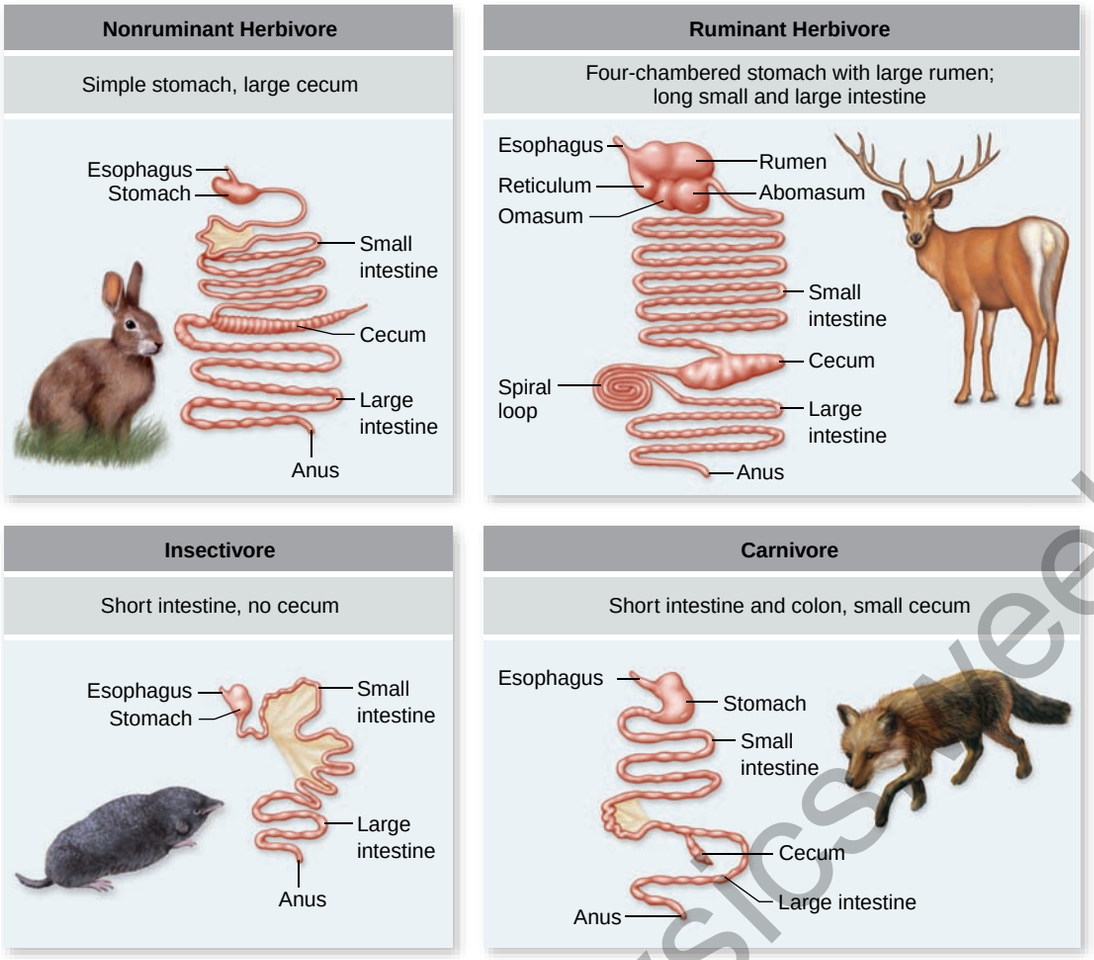


Figure 48.14 The digestive systems of different mammals reflect their diets. Herbivores, such as rabbits and deer, require long digestive tracts with specialized compartments for the breakdown of plant matter. Diets composed of animal matter, thus lacking cellulose, are more easily digested; insectivorous and carnivorous mammals, such as voles and foxes, respectively, have short digestive tracts with few specialized pouches.

protists that convert cellulose into substances the host can absorb. Although digestion by gastrointestinal microorganisms plays a relatively small role in human nutrition, it is an essential element in the nutrition of many other kinds of animals, including insects such as termites and cockroaches, and a few groups of herbivorous mammals. The relationships between these microorganisms and their animal hosts are mutually beneficial and provide an excellent example of symbiosis (see chapter 57).

Plant cellulose is particularly resistant to digestion. As a result, herbivores tend to have much longer digestive tracts than carnivores, allowing greater time for digestion to occur (figure 48.14). In addition, many herbivores have modified their digestive tracts to enhance digestion of plant material.

Ruminants rechew regurgitated food

Ruminants have a four-chambered stomach (figure 48.15). The first three portions include the reticulum, the rumen, and the omasum. These are followed by the true stomach, the abomasum.

The rumen, which may hold up to 50 gallons, serves as a fermentation vat where bacteria and protists convert cellulose and other molecules into a variety of simpler compounds. The location of the rumen at the front of the four chambers allows the animal to regurgitate and rechew the contents of the rumen, an activity called *rumination*, or "chewing the cud." This breaks tougher fiber in the diet into smaller particles, increasing the surface area for microbial attachment.

After chewing, the cud is swallowed for further microbial digestion in the rumen, then passes to the omasum, and then to the abomasum, where it is finally mixed with gastric juice. This process leads to far more efficient digestion of cellulose in ruminants than in mammalian herbivores such as horses, that lack a rumen.

Foregut fermentation has evolved convergently many times

Although the four-chambered stomach has only evolved once, many other types of herbivores—including hippopotamuses, langur monkeys, sloths, kangaroos, and hoatzins (a type of bird)—have evolved large stomachs to enhance microbial fermentation. In many cases, these species have evolved a variety of other anatomical structures that serve to slow down the passage of food through the stomach, leading to increased time for fermentation.

A remarkable case of convergent evolution at the molecular level is exhibited by ruminants and the langur monkey, which subsists primarily on leaves. In most mammals, lysozymes are enzymes found in saliva and tears, which attack invading bacteria. However, in ruminants and langurs, lysozymes have been modified to take on a new role, digesting bacteria in the stomach. In both cases, five identical amino acid changes have

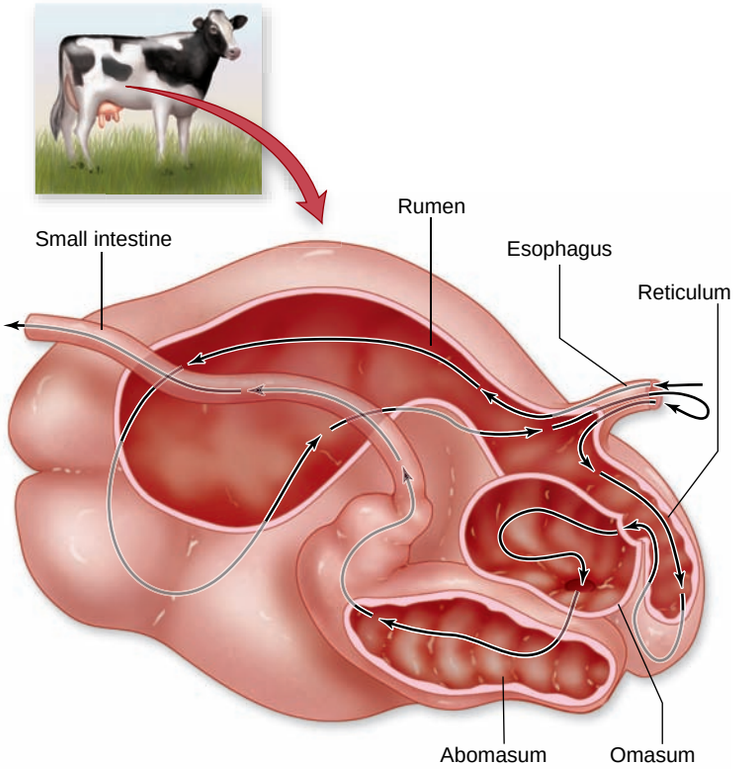


Figure 48.15 Four-chambered stomach of a ruminant. Grass and other plants eaten by ruminants enter the rumen, where they are partially digested. The rumen contains bacteria that break down cellulose from the plant cell walls. Before moving into a second chamber, the reticulum, the food may be regurgitated and rechewed. The food is then transferred to the rear two chambers: the omasum and abomasum. Only the abomasum secretes gastric juice as in the human stomach.

evolved (figure 48.16); the result is that the lysozyme molecules of ruminants and langurs are more similar to each other than they are to lysozymes in more closely related species. In contrast to many cases of convergent evolution, this example illustrates that convergent evolution has occurred in distantly related species by the exact same evolutionary changes.

Other herbivores have alternative strategies for digestion

In some animals, such as rodents, horses, deer, and lagomorphs (rabbits and hares), the digestion of cellulose by microorganisms takes place in the cecum, which is greatly enlarged (see figure 48.14). Because the cecum is located beyond the stomach, regurgitation of its contents is impossible.

Rodents and lagomorphs have evolved another way to capture nutrients from cellulose that achieves a degree of efficiency similar to ruminant digestion. They do this by eating their feces, a practice known as coprophagy—thus passing the food through their digestive tract a second time. The second passage allows the animal to absorb the nutrients produced by the microorganisms in its cecum. Coprophagic animals cannot remain healthy if they are prevented from eating their feces.

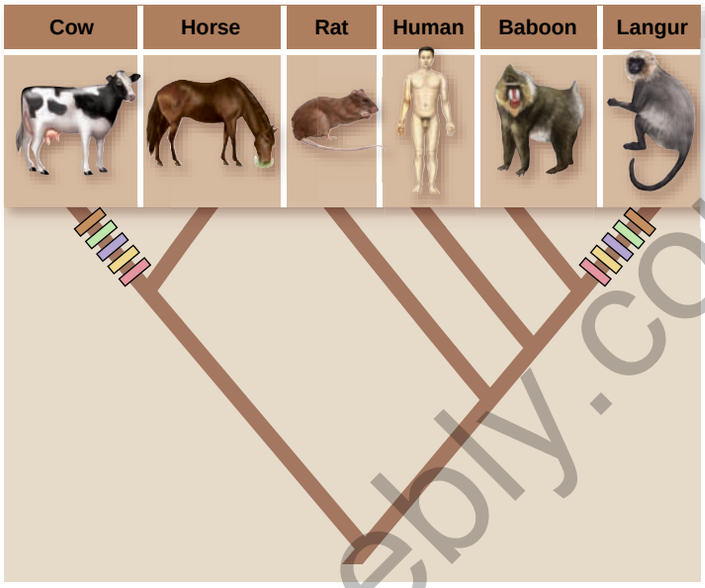


Figure 48.16 Convergent evolution of lysozyme structure in ruminants (represented by the cow) and leaf-eating hanuman langur *(Presbytis entellus).* The same five amino acid changes evolved independently in both groups.

Inquiry question

If you constructed a phylogeny using molecular data from lysozyme, what would it look like?

Animals with diets that don't include cellulose, such as insectivores or carnivores, don't have a cecum, or if they do, it is greatly reduced.

Vitamin K

Another example of the way intestinal microorganisms function in the metabolism of their animal hosts is provided by the synthesis of vitamin K. All mammals rely on intestinal bacteria to synthesize this vitamin, which is necessary for the clotting of blood. Birds, which lack these bacteria, must consume the required quantities of vitamin K in their food.

In humans, prolonged treatment with antibiotics greatly reduces the populations of bacteria in the intestine; under such circumstances, it may be necessary to provide supplementary vitamin K. Restoring the normal flora of the digestive tract with beneficial bacteria may also help replace vitamin K.

Learning Outcomes Review 48.5

The digestive tracts of many herbivores harbor colonies of cellulose-digesting microorganisms. Complex fermentation chambers have also evolved in the digestive tract. In rumination, partially digested food is regurgitated from the rumen for additional processing by the mouth. In distantly related herbivorous species, similar digestive enzymes have evolved by identical but independent changes.

- ***Would you expect identical mutations to be successful in different species? Why or why not?***

48.6 Neural and Hormonal Regulation of the Digestive Tract

Learning Outcomes

1. *Explain how the nervous system stimulates the digestive process.*
2. *Identify the major enterogastrones.*

The activities of the gastrointestinal tract are coordinated by the nervous system and the endocrine system. The nervous system, for example, stimulates salivary and gastric secretions in response to the sight, smell, and consumption of food. When food arrives in the stomach, proteins in the food stimulate the secretion of a stomach hormone called **gastrin,** which in turn stimulates the secretion of pepsinogen and HCl from the gastric glands (figure 48.17). The secreted HCl then lowers the pH of the gastric juice, which acts to inhibit further secretion of gastrin in a negative feedback loop. In this way, the secretion of gastric acid is kept under tight control.

The passage of chyme from the stomach into the duodenum of the small intestine inhibits the contractions of the stomach, so that no additional chyme can enter the duodenum until the previous amount can be processed. This stomach or gastric inhibition is mediated by a neural reflex and by duodenal hormones secreted into the blood. These hormones are collectively known as the **enterogastrones.**

The major enterogastrones include **cholecystokinin (CCK), secretin,** and **gastric inhibitory peptide (GIP).** Chyme with high fat content is the strongest stimulus for CCK and GIP secretions, whereas increasing chyme acidity primarily influences the release of secretin. All three of these enterogastrones inhibit gastric motility (churning action) and gastric juice secretions; the result is that fatty meals remain in the stomach longer than nonfatty meals, allowing more time for digestion of complex fat molecules.

In addition to gastric inhibition, CCK and secretin have other important regulatory functions in digestion. CCK also stimulates increased pancreatic secretions of digestive enzymes and gallbladder contractions. Gallbladder contractions inject more bile into the duodenum, which enhances the emulsification and efficient digestion of fats. The other major function of secretin is to stimulate the pancreas to release more bicarbonate, which neutralizes the acidity of the chyme. Secretin has the distinction of being the first hormone ever discovered. Table 48.1 summarizes the actions of the digestive hormones and enzymes.

Learning Outcomes Review 48.6

Sensory input such as sight, smell, and taste stimulate salivary and gastric activity, as does the arrival of food in the stomach. The major enterogastrones are cholecystokinin (CCK), secretin, and gastric inhibitory peptide (GIP); these regulate passage of chyme into the duodenum and also release of pancreatic enzymes and bile.

- *Would you expect anosmia, an inability to perceive scents, to affect digestion?*

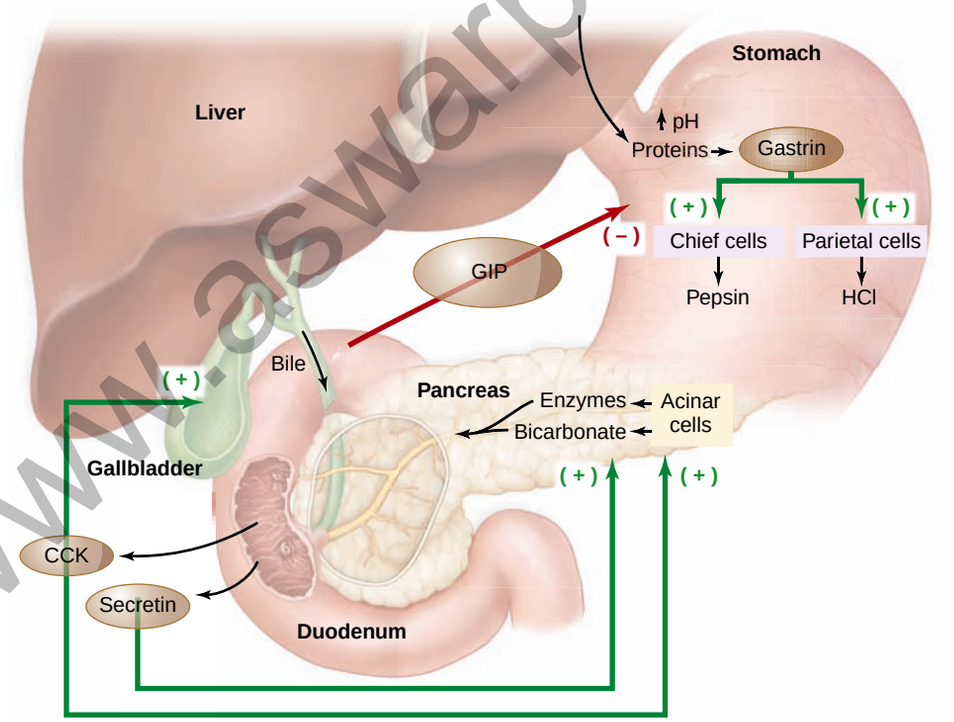


Figure 48.17 Hormonal control of the gastrointestinal tract. Gastrin, secreted by the mucosa of the stomach, stimulates the secretion of HCl and pepsinogen (which is converted into pepsin). The duodenum secretes three hormones: cholecystokinin (CCK), which stimulates contraction of the gallbladder and secretion of pancreatic enzymes; secretin, which stimulates secretion of pancreatic bicarbonate; and gastric inhibitory peptide (GIP), which inhibits stomach emptying.

TABLE 48.1 Hormones and Enzymes of Digestion

HORMONES

Hormone	Class	Source	Stimulus	Action	Note
Gastrin	Polypeptide	Pyloric portion of stomach	Entry of food into stomach	Stimulates secretion of HCl and pepsinogen by stomach	Acts on same organ that secretes it
Cholecystokinin (CCK)	Polypeptide	Duodenum	Fatty chyme in duodenum	Stimulates gallbladder contraction and secretion of digestive enzymes by pancreas	Structurally similar to gastrin
Gastric inhibitory peptide (GIP)	Polypeptide	Duodenum	Fatty chyme in duodenum	Inhibits stomach emptying	Also stimulates insulin secretion
Secretin	Polypeptide	Duodenum	Acidic chyme in duodenum	Stimulates secretion of bicarbonate by pancreas	The first hormone to be discovered (1902)

ENZYMES

Location	Enzymes	Substrates	Digestion Products
Salivary glands	Amylase	Starch, glycogen	Disaccharides
Stomach	Pepsin	Proteins	Short peptides
Pancreas	Lipase	Triglycerides	Fatty acids, monoglycerides
	Trypsin, chymotrypsin	Proteins	Peptides
	DNase	DNA	Nucleotides
	RNase	RNA	Nucleotides
Small intestine (brush border)	Peptidases	Short peptides	Amino acids
	Nucleases	DNA, RNA	Sugars, nucleic acid bases
	Lactase, maltase, sucrase	Disaccharides	Monosaccharides

48.7 Accessory Organ Function

Learning Outcomes

1. ***Describe the liver's role in maintaining homeostasis.***
2. ***Explain how the pancreas acts to control blood glucose concentration.***

The liver and pancreas both have critical roles beyond the production of digestive enzymes. The liver is a key organ in the breakdown of toxins, and the pancreas secretes hormones that regulate the blood glucose level, in part through actions on liver cells.

The liver modifies chemicals to maintain homeostasis

Because the hepatic portal vein carries blood from the stomach and intestine directly to the liver, the liver is in a position to chemically modify the substances absorbed in the gastrointestinal tract before they reach the rest of the body. For example, ingested alcohol and other drugs are taken into liver cells and metabolized; this is one reason that the liver is often damaged as a result of alcohol and drug abuse.

The liver also removes toxins, pesticides, carcinogens, and other poisons, converting them into less toxic forms. For example, the liver's converts the toxic ammonia produced by intestinal bacteria into urea, a compound that can be contained safely and carried by the blood at higher concentrations.

Similarly, the liver regulates the levels of many compounds produced within the body. Steroid hormones, for instance, are converted into less active and more water-soluble forms by the liver. These molecules are then included in the bile and eliminated from the body in the feces or are carried by the blood to the kidneys and excreted in the urine.

The liver also produces most of the proteins found in blood plasma. The total concentration of plasma proteins is significant because it must be kept within certain limits to maintain osmotic balance between blood and interstitial (tissue) fluid. If the concentration of plasma proteins drops too low, as can happen as a result of liver disease such as cirrhosis, fluid accumulates in the tissues, a condition called *edema*.

Blood glucose concentration is maintained by the actions of insulin and glucagon

The neurons in the brain obtain energy primarily from the aerobic respiration of glucose obtained from the blood plasma. It is therefore vitally important that the blood glucose concentration not fall too low, as might happen during fasting or prolonged exercise. It is also important that the blood glucose concentration not stay at too high a level, as it does in people with untreated diabetes mellitus, because too high a level can lead to tissue damage.

After a carbohydrate-rich meal, the liver and skeletal muscles remove excess glucose from the blood and store it as the polysaccharide glycogen. This process is stimulated by the

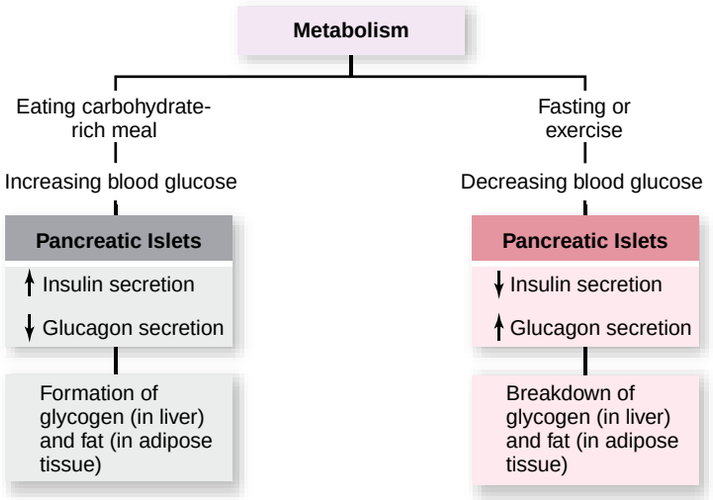


Figure 48.18 The actions of insulin and glucagon.
After a meal, an increased secretion of insulin by the β cells of the pancreatic islets promotes the deposition of glycogen and fat. During fasting or exercising, increased glucagon secretion by the α cells of the pancreatic islets and decreased insulin secretion promote the breakdown (through hydrolysis reactions) of glycogen and fat.

hormone insulin, secreted by the β (beta) cells in the pancreatic islets of Langerhans (figure 48.18).

When blood glucose levels decrease, as they do between meals, during periods of fasting, and during exercise, the liver secretes glucose into the blood. This glucose is obtained in part from the breakdown of liver glycogen to glucose-6-phosphate, a process called **glycogenolysis.** The phosphate group is then removed, and free glucose is secreted into the blood. Skeletal muscles lack the enzyme needed to remove the phosphate group, and so, even though they have glycogen stores, they cannot secrete glucose into the blood. However, muscle cells can use this glucose directly for energy metabolism because glucose-6-phosphate is actually the product of the first reaction in glycolysis. The breakdown of liver glycogen is stimulated by another hormone, glucagon, which is secreted by the α (alpha) cells of the islets of Langerhans in the pancreas (see figure 48.18).

If fasting or exercise continues, the liver begins to convert other molecules, such as amino acids and lactic acid, into glucose. This process is called **gluconeogenesis** ("new formation of glucose"). The amino acids used for gluconeogenesis are obtained from muscle protein, which explains the severe muscle wasting that occurs during prolonged fasting.

Learning Outcomes Review 48.7

The liver is responsible for neutralizing potentially harmful toxins and also for modification of steroid hormones. The liver also produces vital plasma proteins. Pancreatic hormones and the liver regulate blood glucose concentrations. Insulin stimulates the formation of glycogen and fat in the liver. Glucagon stimulates the breakdown of glycogen in the liver, which releases glucose into the blood.

- ***What is one important advantage of the hepatic portal system?***

48.8 *Food Energy, Energy Expenditure, and Essential Nutrients*

Learning Outcomes

1. ***Explain the basal metabolic rate and the effect of exercise.***
2. ***List hormones involved in regulating appetite and body weight.***
3. ***Name the essential nutrients.***

The ingestion of food serves two primary functions: It provides a source of energy and it provides raw materials the animal is unable to manufacture for itself.

Even an animal completely at rest requires energy to support its metabolism; the minimum rate of energy consumption under defined resting conditions is called the **basal metabolic rate (BMR).** The BMR is relatively constant for a given individual, depending primarily on the person's age, sex, and body size.

Exertion increases metabolic rate

Physical exertion raises the metabolic rate above the basal levels, so the amount of energy the body consumes per day is determined not only by the BMR but also by the level of physical activity. If food energy taken in is greater than the energy consumed per day, the excess energy will be stored in glycogen and fat (figure 48.18). Because glycogen reserves are limited, however, continued ingestion of excess food energy results primarily in the accumulation of fat.

The intake of food energy is measured in **kilocalories** (1 kilocalorie = 1000 calories; nutritionists use Calorie with a capital C instead of kilocalorie). The measurement of kilocalories in food is determined by the amount of heat generated when the food is "burned," either literally, in a testing device called a calorimeter, or in the body, when the food is digested and later oxidized during cellular respiration. Caloric intake can be altered by the choice of foods, and the amount of energy expended can be changed by the choice of lifestyle.

The daily energy expenditures (metabolic rates) of humans vary between 1300 and 5000 kilocalories per day, depending on the person's BMR and level of physical activity. When the total kilocalories ingested exceeds the metabolic rate for a sustained period, a person accumulates an amount of fat that is deleterious to health, a condition called obesity. In the United States, about 34% of all adults between 40 and 59 are classified as obese. If 20- to 40-year-olds are added to this group, the percentage of obese individuals drops some but is still fully 30%.

Food intake is under neuroendocrine control

For many years the neuronal and hormonal basis of appetite was a mystery. Experiments with fasting and overfeeding in rats showed an increase in food intake when fasting ends. This

increase restores lost body weight to baseline values and food intake then drops. These experiments indicated the existence of control mechanisms to link food intake to energy balance. The presence of a hormonal *satiety factor* produced by adipose tissue was hypothesized to explain these observations. It has also been shown that regions of the hypothalamus are involved in feeding behavior. Other studies in rodent models had identified a number of genes that can lead to obesity. As modern molecular genetics has allowed the cloning of many of these genes, the outlines of a model to link dietary intake to energy balance have emerged. This model involves afferent signaling from adipose tissue and feeding behavior into the central nervous system (CNS), and efferent signaling outward from the CNS tied to energy expenditure, storage, reproduction and feeding behavior. We will discuss the relevant hormones first, then show how they fit into an overall control circuit.

Leptin

One of the rodent models for obesity, the obese mouse, is caused by a mutation in a single gene named *ob* (for obese). Animals homozygous for the recessive mutant allele become obese compared with wild-type mice (figure 48.19). When the gene responsible for this dramatic phenotype was isolated, it proved to encode a peptide hormone named leptin, leading to the hypothesis that the lack of leptin production in mutant individuals is responsible for obesity. Sure enough, when *ob/ob* animals are injected with leptin, they stop overeating and lose weight (see figure 48.19). These experiments identified leptin as the main satiety factor, and the key to the control of appetite. The gene for the leptin receptor *(db)* has also been isolated and it is expressed in brain neurons in the hypothalamus involved in energy intake.

Leptin is now thought to be the main signaling molecule in the afferent portion of the control circuit for energy sensing, food intake, and energy expenditure. Leptin is produced by adipose tissue in response to feeding, and leptin levels correlate with feeding behavior and amount of body fat. Dietary restriction reduces leptin levels, signaling the brain that food intake is necessary, whereas refeeding after fasting leads to rapid increase in leptin levels and a loss of appetite. The efferent part of this control circuit is complex and includes control of energy expenditure, energy storage, and feeding behavior by the CNS. Reproduction is even affected by this system as reproduction is inhibited under starvation conditions.

The leptin gene has also been isolated in humans and leptin appears to function in humans much as it does in mice. However, recent studies in humans show that the activity of the *ob* gene and the blood concentrations of leptin are actually higher in obese than in lean people, and that the leptin produced by obese people appears to be normal. It has been suggested that, in contrast with the mutant mice, most cases of human obesity may result from a reduced sensitivity to the actions of leptin in the brain, rather than from reduced leptin production by adipose cells. Research on leptin in humans is ongoing and is of great interest to both academic scientists and to the pharmaceutical industry.

Insulin

Although the extreme obesity associated with the loss-of-function mutations in the *ob* gene indicate that other hormonal signals cannot substitute for leptin signaling, other hormones are also involved. Insulin has been implicated in signaling satiety as well, and insulin levels also fall with fasting and rise with obesity. As insulin's primary role is homeostasis of blood glucose, as described earlier, its role in the control circuit of energy balance is complex.

SCIENTIFIC THINKING

Question: *Why are* ob/ob *mice obese?*

Hypothesis: *Lack of leptin production stimulates appetite and leads to overeating.*

Experiment: *Inject mutant mice with leptin.*

Results: *In just two weeks, injected mice lost 30% of their body weight with no apparent side effects.*

Interpretation: *What is the molecular mechanism by which leptin has its effect? Could mutations in other genes have the same effect?*

Figure 48.19 **Effects of the hormone leptin.**

Gut hormones (enterogastrones)

The gut produces a number of hormones that control the physiology of digestion described earlier. Several of these have also been implicated in the regulation of food intake. They are produced directly in response to feeding, necessary for their role in digestion.

The hormones GIP and CCK have receptors in the hypothalamus and seem to send the same kind of inhibitory signals to the brain as leptin and insulin. The levels of these gut hormones also vary with feeding behavior in a pattern similar to leptin and insulin.

The gut hormone ghrelin has the opposite effect of these appetite-suppressing hormones. Ghrelin also has receptors in the hypothalamus, but ghrelin appears to stimulate food intake. This role is supported by studies in rats showing that chronic administration of ghrelin leads to obesity. Ghrelin levels appear to rise before feeding and may be involved in initiating feeding behavior. One of the treatments for severe obesity, gastric bypass surgery, leads to reduced levels of ghrelin. It has been suggested that this is one of the reasons for the suppression of appetite seen after this surgery.

Neuropeptides

The efferent control over feeding and energy balance is less clear than the afferent control detailed earlier. The central

regulator is the hypothalamus and two brain neuropeptides have been implicated: neuropeptide Y (NPY) and alpha-melanocyte-stimulating hormone (α-MSH). These peptides are antagonistic, with NPY inducing feeding activity and α-MSH suppressing it.

Evidence for this comes from experiments that show that production and release of α-MSH is stimulated by leptin and that administration of α-MSH suppresses feeding. Loss of function for the α-MSH receptor also leads to obesity. In contrast, the expression of NPY is negatively regulated by leptin and administration of NPY stimulates feeding behavior.

Model for energy balance

The current model for energy balance and feeding behavior is summarized in figure 48.20. The role of both leptin and insulin is long-term regulation of the afferent portion of this signaling network. Leptin and insulin are produced by adipose tissue and the pancreas, respectively, in response to the effects of feeding behavior, not as a direct response to feeding itself. This leads to circulating levels of leptin that correlate with the amount of adipose tissue. The extreme example of this is the very high level of leptin seen in obese individuals. High levels of leptin and insulin then act on the hypothalamus to increase levels of α-MSH and reduce levels of NPY. This causes a reduction in appetite and increased energy expenditure and allows reproduction and growth. Low levels of these hormones act on the hypothalamus to reduce α-MSH levels and increase NPY levels. This leads to increased appetite and decreased energy expenditure. If very low levels of leptin persist, this can inhibit reproduction and growth.

