52

Circulation

Concept Outline

52.1 The circulatory systems of animals may be open or closed.

Open and Closed Circulatory Systems. All vertebrates have a closed circulation, while many invertebrate animals have open circulatory systems.

52.2 A network of vessels transports blood through the body.

The Blood Plasma. The blood plasma transports a variety of solutes, including ions, metabolites, proteins, and hormones.

The Blood Cells. The blood cells include erythrocytes, which transport oxygen, leukocytes, which provide defenses for the body, and platelets, which function in blood clotting.

Characteristics of Blood Vessels. Blood leaves the heart in arteries and returns in veins; in between, the blood passes through capillaries, where all exchanges with tissues occur.

The Lymphatic System. The lymphatic system returns interstitial fluid to the bloodstream.

52.3 The vertebrate heart has undergone progressive evolutionary change.

The Fish Heart. The fish heart consists of a row of four chambers that receives blood in the posterior end from the body and pumps blood from the anterior end to the gills.

Amphibian and Reptile Circulation. Land vertebrates have a double circulation, where blood from the lungs returns to the heart to be pumped to the rest of the body.

Mammalian and Bird Hearts. Mammals and birds have a complete separation between the two sides of the heart.

52.4 The cardiac cycle drives the cardiovascular system.

The Cardiac Cycle. The right and left sides of the heart rest and receive blood at the same time, then pump the blood into arteries at the same time.

Electrical Excitation and Contraction of the Heart. The impulse begins in one area of the heart and is conducted to the rest of the heart.

Blood Flow and Blood Pressure. Blood flow and blood pressure depend on the diameter of the arterial vessels and on the amount of blood pumped by the heart.

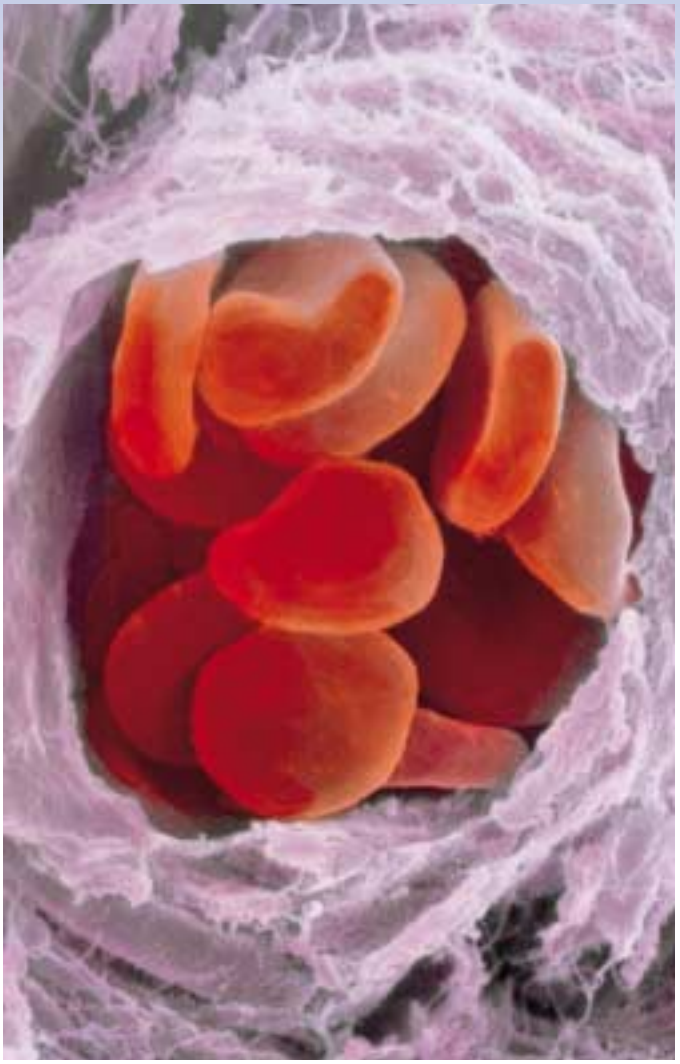


FIGURE 52.1
Red blood cells. This ruptured blood vessel, seen in a scanning electron micrograph, is full of red blood cells, which move through vessels transporting oxygen from one place to another in the body.

Every cell in the animal body must acquire the energy it needs for living from other molecules in food. Like residents of a city whose food is imported from farms in the countryside, cells in the body need trucks to carry the food, highways for the trucks to travel on, and a way to cook the food when it arrives. In animals, the circulatory system provides blood and blood vessels (the trucks and highways), and is discussed in this chapter (figure 52.1). The respiratory system provides the glucose (fuel) and oxygen (fuel to cook the food), and will be discussed in the following chapter.

52.1 The circulatory systems of animals may be open or closed.

Open and Closed Circulatory Systems

Among the unicellular protists, oxygen and nutrients are obtained directly from the aqueous external environment by simple diffusion. The body wall is only two cell layers thick in cnidarians, such as *Hydra*, and flatworms, such as *Planaria*. Each cell layer is in direct contact with either the external environment or the gastrovascular cavity (figure 52.2*a*). The gastrovascular cavity of *Hydra* (see chapter 51) extends from the body cavity into the tentacles, and that of *Planaria* branches extensively to supply every cell with oxygen and nutrients. Larger animals, however, have tissues that are several cell layers thick, so that many cells are too far away from the body surface or digestive cavity to exchange materials directly with the environment. Instead, oxygen and nutrients are transported from the environment and digestive cavity to the body cells by an internal fluid within a *circulatory system*.

There are two main types of circulatory systems: *open* or *closed*. In an **open circulatory system,** such as that found in mollusks and arthropods (figure 52.2*b*), there is no distinction between the circulating fluid (blood) and the extracellular fluid of the body tissues (interstitial fluid or lymph). This fluid is thus called **hemolymph.** In insects, the heart is a muscular tube that pumps hemolymph through a network of channels and cavities in the body. The fluid then drains back into the central cavity.

In a **closed circulatory system,** the circulating fluid, or blood, is always enclosed within blood vessels that transport blood away from and back to a pump, the **heart.** Annelids (see chapter 45) and all vertebrates have a closed circulatory system. In annelids such as an earthworm, a dorsal vessel contracts rhythmically to function as a pump. Blood is pumped through five small connecting arteries which also function as pumps, to a ventral vessel, which transports the blood posteriorly until it eventually reenters the dorsal vessel. Smaller vessels branch from each artery to supply the tissues of the earthworm with oxygen and nutrients and to transport waste products (figure 52.2*c*).

The Functions of Vertebrate Circulatory Systems

The vertebrate circulatory system is more elaborate than the invertebrate circulatory system. It functions in transporting oxygen and nutrients to tissues by the cardiovascular system. Blood vessels form a tubular network that permits blood to flow from the heart to all the cells of the body and then back to the heart. *Arteries* carry blood away from the heart, whereas *veins* return blood to the heart. Blood passes from the arterial to the venous system in *capillaries*, which are the thinnest and most numerous of the blood vessels.

As blood plasma passes through capillaries, the pressure of the blood forces some of this fluid out of the capillary walls. Fluid derived from plasma that passes out of capillary walls into the surrounding tissues is called **interstitial fluid.** Some of this fluid returns directly to capillaries, and some enters into **lymph vessels,** located in the connective tissues around the blood vessels. This fluid, now called *lymph*, is returned to the venous blood at specific sites. The lymphatic system is considered a part of the circulatory system and is discussed later in this chapter.

