

42

Circulation and Gas Exchange



▲ **Figure 42.1** How does a feathery fringe help this animal survive?

KEY CONCEPTS

- 42.1 Circulatory systems link exchange surfaces with cells throughout the body
- 42.2 Coordinated cycles of heart contraction drive double circulation in mammals
- 42.3 Patterns of blood pressure and flow reflect the structure and arrangement of blood vessels
- 42.4 Blood components function in exchange, transport, and defense
- 42.5 Gas exchange occurs across specialized respiratory surfaces
- 42.6 Breathing ventilates the lungs
- 42.7 Adaptations for gas exchange include pigments that bind and transport gases

OVERVIEW

Trading Places

The animal in **Figure 42.1** may look like a creature from a science fiction film, but it's actually an axolotl, a salamander native to shallow ponds in central Mexico. The feathery red appendages jutting out from the head of this albino adult are gills. Although external gills are uncommon in adult animals, they help satisfy the need shared by all animals to exchange substances with their environment.

Exchange between an axolotl or any other animal and its surroundings ultimately occurs at the cellular level. The resources that animal cells require, such as nutrients and oxygen (O_2), enter the cytoplasm by crossing the plasma membrane. Metabolic by-products, such as carbon dioxide (CO_2), exit the cell by crossing the same membrane. In unicellular organisms, exchange occurs directly with the external environment. For most multicellular organisms, however, direct transfer of materials between every cell and the environment is not possible. Instead, these organisms rely on specialized systems that carry out exchange with the environment and that transport materials between sites of exchange and the rest of the body.

The reddish color and branching structure of the axolotl's gills reflect the intimate association between exchange and transport. Tiny blood vessels lie close to the surface of each filament in the gills. Across this surface, there is a net diffusion of O_2 from the surrounding water into the blood and of CO_2 from the blood into the water. The short distances involved allow diffusion to be rapid. Pumping of the axolotl's heart propels the oxygen-rich blood from the gill filaments to all other tissues of the body. There, more short-range exchange occurs, involving nutrients and O_2 as well as CO_2 and other wastes.

Because internal transport and gas exchange are functionally related in most animals, not just axolotls, we will examine both circulatory and respiratory systems in this chapter. We will explore the remarkable variation in form and organization of these systems by considering examples from a number of species. We will also highlight the roles of circulatory and respiratory systems in maintaining homeostasis under a range of physiological and environmental conditions.

CONCEPT 42.1

Circulatory systems link exchange surfaces with cells throughout the body

The molecular trade that an animal carries out with its environment—gaining O_2 and nutrients while shedding CO_2 and other waste products—must ultimately involve every cell in the body. As you learned in Chapter 7, small, nonpolar molecules such as O_2 and CO_2 can move between cells and their

immediate surroundings by diffusion. But diffusion is very slow for distances of more than a few millimeters. That's because the time it takes for a substance to diffuse from one place to another is proportional to the *square* of the distance. For example, if it takes 1 second for a given quantity of glucose to diffuse 100 µm, it will take 100 seconds for the same quantity to diffuse 1 mm and almost 3 hours to diffuse 1 cm! This relationship between diffusion time and distance places a substantial constraint on the body plan of any animal.

Given that diffusion is rapid only over very small distances, how does each cell of an animal participate in exchange? Natural selection has resulted in two general solutions to this problem. The first solution is a body size and shape that keep many or all cells in direct contact with the environment. Each cell can thus exchange materials directly with the surrounding medium. This type of body plan is found only in certain invertebrates, including cnidarians and flatworms. The second solution, found in all other animals, is a circulatory system that moves fluid between each cell's immediate surroundings and the tissues where exchange with the environment occurs.

Gastrovascular Cavities

Let's begin by looking at animals that lack a distinct circulatory system. In hydras, jellies, and other cnidarians, a central gastrovascular cavity functions in the distribution of substances throughout the body and in digestion (see Figure 41.7). An opening at one end connects the cavity to the surrounding water. In a hydra, thin branches of the gastrovascular cavity extend into the animal's tentacles. In jellies and some other cnidarians, the gastrovascular cavity has a much more elaborate branching pattern (**Figure 42.2a**).

In animals with a gastrovascular cavity, fluid bathes both the inner and outer tissue layers, facilitating exchange of gases and cellular waste. Only the cells lining the cavity have direct access to nutrients released by digestion. However, because the body wall is a mere two cells thick, nutrients need diffuse only a short distance to reach the cells of the outer tissue layer.

Planarians and most other flatworms also survive without a circulatory system. Their combination of a gastrovascular cavity and a flat body is well suited for exchange with the environment (**Figure 42.2b**). A flat body

optimizes diffusional exchange by increasing surface area and minimizing diffusion distances.

Evolutionary Variation in Circulatory Systems

EVOLUTION

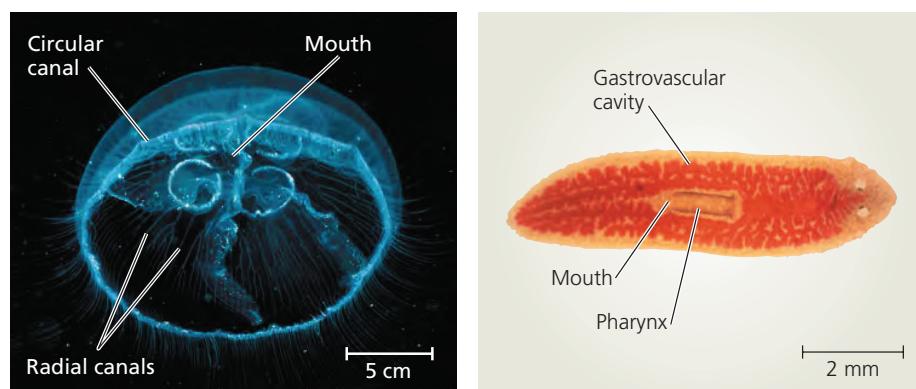
For animals with many cell layers, diffusion distances are too great for adequate exchange of nutrients and wastes by a gastrovascular cavity. In these organisms, a circulatory system minimizes the distances that substances must diffuse to enter or leave a cell.

General Properties of Circulatory Systems

A circulatory system has three basic components: a circulatory fluid, a set of interconnecting vessels, and a muscular pump, the **heart**. The heart powers circulation by using metabolic energy to elevate the hydrostatic pressure of the circulatory fluid, which then flows through the vessels and back to the heart.

By transporting fluid throughout the body, the circulatory system functionally connects the aqueous environment of the body cells to the organs that exchange gases, absorb nutrients, and dispose of wastes. In mammals, for example, O₂ from inhaled air diffuses across only two layers of cells in the lungs before reaching the blood. The circulatory system, powered by the heart, then carries the oxygen-rich blood to all parts of the body. As the blood streams throughout the body tissues in tiny blood vessels, O₂ in the blood diffuses only a short distance before entering the fluid that directly bathes the cells.

Several basic types of circulatory systems have arisen during evolution, each representing adaptations to constraints imposed by anatomy and environment. Circulatory systems are either open or closed, vary with regard to the number of circuits in the body, and rely on pumps that differ in structure and organization. We'll examine each of these variations and their physiological consequences in turn.



► Figure 42.2 Internal transport in gastrovascular cavities.

WHAT IF? Suppose a gastrovascular cavity were open at two ends, with fluid entering one end and leaving the other. How would this affect the gastrovascular cavity's functions in gas exchange and digestion?

(a) The moon jelly *Aurelia*, a cnidarian.
The jelly is viewed here from its underside (oral surface). The mouth leads to an elaborate gastrovascular cavity that consists of radial canals leading to and from a circular canal. Ciliated cells lining the canals circulate fluid within the cavity.

(b) The planarian *Dugesia*, a flatworm. The mouth and pharynx on the ventral side lead to the highly branched gastrovascular cavity, stained dark red in this specimen (LM).

Open and Closed Circulatory Systems

Arthropods and most molluscs have an **open circulatory system**, in which the circulatory fluid bathes the organs directly (Figure 42.3a). In these animals, the circulatory fluid, called **hemolymph**, is also the *interstitial fluid* that bathes body cells. Contraction of one or more hearts pumps the hemolymph through the circulatory vessels into interconnected sinuses, spaces surrounding the organs. Within the sinuses, chemical exchange occurs between the hemolymph and body cells. Relaxation of the heart draws hemolymph

back in through pores, which are equipped with valves that close when the heart contracts. Body movements help circulate the hemolymph by periodically squeezing the sinuses. The open circulatory system of larger crustaceans, such as lobsters and crabs, includes a more extensive system of vessels as well as an accessory pump.

In a **closed circulatory system**, a circulatory fluid called **blood** is confined to vessels and is distinct from the interstitial fluid (Figure 42.3b). One or more hearts pump blood into large vessels that branch into smaller ones that infiltrate the organs. Chemical exchange occurs between the blood and the interstitial fluid, as well as between the interstitial fluid and body cells. Annelids (including earthworms), cephalopods (including squids and octopuses), and all vertebrates have closed circulatory systems.

The fact that both open and closed circulatory systems are widespread among animals suggests that there are advantages to each system. The lower hydrostatic pressures associated with open circulatory systems make them less costly than closed systems in terms of energy expenditure. In some invertebrates, open circulatory systems serve additional functions. For example, spiders use the hydrostatic pressure generated by their open circulatory system to extend their legs.

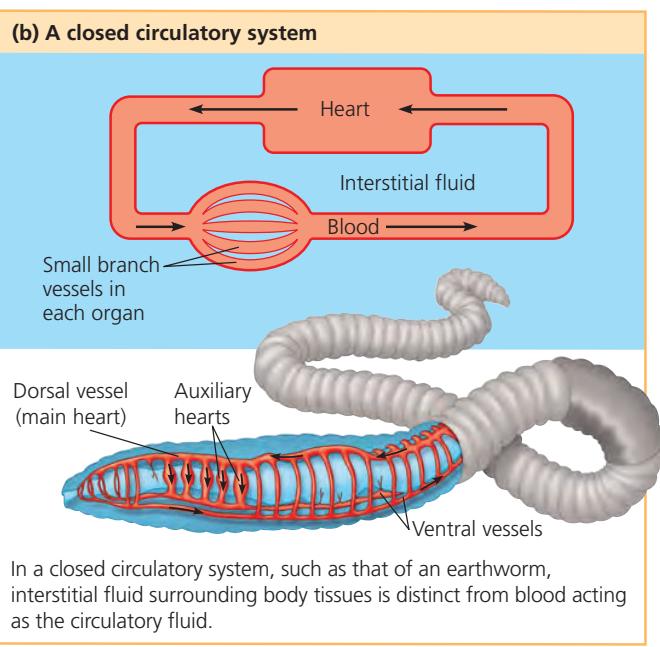
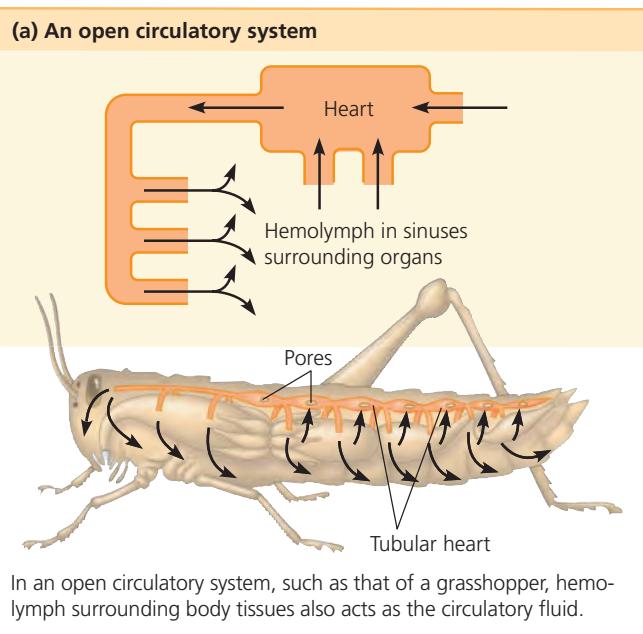
The benefits of closed circulatory systems include relatively high blood pressures, which enable the effective delivery of O₂ and nutrients to the cells of larger and more active animals. Among the molluscs, for instance, closed circulatory systems are found in the largest and most active species, the squids and octopuses. Closed systems are also particularly well suited to regulating the distribution of blood to different organs, as you'll learn later in this chapter. In examining closed circulatory systems in more detail, we will focus on the vertebrates.

Organization of Vertebrate Circulatory Systems

The closed circulatory system of humans and other vertebrates is often called the **cardiovascular system**. Blood circulates to and from the heart through an amazingly extensive network of vessels: The total length of blood vessels in an average human adult is twice Earth's circumference at the equator!

Arteries, veins, and capillaries are the three main types of blood vessels. Within each type, blood flows in only one direction. **Arteries** carry blood away from the heart to organs throughout the body. Within organs, arteries branch into **arterioles**, small vessels that convey blood to the capillaries. **Capillaries** are microscopic vessels with very thin, porous walls. Networks of these vessels, called **capillary beds**, infiltrate every tissue, passing within a few cell diameters of every cell in the body. Across the thin walls of capillaries, chemicals, including dissolved gases, are exchanged by diffusion between the blood and the interstitial fluid around the tissue cells. At their "downstream" end, capillaries converge into **venules**, and venules converge into **veins**, the vessels that carry blood back to the heart.

▼ Figure 42.3 Open and closed circulatory systems.



Arteries and veins are distinguished by the *direction* in which they carry blood, not by the O₂ content or other characteristics of the blood they contain. Arteries carry blood from the heart *toward* capillaries, and veins return blood to the heart *from* capillaries. The only exceptions are the portal veins, which carry blood between pairs of capillary beds. The hepatic portal vein, for example, carries blood from capillary beds in the digestive system to capillary beds in the liver (see Chapter 41). From the liver, blood passes into the hepatic veins, which conduct blood toward the heart.

The hearts of all vertebrates contain two or more muscular chambers. The chambers that receive blood entering the heart are called **atria** (singular, *atrium*). The chambers responsible for pumping blood out of the heart are called **ventricles**. The number of chambers and the extent to which they are separated from one another differ substantially among groups of vertebrates, as we will discuss next. These important differences reflect the close fit of form to function that arises from natural selection.

Single Circulation

In bony fishes, rays, and sharks, the heart consists of two chambers: an atrium and a ventricle. The blood passes through the heart once in each complete circuit, an arrangement called **single circulation** (Figure 42.4a). Blood entering the heart collects in the atrium before transfer to the ventricle. Contraction of the ventricle pumps blood to the gills, where there is a net diffusion of O₂ into the blood and of CO₂ out of the blood. As blood leaves the gills, the capillaries converge into a vessel that carries oxygen-rich blood to capillary beds throughout the body. Blood then returns to the heart.

In single circulation, blood that leaves the heart passes through two capillary beds before returning to the heart. When blood flows through a capillary bed, blood pressure drops substantially, for reasons we will explain shortly. The drop in blood pressure in the gills limits the rate of blood flow in the rest of the animal's body. As the animal swims, however, the contraction and relaxation of its muscles help accelerate the relatively sluggish pace of circulation.

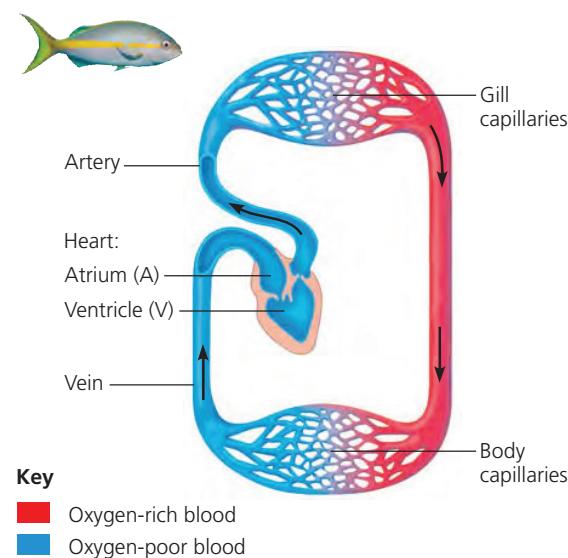
Double Circulation

The circulatory systems of amphibians, reptiles, and mammals have two circuits, an arrangement called **double circulation** (Figure 42.4b). The pumps for the two circuits are combined into a single organ, the heart. Having both pumps within a single heart simplifies coordination of the pumping cycles.

One pump, the right side of the heart, delivers oxygen-poor blood to the capillary beds of the gas exchange tissues, where there is a net movement of O₂ into the blood and of CO₂ out of the blood. This part of the circulation is called a **pulmonary circuit** if the capillary beds involved are all in the lungs, as in reptiles and mammals. It is called a **pulmocutaneous circuit** if it includes capillaries in both the lungs and the skin, as in many amphibians.

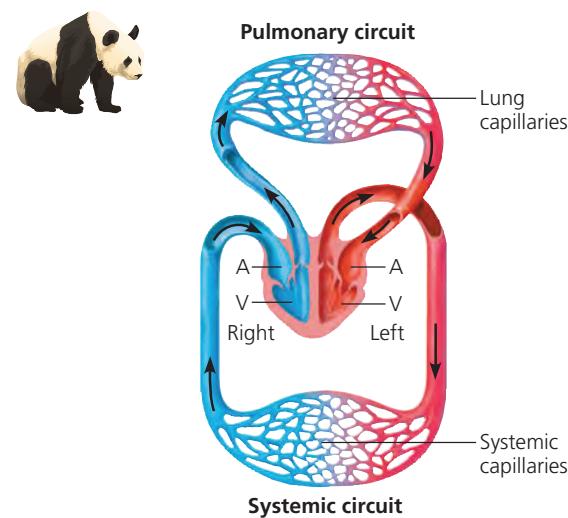
▼ Figure 42.4 Single and double circulation in vertebrates.

(a) Single circulation



Bony fishes, rays, and sharks have a single circuit of blood flow and a single circulatory pump—a heart with two chambers.

(b) Double circulation



Amphibians, reptiles, and mammals have two circuits of blood flow and two pumps fused into a multi-chambered heart. Note that circulatory systems are depicted as if the animal is facing you: The right side of the heart is shown on the left, and vice versa.

After the oxygen-enriched blood leaves the gas exchange tissues, it enters the other pump, the left side of the heart. Contraction of the heart propels this blood to capillary beds in organs and tissues throughout the body. Following the exchange of O₂ and CO₂, as well as nutrients and waste products,

the now oxygen-poor blood returns to the heart, completing the **systemic circuit**.

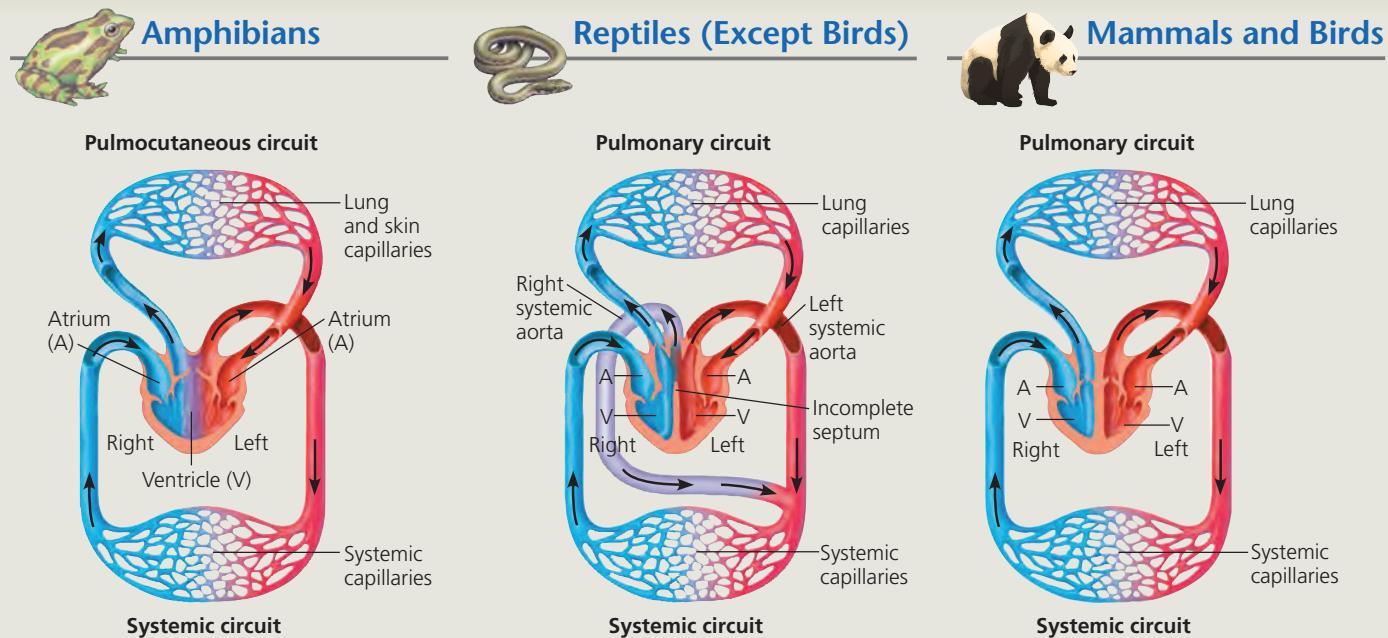
Double circulation provides a vigorous flow of blood to the brain, muscles, and other organs because the heart repressurizes the blood destined for these tissues after it passes through the capillary beds of the lungs or skin. Indeed, blood pressure is often much higher in the systemic circuit than in the gas exchange circuit. This contrasts sharply with single

circulation, in which blood flows under reduced pressure directly from the gas exchange organs to other organs.