The gut hormones CCK and GIP are produced in response to feeding and represent short-term regulators of the afferent portion of the energy balance control circuit. Their action is the same as that of leptin and insulin. The gut hormone ghrelin is also a short-term regulator that stimulates feeding.

Essential nutrients are those that the body cannot manufacture

Over the course of evolution, many animals have lost the ability to synthesize certain substances that nevertheless continue to play critical roles in their metabolism. Substances that an animal cannot manufacture for itself but that are necessary for its health and must be obtained in the diet are referred to as essential nutrients.

Included among the essential nutrients are **vitamins,** certain organic substances required in trace amounts. For example, humans, apes, monkeys, and guinea pigs have lost the ability to synthesize ascorbic acid (vitamin C). If vitamin C is

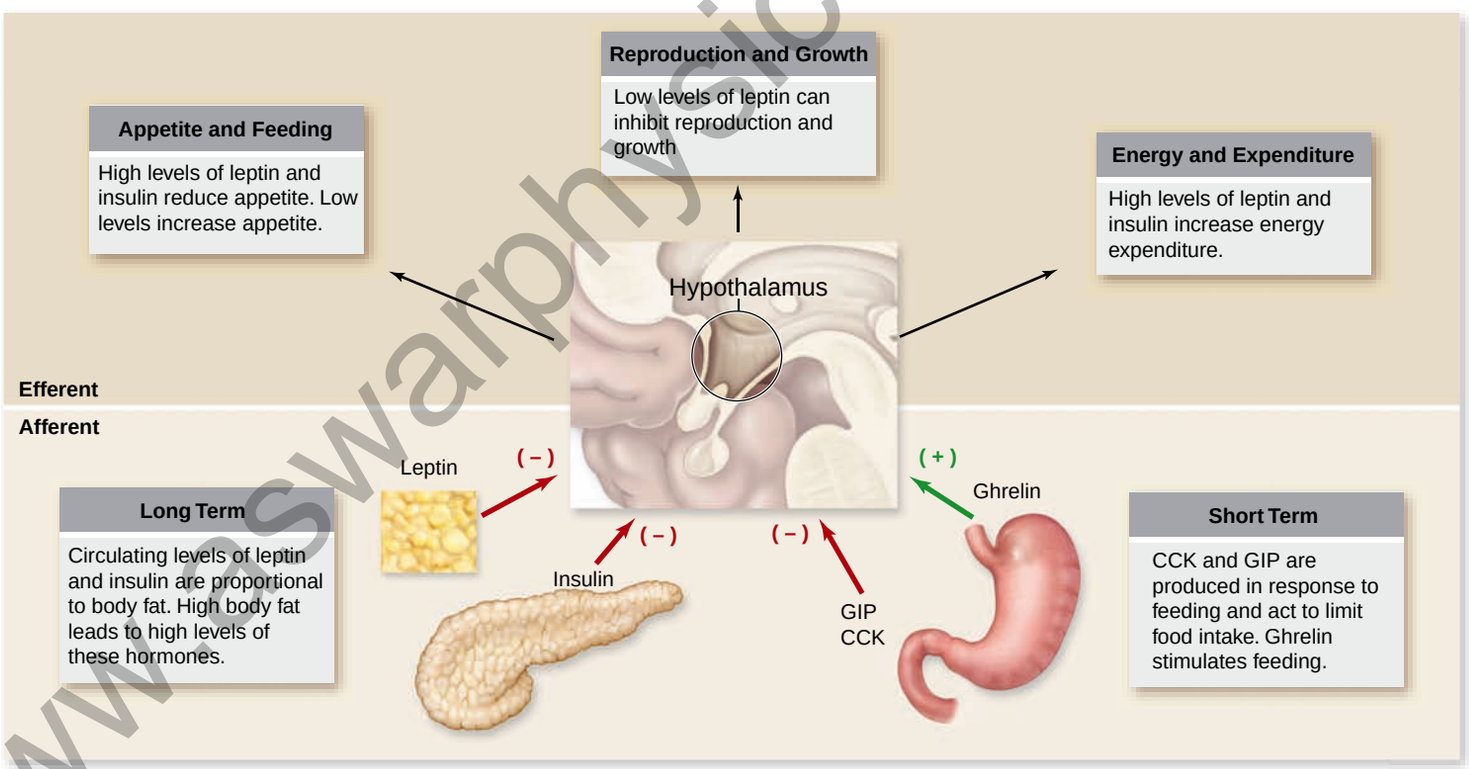


Figure 48.20 Hormonal control of feeding behavior. The control of feeding behavior is under both long-term control related to the amount of adipose tissue, and short-term control related to the act of feeding. This control is mediated by the CNS. The major brain region involved is the hypothalamus.

Inquiry question

Suppose the GIP and CCK sensors in the hypothalamus didn't work. How would this affect levels of leptin production?

TABLE 48.2 Major Vitamins Required by Humans

Vitamin	Function	Source	Deficiency Symptoms
Vitamin A (retinol)	Used in making visual pigments, maintaining epithelial tissues	Green vegetables, milk products, liver	Night blindness, flaky skin
B-complex vitamins			
B_1	Coenzyme in CO_2 removal during cellular respiration	Meat, grains, legumes	Beriberi, weakening of heart, edema
B_2 (riboflavin)	Part of coenzymes FAD and FMN, which play metabolic roles	Many different kinds of foods	Inflammation and breakdown of skin, eye irritation
B_3 (niacin)	Part of coenzymes NAD^+ and $NADP^+$	Liver, lean meats, grains	Pellagra, inflammation of nerves, mental disorders
B_5 (pantothenic acid)	Part of coenzyme-A, a key connection between carbohydrate and fat metabolism	Many different kinds of foods	Rare: fatigue, loss of coordination
B_6 (pyridoxine)	Coenzyme in many phases of amino acid metabolism	Cereals, vegetables, meats	Anemia, convulsions, irritability
B_{12} (cyanocobalamin)	Coenzyme in the production of nucleic acids	Red meats, dairy products	Pernicious anemia
Biotin	Coenzyme in fat synthesis and amino acid metabolism	Meat, vegetables	Rare: depression, nausea
Folic acid	Coenzyme in amino acid and nucleic acid metabolism	Green vegetables	Anemia, diarrhea
Vitamin C	Important in forming collagen, cementum of bone, teeth, connective tissue of blood vessels; may help maintain resistance to infection	Fruit, green leafy vegetables	Scurvy, breakdown of skin, blood vessels
Vitamin D (calciferol)	Increases absorption of calcium and promotes bone formation	Dairy products, cod liver oil	Rickets, bone deformities
Vitamin E (tocopherol)	Protects fatty acids and cell membranes from oxidation	Margarine, seeds, green leafy vegetables	Rare
Vitamin K	Essential to blood clotting	Green leafy vegetables	Severe bleeding

not supplied in sufficient quantities in their diets, these mammals develop scurvy, a potentially fatal disease that results in degeneration of connective tissues. Humans require at least 13 different vitamins (table 48.2).

Some essential nutrients are required in more than trace amounts. Many vertebrates, for example, are unable to synthesize one or more of the 20 amino acids. These *essential amino acids* must be obtained from food they eat. Humans require nine amino acids. People who are strict vegetarians must choose their foods so that the essential amino acids in one food complement those in another. Vegetarians may also need supplements to provide certain vitamins not found in large amounts in plants, such as some B vitamins.

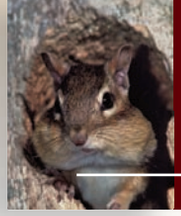
In addition, all vertebrates have lost the ability to synthesize certain long-chain unsaturated fatty acids and therefore must obtain them in food. In contrast, some essential nutrients that vertebrates can synthesize cannot be manufactured by the members of other animal groups. For example, vertebrates can synthesize cholesterol, a key component of steroid hormones, but some carnivorous insects cannot.

Food also supplies essential minerals such as calcium, magnesium, phosphorus, and other inorganic substances, including a wide variety of *trace elements* such as zinc and molybdenum, which are required in very small amounts. Animals obtain trace elements either directly from plants or from animals that have eaten plants.

Learning Outcomes Review 48.8

Basal metabolic rate is the minimum amount of energy consumption under defined resting conditions. Exercise does not increase the basal metabolic rate, but it does add to the body's total energy expenditure. Obesity results if the amount of ingested food energy exceeds energy expenditure over a prolonged period. Hormones involved in regulating appetite are leptin; insulin; the enterogastrones including CCK, GIP, and ghrelin; and neuropeptides associated with the hypothalamus. The essential nutrients for humans are 13 vitamins, essential minerals, and essential amino acids and fatty acids that the body cannot synthesize.

- ***What might explain obesity in a person with normal leptin levels?***



Chapter Review

48.1 Types of Digestive Systems

Invertebrate digestive systems are bags or tubes.

In cnidarians and flatworms, the incomplete digestive system is a gastrovascular cavity with only one opening (see figure 48.1). In contrast, a complete digestive system, with a one-way tube from mouth to anus, allows specialization of digestive organs.

Vertebrate digestive systems include highly specialized structures molded by diet.

The gastrointestinal tract includes the mouth and pharynx, esophagus, stomach, small and large intestines, cloaca or rectum, and anus (see figure 48.3). The four tissue layers of the tract are the mucosa, submucosa, muscularis, and serosa (see figure 48.4).

48.2 The Mouth and Teeth: Food Capture and Bulk Processing

Vertebrate teeth are adapted to different types of food items.

Birds lack teeth but have a gizzard where small pebbles grind food. The teeth of mammals are adapted to reflect their feeding habits (see figure 48.6).

The mouth is a chamber for ingestion and initial processing.

Salivary glands secrete saliva containing amylase that moistens food and begins digestion as the food is chewed. Swallowing, once begun, is involuntary (see figure 48.7).

48.3 The Esophagus and the Stomach: The Early Stages of Digestion

Muscular contractions of the esophagus move food to the stomach.

Rhythmic muscular contractions and relaxation, called peristalsis, propel a bolus of food to the stomach.

The stomach is a "holding station" involved in acidic breakdown of food.

In the stomach, hydrochloric acid breaks down food and converts pepsinogen into pepsin, an active protease. The mixture of food and gastric juice, termed chyme, moves through the pyloric sphincter to the small intestine.

48.4 The Intestines: Breakdown, Absorption, and Elimination

The structure of the small intestine is specialized for digestion and nutrient uptake.

The surface area of the small intestine is increased by fingerlike projections called villi (see figure 48.10). The duodenum receives digestive secretions from the pancreas and liver.

Accessory organs secrete enzymes into the small intestine.

Accessory organs include the salivary glands, pancreas, liver, and gallbladder (see figure 48.11). The pancreas secretes digestive enzymes and bicarbonate. The liver secretes bile, which is stored in the gallbladder. Bile disperses fats into small droplets.

Absorbed nutrients move into blood or lymph capillaries.

Amino acids and monosaccharides move into epithelial cells by active transport and facilitated diffusion (see figure 48.12) and then pass into the bloodstream. Fatty acids and monoglycerides simply diffuse into epithelial cells. They are reassembled into chylomicrons that enter the lymphatic system.

Absorbed molecules that pass into the bloodstream are transported to the liver through the hepatic portal vein.

The large intestine eliminates waste material.

The large intestine absorbs water and concentrates waste material, which is stored in the rectum until it can be eliminated.

48.5 Variations in Vertebrate Digestive Systems

Ruminants rechew regurgitated food.

The four-chambered stomach of ruminants consists of the rumen, reticulum, omasum, and abomasum. Food initially processed in the rumen is regurgitated for further chewing.

Foregut fermentation has evolved convergently many times.

Enlarged foreguts have evolved in many species to provide a chamber for microbial fermentation. In some unrelated herbivores, identical changes in lysozyme have evolved.

Other herbivores have alternative strategies for digestion.

In some herbivores, digestion of cellulose by microorganisms takes place in the cecum, located beyond the stomach.

48.6 Neural and Hormonal Regulation of the Digestive Tract

The activities of the gastrointestinal tract are coordinated by the nervous and endocrine systems.

Duodenal hormones regulate passage of chyme into the duodenum. High fat content in the chyme stimulates the release of CCK and GIP; low chyme pH stimulates the release of secretin. In turn, CCK stimulates release of pancreatic enzymes and bile. Secretin stimulates release of bicarbonate.

48.7 Accessory Organ Function

The liver modifies chemicals to maintain homeostasis.

The liver is involved in detoxification, regulation of steroid hormone levels, and production of proteins found in the blood plasma.

Blood glucose concentration is maintained by the actions of insulin and glucagon.

Insulin lowers blood glucose and increases glycogen storage; glucagon increases blood glucose and utilization of glycogen.

48.8 Food Energy, Energy Expenditure, and Essential Nutrients

Exertion increases metabolic rate.

The basal metabolic rate is the minimum rate of energy consumption under resting conditions. Activity leads to an increase in the metabolic rate.

Food intake is under neuroendocrine control.

Food intake is regulated by the hormones leptin and insulin, by enterogastrones, and by neuropeptides (see figure 48.20).

Essential nutrients are those that the body cannot manufacture.

Essential nutrients are those that cannot be synthesized by animals. For humans, they are 13 vitamins (see table 48.2), the essential amino acids, essential minerals, and certain fatty acids.

Review Questions

UNDERSTAND

1. How is the digestion of fats different from that of proteins and carbohydrates?
   a. Fat digestion occurs in the small intestine, and the digestion of proteins and carbohydrates occurs in the stomach.
   b. Fats are absorbed into cells as fatty acids and monoglycerides but are then modified for absorption; amino acids and glucose are not modified further.
   c. Fats enter the hepatic portal circulation, but digested proteins and carbohydrates enter the lymphatic system.
   d. Digested fats are absorbed in the large intestine, and digested proteins and carbohydrates are absorbed in the small intestine.
2. Although the stomach is normally thought of as the major player in the digestive process, the bulk of chemical digestion actually occurs in the
   a. mouth.
   b. appendix.
   c. duodenum.
   d. large intestine.
3. After being absorbed through the intestinal mucosa, glucose and amino acids are
   a. absorbed directly into the systemic circulation.
   b. used to build glycogen and peptides before being released to the body cells.
   c. transported directly to the liver by the hepatic portal vein.
   d. further digested by bile before release into the circulation.
4. Which of these pairings is incorrect?
   a. Fat transport/lymphatic system
   b. Glucose transport/lymphatic system
   c. Amino acid transport/circulatory system
   d. All of these pairings are correct.
5. Intestinal microorganisms aid digestion and absorption by
   a. digesting cellulose.
   b. producing glucose.
   c. synthesizing vitamin K.
   d. both a and c.
6. The _____ and _____ play important roles in the digestive process by producing chemicals that are required to digest proteins, lipids, and carbohydrates.
   a. liver; pancreas
   b. liver; gallbladder
   c. kidneys; appendix
   d. pancreas; gallbladder
7. Which of the following represents the action of insulin?
   a. Increases blood glucose levels by the hydrolysis of glycogen
   b. Increases blood glucose levels by stimulating glucagon production
   c. Decreases blood glucose levels by forming glycogen
   d. Increases blood glucose levels by promoting cellular uptake of glucose

APPLY

1. The small intestine is specialized for absorption because it
   a. is the last section of the digestive tract and retains food the longest.
   b. has saclike extensions along its length that collect food.
   c. has no outlet so food remains within it for longer periods of time.
   d. has an extremely large surface area that allows extended exposure to food.
2. The primary function of the large intestine is to concentrate wastes into solid form (feces) for release from the body. How does it accomplish this?
   a. By adding additional cells from the mucosal layer
   b. By absorbing water
   c. By releasing salt
   d. All of these are methods used by the large intestine.
3. Inactive forms of some molecules are secreted
   a. because they take less material and energy.
   b. because they must combine with water to be activated.
   c. so their activity can be regulated.
   d. to prevent them from clogging the gland from which they are secreted.
4. Obese humans probably have high levels of leptin because
   a. leptin stimulates eating.
   b. something is wrong with the leptin receptors in their brain, leading to increased leptin production to make up for the apparent shortage.
   c. weight gain leads to the production of leptin.
   d. leptin responds to mechanical stimulation in the adrenal cortex.

SYNTHESIZE

1. Many birds possess crops, although few mammals do. Suggest a reason for this difference between birds and mammals.
2. Suppose that you wanted to develop a new treatment for obesity based on the hormone leptin. What structures in the body produce leptin? What does it do? Should your treatment cause an increase in blood levels of leptin or a decrease? Could this treatment affect any other systems in the body?
3. How could a drop in plasma proteins and a decrease in bile production be related to alcohol and drug abuse?
4. Unlike many cases of convergence (see section 47.5), ruminants and langur monkeys have modified the enzyme lysozyme in the same way to achieve the same end result. Why might this case be different?
5. Birds do not have teeth. Do you think they have adaptations to processing different types of food, comparable to the diversity seen in mammals? If so, what might these adaptive differences be?

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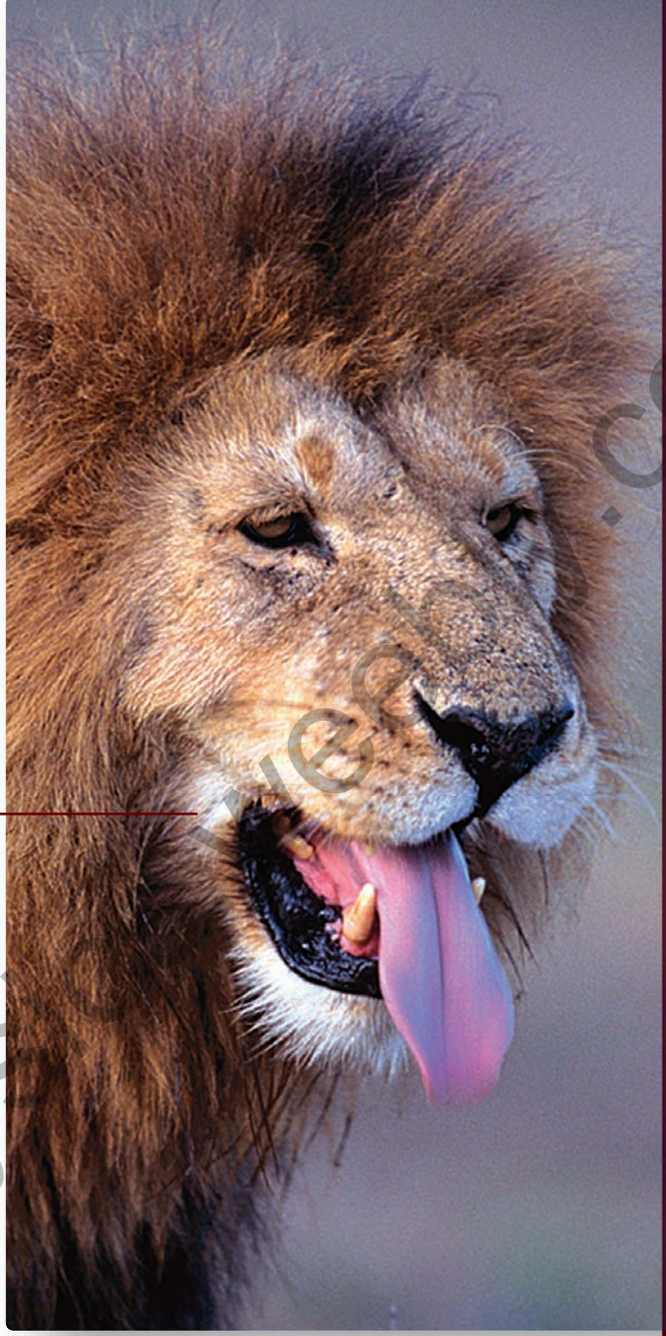
Chapter 49

The Respiratory System



Chapter Outline

Introduction

Every cell in the animal body must exchange materials with its surrounding environment. In single-celled organisms, this exchange occurs directly across the cell membrane to and from the external environment. In multicellular organisms, however, most cells are not in contact with the external environment and must rely on specialized systems for transport and exchange. Although these systems aid in bulk transport, the properties of transport across the plasma membrane do not change. Many structural adaptations throughout the animal kingdom increase surface areas where transport occurs, so that the needs of every cell are met. The interface between air from the environment and blood in the mammalian lungs provides an excellent example of the efficiency associated with increased surface area. In the time it takes you to breathe in, trillions of oxygen molecules have been transported across 80 m^2 of alveolar membrane into blood capillaries. In this and the next chapter, we describe respiration and circulation, the two systems that directly support the other organ systems and tissues of the body.

49.1 Gas Exchange Across Respiratory Surfaces

Learning Outcomes

1. *Describe gas exchange across membranes.*
2. *Explain Fick's Law of Diffusion.*
3. *Compare evolutionary strategies for maximizing gas diffusion.*

One of the major physiological challenges facing all multicellular animals is obtaining sufficient oxygen and disposing of excess carbon dioxide (figure 49.1). Oxygen is used in mitochondria for cellular respiration—a process that also produces CO_2 as waste (see chapter 7). Respiration at the body system level involves a host of processes not found at the cellular level, ranging from the mechanics of breathing to the exchange of oxygen and carbon dioxide in respiratory organs.

Invertebrates display a wide variety of respiratory organs, including the epithelium, tracheae, and gills. Some vertebrates, such as fish and larval amphibians, also use gills; adult amphibians use their skin or other epithelia either as a supplemental or primary external respiratory organ.

Many adult amphibians, reptiles, birds, and mammals have lungs to perform external respiration. In both aquatic and terrestrial animals, these highly vascularized respiratory organs are the site at which oxygen diffuses into the blood, and carbon dioxide diffuses out. In the body tissues, the direction of gas diffusion is the reverse of that in the respiratory organs.

The mechanics, structure, and evolution of respiratory systems, along with the principles of gas diffusion between the blood and tissues, are the subjects of this chapter.

Figure 49.1 Elephant seals are respiratory champions. Diving to great depths, elephant seals can hold their breath for over 2 hr, descend and ascend rapidly in the water, and endure repeated dives without suffering any apparent respiratory distress.

Gas exchange involves diffusion across membranes

Because plasma membranes must be surrounded by water to be stable, the external environment in gas exchange is always aqueous. This is true even in terrestrial vertebrates; in these cases, oxygen from air dissolves in a thin layer of fluid that covers the respiratory surfaces.

In vertebrates, the gases diffuse into the aqueous layer covering the epithelial cells that line the respiratory organs. The diffusion process is passive, driven only by the difference in O_2 and CO_2 concentrations on the two sides of the membranes and their relative solubilities in the plasma membrane. For dissolved gases, concentration is usually expressed as pressure; we explain this more fully a little later.

In general, the rate of diffusion between two regions is governed by a relationship known as **Fick's Law of Diffusion.** Fick's Law states that for a dissolved gas, the rate of diffusion *(R)* is directly proportional to the pressure difference (Δp) between the two sides of the membrane and the area *(A)* over which the diffusion occurs. Furthermore, *R* is inversely proportional to the distance *(d)* across which the diffusion must occur. A molecule-specific diffusion constant, *D*, accounts for the size of molecule, membrane permeability, and temperature. Shown as a formula, Fick's Law is stated as:

$$R = \frac{DA\Delta p}{d}$$

Major evolutionary changes in the mechanism of respiration have occurred to optimize the rate of diffusion (see figure 49.1). *R* can be optimized by changes that (1) increase the surface area, *A;* (2) decrease the distance, *d;* or (3) increase the concentration difference, as indicated by Δp. The evolution of respiratory systems has involved changes in all of these factors.

? Inquiry question

What part of the vertebrate cardiovascular system maximizes surface area?

Evolutionary strategies have maximized gas diffusion

The levels of oxygen needed for cellular respiration cannot be obtained by diffusion alone over distances greater than about 0.5 mm. This restriction severely limits the size and structure of organisms that obtain oxygen entirely by diffusion from the environment. Bacteria, archaea, and protists are small enough that such diffusion can be adequate, even in some colonial forms (figure 49.2*a*), but most multicellular animals require structural adaptations to enhance gas exchange.

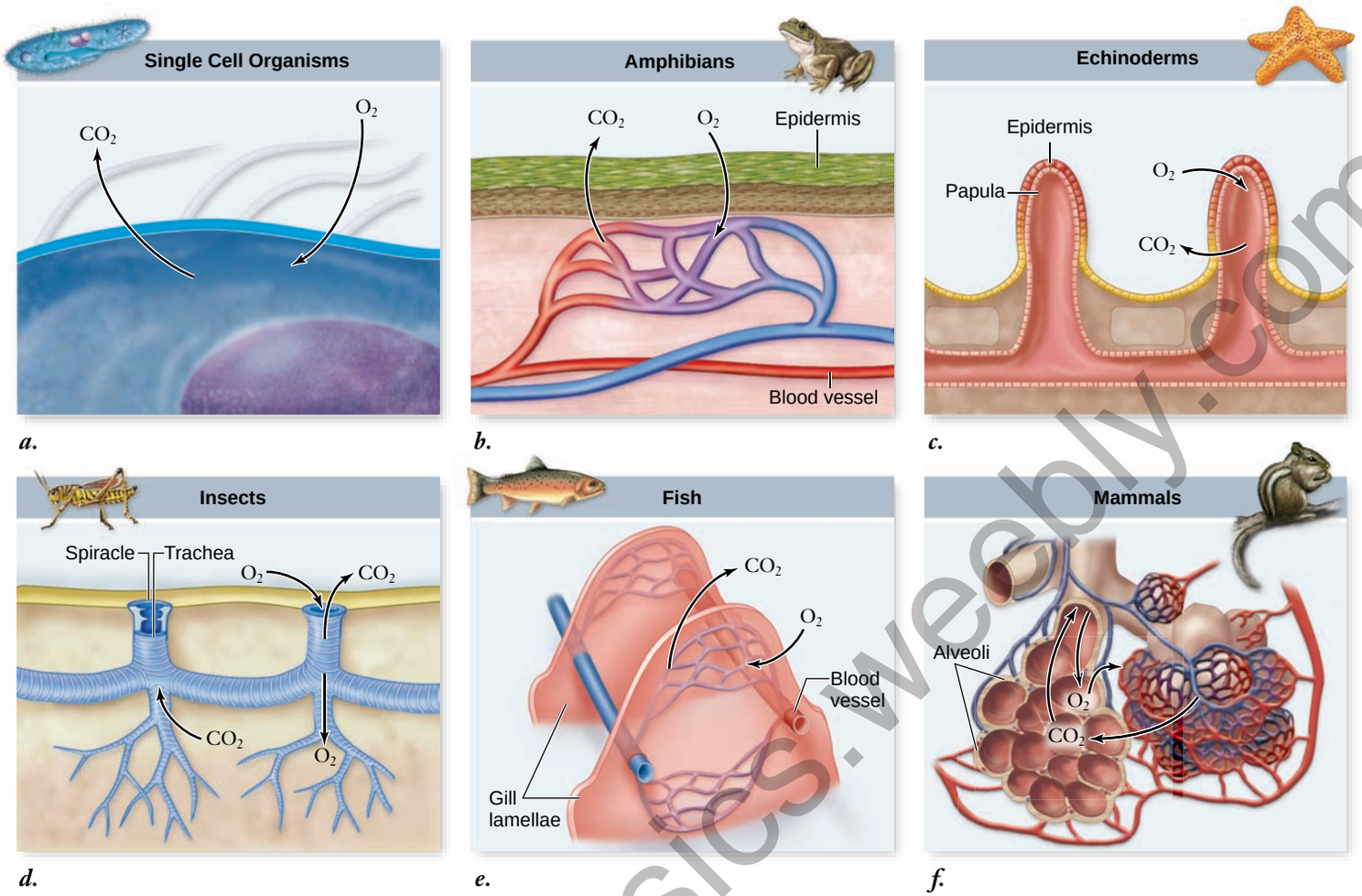


Figure 49.2 Different gas exchange systems in animals. ***a.*** Gases diffuse directly into single-celled organisms. ***b.*** Most amphibians and many other animals respire across their skin. Amphibians also exchange gases via lungs. ***c.*** Echinoderms have protruding papulae, which provide an increased respiratory surface area. ***d.*** Insects respire through an extensive tracheal system. ***e.*** The gills of fishes provide a very large respiratory surface area and countercurrent exchange. ***f.*** The alveoli in mammalian lungs provide a large respiratory surface area but do not permit countercurrent exchange. Inhaled fresh air contains some CO_2, but levels are higher in the lungs, so more CO_2 is exhaled than inhaled; similarly, O_2 levels are higher in fresh air, leading to an influx of O_2.

Increasing oxygen concentration difference

Most phyla of invertebrates lack specialized respiratory organs, but they have developed means of improving diffusion. Many organisms create a water current that continuously replaces the water over the respiratory surfaces; often, beating cilia produce this current. Because of this continuous replenishment of water, the external oxygen concentration does not decrease along the diffusion pathway. Although some of the oxygen molecules that pass into the organism have been removed from the surrounding water, new water continuously replaces the oxygen-depleted water. This maximizes the concentration difference—the Δp of the Fick equation.

Increasing area and decreasing distance

Other invertebrates (mollusks, arthropods, echinoderms) and vertebrates possess respiratory organs—such as gills, tracheae, and lungs—that increase the surface area available for diffusion (see figure 49.2). These adaptations also bring the external environment (either water or air) close to the internal fluid, which is usually circulated throughout the body—such as blood or hemolymph. The respiratory organs thus increase the rate of diffusion by maximizing surface area *(A)* and decreasing the distance *(d)* the diffusing gases must travel.

Learning Outcomes Review 49.1

Gases must be dissolved to diffuse across living membranes. Direction of diffusion is driven by a concentration difference (gradient) between the two sides. Fick's Law states that the rate of diffusion is increased by a greater pressure difference and membrane area, and decreased by greater distance. Evolutionary strategies have therefore aimed to increase gradient and area and to lessen the distance gases must travel.

- ***Which factor is affected by continuously beating cilia?***

49.2 Gills, Cutaneous Respiration, and Tracheal Systems

Learning Outcomes

1. *Describe how gills work.*
2. *Explain the advantage of countercurrent flow.*

Gills are specialized extensions of tissue that project into water. Gills can be simple, as in the papulae of echinoderms (figure 49.2*c*), or complex, as in the highly convoluted gills of fish (figure 49.2*e*). The great increase in diffusion surface area that gills provide enables aquatic organisms to extract far more oxygen from water than would be possible from their body surface alone. In this section we concentrate on gills found in vertebrate animals.

Other moist external surfaces are also involved in gas exchange in some vertebrates and invertebrates. For example, gas exchange across the skin is a common strategy in many amphibian groups.

Terrestrial arthropods such as insects take an alternative approach; their tracheal systems allow gas exchange through their hard exoskeletons (figure 49.2d).

External gills are found in fish and amphibian larvae

External gills are not enclosed within body structures. Examples of vertebrates with external gills are the larvae of many fish and amphibians, as well as amphibians such as the axolotl, which retains larval features throughout life (figure 49.3).

One of the disadvantages of external gills is that they must constantly be moved to ensure contact with fresh water having high oxygen content. The highly branched gills, however, offer significant resistance to movement, making this form of respiration ineffective except in smaller animals. Another disadvantage is that external gills, with their thin epithelium for gas exchange, are easily damaged.

