53

Respiration

Concept Outline

53.1 Respiration involves the diffusion of gases.

Fick's Law of Diffusion. The rate of diffusion across a membrane depends on the surface area of the membrane, the concentration gradients, and the distance across the membrane.

How Animals Maximize the Rate of Diffusion. The diffusion rate increases when surface area or concentration gradient increases.

53.2 Gills are used for respiration by aquatic vertebrates.

The Gill as a Respiratory Structure. Water is forced past the gill surface, and blood flows through the gills.

53.3 Lungs are used for respiration by terrestrial vertebrates.

Respiration in Air-Breathing Animals. In insects, oxygen diffuses directly from the air into body cells; in vertebrates, oxygen diffuses into blood and then into body cells.

Respiration in Amphibians and Reptiles. Amphibians force air into their lungs, whereas reptiles, birds, and mammals draw air in by expanding their rib cage.

Respiration in Mammals. In mammals, gas exchange occurs across millions of tiny air sacs called alveoli.

Respiration in Birds. In birds, air flows through the lung unidirectionally.

53.4 Mammalian breathing is a dynamic process.

Structures and Mechanisms of Breathing. The rib cage and lung volumes are expanded during inspiration by the contraction of the diaphragm and other muscles.

Mechanisms That Regulate Breathing. The respiratory control center in the brain is influenced by reflexes triggered by the blood levels of carbon dioxide and blood pH.

53.5 Blood transports oxygen and carbon dioxide.

Hemoglobin and Oxygen Transport. Hemoglobin, a molecule within the red blood cells, loads with oxygen in the lungs and unloads its oxygen in the tissue capillaries.

Carbon Dioxide and Nitric Oxide Transport. Carbon dioxide is converted into carbonic acid in erythrocytes and is transported as bicarbonate.
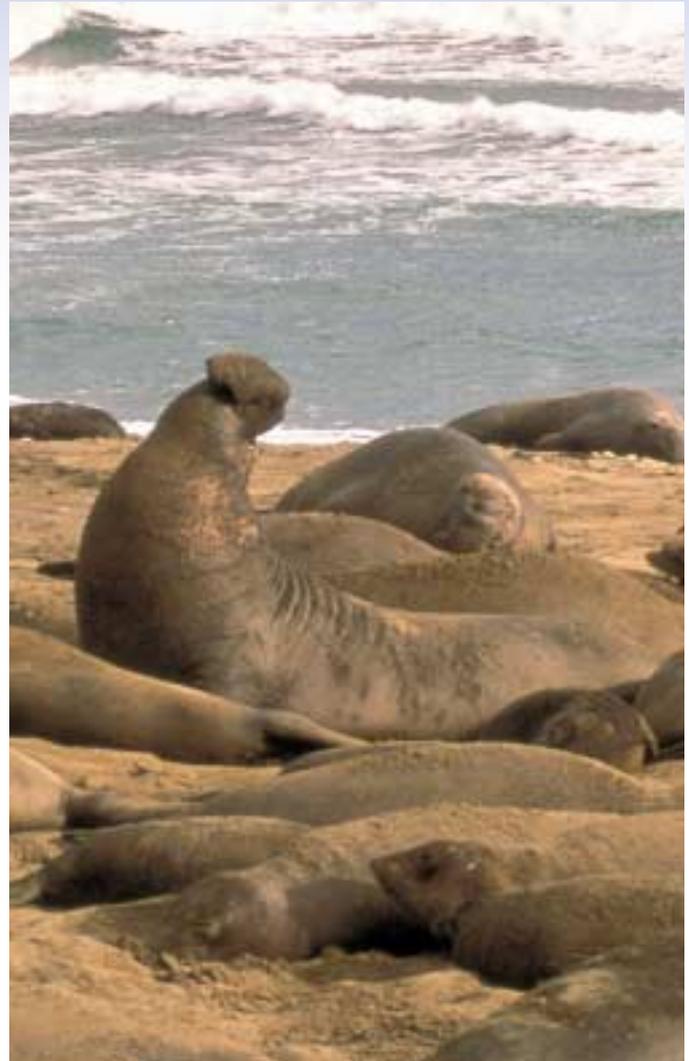

FIGURE 53.1
Elephant seals are respiratory champions. Diving to depths greater than those of all other marine animals, including sperm whales and sea turtles, elephant seals can hold their breath for over two hours, descend and ascend rapidly in the water, and endure repeated dives without suffering any apparent respiratory distress.

Animals pry energy out of food molecules using the biochemical process called cellular respiration. While the term cellular respiration pertains to the use of oxygen and production of carbon dioxide at the cellular level, the general term respiration describes the uptake of oxygen from the environment and the disposal of carbon dioxide into the environment at the body system level. Respiration at the body system level involves a host of processes not found at the cellular level, like the mechanics of breathing and the exchange of oxygen and carbon dioxide in the capillaries. These processes, one of the principal physiological challenges facing all animals (figure 53.1), are the subject of this chapter.

Fick's Law of Diffusion

Respiration involves the diffusion of gases across plasma membranes. Because plasma membranes must be surrounded by water to be stable, the external environment in gas exchange is always aqueous. This is true even in terrestrial animals; in these cases, oxygen from air dissolves in a thin layer of fluid that covers the respiratory surfaces, such as the alveoli in lungs.

In vertebrates, the gases diffuse into the aqueous layer covering the epithelial cells that line the respiratory organs. The diffusion process is passive, driven only by the difference in O_2 and CO_2 concentrations on the two sides of the membranes. In general, the rate of diffusion between two regions is governed by a relationship known as **Fick's Law of Diffusion:**

$$R = D \times A \frac{\Delta p}{d}$$

In this equation,

R = the rate of diffusion; the amount of oxygen or carbon dioxide diffusing per unit of time;

D = the diffusion constant;

A = the area over which diffusion takes place;

Δp = the difference in concentration (for gases, the difference in their partial pressures) between the interior of the organism and the external environment; and

d = the distance across which diffusion takes place.

Major changes in the mechanism of respiration have occurred during the evolution of animals (figure 53.2) that have tended to optimize the rate of diffusion R. By inspecting Fick's Law, you can see that natural selection can optimize R by favoring changes that (1) increase the surface area A; (2) decrease the distance d; or (3) increase the concentration difference, as indicated by Δp. The evolution of respiratory systems has involved changes in all of these factors.

Fick's Law of Diffusion states that the rate of diffusion across a membrane depends on surface area, concentration (partial pressure) difference, and distance.
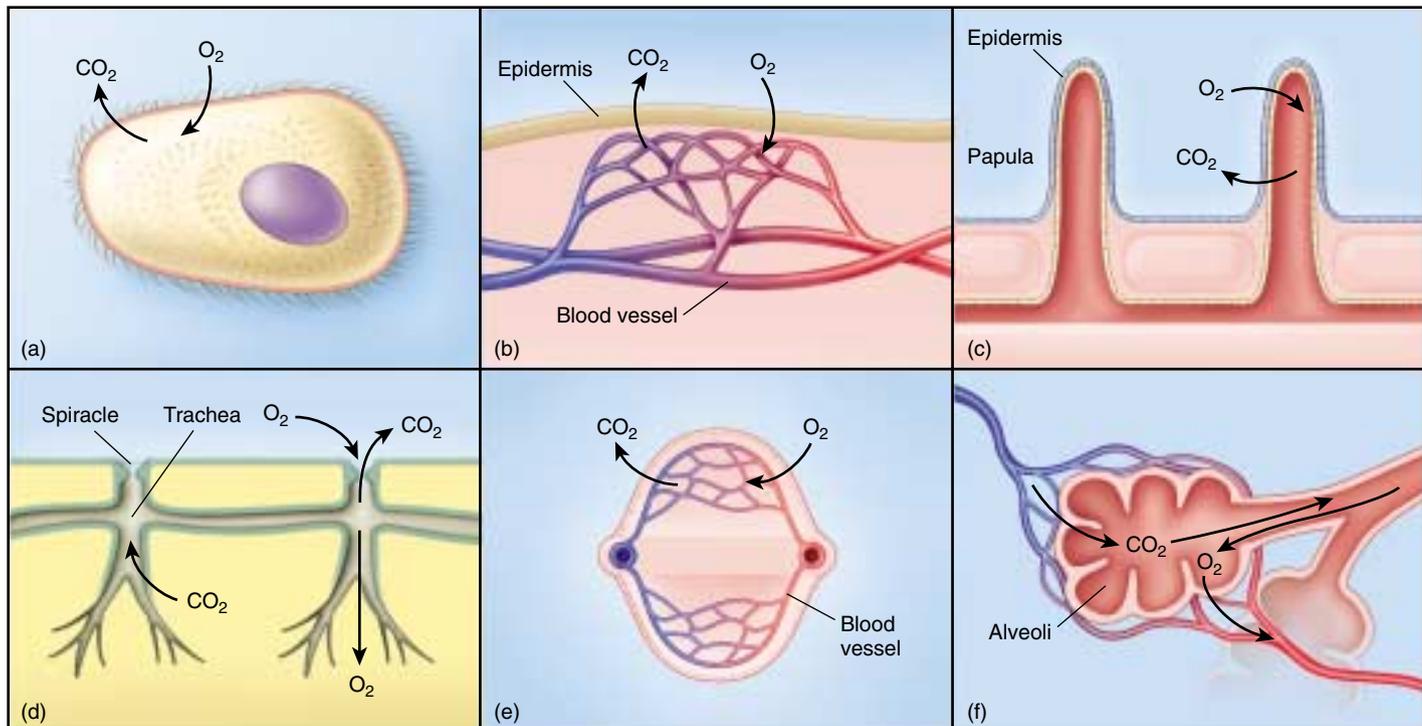

FIGURE 53.2
Gas exchange may take place in a variety of ways. (*a*) Gases diffuse directly into single-celled organisms. (*b*) Amphibians and many other animals respire across their skin. (*c*) Echinoderms have protruding papulae, which provide an increased respiratory surface area. (*d*) Inspects respire through an extensive tracheal system. (*e*) The gills of fishes provide a very large respiratory surface area and countercurrent exchange. (*f*) The alveoli in mammalian lungs provide a large respiratory surface area but do not permit countercurrent exchange.

How Animals Maximize the Rate of Diffusion

The levels of oxygen required by oxidative metabolism cannot be obtained by diffusion alone over distances greater than about 0.5 millimeter. This restriction severely limits the size of organisms that obtain their oxygen entirely by diffusion directly from the environment. Protists are small enough that such diffusion can be adequate (see figure 53.2*a*), but most multicellular animals are much too large.

Most of the more primitive phyla of invertebrates lack special respiratory organs, but they have developed means of improving the movement of water over respiratory structures. In a number of different ways, many of which involve beating cilia, these organisms create a *water current* that continuously replaces the water over the respiratory surfaces. Because of this continuous replenishment with water containing fresh oxygen, *the external oxygen concentration does not decrease along the diffusion pathway*. Although each oxygen molecule that passes into the organism has been removed from the surrounding water, new water continuously replaces the oxygen-depleted water. This increases the rate of diffusion by maximizing the concentration difference—the Δp of the Fick equation.

All of the more advanced invertebrates (mollusks, arthropods, echinoderms), as well as vertebrates, possess respiratory organs that increase the surface area available for diffusion and bring the external environment (either water or air) close to the internal fluid, which is usually circulated throughout the body. The respiratory organs thus increase the rate of diffusion by maximizing surface area and decreasing the distance the diffusing gases must travel (the A and d factors, respectively, in the Fick equation).