The vertebrate circulatory system has three principal functions: transportation, regulation, and protection.

1. **Transportation.** All of the substances essential for cellular metabolism are transported by the circulatory system. These substances can be categorized as follows:
   a. Respiratory. Red blood cells, or *erythrocytes*, transport oxygen to the tissue cells. In the capillaries of

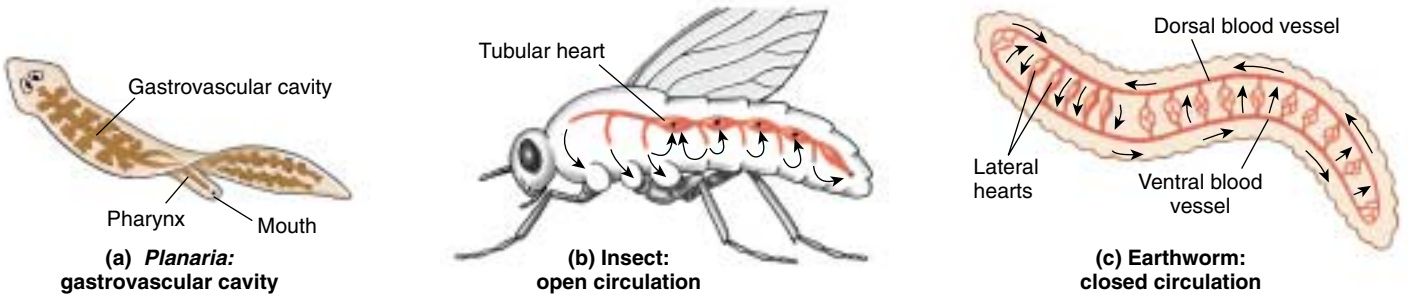


FIGURE 52.2
Circulatory systems of the animal kingdom. (*a*) The gastrovascular cavity of *Planaria* serves as both a digestive and circulatory system, delivering nutrients directly to the tissue cells by diffusion from the digestive cavity. (*b*) In the open circulation of an insect, hemolymph is pumped from a tubular heart into cavities in the insect's body; the hemolymph then returns to the blood vessels so that it can be recirculated. (*c*) In the closed circulation of the earthworm, blood pumped from the hearts remains within a system of vessels that returns it to the hearts. All vertebrates also have closed circulatory systems.

the lungs or gills, oxygen attaches to hemoglobin molecules within the erythrocytes and is transported to the cells for aerobic respiration. Carbon dioxide, a by-product of cell respiration, is carried by the blood to the lungs or gills for elimination.

b. Nutritive. The digestive system is responsible for the breakdown of food into molecules so that nutrients can be absorbed through the intestinal wall and into the blood vessels of the circulatory system. The blood then carries these absorbed products of digestion through the liver and to the cells of the body.

c. Excretory. Metabolic wastes, excessive water and ions, and other molecules in the fluid portion of blood are filtered through the capillaries of the kidneys and excreted in urine.

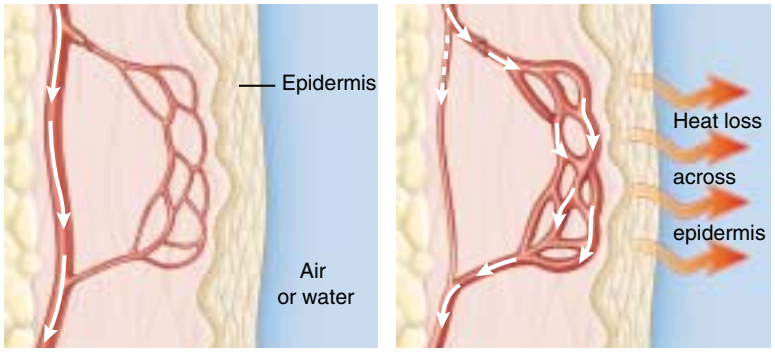


FIGURE 52.3
Regulation of heat loss. The amount of heat lost at the body's surface can be regulated by controlling the flow of blood to the surface. (*a*) Constriction of surface blood vessels limits flow and heat loss; (*b*) dilation of these vessels increases flow and heat loss.

2. Regulation. The cardiovascular system transports regulatory hormones and participates in temperature regulation.

a. Hormone transport. The blood carries hormones from the endocrine glands, where they are secreted, to the distant target organs they regulate.

b. Temperature regulation. In warm-blooded vertebrates, or **endotherms,** a constant body temperature is maintained regardless of the ambient temperature. This is accomplished in part by blood vessels located just under the epidermis. When the ambient temperature is cold, the superficial vessels constrict to divert the warm blood to deeper vessels. When the ambient temperature is warm, the superficial vessels dilate so that the warmth of the blood can be lost by radiation (figure 52.3).

Some vertebrates also retain heat in a cold environment by using a **countercurrent heat exchange** (also see chapter 53). In this process, a vessel carrying warm blood from deep within the body passes next to a vessel carrying cold blood from the surface of the body (figure 52.4). The warm blood going out heats the cold blood returning from the body surface, so that this blood is no longer cold when it reaches the interior of the body.

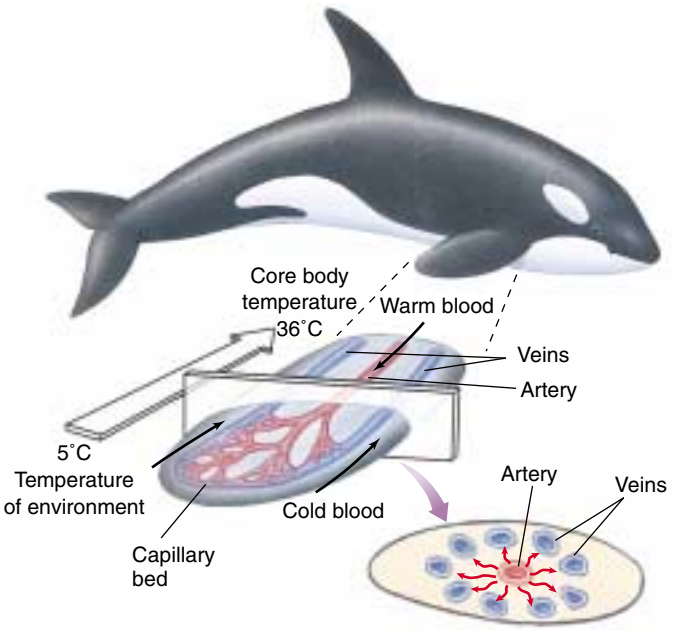


FIGURE 52.4
Countercurrent heat exchange. Many marine animals, such as this killer whale, limit heat loss in cold water using countercurrent heat exchange. The warm blood pumped from within the body in arteries loses heat to the cold blood returning from the skin in veins. This warms the venous blood so that the core body temperature can remain constant in cold water and cools the arterial blood so that less heat is lost when the arterial blood reaches the tip of the extremity.

3. Protection. The circulatory system protects against injury and foreign microbes or toxins introduced into the body.

a. Blood clotting. The clotting mechanism protects against blood loss when vessels are damaged. This clotting mechanism involves both proteins from the blood plasma and cell fragments called platelets (discussed in the next section).

b. Immune defense. The blood contains white blood cells, or leukocytes, that provide immunity against many disease-causing agents. Some white blood cells are phagocytic, some produce antibodies, and some act by other mechanisms to protect the body.

Circulatory systems may be open or closed. All vertebrates have a closed circulatory system, in which blood circulates away from the heart in arteries and back to the heart in veins. The circulatory system serves a variety of functions, including transportation, regulation, and protection.