Figure 49.3 Some amphibians have external gills. External gills are used by aquatic amphibians, both larvae and some species that live their entire lives in water such as this axolotl, to extract oxygen from the water.

Branchial chambers protect gills of some invertebrates

Other types of aquatic animals evolved specialized *branchial chambers*, which provide a means of pumping water past stationary gills. The internal *mantle cavity* of mollusks opens to the outside and contains the gills. Contraction of the muscular walls of the mantle cavity draws water in through the inhalant siphon and then expels it through the exhalant siphon (see chapter 34).

In crustaceans, the branchial chamber lies between the bulk of the body and the hard exoskeleton of the animal. This chamber contains gills and opens to the surface beneath a limb. Movement of the limb draws water through the branchial chamber, thus creating currents over the gills.

Gills of bony fishes are covered by the operculum

The gills of bony fishes are located between the oral cavity, sometimes called the buccal (mouth) cavity, and the *opercular cavities* where the gills are housed (figure 49.4). The two sets

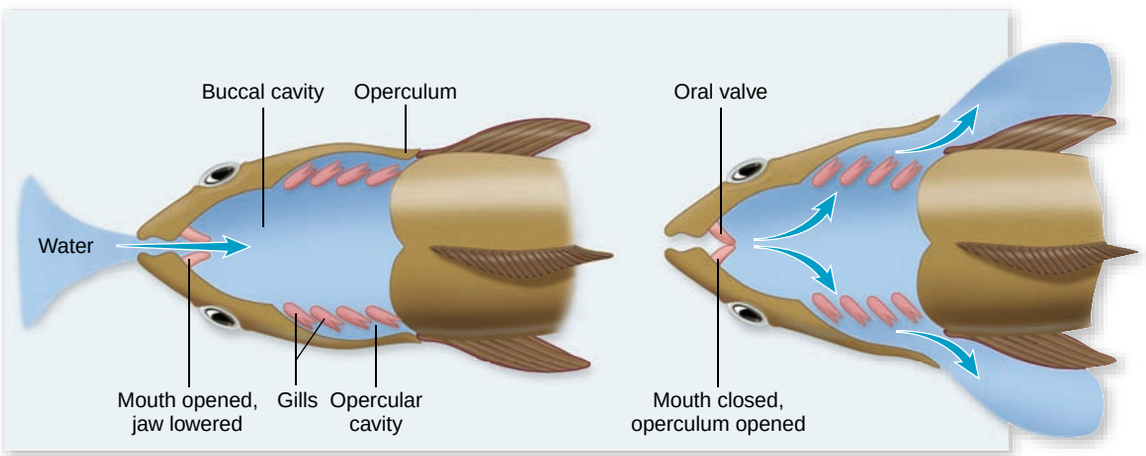


Figure 49.4 How most bony fishes respire. The gills are suspended between the buccal (mouth) cavity and the opercular cavity. Respiration occurs in two stages. The oral valve in the mouth is opened and the jaw is depressed, drawing water into the buccal cavity while the opercular cavity is closed. The oral valve is closed and the operculum is opened, drawing water through the gills to the outside.

of cavities function as pumps that expand alternately to move water into the mouth, through the gills, and out of the fish through the open operculum, or gill cover.

Some bony fishes that swim continuously, such as tuna, have practically immobile opercula. These fishes swim with their mouths partly open, constantly forcing water over the gills in what is known as *ram ventilation*. Most bony fishes, however, have flexible gill covers. For example, the remora, a fish that rides "piggyback" on sharks, uses ram ventilation while the shark is swimming, but employs the pumping action of its opercula when the shark stops swimming.

There are between three and seven gill arches on each side of the fish's head. Each gill arch is composed of two rows of *gill filaments*, and each gill filament contains thin membranous plates, or *lamellae*, that project out into the flow of water (figure 49.5). Water flows past the lamellae in one direction only.

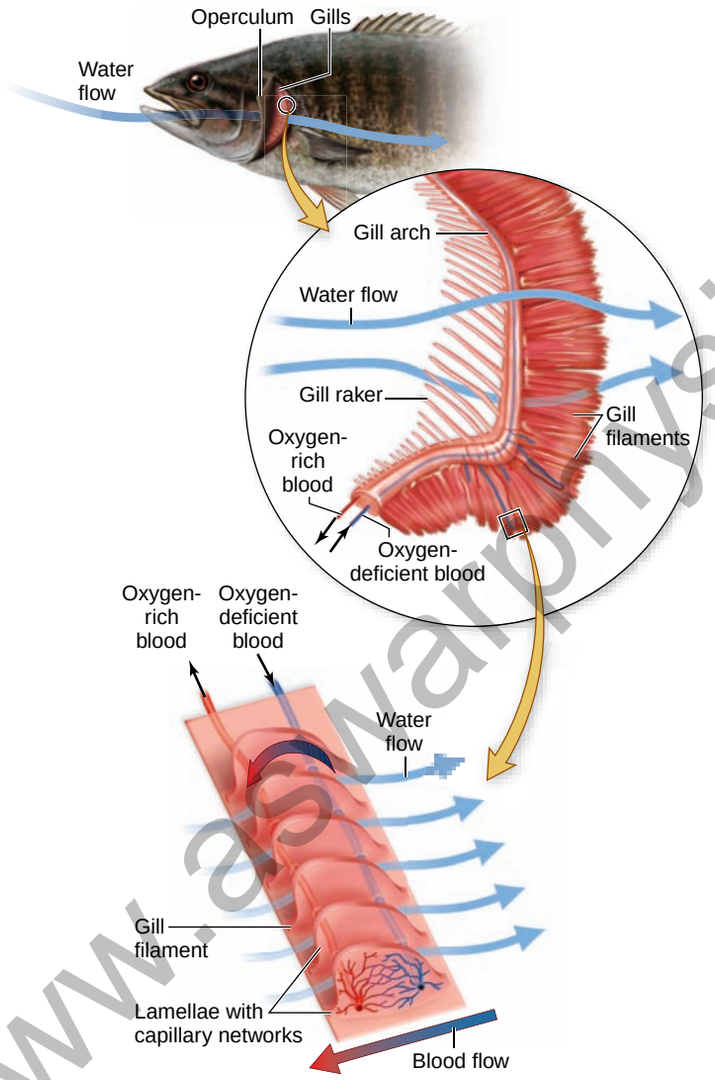
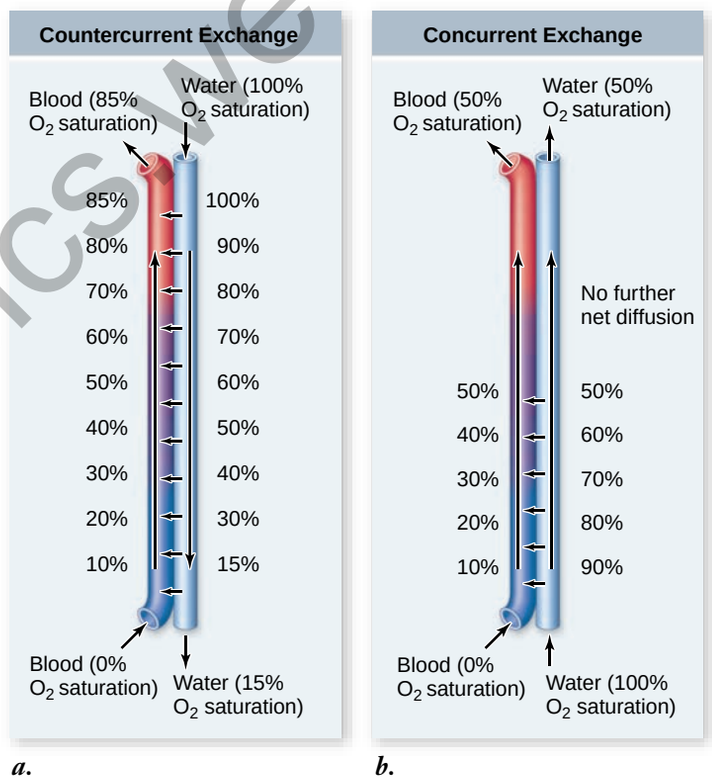


Figure 49.5 Structure of a fish gill. Water passes from the gill arch over the filaments (from left to right in the diagram). Water always passes the lamellae in a direction opposite to the direction of blood flow through the lamellae. The success of the gill's operation critically depends on this countercurrent flow of water and blood.

Within each lamella, blood flows opposite to the direction of water movement. This arrangement is called **countercurrent flow,** and it acts to maximize the oxygenation of the blood by maintaining a positive oxygen gradient along the entire pathway for diffusion, increasing Δp in Fick's Law of Diffusion. The advantages of a countercurrent flow system are illustrated in figure 49.6*a*. Countercurrent flow ensures that an oxygen concentration gradient remains between blood and water throughout the length of the gill lamellae. This permits oxygen to continue to diffuse all along the lamellae, so that the blood leaving the gills has nearly as high an oxygen concentration as the water entering the gills.

If blood and water flowed in the same direction, the flow would be *concurrent* (figure 49.6*b*). In this case, the concentration difference across the gill lamellae would fall rapidly as the water lost oxygen to the blood, and net diffusion of oxygen



a. *b.*

Figure 49.6 Countercurrent exchange. This process allows for the most efficient blood oxygenation. When blood and water flow in opposite directions ***(a)***, the initial oxygen (O_2) concentration difference between water and blood is small, but is sufficient for O_2 to diffuse from water to blood. As more O_2 diffuses into the blood, raising the blood's O_2 concentration, the blood encounters water with ever higher O_2 concentrations. At every point, the O_2 concentration is higher in the water, so that diffusion continues. In this example, blood attains an O_2 concentration of 85%. When blood and water flow in the same direction ***(b)***, O_2 can diffuse from the water into the blood rapidly at first, but the diffusion rate slows as more O_2 diffuses from the water into the blood, until finally the concentrations of O_2 in water and blood are equal. In this example, blood's O_2 concentration cannot exceed 50%.

would cease when the level of oxygen became the same in the water and in the blood.

Because of the countercurrent exchange of gases, fish gills are the most efficient of all respiratory organs.

Cutaneous respiration requires constant moisture

Oxygen and carbon dioxide can diffuse across cutaneous (skin) surfaces in some vertebrates (see figure 49.2*b*). Most commonly, these vertebrates are aquatic, such as amphibians and some turtles, and they have highly vascularized areas of thin epidermis. The process of exchanging oxygen and carbon dioxide across the skin is called **cutaneous respiration.** In amphibians, cutaneous respiration supplements—and sometimes replaces—the action of lungs. Although not common, some terrestrial amphibians, such as plethodontid salamanders, rely on cutaneous respiration exclusively.

Terrestrial reptiles have dry, tough, scaly skins that not only prevent desiccation, but also prohibit cutaneous respiration, which is utilized by many amphibians. Some aquatic reptiles, however, have the ability to respire cutaneously. For example, soft-shelled turtles can remain submerged and inactive in river sediment for hours without having to ventilate their lungs. At that level of activity, cutaneous respiration occurring through the skin lining the throat provides enough oxygen to the tissues. Even the common pond slider uses cutaneous respiration to help stay submerged. During the winter, these turtles can stay submerged for many days without needing to breathe air.

Tracheal systems are found in arthropods

The arthropods have no single respiratory organ. The respiratory system of most terrestrial arthropods consists of small, branched cuticle-lined air ducts called *tracheae* (see figure 49.2*d*). These trachea, which ultimately branch into very small tracheoles, are a series of tubes that transmit gases throughout the body. Tracheoles are in direct contact with individual cells, and oxygen diffuses directly across the plasma membranes.

Air passes into the trachea by way of specialized openings in the exoskeleton called *spiracles*, which, in most terrestrial arthropods, can be opened and closed by valves. The ability to prevent water loss by closing the spiracles was a key adaptation that facilitated the invasion of land by arthropods.

Learning Outcomes Review 49.2

Gills are highly subdivided structures providing a large surface area for exchange. In countercurrent flow, blood in the gills flows opposite to the direction of water to maintain a gradient difference and maximize gas exchange. Some amphibians rely on cutaneous respiration. Highly subdivided tracheal systems have evolved in arthropods, and these have been modified with valves as an adaptation to terrestrial life.

- ***What are the anatomical requirements for a countercurrent flow system?***

49.3 Lungs

Learning Outcomes

1. *Explain why lungs work better than gills in air.*
2. *Compare the breathing mechanisms of amphibians and reptiles.*
3. *Describe the breathing cycle of birds.*

Despite the high efficiency of gills as respiratory organs in aquatic environments, gills were replaced in terrestrial animals for two principal reasons:

1. **Air is less supportive than water.** The fine membranous lamellae of gills lack inherent structural strength and rely on water for their support. A fish out of water, although awash in oxygen, soon suffocates because its gills collapse into a mass of tissue. Unlike gills, internal air passages such as trachaea and lungs can remain open because the body itself provides the necessary structural support.
2. **Water evaporates.** Air is rarely saturated with water vapor, except immediately after a rainstorm. Consequently, terrestrial organisms constantly lose water to the atmosphere. Gills would provide an enormous surface area for water loss.

The lung minimizes evaporation by moving air through a branched tubular passage. The tracheal system of arthropods also uses internal tubes to minimize evaporation.

The air drawn into the respiratory passages becomes saturated with water vapor before reaching the inner regions of the lung. In these areas, a thin, wet membrane permits gas exchange. Unlike the one-way flow of water that is so effective in the respiratory function of gills, gases move in and out of lungs by way of the same airway passages, a two-way flow system. Birds have an exceptional respiratory system, as described later on.

Breathing of air takes advantage of partial pressures of gases

Dry air contains 78.09% nitrogen, 20.95% oxygen, 0.93% argon and other inert gases, and 0.03% carbon dioxide. Convection currents cause the atmosphere to maintain a constant composition to altitudes of at least 100 km, although the *amount* (number of molecules) of air that is present decreases as altitude increases.

Because of the force of gravity, air exerts a pressure downward on objects below it. An apparatus that measures air pressure is called a *barometer*, and 760 mm Hg is the barometric pressure of the air at sea level. A pressure of 760 mm Hg is also defined as one atmosphere (1.0 atm) of pressure.

Each type of gas contributes to the total atmospheric pressure according to its fraction of the total molecules present. The pressure contributed by a gas is called its **partial pressure,** and it is indicated by P_{N_2}, P_{O_2}, P_{CO_2}, and so

on. At sea level, the partial pressures of N_2, O_2, and CO_2 are as follows:

$$P_{N_2} = 760 \times 79.02\% = 600.6 \text{ mm Hg}$$

$$P_{O_2} = 760 \times 20.95\% = 159.2 \text{ mm Hg}$$

$$P_{CO_2} = 760 \times 0.03\% = 0.2 \text{ mm Hg}$$

Humans do not survive for long at altitudes above 6000 m. Although the air at these altitudes still contains 20.95% oxygen, the atmospheric pressure is only about 380 mm Hg, so the P_{O_2} is only 80 mm Hg (380 × 20.95%), half the amount of oxygen available at sea level.

In the following sections, we describe respiration in vertebrates with lungs, beginning with reptiles and amphibians. We then summarize mammalian lungs and the highly adapted and specialized lungs of birds.

Amphibians and reptiles breathe in different ways

The lungs of amphibians are formed as saclike outpouchings of the gut (figure 49.7). Although the internal surface area of these sacs is increased by folds, much less surface area is available for gas exchange in amphibian lungs than in the lungs of other terrestrial vertebrates. Each amphibian lung is connected to the rear of the oral cavity, or pharynx, and the opening to each lung is controlled by a valve, the glottis.

Amphibians do not breathe the same way as other terrestrial vertebrates. Amphibians force air into their lungs; they fill their oral cavity with air (figure 49.7*a*), close their mouth and nostrils, and then elevate the floor of their oral cavity. This pushes air into their lungs in the same way that a pressurized tank of air is used to fill balloons (figure 49.7*b*). This is called **positive pressure breathing;** in humans, it would be analogous to forcing air into a person's lungs by performing mouth-to-mouth resuscitation.

Most reptiles breathe in a different way, by expanding their rib cages by muscular contraction. This action creates a lower pressure inside the lungs compared with the atmosphere, and the greater atmospheric pressure moves air into the lungs. This type of ventilation is termed **negative pressure breathing** because of the air being "pulled in" by the animal, like sucking water through a straw, rather than being "pushed in."

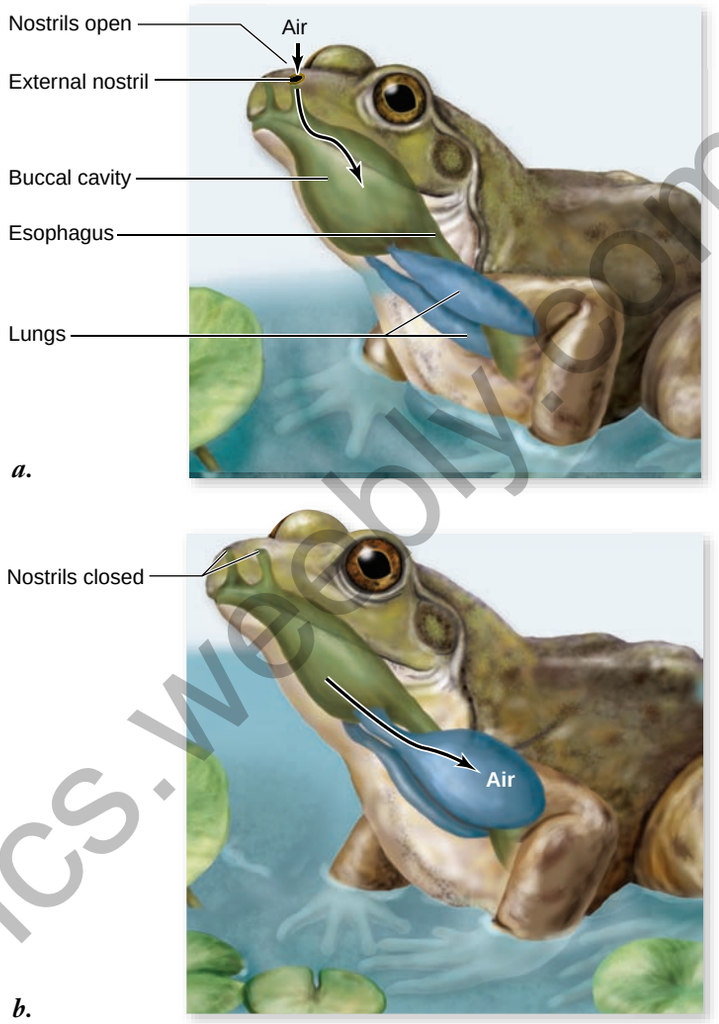


Figure 49.7 Amphibian lungs. Each lung of this frog is an outpouching of the gut and is filled with air by the creation of a positive pressure in the buccal cavity. ***a.*** The buccal cavity is expanded and air flows through the open nostrils. ***b.*** The nostrils are closed and the buccal cavity is compressed, thus creating the positive pressure that fills the lungs. The amphibian lung lacks the structures present in the lungs of other terrestrial vertebrates that provide an enormous surface area for gas exchange, and so are not as efficient as the lungs of other vertebrates.

Mammalian lungs have greatly increased surface area

Endothermic animals, such as birds and mammals, have consistently higher metabolic rates and thus require more oxygen (see chapter 7). Both these vertebrate groups exhibit more complex and efficient respiratory systems than ectothermic animals. The evolution of more efficient respiratory systems accommodates the increased demands on cellular respiration of endothermy.

The lungs of mammals are packed with millions of **alveoli,** tiny sacs clustered like grapes (figure 49.8). This provides each lung with an enormous surface area for gas exchange. Each alveolus is composed of an epithelium only one cell thick, and is surrounded by blood capillaries with walls that are also only one cell layer thick. Thus, the distance *d* across which gas must diffuse is very small—only 0.5 to 1.5 μm.

Inhaled air is taken in through the mouth and nose past the pharynx to the larynx (voice box), where it passes through an opening in the vocal cords, the *glottis*, into a tube supported by C-shaped rings of cartilage, the trachea (windpipe). The term *trachea* is used both for the vertebrate windpipe and the respiratory tubes of arthropods, although the structures are obviously not homologous. The mammalian trachea bifurcates into right and left bronchi (singular, *bronchus*), which enter each lung and further subdivide into bronchioles that deliver the air into the alveoli.

The alveoli are surrounded by an extensive capillary network. All gas exchange between the air and blood takes place

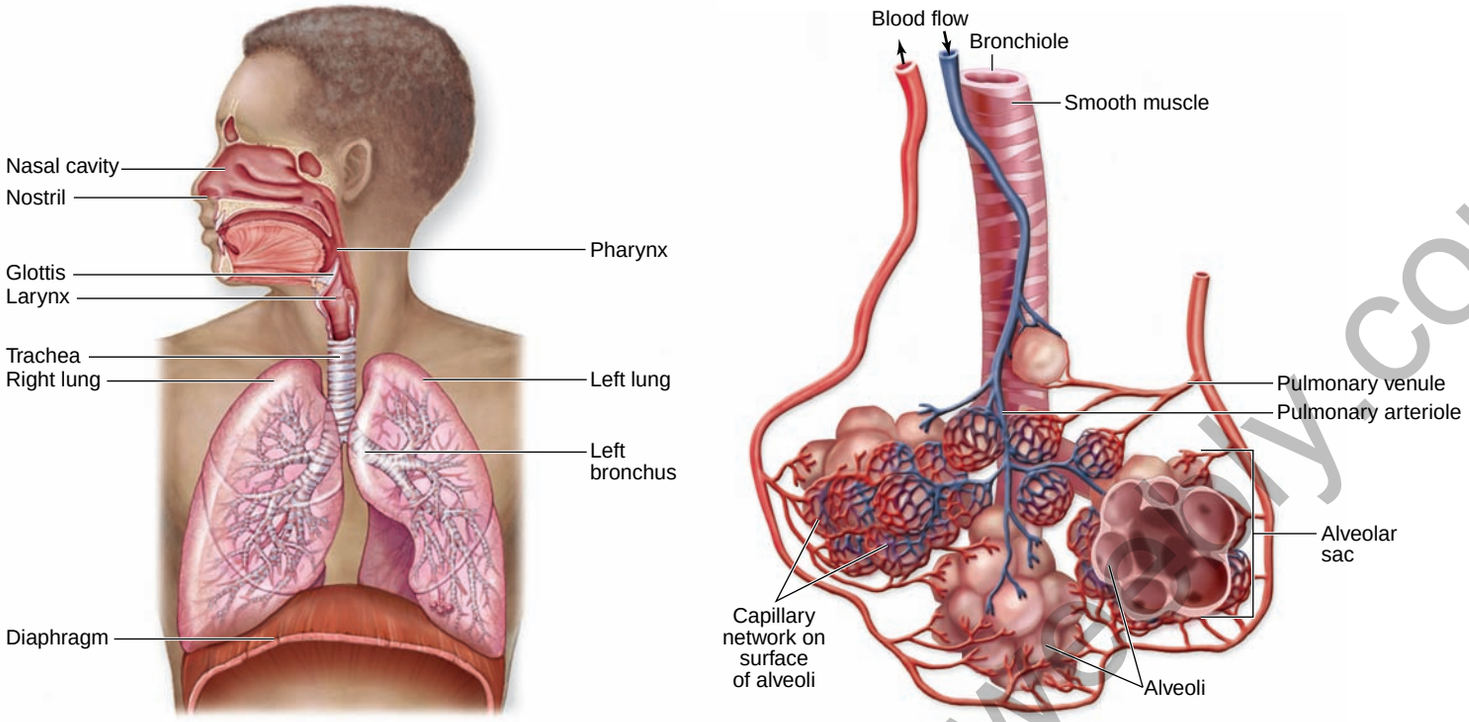


Figure 49.8 The human respiratory system and the structure of the mammalian lung. The lungs of mammals have an enormous surface area because of the millions of alveoli that cluster at the ends of the bronchioles. This provides for efficient gas exchange with the blood.

across the walls of the alveoli. The branching of bronchioles and the vast number of alveoli combine to increase the respiratory surface area far above that of amphibians or reptiles. In humans, each lung has about 300 million alveoli, and the total surface area available for diffusion can be as much as 80 m^2, or about 42 times the surface area of the body. Details of gas exchange at the alveolar interface with blood capillaries is described in sections that follow.

The respiratory system of birds is a highly efficient flow-through system

The avian respiratory system is a unique structure that affords birds the most efficient respiration of all terrestrial vertebrates. Unlike the mammalian lung, which ends in blind alveoli, the bird lung channels air through tiny air vessels called parabronchi, where gas exchange occurs. Air flows through the parabronchi in one direction only. This flow is similar to the unidirectional flow of water through a fish gill.

In other terrestrial vertebrates, inhaled fresh air is mixed with "old," oxygen-depleted air left from the previous breathing cycle. The lungs of amphibians, reptiles, and mammals are never completely empty of the gases within them. In birds, only fresh air enters the parabronchi of the lung, and the "old" air exits the lung by a different route. The unidirectional flow of air is achieved through the action of anterior and posterior air sacs unique to birds (figure 49.9*a*). When these sacs are expanded during inhalation, they take in air, and when they are compressed during exhalation, they push air into and through the lungs.

Respiration in birds occurs in two cycles (figure 49.9*b*). Each cycle has an inhalation and exhalation phase—but the air inhaled in one cycle is not exhaled until the second cycle.

Upon inhalation, both anterior and posterior air sacs expand. The inhaled air, however, only enters the posterior air sacs; the anterior air sacs fill with air pulled from the lungs. Upon exhalation, the air forced out of the anterior air sacs is released outside the body, but the air forced out of the posterior air sacs now enters the lungs. This process is repeated in the second cycle.

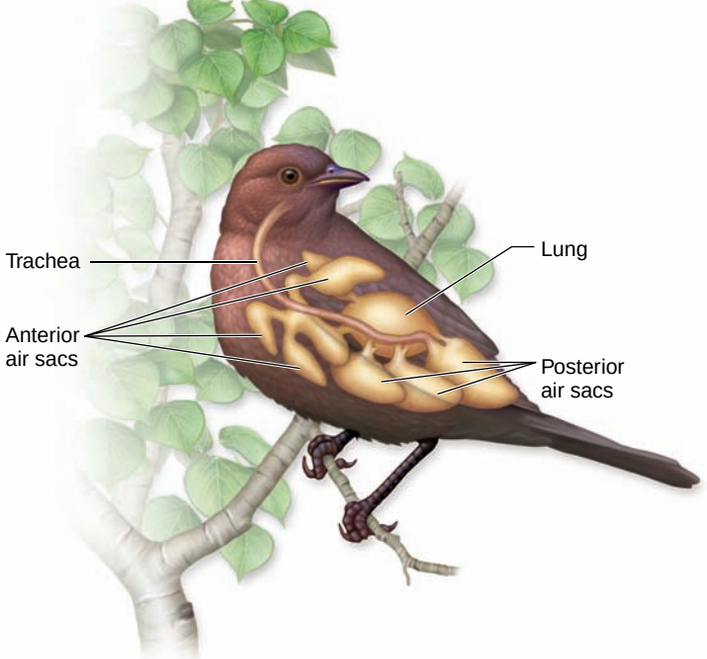
The unidirectional flow of air also permits further respiratory efficiency: The flow of blood through the avian lung runs at a 90° angle to the air flow. This crosscurrent flow is not as efficient as the 180° countercurrent flow in fishes' gills, but it has a greater capacity to extract oxygen from the air than does a mammalian lung.

Because of these respiratory adaptations, a sparrow can be active at an altitude of 6000 m, whereas a mouse, which has a similar body mass and metabolic rate, would die from lack of oxygen in a fairly short time.

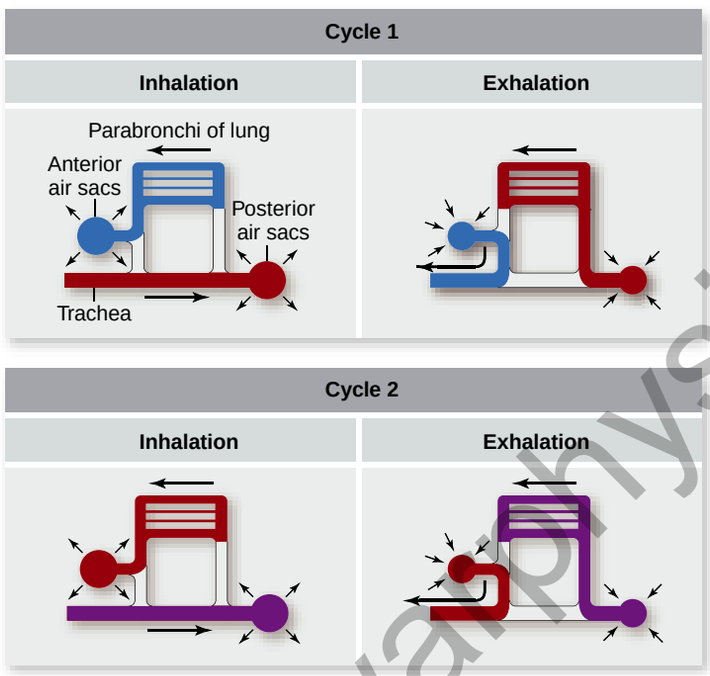
Learning Outcomes Review 49.3

Lungs provide a large surface area for gas exchange while minimizing evaporation; unlike gills, they contain structural support that prevents their collapse. Amphibians push air into their lungs; most reptiles and all birds and mammals pull air into their lungs by expanding the thoracic cavity. The respiratory system of birds has efficient, one-way air flow and crosscurrent blood flow through the lungs.

- ***What selection pressure would bring about the evolution of birds' highly efficient lungs?***



a.



b.

Figure 49.9 How a bird breathes. ***a.*** Birds have a system of air sacs, divided into an anterior group and posterior group, that extend between the internal organs and into the bones. ***b.*** Breathing occurs in two cycles. Cycle 1: Inhaled air (shown in red) is drawn from the trachea into the posterior air sacs (shown expanding as it fills with air) and then is exhaled into the lungs (posterior air sacs deflate). Cycle 2: Air is drawn from the lungs into the anterior air sacs, which expand, and then is exhaled from these air sacs through the trachea. Passage of air through the lungs is always in the same direction, from posterior to anterior (right to left in this diagram). These cycles are always going on simultaneously; during inhalation, fresh air enters the posterior air sacs at the same time that air from the previous breath that was in the lungs moves into the anterior air sacs. In exhalation, the newer air moves from the posterior air sacs to the lung at the same time that air in the anterior air sacs is exhaled from the body. At the same time, another breath of inhaled air (purple) is moving through cycle 1.

49.4 Structures and Mechanisms of Ventilation in Mammals

Learning Outcomes

1. *Explain what is meant by anatomical dead space.*
2. *Describe how the nervous system regulates breathing.*
3. *List and characterize the major respiratory diseases.*

About 30 billion capillaries can be found in each lung, roughly 100 capillaries per alveolus. Thus, an alveolus can be visualized as a microscopic air bubble whose entire surface is bathed by blood. Gas exchange occurs very rapidly at this interface.