Atmospheric Pressure and Partial Pressures

Dry air contains 78.09% nitrogen (N_2), 20.95% oxygen, 0.93% argon and other inert gases, and 0.03% carbon dioxide. Convection currents cause air to maintain a constant composition to altitudes of at least 100 kilometers, although the *amount* (number of molecules) of air that is present decreases with altitude (figure 53.3).

Imagine a column of air extending from the ground to the limits of the atmosphere. All of the gas molecules in this column experience the force of gravity, so they have weight and can exert pressure. If this column were on top of one end of a U-shaped tube of mercury at sea level, it would exert enough pressure to raise the other end of the tube 760 millimeters under a set of specified, standard conditions (see figure 53.3). An apparatus that measures air pressure is called a barometer, and 760 mm Hg (millimeters of mercury) is the barometric pressure of the air at sea level. A pressure of 760 mm Hg is also defined as **one atmosphere** of pressure.
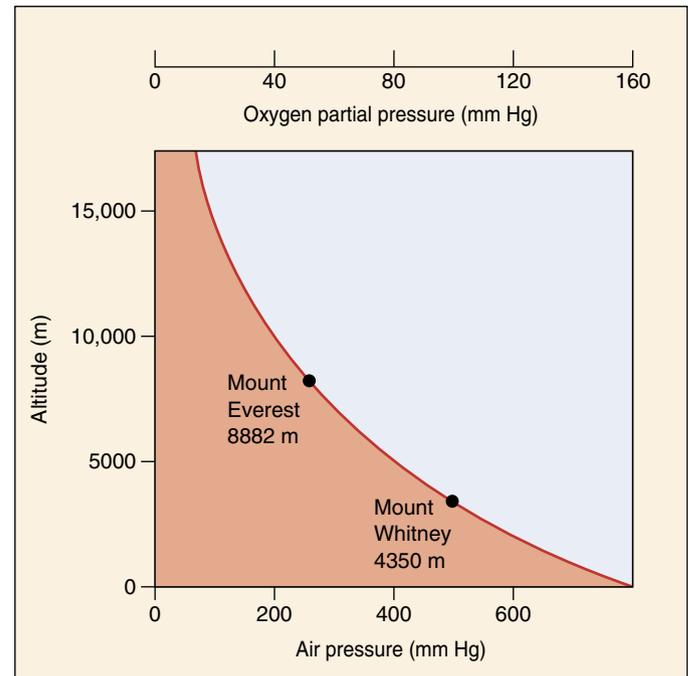

FIGURE 53.3
The relationship between air pressure and altitude above sea level. At the high altitudes characteristic of mountaintops, air pressure is much less than at sea level. At the top of Mount Everest, the world's highest mountain, the air pressure is only one-third that at sea level.

Each type of gas contributes to the total atmospheric pressure according to its fraction of the total molecules present. That fraction contributed by a gas is called its **partial pressure** and is indicated by P_{N_2}, P_{O_2}, P_{CO_2}, and so on. The total pressure is the sum of the partial pressures of all gases present. For dry air, the partial pressures are calculated simply by multiplying the fractional composition of each gas in the air by the atmospheric pressure. Thus, at sea level, the partial pressures of N_2^+ inert gases, O_2, and CO_2 are:

$$P_{N_2} = 760 \times 7902\% = 6006 \text{mm Hg},$$
$$P_{O_2} = 760 \times 2095\% = 1592 \text{mm Hg, and}$$
$$P_{CO_2} = 760 \times 0.03\% = 0.2 \text{mm Hg}.$$

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

The exchange of oxygen and carbon dioxide between an organism and its environment occurs by diffusion of dissolved gases across plasma membranes and is maximized by increasing the concentration gradient and the surface area and by decreasing the distance that the diffusing gases must travel.

The Gill as a Respiratory Structure

Aquatic respiratory organs increase the diffusion surface area by extensions of tissue, called *gills*, that project out into the water. Gills can be simple, as in the papulae of echinoderms (see figure 53.2c), or complex, as in the highly convoluted gills of fish (see figure 53.2e). The great increase in diffusion surface area provided by gills enables aquatic organisms to extract far more oxygen from water than would be possible from their body surface alone.

External gills (gills that are not enclosed within body structures) provide a greatly increased surface area for gas exchange. Examples of vertebrates with external gills are the larvae of many fish and amphibians, as well as developmentally arrested *(neotenic)* amphibian larvae that remain permanently aquatic, such as the axolotl. One of the disadvantages of external gills is that they must constantly be moved or the surrounding water becomes depleted in oxygen as the oxygen diffuses from the water to the blood of the gills. The highly branched gills, however, offer significant resistance to movement, making this form of respiration ineffective except in smaller animals. Another disadvantage is that external gills are easily damaged. The thin epithelium required for gas exchange is not consistent with a protective external layer of skin.

Other types of aquatic animals evolved specialized *branchial chambers*, which provide a means of pumping water past stationary gills. Mollusks, for example, have an internal *mantle cavity* that opens to the outside and contains the gills. Contraction of the muscular walls of the mantle cavity draws water in and then expels it. In crustaceans, the branchial chamber lies between the bulk of the body and the hard exoskeleton of the animal. This chamber contains gills and opens to the surface beneath a limb. Movement of the limb draws water through the branchial chamber, thus creating currents over the gills.

The Gills of Bony Fishes

The gills of bony fishes are located between the *buccal* (mouth) *cavity* and the *opercular cavities* (figure 53.4). The buccal cavity can be opened and closed by opening and closing the mouth, and the opercular cavity can be opened and closed by movements of the **operculum,** or gill cover. The two sets of cavities function as pumps that expand alternately to move water into the mouth, through the gills, and out of the fish through the open operculum. Water is brought into the buccal cavity by lowering the jaw and floor of the mouth, and then is moved through the gills into the opercular cavity by the opening of the operculum. The lower pressure in the opercular cavity causes water to move in the correct direction across the gills, and tissue that acts as valves ensures that the movement is one-way.

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

There are four **gill arches** on each side of the fish head. Each gill arch is composed of two rows of *gill filaments*, and each gill filament contains thin membranous plates, or *lamellae*, that project out into the flow of water (figure 53.5). Water flows past the lamellae in one direction only. Within each lamella, blood flows in a direction that is *opposite* the direction of water movement. This arrangement is called **countercurrent flow,** and it acts to maximize the oxygenation of the blood by increasing the concentration gradient of oxygen along the pathway for diffusion, increasing Δp in Fick's Law of Diffusion.

The advantages of a countercurrent flow system were discussed in chapter 52 in relation to temperature regulation and are again shown here in figure 53.6a. Blood low in oxygen en-
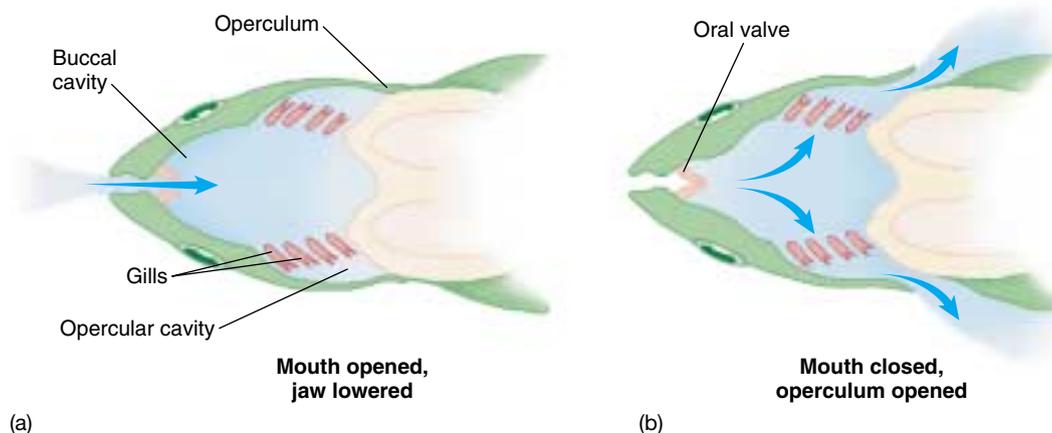

**Mouth opened,
jaw lowered**

(a)

**Mouth closed,
operculum opened**

(b)

**FIGURE 53.4
How most bony fishes respire.** The gills are suspended between the buccal (mouth) cavity and the opercular cavity. Respiration occurs in two stages. (*a*) The oral valve in the mouth is opened and the jaw is depressed, drawing water into the buccal cavity while the opercular cavity is closed. (*b*) The oral valve is closed and the operculum is opened, drawing water through the gills to the outside.
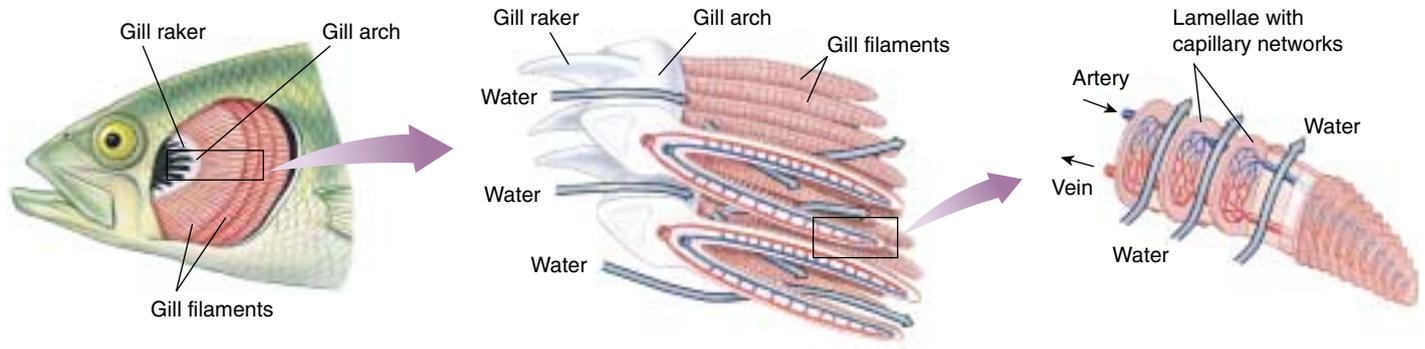
FIGURE 53.5
Structure of a fish gill. Water passes from the gill arch over the filaments (from left to right in the diagram). Water always passes the lamellae in a direction that is opposite to the direction of blood flow through the lamellae. The success of the gill's operation critically depends on this countercurrent flow of water and blood.
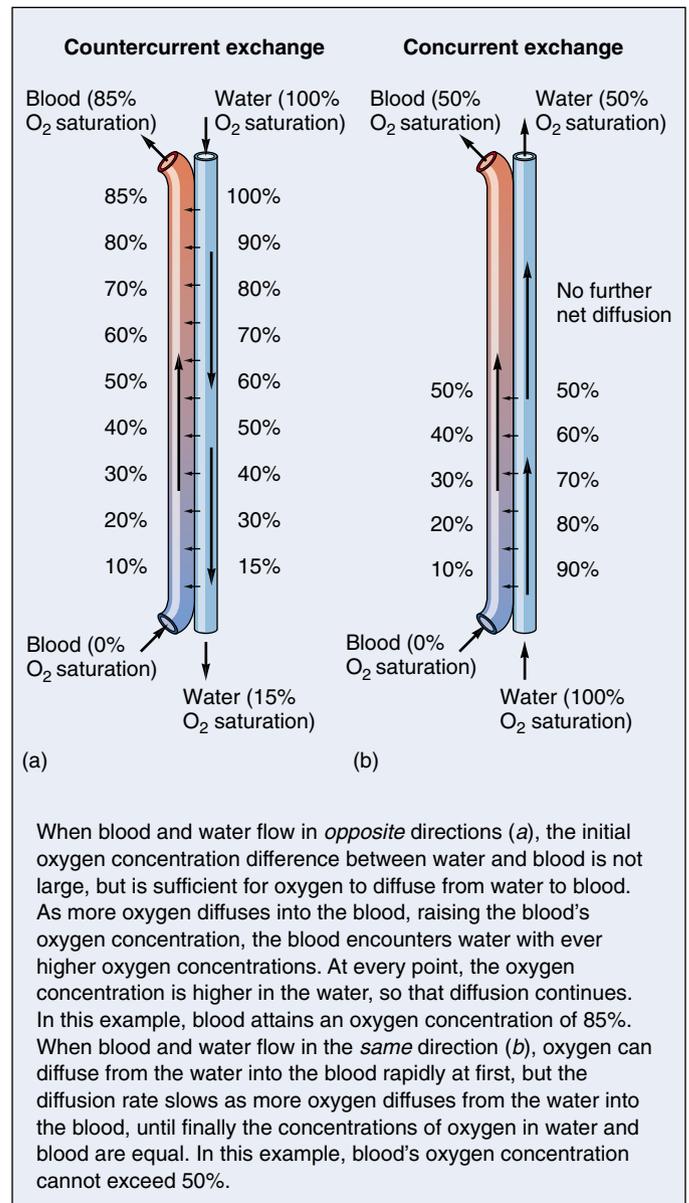
ters the back of the lamella, where it comes in close proximity to water that has already had most of its oxygen removed as it flowed through the lamella in the opposite direction. The water still has a higher oxygen concentration than the blood at this point, however, so oxygen diffuses from the water to the blood. As the blood flows toward the front of the lamella, it runs next to water that has a still higher oxygen content, so oxygen continuously diffuses from the water to the blood. Thus, countercurrent flow ensures that a concentration gradient remains between blood and water throughout the flow. This permits oxygen to continue to diffuse all along the lamellae, so that the blood leaving the gills has nearly as high an oxygen concentration as the water entering the gills.