52.2 A network of vessels transports blood through the body.

The Blood Plasma

Blood is composed of a fluid **plasma** and several different kinds of cells that circulate within that fluid (figure 52.5). Blood platelets, although included in figure 52.5, are not complete cells; rather, they are fragments of cells that reside in the bone marrow. Blood plasma is the matrix in which blood cells and platelets are suspended. Interstitial (extracellular) fluids originate from the fluid present in plasma.

Plasma contains the following solutes:

1. **Metabolites, wastes, and hormones.** Dissolved within the plasma are all of the metabolites used by cells, including glucose, amino acids, and vitamins. Also dissolved in the plasma are hormones that regulate cellular activities, wastes such as nitrogen compounds, and CO_2 produced by metabolizing cells. CO_2 is carried in the blood as bicarbonate because free carbon dioxide would decrease blood pH.
2. **Ions.** Like the water of the seas in which life arose, blood plasma is a dilute salt solution. The predominant plasma ions are sodium, chloride, and bicarbonate ions. In addition, there are trace amounts of other ions such as calcium, magnesium, copper, potassium, and zinc. The composition of the plasma, therefore, is similar to seawater, but plasma has a lower total ion concentration than that of present-day seawater.
3. **Proteins.** The liver produces most of the plasma proteins, including **albumin,** which comprises most of the plasma protein; the alpha (α) and beta (β) **globulins,** which serve as carriers of lipids and steroid hormones; and *fibrinogen*, which is required for blood clotting. Following an injury of a blood vessel, platelets release clotting factors (proteins) into the blood. In the presence of these clotting factors, fibrinogen is converted into insoluble threads of *fibrin*. Fibrin then aggregates to form the clot. Blood plasma which has had fibrinogen removed is called **serum**.

Plasma, the liquid portion of the blood, contains different types of proteins, ions, metabolites, wastes, and hormones. This liquid, and fluids derived from it, provide the extracellular environment of most the cells of the body.

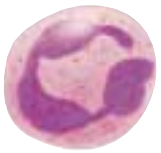
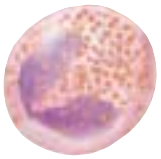
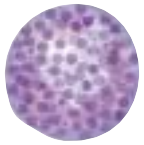
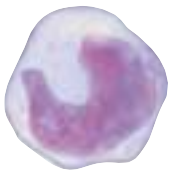
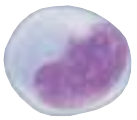
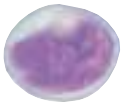
Blood cell	Life span in blood	Function
 Erythrocyte	120 days	O_2 and CO_2 transport
 Neutrophil	7 hours	Immune defenses
 Eosinophil	Unknown	Defense against parasites
 Basophil	Unknown	Inflammatory response
 Monocyte	3 days	Immune surveillance (precursor of tissue macrophage)
 B - lymphocyte	Unknown	Antibody production (precursor of plasma cells)
 T - lymphocyte	Unknown	Cellular immune response
 Platelets	7- 8 days	Blood clotting

FIGURE 52.5
Types of blood cells. Erythrocytes are red blood cells, platelets are fragments of a bone marrow cell, and all the other cells are different types of leukocytes, or white blood cells.

The Blood Cells

Red blood cells function in oxygen transport, white blood cells in immunological defenses, and platelets in blood clotting (see figure 52.5).

Erythrocytes and Oxygen Transport

Each cubic millimeter of blood contains about 5 million **red blood cells,** or **erythrocytes.** The fraction of the total blood volume that is occupied by erythrocytes is called the blood's *hematocrit;* in humans, it is typically around 45%. A disc with a central depression, each erythrocyte resembles a doughnut with a hole that does not go all the way through. As we've already seen, the erythrocytes of vertebrates contain hemoglobin, a pigment which binds and transports oxygen. In vertebrates, hemoglobin is found only in erythrocytes. In invertebrates, the oxygen binding pigment (not always hemoglobin) is also present in plasma.

Erythrocytes develop from unspecialized cells, called *stem cells*. When plasma oxygen levels decrease, the kidney converts a plasma protein into the hormone, *erythropoietin*. Erythropoietin then stimulates the production of erythrocytes in bone marrow. In mammals, maturing erythrocytes lose their nuclei through a process called *erythropoiesis*. This is different from the mature erythrocytes of all other vertebrates, which remain nucleated. As mammalian erythrocytes age, they are removed from the blood by phagocytic cells of the spleen, bone marrow, and liver. Balancing this loss, new erythrocytes are constantly formed in the bone marrow.

Leukocytes Defend the Body

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

There are several kinds of leukocytes, each of which plays a specific role in defending the body against invading microorganisms and other foreign substances, as described in Chapter 57. **Granular leukocytes** include **neutrophils, eosinophils,** and **basophils,** which are named according to the staining properties of granules in their cytoplasm. **Nongranular leukocytes** include **monocytes** and **lymphocytes.** Neutrophils are the most numerous of the leukocytes, followed in order by lymphocytes, monocytes, eosinophils, and basophils.

Platelets Help Blood to Clot

Megakaryocytes are large cells present in bone marrow. Pieces of cytoplasm are pinched off of the megakaryocytes and become **platelets.** Platelets play an important role in blood clotting. When a blood vessel is broken, smooth muscle in the vessel walls contracts, causing the vessel to constrict. Platelets then accumulate at the injured site and form a plug by sticking to each other and to the surrounding tissues. This plug is reinforced by threads of the protein **fibrin** (figure 52.6), which contract to form a tighter mass. The tightening plug of platelets, fibrin, and often trapped erythrocytes constitutes a blood clot.

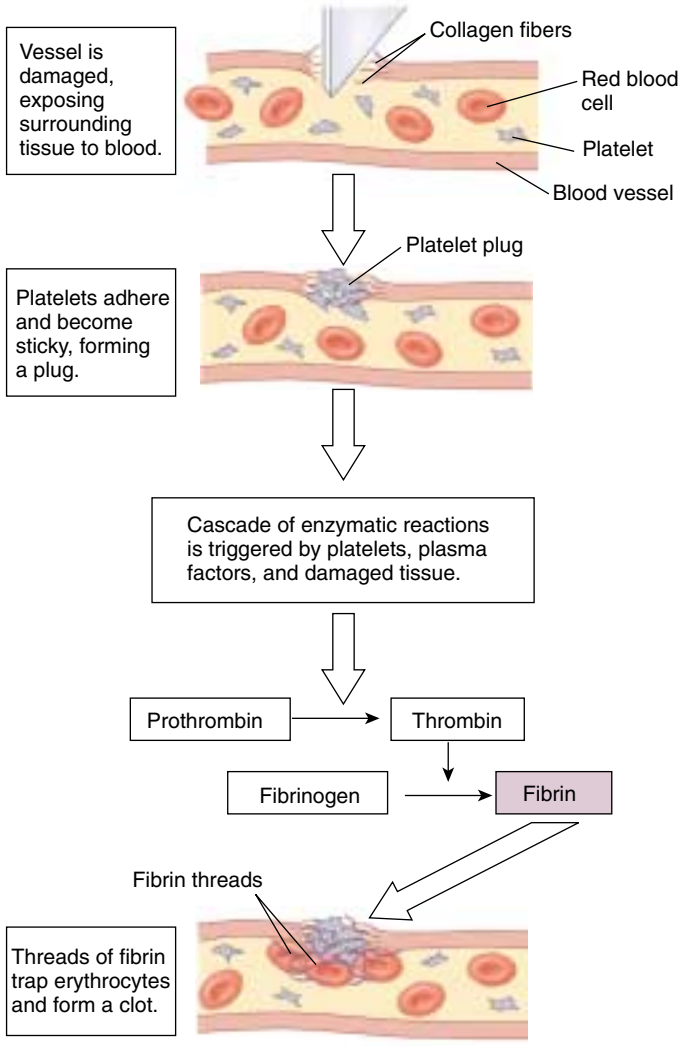


FIGURE 52.6
Blood clotting. Fibrin is formed from a soluble protein, fibrinogen, in the plasma. This reaction is catalyzed by the enzyme thrombin, which is formed from an inactive enzyme called prothrombin. The activation of thrombin is the last step in a cascade of enzymatic reactions that produces a blood clot when a blood vessel is damaged.