To explore the adaptations of double circulation that meet the particular needs of different vertebrates, we conclude our overview of circulatory systems with **Figure 42.5**. In the next section, we will restrict our focus to circulation in mammals and to the anatomy and physiology of the key circulatory organ—the heart.

▼ Figure 42.5

Exploring Double Circulation in Vertebrates



Frogs and other amphibians have a heart with three chambers: two atria and one ventricle. A ridge within the ventricle diverts most (about 90%) of the oxygen-poor blood from the right atrium into the pulmocutaneous circuit and most of the oxygen-rich blood from the left atrium into the systemic circuit. When underwater, a frog adjusts its circulation, for the most part shutting off blood flow to its temporarily ineffective lungs. Blood flow continues to the skin, which acts as the sole site of gas exchange while the frog is submerged.

In the three-chambered heart of turtles, snakes, and lizards, an incomplete septum partially divides the single ventricle into separate right and left chambers. Two major arteries, called aortas, lead to the systemic circulation. The detailed anatomy of the heart varies among these three groups of reptiles, with some adaptations allowing control of the relative amount of blood flowing to the lungs and the body.

In alligators, caimans, and other crocodilians, the ventricles are divided by a complete septum (not shown), but the pulmonary and systemic circuits connect where the arteries exit the heart. This connection enables arterial valves to shunt blood flow away from the lungs temporarily, such as when the animal is underwater.

In mammals and birds, there are two atria and two completely divided ventricles. The left side of the heart receives and pumps only oxygen-rich blood, while the right side receives and pumps only oxygen-poor blood. (In birds, the major vessels near the heart are slightly different than shown.) As endotherms, mammals and birds use about ten times as much energy as equal-sized ectotherms. Their circulatory systems therefore need to deliver about ten times as much fuel and O₂ to their tissues (and remove ten times as much CO₂ and other wastes). This large traffic of substances is made possible by separate and independently powered systemic and pulmonary circuits and by large hearts that pump the necessary volume of blood. A powerful four-chambered heart arose independently in the distinct ancestors of mammals and birds and thus reflects convergent evolution (see Chapter 34).

Key

- █ Oxygen-rich blood
- █ Oxygen-poor blood

CONCEPT CHECK 42.1

- How is the flow of hemolymph through an open circulatory system similar to the flow of water through an outdoor fountain?
- Three-chambered hearts with incomplete septa were once viewed as being less adapted to circulatory function than mammalian hearts. What advantage of such hearts did this viewpoint overlook?
- WHAT IF?** The heart of a normally developing human fetus has a hole between the left and right atria. In some cases, this hole does not close completely before birth. If the hole weren't surgically corrected, how would it affect the O₂ content of the blood entering the systemic circuit?

For suggested answers, see Appendix A.

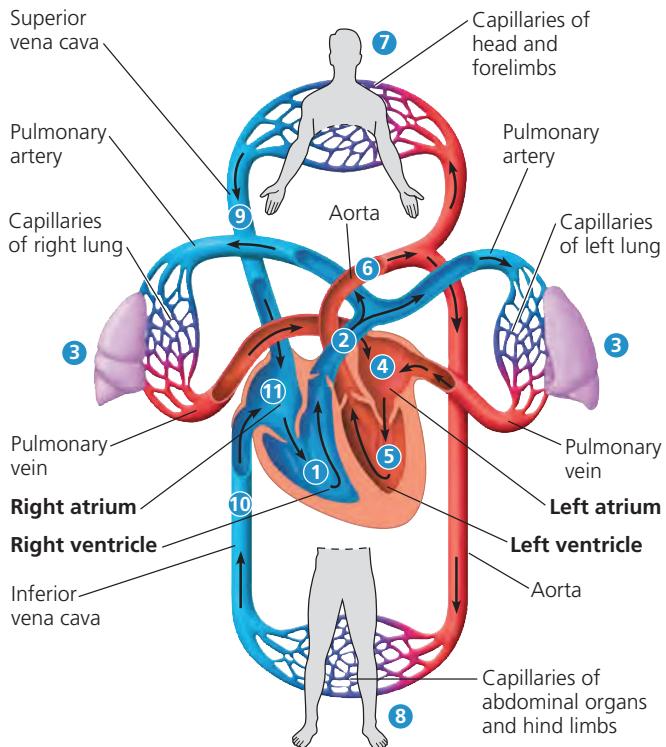
CONCEPT 42.2

Coordinated cycles of heart contraction drive double circulation in mammals

The timely delivery of O₂ to the body's organs is critical: Some brain cells, for example, die if their O₂ supply is interrupted for as little as a few minutes. How does the mammalian cardiovascular system meet the body's continuous but variable demand for O₂? To answer this question, we need to consider how the parts of the system are arranged and how each part functions.

Mammalian Circulation

Let's first examine the overall organization of the mammalian cardiovascular system, beginning with the pulmonary circuit. (The circled numbers refer to corresponding locations in **Figure 42.6**.) ① Contraction of the right ventricle pumps blood to the lungs via ② the pulmonary arteries. As the blood flows through ③ capillary beds in the left and right lungs, it loads O₂ and unloads CO₂. Oxygen-rich blood returns from the lungs via the pulmonary veins to ④ the left atrium of the heart. Next, the oxygen-rich blood flows into ⑤ the heart's left ventricle, which pumps the oxygen-rich blood out to body tissues through the systemic circuit. Blood leaves the left ventricle via ⑥ the aorta, which conveys blood to arteries leading throughout the body. The first branches leading from the aorta are the coronary arteries (not shown), which supply blood to the heart muscle itself. Then branches lead to ⑦ capillary beds in the head and arms (forelimbs). The aorta then descends into the abdomen, supplying oxygen-rich blood to arteries leading to ⑧ capillary beds in the abdominal organs and legs (hind limbs). Within the capillaries, there is a net diffusion of O₂ from the blood to the tissues

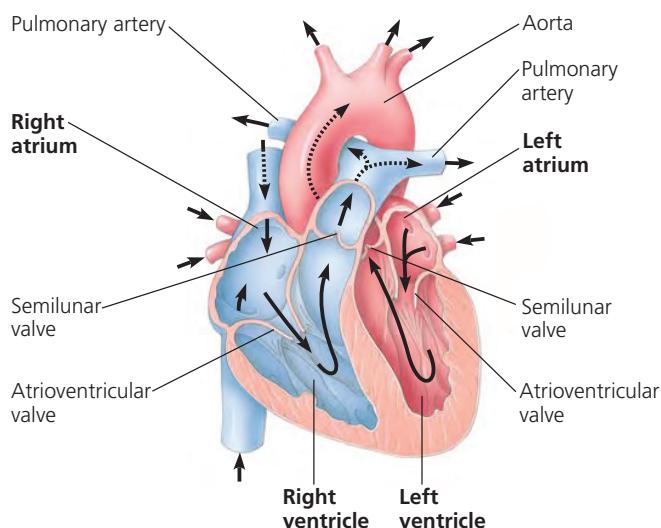


▲ Figure 42.6 The mammalian cardiovascular system: an overview. Note that the dual circuits operate simultaneously, not in the serial fashion that the numbering in the diagram suggests. The two ventricles pump almost in unison; while some blood is traveling in the pulmonary circuit, the rest of the blood is flowing in the systemic circuit.

and of CO₂ (produced by cellular respiration) into the blood. Capillaries rejoin, forming venules, which convey blood to veins. Oxygen-poor blood from the head, neck, and forelimbs is channeled into a large vein, ⑨ the superior vena cava. Another large vein, ⑩ the inferior vena cava, drains blood from the trunk and hind limbs. The two venae cavae empty their blood into ⑪ the right atrium, from which the oxygen-poor blood flows into the right ventricle.

The Mammalian Heart: A Closer Look

Using the human heart as an example, let's now take a closer look at how the mammalian heart works (**Figure 42.7**). Located behind the sternum (breastbone), the human heart is about the size of a clenched fist and consists mostly of cardiac muscle (see Figure 40.5). The two atria have relatively thin walls and serve as collection chambers for blood returning to the heart from the lungs or other body tissues. Much of the blood that enters the atria flows into the ventricles while all heart chambers are relaxed. The remainder is transferred by contraction of the atria before the ventricles begin to contract. The ventricles have thicker walls and contract much more forcefully than the atria—especially the left ventricle, which pumps blood to all body organs through the systemic circuit. Although the left ventricle contracts with



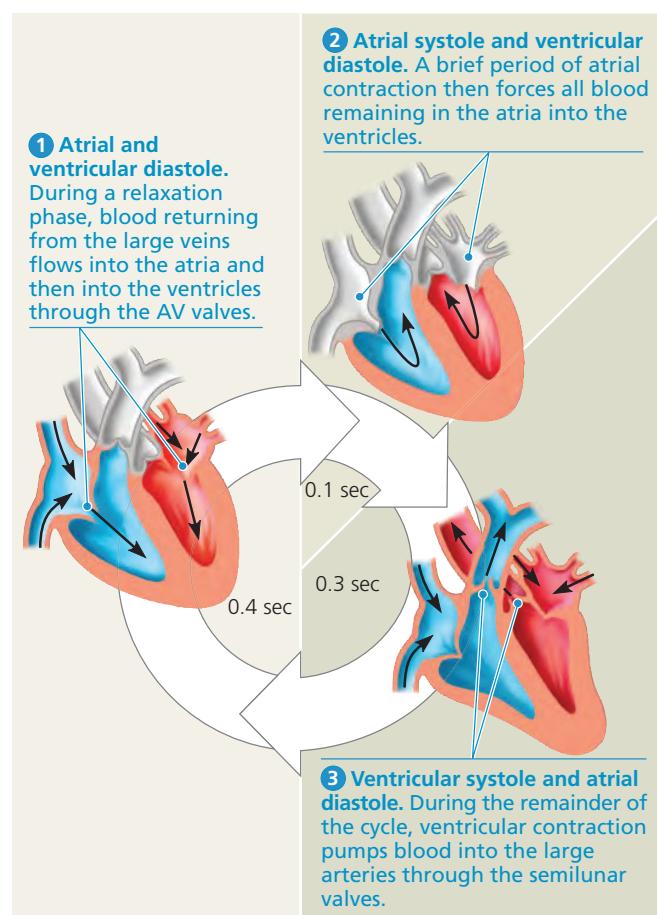
▲ Figure 42.7 The mammalian heart: a closer look. Notice the locations of the valves, which prevent backflow of blood within the heart. Also notice how the atria and left and right ventricles differ in the thickness of their muscular walls.

greater force than the right ventricle, it pumps the same volume of blood as the right ventricle during each contraction.

The heart contracts and relaxes in a rhythmic cycle. When it contracts, it pumps blood; when it relaxes, its chambers fill with blood. One complete sequence of pumping and filling is referred to as the **cardiac cycle**. The contraction phase of the cycle is called **systole**, and the relaxation phase is called **diastole** (Figure 42.8).

The volume of blood each ventricle pumps per minute is the **cardiac output**. Two factors determine cardiac output: the rate of contraction, or **heart rate** (number of beats per minute), and the **stroke volume**, the amount of blood pumped by a ventricle in a single contraction. The average stroke volume in humans is about 70 mL. Multiplying this stroke volume by a resting heart rate of 72 beats per minute yields a cardiac output of 5 L/min—about equal to the total volume of blood in the human body. During heavy exercise, cardiac output increases as much as fivefold.

Four valves in the heart prevent backflow and keep blood moving in the correct direction (see Figures 42.7 and 42.8). Made of flaps of connective tissue, the valves open when pushed from one side and close when pushed from the other. An **atrioventricular (AV) valve** lies between each atrium and ventricle. The AV valves are anchored by strong fibers that prevent them from turning inside out. Pressure generated by the powerful contraction of the ventricles closes the AV valves, keeping blood from flowing back into the atria. **Semilunar valves** are located at the two exits of the heart: where the aorta leaves the left ventricle and where the pulmonary artery leaves the right ventricle. These valves are pushed open by the pressure generated during contraction of



▲ Figure 42.8 The cardiac cycle. For an adult human at rest with a heart rate of about 72 beats per minute, one complete cardiac cycle takes about 0.8 second. Note that during all but 0.1 second of the cardiac cycle, the atria are relaxed and are filling with blood returning via the veins.

the ventricles. When the ventricles relax, blood pressure built up in the aorta closes the semilunar valves and prevents significant backflow.

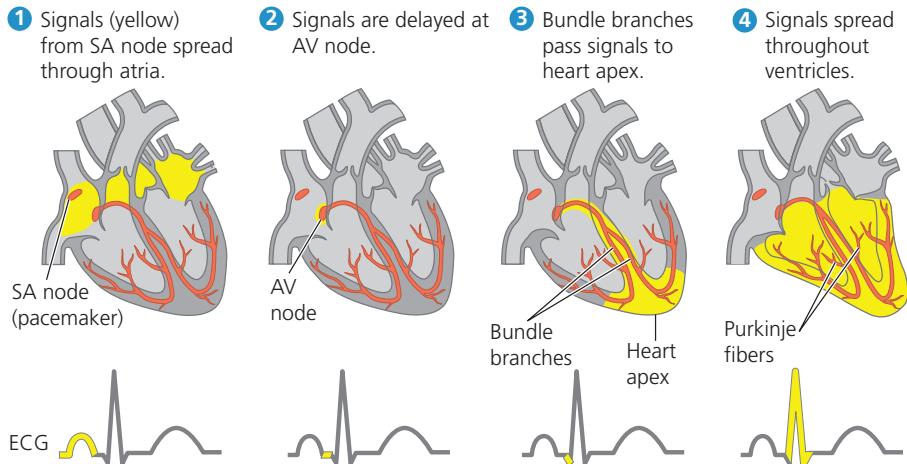
You can follow the closing of the two sets of heart valves either with a stethoscope or by pressing your ear tightly against the chest of a friend (or a friendly dog). The sound pattern is “lub-dup, lub-dup, lub-dup.” The first heart sound (“lub”) is created by the recoil of blood against the closed AV valves. The second sound (“dup”) is produced by the recoil of blood against the closed semilunar valves.

If blood squirts backward through a defective valve, it may produce an abnormal sound called a **heart murmur**. Some people are born with heart murmurs; in others, the valves may be damaged by infection (from rheumatic fever, for instance). When a valve defect is severe enough to endanger health, surgeons may implant a mechanical replacement valve. However, not all heart murmurs are caused by a defect, and most valve defects do not reduce the efficiency of blood flow enough to warrant surgery.

► Figure 42.9 The control of heart rhythm.

rhthm. The sequence of electrical events in the heart is shown at the top; red highlights specialized muscle cells involved in the electrical control of the rhythm. The corresponding components of an electrocardiogram (ECG) are highlighted at the bottom in yellow. In step 4, the portion of the ECG to the right of the “spike” represents electrical activity that reprimed the ventricles for the next round of contraction.

WHAT IF? If a doctor gave you a copy of your ECG recording, how could you determine what your heart rate had been during the test?



Maintaining the Heart's Rhythmic Beat

In vertebrates, the heartbeat originates in the heart itself. Some cardiac muscle cells are autorhythmic, meaning they contract and relax repeatedly without any signal from the nervous system. You can even see these rhythmic contractions in tissue that has been removed from the heart and placed in a dish in the laboratory! Because each of these cells has its own intrinsic contraction rhythm, how are their contractions coordinated in the intact heart? The answer lies in a group of autorhythmic cells located in the wall of the right atrium, near where the superior vena cava enters the heart. This cluster of cells is called the **sinoatrial (SA) node**, or *pacemaker*, and it sets the rate and timing at which all cardiac muscle cells contract. (In contrast to vertebrates, some arthropods have pacemakers located in the nervous system, outside the heart.)

The SA node generates electrical impulses much like those produced by nerve cells. Because cardiac muscle cells are electrically coupled through gap junctions (see Figure 6.32), impulses from the SA node spread rapidly within heart tissue. In addition, these impulses generate currents that are conducted to the skin via body fluids. In an **electrocardiogram (ECG)** or, often, **EKG**, from the German spelling), these currents are recorded by electrodes placed on the skin. The resulting graph of current against time has a characteristic shape that represents the stages in the cardiac cycle (**Figure 42.9**).

Impulses from the SA node first spread rapidly through the walls of the atria, causing both atria to contract in unison. During atrial contraction, the impulses originating at the SA node reach other autorhythmic cells located in the wall between the left and right atria. These cells form a relay point called the **atrioventricular (AV) node**. Here the impulses are delayed for about 0.1 second before spreading to the heart apex. This delay allows the atria to empty completely before the ventricles contract. Then the signals from the AV node are conducted to the heart apex and throughout the ventricular walls by specialized muscle fibers called bundle branches and Purkinje fibers.

Physiological cues alter heart tempo by regulating the SA node. Two portions of the nervous system, the sympathetic and parasympathetic divisions, are largely responsible for this regulation. They function like the spurs and reins used in riding a horse: The sympathetic division speeds up the pacemaker, and the parasympathetic division slows it down. For example, when you stand up and start walking, the sympathetic division increases your heart rate, an adaptation that enables your circulatory system to provide the additional O₂ needed by the muscles that are powering your activity. If you then sit down and relax, the parasympathetic division decreases your heart rate, an adaptation that conserves energy. Hormones secreted into the blood also influence the pacemaker. For instance, epinephrine, the “fight-or-flight” hormone secreted by the adrenal glands, causes the heart rate to increase. A third type of input that affects the pacemaker is body temperature. An increase of only 1°C raises the heart rate by about 10 beats per minute. This is the reason your heart beats faster when you have a fever.

Having examined the operation of the circulatory pump, we turn in the next section to the forces and structures that influence blood flow in the vessels of each circuit.

CONCEPT CHECK 42.2

1. Explain why blood in the pulmonary veins has a higher O₂ concentration than blood in the venae cavae, which are also veins.
2. Why is it important that the AV node delay the electrical impulse moving from the SA node and the atria to the ventricles?
3. **WHAT IF?** After exercising regularly for several months, you find that your resting heart rate has decreased. What other change in the function of your heart at rest would you expect to find? Explain.

For suggested answers, see Appendix A.

CONCEPT 42.3

Patterns of blood pressure and flow reflect the structure and arrangement of blood vessels

The vertebrate circulatory system enables blood to deliver oxygen and nutrients and remove wastes throughout the body. In doing so, the circulatory system relies on a branching network of vessels much like the plumbing system that delivers fresh water to a city and removes its wastes. In fact, the same physical principles that govern the operation of plumbing systems apply to the functioning of blood vessels.

Blood Vessel Structure and Function

Blood vessels contain a central lumen (cavity) lined with an **endothelium**, a single layer of flattened epithelial cells. The smooth surface of the endothelium minimizes resistance to the flow of blood. Surrounding the endothelium are layers of tissue that differ in capillaries, arteries, and veins, reflecting the specialized functions of these vessels.

Capillaries are the smallest blood vessels, having a diameter only slightly greater than that of a red blood cell (**Figure 42.10**). Capillaries also have very thin walls, which consist of just the endothelium and its basal lamina. This structural organization facilitates the exchange of substances between the blood in capillaries and the interstitial fluid.

The walls of arteries and veins have a more complex organization than those of capillaries. Both arteries and veins have two layers of tissue surrounding the endothelium: an outer layer of connective tissue containing elastic fibers, which allow the vessel to stretch and recoil, and a middle layer containing smooth muscle and more elastic fibers. However, the walls of arteries and veins also differ, reflecting distinct adaptations of these vessels to their particular functions in circulation.