Blood returning from the systemic circulation, depleted in oxygen, has a partial oxygen pressure (P_{O_2}) of about 40 mm Hg. By contrast, the P_{O_2} in the alveoli is about 105 mm Hg. The difference in pressures, namely the Δp of Fick's Law, is 65 mm Hg, leading to oxygen moving into the blood. The blood leaving the lungs, as a result of this gas exchange, normally contains a P_{O_2} of about 100 mm Hg. As you can see, the lungs do a very effective, but not perfect, job of oxygenating the blood. These changes in the P_{O_2} of the blood, as well as the changes in plasma carbon dioxide (indicated as the P_{CO_2}), are shown in figure 49.10.

Lung structure and function supports the respiratory cycle

In humans and other mammals, the outside of each lung is covered by a thin membrane called the **visceral pleural membrane.** A second membrane, the **parietal pleural membrane,** lines the inner wall of the thoracic cavity. The space between these two membrane sheets, the **pleural cavity,** is normally very small and filled with fluid. This fluid causes the two membranes to adhere, effectively coupling the lungs to the thoracic cavity. The pleural membranes package each lung separately—if one lung collapses due to a perforation of the membranes, the other lung can still function.

During inhalation, the thoracic volume is increased through contraction of two sets of muscles: the *external intercostal muscles* and the *diaphragm.* Contraction of the external intercostal muscles between the ribs raises the ribs and expands the rib cage. Contraction of the **diaphragm,** a convex sheet of striated muscle separating the thoracic cavity from the abdominal cavity, causes the diaphragm to lower and assume a more flattened shape. This expands the volume of the thorax and lungs, bringing about negative pressure ventilation, while it increases the pressure on the abdominal organs (figure 49.11*a*).

The thorax and lungs have a degree of elasticity; expansion during inhalation places these structures under elastic tension. The relaxation of the external intercostal muscles and diaphragm produces unforced exhalation because the elastic tension is released, allowing the thorax and lungs to recoil. You can produce a greater exhalation force by actively contracting your abdominal muscles—such as when blowing up a balloon (figure 49.11*b*).

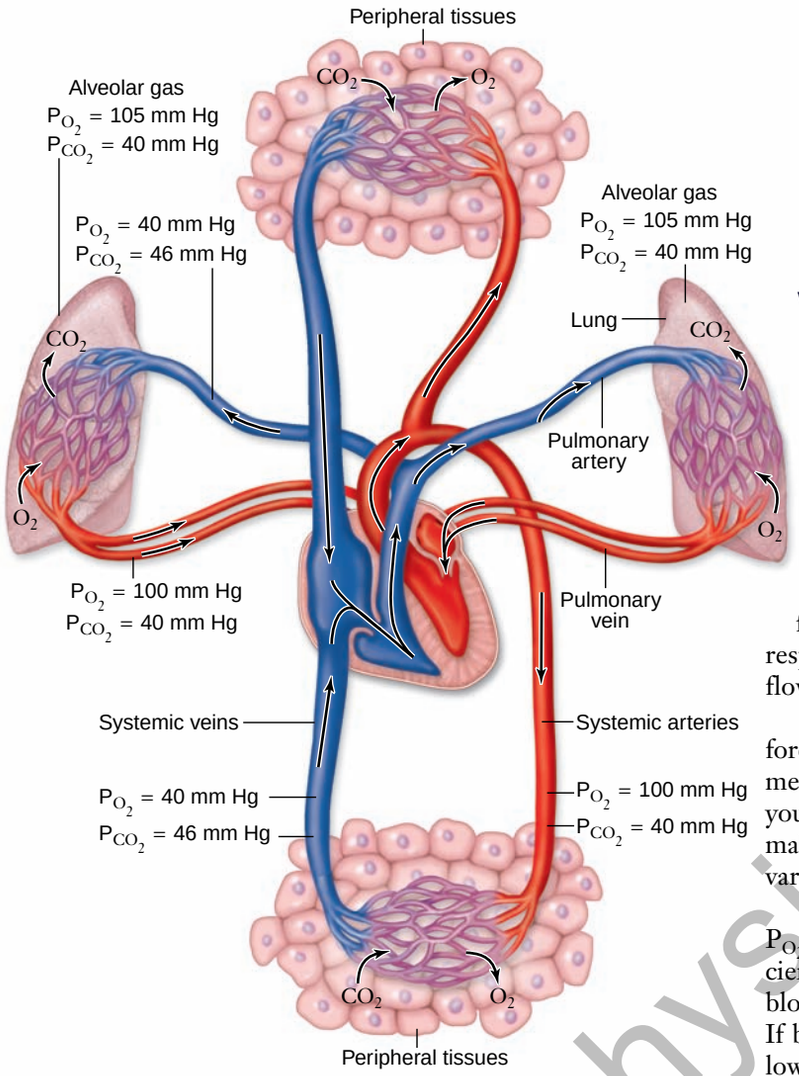


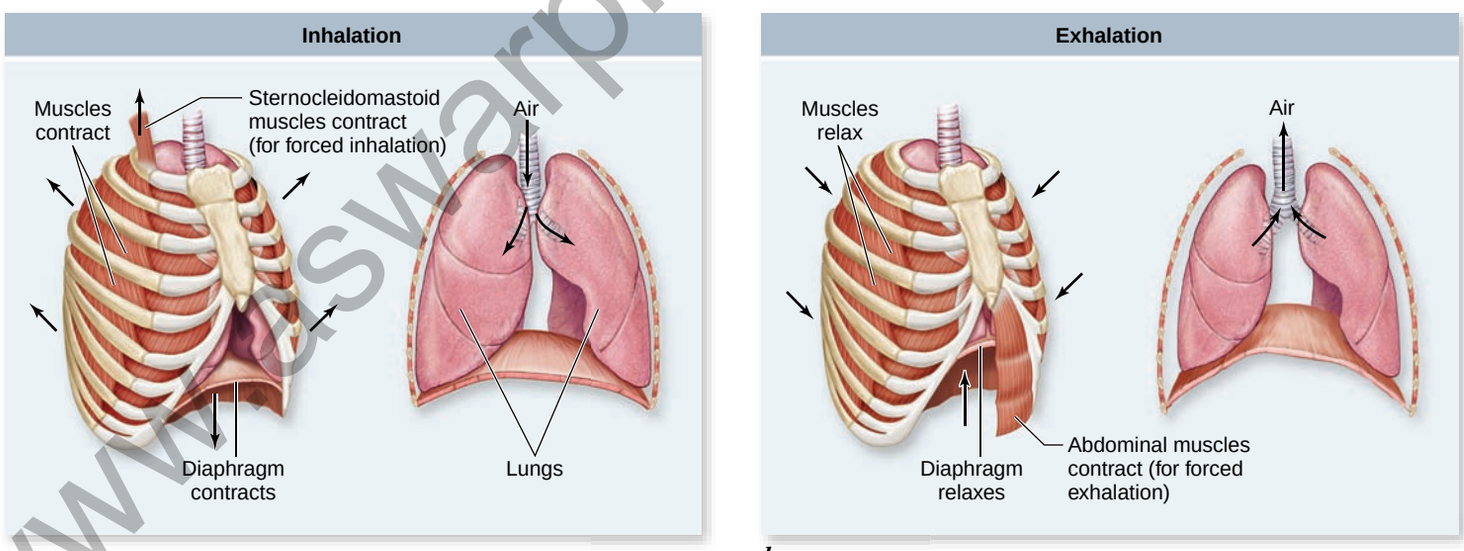
Figure 49.10 Gas exchange in the blood capillaries of the lungs and systemic circulation. As a result of gas exchange in the lungs, the systemic arteries carry oxygenated blood with a relatively low carbon dioxide (CO_2) concentration. After the oxygen (O_2) is unloaded to the tissues, the blood in the systemic veins has a lowered O_2 content and an increased CO_2 concentration.

Ventilation efficiency depends on lung capacity and breathing rate

A variety of terms are used to describe the volume changes of the lung during breathing. In a person at rest, each breath moves a tidal volume of about 500 mL of air into and out of the lungs. About 150 mL of the tidal volume is contained in the tubular passages (trachea, bronchi, and bronchioles), where no gas exchange occurs—termed the *anatomical dead space*. The gases in this space mix with fresh air during inhalation. This mixing is one reason that respiration in mammals is not as efficient as in birds, where air flow through the lungs is one-way.

The maximum amount of air that can be expired after a forceful, maximum inhalation is called the vital capacity. This measurement, which averages 4.6 L in young men and 3.1 L in young women, can be clinically important because an abnormally low vital capacity may indicate damage to the alveoli in various pulmonary disorders.

The rate and depth of breathing normally keeps the blood P_{O_2} and P_{CO_2} within a normal range. If breathing is insufficient to maintain normal blood gas measurements (a rise in the blood P_{CO_2} is the best indicator), the person is hypoventilating. If breathing is excessive, so that the blood P_{CO_2} is abnormally lowered, the person is said to be **hyperventilating.**



a. *b.*

Figure 49.11 How a human breathes. ***a.*** Inhalation. The diaphragm contracts and the walls of the chest cavity expand, increasing the volume of the chest cavity and lungs. As a result of the larger volume, air is drawn into the lungs. ***b.*** Exhalation. The diaphragm and chest walls return to their normal positions as a result of elastic recoil, reducing the volume of the chest cavity and forcing air out of the lungs through the trachea. Note that inhalation can be forced by contracting accessory respiratory muscles (such as the sternocleidomastoid), and exhalation can be forced by contracting abdominal muscles.

The increased breathing that occurs during moderate exertion is not necessarily hyperventilation because the faster and more forceful breathing is matched to the higher metabolic rate, and blood gas measurements remain normal. Next, we describe how breathing is regulated to keep pace with metabolism.

Ventilation is under nervous system control

Each breath is initiated by neurons in a *respiratory control center* located in the medulla oblongata. These neurons stimulate the diaphragm and external intercostal muscles to contract, causing inhalation. When these neurons stop producing impulses, the inspiratory muscles relax and exhalation occurs. Although the muscles of breathing are skeletal muscles, they are usually controlled automatically. This control can be voluntarily overridden, however, as in hypoventilation (breath holding) or hyperventilation.

Neurons of the medulla oblongata must be responsive to changes in blood P_{O_2} and P_{CO_2} in order to maintain homeostasis. You can demonstrate this mechanism by simply holding your breath. Your blood carbon dioxide level immediately rises, and your blood oxygen level falls. After a short time, the urge to breathe induced by the changes in blood gases becomes overpowering. The rise in blood carbon dioxide, as indicated by a rise in P_{CO_2}, is the primary initiator, rather than the fall in oxygen levels.

A rise in P_{CO_2} causes an increased production of carbonic acid (H_2CO_3), which lowers the blood pH. A fall in blood pH stimulates chemosensitive neurons in the **aortic** and **carotid bodies,** in the aorta and the carotid artery (figure 49.12*b*). These

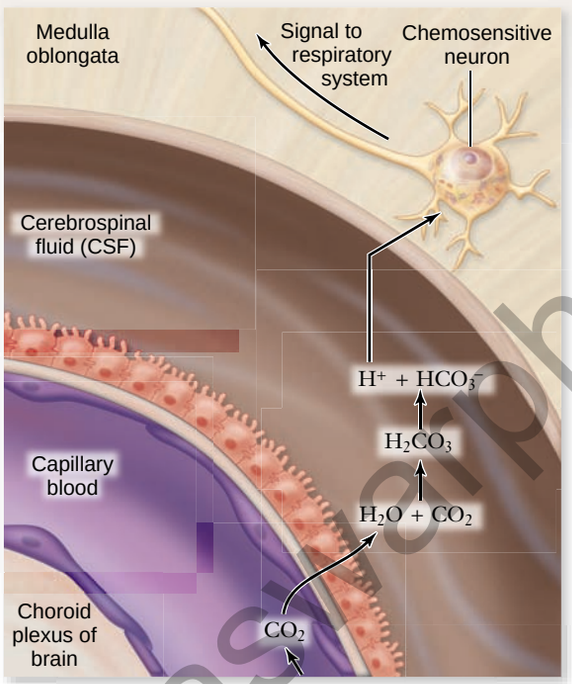
SCIENTIFIC THINKING

Question: *What is the relationship between cerebrospinal fluid (CSF) pH, rate of respiration, and partial pressure of carbon dioxide in the blood (P_{CO_2})?*

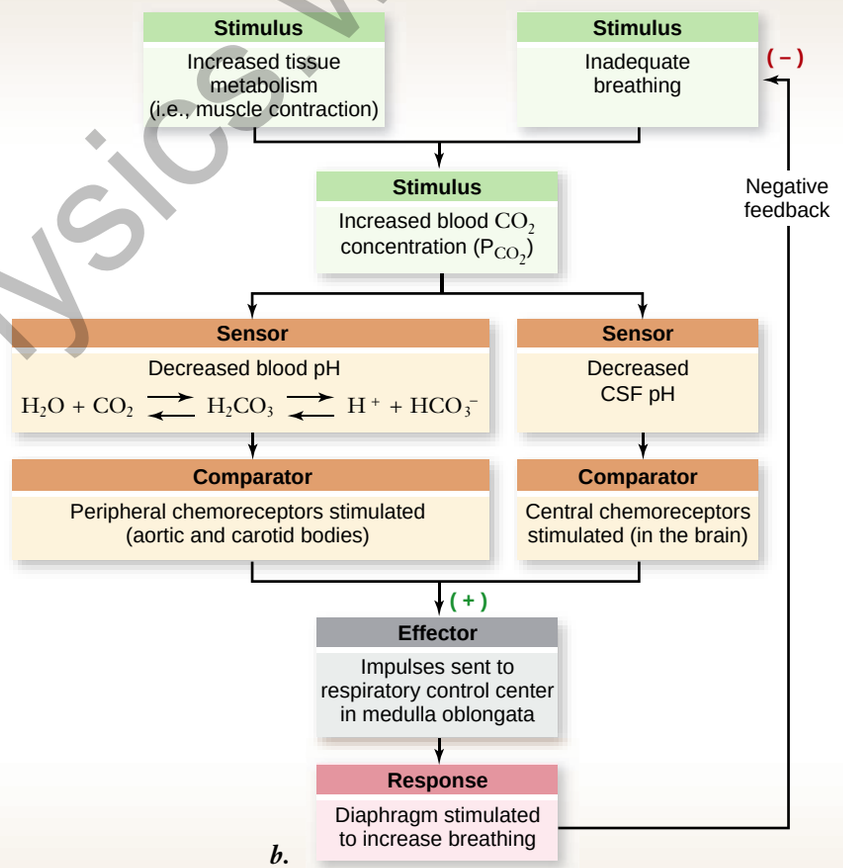
Hypothesis: *The pH of CSF, detected by pH-sensitive chemoreceptors in the brain, affects the rate of respiration.*

Prediction: *Lowering the pH of the CSF (by reducing the concentration of HCO_3^-) will stimulate increased respiration and, subsequently, reduce blood P_{CO_2}.*

Experiment: *Patients with chronic obstructive respiratory disease (COPD) have higher than average CSF levels of HCO_3^-. Some of the CSF in these patients was replaced with CSF with normal HCO_3^- levels, and subsequent P_{CO_2} levels were measured.*



a.



b.

Result: *The reduced HCO_3^- levels (and corresponding drop in CSF pH) resulted in increased respiration, which subsequently resulted in lower arterial P_{CO_2}.*

Conclusion: *The drop in pH (caused by the change in HCO_3^- levels) is detected by H^+ ion chemoreceptors in the brain. The brain sends impulses to the respiratory control center in the medulla oblongata, which directs an increase in breathing. Likewise, when the concentration of CO_2 in the blood rises as a result of inadequate breathing or increased tissue metabolism, the pH of the blood and the CSF decreases, stimulating the central chemoreceptors in the brain and the peripheral chemoreceptors in the aortic and carotid bodies. The receptors signal the brain stem control center, increasing ventilation and reducingthe P_{CO_2} to normal levels.*

Figure 49.12 **Regulation of breathing by pH-sensitive chemoreceptors.**

peripheral receptors send impulses to the respiratory control center, which then stimulates increased breathing. The brain also contains central chemoreceptors that are stimulated by a drop in the pH of cerebrospinal fluid (CSF) (figure 49.12*a*).

A person cannot voluntarily hyperventilate for too long. The decrease in plasma P_{CO_2} and increase in pH of plasma and CSF caused by hyperventilation suppress the reflex drive to breathe. Deliberate hyperventilation allows people to hold their breath longer—not because it increases oxygen in the blood, but because the carbon dioxide level is lowered and takes longer to build back up, postponing the need to breathe.

In people with normal lungs, P_{O_2} becomes a significant stimulus for increased breathing rates only at high altitudes, where the P_{O_2} of the atmosphere is low. The symptoms of low oxygen at high altitude are known as mountain sickness, which may include feelings of weakness, headache, nausea, vomiting, and reduced mental function. All of these symptoms are related to the low P_{O_2}, and breathing supplemental oxygen often may remove all symptoms.

Respiratory diseases restrict gas exchange

Chronic obstructive pulmonary disease (COPD) refers to any disorder that obstructs airflow on a long-term basis. The major COPDs are asthma, chronic bronchitis, and emphysema. In **asthma,** an allergen triggers the release of histamine and other inflammatory chemicals that cause intense constriction of the bronchi and sometimes suffocation. Other COPDs are commonly caused by cigarette smoking but can also result from air pollution or occupational exposure to airborne irritants.

Emphysema

In **emphysema,** alveolar walls break down and the lung exhibits larger but fewer alveoli. The lungs also become fibrotic and less elastic. The air passages open adequately during inhalation but they tend to collapse and obstruct the outflow of air. People with emphysema become exhausted because they expend three to four times the normal amount of energy just to breathe. Eighty to 90% of emphysema deaths are caused by cigarette smoking.

Inquiry question

How does emphysema affect the diffusion of gases in and out of the lung, based on Fick's Law?

Lung cancer

Lung cancer accounts for more deaths than any other form of cancer. The most important cause of lung cancer is cigarette smoking, distantly followed by air pollution (figure 49.13). Lung cancer follows or accompanies COPD.

Over 90% of lung tumors originate in the mucous membranes of the large bronchi. As a tumor invades the bronchial wall and grows around it, it compresses the airway and may cause collapse of more distal parts of the lung. Growth of a tumor often produces coughing, but coughing is such an everyday occurrence for smokers, it seldom causes alarm. Often, the first sign of serious trouble is the coughing up of blood.

Lung cancer metastasizes (spreads) so rapidly that it has usually invaded other organs by the time it is diagnosed. The chance of recovery from metastasized lung cancer is poor, with only 3% of patients surviving for 5 years after diagnosis.

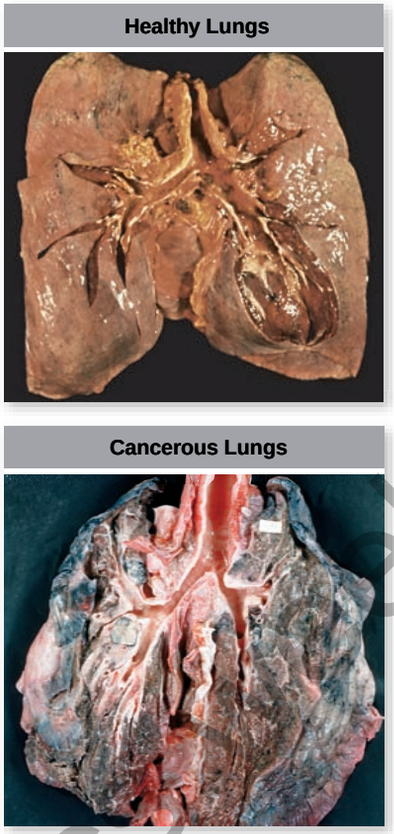


Figure 49.13
Comparison of healthy lung (*a*) and a lung with cancer (*b*).

Learning Outcomes Review 49.4

In humans, each breath moves a tidal volume of about 500 mL in and out of the lungs; 150 mL remains in the tubular passages where no gases are exchanged (anatomical dead space). Depth and rate of ventilation is regulated primarily by neurons in the medulla oblongata that detect CO_2 concentration. Diseases such as COPD limit gas exchange by obstructing airflow. Lung cancer, associated with tobacco use, has a low survival rate.

- ***How do mammals breathe differently from birds?***

49.5 *Transport of Gases in Body Fluids*

Learning Outcomes

1. ***Depict the structure of hemoglobin.***
2. ***Describe how hemoglobin's oxygen affinity changes depending on environmental conditions.***
3. ***Explain how carbon dioxide is transported by the blood.***

The amount of oxygen that can be dissolved in the blood plasma depends directly on the P_{O_2} of the air in the alveoli, as explained earlier. When mammalian lungs are functioning normally,

the blood plasma leaving the lungs has almost as much dissolved oxygen as is theoretically possible, given the P_{O_2} of the air. Because of oxygen's low solubility, however, blood plasma can contain a maximum of only about 3 mL of O_2 per liter. But whole blood normally carries almost 200 mL of O_2 per liter. Most of the oxygen in the blood is bound to molecules of hemoglobin inside red blood cells.

Respiratory pigments bind oxygen for transport

Hemoglobin is a protein composed of four polypeptide chains and four organic compounds called *heme groups*. At the center of each heme group is an atom of iron, which can bind to a molecule of oxygen (figure 49.14). Thus, each hemoglobin molecule can carry up to four molecules of oxygen.

Hemoglobin loads up with oxygen in the alveolar capillaries of the pulmonary circulation, forming oxyhemoglobin. This molecule has a bright red color. As blood passes through capillaries in the systemic circulation, some of the oxyhemoglobin releases oxygen, becoming **deoxyhemoglobin.** Deoxyhemoglobin has a darker red color; but it imparts a bluish tinge to tissues. Illustrations of the cardiovascular system show vessels carrying oxygenated blood with a red color and vessels that carry oxygen-depleted blood with a blue color.

Hemoglobin is an ancient protein; it is not only the oxygen-carrying molecule in all vertebrates, but is also used as an oxygen carrier by many invertebrates, including annelids, mollusks, echinoderms, flatworms, and even some protists. Many other invertebrates, however, employ different oxygen carriers, such as **hemocyanin.** In hemocyanin, the oxygen-binding atom is copper instead of iron. Hemocyanin is not found associated with blood cells, but is instead one of the free proteins in the circulating fluid (hemolymph) of arthropods and some mollusks.

Inquiry question

If oxygen-depleted vessels have a bluish color, does this mean that all veins in the body have a bluish color? Why or why not?

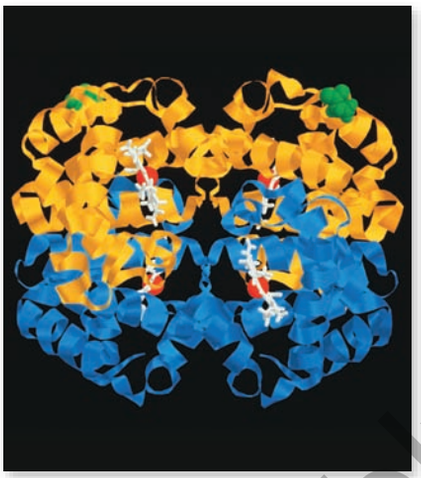


Figure 49.14 The structure of the adult hemoglobin protein. Hemoglobin consists of four polypeptide chains: two α chains and two β chains. Each chain is associated with a heme group (in white), and each heme group has a central iron atom (red ball), which can bind to a molecule of O_2.

Hemoglobin and myoglobin provide an oxygen reserve

At a blood P_{O_2} of 100 mm Hg, the level found in blood leaving the alveoli, approximately 97% of the hemoglobin within red blood cells is in the form of oxyhemoglobin—indicated as a percent oxyhemoglobin saturation of 97%.

In a person at rest, blood that returns to the heart in the systemic veins has a P_{O_2} that is decreased to about 40 mm Hg. At this lower P_{O_2}, the percent saturation of hemoglobin is only 75%. In a person at rest, therefore, 22% (97% minus 75%) of the oxyhemoglobin has released its oxygen to the tissues. Put another way, roughly one-fifth of the oxygen is unloaded in the tissues, leaving four-fifths of the oxygen in the blood as a reserve. A graphic representation of these changes is called an oxyhemoglobin dissociation curve (figure 49.15).

This large reserve of oxygen serves an important function. It enables the blood to supply the body's oxygen needs during exertion as well as at rest. During exercise, for example, the muscles' accelerated metabolism uses more oxygen and decreases the venous blood P_{O_2}. The P_{O_2} of the venous blood

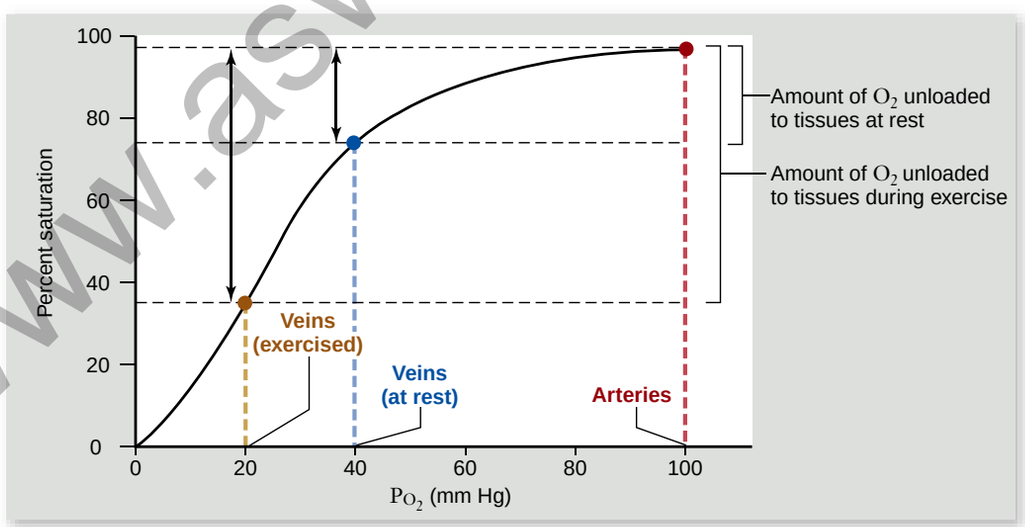


Figure 49.15 The oxyhemoglobin dissociation curve. Hemoglobin combines with O_2 in the lungs, and this oxygenated blood is carried by arteries to the body cells. After O_2 is removed from the blood to support cellular respiration, the blood entering the veins contains less O_2.

Inquiry question

How would you determine how much oxygen was unloaded to the tissues?

could drop to 20 mm Hg; in this case, the percent saturation of hemoglobin would be only 35% (see figure 49.15). Because arterial blood would still contain 97% oxyhemoglobin, the amount of oxygen unloaded would now be 62% (97% minus 35%), instead of the 22% at rest.

In addition to this function, the oxygen reserve also ensures that the blood contains enough oxygen to maintain life for 4 to 5 min if breathing is interrupted or if the heart stops pumping.

A second oxygen reserve is available in myoglobin, an oxygen-binding molecule found in muscle cells. Myoglobin is composed of a single polypeptide chain with an iron atom that can bind to an O_2 molecule. Myoglobin has a higher affinity for oxygen than hemoglobin, which means that when oxygen levels fall in muscle cells, myoglobin will contain oxygen after the hemoglobin supplies have been exhausted. Deep sea-diving mammals, such as the elephant seal in figure 49.1, are able to stay under water for long periods in part because of the high levels of oxygen stored in the myoglobin in their muscles.

Inquiry question

Based on the preceding information, would an otherwise healthy person benefit significantly from breathing 100% oxygen following a bout of intense exercise such as a 400-m sprint?

Hemoglobin's affinity for oxygen is affected by pH and temperature

Oxygen transport in the blood is affected by other conditions including temperature and pH. The CO_2 produced by metabolizing tissues combines with H_2O to form carbonic acid (H_2CO_3). H_2CO_3 dissociates into bicarbonate (HCO_3^-) and H^+, thereby lowering blood pH. This reaction occurs primarily inside red blood cells, where the lowered pH reduces hemoglobin's affinity for oxygen, causing it to release oxygen more readily.

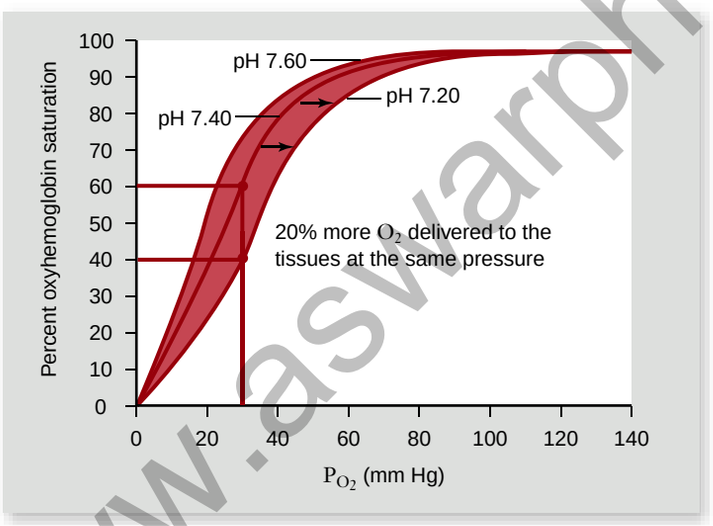
The effect of pH on hemoglobin's affinity for oxygen, known as the **Bohr effect** or **Bohr shift,** is the result of H^+ binding to hemoglobin. It is shown graphically by a shift of the oxyhemoglobin dissociation curve to the right (figure 49.16*a*).

Increasing temperature has a similar effect on hemoglobin's affinity for oxygen (figure 49.16*b*). Because skeletal muscles produce carbon dioxide more rapidly during exercise, and because active muscles produce heat, the blood unloads a higher percentage of the oxygen it carries during exercise.

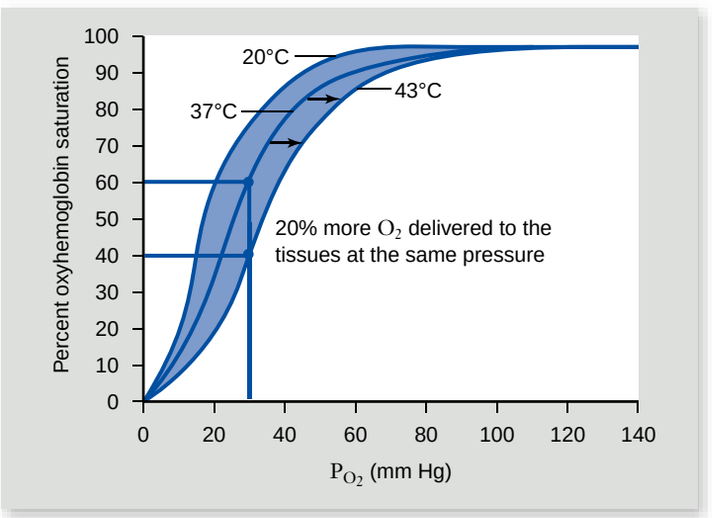
Carbon dioxide is primarily transported as bicarbonate ion

About 8% of the CO_2 in blood is simply dissolved in plasma; another 20% is bound to hemoglobin. Because CO_2 binds to the protein portion of hemoglobin, and not to the iron atoms of the heme groups, it does not compete with oxygen; however, it does cause hemoglobin's shape to change, lowering its affinity for oxygen.