Erythrocytes contain hemoglobin and serve in oxygen transport. The different types of leukocytes have specialized functions that serve to protect the body from invading pathogens, and the platelets participate in blood clotting.

Characteristics of Blood Vessels

Blood leaves the heart through vessels known as **arteries.** These continually branch, forming a hollow "tree" that enters each of the organs of the body. The finest, microscopically-sized branches of the arterial trees are the **arterioles.** Blood from the arterioles enters the **capillaries** (from the Latin *capillus*, "a hair"), an elaborate latticework of very narrow, thin-walled tubes. After traversing the capillaries, the blood is collected into **venules;** the venules lead to larger vessels called **veins,** which carry blood back to the heart.

Arteries, arterioles, veins, and venules all have the same basic structure (figure 52.7). The innermost layer is an epithelial sheet called the *endothelium.* Covering the endothelium is a thin layer of elastic fibers, a smooth muscle layer, and a connective tissue layer. The walls of these vessels are thus too thick to permit any exchange of materials between the blood and the tissues outside the vessels. The walls of capillaries, however, are made up of only the endothelium, so molecules and ions can leave the blood plasma by diffusion, by filtration through pores in the capillary walls, and by transport through the endothelial cells. Therefore, it is while blood is in the capillaries that gases and metabolites are exchanged with the cells of the body.

Arteries and Arterioles

Arteries function in transporting blood away from the heart. The larger arteries contain extra elastic fibers in their walls, allowing them to recoil each time they receive a volume of blood pumped by the heart. Smaller arteries and arterioles are less elastic, but their disproportionately thick smooth muscle layer enables them to resist bursting.

The vast tree of arteries presents a frictional resistance to blood flow. The narrower the vessel, the greater the frictional resistance to flow. In fact, a vessel that is half the diameter of another has 16 times the frictional resistance! This is because the resistance to blood flow is inversely proportional to the radius of the vessel. Therefore, within the arterial tree, it is the small arteries and arterioles that provide the greatest resistance to blood flow. Contraction of the smooth muscle layer of the arterioles results in **vasoconstriction,** which greatly increases resistance and decreases flow. Relaxation of the smooth muscle layer results in **vasodilation,** decreasing resistance and increasing blood flow to an organ (see figure 52.3).

In addition, blood flow through some organs is regulated by rings of smooth muscle around arterioles near the region where they empty into capillaries. These **precapillary sphincters** (figure 52.8) can close off specific capillary beds completely. For example, the closure of precapillary sphincters in the skin contributes to the vasoconstriction that limits heat loss in cold environments.

Exchange in the Capillaries

Each time the heart contracts, it must produce sufficient pressure to pump blood against the resistance of the arterial tree and into the capillaries. The vast number and extensive branching of the capillaries ensure that *every cell in the body is within 100 μm of a capillary.* On the average, capillaries are about 1 mm long and 8 μm in diameter, only slightly larger than a red blood cell (5 to 7 μm in diameter). Despite the close fit, red blood cells can squeeze through capillaries without difficulty.

Although each capillary is very narrow, there are so many of them that the capillaries have the greatest *total* cross-sectional area of any other type of vessel. Conse-

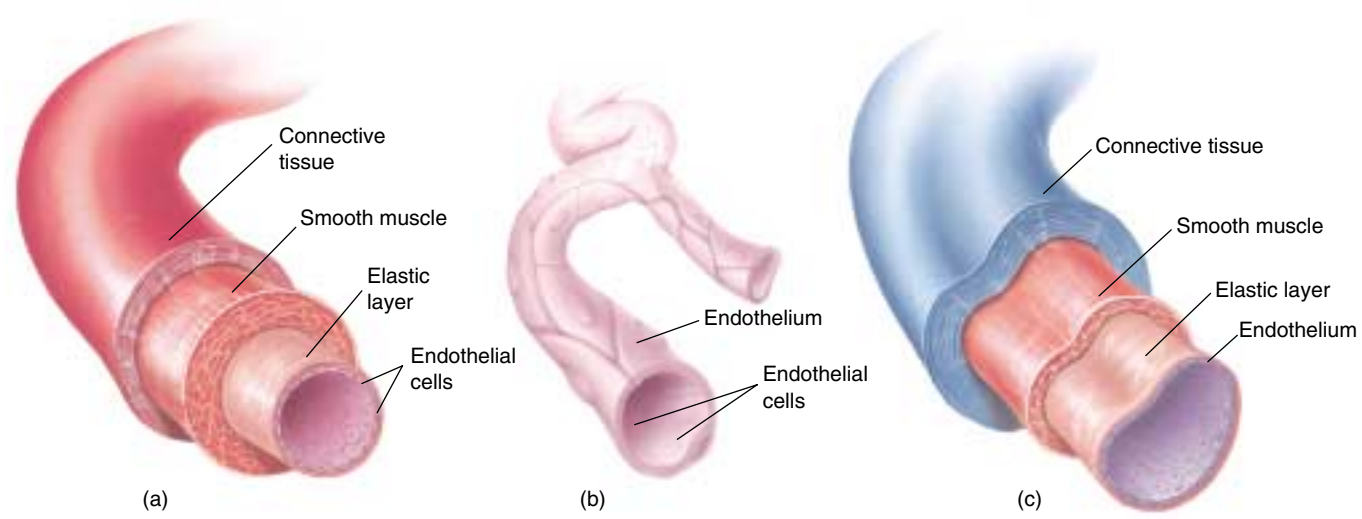


FIGURE 52.7
The structure of blood vessels. (*a*) Arteries and (*c*) veins have the same tissue layers. (*b*) Capillaries are composed of only a single layer of endothelial cells. (not to scale)