This concept is easier to understand if we look at what would happen if blood and water flowed in the same direction, that is, had a *concurrent flow*. The difference in oxygen concentration would be very high at the front of each lamella, where oxygen-depleted blood would meet oxygen-rich water entering the gill (figure 53.6b). The concentration difference would fall rapidly, however, as the water lost oxygen to the blood. Net diffusion of oxygen would cease when the oxygen concentration of blood matched that of the water. At this point, much less oxygen would have been transferred to the blood than is the case with countercurrent flow. The flow of blood and water in a fish gill is in fact countercurrent, and because of the countercurrent exchange of gases, fish gills are the most efficient of all respiratory organs.

In bony fishes, water is forced past gills by the pumping action of the buccal and opercular cavities, or by active swimming in ram ventilation. In the gills, blood flows in an opposite direction to the flow of water. This countercurrent flow maximizes gas exchange, making the fish's gill an efficient respiratory organ.

FIGURE 53.6
Countercurrent exchange. This process allows for the most efficient blood oxygenation known in nature.

Countercurrent exchange

Blood (85% O₂ saturation)   Water (100% O₂ saturation)

85%	100%
80%	90%
70%	80%
60%	70%
50%	60%
40%	50%
30%	40%
20%	30%
10%	15%

Blood (0% O₂ saturation)
Water (15% O₂ saturation)
(a)

Concurrent exchange

Blood (50% O₂ saturation)   Water (50% O₂ saturation)

No further net diffusion

50%	50%
40%	60%
30%	70%
20%	80%
10%	90%

Blood (0% O₂ saturation)
Water (100% O₂ saturation)
(b)

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

Respiration in Air-Breathing Animals

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

1. **Air is less buoyant than water.**   The fine membranous lamellae of gills lack structural strength and rely on water for their support. A fish out of water, although awash in oxygen (water contains only 5 to 10 mL O_2/L, compared with air with 210 mL O_2/L), soon suffocates because its gills collapse into a mass of tissue. This collapse greatly reduces the diffusion surface area of the gills. Unlike gills, internal air passages can remain open, because the body itself provides the necessary structural support.
2. **Water diffuses into air through evaporation.**   Atmospheric air is rarely saturated with water vapor, except immediately after a rainstorm. Consequently, terrestrial organisms that are surrounded by air constantly lose water to the atmosphere. Gills would provide an enormous surface area for water loss.

Two main types of respiratory organs are used by terrestrial animals, and both sacrifice respiratory efficiency to some extent in exchange for reduced evaporation. The first are the **tracheae** of insects (see chapter 46 and figure 53.2*d*). Tracheae comprise an extensive series of air-filled passages connecting the surface of an insect to all portions of its body. Oxygen diffuses from these passages directly into cells, without the intervention of a circulatory system. Piping air directly from the external environment to the cells works very well in insects because their small bodies give them a high surface area-to-volume ratio. Insects prevent excessive water loss by closing the external openings of the tracheae whenever their internal CO_2 levels fall below a certain point.

The other main type of terrestrial respiratory organ is the **lung** (figure 53.7). A lung minimizes evaporation by moving air through a branched tubular passage; the air becomes saturated with water vapor before reaching the portion of the lung where a thin, wet membrane permits gas exchange. The lungs of all terrestrial vertebrates ex-

FIGURE 53.7
Human lungs. This chest X ray (dorsal view) was color-enhanced to show the lungs clearly. The heart is the pear-shaped object behind the vertical white column that is the esophagus.

cept birds use a **uniform pool** of air that is in contact with the gas exchange surface. Unlike the one-way flow of water that is so effective in the respiratory function of gills, air moves in and out by way of the same airway passages, a two-way flow system. Let us now examine the structure and function of lungs in the four classes of terrestrial vertebrates.

Air is piped directly to the body cells of insects, but the cells of terrestrial vertebrates obtain oxygen from the blood. The blood obtains its oxygen from a uniform pool of air by diffusion across the wet membranes of the lungs, which are filled with air in the process of ventilation.

Respiration in Amphibians and Reptiles

The lungs of amphibians are formed as saclike outpouchings of the gut (figure 53.8). Although the internal surface area of these sacs is increased by folds, much less surface area is available for gas exchange in amphibian lungs than in the lungs of other terrestrial vertebrates. Each amphibian lung is connected to the rear of the oral cavity, or pharynx, and the opening to each lung is controlled by a valve, the glottis.

Amphibians do not breathe the same way other terrestrial vertebrates do. Amphibians force air into their lungs by creating a greater-than-atmospheric pressure (positive pressure) in the air outside their lungs. They do this by filling their *buccal cavity* with air, closing their mouth and nostrils, and then elevating the floor of their oral cavity. This pushes air into their lungs in the same way that a pressurized tank of air is used to fill balloons. This is called positive pressure breathing; in humans, it would be analogous to forcing air into a victim's lungs by performing mouth-to-mouth resuscitation.

All other terrestrial vertebrates breathe by expanding their lungs and thereby creating a lower-than-atmospheric pressure (a negative pressure) within the lungs. This is called negative pressure breathing and is analogous to taking air into an accordion by pulling the accordion out to a greater volume. In reptiles, birds, and mammals, this is accomplished by expanding the thoracic (chest) cavity through muscular contractions, as will be described in a later section.

The oxygenation of amphibian blood by the lungs is supplemented by cutaneous respiration—the exchange of gases across the skin, which is wet and well vascularized in amphibians. Cutaneous respiration is actually more significant than pulmonary (lung) ventilation in frogs during winter, when their metabolisms are slow. Lung function becomes more important during the summer as the frog's metabolism increases. Although not common, some terrestrial amphibians, such as plethodontid salamanders, rely on cutaneous respiration exclusively.

Reptiles expand their rib cages by muscular contraction, and thereby take air into their lungs through negative pressure breathing. Their lungs have somewhat more surface area than the lungs of amphibians and so are more efficient at gas exchange. Terrestrial reptiles have dry, tough, scaly skins that prevent desiccation, and so cannot have cutaneous respiration. Cutaneous respiration, however, has been demonstrated in marine sea snakes.

Amphibians force air into their lungs by positive pressure breathing, whereas reptiles and all other terrestrial vertebrates take air into their lungs by expanding their lungs when they increase rib cage volume through muscular contractions. This creates a subatmospheric pressure in the lungs.
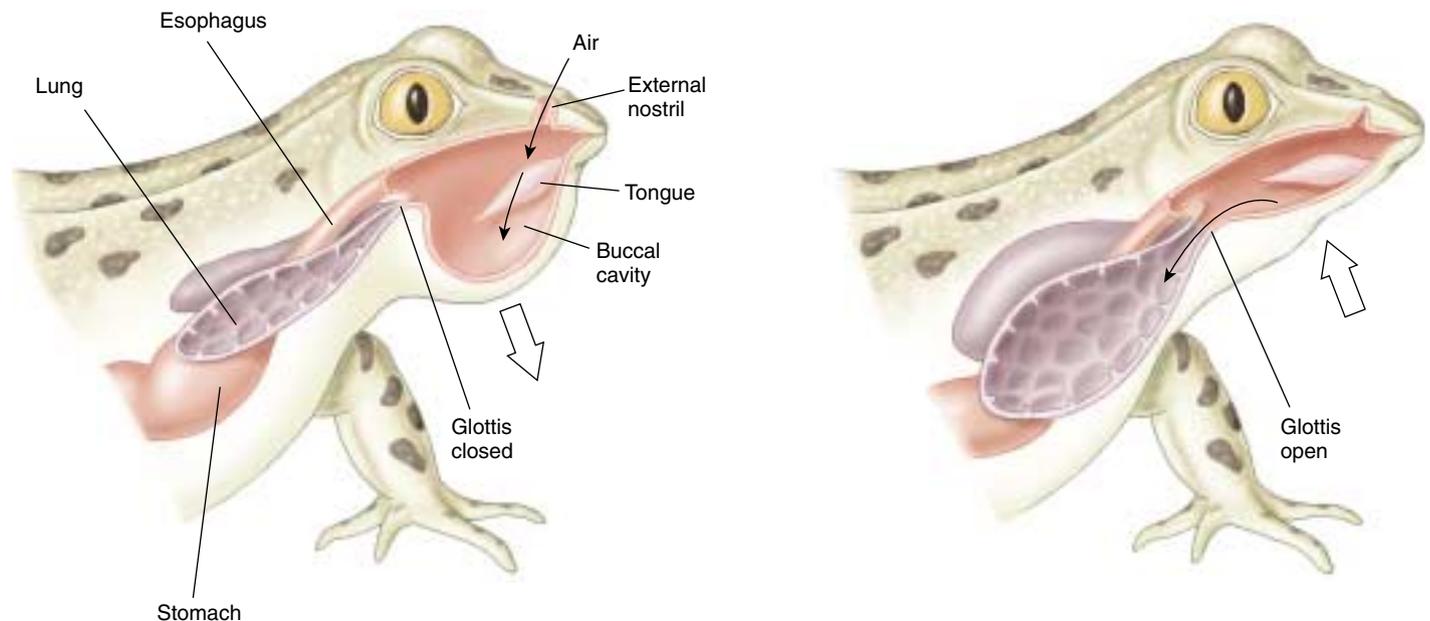

FIGURE 53.8
Amphibian lungs. Each lung of this frog is an outpouching of the gut and is filled with air by the creation of a positive pressure in the buccal cavity. The amphibian lung lacks the structures present in the lungs of other terrestrial vertebrates that provide an enormous surface area for gas exchange, and so are not as efficient as the lungs of other vertebrates.