The walls of arteries are thick and strong, accommodating blood pumped at high pressure by the heart. Arterial walls also have an elastic recoil that helps maintain blood pressure and flow to capillaries when the heart relaxes between contractions. Signals from the nervous system and hormones circulating in the blood act on the smooth muscle

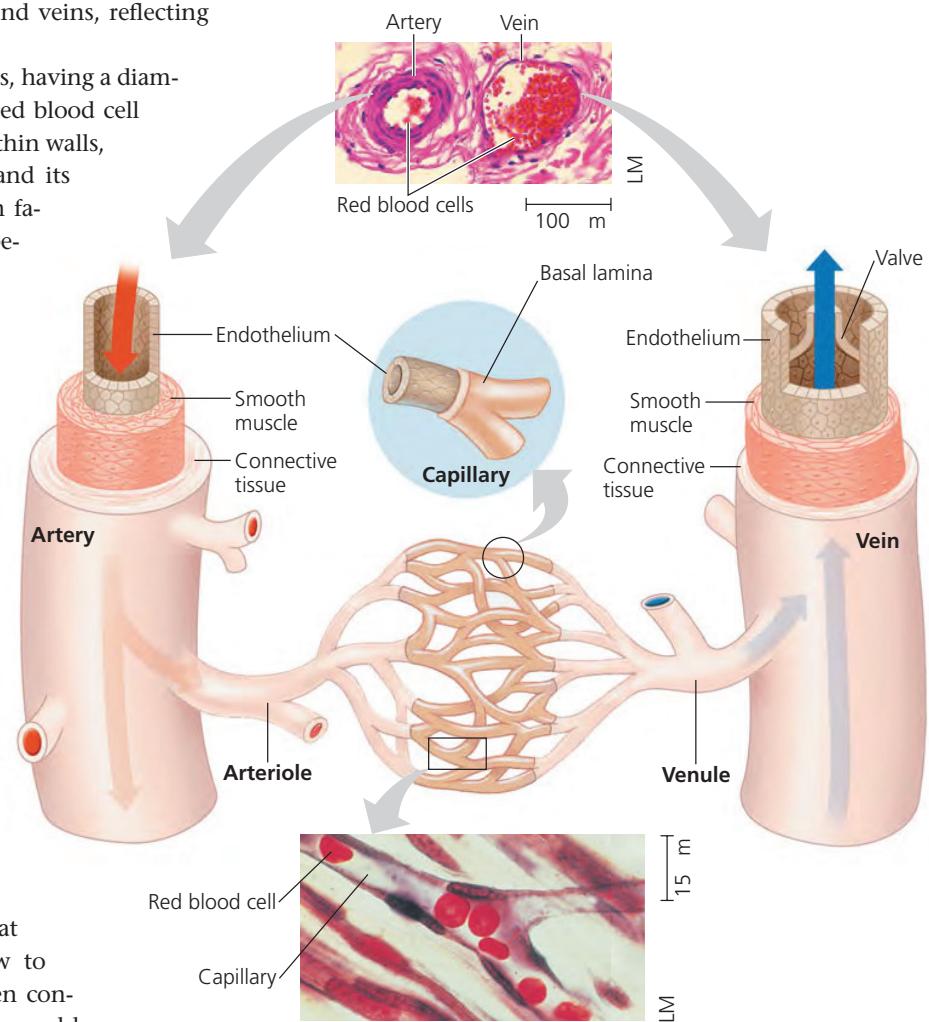
in arteries and arterioles, dilating or constricting these vessels and thus controlling blood flow to different parts of the body.

Because veins convey blood back to the heart at a lower pressure, they do not require thick walls. For a given blood vessel diameter, a vein has a wall only about a third as thick as that of an artery. Valves inside the veins maintain a unidirectional flow of blood despite the low blood pressure.

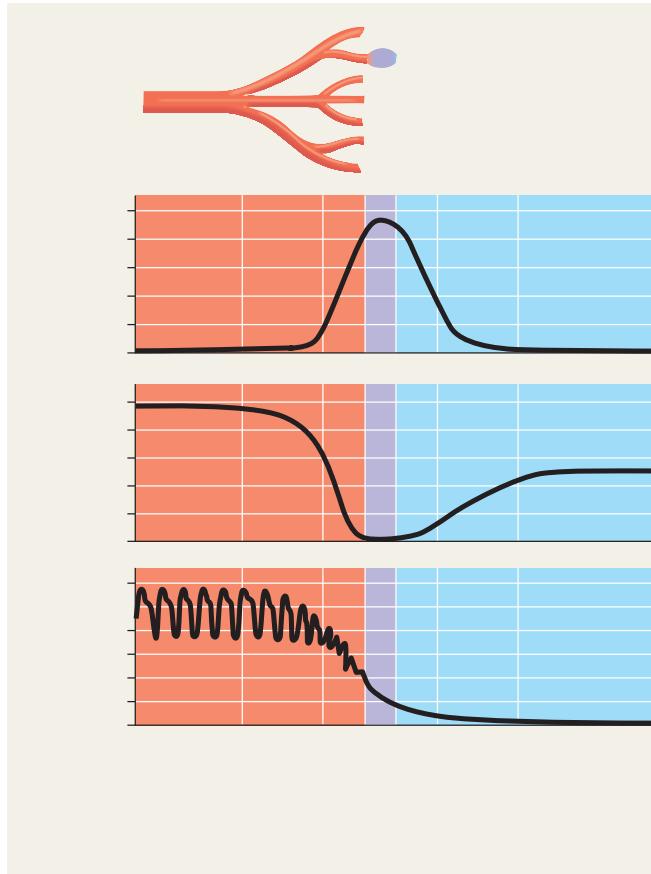
We consider next how blood vessel diameter, vessel number, and pressure influence the speed at which blood flows in different locations within the body.

Blood Flow Velocity

To understand how blood vessel diameter influences blood flow, consider how water flows through a thick hose connected to a faucet. When the faucet is turned on, water flows at the same velocity at each point along the hose. However, if a narrow nozzle is attached to the end of the hose, the water



▲ **Figure 42.10** The structure of blood vessels.



emotional stress can trigger nervous and hormonal responses that cause smooth muscles in arteriole walls to contract. When that happens, the arterioles narrow, a process called **vasoconstriction**. Narrowing of the arterioles increases blood pressure upstream in the arteries. When the smooth muscles relax, the arterioles undergo **vasodilation**, an increase in diameter that causes blood pressure in the arteries to fall.

Researchers have identified a gas, nitric oxide (NO), as a major inducer of vasodilation and a peptide, endothelin, as the most potent inducer of vasoconstriction. Both NO and endothelin are signaling molecules produced in blood vessels in response to cues from the nervous and endocrine systems. Each kind of molecule binds to a specific receptor, activating a signal transduction pathway that alters smooth muscle contraction and thus changes blood vessel diameter.

Vasoconstriction and vasodilation are often coupled to changes in cardiac output that also affect blood pressure. This coordination of regulatory mechanisms maintains adequate blood flow as the body's demands on the circulatory system change. During heavy exercise, for example, the arterioles in working muscles dilate, causing a greater flow of oxygen-rich blood to the muscles. By itself, this increased flow to the muscles would cause a drop in blood pressure (and therefore blood flow) in the body as a whole. However, cardiac output increases at the same time, maintaining blood pressure and supporting the necessary increase in blood flow.

Blood Pressure and Gravity

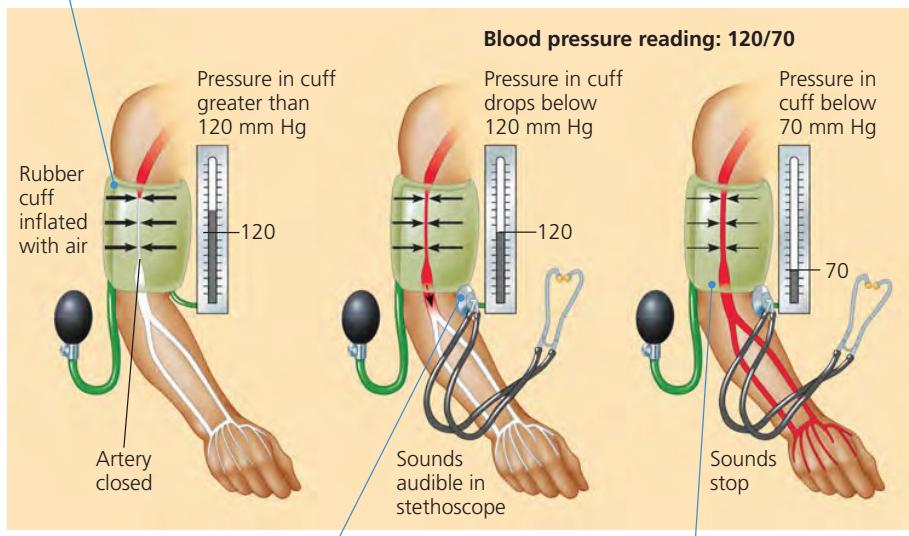
Blood pressure is generally measured for an artery in the arm at the same height as the heart (**Figure 42.12**). For a healthy 20-year-old human at rest, arterial blood pressure in the systemic circuit is typically about 120 millimeters of mercury (mm Hg) at systole and 70 mm Hg at diastole, expressed as 120/70. (Arterial blood pressure in the pulmonary circuit is six to ten times lower.)

Gravity has a significant effect on blood pressure. When you are standing, for example, your head is roughly 0.35 m higher than your chest, and the arterial blood pressure in your brain is about 27 mm Hg less than that near your heart. If the blood pressure in your brain is too low to provide adequate blood flow, you will likely faint. By causing your body to collapse to the ground, fainting effectively places your head at the level of your heart, quickly increasing blood flow to your brain.

The challenge of pumping blood against gravity is particularly great for animals with very long necks. A giraffe, for example, requires a systolic pressure of more than 250 mm Hg near the heart to get blood to its head. When a giraffe lowers its head to drink, one-way valves and sinuses, along with feedback mechanisms that reduce cardiac output, prevent this high pressure from damaging its brain. We can calculate that a dinosaur with a neck nearly 10 m long would have required even greater systolic pressure—nearly 760 mm Hg—to pump blood to its brain when its head was fully raised. However, calculations based on anatomy and inferred metabolic rate suggest that dinosaurs did not have a heart powerful enough to generate such high pressure. Based on this evidence as well as studies of neck bone structure, some biologists have concluded that the long-necked dinosaurs fed close to the ground rather than on high foliage.

Gravity is also a consideration for blood flow in veins, especially those in the legs. Although blood pressure in veins is relatively low, several mechanisms assist the return of venous blood to the heart. First, rhythmic contractions of smooth muscles in the walls of venules and veins aid in the movement of the blood. Second, and more important, the contraction of skeletal muscles during exercise squeezes blood through the

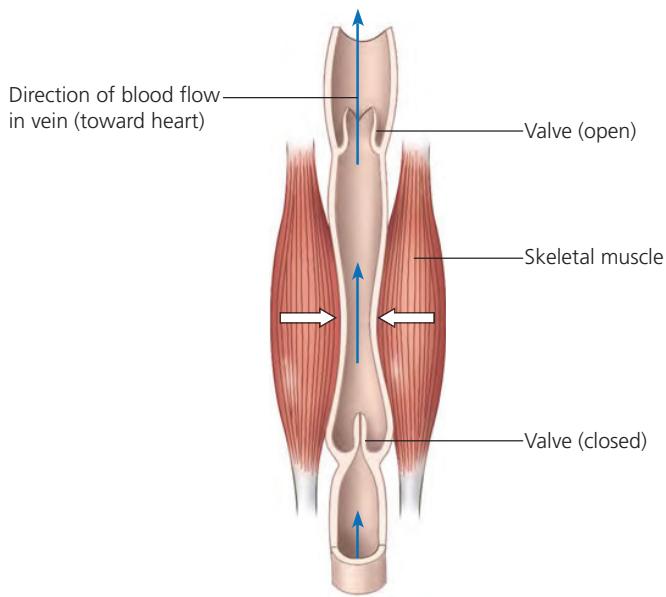
1 A sphygmomanometer, an inflatable cuff attached to a pressure gauge, measures blood pressure in an artery. The cuff is inflated until the pressure closes the artery, so that no blood flows past the cuff. When this occurs, the pressure exerted by the cuff exceeds the pressure in the artery.



2 The cuff is allowed to deflate gradually. When the pressure exerted by the cuff falls just below that in the artery, blood pulses into the forearm, generating sounds that can be heard with the stethoscope. The pressure measured at this point is the systolic pressure.

3 The cuff is allowed to deflate further, just until the blood flows freely through the artery and the sounds below the cuff disappear. The pressure at this point is the diastolic pressure.

▲ Figure 42.12 Measurement of blood pressure. Blood pressure is recorded as two numbers separated by a slash. The first number is the systolic pressure; the second is the diastolic pressure.



▲ Figure 42.13 Blood flow in veins. Skeletal muscle contraction squeezes and constricts veins. Flaps of tissue within the veins act as one-way valves that keep blood moving only toward the heart. If you sit or stand too long, the lack of muscular activity may cause your feet to swell as blood pools in your veins.

veins toward the heart (**Figure 42.13**). Third, the change in pressure within the thoracic (chest) cavity during inhalation causes the *venae cavae* and other large veins near the heart to expand and fill with blood.

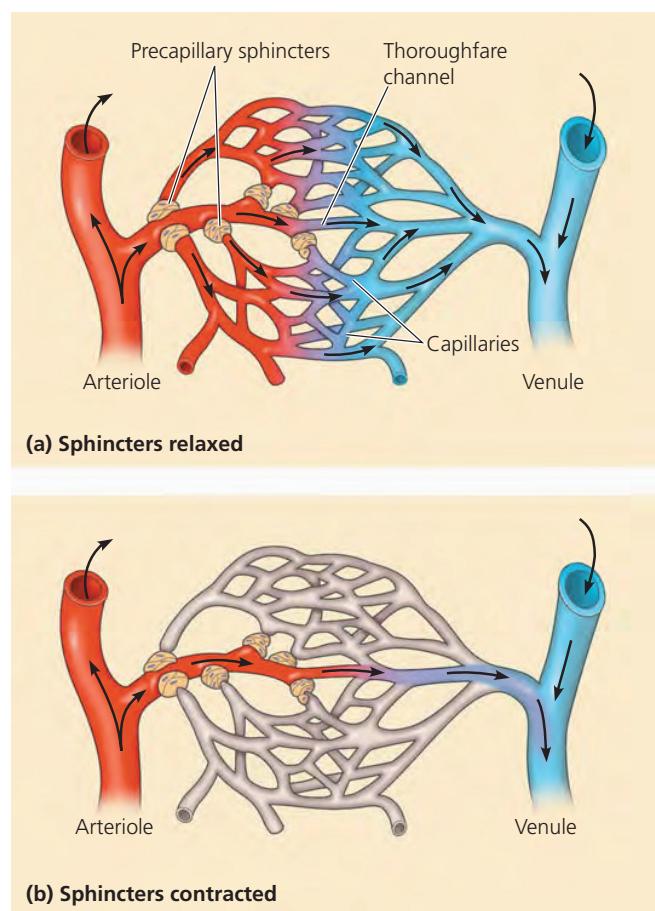
In rare instances, runners and other athletes can suffer heart failure if they stop vigorous exercise abruptly. When the leg muscles suddenly cease contracting and relaxing, less blood returns to the heart, which continues to beat rapidly. If the heart is weak or damaged, this inadequate blood flow may cause the heart to malfunction. To reduce the risk of stressing the heart excessively, athletes are encouraged to follow hard exercise with moderate activity, such as walking, to “cool down” until their heart rate approaches its resting level.

Capillary Function

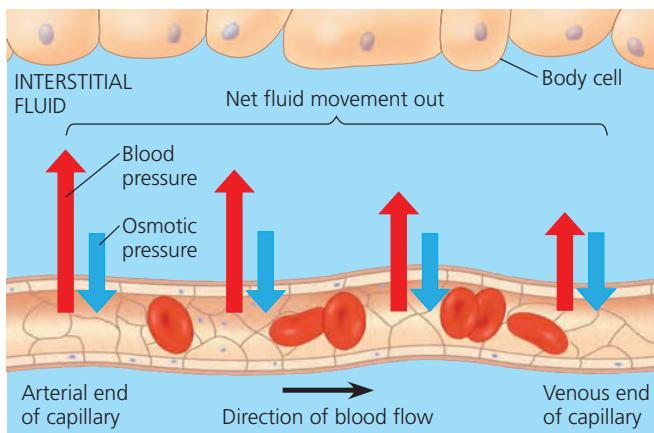
At any given time, only about 5–10% of the body’s capillaries have blood flowing through them. However, each tissue has many capillaries, so every part of the body is supplied with blood at all times. Capillaries in the brain, heart, kidneys, and liver are usually filled to capacity, but at many other sites the blood supply varies over time as blood is diverted from one destination to another. For example, blood flow to the skin is regulated to help control body temperature, and blood supply to the digestive tract increases after a meal. During strenuous exercise, blood is diverted from the digestive tract and supplied more generously to skeletal muscles and skin. This is one reason why exercising heavily immediately after eating a big meal may cause indigestion.

Given that capillaries lack smooth muscle, how is blood flow in capillary beds altered? There are two mechanisms, both of which rely on signals that regulate the flow into capillaries. One mechanism involves contraction of the smooth muscle in the wall of an arteriole, which reduces the vessel’s diameter and decreases blood flow to the adjoining capillary beds. When the smooth muscle relaxes, the arterioles dilate, allowing blood to enter the capillaries. The other mechanism for altering flow, shown in **Figure 42.14**, involves the action of *precapillary sphincters*, rings of smooth muscle located at the entrance to capillary beds. The signals that regulate blood flow include nerve impulses, hormones traveling throughout the bloodstream, and chemicals produced locally. For example, the chemical histamine released by cells at a wound site causes smooth muscle relaxation, dilating blood vessels and increasing blood flow. The dilated vessels also give disease-fighting white blood cells greater access to invading microorganisms.

As you have read, the critical exchange of substances between the blood and interstitial fluid takes place across the



▲ Figure 42.14 Blood flow in capillary beds. Precapillary sphincters regulate the passage of blood into capillary beds. Some blood flows directly from arterioles to venules through capillaries called thoroughfare channels, which are always open.



▲ Figure 42.15 Fluid exchange between capillaries and the interstitial fluid. This diagram shows a hypothetical capillary in which blood pressure exceeds osmotic pressure throughout the entire length of the capillary. In other capillaries, blood pressure may be lower than osmotic pressure along all or part of the capillary.

thin endothelial walls of the capillaries. Some substances are carried across the endothelium in vesicles that form on one side by endocytosis and release their contents on the opposite side by exocytosis. Small molecules, such as O_2 and CO_2 , simply diffuse across the endothelial cells or, in some tissues, through microscopic pores in the capillary wall. These openings also provide the route for transport of small solutes such as sugars, salts, and urea, as well as for bulk flow of fluid into tissues driven by blood pressure within the capillary.

Two opposing forces control the movement of fluid between the capillaries and the surrounding tissues: Blood pressure tends to drive fluid out of the capillaries, and the presence of blood proteins tends to pull fluid back (**Figure 42.15**). Many blood proteins (and all blood cells) are too large to pass readily through the endothelium, and they remain in the capillaries. These dissolved proteins are responsible for much of the blood's **osmotic pressure** (the pressure produced by the difference in solute concentration across a membrane). The difference in osmotic pressure between the blood and the interstitial fluid opposes fluid movement out of the capillaries. On average, blood pressure is greater than the opposing forces, leading to a net loss of fluid from capillaries. The net loss is generally greatest at the arterial end of these vessels, where blood pressure is highest.

Fluid Return by the Lymphatic System

Each day, the adult human body loses approximately 4–8 L of fluid from capillaries to the surrounding tissues. There is also some leakage of blood proteins, even though the capillary wall is not very permeable to large molecules. The lost fluid and proteins return to the blood via the **lymphatic system**, which includes a network of tiny vessels intermingled among capillaries of the cardiovascular system.

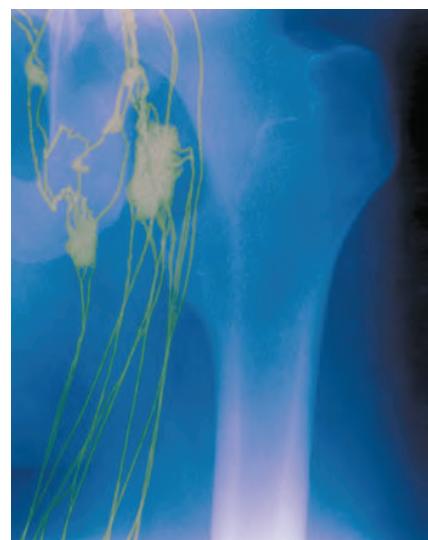
After entering the lymphatic system by diffusion, the fluid lost by capillaries is called **lymph**; its composition is about the same as that of interstitial fluid. The lymphatic system drains into large veins of the circulatory system at the base of the neck (see Figure 43.7). As you read in Chapter 41, this joining of the lymphatic and circulatory systems functions in the transfer of lipids from the small intestine to the blood.