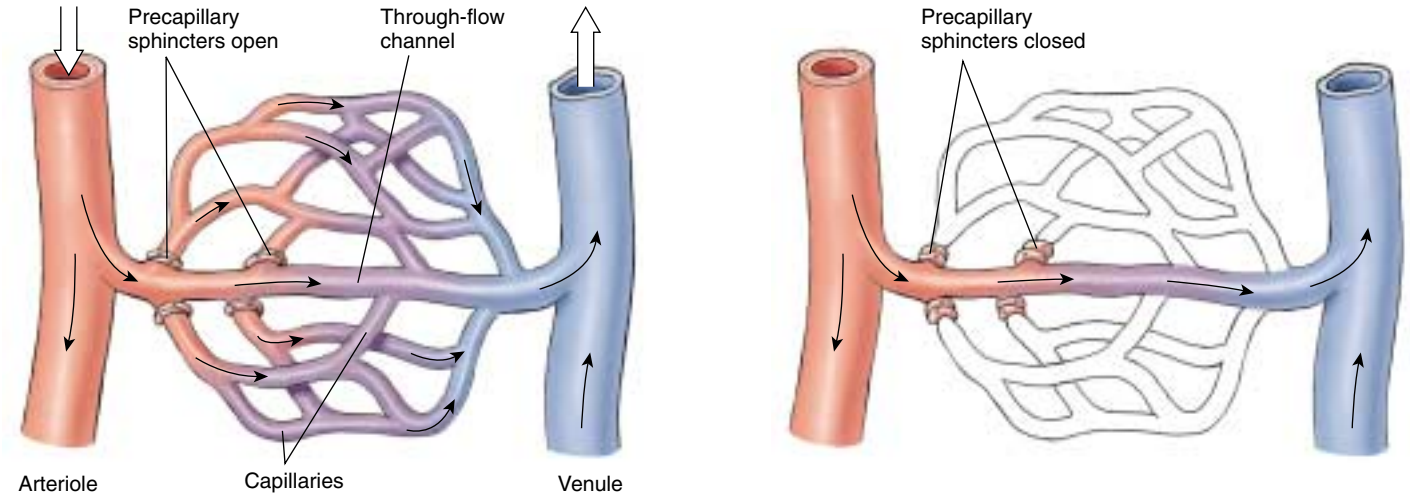


FIGURE 52.8
The capillary network connects arteries with veins. (*a*) Most of the exchange between the blood and the extracellular fluid occurs while the blood is in the capillaries. Entrance to the capillaries is controlled by bands of muscle called precapillary sphincters at the entrance to each capillary. (*b*) When a sphincter contracts, it closes off the capillary. By contracting these sphincters, the body can limit the amount of blood in the capillary network of a particular tissue, and thus control the rate of exchange in that tissue.

quently, the blood decreases in velocity as it passes through the capillary beds, allowing more time for it to exchange materials with the surrounding extracellular fluid. By the time the blood reaches the end of a capillary, it has released some of its oxygen and nutrients and picked up carbon dioxide and other waste products. Blood also loses most of its pressure in passing through the vast capillary networks, and so is under very low pressure when it enters the veins.

Venules and Veins

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

When the blood pressure in the veins is so low, how does the blood return to the heart from the feet and legs? The venous pressure alone is not sufficient, but several sources provide help. Most significantly, skeletal muscles surrounding the veins can contract to move blood by squeezing the veins. Blood moves in one direction through the veins back to the heart with the help of **venous valves** (figure 52.9). When a person's veins expand too much with blood, the venous valves may no longer work and the blood may pool in the veins. Veins in this condition are known as varicose veins.

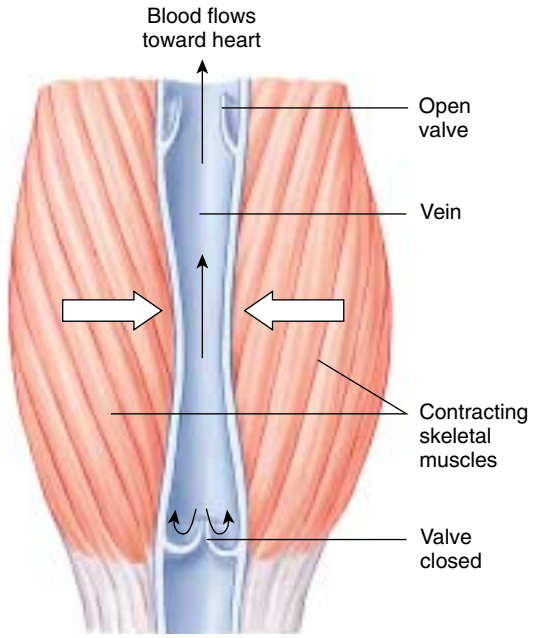


FIGURE 52.9
One-way flow of blood through veins. Venous valves ensure that blood moves through the veins in only one direction, back to the heart.

Blood is pumped from the heart into the arterial system, which branches into fine arterioles. This blood is delivered into the thinnest and most numerous of vessels, the capillaries, where exchanges with the tissues occur. Blood returns to the heart through veins.

The Lymphatic System

The cardiovascular system is considered to be a closed system because all of its vessels are connected with one another—none are simply open-ended. However, some water and solutes in the blood plasma do filter through the walls of the capillaries to form the interstitial (tissue) fluid. This filtration is driven by the pressure of the blood, and it helps supply the tissue cells with oxygen and nutrients. Most of the fluid is filtered from the capillaries near their arteriolar ends, where the blood pressure is higher, and returned to the capillaries near their venular ends. This return of fluid occurs by osmosis, which is driven by a higher solute concentration within the capillaries. Most of the plasma proteins cannot escape through the capillary pores because of their large size and so the concentration of proteins in the plasma is greater than the protein concentration in the interstitial fluid. The difference in protein concentration produces an osmotic pressure, called the *oncotic pressure*, that causes osmosis of water into the capillaries (figure 52.10).

Because interstitial fluid is produced because of the blood pressure, high capillary blood pressure could cause too much interstitial fluid to be produced. A common example of this occurs in pregnant women, when the fetus compresses veins and thereby increases the capillary blood pressure in the mother's lower limbs. The increased interstitial fluid can cause swelling of the tissues, or *edema*, of the feet. Edema may also result if the plasma protein concentration (and thus the oncotic pressure) is too low. Fluids will not return to the capillaries but will remain as interstitial fluid. This may be caused either by liver disease, because the liver produces most of the plasma proteins, or by protein malnutrition (*kwashiorkor*).

Even under normal conditions, the amount of fluid filtered out of the capillaries is greater than the amount that returns to the capillaries by osmosis. The remainder does eventually return to the cardiovascular system, however, by way of an *open* circulatory system called the **lymphatic system.** The lymphatic system consists of lymphatic capillaries, lymphatic vessels, lymph nodes, and lymphatic organs, including the spleen and thymus. Excess fluid in the tissues drains into blind-ended lymph capillaries with highly permeable walls. This fluid, now called **lymph,** passes into progressively larger lymphatic vessels, which resemble veins and have one-way valves (figure 52.11). The lymph eventually enters two major lymphatic vessels, which drain into veins on each side of the neck.

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

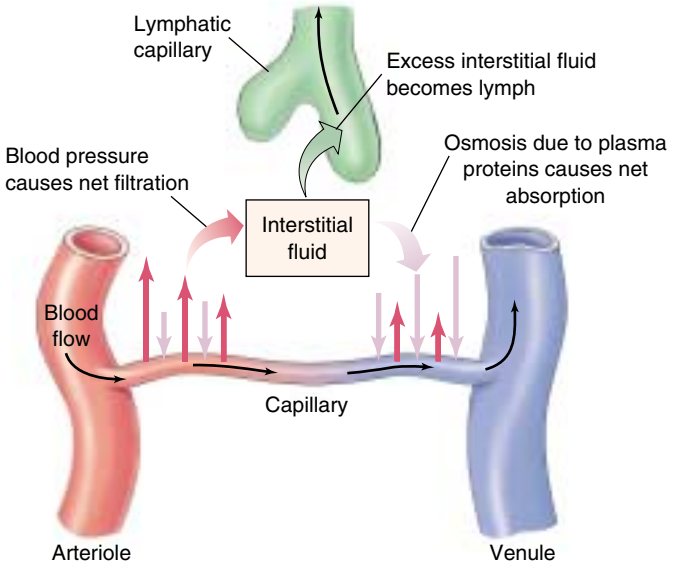


FIGURE 52.10
Plasma fluid, minus proteins, is filtered out of capillaries. This forms interstitial fluid, which bathes the tissues. Much of the interstitial fluid is returned to the capillaries by the osmotic pressure generated by the higher protein concentration in plasma. The excess interstitial fluid is drained into open-ended lymphatic capillaries, which ultimately return the fluid to the cardiovascular system.