Respiration in Mammals

The metabolic rate, and therefore the demand for oxygen, is much greater in birds and mammals, which are endothermic and thus require a more efficient respiratory system.

The lungs of mammals are packed with millions of *alveoli*, tiny sacs clustered like grapes (figure 53.9). This provides each lung with an enormous surface area for gas exchange. Air is brought to the alveoli through a system of air passages. Inhaled air is taken in through the mouth and nose past the pharynx to the **larynx** (voice box), where it passes through an opening in the vocal cords, the *glottis*, into a tube supported by C-shaped rings of cartilage, the **trachea** (windpipe). The trachea bifurcates into right and left **bronchi** (singular, *bronchus*), which enter each lung and further subdivide into **bronchioles** that deliver the air into blind-ended sacs called **alveoli.** The alveoli are surrounded by an extremely extensive capillary network. All gas exchange between the air and blood takes place across the walls of the alveoli.

The branching of bronchioles and the vast number of alveoli combine to increase the respiratory surface area (*A* in Fick's Law) far above that of amphibians or reptiles. In humans, there are about 300 million alveoli in each of the two lungs, and the total surface area available for diffusion can be as much as 80 square meters, or about 42 times the surface area of the body. Respiration in mammals will be considered in more detail in a separate section later.

Mammalian lungs are composed of millions of alveoli that provide a huge surface area for gas exchange. Air enters and leaves these alveoli through the same system of airways.
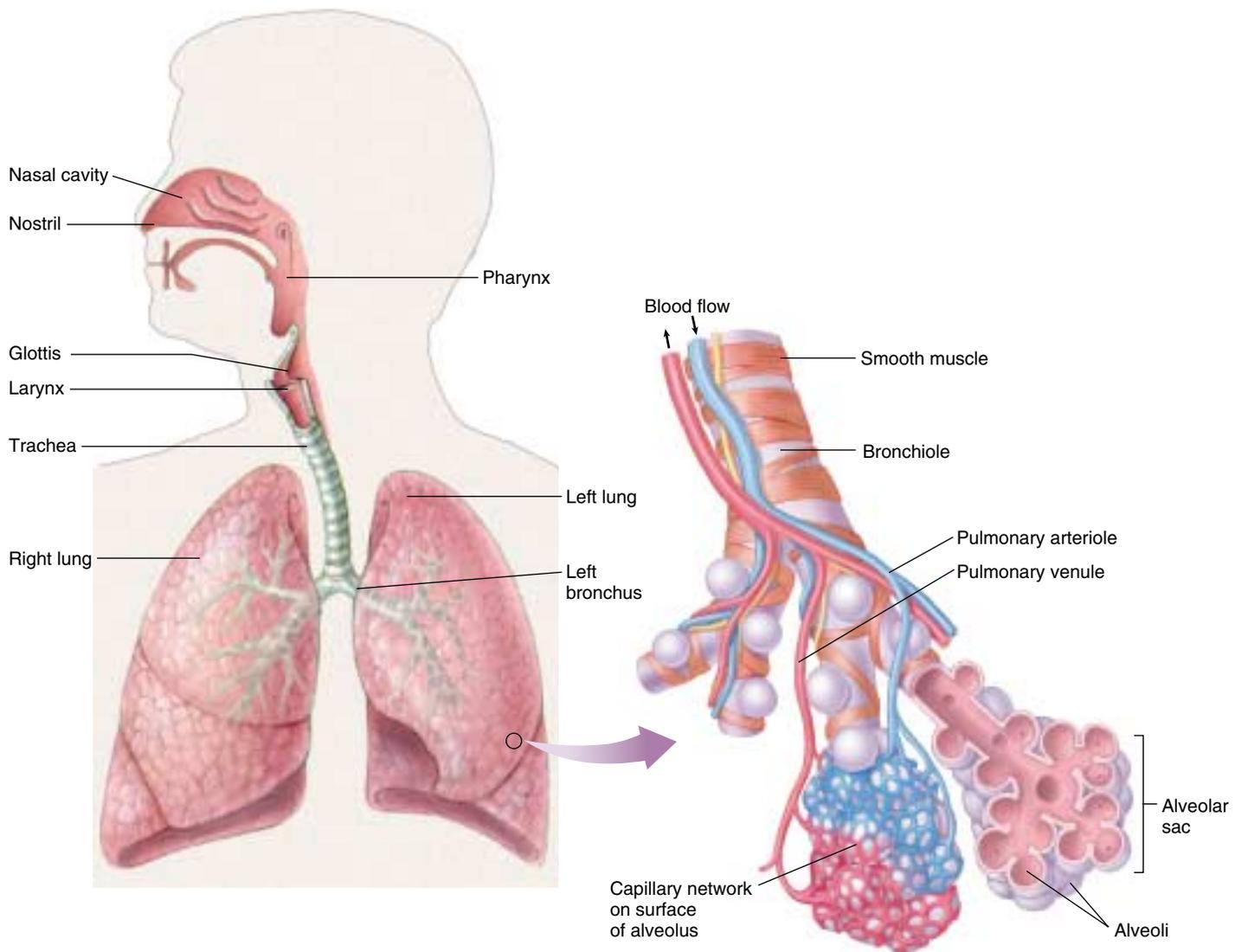

FIGURE 53.9
The human respiratory system and the structure of the mammalian lung. The lungs of mammals have an enormous surface area because of the millions of alveoli that cluster at the ends of the bronchioles. This provides for efficient gas exchange with the blood.

Respiration in Birds

The avian respiratory system has a unique structure that affords birds the most efficient respiration of all terrestrial vertebrates. Unlike the blind-ended alveoli in the lungs of mammals, the bird lung channels air through tiny air vessels called parabronchi, where gas exchange occurs (figure 53.10*a*). Air flows through the parabronchi in one direction only; this is similar to the unidirectional flow of water through a fish gill, but markedly different from the two-way flow of air through the airways of other terrestrial vertebrates. In other terrestrial vertebrates, the inhaled fresh air is mixed with "old" oxygen-depleted air that was not exhaled from the previous breathing cycle. In birds, only fresh air enters the parabronchi of the lung, and the old air exits the lung by a different route.

The unidirectional flow of air through the parabronchi of an avian lung is achieved through the action of air sacs, which are unique to birds (figure 53.10*b*). There are two groups of air sacs, anterior and posterior. When they are expanded during *inspiration* they take in air, and when they are compressed during *expiration* they push air into and through the lungs.

If we follow the path of air through the avian respiratory system, we will see that respiration occurs in *two cycles*. Each cycle has an inspiration and expiration phase—but the air inhaled in one cycle is not exhaled until the second cycle. Upon inspiration, both anterior and posterior air sacs expand and take in air. The inhaled air, however, only enters the posterior air sacs; the anterior air sacs fill with air from the lungs (figure 53.10*c*). Upon expiration, the air forced out of the anterior air sacs is exhaled, but the air forced out of the posterior air sacs enters the lungs. This process is repeated in the second cycle, so that air flows through the lungs in one direction and is exhaled at the end of the second cycle.

The unidirectional flow of air also permits a second respiratory efficiency: the flow of blood through the avian lung runs at a 90° angle to the air flow. This **cross-current flow** is not as efficient as the 180° countercurrent flow in fish gills, but it has the capacity to extract more oxygen from the air than a mammalian lung can. Because of the unidirectional air flow in the parabronchi and cross-current blood flow, a sparrow can be active at an altitude of 6000 meters while a mouse, which has a similar body mass and metabolic rate, cannot respire successfully at that elevation.
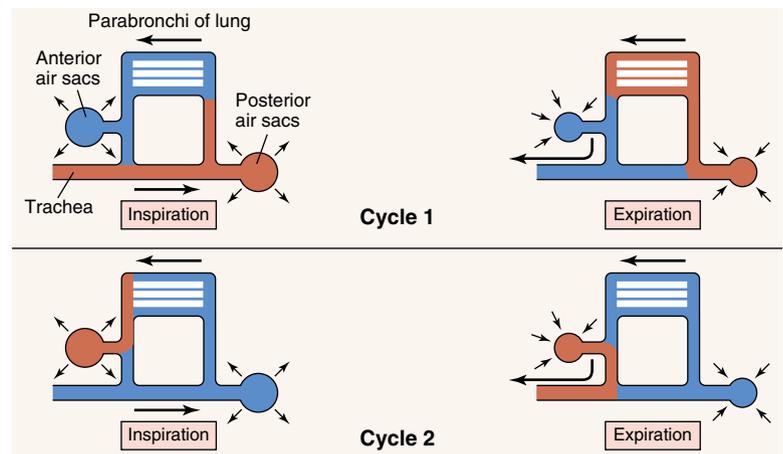
> The avian respiration system is the most efficient among terrestrial vertebrates because it has unidirectional air flow and cross-current blood flow through the lungs.
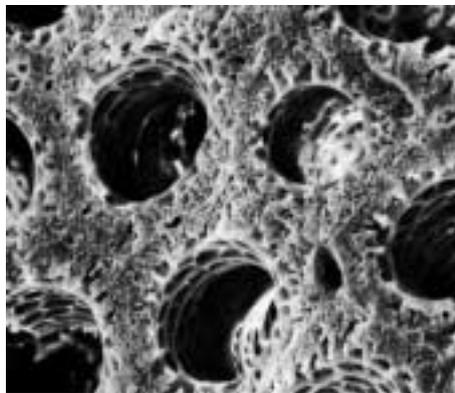
(a)
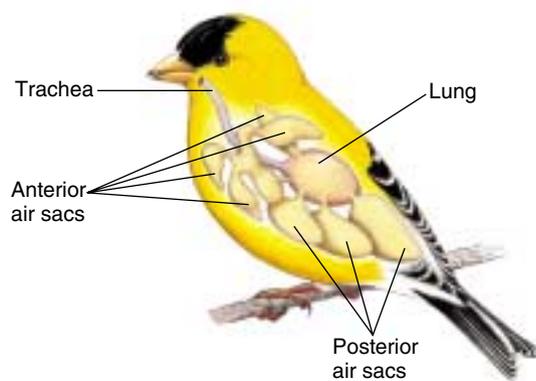
(b)

(c)

FIGURE 53.10
How a bird breathes. (*a*) Cross section of lung of a domestic chicken (75×). Air travels through tiny tunnels in the lungs, called parabronchi, while blood circulates within the fine lattice at right angles to the air flow. This cross-current flow makes the bird lung very efficient at extracting oxygen. (*b*) Birds have a system of air sacs, divided into an anterior group and posterior group, that extend between the internal organs and into the bones. (*c*) Breathing occurs in two cycles. *Cycle 1:* Inhaled air (shown in red) is drawn from the trachea into the posterior air sacs and then is exhaled into the lungs. *Cycle 2:* Air is drawn from the lungs into the anterior air sacs and then is exhaled through the trachea. Passage of air through the lungs is always in the same direction, from posterior to anterior (right to left in this diagram).

53.4 Mammalian breathing is a dynamic process.

Structures and Mechanisms of Breathing

In mammals, inspired air travels through the trachea, bronchi, and bronchioles to reach the alveoli, where gas exchange occurs. Each alveolus is composed of an epithelium only one cell thick, and is surrounded by blood capillaries with walls that are also only one cell layer thick. There are about 30 billion capillaries in both lungs, or about 100 capillaries per alveolus. Thus, an alveolus can be visualized as a microscopic air bubble whose entire surface is bathed by blood. Because the alveolar air and the capillary blood are separated by only two cell layers, the distance between the air and blood is only 0.5 to 1.5 micrometers, allowing for the rapid exchange of gases by diffusion by decreasing d in Fick's Law.