The remaining 72% of the CO_2 diffuses into the red blood cells, where the enzyme carbonic anhydrase catalyzes the combining of CO_2 with water to form H_2CO_3. H_2CO_3 dissociates into HCO_3^- and H^+ ions. The H^+ binds to deoxyhemoglobin, and the HCO_3^- moves out of the erythrocyte into the plasma via a transporter that exchanges one Cl^- for a HCO_3^- (this is called the "chloride shift").



a. pH shift



b. Temperature shift

Figure 49.16 The effect of pH and temperature on the oxyhemoglobin dissociation curve. *a.* Lower blood pH and (*b*) higher blood temperatures shift the oxyhemoglobin dissociation curve to the right, facilitating O_2 unloading. In this example, this can be seen as a lowering of the oxyhemoglobin percent saturation from 60% to 40%, indicating that the difference of 20% more O_2 is unloaded to the tissues.

Inquiry question

What effect does high blood pressure have on oxygen unloading to the tissues during exercise?

This reaction removes large amounts of CO_2 from the plasma, maintaining a diffusion gradient that allows additional CO_2 to move into the plasma from the surrounding tissues (figure 49.17*a*). The formation of H_2CO_3 is also important in maintaining the acid–base balance of the blood; HCO_3^- serves as the major buffer of the blood plasma.

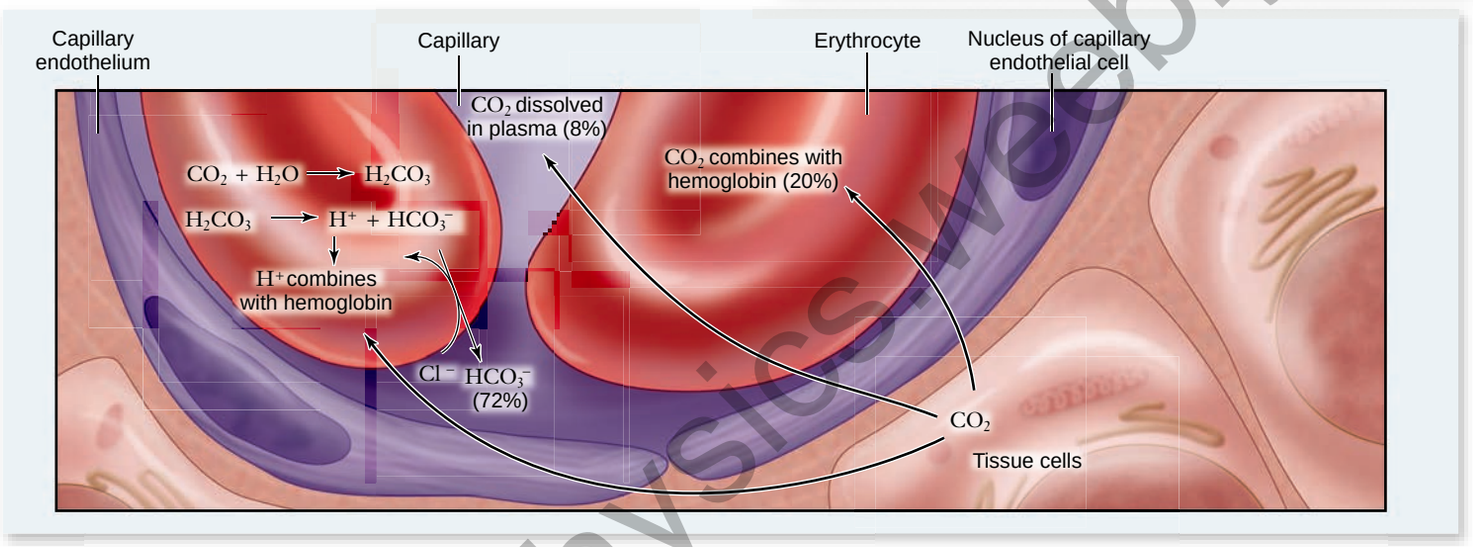
In the lungs, the lower P_{CO_2} of the gas mixture inside the alveoli causes the carbonic anhydrase reaction to proceed in the reverse direction, converting H_2CO_3 into H_2O and CO_2 (figure 49.17*b*). The CO_2 diffuses out of the red blood cells and into the alveoli, so that it can leave the body in the next exhalation.

Other dissolved gases are also transported by hemoglobin, most notably nitric oxide (NO), which plays an important role in vessel dilation. Carbon monoxide (CO) binds more strongly to hemoglobin than does oxygen, which is why carbon monoxide poisoning can be deadly. Victims of carbon monoxide poisoning often have bright red skin due to hemoglobin's binding with CO.

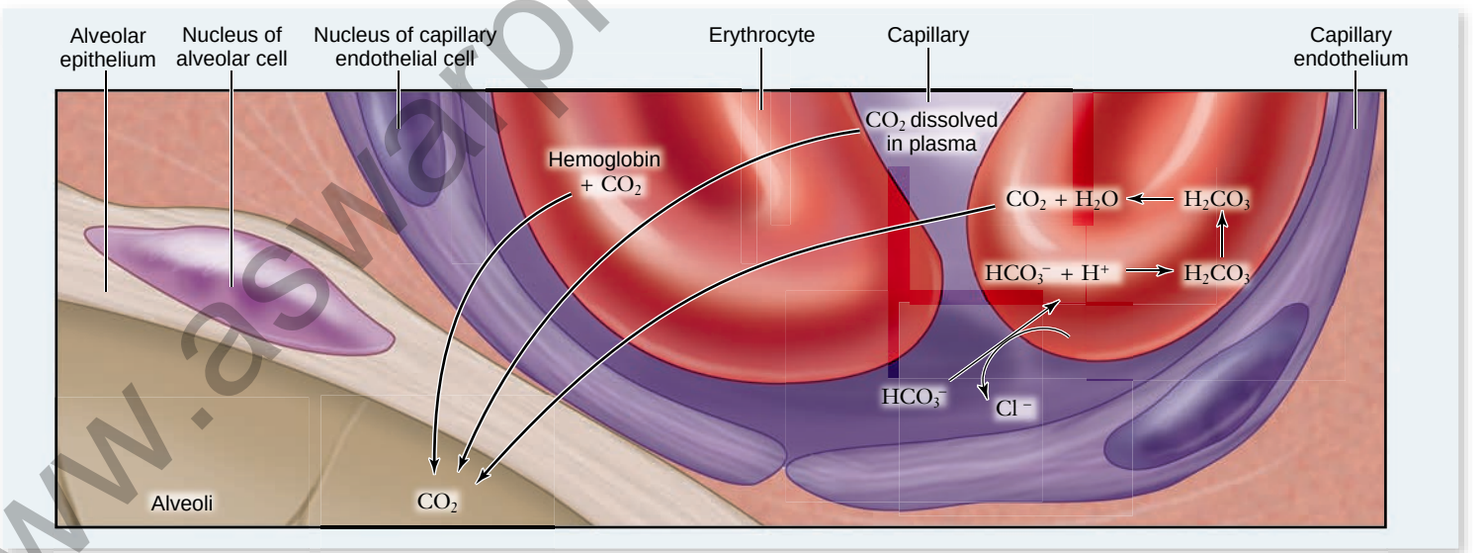
Learning Outcomes Review 49.5

Hemoglobin consists of four polypeptide chains, each associated with an iron-containing heme group that can bind O_2. Hemoglobin's affinity for oxygen is affected by pH and temperature; more O_2 is released into tissues at lower pH and at higher temperature. Carbon dioxide is transported in the blood in three ways: dissolved in the plasma, bound to hemoglobin, and as bicarbonate in the plasma following a reaction with carbonic anhydrase in the red blood cells.

- ***What are the differences in the way that oxygen and carbon dioxide are transported in blood?***



a.



b.

Figure 49.17 The transport of carbon dioxide by the blood. ***a.*** Passage into bloodstream. CO_2 is transported in three ways: dissolved in plasma, bound to the protein portion of hemoglobin, and as bicarbonate (HCO_3^-), which forms in red blood cells. The reaction of CO_2 with H_2O to form H_2CO_3 (carbonic acid) is catalyzed by the enzyme carbonic anhydrase in red blood cells. ***b.*** Removal from bloodstream. When the blood passes through the pulmonary capillaries, these reactions are reversed so that CO_2 gas is formed, which is exhaled.

Chapter Review

49.1 Gas Exchange Across Respiratory Surfaces

Gas exchange involves diffusion across membranes.

Diffusion is a passive process; the rate of diffusion *(R)* increases with a higher concentration gradient and greater surface area, but decreases with distance (Fick's Law).

Evolutionary strategies have maximized gas diffusion.

Most invertebrate phyla lack specialized respiratory organs, but have evolved ways to increase oxygen concentration differences. Most other animals possess respiratory organs.

49.2 Gills, Cutaneous Respiration, and Tracheal Systems

External gills are found in fish and amphibian larvae.

Gills increase the respiratory surface area for gas exchange; however, they require an aqueous environment.

Branchial chambers protect gills of some invertebrates.

Some aquatic invertebrates have branchial chambers in which oxygenated water is pumped past stationary gills. Mollusks possess a mantle in which water is drawn in and expelled.

Gills of bony fishes are covered by the operculum.

In bony fishes, diffusion of gases is maximized by countercurrent exchange, in which blood in gills flows in a direction opposite the flow of water over the gills (see figures 49.4 and 49.5).

Cutaneous respiration requires constant moisture.

Many amphibians and a few reptiles use cutaneous respiration for gas exchange.

Tracheal systems are found in arthropods.

Tracheae and tracheoles are a series of small tubes, connected with the outside environment by spiracles, that carry air directly to the cells. The ability to open and close the spiracles allowed arthropods to invade the land.

49.3 Lungs

Lungs minimize evaporation and contain supporting tissues to prevent collapse of exchange membranes, and thus have become well adapted to terrestrial living (see figure 49.8).

Breathing of air takes advantage of partial pressures of gases.

The partial pressure of gases refers to the proportion of atmospheric pressure attributed to each gas. It is responsible for the pressure gradient that brings about gas exchange.

Amphibians and reptiles breathe in different ways.

Amphibians force air into their lungs by positive pressure; reptiles pull air in using negative pressure (see figure 49.7).

Mammalian lungs have greatly increased surface area.

The surface area of mammalian lungs is enormous due to numerous alveoli, encased by an extensive capillary network (see figure 49.8).

The respiratory system of birds is a highly efficient flow-through system.

The respiratory system of birds involves one-way direction of air flow. Air moves through the respiratory system in a two-cycle process so that fresh and used air never mix (see figure 49.9).

49.4 Structures and Mechanisms of Ventilation in Mammals

Lung structure and function supports the respiratory cycle.

Gas exchange is driven by differences in partial pressures. Lungs are filled by contraction of the diaphragm and external intercostal muscles, creating negative pressure (see figure 49.11).

Ventilation efficiency depends on lung capacity and breathing rate.

Normal rates of breathing keep the partial pressure of oxygen and carbon dioxide within a limited range of values. Hypoventilation occurs when carbon dioxide levels are too high, and hyperventilation when they are too low.

Ventilation is under nervous system control.

Each breath is initiated by neurons in the respiratory control center, primarily those that detect CO_2 levels. Humans can voluntarily hypo- or hyperventilate, but only for a limited time.

Respiratory diseases restrict gas exchange.

Emphysema occurs when alveolar walls break down, which makes breathing very energetically expensive. Lung cancer is highly deadly and caused primarily by smoking.

49.5 Transport of Gases in Body Fluids

Respiratory pigments bind oxygen for transport.

Hemoglobin increases the ability of the blood to transport oxygen beyond what can dissolve in plasma (see figure 49.15).

Hemoglobin consists of four polypeptide chains, two α chains and two β chains; each of these is associated with an iron-containing heme group that can bind to O_2 (see figure 49.14).

Hemoglobin and myoglobin provide an oxygen reserve.

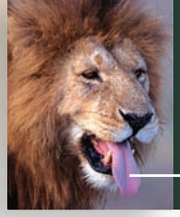
Most oxygen carried by hemoglobin remains in the blood and is available when needed. In addition, myoglobin molecules in muscle cells retain oxygen at lower partial pressures than hemoglobin and thus serve as an additional oxygen reserve.

Hemoglobin's affinity for oxygen is affected by pH and temperature.

The affinity of hemoglobin for oxygen decreases as pH decreases and as temperature increases (see figure 49.16). Therefore at lower pH and higher temperature, more oxygen is released.

Carbon dioxide is primarily transported as bicarbonate ion.

Most carbon dioxide diffuses into red blood cells and combines with water to form bicarbonate atoms in a reaction catalyzed by the enzyme carbonic anhydrase.



Review Questions

UNDERSTAND

1. If you hold your breath for a long time, body CO_2 levels are likely to ____, and the pH of body fluids is likely to ____.
   a. increase; increase
   b. decrease; increase
   c. increase; decrease
   d. decrease; decrease
2. Increased efficiency of gas exchange in vertebrates has been brought about by all of the following mechanisms except
   a. cutaneous respiration.
   b. unidirectional air flow.
   c. crosscurrent blood flow.
   d. cartilaginous rings in the trachea.
3. Which of the following is the primary method by which carbon dioxide is transported to the lungs?
   a. Dissolved in plasma
   b. Bound to hemoglobin
   c. As carbon monoxide
   d. As bicarbonate
4. Gills are found in
   a. fish.
   b. amphibians.
   c. aquatic invertebrates.
   d. all of these.
5. Fick's Law of Diffusion states the rate of diffusion is directly proportional to
   a. the area differences between the cross section of the blood vessel and the tissue.
   b. the pressure differences between the two sides of the membrane and area over which the diffusion occurs.
   c. the pressure differences between the inside of the organism and the outside.
   d. the temperature of the gas molecule.
6. Cutaneous respiration requires
   a. moist and highly vascularized skin.
   b. the absence of gills and lungs.
   c. an environment rich in oxygen.
   d. low temperatures.
7. Hyperventilation occurs
   a. as a result of breathing rapidly.
   b. when oxygen levels become low.
   c. when tidal volumes are unusually low.
   d. when the partial pressure of carbon dioxide is low.
8. Most carbon dioxide is
   a. dissolved in the plasma.
   b. bound to hemoglobin.
   c. combined with water in red blood cells to form carbonic acid.
   d. stored in the lungs prior to exhalation.

APPLY

1. When you take a deep breath, your stomach moves out because
   a. swallowing air increases the volume of the thoracic cavity.
   b. your stomach shouldn't move out when you take a deep breath because you want the volume of your chest cavity to increase, not your abdominal cavity.
   c. contracting your abdominal muscles pushes your stomach out, generating negative pressure in your lungs.
   d. when your diaphragm contracts, it moves down, pressing your abdominal cavity out.
2. Marine mammals are able to hold their breath for extended periods underwater because
   a. unlike humans, they don't hypoventilate.
   b. partial pressure of carbon dioxide does not increase underwater.
   c. myoglobin in muscle tissue provides an oxygen reserve.
   d. the brains of marine mammals do not have receptors that respond to impulses initiated in the aortic and carotid bodies.
3. Countercurrent flow systems do not occur in lungs because they
   a. require oxygen suspended in flowing water.
   b. are limited to fish.
   c. only work in moving organisms.
   d. cannot operate in the presence of carbon dioxide.
4. Respiratory organs of invertebrates and vertebrates are similar in that
   a. they use negative pressure breathing.
   b. they take advantage of countercurrent flow systems.
   c. they increase the surface area available for diffusion.
   d. the air flows through the organ in one direction.
5. Mountain climbers may have difficulty at high elevations because
   a. the partial pressure of oxygen is lower at higher elevations.
   b. more CO_2 occurs at higher altitudes.
   c. the concentration of all elements of the air is lower at higher elevations.
   d. cooler temperatures restrict the metabolic activity of oxygen at high elevations.
6. During exercise more oxygen is delivered to the muscles because
   a. active muscles produce more CO_2, lowering the pH of the blood.
   b. active muscles produce heat.
   c. both a and b
   d. neither a nor b

SYNTHESIZE

1. Compare the operation and efficiency of fish gills with amphibian, bird, and mammal lungs.
2. What happens when, during exercise, the oxygen needs of the peripheral tissues increase greatly?
3. Explain how bacteria, archaea, protists, and many phyla of invertebrates can survive without respiratory organs.

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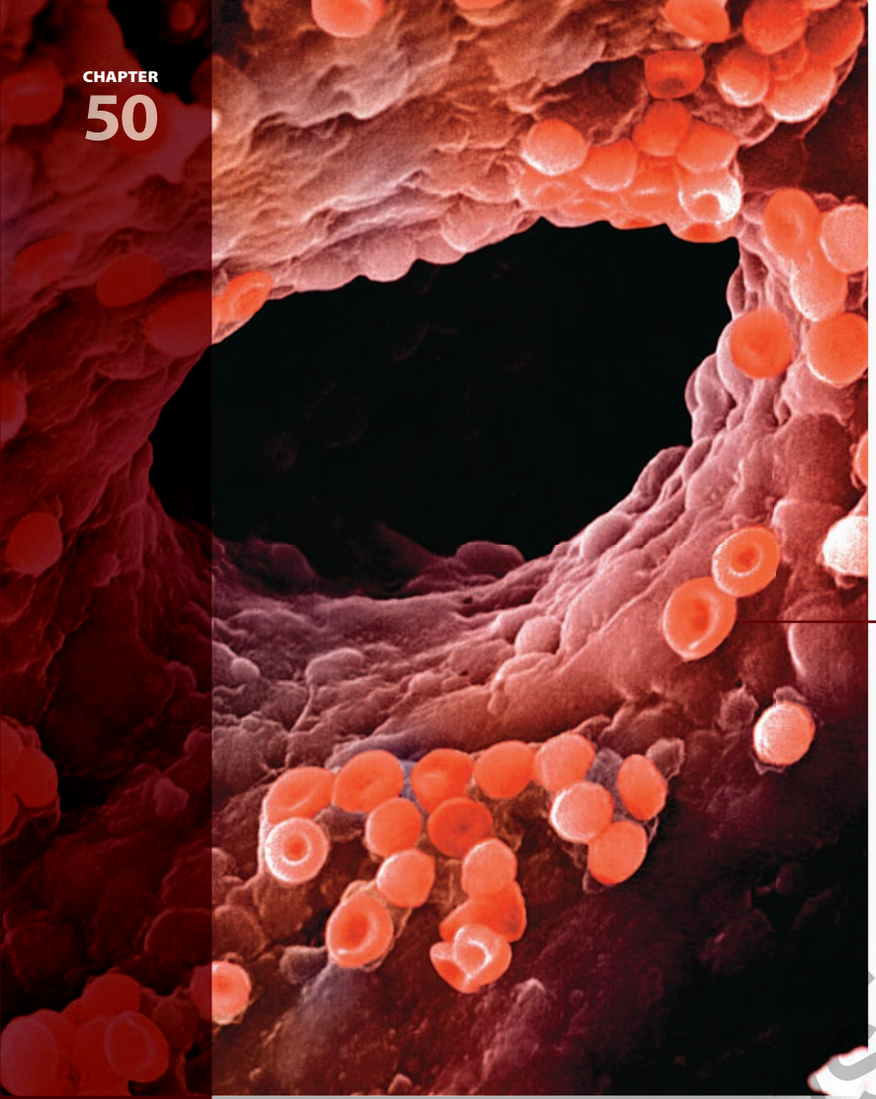


Chapter 50

The Circulatory System

Chapter Outline

Introduction

In multicellular organisms, oxygen obtained by the respiratory system and nutrients processed by the digestive system must be transported to cells throughout the body. Conversely, carbon dioxide and other waste products produced within the cells must be returned to the respiratory, digestive, and urinary systems for elimination from the body. These tasks are the responsibility of the circulatory system. All multicellular organisms have a heart that pumps fluids through the body. Many invertebrates have an open system in which fluids move through the body cavity. Vertebrates also have a system like this that moves lymph through the body; however, the primary circulatory fluid is blood, which means through a closed system of blood vessels.

50.1 The Components of Blood

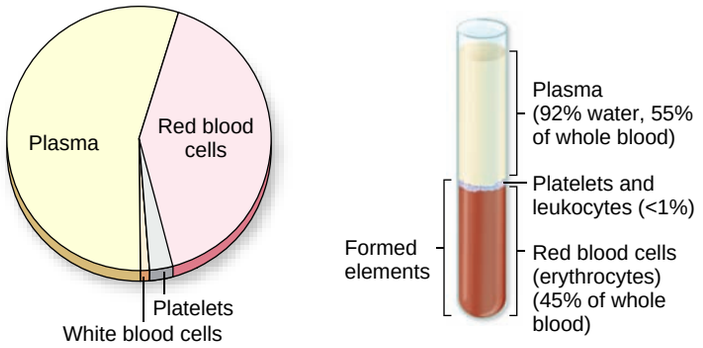
Learning Outcomes

1. *Describe the functions of circulating blood.*
2. *Distinguish between the types of formed elements.*
3. *Delineate the process of blood clotting.*

Blood is a connective tissue composed of a fluid matrix, called **plasma,** and several different kinds of cells and other **formed elements** that circulate within that fluid (figure 50.1). Blood **platelets,** although included in figure 50.1, are not complete cells; rather, they are fragments of cells that are produced in the bone marrow. (We describe the action of platelets in blood clotting later in this section.)

Circulating blood has many functions:

1. **Transportation.** All of the substances essential for cellular metabolism are transported by blood. Red blood cells transport oxygen attached to hemoglobin; nutrient molecules are carried in the plasma, sometimes bound to carriers; and metabolic wastes are eliminated as blood passes through the liver and kidneys.
2. **Regulation.** The cardiovascular system transports regulatory hormones from the endocrine glands and also



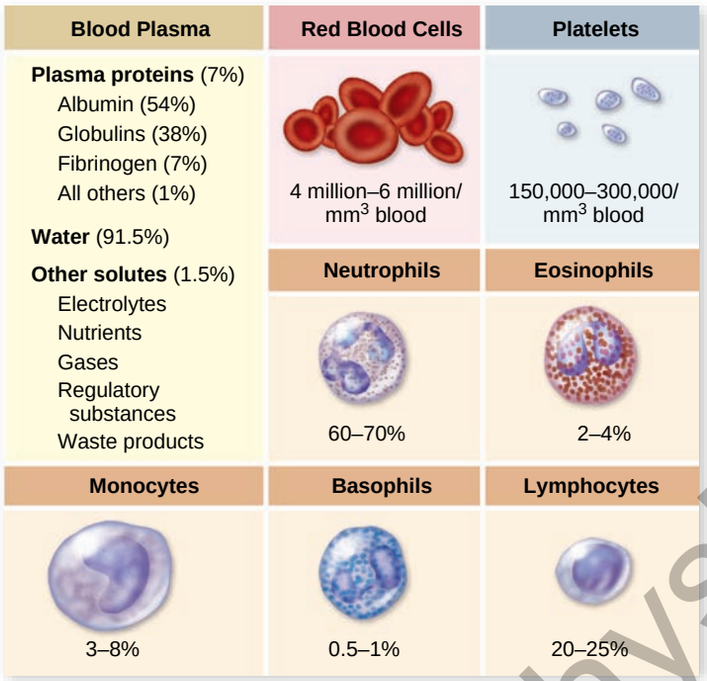


Figure 50.1 Composition of blood.

participates in temperature regulation. Contraction and dilation of blood vessels near the surface of the body, beneath the epidermis, helps to conserve or to dissipate heat as needed.

3. **Protection.** The circulatory system protects against injury and foreign microbes or toxins introduced into the body. Blood clotting helps to prevent blood loss when vessels are damaged. White blood cells, or leukocytes, help to disarm or disable invaders such as viruses and bacteria (see chapter 52).

Blood plasma is a fluid matrix

Blood plasma is the matrix in which blood cells and platelets are suspended. Interstitial (extracellular) fluids originate from the fluid present in plasma.

Although plasma is 92% water, it also contains the following solutes:

1. **Nutrients, wastes, and hormones.** Dissolved within the plasma are all of the nutrients resulting from digestive breakdown that can be used by cells, including glucose, amino acids, and vitamins. Also dissolved in the plasma are wastes such as nitrogen compounds and CO_2 produced by metabolizing cells. Endocrine hormones released from glands are also carried through the blood to their target cells.
2. **Ions.** Blood plasma is a dilute salt solution. The predominant plasma ions are Na^+, Cl^-, and bicarbonate ions (HCO_3^-). In addition, plasma contains trace amounts of other ions such as Ca^{2+}, Mg^{2+}, Cu^{2+}, K^+, and Zn^{2+}.
3. **Proteins.** As mentioned earlier, the liver produces most of the plasma proteins, including **albumin,** which constitutes most of the plasma protein; the alpha (α) and beta (β) **globulins,** which serve as carriers of lipids and steroid hormones; and **fibrinogen,** which is required for blood clotting. Blood plasma with the fibrinogen removed is called **serum.**

Formed elements include circulating cells and platelets

The formed elements of blood cells and cell fragments include red blood cells, white blood cells, and platelets. Each element has a specific function in maintaining the body's health and homeostasis.

Erythrocytes

Each microliter of blood contains about 5 million **red blood cells,** or **erythrocytes.** The fraction of the total blood volume that is occupied by erythrocytes is called the blood's *hematocrit;* in humans, the hematocrit is typically around 45%.

Each erythrocyte resembles a doughnut-shaped disk with a central depression that does not go all the way through. Mature mammalian erythrocytes lack nuclei. The erythrocytes of vertebrates contain hemoglobin, a pigment that binds and transports oxygen. (Hemoglobin was described more fully in the previous chapter when we discussed respiration.) In vertebrates, hemoglobin is found only in erythrocytes. In invertebrates, the oxygen-binding pigment (not always hemoglobin) is also present in plasma.

Leukocytes

Less than 1% of the cells in human blood are **white blood cells,** or **leukocytes;** there are only 1 or 2 leukocytes for every 1000 erythrocytes. Leukocytes are larger than erythrocytes and have nuclei. Furthermore, leukocytes are not confined to the blood as erythrocytes are, but can migrate out of capillaries through the intercellular spaces into the surrounding interstitial (tissue) fluid.

Leukocytes come in several varieties, each of which plays a specific role in defending against invading microorganisms and other foreign substances, as described in chapter 52. **Granular leukocytes** include neutrophils, eosinophils, and basophils, which are named according to the staining properties of granules in their cytoplasm. **Nongranular leukocytes** include monocytes and lymphocytes. In humans, neutrophils are the most numerous of the leukocytes, followed in order by lymphocytes, monocytes, eosinophils, and basophils.

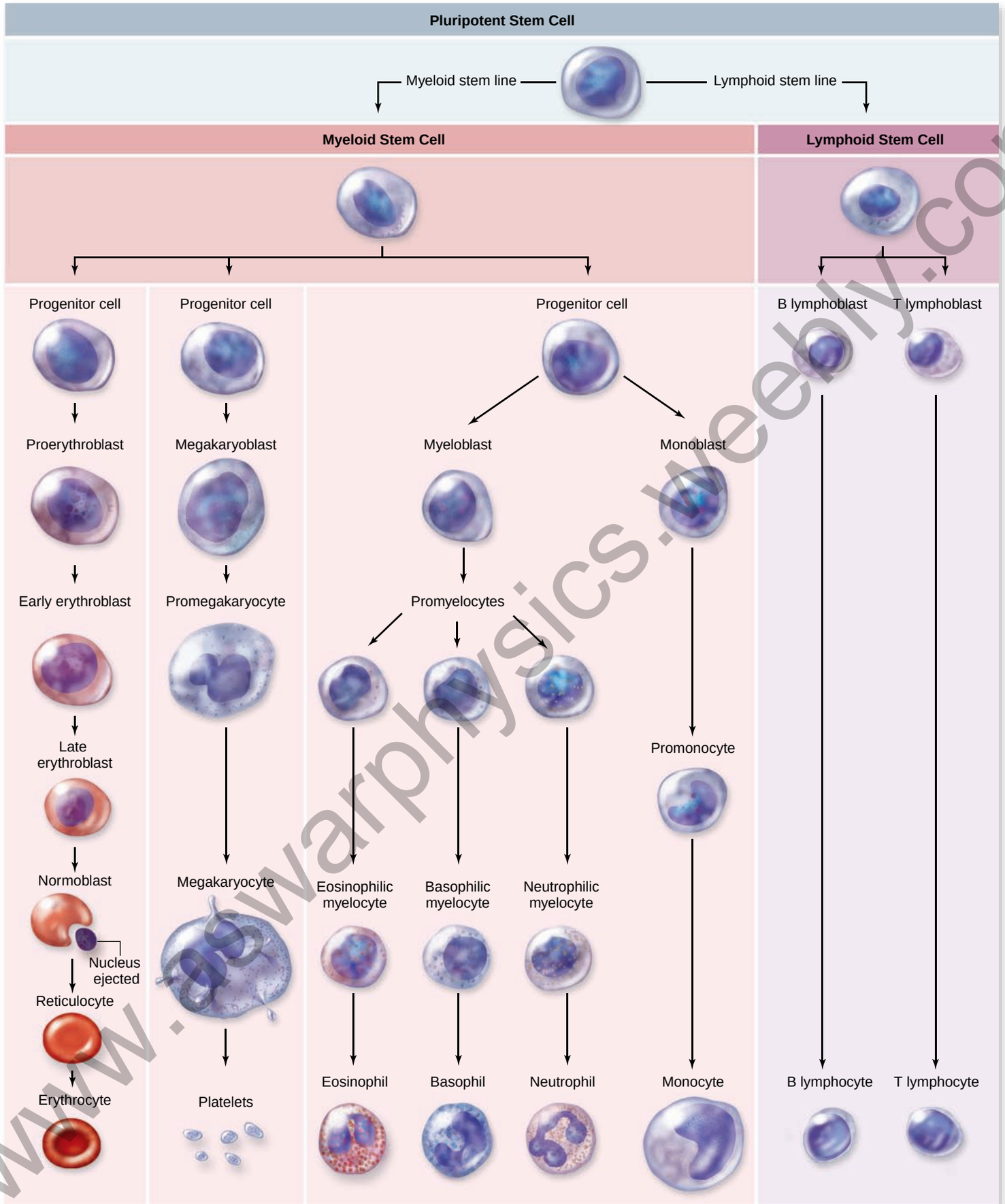


Figure 50.2 **Stem cells and the production of formed elements.**

Platelets

Platelets are cell fragments that pinch off from larger cells in the bone marrow. They are approximately 3 μm in diameter, and following an injury to a blood vessel, the liver releases *prothrombin* into the blood. In the presence of this clotting factor, fibrinogen is converted into insoluble threads of **fibrin.** Fibrin then aggregates to form the clot.

Formed elements arise from stem cells

The formed elements of blood each have a finite life span and therefore must be constantly replaced. Many of the old cell fragments are digested by phagocytic cells of the spleen; however, many products from the old cells, such as iron and amino acids, are incorporated into new formed elements. The creation of new formed elements begins in the bone marrow (see chapter 47).