The movement of lymph from peripheral tissues to the heart relies on much the same mechanisms that assist blood flow in veins. Lymph vessels, like veins, have valves that prevent the backflow of fluid. Rhythmic contractions of the vessel walls help draw fluid into the small lymphatic vessels. In addition, skeletal muscle contractions play a role in moving lymph.

Disorders that interfere with the lymphatic system highlight its role in maintaining proper fluid distribution in the body. Disruptions in the movement of lymph often cause edema, swelling resulting from the excessive accumulation of fluid in tissues. Severe blockage of lymph flow, as occurs when certain parasitic worms lodge in lymph vessels, results in extremely swollen limbs or other body parts, a condition known as elephantiasis.

Along a lymph vessel are organs called **lymph nodes** (**Figure 42.16**). By filtering the lymph and by housing cells that attack viruses and bacteria, lymph nodes play an important role in the body's defense. Inside each lymph node is a honeycomb of connective tissue with spaces filled by white blood cells. When the body is fighting an infection, these cells multiply rapidly, and the lymph nodes become swollen and tender (which is why your doctor may check for swollen lymph nodes in your neck, armpits, or groin when you feel sick). Because lymph nodes have filtering and surveillance functions, doctors may examine the lymph nodes of cancer patients to detect the spread of diseased cells.

In recent years, evidence has surfaced demonstrating that the lymphatic system also plays a role in harmful immune responses, such as those responsible for asthma. Because of these and other findings, the lymphatic system, largely ignored until the 1990s, has become a very active and promising area of biomedical research.



► Figure 42.16 Human lymph nodes and vessels. In this colorized X-ray image of the groin, lymph nodes and vessels (yellow) are visible next to the upper thigh bone (femur).

CONCEPT CHECK 42.3

- What is the primary cause of the low velocity of blood flow through capillaries?
- What short-term changes in cardiovascular function might best enable skeletal muscles to help an animal escape from a dangerous situation?
- WHAT IF?** If you had additional hearts distributed throughout your body, what would be one likely advantage and one likely disadvantage?

For suggested answers, see Appendix A.

much more highly specialized, as is the case for the blood of vertebrates.

Blood Composition and Function

Vertebrate blood is a connective tissue consisting of cells suspended in a liquid matrix called **plasma**. Dissolved in the plasma are ions and proteins that, together with the blood cells, function in osmotic regulation, transport, and defense. Separating the components of blood using a centrifuge reveals that cellular elements (cells and cell fragments) occupy about 45% of the volume of blood (Figure 42.17). The remainder is plasma.

Plasma

Among the many solutes in plasma are inorganic salts in the form of dissolved ions, sometimes referred to as blood electrolytes (see Figure 42.17). Although plasma is about 90% water, the dissolved salts are an essential component of the blood. Some of these ions buffer the blood, which in humans normally has a pH of 7.4. Salts are also important in maintaining the osmotic balance of the blood. In addition, the concentration of ions in plasma directly affects the composition of

CONCEPT 42.4

Blood components function in exchange, transport, and defense

As we discussed earlier, the fluid transported by an open circulatory system is continuous with the fluid that surrounds all of the body cells and therefore has the same composition. In contrast, the fluid in a closed circulatory system can be

The diagram illustrates the separation of blood components. On the left, a test tube contains a red liquid (red blood cells) at the bottom and a yellowish layer (plasma) at the top. Dashed lines extend from the test tube to two tables. The left table, titled 'Plasma 55%', details the components of plasma. The right table, titled 'Cellular elements 45%', details the various blood cells and platelets.

Plasma 55%	
Constituent	Major functions
Water	Solvent for carrying other substances
Ions (blood electrolytes)	Osmotic balance, pH buffering, and regulation of membrane permeability
Sodium Potassium Calcium Magnesium Chloride Bicarbonate	
Plasma proteins	Osmotic balance, pH buffering
Albumin	
Fibrinogen	Clotting
Immunoglobulins (antibodies)	Defense
Substances transported by blood	
Nutrients (such as glucose, fatty acids, vitamins)	
Waste products of metabolism	
Respiratory gases (O_2 and CO_2)	
Hormones	

Cellular elements 45%		
Cell type	Number per L (mm^3) of blood	Functions
Leukocytes (white blood cells)	5,000–10,000	Defense and immunity
Basophils		
Lymphocytes		
Eosinophils		
Neutrophils		
Monocytes		
Platelets	250,000–400,000	Blood clotting
Erythrocytes (red blood cells)	5–6 million	Transport of O_2 and some CO_2

▲ Figure 42.17 The composition of mammalian blood.

the interstitial fluid, where many of these ions have a vital role in muscle and nerve activity. To serve all of these functions, plasma electrolytes must be kept within narrow concentration ranges, a homeostatic function we will explore in Chapter 44.

Plasma proteins act as buffers against pH changes, help maintain the osmotic balance between blood and interstitial fluid, and contribute to the blood's viscosity (thickness). Particular plasma proteins have additional functions. The immunoglobulins, or antibodies, help combat viruses and other foreign agents that invade the body (see Chapter 43). Others are escorts for lipids, which are insoluble in water and can travel in blood only when bound to proteins. A third group of plasma proteins are clotting factors that help plug leaks when blood vessels are injured. (The term *serum* refers to blood plasma from which these clotting factors have been removed.)

Plasma also contains a wide variety of other substances in transit from one part of the body to another, including nutrients, metabolic wastes, respiratory gases, and hormones. Plasma has a much higher protein concentration than interstitial fluid, although the two fluids are otherwise similar. (Capillary walls, remember, are not very permeable to proteins.)

Cellular Elements

Blood contains two classes of cells: red blood cells, which transport O₂, and white blood cells, which function in defense (see Figure 42.17). Also suspended in blood plasma are **platelets**, fragments of cells that are involved in the clotting process.

Erythrocytes Red blood cells, or **erythrocytes**, are by far the most numerous blood cells. Each microliter (μL, or mm³) of human blood contains 5–6 million red cells, and there are about 25 trillion of these cells in the body's 5 L of blood. Their main function is O₂ transport, and their structure is closely related to this function. Human erythrocytes are small disks (7–8 μm in diameter) that are biconcave—thinner in the center than at the edges. This shape increases surface area, enhancing the rate of diffusion of O₂ across their plasma membranes. Mature mammalian erythrocytes lack nuclei. This unusual characteristic leaves more space in these tiny cells for **hemoglobin**, the iron-containing protein that transports O₂ (see Figure 5.20). Erythrocytes also lack mitochondria and generate their ATP exclusively by anaerobic metabolism. Oxygen transport would be less efficient if erythrocytes were aerobic and consumed some of the O₂ they carry.

Despite its small size, an erythrocyte contains about 250 million molecules of hemoglobin. Because each molecule of hemoglobin binds up to four molecules of O₂, one erythrocyte can transport about a billion O₂ molecules. As erythrocytes pass through the capillary beds of lungs, gills, or other respiratory organs, O₂ diffuses into the erythrocytes and binds to hemoglobin. In the systemic capillaries, O₂ dissociates from hemoglobin and diffuses into body cells.

In **sickle-cell disease**, an abnormal form of hemoglobin (Hb^S) polymerizes into aggregates. Because the concentration of hemoglobin in erythrocytes is so high, these aggregates are large enough to distort the erythrocyte into an elongated, curved shape that resembles a sickle. As you learned in Chapter 5, this abnormality results from an alteration in the amino acid sequence of hemoglobin at a single position (see Figure 5.21).

Sickle-cell disease significantly impairs the function of the circulatory system. Sickled cells often lodge in arterioles and capillaries, preventing delivery of O₂ and nutrients and removal of CO₂ and wastes. Blood vessel blockage and resulting organ swelling often result in severe pain. In addition, sickled cells frequently rupture, reducing the number of red blood cells available for transporting O₂. The average life span of a sickled erythrocyte is only 20 days—one-sixth that of a normal erythrocyte. The rate of erythrocyte loss outstrips the replacement capacity of the bone marrow. Short-term therapy includes replacement of erythrocytes by blood transfusion; long-term treatments are generally aimed at inhibiting aggregation of Hb^S.

Leukocytes The blood contains five major types of white blood cells, or **leukocytes**. Their function is to fight infections. Some are phagocytic, engulfing and digesting microorganisms as well as debris from the body's own dead cells. As we will see in Chapter 43, other leukocytes, called lymphocytes, develop into specialized B cells and T cells that mount immune responses against foreign substances. Normally, 1 μL of human blood contains about 5,000–10,000 leukocytes; their numbers increase temporarily whenever the body is fighting an infection. Unlike erythrocytes, leukocytes are also found outside the circulatory system, patrolling both interstitial fluid and the lymphatic system.

Platelets Platelets are pinched-off cytoplasmic fragments of specialized bone marrow cells. They are about 2–3 μm in diameter and have no nuclei. Platelets serve both structural and molecular functions in blood clotting.

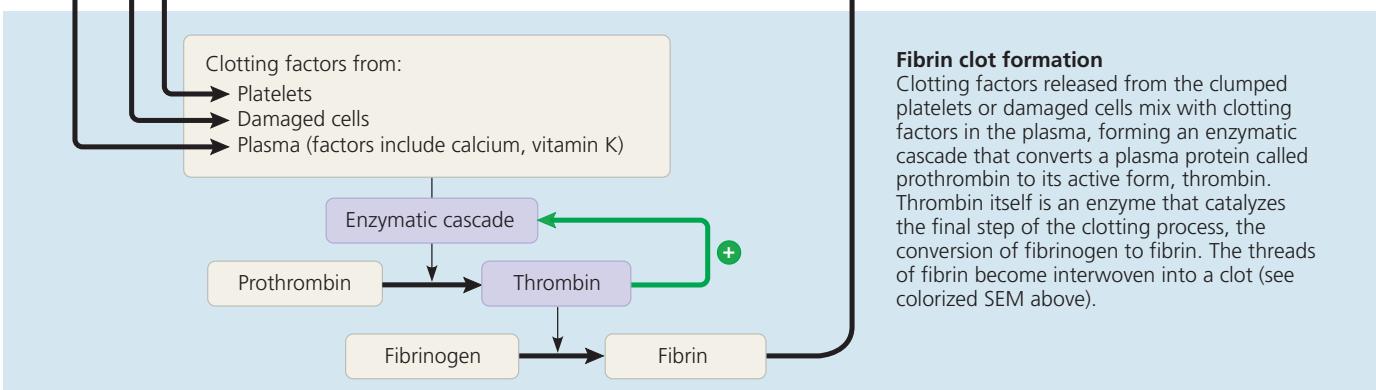
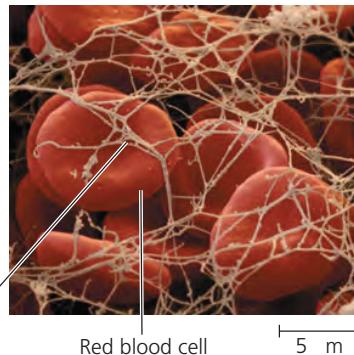
Blood Clotting

The occasional cut or scrape is not life-threatening because blood components seal the broken blood vessels. A break in a blood vessel wall exposes proteins that attract platelets and initiate coagulation, the conversion of liquid components of blood to a solid clot. The coagulant, or sealant, circulates in an inactive form called *fibrinogen*. In response to a broken blood vessel, platelets release clotting factors that trigger reactions leading to the formation of *thrombin*, an enzyme that converts fibrinogen to *fibrin*. Newly formed fibrin aggregates into threads that form the framework of the clot. Thrombin also activates a factor that catalyzes the formation of more thrombin, driving clotting to completion through positive feedback (see Chapter 40). The steps in the production of a

- 1 The clotting process begins when the endothelium of a vessel is damaged, exposing connective tissue in the vessel wall to blood. Platelets adhere to collagen fibers in the connective tissue and release a substance that makes nearby platelets sticky.

- 2 The platelets form a plug that provides emergency protection against blood loss.

- 3 This plug is reinforced by a fibrin clot when vessel damage is severe.



▲ Figure 42.18 Blood clotting.

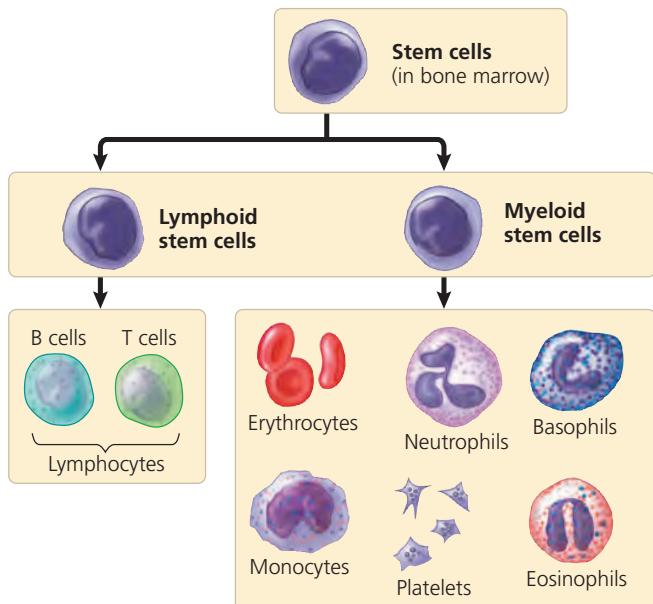
blood clot are diagrammed in **Figure 42.18**. Any genetic mutation that blocks a step in the clotting process can cause hemophilia, a disease characterized by excessive bleeding and bruising from even minor cuts and bumps (see Chapter 15).

Anticlotting factors in the blood normally prevent spontaneous clotting in the absence of injury. Sometimes, however, clots form within a blood vessel, blocking the flow of blood. Such a clot is called a **thrombus**. We will explore how a thrombus forms and the danger that it poses later in this chapter.

Stem Cells and the Replacement of Cellular Elements

Erythrocytes, leukocytes, and platelets all develop from a common source: multipotent **stem cells** that are dedicated to replenishing the body's blood cell populations (**Figure 42.19**). The stem cells that produce blood cells are located in the red marrow of bones, particularly the ribs, vertebrae, sternum, and pelvis. Multipotent stem cells are so named because they have the ability to form multiple types of cells—in this case, the myeloid and lymphoid cell lineages. When a stem cell divides, one daughter cell remains a stem cell while the other takes on a specialized function.

Throughout a person's life, erythrocytes, leukocytes, and platelets arising from stem cell divisions replace the worn-out



▲ Figure 42.19 Differentiation of blood cells. Some of the multipotent stem cells differentiate into lymphoid stem cells, which then develop into B cells and T cells, two types of lymphocytes that function in immunity (see Chapter 43). All other blood cells and platelets arise from myeloid stem cells.

cellular elements of blood. Erythrocytes, for example, circulate for only 120 days on average before being replaced; the old cells are consumed by phagocytic cells in the liver and spleen. The production of new erythrocytes involves recycling of materials, such as the use of iron scavenged from old erythrocytes in new hemoglobin molecules.

A negative-feedback mechanism, sensitive to the amount of O₂ reaching the body's tissues via the blood, controls erythrocyte production. If the tissues do not receive enough O₂, the kidneys synthesize and secrete a hormone called **erythropoietin (EPO)** that stimulates erythrocyte production. If the blood is delivering more O₂ than the tissues can use, the level of EPO falls and erythrocyte production slows. Physicians use synthetic EPO to treat people with health problems such as *anemia*, a condition of lower-than-normal erythrocyte or hemoglobin levels that lowers the oxygen-carrying capacity of the blood. Some athletes inject themselves with EPO to increase their erythrocyte levels, although this practice, a form of blood doping, has been banned by the International Olympic Committee and other sports organizations. In recent years, a number of well-known runners and cyclists have tested positive for EPO-related drugs and have forfeited both their records and their right to participate in future competitions.

Cardiovascular Disease

More than half of all human deaths in the United States are caused by cardiovascular diseases—disorders of the heart and blood vessels. Cardiovascular diseases range from a minor

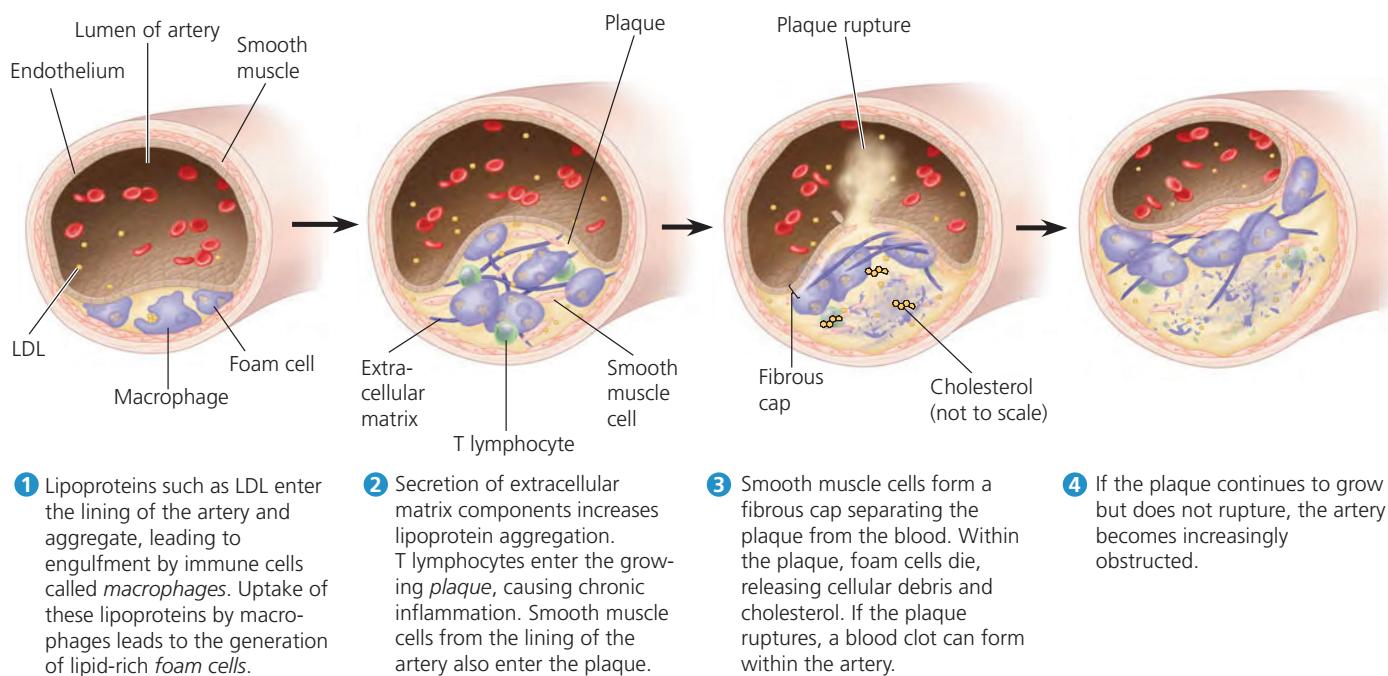
disturbance of vein or heart valve function to a life-threatening disruption of blood flow to the heart or brain.

Cholesterol metabolism plays a central role in cardiovascular disease. As you learned in Chapter 7, the presence of this steroid in animal cell membranes helps maintain normal membrane fluidity. Cholesterol travels in blood plasma mainly in particles that consist of thousands of cholesterol molecules and other lipids bound to a protein. One type of particle—**low-density lipoprotein (LDL)**—delivers cholesterol to cells for membrane production. Another type—**high-density lipoprotein (HDL)**—scavenges excess cholesterol for return to the liver. Individuals with a high ratio of LDL to HDL are at substantially increased risk for heart disease.

Another factor in cardiovascular disease is *inflammation*, the body's reaction to injury. As you will learn in the next chapter, tissue damage leads to recruitment of two types of circulating immune cells, macrophages and leukocytes. Signals released by these cells trigger a flow of fluid out of blood vessels at the site of injury, resulting in the tissue swelling characteristic of inflammation (see Figure 43.8). Although inflammation is often a normal and healthy response to injury, it can significantly disrupt circulatory function, as explained in the next section.