The blood leaving the lungs, as a result of this gas exchange, normally contains a partial oxygen pressure (P_{O_2}) of about 100 millimeters of mercury. As previously discussed, the P_{O_2} is a measure of the concentration of dissolved oxygen—you can think of it as indicating the plasma oxygen. Because the P_{O_2} of the blood leaving the lungs is close to the P_{O_2} of the air in the alveoli (about 105 mm Hg), the lungs do a very effective, but not perfect, job of oxygenating the blood. After gas exchange in the systemic capillaries, the blood that returns to the right side of the heart is depleted in oxygen, with a P_{O_2} of about 40 millimeters of mercury. These changes in the P_{O_2} of the blood, as well as the changes in plasma carbon dioxide (indicated as the P_{CO_2}), are shown in figure 53.11.

The outside of each lung is covered by a thin membrane called the **visceral pleural membrane.** A second, **parietal pleural membrane** lines the inner wall of the thoracic cavity. The space between these two membranes, the **pleural cavity,** is normally very small and filled with fluid. This fluid links the two membranes in the same way a thin film of water can hold two plates of glass together, effectively coupling the lungs to the thoracic cavity. The pleural membranes package each lung separately—if one collapses due to a perforation of the membranes, the other lung can still function.

Mechanics of Breathing

As in all other terrestrial vertebrates except amphibians, air is drawn into the lungs by the creation of a negative, or subatmospheric, pressure. In accordance with *Boyle's Law,* when the volume of a given quantity of gas increases its pressure decreases. This occurs because the volume of the thorax is increased during inspiration (inhalation), and the lungs likewise expand because of the adherence of the visceral and parietal pleural membranes. When the pressure within the lungs is lower than the atmospheric pressure, air enters the lungs.
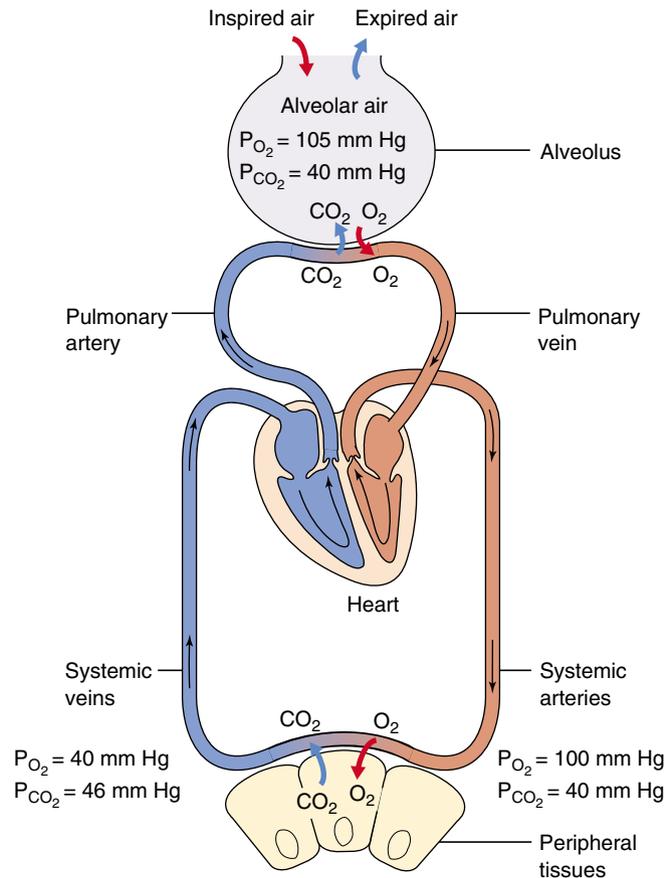

FIGURE 53.11
Gas exchange in the blood capillaries of the lungs and systemic circulation. As a result of gas exchange in the lungs, the systemic arteries carry oxygenated blood with a relatively low carbon dioxide concentration. After the oxygen is unloaded to the tissues, the blood in the systemic veins has a lowered oxygen content and an increased carbon dioxide concentration.

The thoracic volume is increased through contraction of two sets of muscles: the *external intercostals* and the *diaphragm.* During inspiration, contraction of the external intercostal muscles between the ribs raises the ribs and expands the rib cage. Contraction of the diaphragm, a convex sheet of striated muscle separating the thoracic cavity from the abdominal cavity, causes the diaphragm to lower and assume a more flattened shape. This expands the volume of the thorax and lungs while it increases the pressure on the abdomen (causing the belly to protrude). You can force a deeper inspiration by contracting other muscles that insert on the sternum or rib cage and expand the thoracic cavity and lungs to a greater extent (figure 53.12a).

The thorax and lungs have a degree of *elasticity*—they tend to resist distension and they recoil when the distend-
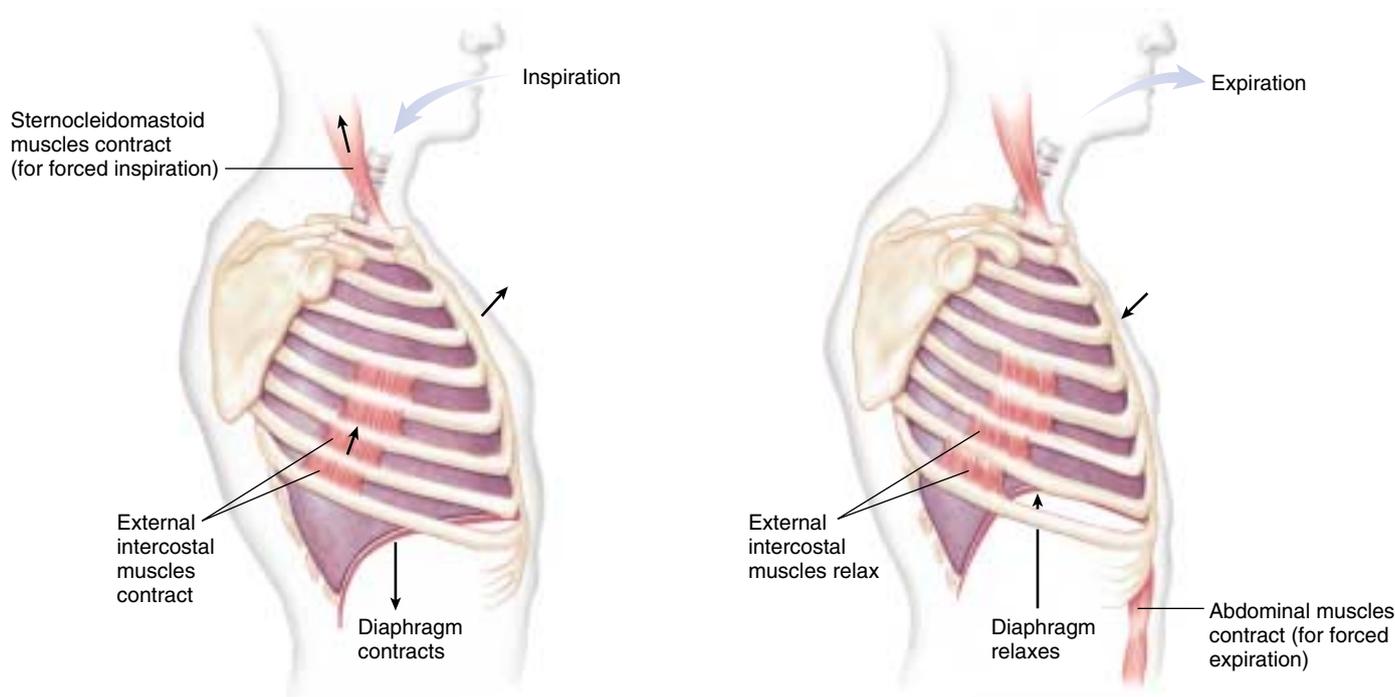
FIGURE 53.12
How a human breathes. (*a*) Inspiration. The diaphragm contracts and the walls of the chest cavity expand, increasing the volume of the chest cavity and lungs. As a result of the larger volume, air is drawn into the lungs. (*b*) Expiration. The diaphragm and chest walls return to their normal positions as a result of elastic recoil, reducing the volume of the chest cavity and forcing air out of the lungs through the trachea. Note that inspiration can be forced by contracting accessory respiratory muscles (such as the sternocleidomastoid), and expiration can be forced by contracting abdominal muscles.

ing force subsides. Expansion of the thorax and lungs during inspiration places these structures under elastic tension. It is the relaxation of the external intercostal muscles and diaphragm that produces unforced expiration, because it relieves that elastic tension and allows the thorax and lungs to recoil. You can force a greater expiration by contracting your abdominal muscles and thereby pressing the abdominal organs up against the diaphragm (figure 53.12*b*).

Breathing Measurements

A variety of terms are used to describe the volume changes of the lung during breathing. At rest, each breath moves a **tidal volume** of about 500 milliliters of air into and out of the lungs. About 150 milliliters of the tidal volume is contained in the tubular passages (trachea, bronchi, and bronchioles), where no gas exchange occurs. The air in this *anatomical dead space* mixes with fresh air during inspiration. This is one of the reasons why respiration in mammals is not as efficient as in birds, where air flow through the lungs is one-way.

The maximum amount of air that can be expired after a forceful, maximum inspiration is called the **vital capacity.** This measurement, which averages 4.6 liters in young men and 3.1 liters in young women, can be clinically important, because an abnormally low vital capacity may indicate dam-

age to the alveoli in various pulmonary disorders. For example, in **emphysema,** a potentially fatal condition usually caused by cigarette smoking, vital capacity is reduced as the alveoli are progressively destroyed.

A person normally breathes at a rate and depth that properly oxygenate the blood and remove carbon dioxide, keeping the blood P_{O_2} and P_{CO_2} within a normal range. If breathing is insufficient to maintain normal blood gas measurements (a rise in the blood P_{CO_2} is the best indicator), the person is **hypoventilating.** If breathing is excessive for a particular metabolic rate, so that the blood P_{CO_2} is abnormally lowered, the person is said to be **hyperventilating.** Perhaps surprisingly, the increased breathing that occurs during moderate exercise is not necessarily hyperventilation, because the faster breathing is matched to the faster metabolic rate, and blood gas measurements remain normal. The next section describes how breathing is regulated to keep pace with metabolism.

Humans inspire by contracting muscles that insert on the rib cage and by contracting the diaphragm. Expiration is produced primarily by muscle relaxation and elastic recoil. As a result, the blood oxygen and carbon dioxide levels are maintained in a normal range through adjustments in the depth and rate of breathing.

Mechanisms That Regulate Breathing

Each breath is initiated by neurons in a *respiratory control center* located in the medulla oblongata, a part of the brain stem (see chapter 54). These neurons send impulses to the diaphragm and external intercostal muscles, stimulating them to contract, and contractions of these muscles expand the chest cavity, causing inspiration. When these neurons stop producing impulses, the inspiratory muscles relax and expiration occurs. Although the muscles of breathing are skeletal muscles, they are usually controlled automatically. This control can be voluntarily overridden, however, as in hypoventilation (breath holding) or hyperventilation.