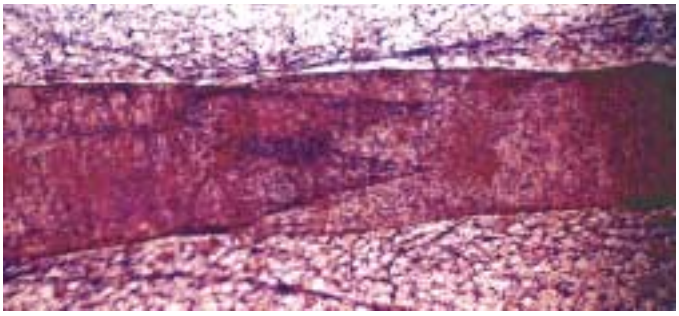


FIGURE 52.11
A lymphatic vessel valve (25×). Valves allow lymph to flow in one direction (from left to right in this figure) but not in the reverse direction.

As the lymph moves through lymph nodes and lymphatic organs, it is modified by phagocytic cells that line the channels of those organs. In addition, the lymph nodes and lymphatic organs contain *germinal centers* for the production of lymphocytes, a type of white blood cell critically important in immunity.

Lymphatic vessels carry excess interstitial fluid back to the vascular system. This fluid, called lymph, travels through lymph nodes and lymphatic organs where it encounters the immune cells called lymphocytes that are produced in these organs.

52.3 The vertebrate heart has undergone progressive evolutionary change.

The Fish Heart

The chordates that were ancestral to the vertebrates are thought to have had simple tubular hearts, similar to those now seen in lancelets (see chapter 48). The heart was little more than a specialized zone of the ventral artery, more heavily muscled than the rest of the arteries, which contracted in simple peristaltic waves. A pumping action results because the uncontracted portions of the vessel have a larger diameter than the contracted portion, and thus present less resistance to blood flow.

The development of gills by fishes required a more efficient pump, and in fishes we see the evolution of a true chamber-pump heart. The fish heart is, in essence, a tube with four chambers arrayed one after the other (figure 52.12*a*). The first two chambers—the **sinus venosus** and **atrium**—are collection chambers, while the second two, the **ventricle** and **conus arteriosus,** are pumping chambers.

As might be expected, the sequence of the heartbeat in fishes is a peristaltic sequence, starting at the rear and moving to the front, similar to the early chordate heart. The first of the four chambers to contract is the sinus venosus, followed by the atrium, the ventricle, and finally the conus arteriosus. Despite shifts in the relative positions of the chambers in the vertebrates that evolved later, this heartbeat sequence is maintained in all vertebrates. In fish, the electrical impulse that produces the contraction is initiated in the sinus venosus; in other vertebrates, the electrical impulse is initiated by their equivalent of the sinus venosus.

The fish heart is remarkably well suited to the gill respiratory apparatus and represents one of the major evolutionary innovations in the vertebrates. Perhaps its greatest advantage is that the blood that moves through the gills is fully oxygenated when it moves into the tissues. After blood leaves the conus arteriosus, it moves through the gills, where it becomes oxygenated; from the gills, it flows through a network of arteries to the rest of the body; then it returns to the heart through the veins (figure 52.12*b*). This arrangement has one great limitation, however. In passing through the capillaries in the gills, the blood loses much of the pressure developed by the contraction of the heart, so the circulation from the gills through the rest of the body is sluggish. This feature limits the rate of oxygen delivery to the rest of the body.

The fish heart is a modified tube, consisting of a series of four chambers. Blood first enters the heart at the sinus venosus, where the wavelike contraction of the heart begins.

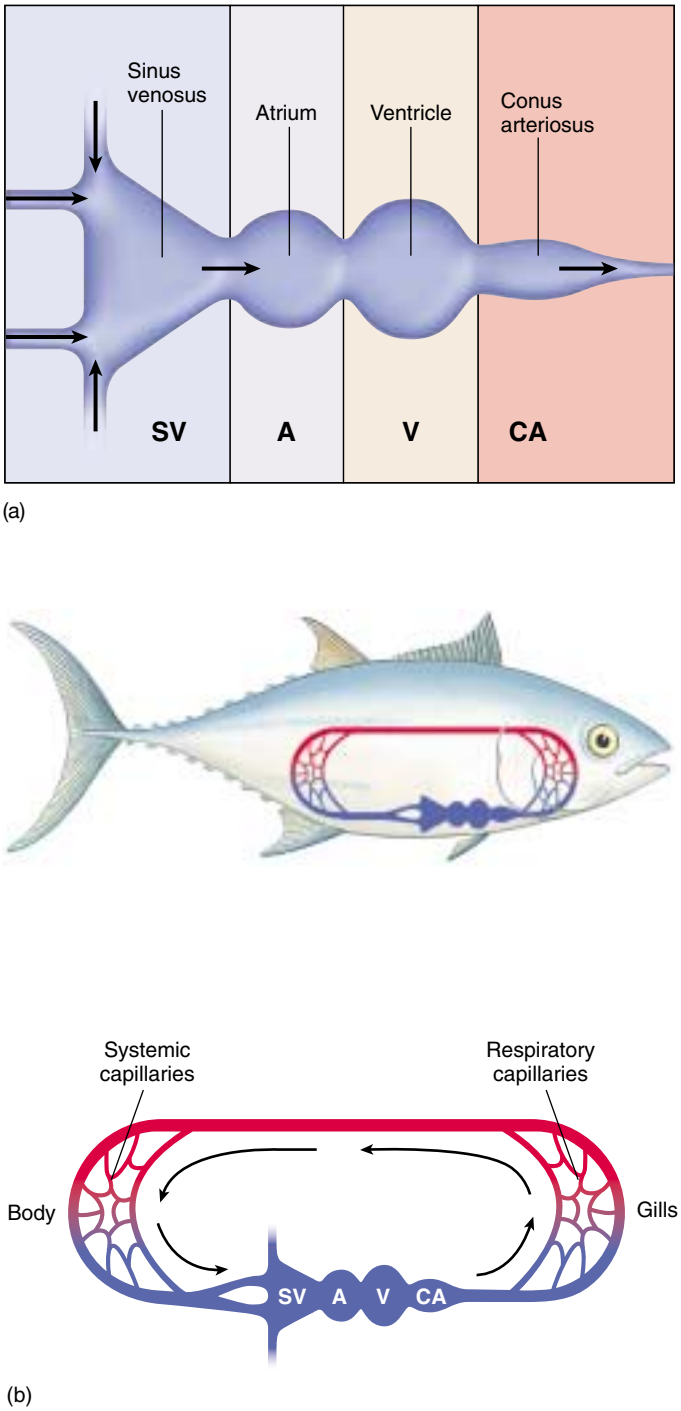


FIGURE 52.12
The heart and circulation of a fish. (*a*) Diagram of a fish heart, showing the chambers in series with each other. (*b*) Diagram of fish circulation, showing that blood is pumped by the ventricle through the gills and then to the body. Blood rich in oxygen (oxygenated) is shown in red; blood low in oxygen (deoxygenated) is shown in blue.