Atherosclerosis, Heart Attacks, and Stroke

Circulating cholesterol and inflammation can act together to produce a cardiovascular disease called **atherosclerosis**, the hardening of the arteries by accumulation of fatty deposits (**Figure 42.20**). Healthy arteries have a smooth inner lining



▲ **Figure 42.20 Atherosclerosis.** In atherosclerosis, thickening of an arterial wall by plaque formation can restrict blood flow through the artery. Fragments of a ruptured plaque can travel via the bloodstream and become lodged in other arteries. If those arteries supply the heart or brain, the resulting obstruction could cause a heart attack or stroke, respectively.

that reduces resistance to blood flow. Damage or infection can roughen the lining and lead to inflammation. Leukocytes are attracted to the damaged lining and begin to take up lipids, including cholesterol. A fatty deposit, called a plaque, grows steadily, incorporating fibrous connective tissue and additional cholesterol. As the plaque grows, the walls of the artery become thick and stiff, and the obstruction of the artery increases.

The result of untreated atherosclerosis is often a heart attack or a stroke. A **heart attack**, also called a *myocardial infarction*, is the damage or death of cardiac muscle tissue resulting from blockage of one or more coronary arteries, which supply oxygen-rich blood to the heart muscle. Because the coronary arteries are small in diameter, they are especially vulnerable to obstruction. Such blockage can destroy cardiac muscle quickly because the constantly beating heart muscle cannot survive long without O₂. If the heart stops beating, the victim may nevertheless survive if a heartbeat is restored by cardiopulmonary resuscitation (CPR) or some other emergency procedure within a few minutes of the attack. A **stroke** is the death of nervous tissue in the brain due to a lack of O₂. Strokes usually result from rupture or blockage of arteries in the head. The effects of a stroke and the individual's chance of survival depend on the extent and location of the damaged brain tissue. Rapid administration of a clot-dissolving drug may reduce the effects of a stroke or heart attack.

Although atherosclerosis often isn't detected until critical blood flow is disrupted, there can be warning signs. Partial blockage of the coronary arteries may cause occasional chest pain, a condition known as angina pectoris. The pain is most likely to be felt when the heart is laboring hard during physical or emotional stress, and it signals that part of the heart is not receiving enough O₂. An obstructed coronary artery may be treated surgically, either by inserting a metal mesh tube called a stent to expand the artery or by transplanting a healthy blood vessel from the chest or a limb to bypass the blockage.

Risk Factors and Treatment of Cardiovascular Disease

Although the tendency to develop particular cardiovascular diseases is inherited, it is also strongly influenced by lifestyle. Smoking and consumption of certain processed vegetable oils called *trans fats* (see Chapter 5) increase the ratio of LDL to HDL, raising the risk of cardiovascular disease. In contrast, exercise decreases the LDL/HDL ratio.

There has been considerable progress in the last decade in preventing cardiovascular disease. Many individuals at high risk are now treated with drugs called statins, which lower LDL levels and thereby reduce the risk of heart attacks. A recent discovery highlighted in **Figure 42.21** may lead to the development of additional drugs effective at lowering LDL levels in the blood.

The recognition that inflammation plays a central role in atherosclerosis and thrombus formation is also changing the

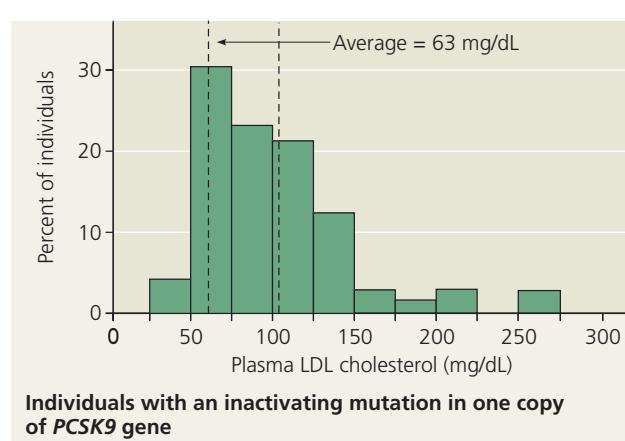
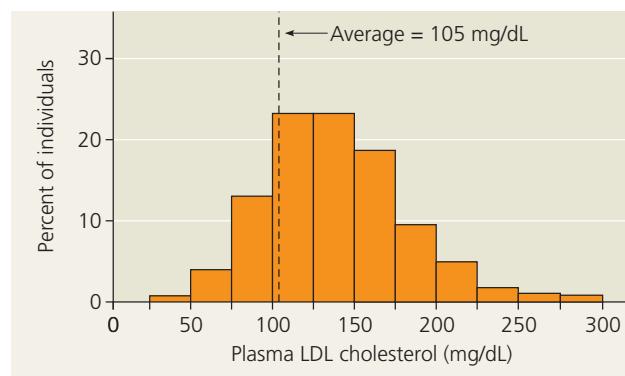
▼ Figure 42.21

INQUIRY

Can inactivating a liver enzyme lower plasma LDL levels?

EXPERIMENT In 2003, French researchers found that plasma LDL levels are higher in people who have mutations that increase the activity of a human liver enzyme called PCSK9. Helen Hobbs and co-workers in Dallas, Texas, then asked whether mutations that *inactivate* the PCSK9 gene could *lower* LDL levels. By screening 15,000 participants in a 15-year study of cardiovascular disease, they discovered that 2% of individuals of African descent have mutations that inactivate one copy of the PCSK9 gene. They then measured plasma LDL levels in individuals with one of these mutations and in control individuals.

RESULTS



CONCLUSION Inactivating one copy of the PCSK9 gene lowers the average plasma LDL level by 40%. Based on this result, Hobbs and colleagues hypothesized that decreasing PCSK9 activity reduces the risk for heart disease. Further analysis of data from the 15-year study supported this hypothesis: Individuals carrying PCSK9 mutations had an 88% lower risk for heart disease compared with the control group. A search is now under way for molecules that inhibit PCSK9 as potential drugs to prevent heart disease.

SOURCE J. Cohen, A. Pertsemlidis, I. Kotowski, R. Graham, C. Garcia, and H. Hobbs, Low LDL cholesterol in individuals of African descent resulting from frequent nonsense mutations in PCSK9, *Nature Genetics* 37:161–165 (2005).

WHAT IF? Suppose you could measure the activity of PCSK9 in blood samples. How would you expect the activity to compare for the individuals studied by the French researchers and by Dr. Hobbs's team?

treatment of cardiovascular disease. For example, aspirin, which inhibits the inflammatory response, has been found to help prevent the recurrence of heart attacks and stroke. Researchers have also focused on C-reactive protein (CRP), which is produced by the liver and found in the blood during episodes of acute inflammation. Like a high level of LDL cholesterol, the presence of significant amounts of CRP in blood is a useful risk indicator for cardiovascular disease.

Hypertension (high blood pressure) is yet another contributor to heart attack and stroke as well as other health problems. According to one hypothesis, chronic high blood pressure damages the endothelium that lines the arteries, promoting plaque formation. The usual definition of hypertension in adults is a systolic pressure above 140 mm Hg or a diastolic pressure above 90 mm Hg. Fortunately, hypertension is simple to diagnose and can usually be controlled by dietary changes, exercise, medication, or a combination of these approaches.

CONCEPT CHECK 42.4

1. Explain why a physician might order a white cell count for a patient with symptoms of an infection.
2. Clots in arteries can cause heart attacks and strokes. Why, then, does it make sense to treat hemophiliacs by introducing clotting factors into their blood?
3. **WHAT IF?** Nitroglycerin (the key ingredient in dynamite) is sometimes prescribed for heart disease patients. Within the body, the nitroglycerin is converted to nitric oxide. Why would you expect nitroglycerin to relieve chest pain in these patients?
4. **MAKE CONNECTIONS** The allele that encodes Hb^S is codominant with the allele encoding normal hemoglobin (Hb) (see Concept 14.4, pp. 277–278). What can you deduce about the properties of Hb and Hb^S with regard to aggregate formation and sickling?
5. **MAKE CONNECTIONS** How do stem cells from the bone marrow of an adult differ from embryonic stem cells (see Concept 20.3, p. 415–416)?

For suggested answers, see Appendix A.

CONCEPT 42.5

Gas exchange occurs across specialized respiratory surfaces

In the remainder of this chapter, we will focus on the process of **gas exchange**. Although this process is often called respiratory exchange or respiration, it should not be confused with the energy transformations of cellular respiration. Gas exchange is the uptake of molecular O₂ from the environment and the discharge of CO₂ to the environment.

Partial Pressure Gradients in Gas Exchange

To understand the driving forces for gas exchange, we must calculate **partial pressure**, which is simply the pressure exerted by a particular gas in a mixture of gases. To do so, we need to know the pressure that the mixture exerts and the fraction of the mixture represented by a particular gas. Let's consider O₂ as an example. At sea level, the atmosphere exerts a downward force equal to that of a column of mercury (Hg) 760 mm high. Therefore, atmospheric pressure at sea level is 760 mm Hg. Since the atmosphere is 21% O₂ by volume, the partial pressure of O₂ is 0.21×760 , or about 160 mm Hg. This value is called the *partial pressure* of O₂ (abbreviated P_{O₂}) because it is the part of atmospheric pressure contributed by O₂. The partial pressure of CO₂ (abbreviated P_{CO₂}) is much less, only 0.29 mm Hg at sea level.

Partial pressures also apply to gases dissolved in a liquid, such as water. When water is exposed to air, an equilibrium is reached in which the partial pressure of each gas in the water equals the partial pressure of that gas in the air. Thus, water exposed to air at sea level has a P_{O₂} of 160 mm Hg, the same as in the atmosphere. However, the *concentrations* of O₂ in the air and water differ substantially because O₂ is much less soluble in water than in air.

Once we have calculated partial pressures, we can readily predict the net result of diffusion at gas exchange surfaces: A gas always diffuses from a region of higher partial pressure to a region of lower partial pressure.

Respiratory Media

The conditions for gas exchange vary considerably, depending on whether the respiratory medium—the source of O₂—is air or water. As already noted, O₂ is plentiful in air, making up about 21% of Earth's atmosphere by volume. Compared to water, air is much less dense and less viscous, so it is easier to move and to force through small passageways. As a result, breathing air is relatively easy and need not be particularly efficient. Humans, for example, extract only about 25% of the O₂ in inhaled air.

Gas exchange with water as the respiratory medium is much more demanding. The amount of O₂ dissolved in a given volume of water varies but is always less than in an equivalent volume of air. Water in many marine and freshwater habitats contains only 4–8 mL of dissolved O₂ per liter, a concentration roughly 40 times less than in air. The warmer and saltier the water is, the less dissolved O₂ it can hold. Water's lower O₂ content, greater density, and greater viscosity mean that aquatic animals such as fishes and lobsters must expend considerable energy to carry out gas exchange. In the context of these challenges, adaptations have evolved that enable most aquatic animals to be very efficient in gas exchange. Many of these adaptations involve the organization of the surfaces dedicated to exchange.

Respiratory Surfaces

Specialization for gas exchange is apparent in the structure of the respiratory surface, the part of an animal's body where gas exchange occurs. Like all living cells, the cells that carry out gas exchange have a plasma membrane that must be in contact with an aqueous solution. Respiratory surfaces are therefore always moist.

The movement of O₂ and CO₂ across moist respiratory surfaces takes place entirely by diffusion. The rate of diffusion is proportional to the surface area across which it occurs and inversely proportional to the square of the distance through which molecules must move. In other words, gas exchange is fast when the area for diffusion is large and the path for diffusion is short. As a result, respiratory surfaces tend to be large and thin.

In some relatively simple animals, such as sponges, cnidarians, and flatworms, every cell in the body is close enough to the external environment that gases can diffuse quickly between all cells and the environment. In many animals, however, the bulk of the body's cells lack immediate access to the environment. The respiratory surface in these animals is a thin, moist epithelium that constitutes a respiratory organ.

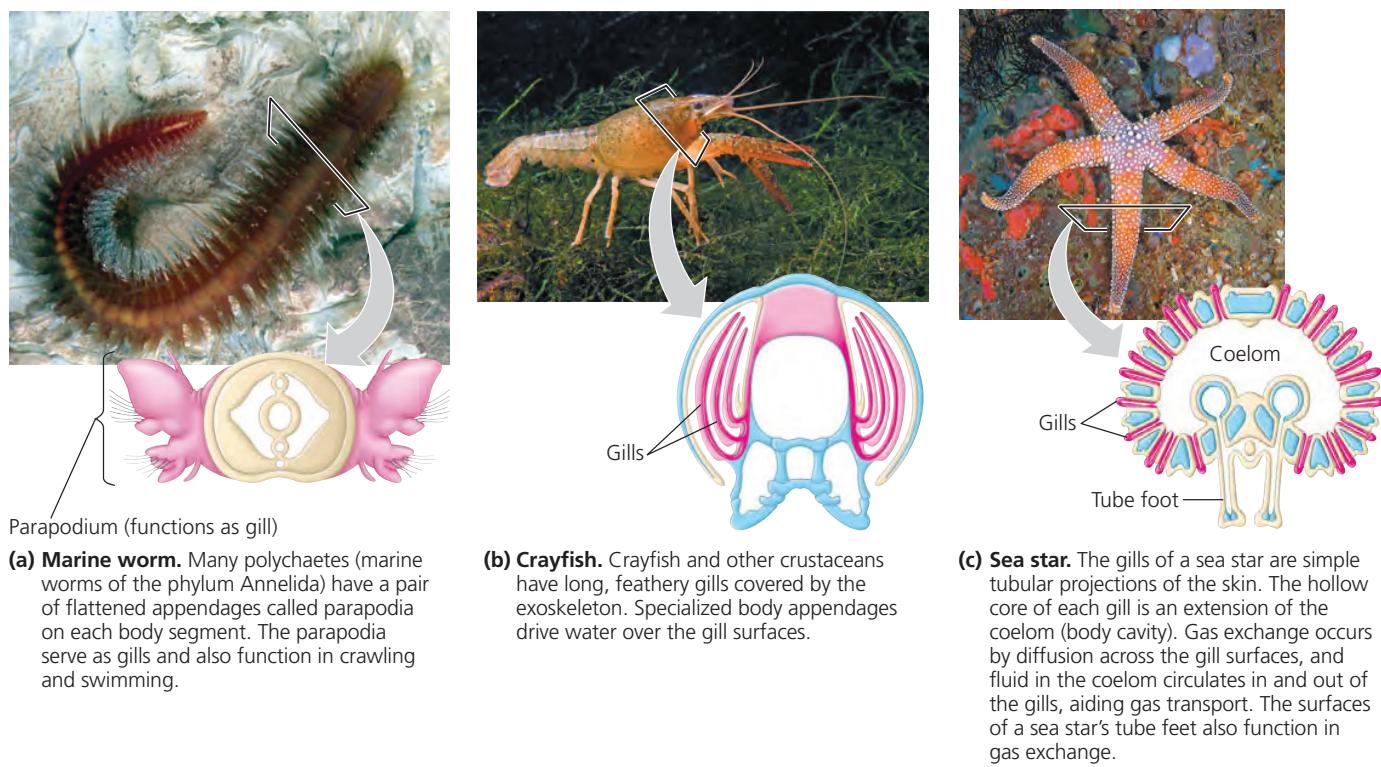
The skin serves as a respiratory organ in some animals, including earthworms and some amphibians. Just below the skin, a dense network of capillaries facilitates the exchange of gases between the circulatory system and the environment. Because the respiratory surface must remain moist, earthworms and many other skin-breathers can survive for extended periods only in damp places.

The general body surface of most animals lacks sufficient area to exchange gases for the whole organism. The evolutionary solution to this limitation is a respiratory organ that is extensively folded or branched, thereby enlarging the available surface area for gas exchange. Gills, tracheae, and lungs are three such organs.

Gills in Aquatic Animals

Gills are outfoldings of the body surface that are suspended in the water. As illustrated in **Figure 42.22**, the distribution of gills over the body can vary considerably. Regardless of their distribution, gills often have a total surface area much greater than that of the rest of the body's exterior.

Movement of the respiratory medium over the respiratory surface, a process called **ventilation**, maintains the partial pressure gradients of O₂ and CO₂ across the gill that



▲ Figure 42.22 Diversity in the structure of gills, external body surfaces that function in gas exchange.

MAKE CONNECTIONS As shown in Figure 32.11, animals with bilateral symmetry are divided into three main lineages. What are those lineages? How many are represented by the gilled animals shown above?

are necessary for gas exchange. To promote ventilation, most gill-bearing animals either move their gills through the water or move water over their gills. For example, crayfish and lobsters have paddle-like appendages that drive a current of water over the gills, whereas mussels and clams move water with cilia. Octopuses and squids ventilate their gills by taking in and ejecting water, with the side benefit of locomotion by jet propulsion. Fishes use the motion of swimming or coordinated movements of the mouth and gill covers to ventilate their gills. In both cases, a current of water enters the mouth, passes through slits in the pharynx, flows over the gills, and then exits the body (**Figure 42.23**).

The arrangement of capillaries in a fish gill allows for **countercurrent exchange**, the exchange of a substance or heat between two fluids flowing in opposite directions. In a fish gill, this process maximizes gas exchange efficiency. Because blood flows in the direction opposite to that of water passing over the gills, at each point in its travel blood is less saturated with O₂ than the water it meets (see Figure 42.23). As blood enters a gill capillary, it encounters water that is completing its passage through the gill. Depleted of much of its dissolved O₂, this water nevertheless has a higher P_{O₂} than the incoming blood, and O₂ transfer takes place. As the blood continues its passage, its P_{O₂} steadily increases, but so does that of the water it encounters, since each successive position

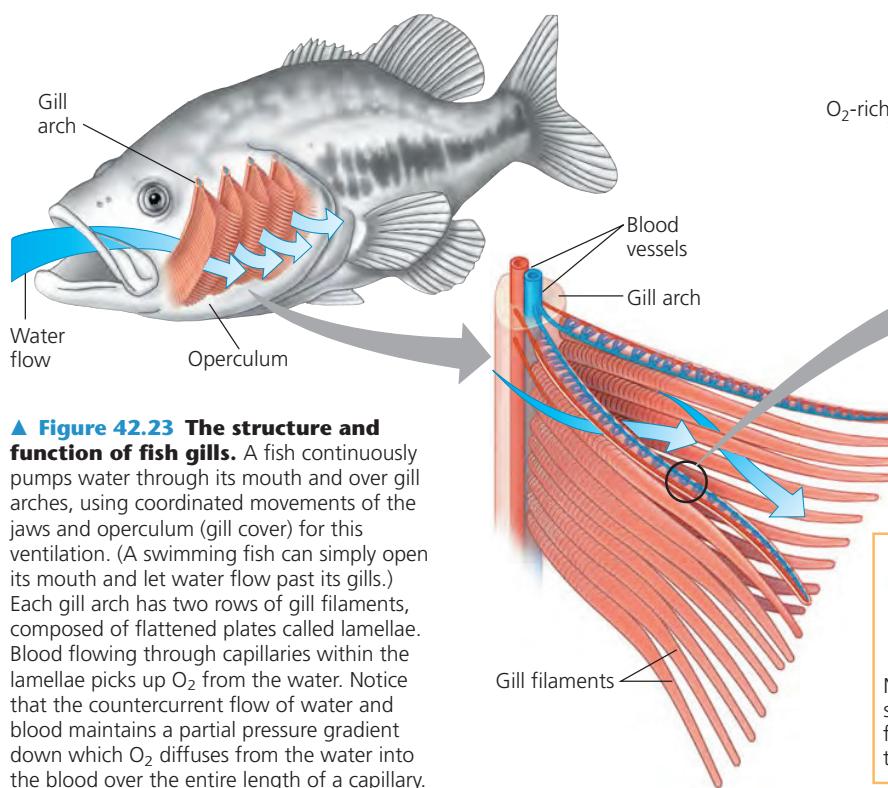
in the blood's travel corresponds to an earlier position in the water's passage over the gills. Thus, a partial pressure gradient favoring the diffusion of O₂ from water to blood exists along the entire length of the capillary.

Countercurrent exchange mechanisms are remarkably efficient. In the fish gill, more than 80% of the O₂ dissolved in the water is removed as it passes over the respiratory surface. In other settings, countercurrent exchange contributes to temperature regulation (see Chapter 40) and to the functioning of the mammalian kidney, as we will see in Chapter 44.