All of the formed elements develop from **pluripotent stem cells** (see chapter 19). The production of blood cells occurs in the bone marrow and is called **hematopoiesis.** This process generates two types of stem cells with a more restricted fate: a lymphoid stem cell that gives rise to lymphocytes and a myeloid stem cell that gives rise to the rest of the blood cells (figure 50.2).

When the oxygen available in the blood decreases, the kidney converts a plasma protein into the hormone **erythropoietin.** Erythropoietin then stimulates the production of erythrocytes from the myeloid stem cells through a process called **erythropoiesis.**

In mammals, maturing erythrocytes lose their nuclei prior to release into circulation. In contrast, the mature erythrocytes of all other vertebrates remain nucleated. *Megakaryocytes* are examples of committed cells formed in bone marrow from stem cells. Pieces of cytoplasm are pinched off the megakaryocytes to form the platelets.

Inquiry question

Why do you think the use of erythropoietin as a drug is banned in the Olympics and in some other sports?

Blood clotting is an example of an enzyme cascade

When a blood vessel is broken or cut, smooth muscle in the vessel walls contracts, causing the vessel to constrict. Platelets then accumulate at the injured site and form a plug by sticking to one another and to the surrounding tissues (figure 50.3). A cascade of enzymatic reactions is triggered by the platelets, plasma factors, and molecules released from the damaged tissue.

One of the results of this cascade is that fibrinogen, normally dissolved in the plasma, comes out of solution in a reaction that forms fibrin. The platelet plug is then reinforced by fibrin threads, which contract to form a tighter mass. The tightening plug of platelets, fibrin, and often trapped erythrocytes constitutes a blood clot.

Once the tissue damage is healed, the careful process of dissolving the blot clot begins. This process is significant because if a clot breaks loose and travels in the circulatory system, it may end up blocking a blood vessel in the brain, causing a stroke, or in the heart, causing a heart attack.

Learning Outcomes Review 50.1

The circulatory system functions in transport of materials, regulation of temperature and body processes, and protection of the body. Formed elements in blood include red blood cells, white blood cells, and platelets. Blood clotting involves a cascade of enzymatic reactions triggered by platelets and plasma factors to produce insoluble fibrin from fibrinogen.

- ***How does a blood clot form?***

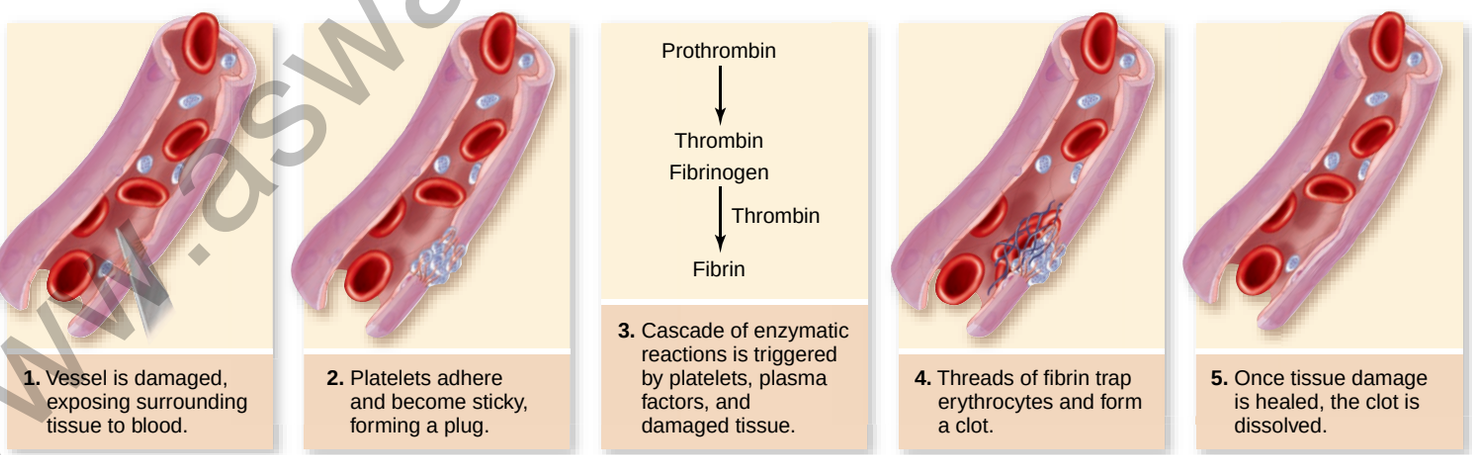


Figure 50.3 Blood clotting. Fibrin is formed from a soluble protein, fibrinogen, in the plasma. This reaction is catalyzed by the enzyme thrombin, which is formed from an inactive enzyme called prothrombin. The activation of thrombin is the last step in a cascade of enzymatic reactions that produces a blood clot when a blood vessel is damaged.

50.2 Invertebrate Circulatory Systems

Learning Outcomes

1. *Distinguish between open and closed circulatory systems.*
2. *Define hemolymph.*

The nature of the circulatory system in multicellular invertebrates is directly related to the size, complexity, and lifestyle of the organism in question. Sponges and most cnidarians utilize water from the environment as a circulatory fluid. Sponges pass water through a series of channels in their bodies, and *Hydra* and other cnidarians circulate water through a **gastrovascular cavity** (figure 50.4*a*). Because the body wall in *Hydra* species is only two cell layers thick, each cell layer is in direct contact with either the external environment or the gastrovascular cavity.

Pseudocoelomate invertebrates (roundworms, rotifers) use the fluids of the body cavity for circulation. Most of these invertebrates are quite small or are long and thin, and therefore adequate circulation is accomplished by movements of the body against the body fluids, which are in direct contact with the internal tissues and organs. Larger animals, however, have tissues that are several cell layers thick, so that many cells are

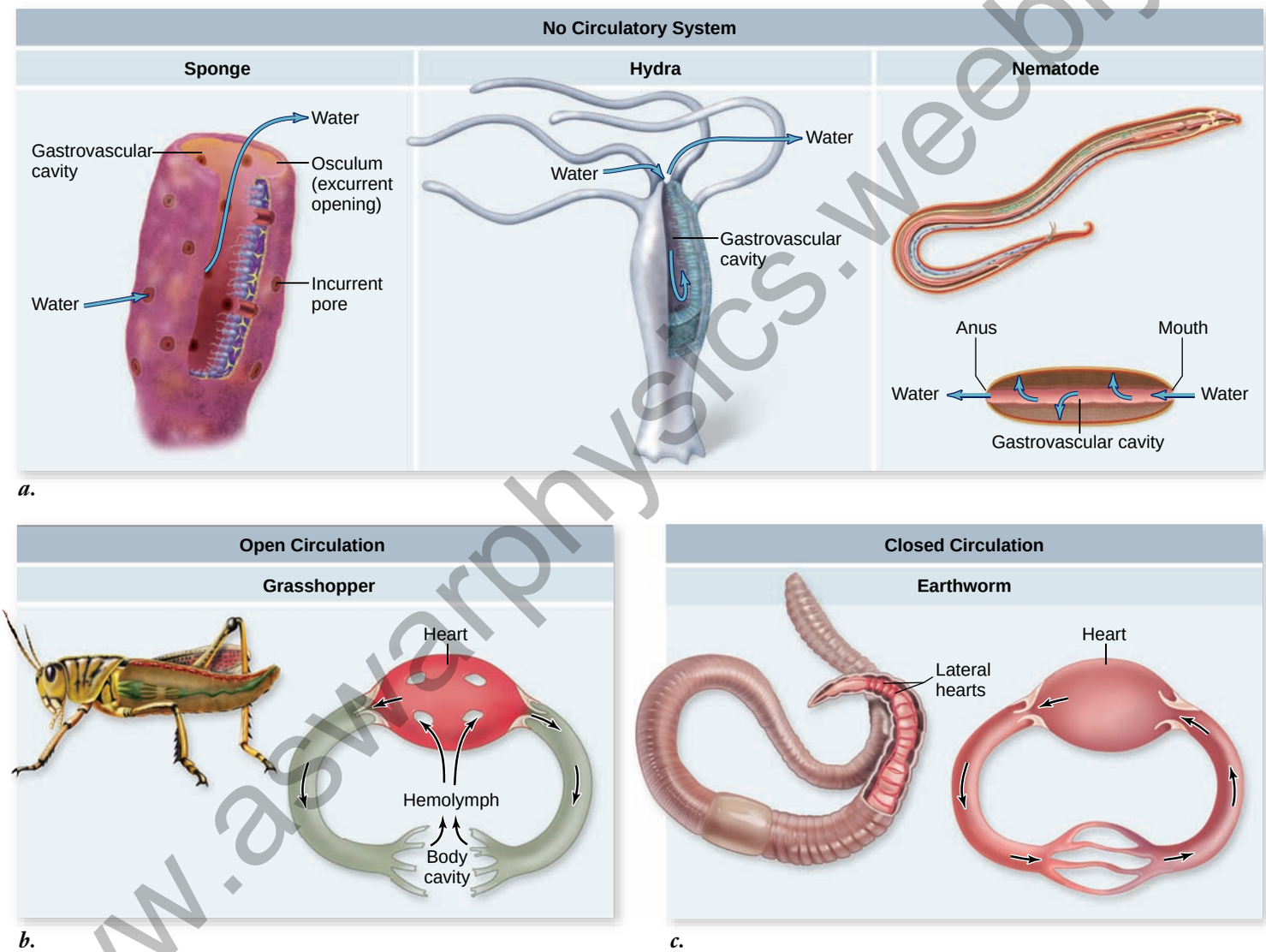


Figure 50.4 Circulatory systems of the animal kingdom. ***a.*** Sponges (left panel) do not have a separate circulatory system. They circulate water using many incurrent pores and one excurrent pore. The gastrovascular cavity of a hydra (middle panel) serves as both a digestive and a circulatory system, delivering nutrients directly to the tissue cells by diffusion from the digestive cavity. The nematode (right panel) is thin enough that the digestive tract can also be used as a circulatory system. Larger animals require a separate circulatory system to carry nutrients to and wastes away from tissues. ***b.*** In the open circulation of an insect, hemolymph is pumped from a tubular heart into cavities in the insect's body; the hemolymph then returns to the blood vessels so that it can be recirculated. ***c.*** In the closed circulation of the earthworm, blood pumped from the hearts remains within a system of vessels that returns it to the hearts. All vertebrates also have closed circulatory systems.

too far away from the body surface or digestive cavity to directly exchange materials with the environment. Instead, oxygen and nutrients are transported from the environment and digestive cavity to the body cells by an internal fluid within a circulatory system.

Open circulatory systems move fluids in a one-way path

The two main types of circulatory systems are *open* and *closed.* In an open circulatory system, such as that found in most mollusks and in arthropods (figure 50.4*b*), there is no distinction between the circulating fluid and the extracellular fluid of the body tissues. This fluid is thus called **hemolymph.**

In insects, a muscular tube, or **heart,** pumps hemolymph through a network of channels and cavities in the body. The fluid then drains back into the central cavity.

Closed circulatory systems move fluids in a loop

In a closed circulatory system, the circulating fluid, blood, is always enclosed within blood vessels that transport it away from and back to the heart (figure 50.4*c*). Some invertebrates, such as cephalopod mollusks and annelids (see chapter 34), and all vertebrates have a closed circulatory system.

In annelids such as earthworms, a dorsal vessel contracts rhythmically to function as a pump. Blood is pushed through five small connecting arteries, which also function as pumps, to a ventral vessel, which transports the blood posteriorly until it eventually reenters the dorsal vessel. Smaller vessels branch from each artery to supply the tissues of the earthworm with oxygen and nutrients and to remove waste products.

Learning Outcomes Review 50.2

In invertebrates, open circulatory systems pump hemolymph into tissues, from which it then drains into a central cavity. Closed circulatory systems move fluid in a loop to and from a muscular pumping region such as a heart. Hemolymph (invertebrates) is identical to the extracellular fluid in the tissues.

- ***In the open circulatory system of insects, how does hemolymph get back to the heart?***

50.3 *Vertebrate Circulatory Systems*

Learning Outcomes

1. ***Trace the evolution of the chambered heart from lancelets to birds and mammals.***
2. ***Delineate the flow of blood through the circulatory system in birds and mammals.***

The evolution of large and complex hearts and closed circulatory systems put a premium on efficient circulation. In response, vertebrates have evolved a remarkable set of adaptations inextricably linking circulation and respiration, which has facilitated diversification throughout aquatic and terrestrial habitats and permitted the evolution of large body size.

In fishes, more efficient circulation developed concurrently with gills

Chordates ancestral to the vertebrates are thought to have had simple tubular hearts, similar to those now seen in lancelets (see chapter 35). The heart was little more than a specialized zone of the ventral artery that was more heavily muscled than the rest of the arteries; it contracted in simple peristaltic waves.

The development of gills by fishes required a more efficient pump, and in fishes we see the evolution of a true chamber-pump heart. The fish heart is, in essence, a tube with four structures arrayed one after the other to form two pumping chambers (figure 50.5). The first two structures—the **sinus venosus** and **atrium**—form the first chamber; the second two, the **ventricle** and **conus arteriosus,** form the second chamber. The sinus venosus is the first to contract, followed by the atrium, the ventricle, and finally the conus arteriosus.

Despite shifts in the relative positions of these structures, this heartbeat sequence is maintained in all vertebrates. In fish, the electrical impulse that produces the contraction is initiated in the sinus venosus; in other vertebrates, the electrical impulse is initiated by a structure homologous to the sinus venosus—the **sinoatrial (SA) node.**

After blood leaves the conus arteriosus, it moves through the gills, becoming oxygenated. Blood leaving the gills then flows through a network of arteries to the rest of the body, finally returning to the sinus venosus. This simple loop has one serious limitation: in passing through the capillaries in the gills, blood pressure drops significantly. This slows circulation from the gills to the rest of the body and can limit oxygen delivery to tissues.

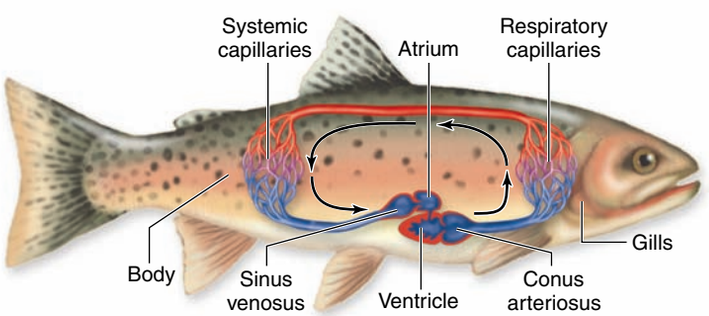


Figure 50.5 The heart and circulation of a fish. Diagram of a fish heart, showing the structures in series with each other (sinus venosus; atrium; ventricles; conus arteriosus) that form two pumping chambers. Blood is pumped by the ventricle through the gills and then to the body. Blood rich in oxygen (oxygenated) is shown in red; blood low in oxygen (deoxygenated) is shown in blue.

In amphibians and most reptiles, lungs required a separate circulation

The advent of lungs in amphibians (see chapter 49) involved a major change in the pattern of circulation, a second pumping circuit. After blood is pumped by the heart through the *pulmonary arteries* to the lungs, it does not go directly to the tissues of the body. Instead, it is returned via the *pulmonary veins* to the heart. Blood leaves the heart a second time to be circulated through other tissues. This system is termed **double circulation:** One system, the **pulmonary circulation,** moves blood between heart and lungs, and another, the **systemic circulation,** moves blood between the heart and the rest of the body.

Amphibian circulation

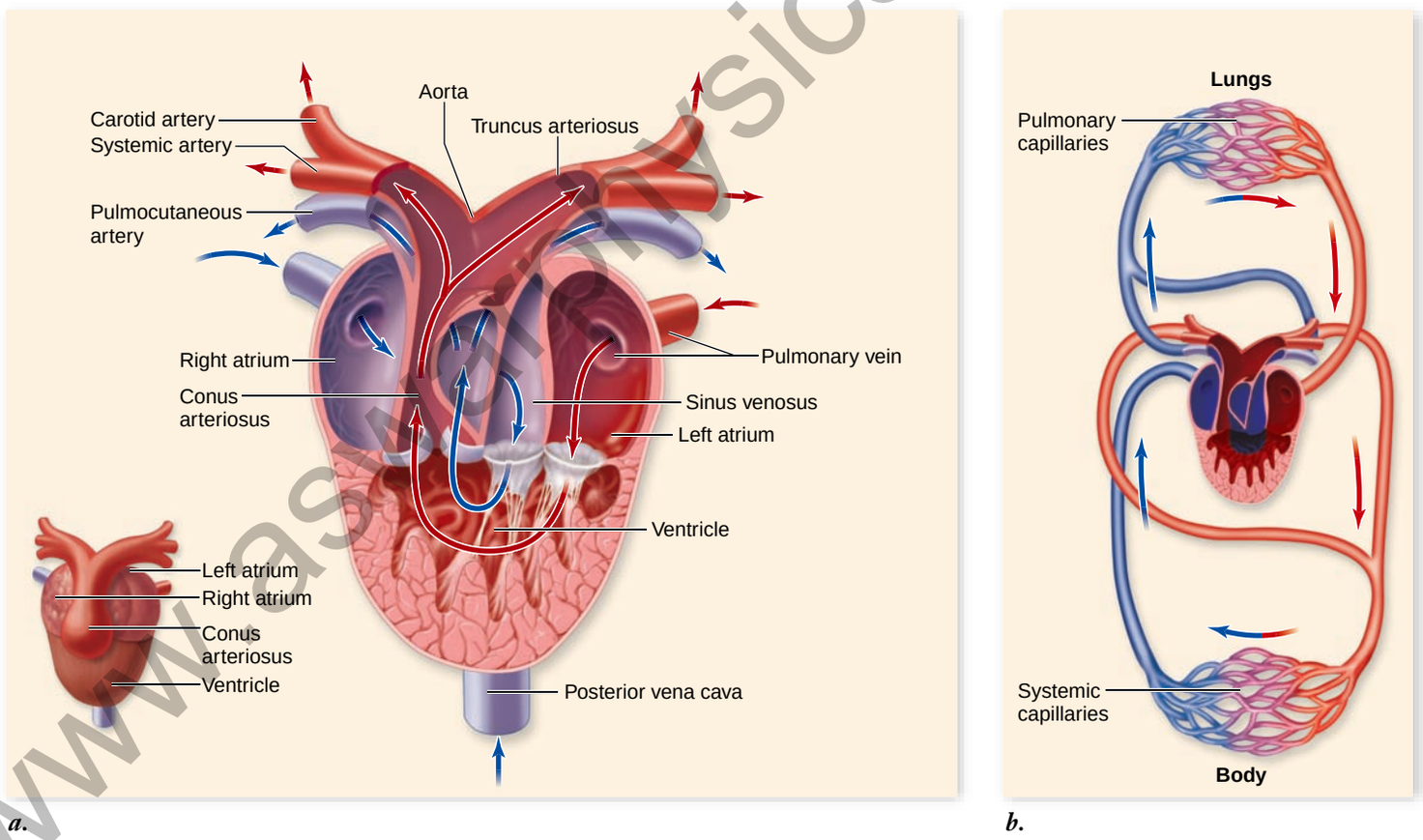
Optimally, oxygenated blood from lungs would go directly to tissues, rather than being mixed in the heart with deoxygenated blood returning from the body. The amphibian heart has two structural features that significantly reduce this mixing (figure 50.6). First, the atrium is divided into two chambers: The right atrium receives deoxygenated blood from the systemic circulation, and the left atrium receives oxygenated blood from the lungs. These two types of blood, therefore, do not mix in the atria.

Because an amphibian heart has a single ventricle, the separation of the pulmonary and systemic circulations is incomplete. The extent of mixing when the contents of each atrium enter the ventricle is reduced by internal channels created by recesses in the ventricular wall. The conus arteriosus is partially separated by a dividing wall, which directs deoxygenated blood into the pulmonary arteries and oxygenated blood into the *aorta*, the major artery of the systemic circulation.

Amphibians living in water can obtain additional oxygen by diffusion through their skin. Thus, amphibians have a *pulmocutaneous circuit* that sends blood to both the lungs and the skin. Cutaneous respiration is also seen in many aquatic reptiles such as turtles.

Reptilian circulation

Among reptiles, additional modifications have further reduced the mixing of blood in the heart. In addition to having two separate atria, reptiles have a septum that partially subdivides the ventricle. This separation is complete in one order of reptiles, the crocodilians, which have two separate ventricles divided by a complete septum (see the following section). Another change in the circulation of reptiles is that the conus arteriosus has become incorporated into the trunks of the large arteries leaving the heart.



a. *b.*

Figure 50.6 The heart and circulation of an amphibian. ***a.*** The frog has a three-chambered heart with two atria but only one ventricle, which pumps blood both to the lungs and to the body. ***b.*** Despite the potential for mixing, the oxygenated and deoxygenated bloods (red and blue lines, respectively) mix little as they are pumped to the body and lungs. Oxygenation of blood also occurs by gas exchange through the skin.

Mammals, birds, and crocodilians have two completely separated circulatory systems

Mammals, birds, and crocodilians have a four-chambered heart with two separate atria and two separate ventricles (figure 50.7). The hearts of birds and crocodiles exhibit some differences, but overall are quite similar, which is not surprising given their close evolutionary relationship (figure 50.8). However, the extreme similarity of the hearts of birds and mammals—so alike that a single illustration can suffice for both (see figure 50.7)—is a remarkable case of convergent evolution (see figure 50.8).

In a four-chambered heart, the right atrium receives deoxygenated blood from the body and delivers it to the right ventricle, which pumps the blood to the lungs. The left atrium receives oxygenated blood from the lungs and delivers it to the left ventricle, which pumps the oxygenated blood to the rest of the body (see figure 50.7).

The heart in these vertebrates is a two-cycle pump. Both atria fill with blood and simultaneously contract, emptying their blood into the ventricles. Both ventricles also contract at the same time, pushing blood simultaneously into the pulmonary and systemic circulations.

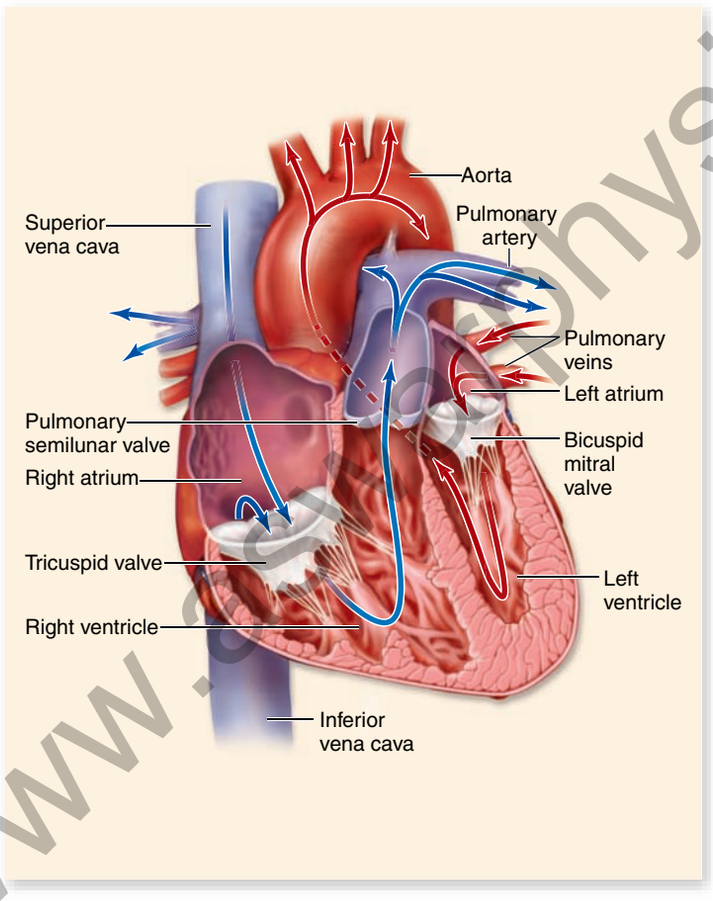
The increased efficiency of the double circulatory system in mammals and birds is thought to have been important in the evolution of endothermy. More efficient circulation is necessary to support the high metabolic rate required for maintenance of internal body temperature about a set point.

Throughout the evolutionary history of the vertebrate heart, the sinus venosus has served as a pacemaker, the site where the impulses that initiate the heartbeat originate. Although the sinus venosus constitutes a major chamber in the fish heart, it is reduced in size in amphibians and is further reduced in reptiles. In mammals and birds, the sinus venosus is no longer present as a separate chamber, although some of its tissue remains in the wall of the right atrium. This tissue, the sinoatrial (SA) node, is still the site where each heartbeat originates as detailed later in the chapter.

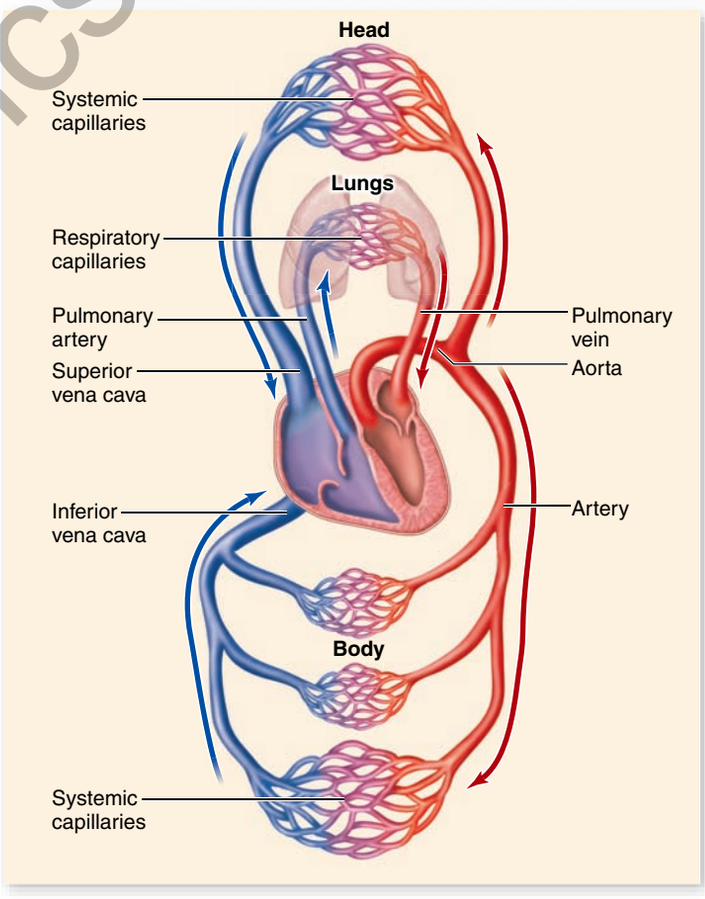
Learning Outcomes Review 50.3

The chordate heart has evolved from a muscular region of a vessel, to the two-chambered heart of fish, the three-chambered heart of amphibians and most reptiles, and the four-chambered heart of crocodilians, birds, and mammals. Deoxygenated blood travels in the pulmonary circuit from the right atrium into the right ventricle and then to the lungs; it returns to the left atrium. Oxygenated blood travels in the systemic circuit from the left atrium into the left ventricle and then to the body; it returns to the right atrium.

- ***What is the physiological advantage of having separated ventricles?***



a.



b.

Figure 50.7 The heart and circulation of mammals and birds. *a.* The path of blood through the four-chambered heart. *b.* The right side of the heart receives deoxygenated blood and pumps it to the lungs; the left side of the heart receives oxygenated blood and pumps it to the body. In this way, the pulmonary and systemic circulations are kept completely separate.

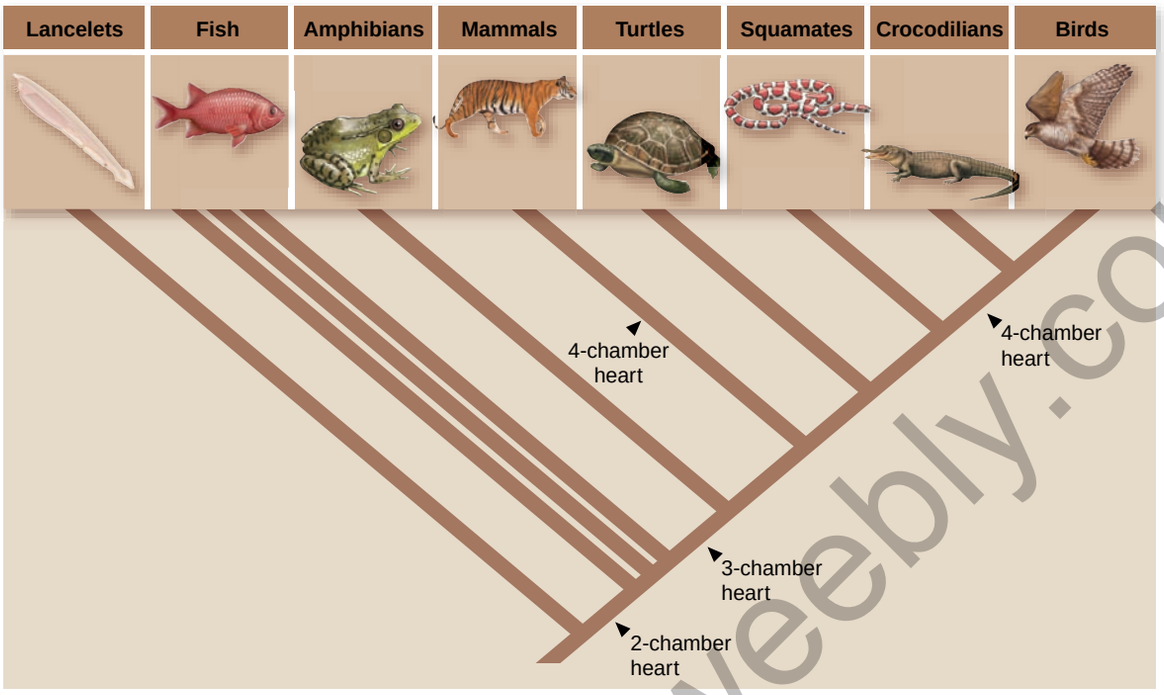


Figure 50.8
Evolution of the heart in vertebrates. Despite their similarity, the four-chambered hearts of mammals and birds evolved convergently.

50.4 The Four-Chambered Heart and the Blood Vessels

Learning Outcomes

1. *Explain the cardiac cycle.*
2. *Describe the role of autorhythmic cells of the SA node.*
3. *Define blood pressure and how it is measured*

As mentioned earlier, the heart of mammals, birds, and crocodilians goes through two contraction cycles, one of atrial contraction to send blood to the ventricles, and one of ventricular contraction to send blood to the pulmonary and systemic circuits. These two contractions plus the resting period between these make up the complete **cardiac cycle** encompassed by the heartbeat.