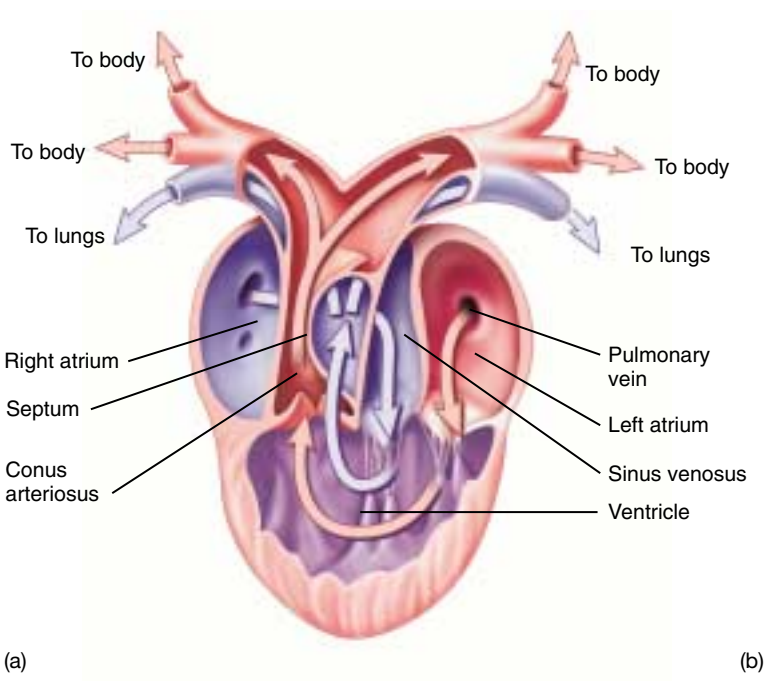


FIGURE 52.13
The heart and circulation of an amphibian. (*a*) The frog heart has two atria but only one ventricle, which pumps blood both to the lungs and to the body. (*b*) Despite the potential for mixing, the oxygenated and deoxygenated bloods (red and blue, respectively) mix very little as they are pumped to the body and lungs. The slight mixing is shown in purple. RA = right atrium; LA = left atrium; V = ventricle.

Amphibian and Reptile Circulation

The advent of lungs involved a major change in the pattern of circulation. After blood is pumped by the heart through the *pulmonary arteries* to the lungs, it does not go directly to the tissues of the body but is instead returned via the *pulmonary veins* to the heart. This results in two circulations: one between heart and lungs, called the **pulmonary circulation,** and one between the heart and the rest of the body, called the **systemic circulation.**

If no changes had occurred in the structure of the heart, the oxygenated blood from the lungs would be mixed in the heart with the deoxygenated blood returning from the rest of the body. Consequently, the heart would pump a mixture of oxygenated and deoxygenated blood rather than fully oxygenated blood. The amphibian heart has two structural features that help reduce this mixing (figure 52.13). First, the atrium is divided into two chambers: the right atrium receives deoxygenated blood from the systemic circulation, and the left atrium receives oxygenated blood from the lungs. These two stores of blood therefore do not mix in the atria, and little mixing occurs when the contents of each atrium enter the single, common ventricle, due to internal channels created by recesses in the ventricular wall. The conus arteriosus is partially separated by a dividing wall which directs deoxygenated blood into the pulmonary arteries to the lungs and oxygenated blood into the *aorta*, the major artery of the systemic circulation to the body.

Because there is only one ventricle in an amphibian heart, the separation of the pulmonary and systemic circulations is incomplete. Amphibians in water, however, can obtain additional oxygen by diffusion through their skin. This process, called **cutaneous respiration,** helps to supplement the oxygenation of the blood in these vertebrates.

Among reptiles, additional modifications have reduced the mixing of blood in the heart still further. In addition to having two separate atria, reptiles have a septum that partially subdivides the ventricle. This results in an even greater separation of oxygenated and deoxygenated blood within the heart. The separation is complete in one order of reptiles, the crocodiles, which have two separate ventricles divided by a complete septum. Crocodiles therefore have a completely divided pulmonary and systemic circulation. Another change in the circulation of reptiles is that the conus arteriosus has become incorporated into the trunks of the large arteries leaving the heart.

Amphibians and reptiles have two circulations, pulmonary and systemic, that deliver blood to the lungs and rest of the body, respectively. The oxygenated blood from the lungs is kept relatively separate from the deoxygenated blood from the rest of the body by incomplete divisions within the heart.

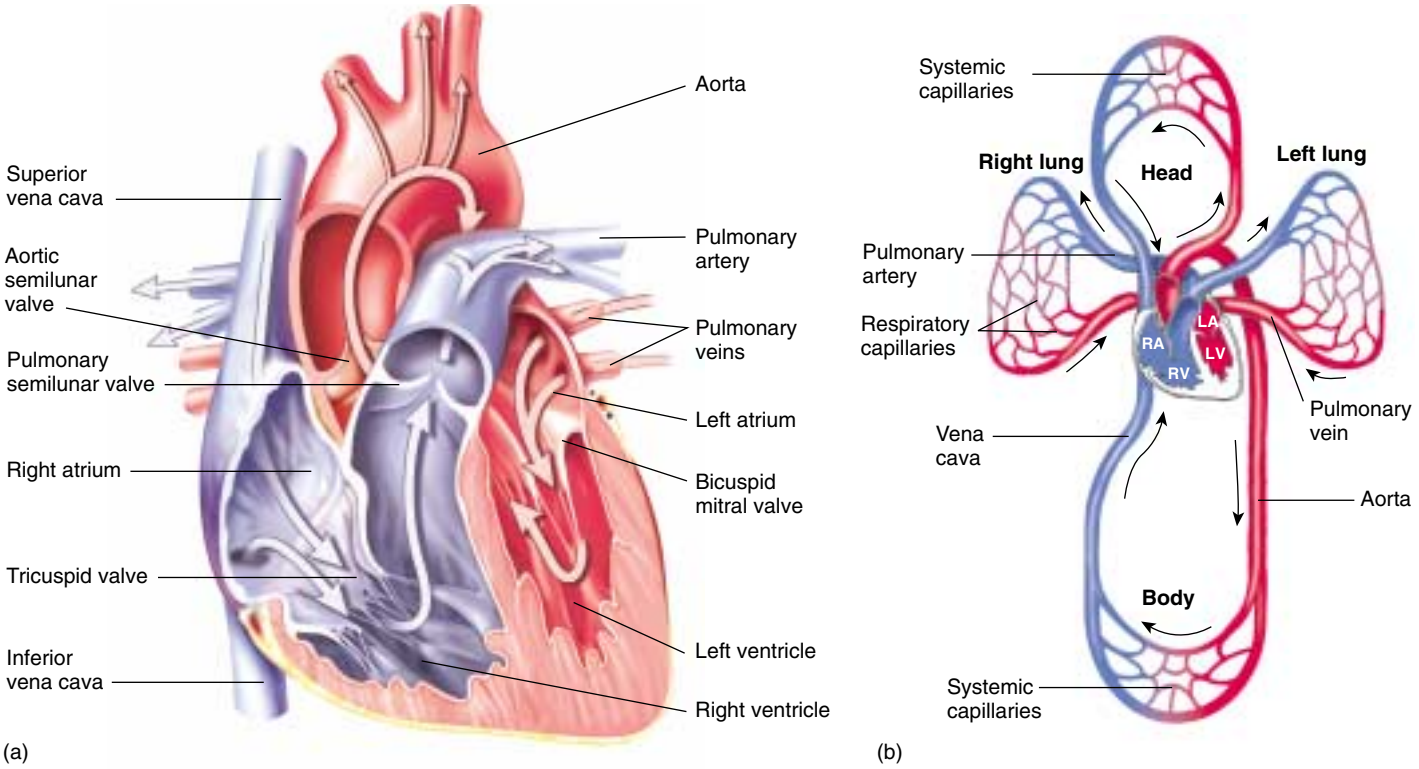


FIGURE 52.14
The heart and circulation of mammals and birds. (*a*) The path of blood through the four-chambered heart. (*b*) The right side of the heart receives deoxygenated blood and pumps it to the lungs; the left side of the heart receives oxygenated blood and pumps it to the body. In this way, the pulmonary and systemic circulations are kept completely separate. RA = right atrium; LA = left atrium; RV = right ventricle; LV = left ventricle.