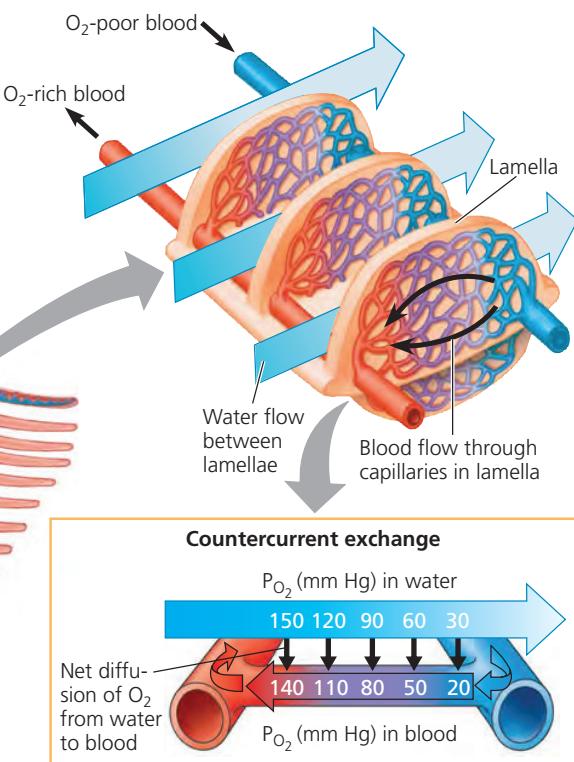
Gills are generally unsuitable for an animal living on land. An expansive surface of wet membrane exposed directly to air currents in the environment would lose too much water by evaporation. Furthermore, the gills would collapse as their fine filaments, no longer supported by water, stuck together. In most terrestrial animals, respiratory surfaces are enclosed within the body, exposed to the atmosphere only through narrow tubes.

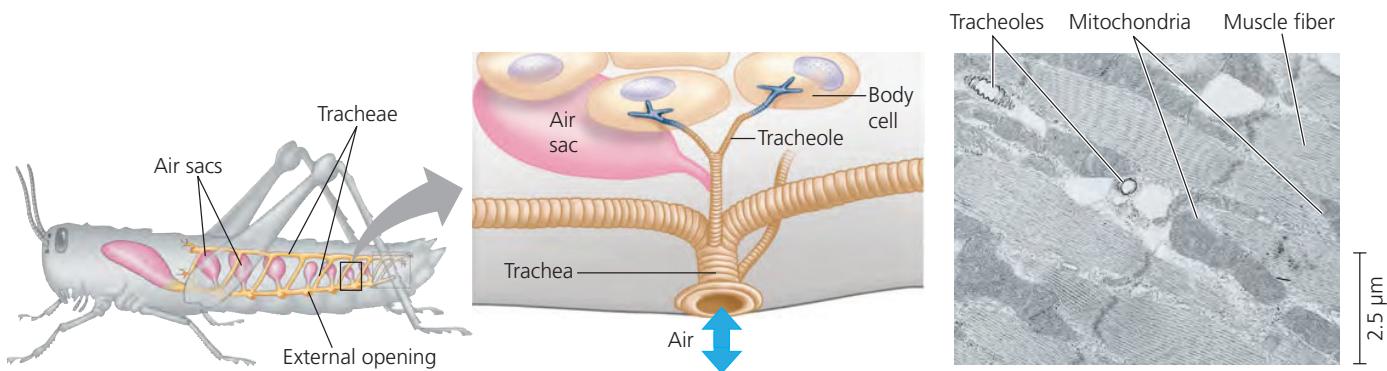
Tracheal Systems in Insects

Although the most familiar respiratory structure among terrestrial animals is the lung, the most common is actually the **tracheal system** of insects. Made up of air tubes that branch throughout the body, this system is one variation on the theme of an internal respiratory surface. The largest



▲ Figure 42.23 The structure and function of fish gills. A fish continuously pumps water through its mouth and over gill arches, using coordinated movements of the jaws and operculum (gill cover) for this ventilation. (A swimming fish can simply open its mouth and let water flow past its gills.) Each gill arch has two rows of gill filaments, composed of flattened plates called lamellae. Blood flowing through capillaries within the lamellae picks up O₂ from the water. Notice that the countercurrent flow of water and blood maintains a partial pressure gradient down which O₂ diffuses from the water into the blood over the entire length of a capillary.





(a) The respiratory system of an insect consists of branched internal tubes. The largest tubes, called tracheae, connect to external openings spaced along the insect's body surface. Air sacs formed from enlarged portions of the tracheae are found near organs that require a large supply of oxygen.

(b) Rings of chitin keep the tracheae open, allowing air to enter and pass into smaller tubes called tracheoles. The branched tracheoles deliver air directly to cells throughout the body. Tracheoles have closed ends filled with fluid (blue-gray). When the animal is active and using more O₂, most of the fluid is withdrawn into the body. This increases the surface area of air-filled tracheoles in contact with cells.

(c) The TEM above shows cross sections of tracheoles in a tiny piece of insect flight muscle. Each of the numerous mitochondria in the muscle cells lies within about 5 m of a tracheole.

▲ **Figure 42.24 Tracheal systems.**

tubes, called tracheae, open to the outside (**Figure 42.24a**). The finest branches extend close to the surface of nearly every cell, where gas is exchanged by diffusion across the moist epithelium that lines the tips of the tracheal branches (**Figure 42.24b**). Because the tracheal system brings air within a very short distance of virtually every body cell in an insect, it can transport O₂ and CO₂ without the participation of the animal's open circulatory system.

For small insects, diffusion through the tracheae brings in enough O₂ and removes enough CO₂ to support cellular respiration. Larger insects meet their higher energy demands by ventilating their tracheal systems with rhythmic body movements that compress and expand the air tubes like bellows. For example, consider an insect in flight, which has a very high metabolic rate, consuming 10 to 200 times more O₂ than it does at rest. In many flying insects, alternating contraction and relaxation of the flight muscles pumps air rapidly through the tracheal system. The flight muscle cells are packed with mitochondria that support the high metabolic rate, and the tracheal tubes supply these ATP-generating organelles with ample O₂ (**Figure 42.24c**). Thus, adaptations of tracheal systems are directly related to bioenergetics.

Lungs

Unlike tracheal systems, which branch throughout the insect body, **lungs** are localized respiratory organs. Representing an infolding of the body surface, they are typically subdivided into numerous pockets. Because the respiratory surface of a lung is not in direct contact with all other parts of the body, the gap must be bridged by the circulatory system, which transports gases between the lungs and the rest of the body. Lungs have evolved in organisms with open

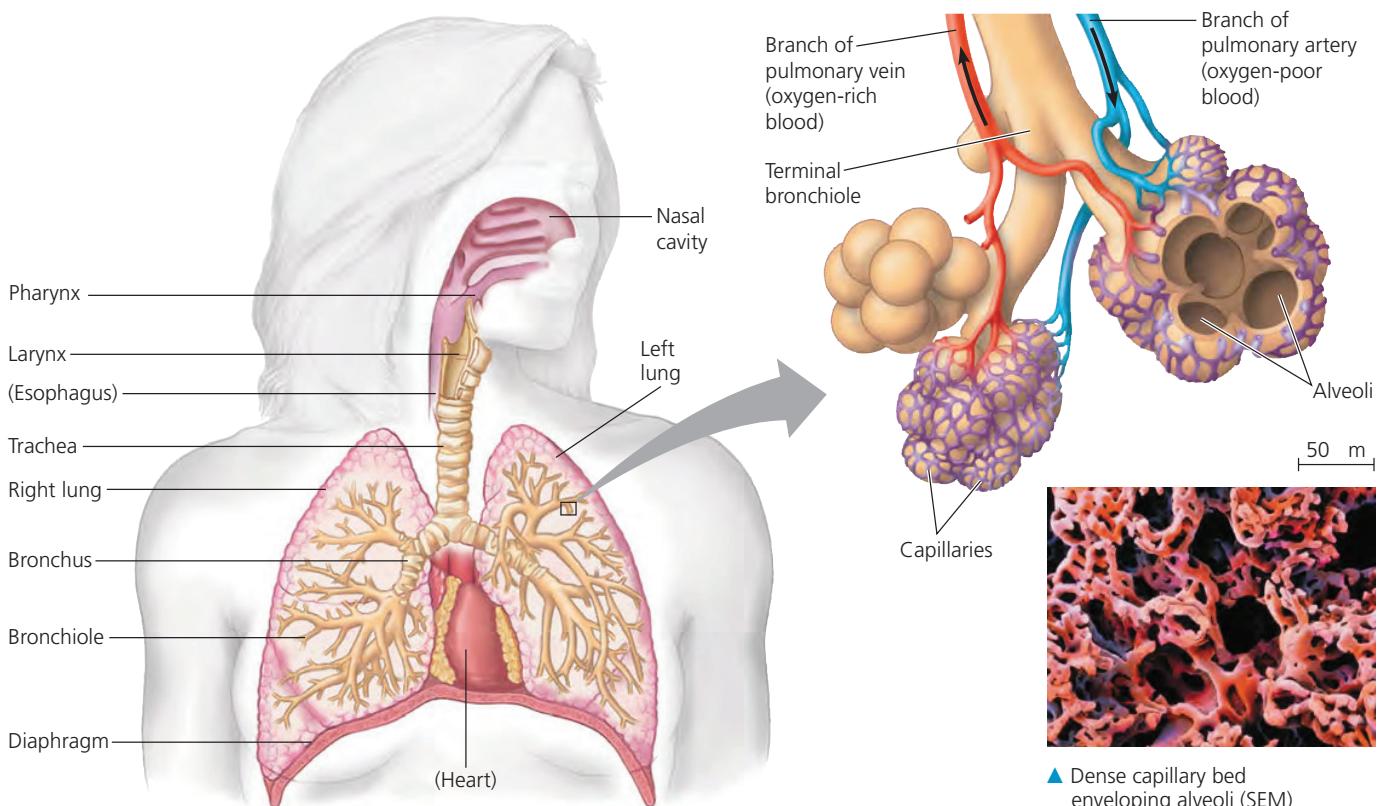
circulatory systems, such as spiders and land snails, as well as in vertebrates.

Among vertebrates that lack gills, the use of lungs for gas exchange varies. Amphibian lungs, when present, are relatively small and lack an extensive surface for exchange. Amphibians instead rely heavily on diffusion across other body surfaces, such as the skin, to carry out gas exchange. In contrast, most reptiles (including all birds) and all mammals depend entirely on lungs for gas exchange. Turtles are an exception; they supplement lung breathing with gas exchange across moist epithelial surfaces continuous with their mouth or anus. Lungs and air breathing have evolved in a few aquatic vertebrates (including lungfishes) as adaptations to living in oxygen-poor water or to spending part of their time exposed to air (for instance, when the water level of a pond recedes).

Mammalian Respiratory Systems: A Closer Look

In mammals, a system of branching ducts conveys air to the lungs, which are located in the thoracic cavity (**Figure 42.25**). Air enters through the nostrils and is then filtered by hairs, warmed, humidified, and sampled for odors as it flows through a maze of spaces in the nasal cavity. The nasal cavity leads to the pharynx, an intersection where the paths for air and food cross. When food is swallowed, the **larynx** (the upper part of the respiratory tract) moves upward and tips the epiglottis over the glottis (the opening of the **trachea**, or windpipe). This allows food to go down the esophagus to the stomach (see Figure 41.11). The rest of the time, the glottis is open, enabling breathing.

From the larynx, air passes into the trachea. Cartilage reinforcing the walls of both the larynx and the trachea keeps this part of the airway open. Within the larynx of most mammals,



▲ Figure 42.25 The mammalian respiratory system. From the nasal cavity and pharynx, inhaled air passes through the larynx, trachea, and bronchi to the bronchioles, which end in microscopic alveoli lined by a thin, moist epithelium. Branches of the pulmonary arteries convey oxygen-poor blood to the alveoli; branches of the pulmonary veins transport oxygen-rich blood from the alveoli back to the heart.

exhaled air rushes by a pair of elastic bands of muscle called **vocal folds**, or, in humans, **vocal cords**. Sounds are produced when muscles in the larynx are tensed, stretching the cords so they vibrate. High-pitched sounds result from tightly stretched cords vibrating rapidly; low-pitched sounds come from less tense cords vibrating slowly.

The trachea branches into two **bronchi** (singular, **bronchus**), one leading to each lung. Within the lung, the bronchi branch repeatedly into finer and finer tubes called **bronchioles**. The entire system of air ducts has the appearance of an inverted tree, the trunk being the trachea. The epithelium lining the major branches of this respiratory tree is covered by cilia and a thin film of mucus. The mucus traps dust, pollen, and other particulate contaminants, and the beating cilia move the mucus upward to the pharynx, where it can be swallowed into the esophagus. This process, sometimes referred to as the “mucus escalator,” plays a crucial role in cleansing the respiratory system.

Gas exchange in mammals occurs in **alveoli** (singular, **alveolus**; see Figure 42.25), air sacs clustered at the tips of the tiniest bronchioles. Human lungs contain millions of alveoli, which together have a surface area of about 100 m^2 , 50 times

that of the skin. Oxygen in the air entering the alveoli dissolves in the moist film lining their inner surfaces and rapidly diffuses across the epithelium into a web of capillaries that surrounds each alveolus. Net diffusion of carbon dioxide occurs in the opposite direction, from the capillaries across the epithelium of the alveolus and into the air space.

Lacking cilia or significant air currents to remove particles from their surface, alveoli are highly susceptible to contamination. White blood cells patrol alveoli, engulfing foreign particles. However, if too much particulate matter reaches the alveoli, the defenses can be overwhelmed, leading to inflammation and irreversible damage. For example, particulates from cigarette smoke that enter alveoli can cause a permanent reduction in lung capacity. For coal miners, inhalation of large amounts of coal dust can lead to silicosis, a disabling, irreversible, and sometimes fatal lung disease.

The film of liquid that lines alveoli is subject to surface tension, an attractive force that acts to minimize the surface area of a liquid (see Chapter 3). Given their tiny diameter (about 0.25 mm), why don't alveoli collapse under high surface tension? Researchers reasoned that alveoli must be coated with a material that reduces surface tension. In 1955, English

biophysicist Richard Pattle obtained experimental evidence for such a material, now called a **surfactant**, for surface-active agent. In addition, he proposed that the absence of surfactant might cause *respiratory distress syndrome* (RDS), a disease common among preterm infants born 6 weeks or more before their due dates. In the 1950s, RDS killed 10,000 infants annually in the United States alone.

In the late 1950s, Mary Ellen Avery carried out the first experiment linking RDS to a surfactant deficiency (Figure 42.26). Subsequent studies revealed that surfactant contains a mixture of phospholipids and proteins and typically appears in the lungs after 33 weeks of development. (The average full-term pregnancy lasts 38 weeks in humans.) Artificial surfactants are now used routinely to treat early preterm infants. Treated babies with a body mass over 900 g (2 pounds) at birth usually survive without long-term health problems. For her contributions, Avery received the National Medal of Science in 1991.

Having surveyed the route that air follows when we breathe, we will turn next to the process of breathing itself.

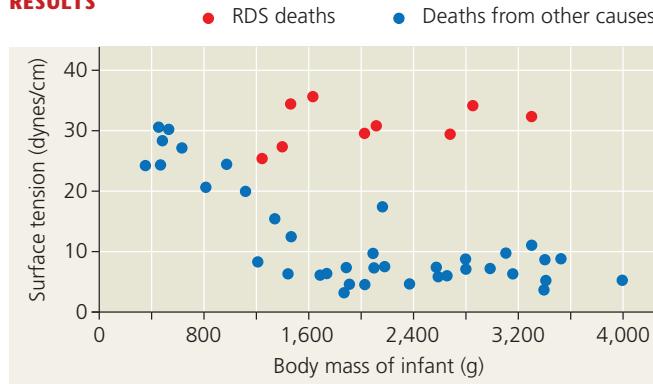
▼ Figure 42.26

INQUIRY

What causes respiratory distress syndrome?

EXPERIMENT Mary Ellen Avery, a research fellow working with Jere Mead at Harvard University Medical School, wondered whether a lack of surfactant caused respiratory distress syndrome (RDS) in preterm infants. She obtained autopsy samples of lungs from infants that had died of RDS and from infants that had died of other causes. She extracted material from the samples and allowed it to form a film on a water surface. Then Dr. Avery measured the tension (in dynes per centimeter) across the surface of the water and recorded the lowest surface tension observed for each sample.

RESULTS



CONCLUSION The lungs of infants with a body mass over 1,200 g (2.7 pounds) contain a substance that reduces surface tension. That substance is absent in the lungs of infants with RDS.

SOURCE M. E. Avery and J. Mead, Surface properties in relation to atelectasis and hyaline membrane disease, *American Journal of Diseases of Children* 97:517–523 (1959).

WHAT IF? Suppose you repeated this experiment but instead measured the amount of surfactant in lung samples. Describe the graph you would expect if you plotted the amount of surfactant versus infant weight.

CONCEPT CHECK 42.5

- Why is the position of lung tissues *within* the body an advantage for terrestrial animals?
- After a heavy rain, earthworms come to the surface. How would you explain this behavior in terms of an earthworm's requirements for gas exchange?
- MAKE CONNECTIONS** Describe how countercurrent exchange can facilitate both thermoregulation (see Concept 40.3, p. 865) and respiration.

For suggested answers, see Appendix A.

CONCEPT 42.6

Breathing ventilates the lungs

Like fishes, terrestrial vertebrates rely on ventilation to maintain high O₂ and low CO₂ concentrations at the gas exchange surface. The process that ventilates lungs is **breathing**, the alternating inhalation and exhalation of air. A variety of mechanisms for moving air in and out of lungs have evolved, as we will see by considering breathing in amphibians, mammals, and birds.

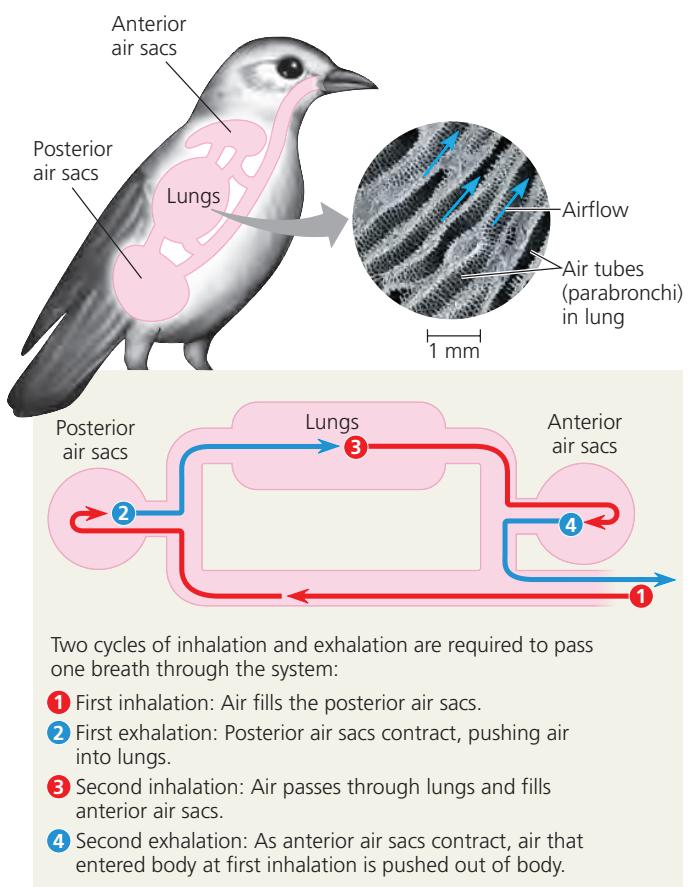
How an Amphibian Breathes

An amphibian such as a frog ventilates its lungs by **positive pressure breathing**, inflating the lungs with forced airflow. During the first stage of inhalation, muscles lower the floor of an amphibian's oral cavity, drawing in air through its nostrils. Next, with the nostrils and mouth closed, the floor of the oral cavity rises, forcing air down the trachea. During exhalation, air is forced back out by the elastic recoil of the lungs and by compression of the muscular body wall. When male frogs puff themselves up in aggressive or courtship displays, they disrupt this breathing cycle, taking in air several times without allowing any release.