The cardiac cycle drives the cardiovascular system

The heart has two pairs of valves. One pair, the **atrioventricular (AV) valves,** maintains unidirectional blood flow between the atria and ventricles. The AV valve on the right side is the **tricuspid valve,** and the AV valve on the left is the **bicuspid,** or **mitral, valve.** Another pair of valves, together called the **semilunar valves,** ensure one-way flow out of the ventricles to the arterial systems. The **pulmonary valve** is located at the exit of the right ventricle, and the **aortic valve** is located at the exit of the left ventricle. These valves open and close as the heart goes through its cycle. The closing of these valves produces the "lub-dub" sounds heard with a stethoscope.

The cardiac cycle is portrayed in figure 50.9. It begins as blood returns to the resting heart through veins that empty into the right and left atria. As the atria fill and the pressure in them rises, the AV valves open and blood flows into the ventricles. The ventricles become about 80% filled during this time. Contraction of the atria tops up the final 20% of the 80 mL of blood the ventricles receive, on average, in a resting person. These events occur while the ventricles are relaxing, a period called ventricular **diastole.**

After a slight delay, the ventricles contract, a period called ventricular **systole.** Contraction of each ventricle increases the pressure within each chamber, causing the AV valves to forcefully close (the "lub" sound), preventing blood from backing up into the atria. Immediately after the AV valves close, the pressure in the ventricles forces the semilunar valves open and blood flows into the arterial systems. As the ventricles relax, closing of the semilunar valves prevents backflow (the "dub" sound).

Contraction of heart muscle is initiated by autorhythmic cells

As in other types of muscle, contraction of heart muscle is stimulated by membrane depolarization (see chapters 44 and 47). In skeletal muscles, only nerve impulses from motor neurons can normally initiate depolarization. The heart, by contrast, contains specialized "self-excitable" muscle cells called autorhythmic fibers, which can initiate periodic action potentials without neural activation.

The most important group of autorhythmic cells is the sinoatrial (SA) node, described earlier (figure 50.10). Located in the wall of the right atrium, the SA node acts as a pacemaker for the rest of the heart by producing spontaneous action potentials at a faster rate than other autorhythmic cells. These spontaneous action potentials are due to a constant leakage of Na^+ ions into the cell that depolarize the membrane. When the

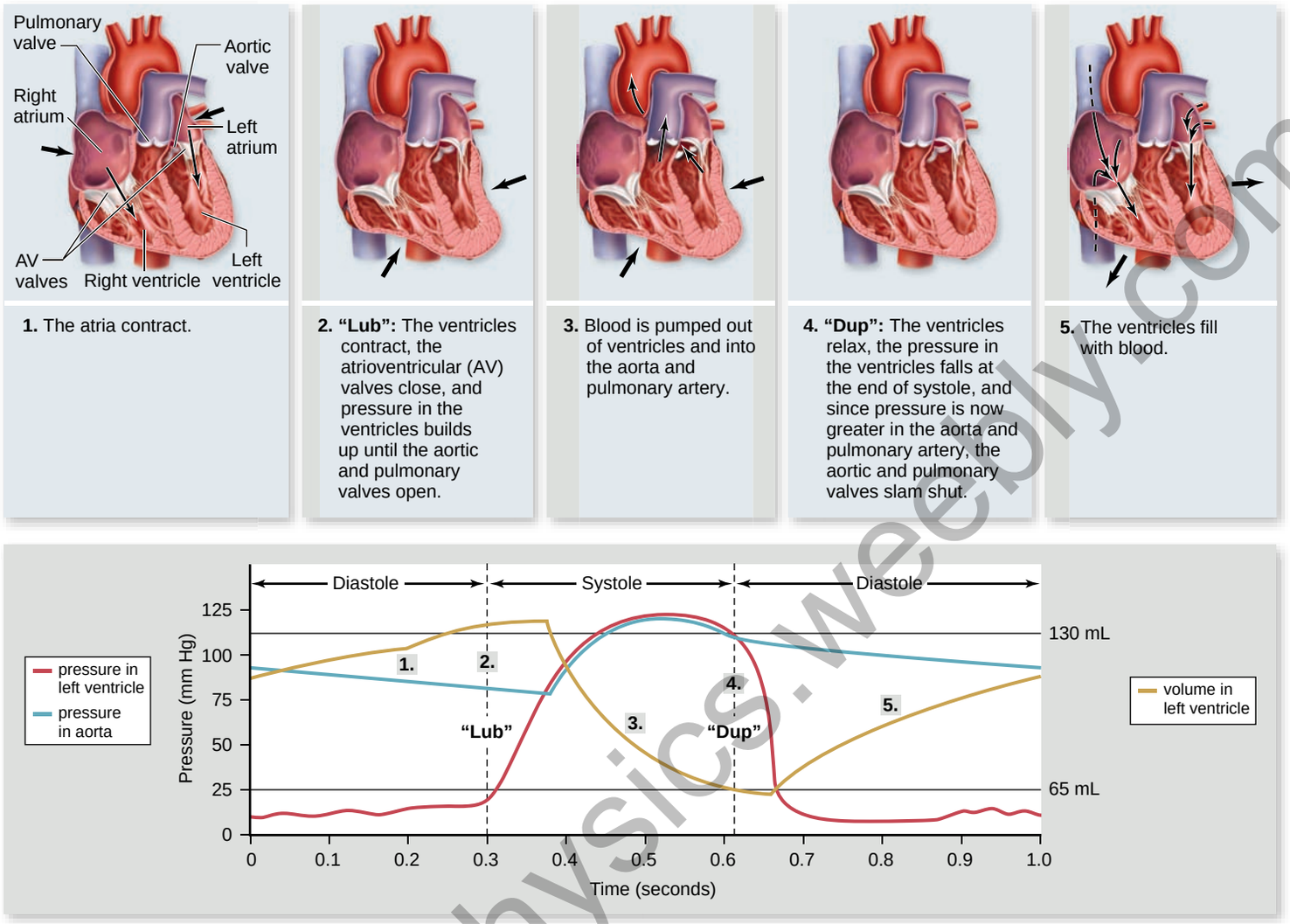


Figure 50.9 The cardiac cycle. *a.* Contraction and relaxation of the atria and ventricles moves blood through the heart. *b.* Blood pressure and volume changes through the cardiac cycle, shown here for the left ventricle.

threshold is reached, an action potential occurs. At the end of the action potential, the membrane is again below threshold and the process begins again. The cells of the SA node generate an action potential every 0.6 sec, equivalent to about 100 a minute. As we will see later in the chapter, the autonomic nervous system can modulate this rate.

Each depolarization initiated by this pacemaker is transmitted through two pathways: one to the cardiac muscle fibers of the left atrium, and the other to the right atrium and the atrioventricular (AV) node. Once initiated, depolarizations spread quickly from one muscle fiber to another in a wave that envelops the right and left atria nearly simultaneously. The rapid spread of depolarization is made possible because special conducting fibers are present and because the cardiac muscle cells are coupled by groups of gap junctions located within *intercalated disks* (see chapter 44).

A sheet of connective tissue separating the atria from the ventricles blocks the spread of excitation through muscle fibers from one chamber to the other. The AV node provides the only pathway for conduction of the depolarization from the atria to the ventricles. The fibers of the AV node slow down the conduction of the depolarizing signals, delaying the contraction of the ventricle by about 0.1 sec. This delay permits the atria to finish contracting and emptying their blood into the ventricles before the ventricles contract.

From the AV node, the wave of depolarization is conducted rapidly over both ventricles by a network of fibers called the atrioventricular bundle, or bundle of His. These fibers relay the depolarization to Purkinje fibers, which directly stimulate the myocardial cells of the left and right ventricles, causing their almost simultaneous contraction.

The stimulation of myocardial cells produces an action potential that leads to contraction. Contraction is controlled by Ca^{2+} and the troponin/tropomyosin system similar to skeletal muscle (see chapter 47), but the shape of the action potential is different. The initial rising phase due to an influx of Na^+ from voltage-gated Na^+ channels is followed by a plateau phase that leads to more sustained contraction. The plateau phase is due to the opening of voltage-gated Ca^{2+} channels. The resulting influx of Ca^{2+} keeps the membrane depolarized when the Na^+ channels inactivate. This, in turn, leads to more voltage-gated Ca^{2+} channels in the sarcoplasmic reticulum opening. The additional Ca^{2+} in the cytoplasm produces a more sustained contraction. The Ca^{2+} is

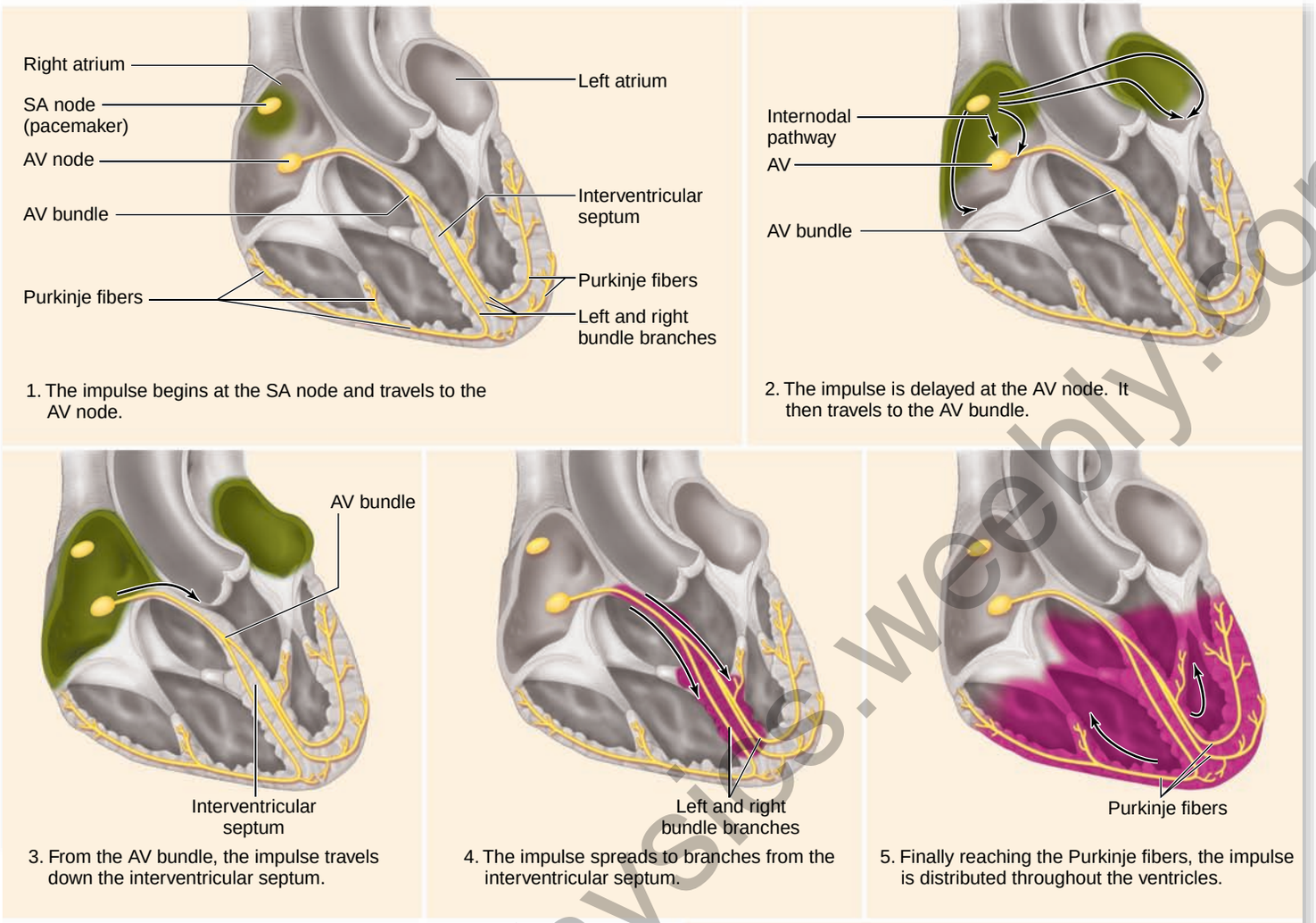


Figure 50.10 The path of electrical excitation in the heart. The events occurring during contraction of the heart are correlated with the measurement of electrical activity by an electrocardiogram (ECG also called EKG). The depolarization/contraction of the atrium is shown in green above and corresponds to the P wave of the ECG (also in green). The depolarization/contraction of the ventricle is shown in red above and corresponds to the QRS wave of the ECG (also in red). The T wave on the ECG corresponds to the repolarization of the ventricles. The atrial repolarization is masked by the QRS wave.

removed from the cytoplasm by a pump in the sarcoplasmic reticulum similar to skeletal muscle, and an additional carrier in the plasma membrane pumps Ca^{2+} into the interstitial space.

The electrical activity of the heart can be recorded from the surface of the body with electrodes placed on the limbs and chest. The recording, called an electrocardiogram (ECG or EKG), shows how the cells of the heart depolarize and repolarize during the cardiac cycle (see figure 50.10). Depolarization causes contraction of the heart, and repolarization causes relaxation.

The first peak in the recording, P, is produced by the depolarization of the atria, and is associated with atrial systole. The second, larger peak, QRS, is produced by ventricular depolarization; during this time, the ventricles contract (ventricular systole). The last peak, T, is produced by ventricular repolarization; at this time, the ventricles begin diastole.

Arteries and veins branch to and from all parts of the body

The right and left **pulmonary arteries** deliver oxygen-depleted blood from the right ventricle to the right and left lungs. As

previously mentioned, the **pulmonary veins** return oxygenated blood from the lungs to the left atrium of the heart.

The **aorta** and all its branches are systemic arteries, carrying oxygen-rich blood from the left ventricle to all parts of the body. The **coronary arteries** are the first branches off the aorta; these supply oxygenated blood to the heart muscle itself (see figure 50.7*b*). Other systemic arteries branch from the aorta as it makes an arch above the heart and as it descends and traverses the thoracic and abdominal cavities.

The blood from the body's organs, now lower in oxygen, returns to the heart in the systemic veins. These eventually empty into two major veins: the **superior vena cava,** which drains the upper body, and the **inferior vena cava,** which drains the lower body. These veins empty into the right atrium, completing the systemic circulation.

The flow of blood through the arteries, capillaries, and veins is driven by the pressure generated by ventricular contraction. The ventricles must contract forcefully enough to move the blood through the entire circulatory system.

Arterial blood pressure can be measured

As the ventricles contract, great pressure is generated within them and transferred through the arteries once the aortic valve opens. The pulse that you can detect in your wrist or neck results from changes in pressure as elastic arteries expand and contract with the periodic blood flow. Doctors use blood pressure as an general indicator of cardiovascular health because a variety of conditions can cause increases or decreases in pressure.

A *sphygmomanometer* measures the blood pressure in the brachial artery found on the inside part of the arm, above the elbow (figure 50.11). A cuff wrapped around the upper part of the arm is tightened enough to stop the flow of blood to the lower part of the arm. As the cuff is slowly loosened, eventually the blood pressure produced by the heart is greater than the constricting pressure of cuff and blood begins pulsating through the artery, producing a sound that can be detected using a stethoscope. The point at which this pulsing sound begins marks the peak pressure, or **systolic pressure,** at which ventricles are contracting. As the cuff is loosened further, the point is reached where the pressure of the cuff is lower than the blood pressure throughout the cardiac cycle, at which time the blood vessel is no longer distorted and the pulsing sound stops. This point marks the minimum pressure between heartbeats or **diastolic pressure,** at which the ventricles are relaxed.

The blood pressure is written as a ratio of systolic over diastolic pressure, and for a healthy person in his or her twenties, a typical blood pressure is 120/75 (measured in millimeters

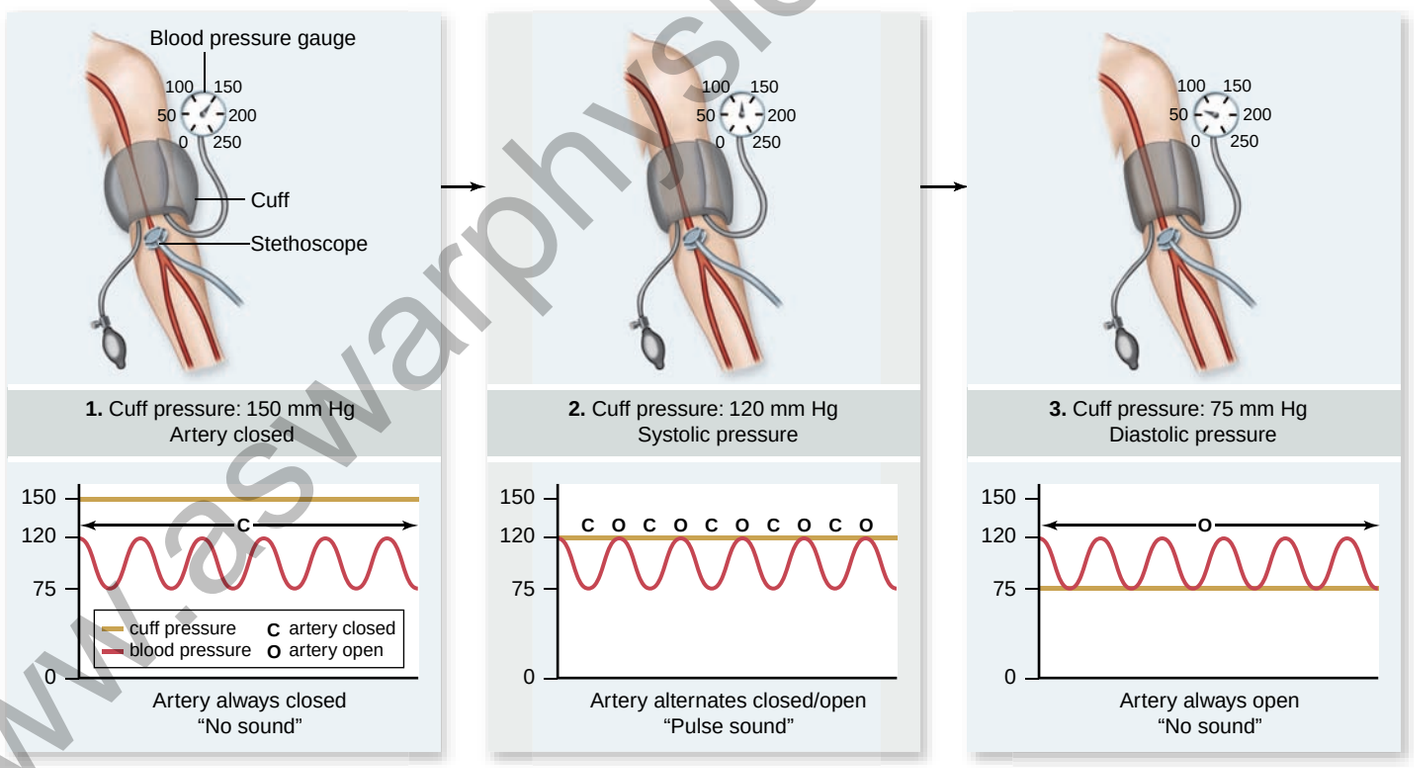


Figure 50.11 Measurement of blood pressure. The blood pressure cuff is tightened to stop the blood flow through the brachial artery. As the cuff is loosened, the maximal (systolic) pressure becomes greater than the cuff pressure and blood can momentarily pass through, producing a pulse that can be heard with a stethoscope. The pressure at this point is recorded as the systolic pressure. As the cuff pressure continues to drop, blood pressure is greater than cuff pressure for larger portions of the cardiac cycle. Eventually, even the minimum pressure during the cycle is greater than the cuff pressure, at which time the blood vessel is no longer distorted and silent laminar flow returns, replacing the pulsing sound. The diastolic pressure is recorded as the pressure at which a sound is no longer heard.

of mercury, or mm Hg). The medical condition called **hypertension** (high blood pressure) is defined as either a systolic pressure greater than 150 mm Hg or a diastolic pressure greater than 90 mm Hg.

Learning Outcomes Review 50.4

The cardiac cycle consists of systole and diastole; the ventricles contract at systole and relax at diastole. The SA node in the right atrium initiates waves of depolarization that stimulate first the atria and then travel to the AV node, which stimulates the ventricles. Blood pressure is expressed as the ratio of systolic pressure over diastolic pressure and is measured with a device called a sphygmomanometer.

- ***What would happen without a delay between auricular and ventricular contraction?***

50.5 *Characteristics of Blood Vessels*

Learning Outcomes

1. ***Describe the four tissue layers in blood vessels.***
2. ***Explain the distinctions among arteries, capillaries, and veins.***
3. ***Describe how the lympathic system operates.***

You already know that blood leaves the heart through vessels known as **arteries.** These continually branch, forming a hollow "tree" that enters each organ of the body. The finest, microscopic branches of the arterial tree are the **arterioles.** Blood from the arterioles enters the **capillaries,** an elaborate latticework of very narrow, thin-walled tubes. After traversing the capillaries, the blood is collected into microscopic **venules,** which lead to larger vessels called **veins,** and these carry blood back to the heart.

Larger vessels are composed of four tissue layers

Arteries, arterioles, veins, and venules all have the same basic structure (figure 50.12). The innermost layer is an epithelial sheet called the *endothelium.* Covering the endothelium is a thin layer of elastic fibers, a smooth muscle layer, and a connective tissue layer. The walls of these vessels, therefore, are thick enough to significantly reduce exchange of materials between the blood and the tissues outside the vessels.

The walls of capillaries, in contrast, are composed only of endothelium, so molecules and ions can leave the blood plasma by diffusion, by filtration through pores between the cells of the capillary walls, and by transport through the endothelial cells. Therefore, exchange of gases and metabolites between the blood and the interstitial fluids and cells of the body takes place through the capillaries.

Arteries and arterioles have evolved to withstand pressure

The larger arteries contain more elastic fibers in their walls than other blood vessels, allowing them to recoil each time they receive a volume of blood pumped by the heart. Smaller arteries and arterioles are less elastic, but their relatively thick smooth muscle layer enables them to resist bursting.

The narrower the vessel, the greater the frictional resistance to flow. In fact, a vessel that is half the diameter of another has *16 times* the frictional resistance. Resistance to blood flow is inversely proportional to the fourth power of the radius of the vessel. Therefore, within the arterial tree, the small arteries and arterioles provide the greatest resistance to blood flow.

Contraction of the smooth muscle layer of the arterioles results in **vasoconstriction,** which greatly increases resistance and decreases flow. Relaxation of the smooth muscle layer results in **vasodilation,** decreasing resistance and increasing blood flow to an organ. Chronic vasoconstriction of the arterioles can result in hypertension, or high blood pressure.

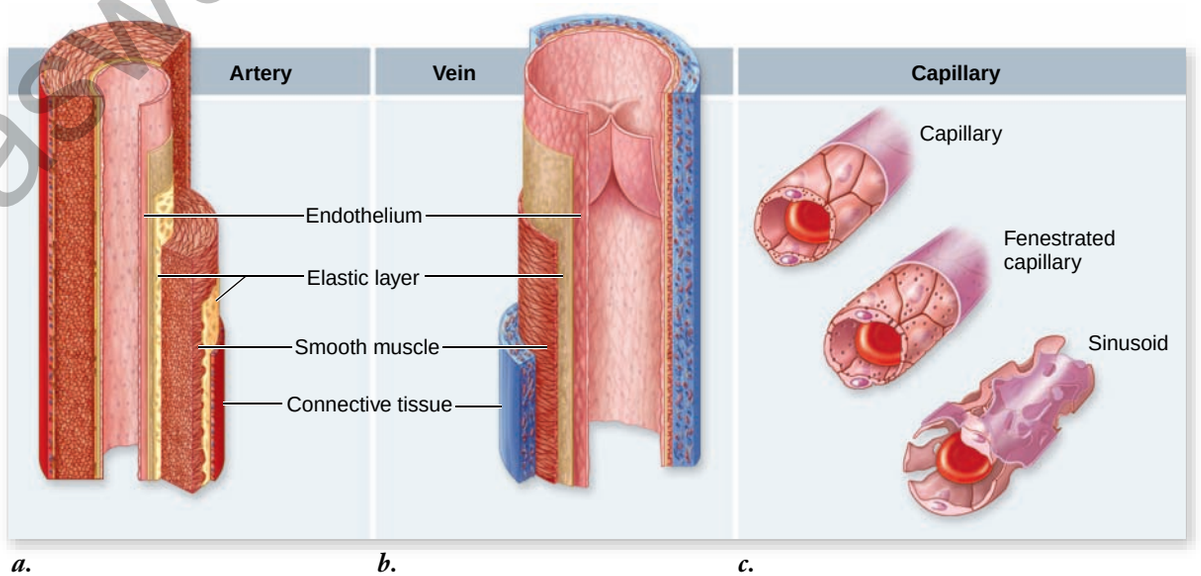


Figure 50.12 The structure of blood vessels. Arteries *(a)* and veins *(b)* have the same tissue layers, but the smooth muscle layer in arteries is much thicker and there are two elastic layers. *c.* Capillaries are composed of only a single layer of endothelial cells. (Not to scale.)

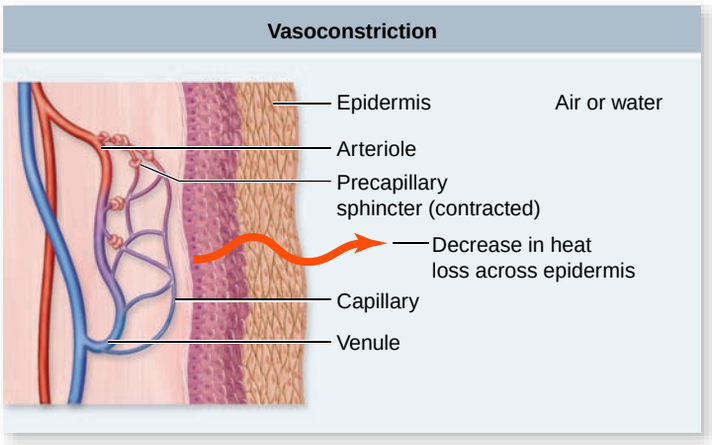


Figure 50.13 Regulation of heat exchange. The amount of heat gained or lost at the body's surface can be regulated by controlling the flow of blood to the surface. ***a.*** Constriction of surface blood vessels limits flow and heat loss when the animal is warmer than the surrounding air; when the animal is cooler than the surrounding air (not shown here), constriction minimizes heat gain; ***(b)*** dilation of these vessels increases flow and heat exchange.

Vasoconstriction and vasodilation are important means of regulating body heat in both ectotherms and endotherms (figure 50.13). By increasing blood flow to the skin, an animal can increase the rate of heat exchange, which is beneficial for gaining or losing heat. Conversely, shunting blood away from the skin is effective when an animal needs to minimize heat exchange, as might happen in cold weather.

Capillaries form a vast network for exchange of materials

The huge number and extensive branching of the capillaries ensure that every cell in the body is within 100 micrometers (μm) of a capillary. On the average, capillaries are about 1 mm long and 8 μm in diameter, this diameter is only slightly larger than a red blood cell (5 to 7 μm in diameter). Despite the close fit, normal red blood cells are flexible enough to squeeze through capillaries without difficulty.

The rate of blood flow through vessels is governed by hydrodynamics. The smaller the cross-sectional area of a vessel, the faster fluid moves through it. Given this, flow in the capillaries would be expected to be the fastest in the system. This would not be ideal for diffusion, and is actually not the case. Although each capillary is very narrow, so many of them exist that the capillaries have the greatest *total* cross-sectional area of any other type of vessel. Consequently, blood moving through capillaries goes more slowly and has more time to exchange materials with the surrounding extracellular fluid. By the time the blood reaches the end of a capillary, it has released some of its oxygen and nutrients and picked up carbon dioxide and other waste products. Blood loses pressure and velocity as it moves through the arterioles and capillaries, but as cross-sectional area decreases in the venous side, velocity increases.

Venules and veins have less muscle in their walls

Venules and veins have the same tissue layers as arteries, but they have a thinner layer of smooth muscle. Less muscle is needed because the pressure in the veins is only about one-tenth that in the arteries. Most of the blood in the cardiovascular system is contained within veins, which can expand to hold additional amounts of blood. You can see the expanded veins in your feet when you stand for a long time.

The venous pressure alone is not sufficient to return blood to the heart from the feet and legs, but several other sources of pressure provide help. Most significantly, skeletal muscles surrounding the veins can contract to move blood by squeezing the veins, a mechanism called the **venous pump.** Blood moves in one direction through the veins back to the heart with the help of **venous valves** (figure 50.14). When a

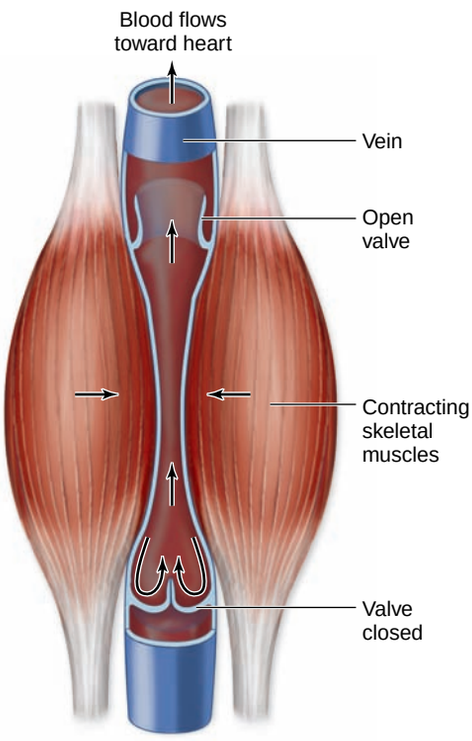


Figure 50.14 One-way flow of blood through veins. Venous valves ensure that blood moves through the veins in only one direction, back to the heart.

person's veins expand too much with blood, the venous valves may no longer work and the blood may pool in the veins. Veins in this condition are known as varicose veins.

The lymphatic system handles fluids that leave the cardiovascular system

The cardiovascular system is considered a closed system because all its vessels are connected with one another—none are simply open-ended. But a significant amount of water and solutes in the blood plasma filter through the walls of the capillaries to form the interstitial (tissue) fluid. Most of the fluid leaves the capillaries near their arteriolar ends, where the blood pressure is higher; it is returned to the capillaries near their venular ends (figure 50.15).

Fluid returns by osmosis (see chapter 5). Most of the plasma proteins cannot escape through the capillary pores because of their large size, and so the concentration of proteins in the plasma is greater than the protein concentration in the interstitial fluid. The difference in protein concentration produces an osmotic pressure gradient that causes water to move into the capillaries from the interstitial space.

High capillary blood pressure can cause too much interstitial fluid to accumulate. In pregnant women, for example, the enlarged uterus, carrying the fetus, compresses veins in the abdominal cavity, thereby adding to the capillary blood pressure in the woman's lower limbs. The increased interstitial fluid can cause swelling of the tissues, or **edema,** of the feet.