A proper rate and depth of breathing is required to maintain the blood oxygen and carbon dioxide levels in the normal range. Thus, although the automatic breathing cycle is driven by neurons in the brain stem, these neurons must be responsive to changes in blood P_{O_2} and P_{CO_2} in order to maintain homeostasis. You can demonstrate this mechanism by simply holding your breath. Your blood carbon dioxide immediately rises and your blood oxygen falls. After a short time, the urge to breathe induced by the changes in blood gases becomes overpowering. This is due primarily to the rise in blood carbon dioxide, as indicated by a rise in P_{CO_2}, rather than to the fall in oxygen levels.

A rise in P_{CO_2} causes an increased production of carbonic acid (H_2CO_3), which is formed from carbon dioxide and water and acts to lower the blood pH (carbonic acid dissociates into HCO_3^- and H^+, thereby increasing blood H^+ concentration). A fall in blood pH stimulates neurons in the **aortic** and **carotid bodies,** which are sensory structures known as *peripheral chemoreceptors* in the aorta and the carotid artery. These receptors send impulses to the respiratory control center in the medulla oblongata, which then stimulates increased breathing. The brain also contains chemoreceptors, but they cannot be stimulated by blood H^+ because the blood is unable to enter the brain. After a brief delay, however, the increased blood P_{CO2} also causes a decrease in the pH of the cerebrospinal fluid (CSF) bathing the brain. This stimulates the **central chemoreceptors** in the brain (figure 53.13).

The peripheral chemoreceptors are responsible for the immediate stimulation of breathing when the blood P_{CO_2} rises, but this immediate stimulation only account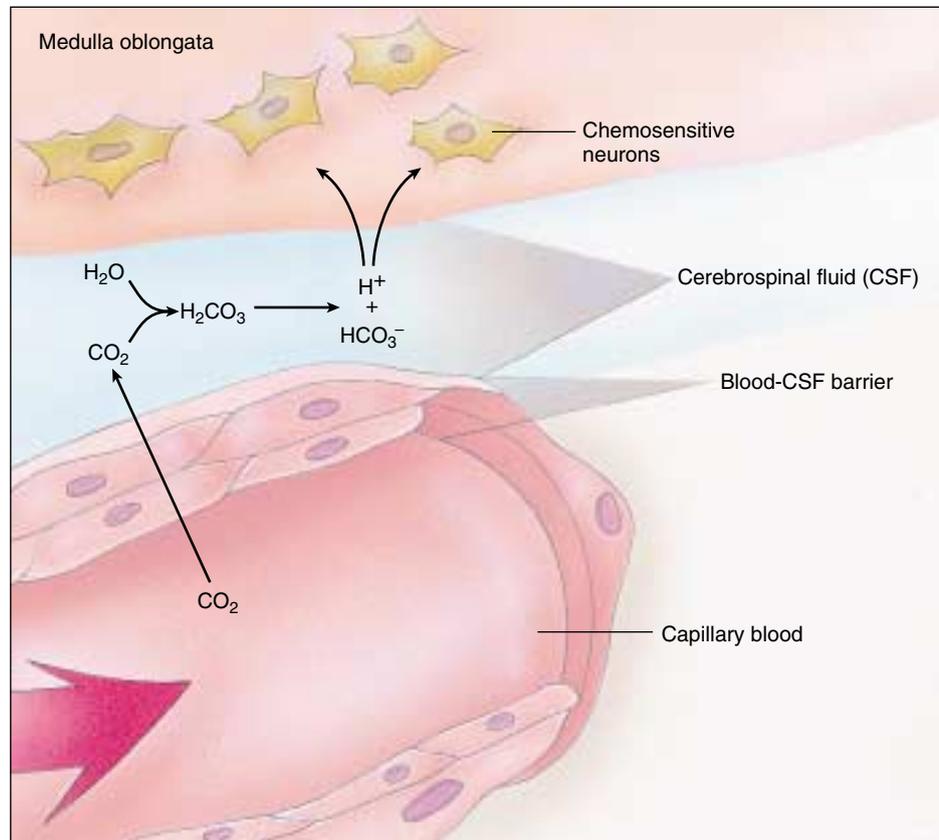s for about 30% of increased ventilation. The central chemoreceptors are responsible for the sustained increase in ventilation if P_{CO_2} remains elevated. The increased respiratory rate then acts to eliminate the extra CO_2, bringing the blood pH back to normal (figure 53.14).

A person cannot voluntarily hyperventilate for too long. The decrease in plasma P_{CO_2} and increase in pH of plasma and CSF caused by hyperventilation extinguish the reflex drive to breathe. They also lead to constriction of cerebral blood vessels, causing dizziness. People can hold their breath longer if they hyperventilate first, because it takes longer for the CO_2 levels to build back up, not because hyperventilation increases the P_{O_2} of the blood. Actually, in people with normal lungs, P_{O_2} becomes a significant stimulus for breathing only at high altitudes, where the P_{O_2} is low. Low P_{O_2} can also stimulate breathing in patients with emphysema, where the lungs are so damaged that blood CO_2 can never be adequately eliminated.

Breathing serves to keep the blood gases and pH in the normal range and is under the reflex control of peripheral and central chemoreceptors. These chemoreceptors sense the pH of the blood and cerebrospinal fluid, and they regulate the respiratory control center in the medulla oblongata of the brain.
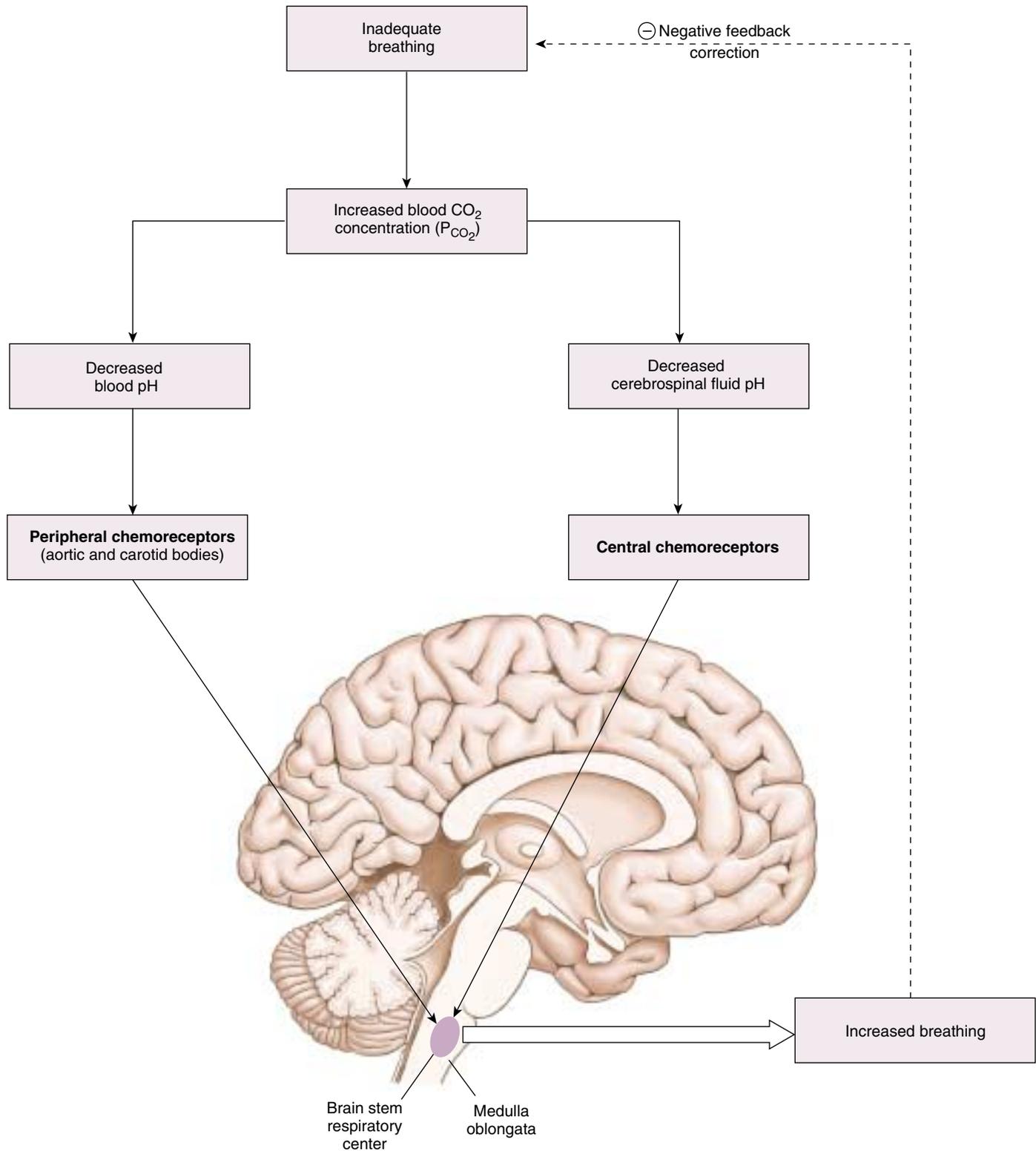

FIGURE 53.13
The effect of blood CO_2 on cerebrospinal fluid (CSF). Changes in the pH of the CSF are detected by chemosensitive neurons in the brain that help regulate breathing.

FIGURE 53.14
The regulation of breathing by chemoreceptors. Peripheral and central chemoreceptors sense a fall in the pH of blood and cerebrospinal fluid, respectively, when the blood carbon dioxide levels rise as a result of inadequate breathing. In response, they stimulate the respiratory control center in the medulla oblongata, which directs an increase in breathing. As a result, the blood carbon dioxide concentration is returned to normal, completing the negative feedback loop.

53.5 Blood transports oxygen and carbon dioxide.

Hemoglobin and Oxygen Transport

When oxygen diffuses from the alveoli into the blood, its journey is just beginning. The circulatory system delivers oxygen to tissues for respiration and carries away carbon dioxide. The transport of oxygen and carbon dioxide by the blood is itself an interesting and physiologically important process.

The amount of oxygen that can be dissolved in the blood plasma depends directly on the P_{O_2} of the air in the alveoli, as we explained earlier. When the lungs are functioning normally, the blood plasma leaving the lungs has almost as much dissolved oxygen as is theoretically possible, given the P_{O_2} of the air. Because of oxygen's low solubility in water, however, blood plasma can contain a maximum of only about 3 milliliters O_2 per liter. Yet whole blood carries almost 200 milliliters O_2 per liter! Most of the oxygen is bound to molecules of hemoglobin inside the red blood cells.

Hemoglobin is a protein composed of four polypeptide chains and four organic compounds called *heme groups.* At the center of each heme group is an atom of iron, which can bind to a molecule of oxygen (figure 53.15). Thus, each hemoglobin molecule can carry up to four molecules of oxygen. Hemoglobin loads up with oxygen in the lungs, forming **oxyhemoglobin.** This molecule has a bright red, tomato juice color. As blood passes through capillaries in the rest of the body, some of the oxyhemoglobin releases oxygen and becomes **deoxyhemoglobin.** Deoxyhemoglobin has a dark red color (the color of blood that is collected from the veins of blood donors), but it imparts a bluish tinge to tissues. Because of these color changes, vessels that carry oxygenated blood are always shown in artwork with a red color, and vessels that carry oxygen-depleted blood are indicated with a blue color.