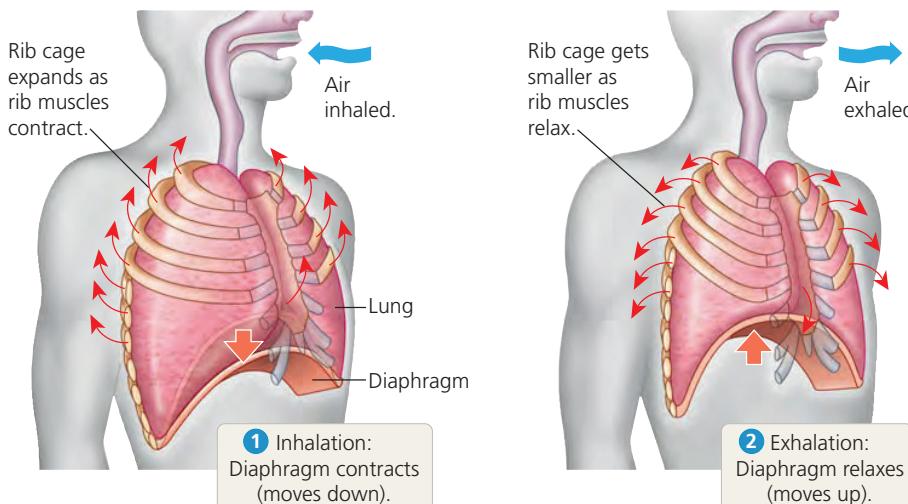
How a Bird Breathes

Two features of ventilation in birds make it highly efficient. First, when birds breathe, they pass air over the gas exchange surface in only one direction. Second, incoming fresh air does not mix with air that has already carried out gas exchange.

To bring fresh air to their lungs, birds use eight or nine air sacs situated on either side of the lungs (Figure 42.27). The air sacs do not function directly in gas exchange but act as bellows that keep air flowing through the lungs. Instead of alveoli, which are dead ends, the sites of gas exchange in bird lungs are tiny channels called *parabronchi*. Passage of air through the entire system—lungs and air sacs—requires two cycles of inhalation and exhalation. In some passageways, the direction in



▲ Figure 42.27 The avian respiratory system. This diagram traces a breath of air through the respiratory system of a bird. As shown, two cycles of inhalation and exhalation are required for the air to pass all the way through the system and out of the bird.



▲ Figure 42.28 Negative pressure breathing. A mammal breathes by changing the air pressure within its lungs relative to the pressure of the outside atmosphere.

WHAT IF? The walls of alveoli contain elastic fibers that allow the alveoli to expand and contract with each breath. If alveoli lost their elasticity, how would that affect gas exchange in the lungs?

which air moves alternates (see Figure 42.27). Within the parabronchi, however, air always flows in the same direction.

How a Mammal Breathes

Unlike amphibians and birds, mammals employ **negative pressure breathing**—pulling, rather than pushing, air into their lungs (Figure 42.28). Using muscle contraction to actively expand the thoracic cavity, mammals lower air pressure in their lungs below that of the air outside their body. Because gas flows from a region of higher pressure to a region of lower pressure, air rushes through the nostrils and mouth and down the breathing tubes to the alveoli. During exhalation, the muscles controlling the thoracic cavity relax, and the volume of the cavity is reduced. The increased air pressure in the alveoli forces air up the breathing tubes and out of the body. Thus, inhalation is always active and requires work, whereas exhalation is usually passive.

Expanding the thoracic cavity during inhalation involves the animal's rib muscles and the **diaphragm**, a sheet of skeletal muscle that forms the bottom wall of the cavity. Contracting the rib muscles expands the rib cage, the front wall of the thoracic cavity, by pulling the ribs upward and the sternum outward. At the same time, the diaphragm contracts, expanding the thoracic cavity downward. The effect of the descending diaphragm is similar to that of a plunger being drawn out of a syringe.

Within the thoracic cavity, a double membrane surrounds the lungs. The inner layer of this membrane adheres to the outside of the lungs, and the outer layer adheres to the wall of the thoracic cavity. A thin space filled with fluid separates the two layers. Surface tension in the fluid causes the two layers to stick together like two plates of glass separated by a film of water: The layers can slide smoothly past each other, but they cannot be pulled apart easily. Consequently, the volume of the thoracic cavity and the volume of the lungs change in unison.

Depending on activity level, additional muscles may be recruited to aid breathing. The rib muscles and diaphragm are sufficient to change lung volume when a mammal is at rest. During exercise, other muscles of the neck, back, and chest increase the volume of the thoracic cavity by raising the rib cage. In kangaroos and some other species, locomotion causes a rhythmic movement of organs in the abdomen, including the stomach and liver. The result is a piston-like pumping motion that pushes and pulls on the diaphragm, further increasing the volume of air moved in and out of the lungs.

The volume of air inhaled and exhaled with each breath is called **tidal volume**. It averages about 500 mL in resting humans. The tidal volume during maximal inhalation and exhalation is the **vital capacity**, which is about 3.4 L and 4.8 L for college-age women and men, respectively. The air that remains after a forced exhalation is called the **residual volume**. As we age, our lungs lose their resilience, and residual volume increases at the expense of vital capacity.

Because the lungs in mammals do not completely empty with each breath, and because inhalation occurs through the same airways as exhalation, each inhalation mixes fresh air with oxygen-depleted residual air. As a result, the maximum P_{O_2} in alveoli is always considerably less than in the atmosphere. The maximum P_{O_2} in lungs is also less for mammals than for birds, which renew the air in their lungs with every exhalation. This is one reason mammals function less well than birds at high altitude. For example, humans have great difficulty obtaining enough O_2 when climbing Earth's highest peaks, such as Mount Everest (8,850 m), in the Himalayas. However, bar-headed geese and several other bird species easily fly over the Himalayas during their migrations.

Control of Breathing in Humans

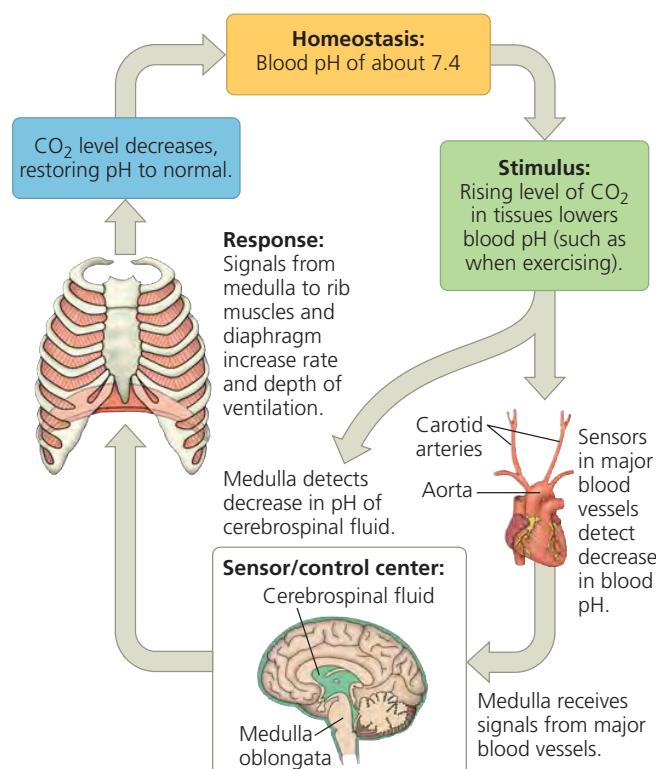
Although you can voluntarily hold your breath or breathe faster and deeper, most of the time your breathing is regulated by involuntary mechanisms. These control mechanisms ensure that gas exchange is coordinated with blood circulation and with metabolic demand.

The neurons mainly responsible for regulating breathing are in the medulla oblongata, near the base of the brain (Figure 42.29). Neural circuits in the medulla form a *breathing control center* that establishes the breathing rhythm. When you breathe deeply, a negative-feedback mechanism prevents the lungs from overexpanding: During inhalation, sensors that detect stretching of the lung tissue send nerve impulses to the control circuits in the medulla, inhibiting further inhalation.

In regulating breathing, the medulla uses the pH of the surrounding tissue fluid as an indicator of blood CO_2 concentration. The reason pH can be used in this way is that blood CO_2 is the main determinant of the pH of *cerebrospinal fluid*, the fluid surrounding the brain and spinal cord. Carbon dioxide diffuses from the blood to the cerebrospinal fluid, where it reacts with water and forms carbonic acid (H_2CO_3). The H_2CO_3 can then dissociate into a bicarbonate ion (HCO_3^-) and a hydrogen ion (H^+):



Increased metabolic activity, such as occurs during exercise, lowers pH by increasing the concentration of CO_2 in the blood. Sensors in blood vessels and the medulla detect this pH change. In response, the medulla's control circuits increase the depth and rate of breathing. Both remain high until the excess CO_2 is eliminated in exhaled air and pH returns to a normal value.



▲ Figure 42.29 Homeostatic control of breathing.

WHAT IF? Suppose a person began breathing very rapidly while resting. Describe the effect on blood CO_2 levels and the steps by which the negative feedback circuit in this figure would restore homeostasis.

The blood O_2 level usually has little effect on the breathing control centers. However, when the O_2 level drops very low (at high altitudes, for instance), O_2 sensors in the aorta and the carotid arteries in the neck send signals to the breathing control centers, which respond by increasing the breathing rate.

The pons, a part of the brain next to the medulla, also regulates breathing, although its exact role remains an open question. The pons may act in the regulatory circuit with the medulla or modulate the output of that circuit.

Breathing control is effective only if ventilation is matched to blood flow through alveolar capillaries. During exercise, for instance, such coordination couples an increased breathing rate, which enhances O_2 uptake and CO_2 removal, with an increase in cardiac output.

CONCEPT CHECK 42.6

- How does an increase in the CO_2 concentration in the blood affect the pH of cerebrospinal fluid?
- A drop in blood pH causes an increase in heart rate. What is the function of this control mechanism?
- WHAT IF?** If an injury tore a small hole in the membranes surrounding your lungs, what effect on lung function would you expect?

For suggested answers, see Appendix A.

CONCEPT 42.7

Adaptations for gas exchange include pigments that bind and transport gases

The high metabolic demands of many animals necessitate the exchange of large quantities of O₂ and CO₂. Here we'll examine how blood molecules called respiratory pigments facilitate this exchange through their interaction with O₂ and CO₂. We will also investigate physiological adaptations that enable animals to be active under conditions of high metabolic load or very limiting P_{O₂}. As a basis for exploring these topics, let's summarize the basic gas exchange circuit in humans.

Coordination of Circulation and Gas Exchange

The partial pressures of O₂ and CO₂ in the blood vary at different points in the circulatory system, as shown in **Figure 42.30**. Blood flowing through the alveolar capillaries has a lower P_{O₂} and a higher P_{CO₂} than the air in the alveoli. As a result, CO₂ diffuses down its partial pressure gradient from the blood to the air in the alveoli. Meanwhile, O₂ in the air dissolves in the fluid that coats the alveolar epithelium and diffuses into the blood. By the time the blood leaves the lungs in the pulmonary veins, its P_{O₂} has been raised and its P_{CO₂} has been lowered. After returning to the heart, this blood is pumped through the systemic circuit.

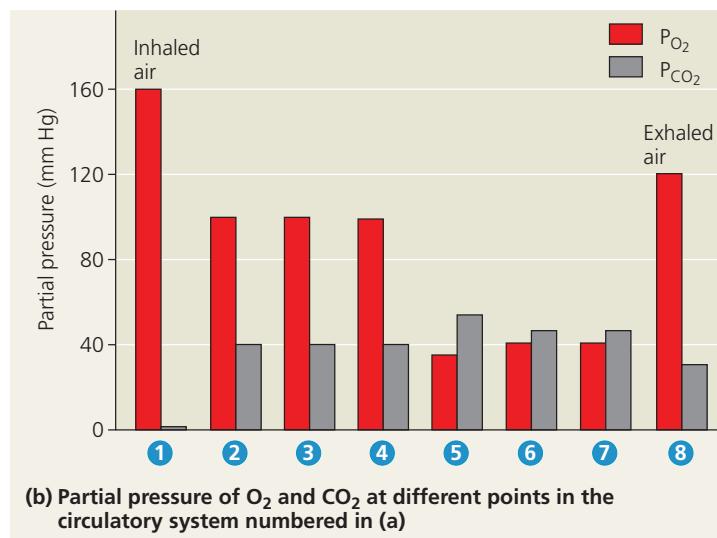
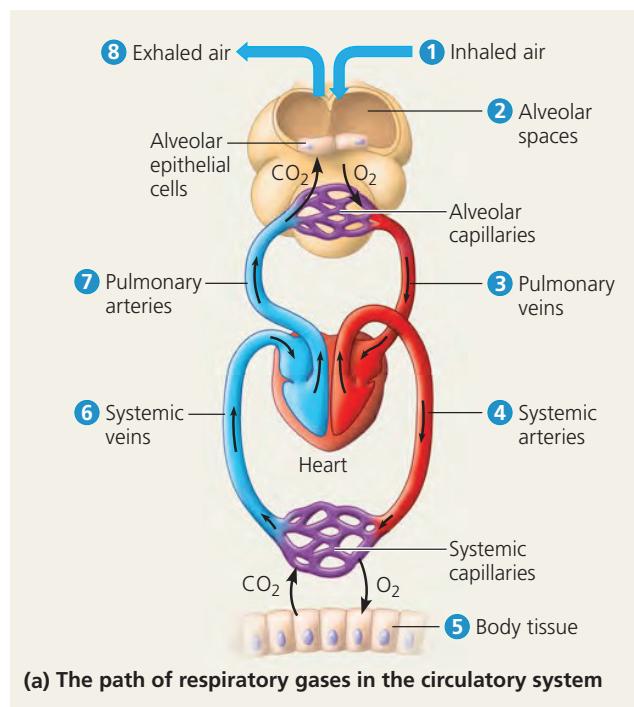
In the tissue capillaries, gradients of partial pressure favor the diffusion of O₂ out of the blood and CO₂ into the blood. These gradients exist because cellular respiration in the mitochondria of cells near each capillary removes O₂ from and adds CO₂ to the surrounding interstitial fluid. After the blood unloads O₂ and loads CO₂, it is returned to the heart and pumped to the lungs again.

Although this description faithfully characterizes the driving forces for gas exchange in different tissues, it omits the critical role of the specialized carrier proteins we will discuss next.

Respiratory Pigments

The low solubility of O₂ in water (and thus in blood) poses a problem for animals that rely on the circulatory system to deliver O₂. For example, a person requires almost 2 L of O₂ per minute during intense exercise, and all of it must be carried in the blood from the lungs to the active tissues. At normal body temperature and air pressure, however, only 4.5 mL of O₂ can dissolve into a liter of blood in the lungs. Even if 80% of the dissolved O₂ were delivered to the tissues (an unrealistically high percentage), the heart would still need to pump 555 L of blood per minute!

In fact, animals transport most of their O₂ bound to proteins called **respiratory pigments**. Respiratory pigments circulate with the blood or hemolymph and are often contained within specialized cells. The pigments greatly increase the amount of O₂ that can be carried in the circulatory fluid (to about 200 mL of O₂ per liter in mammalian blood).



▲ **Figure 42.30 Loading and unloading of respiratory gases.**

WHAT IF? If you consciously forced more air out of your lungs each time you exhaled, how would that affect the values shown in (b)?

In our example of an exercising human with an O₂ delivery rate of 80%, the presence of a respiratory pigment reduces the cardiac output necessary for O₂ transport to a manageable 12.5 L of blood per minute.

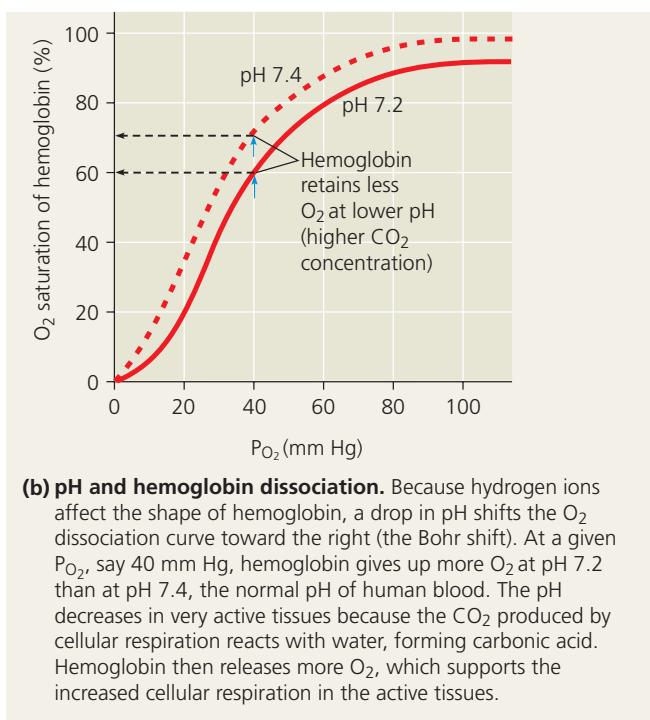
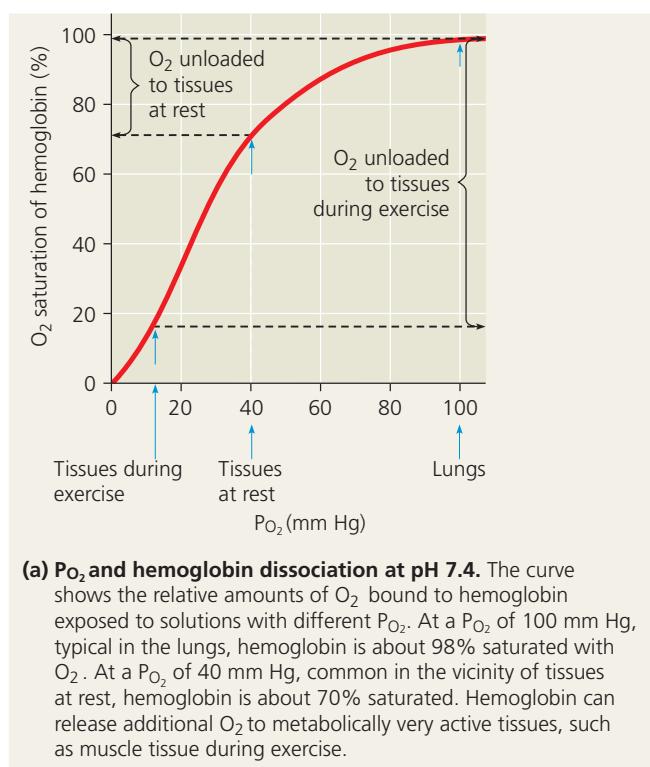
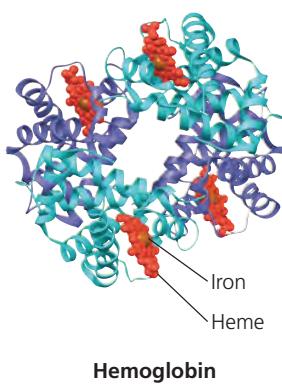
A variety of respiratory pigments have evolved among the animal taxa. With a few exceptions, these molecules have a distinctive color (hence the term *pigment*) and consist of a protein bound to a metal. One example is the blue pigment *hemocyanin*, which has copper as its oxygen-binding component and is found in arthropods and many molluscs. The respiratory pigment of almost all vertebrates and many invertebrates is hemoglobin. In vertebrates, it is contained in the erythrocytes.

Hemoglobin

Vertebrate hemoglobin consists of four subunits (polypeptide chains), each with a cofactor called a heme group that has an iron atom at its center. Each iron atom binds one molecule of O₂; hence, a single hemoglobin molecule can carry four molecules of O₂. Like all respiratory pigments, hemoglobin binds O₂ reversibly, loading O₂ in the lungs or gills and unloading it in other parts of the body. This process depends on cooperativity between the hemoglobin subunits (see pp. 158–159). When O₂ binds to one subunit, the others change shape slightly, increasing their affinity for O₂. When four O₂ molecules are bound and one subunit unloads its O₂, the other three subunits more readily unload O₂, as an associated shape change lowers their affinity for O₂.

Cooperativity in O₂ binding and release is evident in the dissociation curve for hemoglobin (Figure 42.31a). Over the range of P_{O₂} where the dissociation curve has a steep slope, even a slight change in P_{O₂} causes hemoglobin to load or unload a substantial amount of O₂. Notice that the steep part of the curve corresponds to the range of P_{O₂} found in body tissues. When cells in a particular location begin working harder—during exercise, for instance—P_{O₂} dips in their vicinity as the O₂ is consumed in cellular respiration. Because of the effect of subunit cooperativity, a slight drop in P_{O₂} causes a relatively large increase in the amount of O₂ the blood unloads.