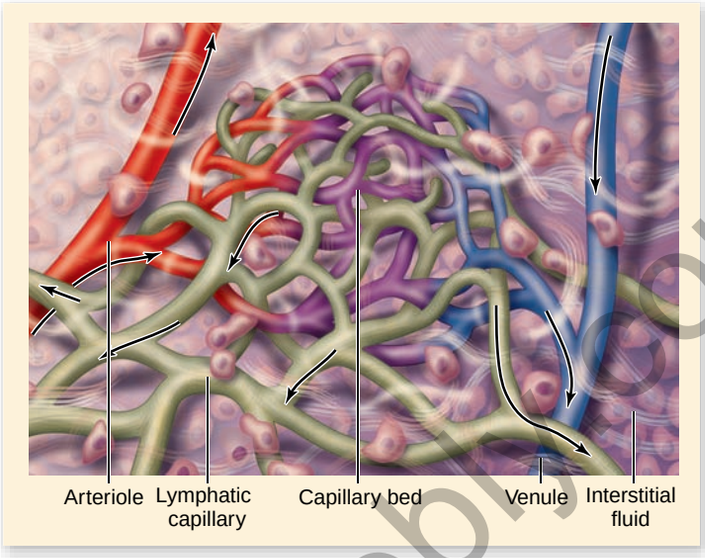
Edema may also result if the plasma protein concentration is too low. Fluids do not return to the capillaries, but remain as interstitial fluid. Low protein concentration in the plasma may be caused either by liver disease, because the liver produces most of the plasma proteins, or by insufficient dietary protein such as occurs in starvation.

Even under normal conditions, the amount of fluid filtered out of the capillaries is greater than the amount that returns to the capillaries by osmosis. The remainder does eventually return to the cardiovascular system by way of an open circulatory system called the **lymphatic system.**

The lymphatic system consists of lymphatic capillaries, lymphatic vessels, lymph nodes, and lymphatic organs, including the spleen and thymus. Excess fluid in the tissues drains into blind-ended lymph capillaries with highly permeable walls. This fluid, now called **lymph,** passes into progressively larger lymphatic vessels, which resemble veins and have one-way valves (similar to figure 50.14). The lymph eventually enters two major lymphatic vessels, which drain into the left and right subclavian veins located under the collarbones.

Movement of lymph in mammals results as skeletal muscles squeeze against the lymphatic vessels, a mechanism similar to the venous pump that moves blood through veins. In some cases, the lymphatic vessels also contract rhythmically. In many fishes, all amphibians and reptiles, bird embryos, and some adult birds, movement of lymph is propelled by **lymph hearts.**

As the lymph moves through lymph nodes and lymphatic organs, it is modified by phagocytic cells (see chapter 4) that line the channels of those organs. In addition, the lymph nodes



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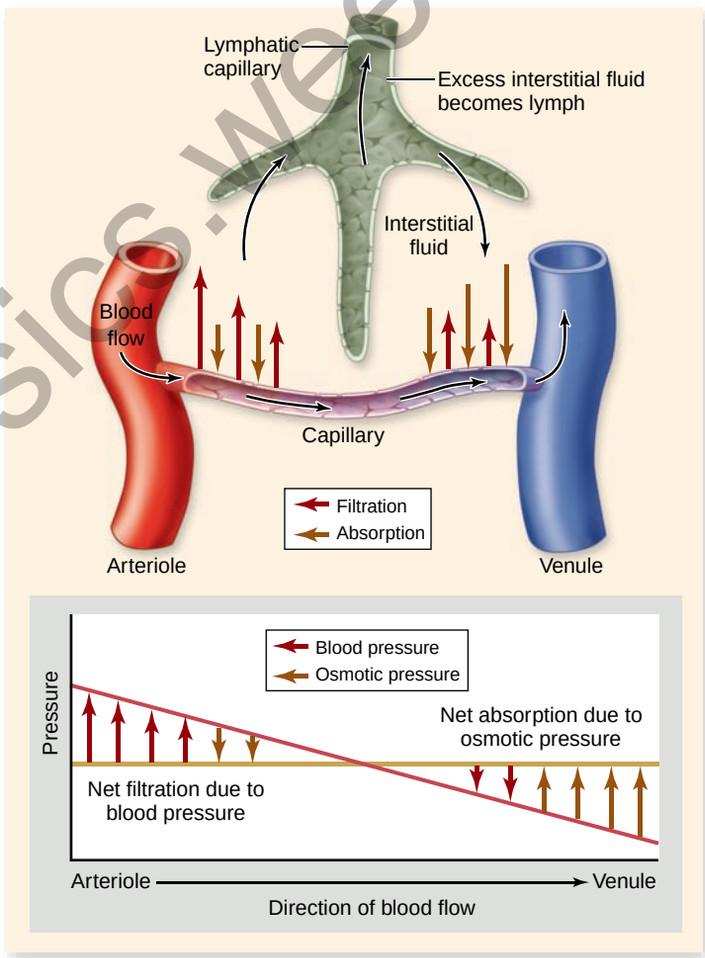


b.

Figure 50.15 Relationship between blood, lymph, and interstitial fluid. ***a.*** Vessels of the circulatory and lymphatic systems with arrows indicating the direction of flow of fluid in the vessels. ***b.*** Plasma fluid, minus proteins, is filtered out of capillaries, forming interstitial fluid that bathes tissues. Much of this fluid is returned to the capillaries by osmosis due to the higher protein concentration in plasma. Excess interstitial fluid drains into open-ended lymphatic capillaries, which ultimately return the fluid to the cardiovascular system.

and lymphatic organs contain *germinal centers*, where the activation and proliferation of lymphocytes occurs.

Cardiovascular diseases affect the delivery system

Cardiovascular diseases are the leading cause of death in the United States; more than 80 million people have some form of cardiovascular disease. Many disease conditions result from problems in arteries, such as blockage or rupture.

Atherosclerosis, or hardening of the arteries, is an accumulation within the arteries of fatty materials, abnormal amounts of smooth muscle, deposits of cholesterol or fibrin, or various kinds of cellular debris. These accumulations cause an increase in vascular resistance, which impedes blood flow (figure 50.16). The lumen (interior) of the artery may be further narrowed by a clot that forms as a result of the atherosclerosis. In the severest cases, the artery becomes completely blocked.

The accumulation of cholesterol in vessels is affected by a number of factors including total serum cholesterol and the levels of different cholesterol carrier proteins. Because cholesterol is not very water-soluble, it is carried in blood in the form of lipoprotein complexes. Two main forms are observed that differ in density: low-density lipoproteins (LDL) and high-density lipoproteins (HDL)—often called "bad cholesterol" and "good cholesterol," respectively. The reason for this is that HDLs tend to take cholesterol out of circulation, transporting it to the liver for elimination, and LDL is the carrier that brings cholesterol to all cells in the body. The problem arises when cells have enough cholesterol. This causes a reduction in the amount of LDL receptors, leading to high levels of circulating LDLs, which can end up being deposited in blood vessels.

Atherosclerosis is promoted by genetic factors, smoking, hypertension (high blood pressure), and the effects of cholesterol just discussed. Stopping smoking is the single most effective action a smoker can take to reduce the risk of atherosclerosis.

Arteriosclerosis occurs when calcium is deposited in arterial walls. It tends to occur when atherosclerosis is severe. Not only do such arteries have restricted blood flow, but they also lack the ability to expand as normal arteries do. This decrease in flexibility forces the heart to work harder because blood pressure increases to maintain flow.

Heart attacks (myocardial infarctions) are the main cause of cardiovascular deaths in the United States, accounting for about one-fifth of all deaths. Heart attacks result from an insufficient supply of blood to one or more parts of the heart muscle, which causes myocardial cells in those parts to die. Heart attacks may be caused by a blood clot forming somewhere in the coronary arteries and may also result if an artery is blocked by atherosclerosis. Recovery from a heart attack is possible if the portion of the heart that was damaged is small enough that the heart can still contract as a functional unit.

Angina pectoris, which literally means "chest pain," occurs for reasons similar to those that cause heart attacks, but it is not as severe. The pain may occur in the heart and often also in the left arm and shoulder. Angina pectoris is a warning sign that the blood supply to the heart is inadequate but is still sufficient to avoid myocardial cell death.

Strokes are caused by an interference with the blood supply to the brain. They may occur when a blood vessel bursts in the brain (hemorrhagic stroke), when blood flow in a cerebral artery is blocked by a blood clot or by atherosclerosis (ischemic stroke). The effects of a stroke depend on the severity of the damage and where in the brain the stroke occurs.

Learning Outcomes Review 50.5

The four layers of blood vessels are (1) endothelium, (2) an elastic layer, (3) smooth muscle, and (4) connective tissue. In contrast, capillaries have only endothelium. Arteries have more muscle in their walls than do veins to help withstand greater pressure; large arteries also have more elastic fibers for recoil. Excess interstitial fluid, called lymph, is returned to the cardiovascular system via the lymphatic system, a one-way system.

- ***What is the connection between the lymphatic and circulatory systems?***

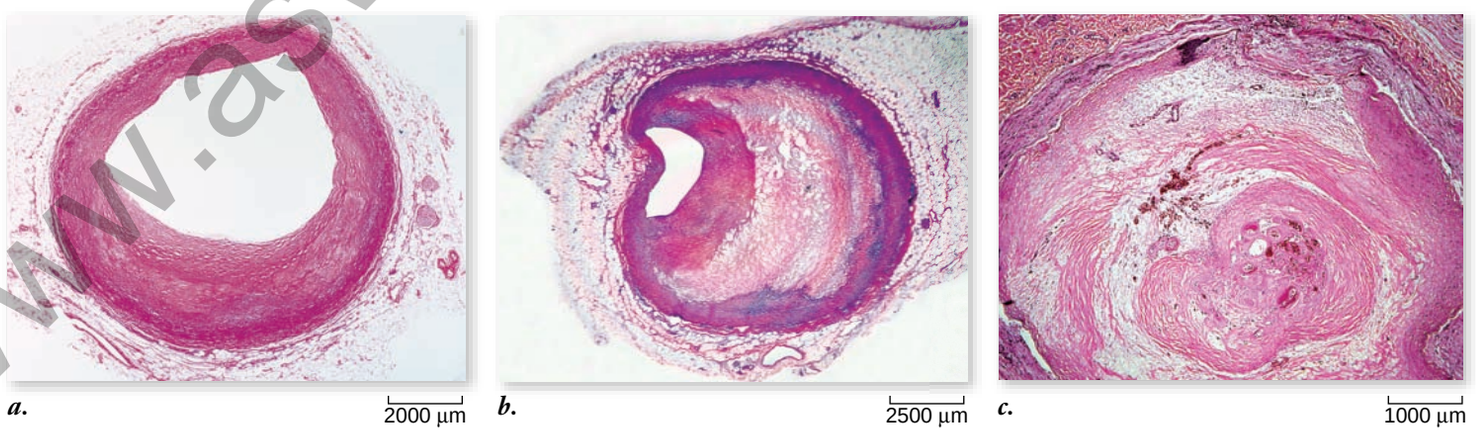


Figure 50.16 Atherosclerosis. *a.* The coronary artery shows only minor blockage. *b.* The artery exhibits severe atherosclerosis—much of the passage is blocked by buildup on the interior walls of the artery. *c.* The coronary artery is essentially completely blocked.

50.6 Regulation of Blood Flow and Blood Pressure

Learning Outcomes

1. *Describe how exertion affects cardiac output.*
2. *Explain how hormones regulate blood volume.*

Although the autonomic nervous system does not initiate the heartbeat, it does modulate its rhythm and force of contraction. In addition, several mechanisms regulate characteristics of the cardiovascular system, including cardiac output, blood pressure, and blood volume.

The nervous system may speed up or slow down heart rate

Heart rate is under the control of the autonomic nervous system. The cardiac center of the medulla oblongata (a part of the hindbrain; see chapter 44) consists of two neuronal centers that modulate heart rate. The **cardioacceleratory center** sends signals by way of the sympathetic cardiac accelerator nerves to the SA node, AV node, and myocardium. These nerves secrete norepinephrine, which increases the heart rate. Sympathetic nervous system stimulation can also increase contractility of the heart muscle itself, thus ejecting more blood per contraction (stroke volume).

The **cardioinhibitory center** sends signals via the parasympathetic fibers in the vagus nerve to the SA and AV nodes. The vagus nerve secretes acetylcholine, which inhibits the development of action potentials and so slows the heart down.

Cardiac output increases with exertion

Cardiac output is the volume of blood pumped by each ventricle per minute. It is calculated by multiplying the heart rate by the *stroke volume*, which is the volume of blood ejected by each ventricle per beat. For example, if the heart rate is 72 beats per minute and the stroke volume is 70 mL, the cardiac output is 5 L/min, which is about average in a resting human.

Cardiac output increases during exertion because of an increase in both heart rate and stroke volume. When exertion begins, such as running, the heart rate increases up to about 100 beats per minute to provide more oxygen to cells in the body. As movement becomes more intense, skeletal muscles squeeze on veins more vigorously, returning blood to the heart more rapidly. In addition, the ventricles contract more strongly, so they empty more completely with each beat.

During exercise, the cardiac output increases to a maximum of about 25 L/min in an average young adult. Although the cardiac output has increased fivefold, not all organs receive five times the blood flow; some receive more, others less. Arterioles in some organs, such as in the digestive system, constrict, while the arterioles in the working muscles and heart dilate.

The baroreceptor reflex maintains homeostasis in blood pressure

The arterial blood pressure (BP) depends on two factors: the cardiac output (CO) and the resistance (R) to blood flow in the vascular system. This relationship can be expressed as:

$$BP = CO \times R$$

An increased blood pressure, therefore, could be produced by an increase in either heart rate or blood volume (because both increase the cardiac output), or by vasoconstriction, which increases the resistance to blood flow. Conversely, blood pressure falls if the heart rate slows or if the blood volume is reduced—for example, by dehydration or excessive bleeding (hemorrhage).

Changes in arterial blood pressure are detected by **baroreceptors** located in the arch of the aorta and in the carotid arteries (see chapter 46). These sensors are stretch receptors sensitive to expansion and contraction of arteries. When the baroreceptors detect a fall in blood pressure, the number of impulses to the cardiac center is decreased, resulting in increased sympathetic stimulation and decreased parasympathetic stimulation of the heart and other targets. This increases heart rate and stroke volume to amplify cardiac output. This also causes vasoconstriction of blood vessels in the skin and viscera, raising resistance. These combine to increase blood pressure, closing the feedback loop in this direction (figure 50.17, top).

When baroreceptors detect a rise in blood pressure, the number of impulses to the cardiac center is increased. This has the opposite effect of decreasing sympathetic stimulation and increasing parasympathetic simulation of the heart. This lowers heart rate and stroke volume to reduce cardiac output. The cardiac center also sends signals causing vasodilation of blood vessels in the skin and viscera, lowering resistance. These combine to decrease blood pressure closing the feedback loop in this direction. Thus, the baroreceptor reflex forms a negative feedback loop responding to changes in blood pressure (figure 50.17, bottom).

Blood volume is regulated by hormones

Blood pressure depends in part on the total blood volume because this can affect the cardiac output. A decrease in blood volume decreases blood pressure, if all else remains equal. Blood volume regulation involves the effects of four hormones: (1) antidiuretic hormone, (2) aldosterone, (3) atrial natriuretic hormone, and (4) nitric oxide.

Antidiuretic hormone (ADH), also called **vasopressin,** is secreted by the posterior-pituitary gland in response to an increase in the osmolarity of the blood plasma (see chapter 46). Dehydration, for example, causes the blood volume to decrease. Osmoreceptors in the hypothalamus promote thirst and stimulate ADH secretion from the posterior pituitary gland. ADH, in turn, stimulates the kidneys to retain more water in the blood, excreting less in the urine. A dehydrated person thus drinks more and urinates less, helping to raise the blood volume and restore homeostasis.

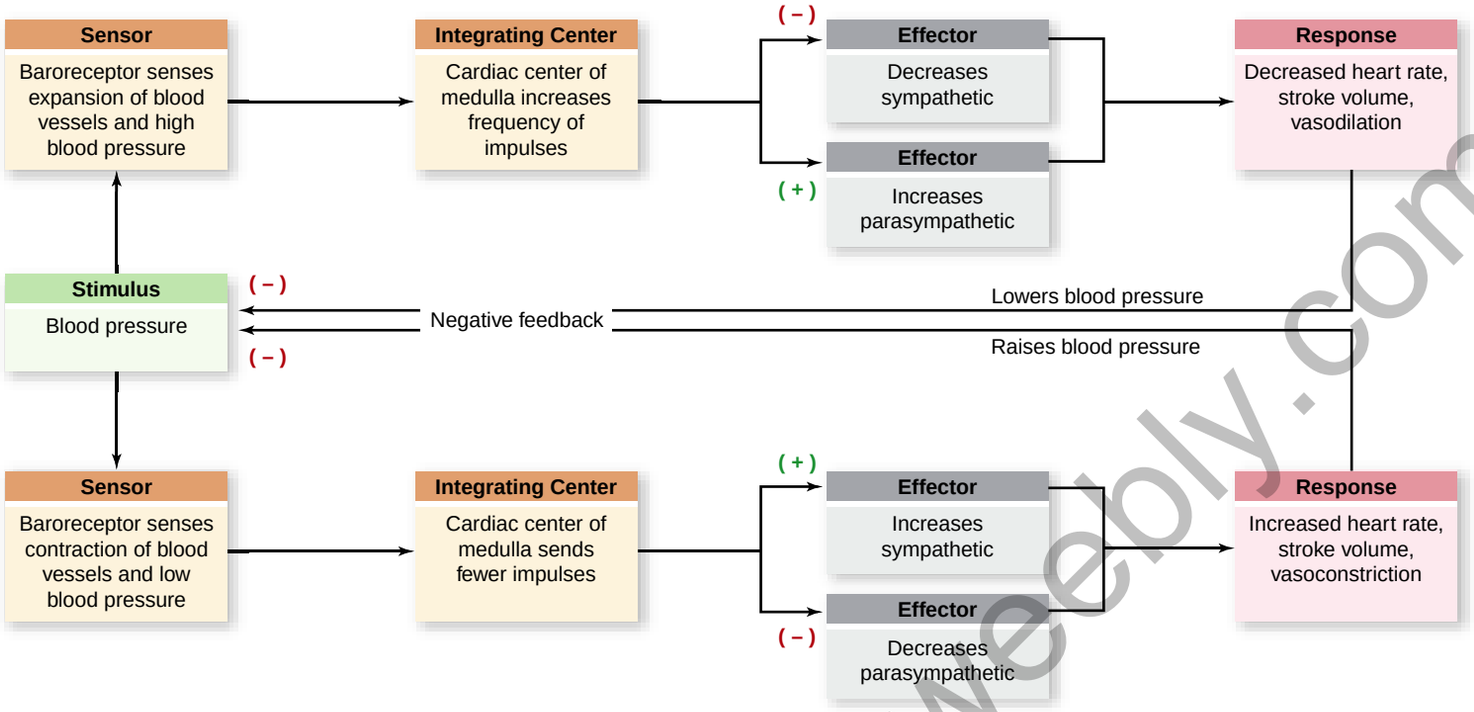


Figure 50.17 Baroreceptor negative feedback loops control blood pressure. Baroreceptors form the afferent portion of a feedback loop controlling blood pressure. The frequency of nerve impulses from these stretch receptors correlates with blood pressure. This information is processed in the cardiac center of the medulla. The efferent portion of the loop involves sympathetic and parasympathetic nerves that innervate the heart. This control can raise or lower heart rate and stroke volume to raise and lower blood pressure in response to baroreceptors signaling.

Whenever the kidneys experience a decreased blood flow, a group of kidney cells initiate the release of an enzyme known as renin into the blood. Renin activates a blood protein, angiotensin, which stimulates vasoconstriction throughout the body while stimulating the adrenal cortex to secrete **aldosterone.** This steroid hormone acts on the kidneys to promote the retention of Na^+ and water in the blood (see chapter 46).

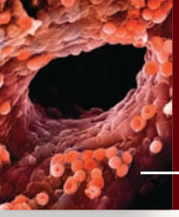
When excess Na^+ is present, less aldosterone is secreted by the adrenals, so that less Na^+ is retained by the kidneys. Na^+ excretion in the urine is promoted by another hormone, **atrial natriuretic hormone.** This hormone is secreted by the right atrium of the heart in response to stretching caused by an increased blood volume. The action of atrial natriuretic hormone completes a negative feedback loop, lowering the blood volume and pressure.

Nitric oxide (NO) is a gas produced by endothelial cells of blood vessels. As described in chapter 46, it is one of a number of paracrine regulators of blood vessels. In solution, NO passes outward through the cell layers of the vessel, causing the smooth muscles that encase it to relax and the blood vessels to dilate (become wider). For over a century, heart patients have been prescribed nitroglycerin to relieve chest pain, but only now has it become clear that nitroglycerin acts by releasing nitric oxide.

Learning Outcomes Review 50.6

Cardiac output is the heart rate times the heart's stroke volume. As exertion increases, cardiac output increases to meet the body's demands. Blood pressure depends on cardiac output and the resistance to blood flow due to constriction of the arteries. The blood volume is regulated by antidiuretic hormone, aldosterone, and atrial natriuretic hormone; nitric oxide causes vasodilation that lessens resistance.

- ***What are the connections between regulation of heart rate and breathing rate?***



Chapter Review

50.1 The Components of Blood

Blood plasma is a fluid matrix.

Plasma is 92% water plus nutrients, hormones, ions, plasma proteins, and wastes (see figure 50.1).

Formed elements include circulating cells and platelets.

Blood cells include erythrocytes (red cells), leukocytes (white cells), and platelets. Erythrocytes contain hemoglobin for oxygen transport, and leukocytes are part of the immune system. Platelets help initiate blood clotting (see figure 50.3).

Formed elements arise from stem cells.

Blood cells are derived from pluripotent stem cells in bone marrow by hematopoiesis (see figure 50.2).

Blood clotting is an example of an enzyme cascade.

Upon initiation of clotting, fibrinogen, normally dissolved in the plasma, is turned into fibrin, an insoluble protein, via an enzyme cascade. As a wound heals, the clot must be dissolved.

50.2 Invertebrate Circulatory Systems

Open circulatory systems move fluids in a one-way path.

Sponges pass water through channels, and cnidarians circulate water through a gastrovascular cavity. Small animals can use body cavity fluids for circulation.

Closed circulatory systems move fluids in a loop.

Closed systems have a distinct circulatory fluid, such as blood, enclosed in vessels and transported in a loop.

50.3 Vertebrate Circulatory Systems

In fishes, more efficient circulation developed concurrently with gills.

Fishes have a linear heart with two pumping chambers to increase efficiency of blood flow through the gills; from the gills, the blood moves into the rest of the body (see figure 50.5).

In amphibians and most reptiles, lungs required a separate circulation.

Pulmonary circulation pumps blood to the lungs, and systemic circulation pumps blood to the body.

Amphibian hearts have two atria that separate blood flow to the lungs and body, and a single ventricle (figure 50.6). The heart of most reptiles has a septum that partially divides the ventricle, reducing mixing of blood from the atria.

Mammals, birds, and crocodilians have two completely separated circulatory systems.

The four-chambered heart has two ventricles (see figure 50.7). The extreme similarity between the heart of mammals and birds is an example of convergent evolution.

50.4 The Four-Chambered Heart and the Blood Vessels

The cardiac cycle drives the cardiovascular system.

The unidirectional flow of blood through the heart is maintained by two atrioventricular valves (see figure 50.9). During diastole ventricles relax and atria contract; during systole ventricles contract.

Contraction of heart muscle is initiated by autorhythmic cells.

Contraction is initiated by the SA node, a natural pacemaker, and impulses then travel to the AV node (see figure 50.10).

Arteries and veins branch to and from all parts of the body.

Arteries and arterioles carry oxygenated blood to the body; veins and venules return deoxygenated blood to the heart (see figure 50.7).

Arterial blood pressure can be measured.

A sphygmomanometer measures the peak (systolic) and minimum (diastolic) blood pressure. Blood pressure is expressed as the ratio of systolic to diastolic.

50.5 Characteristics of Blood Vessels

Larger vessels are composed of four tissue layers.

Arteries and veins consist of endothelium, elastic fibers, smooth muscle, and connective tissues (see figure 50.12). Capillaries have only one layer of endothelium.

Arteries and arterioles have evolved to withstand pressure.

Arteries and arterioles have thicker muscular layer and more elastic fibers to control blood flow and to recoil with changes in blood pressure.

Capillaries form a vast network for exchange of materials.

Capillaries are the region of the circulatory system where exchange takes place with the body's tissues (see figure 50.13).

Venules and veins have less muscle in their walls.

The return of blood to the heart through veins is facilitated by skeletal muscle contractions and one-way valves (see figure 50.14).

The lymphatic system handles fluids that leave the cardiovascular system.

Fluid from plasma filters out of capillaries, then returns via the separate, one-way lymphatic system (see figure 50.15). The lymphatic system connects with the blood circulation at the subclavian veins.

Cardiovascular diseases affect the delivery system.

Atherosclerosis is an accumulation of fatty materials in arteries; it is one cause of a heart attack, which results from an insufficient supply of blood to heart muscle. Strokes are caused by blockage of the blood supply to the brain.

50.6 Regulation of Blood Flow and Blood Pressure

The nervous system may speed up or slow down heart rate.

Norepinephrine from sympathetic neurons increases heart rate; acetylcholine from parasympathetic neurons decreases the rate.

Cardiac output increases with exertion.

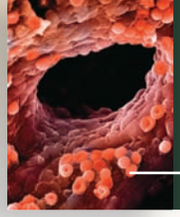
Both heart rate and stroke volume increase with exertion.

The baroreceptor reflex maintains homeostasis in blood pressure.

Arterial blood pressure is monitored by baroreceptors in the aortic arch and carotid arteries, which relay impulses to the cardiac center (see figure 50.17).

Blood volume is regulated by hormones.

Blood volume regulation and arterial resistance involves the effects of four hormones: (1) antidiuretic hormone, (2) aldosterone, (3) atrial natriuretic hormone, and (4) nitric oxide.



Review Questions

UNDERSTAND

1. An ECG measures
   a. changes in electrical potential during the cardiac cycle.
   b. Ca^{2+} concentration of the ventricles in diastole.
   c. the force of contraction of the atria during systole.
   d. the volume of blood being pumped during the contraction cycle.
2. Systole is vitally important to heart function and begins in the heart with the
   a. activation of the AV node.
   b. activation of the SA node.
   c. opening of the voltage-gated potassium gates.
   d. opening of the semilunar valves.
3. Which of the following is the correct sequence of events in the circulation of blood?
   a. Heart ⟶ arteries ⟶ arterioles ⟶ capillaries ⟶ venules ⟶ lymph ⟶ heart
   b. Heart ⟶ arteries ⟶ arterioles ⟶ capillaries ⟶ veins ⟶ venules ⟶ heart
   c. Heart ⟶ arteries ⟶ arterioles ⟶ capillaries ⟶ venules ⟶ veins ⟶ heart
   d. Heart ⟶ arterioles ⟶ arteries ⟶ capillaries ⟶ venules ⟶ veins ⟶ heart
4. Which of the following statements is not true?
   a. Only arteries carry oxygenated blood.
   b. Both arteries and veins have a layer of smooth muscle.
   c. Both arteries and veins branch out into capillary beds.
   d. Precapillary sphincters regulate blood flow through capillaries.
5. The lymphatic system is like the circulatory system in that they both
   a. have nodes that filter out pathogens.
   b. have a network of arteries.
   c. have capillaries.
   d. are closed systems.
6. Which pairing of structure and function is incorrect?
   a. Erythrocytes: oxygen transport
   b. Platelets: blood clotting
   c. Plasma: waste transport
   d. All of these are correct.
7. When a sphygmomanometer is used,
   a. blood pulses through the vein when systolic pressure is greater than the pressure caused by the cuff.
   b. pulsing ceases when blood pressure falls below the systolic pressure.
   c. blood does not move through the vein when cuff pressure is greater than maximal blood pressure.
   d. cuff pressure stops decreasing when it equals systolic pressure.

APPLY

1. In vertebrate hearts, atria contract from the top, and ventricles contract from the bottom. How is this accomplished?
   a. Depolarization from the SA node proceeds across the atria from the top; depolarization from the AV node is carried to the bottom of the ventricles before it emanates over ventricular tissue.
   b. The depolarization from the SA node is initiated from motor neurons coming down from our brain; depolarization from the AV node is initiated from motor neurons coming up from our spinal cord.
   c. Gravity carries the depolarization from the SA node down from the top of the heart; contraction of the diaphragm forces depolarization from the AV node from the bottom up.
   d. This statement is false; both contract from the bottom.
2. A molecule of CO_2 that is generated in the cardiac muscle of the left ventricle would *not* pass through which of the following structures before leaving the body?
   a. Right atrium
   b. Left atrium
   c. Right ventricle
   d. Left ventricle
3. Blood clots are made of
   a. fibrin.
   b. fibrinogen.
   c. prothrombin.
   d. all of these.
4. The difference between the amphibian and mammal hearts is that
   a. in the amphibian heart, oxygenated and deoxygenated blood mix completely in the single ventricle.
   b. in the amphibian heart, there are two SA nodes so that contractions occur simultaneously throughout the heart.
   c. in the ventricle in the amphibian heart, internal channels reduce mixing of blood.
   d. in the amphibian heart, only the left aorta pumps oxygen obtained by diffusion through the skin.
5. Contraction of the smooth muscle layers of the arterioles
   a. increases the frictional resistance to blood flow.
   b. may be a way of increasing heat exchange through the skin.
   c. can increase blood flow to an organ.
   d. includes all of the above.

SYNTHESIZE

1. Humans have a number of mechanisms that help to maintain blood pressure, particularly when it falls too low. Explain how the kidney and the endocrine systems help to maintain blood pressure.
2. What is the difference among blood, lymph, and hemolymph?
3. Is the evolution of the four-chambered heart related to the evolution of endothermy?
4. What do you think are the clinical symptoms indicating that a person requires the surgical implantation of a mechanical pacemaker?

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Chapter 51

Osmotic Regulation and the Urinary System

Chapter Outline

Introduction

The majority of your body weight is actually water, but you exist in a very dehydrating environment. The kangaroo rat pictured lives in a desert environment that is even more dehydrating and yet is so parsimonious with water that it never needs to drink; it generates sufficient water as a by-product of oxidizing its food. Fish can exist in both freshwater and marine environments, facing the challenge of either gaining or losing water, respectively. Life in these different environments is possible because elaborate mechanisms enable organisms to control the osmotic strength of their blood and extracellular fluids. The regulation of internal fluid and its composition is an example of homeostasis—the ability of living organisms to maintain internal conditions within an optimal range. In this chapter, we describe the osmoregulatory systems of a number of animals, including the mammalian urinary system. These organ systems maintain the water and ionic balance of fluids in the body.

51.1 Osmolarity and Osmotic Balance

Learning Outcomes

1. *Explain the importance of osmotic balance.*
2. *Describe how organisms are classified based on their method of osmotic regulation.*

Water in a multicellular animal's body is distributed between the intracellular and extracellular compartments (figure 51.1). To maintain osmotic balance, the extracellular compartment of an animal's body (including its blood plasma) must be able to take water from the environment and to excrete excess water into the environment. Inorganic ions must also be exchanged between the extracellular body fluids and the external environment to maintain homeostasis. Exchanges of water and electrolytes between the body and the external environment occur across specialized epithelial cells and, in most vertebrates, through a filtration process in the kidneys.