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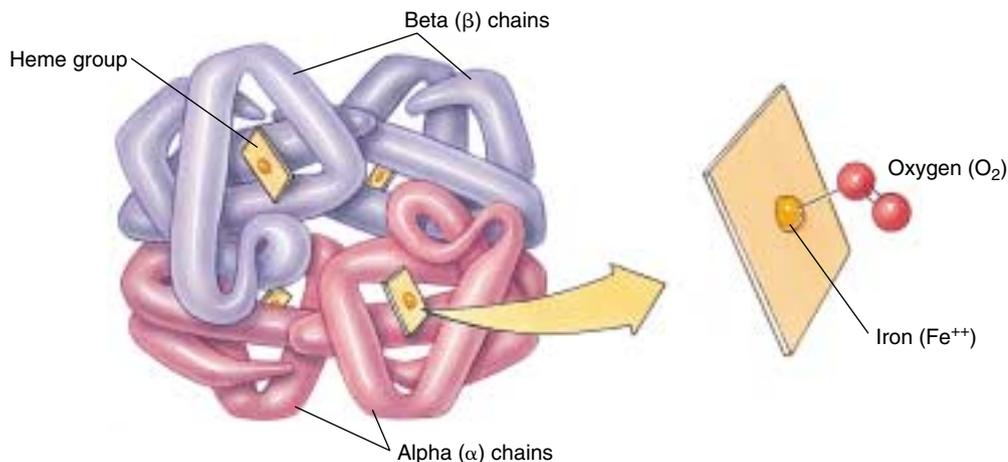

FIGURE 53.15

Hemoglobin consists of four polypeptide chains—two alpha (α) chains and two beta (β) chains. Each chain is associated with a heme group, and each heme group has a central iron atom, which can bind to a molecule of O_2.

Oxygen Transport

The P_{O_2} of the air within alveoli at sea level is approximately 105 millimeters of mercury (mm Hg), which is less than the P_{O_2} of the atmosphere because of the mixing of freshly inspired air with "old" air in the anatomical dead space of the respiratory system. The P_{O_2} of the blood leaving the alveoli is slightly less than this, about 100 mm Hg, because the blood plasma is not completely saturated with oxygen due to slight inefficiencies in lung function. At a blood P_{O_2} of 100 mm Hg, approximately 97% of the hemoglobin within red blood cells is in the form of oxyhemoglobin—indicated as a percent oxyhemoglobin saturation of 97%.

As the blood travels through the systemic blood capillaries, oxygen leaves the blood and diffuses into the tissues. Consequently, the blood that leaves the tissue in the veins has a P_{O_2} that is decreased (in a resting person) to about 40 mm Hg. At this lower P_{O_2}, the percent saturation of hemoglobin is only 75%. A graphic representation of these changes is called an oxyhemoglobin dissociation curve (figure 53.16). In a person at rest, therefore, 22% (97% minus 75%) of the oxyhemoglobin has released its oxygen to the tissues. Put another way, roughly one-fifth of the oxygen is unloaded in the tissues, leaving four-fifths of the oxygen in the blood as a reserve.

This large reserve of oxygen serves an important function. It enables the blood to supply the body's oxygen needs during exercise as well as at rest. During exercise, the muscles' accelerated metabolism uses more oxygen from the capillary blood and thus decreases the venous blood P_{O_2}. For example, the P_{O_2} of the venous blood could drop to 20 mm Hg; in this case, the percent saturation of hemoglobin will be only 35% (see figure 53.16).

Because arterial blood still contains 97% oxyhemoglobin (ventilation increases proportionately with exercise), the amount of oxygen unloaded is now 62% (97% minus 35%), instead of the 22% at rest. In addition to this function, the oxygen reserve also ensures that the blood contains enough oxygen to maintain life for four to five minutes if breathing is interrupted or if the heart stops pumping.

Oxygen transport in the blood is affected by other conditions. The CO_2 produced by metabolizing tissues as a product of aerobic respiration combines with H_2O to ultimately form bicarbonate and H^+, lowering the pH of the blood. This reaction occurs primarily inside red blood cells, where the lowered pH reduces hemoglobin's affinity for oxygen and thus causes it to release oxygen more readily. The effect of pH on hemoglobin's affinity for oxygen is known as the Bohr effect and is shown graphically by a shift of the oxyhemoglobin dissociation curve to the right (figure 53.17a). Increasing temperature has a similar affect on hemoglobin's affinity for oxygen (figure 53.17b) Because skeletal muscles produce carbon dioxide more rapidly during exercise and active muscles produce heat, the blood unloads a higher percentage of the oxygen it carries during exercise.

Deoxyhemoglobin combines with oxygen in the lungs to form oxyhemoglobin, which dissociates in the tissue capillaries to release its oxygen. The degree to which the loading reaction occurs depends on ventilation; the degree of unloading is influenced by such factors as pH and temperature.
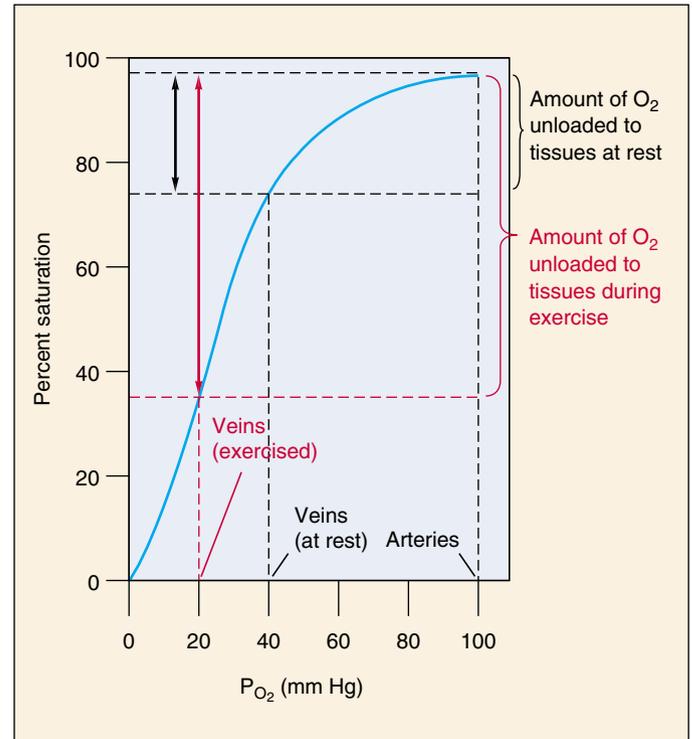

FIGURE 53.16
The oxyhemoglobin dissociation curve. Hemoglobin combines with O_2 in the lungs, and this oxygenated blood is carried by arteries to the body cells. After oxygen is removed from the blood to support cell respiration, the blood entering the veins contains less oxygen. The difference in O_2 content between arteries and veins during rest and exercise shows how much O_2 was unloaded to the tissues.
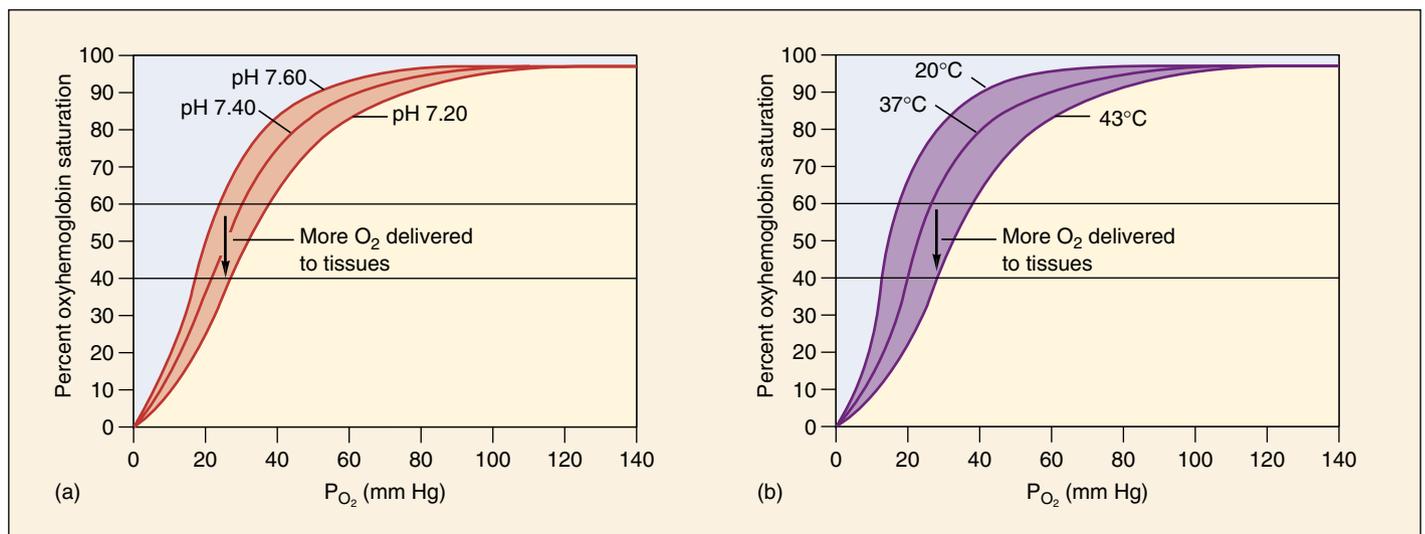

FIGURE 53.17
The effect of pH and temperature on the oxyhemoglobin dissociation curve. Lower blood pH (a) and higher blood temperatures (b) shift the oxyhemoglobin dissociation curve to the right, facilitating oxygen unloading. This can be seen as a lowering of the oxyhemoglobin percent saturation from 60 to 40% in the example shown, indicating that the difference of 20% more oxygen is unloaded to the tissues.

Carbon Dioxide and Nitric Oxide Transport

The systemic capillaries deliver oxygen to the tissues and remove carbon dioxide. About 8% of the CO_2 in blood is simply dissolved in plasma; another 20% is bound to hemoglobin. (Because CO_2 binds to the protein portion of hemoglobin, however, and not to the heme irons, it does not compete with oxygen.) The remaining 72% of the CO_2 diffuses into the red blood cells, where the enzyme carbonic anhydrase catalyzes the combination of CO_2 with water to form carbonic acid (H_2CO_3). Carbonic acid dissociates into bicarbonate (HCO_3^-) and hydrogen (H^+) ions. The H^+ binds to deoxyhemoglobin, and the bicarbonate moves out of the erythrocyte into the plasma via a transporter that exchanges one chloride ion for a bicarbonate (this is called the "chloride shift"). This reaction removes large amounts of CO_2 from the plasma, facilitating the diffusion of additional CO_2 into the plasma from the surrounding tissues (figure 53.18). The formation of carbonic acid is also important in maintaining the acid-base balance of the blood, because bicarbonate serves as the major buffer of the blood plasma.

The blood carries CO_2 in these forms to the lungs. The lower P_{CO_2} of the air inside the alveoli causes the carbonic anhydrase reaction to proceed in the reverse direction, converting H_2CO_3 into H_2O and CO_2 (see figure 53.18). The CO_2 diffuses out of the red blood cells and into the alveoli, so that it can leave the body in the next exhalation (figure 53.19).

Nitric Oxide Transport

Hemoglobin also has the ability to hold and release nitric oxide gas (NO). Although a noxious gas in the atmosphere, nitric oxide has an important physiological role in the body and acts on many kinds of cells to change their shapes and functions. For example, in blood vessels the presence of NO causes the blood vessels to expand because it relaxes the surrounding muscle cells (see chapters 7 and 52). Thus, blood flow and blood pressure are regulated by the amount of NO released into the bloodstream.