The production of CO₂ during cellular respiration promotes the unloading of O₂ by hemoglobin in active tissues. As we have seen, CO₂ reacts with water, forming carbonic acid, which lowers the pH of its surroundings. Low pH, in turn, decreases the affinity of hemoglobin for O₂, an effect called the **Bohr shift** (Figure 42.31b). Thus, where CO₂ production is greater, hemoglobin releases more O₂, which can then be used to support more cellular respiration.



▲ **Figure 42.31** Dissociation curves for hemoglobin at 37°C.

Carbon Dioxide Transport

In addition to its role in O₂ transport, hemoglobin helps transport CO₂ and assists in buffering the blood—that is, preventing harmful changes in pH. Only about 7% of the CO₂

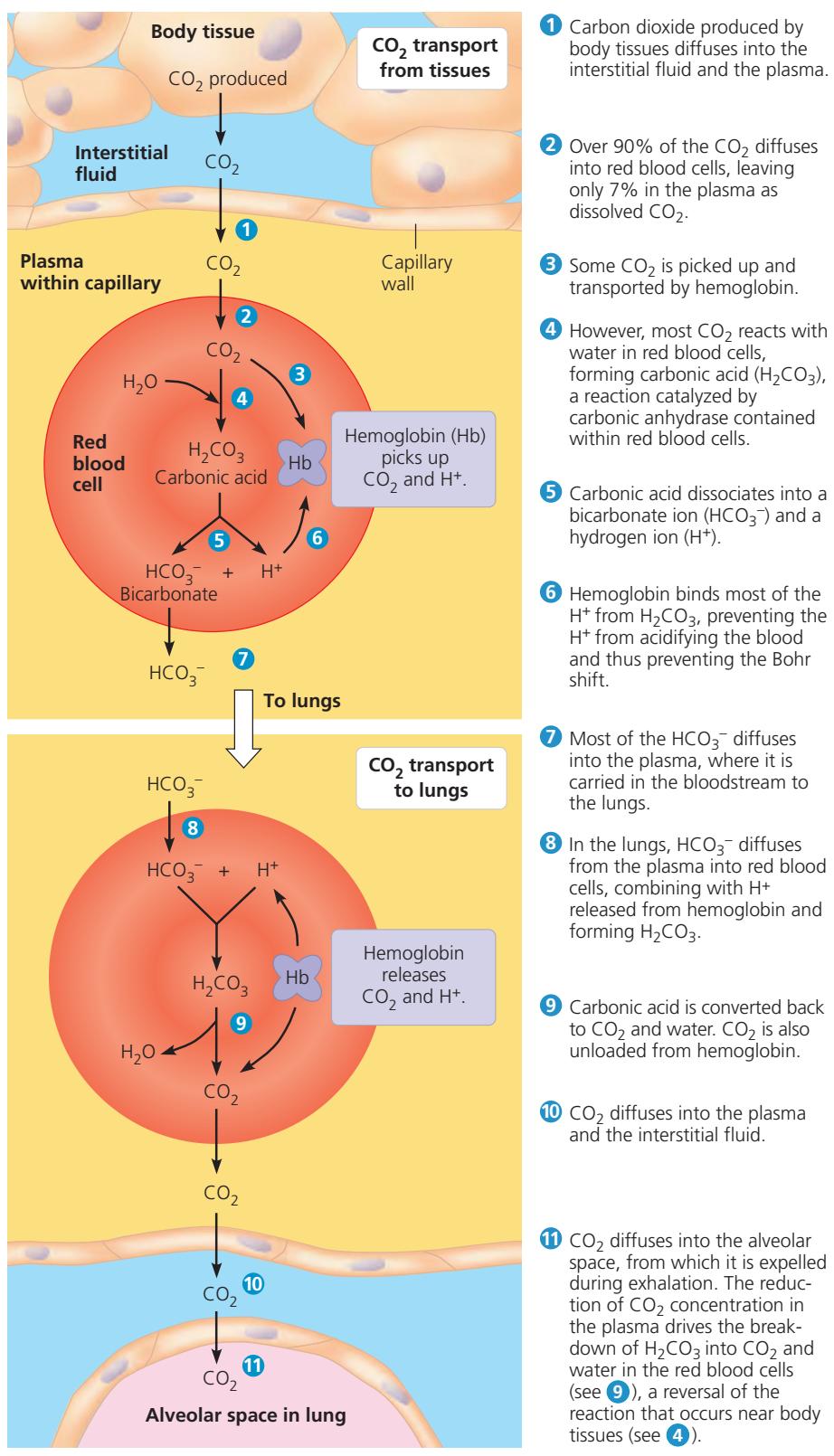
released by respiring cells is transported in solution in blood plasma. Another 23% binds to the amino ends of the hemoglobin polypeptide chains, and about 70% is transported in the blood in the form of bicarbonate ions (HCO_3^-).

As shown in **Figure 42.32**, carbon dioxide from respiring cells diffuses into the blood plasma and then into erythrocytes. There the CO_2 reacts with water (assisted by the enzyme carbonic anhydrase) and forms H_2CO_3 , which dissociates into H^+ and HCO_3^- . Most of the H^+ binds to hemoglobin and other proteins, minimizing the change in blood pH. The HCO_3^- diffuses into the plasma.

When blood flows through the lungs, the relative partial pressures of CO_2 favor the diffusion of CO_2 out of the blood. As CO_2 diffuses into alveoli, the amount of CO_2 in the blood decreases. This decrease shifts the chemical equilibrium in favor of the conversion of HCO_3^- to CO_2 , enabling further net diffusion of CO_2 into alveoli. Overall, the P_{CO_2} gradient is sufficient to reduce P_{CO_2} by roughly 15% during passage of blood through the lungs.

Respiratory Adaptations of Diving Mammals

EVOLUTION Animals vary greatly in their ability to temporarily inhabit environments in which there is no access to their normal respiratory medium—for example, when an air-breathing mammal swims underwater. Whereas most humans, even well-trained divers, cannot hold their breath longer than 2 or 3 minutes or swim deeper than 20 m, the Weddell seal of Antarctica routinely plunges to 200–500 m and remains there for about 20 minutes (and sometimes for more than an hour). (Humans can remain submerged for comparable periods, but only with the aid of specialized gear and compressed air tanks.) Some whales and other species of seals make even more impressive dives. Elephant seals can reach depths of 1,500 m—almost a mile—and stay submerged for as long as 2 hours! One elephant seal carrying a recording device spent 40 days at sea,



▲ **Figure 42.32** Carbon dioxide transport in the blood.

? In what three forms is CO₂ transported in the bloodstream?



diving almost continuously with no surface period longer than 6 minutes. What evolutionary adaptations enable these animals to perform such amazing feats?

One adaptation of diving mammals to prolonged stays underwater is an ability to store large amounts of O₂. Compared with humans, the Weddell seal can store about twice as much O₂ per kilogram of body mass. About 36% of our total O₂ is in our lungs, and 51% is in our blood. In contrast, the Weddell seal holds only about 5% of its O₂ in its relatively small lungs (and may exhale before diving, which reduces buoyancy), stockpiling 70% in the blood. And the seal has about twice the volume of blood per kilogram of body mass as a human. Diving mammals also have a high concentration of an oxygen-storing protein called **myoglobin** in their muscles. The Weddell seal can store about 25% of its O₂ in muscle, compared with only 13% in humans.

Diving mammals not only have a relatively large O₂ stockpile but also have adaptations that conserve O₂. They swim with little muscular effort and glide passively upward or downward by changing their buoyancy. Their heart rate and O₂ consumption rate decrease during a dive. At the same time, regulatory mechanisms route most blood to the brain, spinal cord, eyes, adrenal glands, and, in pregnant seals, the placenta. Blood supply to the muscles is restricted or, during

the longest dives, shut off altogether. During dives of more than about 20 minutes, a Weddell seal's muscles deplete the O₂ stored in myoglobin and then derive their ATP from fermentation instead of respiration (see Chapter 9).

The unusual abilities of the Weddell seal and other air-breathing divers to power their bodies during long dives showcase two related themes in our study of organisms—the response to environmental challenges over the short term by physiological adjustments and over the long term as a result of natural selection.

CONCEPT CHECK 42.7

- What determines whether O₂ and CO₂ diffuse into or out of the capillaries in the tissues and near the alveoli? Explain.
- How does the Bohr shift help deliver O₂ to very active tissues?
- WHAT IF?** A doctor might give bicarbonate (HCO₃⁻) to a patient who is breathing very rapidly. What assumption is the doctor making about the blood chemistry of the patient?

For suggested answers, see Appendix A.

42 CHAPTER REVIEW

SUMMARY OF KEY CONCEPTS

CONCEPT 42.1

Circulatory systems link exchange surfaces with cells throughout the body (pp. 897–902)

- In animals with simple body plans, gastrovascular cavities mediate exchange between the environment and cells that can be reached by diffusion. Because diffusion is slow over long distances, most complex animals have a circulatory system that moves fluid between cells and the organs that carry out exchange with the environment. Arthropods and most molluscs have an **open circulatory system**, in which **hemolymph** bathes organs directly. Vertebrates have a **closed circulatory system**, in which **blood** circulates in a closed network of pumps and vessels.
- The closed circulatory system of vertebrates consists of blood, **blood vessels**, and a two- to four-chambered **heart**. Blood pumped by a heart **ventricle** passes to **arteries** and then to **capillaries**, the sites of chemical exchange between blood and interstitial fluid. **Veins** return blood from capillaries to an **atrium**, which passes blood to a ventricle. Fishes, rays, and sharks have a single pump in their circulation. Air-breathing vertebrates have two pumps combined in a single heart. Variations in ventricle number and separation reflect adaptations to different environments and metabolic needs.

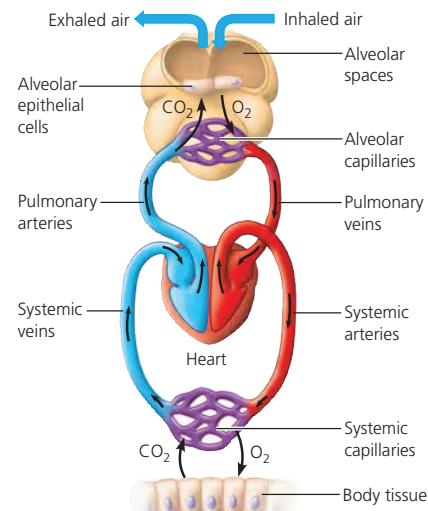
?

How does the flow of a fluid in a closed circulatory system differ from the movement of molecules between cells and their environment with regard to distance traveled, direction traveled, and driving force?

CONCEPT 42.2

Coordinated cycles of heart contraction drive double circulation in mammals (pp. 902–904)

- The right ventricle pumps blood to the lungs, where it loads O₂ and unloads CO₂. Oxygen-rich blood from the lungs enters the heart at the left atrium and is pumped to the body tissues by the left ventricle. Blood returns to the heart through the right atrium.



- The **cardiac cycle**, one complete sequence of the heart's pumping and filling, consists of a period of contraction, called **systole**, and a period of relaxation, called **diastole**. Heart function can be assessed by measuring the **pulse** (number of times the heart beats each minute) and **cardiac output** (volume of blood pumped by each ventricle per minute).
- The heartbeat originates with impulses at the **sinoatrial (SA) node** (pacemaker) of the right atrium. The impulses trigger contraction of both atria before passing to the **atrioventricular (AV) node**, where the impulses are temporarily delayed. They are then conducted along the bundle branches and Purkinje fibers, triggering contraction of the ventricles. The nervous system, hormones, and body temperature influence pacemaker activity.

? What changes in cardiac function might you expect after surgical replacement of a defective heart valve?

CONCEPT 42.3

Patterns of blood pressure and flow reflect the structure and arrangement of blood vessels (pp. 905–910)

- Blood vessels have structures well adapted to function. Capillaries have narrow diameters and thin walls that facilitate exchange. Arteries contain thick elastic walls that maintain blood pressure. Veins contain one-way valves that contribute to the return of blood to the heart.
- Physical laws governing the movement of fluids through pipes influence blood flow and blood pressure. The velocity of blood flow varies in the circulatory system, being lowest in the capillary beds as a result of their large total cross-sectional area. Blood pressure is altered by changes in cardiac output and by variable constriction of arterioles.
- Fluid leaks out of capillaries and is returned to blood by the **lymphatic system**. This system parallels the circulatory system in its extent and its mechanisms for fluid flow under low hydrostatic pressure. It also plays a vital role in defense against infection.

? If you placed your forearm on your head, how, if at all, would the blood pressure in that arm change? Explain.

CONCEPT 42.4

Blood components function in exchange, transport, and defense (pp. 910–915)

- Whole blood consists of cells and cell fragments (**platelets**) suspended in a liquid matrix called **plasma**. Plasma proteins influence blood pH, osmotic pressure, and viscosity, and they function in lipid transport, immunity (antibodies), and blood clotting (fibrinogen). Red blood cells, or **erythrocytes**, transport O₂. Five types of white blood cells, or **leukocytes**, function in defense against microbes and foreign substances in the blood. Platelets function in blood clotting, a cascade of reactions that converts plasma fibrinogen to fibrin.
- A variety of diseases impair function of the circulatory system. In **sickle-cell disease**, an aberrant form of **hemoglobin** disrupts erythrocyte shape and function, leading to blockage of small blood vessels and a decrease in the oxygen-carrying capacity of the blood. In cardiovascular disease, inflammation caused by damage to the lining of arteries enhances deposition of lipids and cells, resulting in the potential for life-threatening damage to the heart or brain.

? In the absence of infection, what percentage of cells in human blood are leukocytes?

CONCEPT 42.5

Gas exchange occurs across specialized respiratory surfaces (pp. 915–920)

- At all sites of **gas exchange**, a gas diffuses from where its **partial pressure** is higher to where it is lower. Air is more conducive to gas exchange than water because air has a higher O₂ content, lower density, and lower viscosity. Regardless of whether the respiratory medium is air or water, adequate diffusion of O₂ and CO₂ between the medium and an animal's cells requires large, moist respiratory surfaces.
- The structure and organization of respiratory surfaces differ among animal species. Gills are outfoldings of the body surface specialized for gas exchange in water. The effectiveness of gas exchange in some gills, including those of fishes, is increased by **ventilation** and **countercurrent exchange** between blood and water. Gas exchange in insects relies on a **tracheal system** consisting of tiny, branching tubes that penetrate the body, bringing O₂ directly to cells. Spiders, land snails, and most terrestrial vertebrates have internal **lungs**. In mammals, air inhaled through the nostrils passes through the pharynx into the **trachea**, **bronchi**, **bronchioles**, and dead-end **alveoli**, where gas exchange occurs.

? Why does altitude have almost no effect on an animal's ability to rid itself of CO₂ through gas exchange?

CONCEPT 42.6

Breathing ventilates the lungs (pp. 920–922)

- Breathing mechanisms vary substantially among vertebrates. An amphibian ventilates its lungs by **positive pressure breathing**, which forces air down the trachea. Birds use a system of air sacs as bellows to keep air flowing through the lungs in one direction only. Every exhalation completely renews the air in the lungs. Mammals ventilate their lungs by **negative pressure breathing**, which pulls air into the lungs. Lung volume increases as the rib muscles and **diaphragm** contract. Incoming and outgoing air mix, decreasing the efficiency of ventilation.
- Control centers in the medulla oblongata and pons of the human brain regulate the rate and depth of breathing. Sensors detect the pH of cerebrospinal fluid (reflecting CO₂ concentration in the blood), and the medulla adjusts breathing rate and depth to match metabolic demands. Secondary control over breathing is exerted by sensors in the aorta and carotid arteries that monitor blood levels of O₂ as well as CO₂ (via blood pH).

? How does tidal volume differ from the volume of fresh air that enters the body during inspiration?

CONCEPT 42.7

Adaptations for gas exchange include pigments that bind and transport gases (pp. 923–926)

- In the lungs, gradients of partial pressure favor the diffusion of O₂ into the blood and CO₂ out of the blood. The opposite situation exists in the rest of the body. **Respiratory pigments** transport O₂, greatly increasing the amount of O₂ that blood or hemolymph can carry. Many arthropods and molluscs have copper-containing hemocyanin; vertebrates and a wide variety of invertebrates have hemoglobin. Hemoglobin also helps transport CO₂ and assists in buffering the blood.

- Evolutionary adaptations enable some animals to satisfy extraordinary O₂ demands. Deep-diving air-breathers stockpile O₂ in blood and other tissues and deplete it slowly.

? In what way is the role of a respiratory pigment like that of an enzyme?

TEST YOUR UNDERSTANDING

LEVEL 1: KNOWLEDGE/COMPREHENSION

- Which of the following respiratory systems is not closely associated with a blood supply?
 - the lungs of a vertebrate
 - the gills of a fish
 - the tracheal system of an insect
 - the skin of an earthworm
 - the parapodia of a polychaete worm
- Blood returning to the mammalian heart in a pulmonary vein drains first into the
 - vena cava.
 - left atrium.
 - right atrium.
 - left ventricle.
 - right ventricle.
- Pulse is a direct measure of
 - blood pressure.
 - stroke volume.
 - cardiac output.
 - heart rate.
 - breathing rate.
- When you hold your breath, which of the following blood gas changes first leads to the urge to breathe?
 - rising O₂
 - falling O₂
 - rising CO₂
 - falling CO₂
 - rising CO₂ and falling O₂
- One feature that amphibians and humans have in common is
 - the number of heart chambers.
 - the type of gas exchange tissues.
 - a complete separation of circuits for circulation.
 - the number of circuits for circulation.
 - a low blood pressure in the systemic circuit.

LEVEL 2: APPLICATION/ANALYSIS

- If a molecule of CO₂ released into the blood in your left toe is exhaled from your nose, it must pass through all of the following except
 - the pulmonary vein.
 - an alveolus.
 - the trachea.
 - the right atrium.
 - the right ventricle.
- Compared with the interstitial fluid that bathes active muscle cells, blood reaching these cells in arteries has a
 - higher P_{O₂}.
 - higher P_{CO₂}.
 - greater bicarbonate concentration.
 - lower pH.
 - lower osmotic pressure.
- Which of the following reactions prevails in red blood cells traveling through alveolar capillaries? (Hb = hemoglobin)
 - Hb + 4 O₂ → Hb(O₂)₄
 - Hb(O₂)₄ → Hb + 4 O₂
 - CO₂ + H₂O → H₂CO₃
 - H₂CO₃ → H⁺ + HCO₃⁻
 - Hb + 4 CO₂ → Hb(CO₂)₄

LEVEL 3: SYNTHESIS/EVALUATION

- DRAW IT** Plot blood pressure against time for one cardiac cycle in humans, drawing separate lines for the pressure in the aorta, the left ventricle, and the right ventricle. Below the

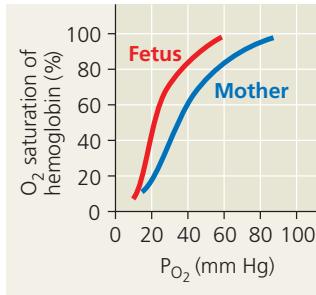
time axis, add a vertical arrow pointing to the time when you expect a peak in atrial blood pressure.

10. EVOLUTION CONNECTION

One of the many mutant opponents that the movie monster Godzilla contends with is Mothra, a giant mothlike creature with a wingspan of several dozen meters. Science fiction creatures like these can be critiqued on the grounds of biomechanical and physiological principles. What problems of respiration and gas exchange would Mothra face? The largest insects that have ever lived are Paleozoic dragonflies with half-meter wingspans. Why do you think truly giant insects are improbable?

11. SCIENTIFIC INQUIRY

The hemoglobin of a human fetus differs from adult hemoglobin. Compare the dissociation curves of the two hemoglobins in the graph at right. Propose a hypothesis to explain the benefit of this difference between these two hemoglobins.



12. SCIENCE, TECHNOLOGY, AND SOCIETY

Hundreds of studies have linked smoking with cardiovascular and lung disease. According to most health authorities, smoking is the leading cause of preventable, premature death in the United States. Antismoking groups have proposed that cigarette advertising in all media be banned entirely. What are some arguments in favor of a total ban on cigarette advertising? What are arguments in opposition? Do you favor or oppose such a ban? Defend your position.

13. WRITE ABOUT A THEME

Environmental Interactions Some athletes prepare for competition at sea level by sleeping in a tent in which P_{O₂} is kept artificially low. When climbing very high peaks, some mountaineers breathe from bottles of pure O₂. In a short essay (100–150 words), relate these behaviors to the mechanism of O₂ transport in the human body and to our physiological interactions with our gaseous environment.

For selected answers, see Appendix A.

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1. MasteringBiology® Assignments

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Tutorial Gas Transport in Blood

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