A current hypothesis proposes that hemoglobin carries NO in a special form called super nitric oxide. In this form, NO has acquired an extra electron and is able to bind to the amino acid cysteine in hemoglobin. In the lungs, hemoglobin that is dumping CO_2 and picking up O_2 also picks up NO as super nitric oxide. In blood vessels at the tissues, hemoglobin that is releasing its O_2 and picking up CO_2 can do one of two things with nitric oxide. To increase blood flow, hemoglobin can release the
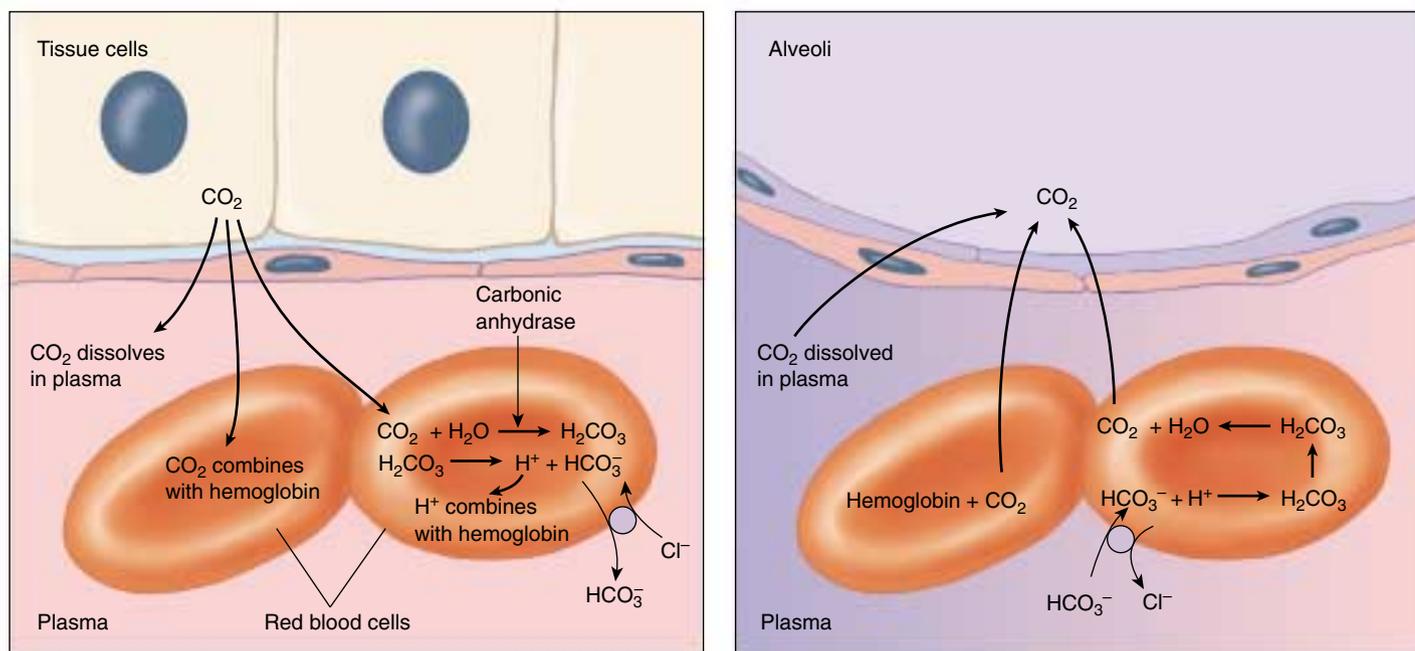

FIGURE 53.18
The transport of carbon dioxide by the blood. CO_2 is transported in three ways: dissolved in plasma, bound to the protein portion of hemoglobin, and as carbonic acid and bicarbonate, which form in the red blood cells. When the blood passes through the pulmonary capillaries, these reactions are reversed so that CO_2 gas is formed, which is exhaled.
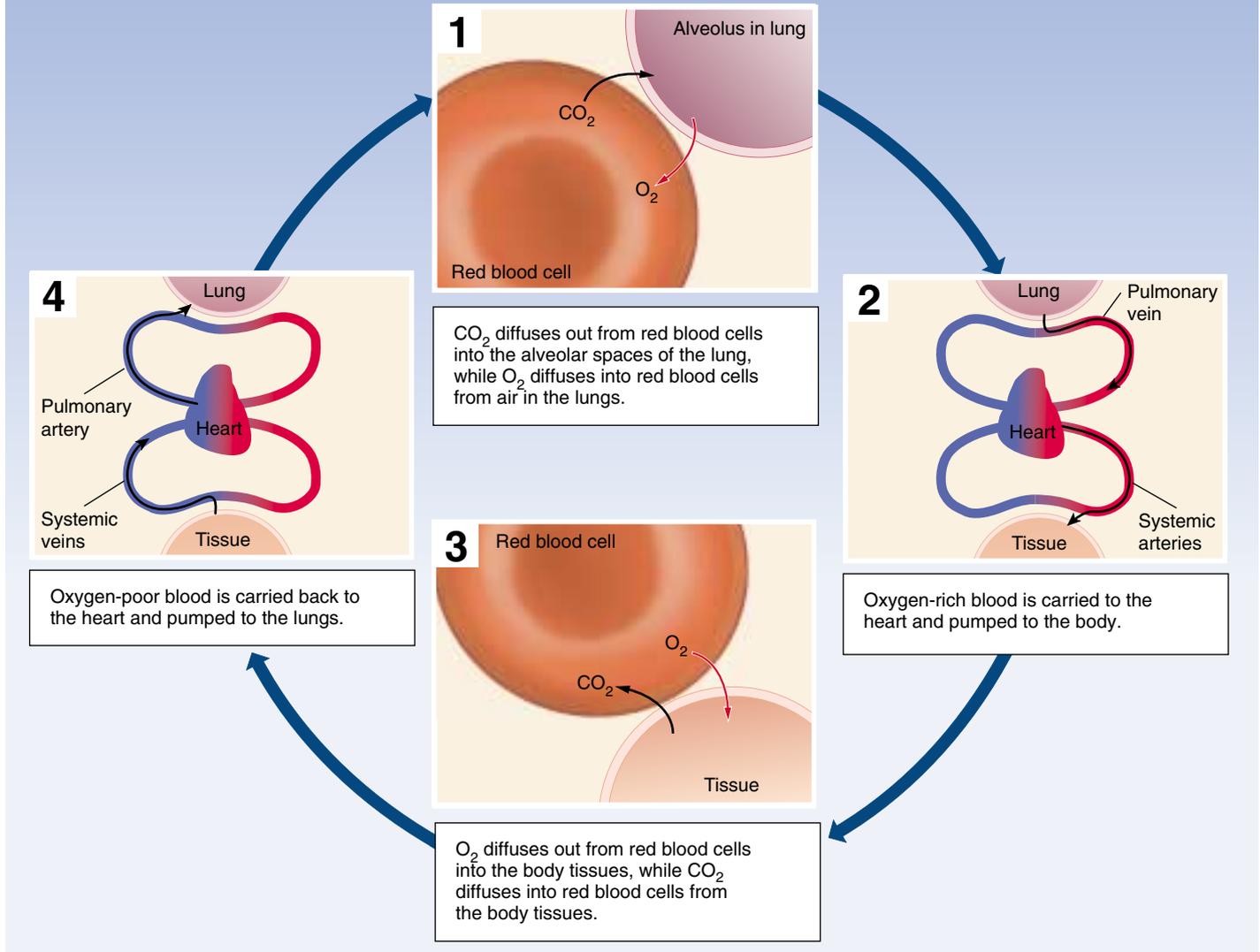
GAS EXCHANGE DURING RESPIRATION

1

Alveolus in lung

CO_2

O_2

Red blood cell

CO_2 diffuses out from red blood cells into the alveolar spaces of the lung, while O_2 diffuses into red blood cells from air in the lungs.

4

Lung

Pulmonary artery

Heart

Systemic veins

Tissue

Oxygen-poor blood is carried back to the heart and pumped to the lungs.

2

Lung

Pulmonary vein

Heart

Systemic arteries

Tissue

Oxygen-rich blood is carried to the heart and pumped to the body.

3

Red blood cell

O_2

CO_2

Tissue

O_2 diffuses out from red blood cells into the body tissues, while CO_2 diffuses into red blood cells from the body tissues.

FIGURE 53.19
Summary of respiratory gas exchange.

super nitric oxide as NO into the blood, making blood vessels expand because NO acts as a relaxing agent. Or, hemoglobin can trap any excess of NO on its iron atoms left vacant by the release of oxygen, causing blood vessels to constrict. When the red blood cells return to the lungs, hemoglobin dumps its CO_2 and the regular form of NO bound to the iron atoms. It is then ready to pick up O_2 and super nitric oxide and continue the cycle.

Carbon dioxide is transported in the blood in three ways: dissolved in the plasma, bound to hemoglobin, and the majority as bicarbonate in the plasma following an enzyme-catalyzed reaction in the red blood cells. Nitric oxide is also transported in the blood providing yet another explanation of NO actions on blood vessels.

Chapter 53

Summary | Questions | Media Resources

53.1 Respiration involves the diffusion of gases.

- The factors that influence the rate of diffusion, surface area, concentration gradient, and diffusion distance, are described by Fick's Law.
- Animals have evolved to maximize the diffusion rate across respiratory membranes by increasing the respiratory surface area, increasing the concentration gradient across the membrane, or decreasing the diffusion distance.

1. Approximately what percentage of dry air is oxygen, and what percentage is carbon dioxide?

2. Why is it that only very small organisms can satisfy their respiratory requirements by direct diffusion to all cells from the body surface?

- Respiration

- Gas exchange systems
- Respiratory overview
- Gas exchange

53.2 Gills are used for respiration by aquatic vertebrates.

- As water flows past a gill's lamellae, it comes close to blood flowing in an opposite, or countercurrent, direction; this maximizes the concentration difference between the two fluids, thereby maximizing the diffusion of gases.

3. What is countercurrent flow, and how does it help make the fish gill the most efficient respiratory organ?

53.3 Lungs are used for respiration by terrestrial vertebrates.

- Reptiles, birds, and mammals use negative pressure breathing; air is taken into the lungs when the lung volume is expanded to create a partial vacuum.
- Mammals have lungs composed of millions of alveoli, where gas exchange occurs; this is very efficient, but because inspiration and expiration occur through the same airways, new air going into the lungs is mixed with some old air.

4. How do amphibians get air into their lungs? How do other terrestrial vertebrates get air into their lungs?

5. What two features in birds make theirs the most efficient of all terrestrial respiratory systems?

- Art Activities:
  Respiratory tract
  Upper respiratory tract
  Section of larynx

- Gas exchange

53.4 Mammalian breathing is a dynamic process.

- The lungs are covered with a wet membrane that sticks to the wet membrane lining the thoracic cavity, so the lungs expand as the chest expands through muscular contractions.
- Breathing is controlled by centers in the medulla oblongata of the brain; breathing is stimulated by a rise in blood CO_2, and consequent fall in blood pH, as sensed by chemoreceptors located in the aorta and carotid artery.

6. How are the lungs connected to and supported within the thoracic cavity?

7. How does the brain control inspiration and expiration? How do peripheral and central chemoreceptors influence the brain's control of breathing?

- Boyle's Law
- Breathing

- Breathing
- Mechanics of ventilation
- Control of respiration

53.5 Blood transports oxygen and carbon dioxide.

- Hemoglobin loads with oxygen in the lungs; this oxyhemoglobin then unloads oxygen as the blood goes through the systemic capillaries.
- Carbon dioxide combines with water as the carbon dioxide is transported to the lungs for exhalation.

8. In what form does most of the carbon dioxide travel in the blood? How and where is this molecule produced?

- Art Activity:
  Hemoglobin module

- Hemoglobin