Mammalian and Bird Hearts

Mammals, birds, and crocodiles have a four-chambered heart with two separate atria and two separate ventricles (figure 52.14). The right atrium receives deoxygenated blood from the body and delivers it to the right ventricle, which pumps the blood to the lungs. The left atrium receives oxygenated blood from the lungs and delivers it to the left ventricle, which pumps the oxygenated blood to the rest of the body. This completely double circulation is powered by a two-cycle pump. Both atria fill with blood and simultaneously contract, emptying their blood into the ventricles. Both ventricles contract at the same time, pushing blood simultaneously into the pulmonary and systemic circulations. The increased efficiency of the double circulatory system in mammals and birds is thought to have been important in the evolution of endothermy (warm-bloodedness), because a more efficient circulation is necessary to support the high metabolic rate required.

Because the overall circulatory system is closed, the same volume of blood must move through the pulmonary circulation as through the much larger systemic circulation with each heartbeat. Therefore, the right and left ventricles must pump the same amount of blood each time they contract. If the output of one ventricle did not match that of the other, fluid would accumulate and pressure would increase in one of the circuits. The result would be increased filtration out of the capillaries and edema (as occurs in congestive heart failure, for example). Although the volume of blood pumped by the two ventricles is the same, the pressure they generate is not. The left ventricle, which pumps blood through the higher-resistance systemic pathway, is more muscular and generates more pressure than does the right ventricle.

Throughout the evolutionary history of the vertebrate heart, the sinus venosus has served as a pacemaker, the site where the impulses that initiate the heartbeat originate. Although it constitutes a major chamber in the fish heart, it is reduced in size in amphibians and further reduced in reptiles. In mammals and birds, the sinus venosus is no longer evident as a separate chamber, but its disappearance is not really complete. Some of its tissue remains in the wall of the right atrium, near the point where the systemic veins empty into the atrium. This tissue, which is called the *sinoatrial (SA) node*, is still the site where each heartbeat originates.

The oxygenated blood from the lungs returns to the left atrium and is pumped out the left ventricle. The deoxygenated blood from the body returns to the right atrium and out the right ventricle to the lungs.

52.4 The cardiac cycle drives the cardiovascular system.

The Cardiac Cycle

The human heart, like that of all mammals and birds, is really two separate pumping systems operating within a single organ. The right pump sends blood to the lungs, and the left pump sends blood to the rest of the body.

The heart has two pairs of valves. One pair, the **atrioventricular (AV) valves,** guards the opening between the atria and ventricles. The AV valve on the right side is the **tricuspid valve,** and the AV valve on the left is the **bicuspid,** or **mitral, valve.** Another pair of valves, together called the **semilunar valves,** guard the exits from the ventricles to the arterial system; the **pulmonary valve** is located at the exit of the right ventricle, and the **aortic valve** is located at the exit of the left ventricle. These valves open and close as the heart goes through its **cardiac cycle** of rest *(diastole)* and contraction *(systole)*. The sound of these valves closing produces the "lub-dub" sounds heard with a stethoscope.

Blood returns to the resting heart through veins that empty into the right and left atria. As the atria fill and the pressure in them rises, the AV valves open to admit the blood into the ventricles. The ventricles become about 80% filled during this time. Contraction of the atria wrings out the final 20% of the 80 milliliters of blood the ventricles will receive, on average, in a resting person. These events occur while the ventricles are relaxing, a period called ventricular **diastole.**

After a slight delay, the ventricles contract; this period of contraction is known as ventricular **systole.** Contraction of each ventricle increases the pressure within each chamber, causing the AV valves to forcefully close (the "lub" sound), thereby preventing blood from backing up into the atria. Immediately after the AV valves close, the pressure in the ventricles forces the semilunar valves open so that blood can be pushed out into the arterial system. As the ventricles relax, closing of the semilunar valves prevents back flow (the "dub" sound).

The right and left **pulmonary arteries** deliver oxygen-depleted blood to the right and left lungs. As previously mentioned, these return blood to the left atrium of the heart via the **pulmonary veins.** The **aorta** and all its branches are systemic arteries (figure 52.15), carrying oxygen-rich blood from the left ventricle to all parts of the body. The **coronary arteries** are the first branches off the aorta; these supply the heart muscle itself. Other systemic arteries branch from the aorta as it makes an arch above the heart, and as it descends and traverses the thoracic and abdominal cavities. These branches provide all body organs with oxygenated blood. The blood from the body organs, now lower in oxygen, returns to the heart in the systemic veins. These eventually empty into two major veins: the **superior vena cava,** which drains the upper body, and the **inferior vena cava,** which drains the lower body. These veins empty into the right atrium and thereby complete the systemic circulation.

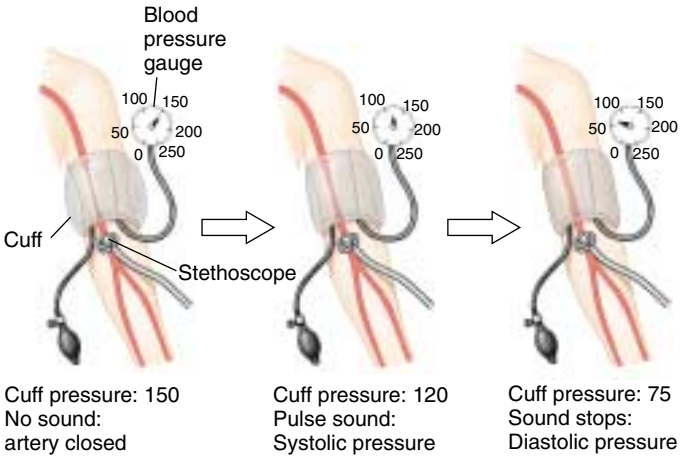


FIGURE 52.15
Measurement of blood pressure.

Measuring Arterial Blood Pressure

As the ventricles contract, great pressure is generated in the arteries throughout the body. You can tell this by feeling your pulse, either on the inside of your wrist, below the thumb or on the sides of your neck below your ear and jawbone. The contraction of the ventricles has to be strong enough to force blood through capillary beds but not too strong as to cause damage to smaller arteries and arterioles. Doctors measure your blood pressure to determine how hard your heart is working.

The measuring device used is called a sphygmomanometer and measures the blood pressure of the brachial artery found on the inside part of the arm, at the elbow (figure 52.15). A cuff wrapped around the upper part of the arm is tightened enough to stop the flow of blood to the lower part of the arm. As the cuff is loosened, blood will begin pulsating through the artery and can be detected using a stethoscope. Two measurements are recorded: the systolic and the diastolic pressure. The systolic pressure is the peak pressure during ventricular systole (contraction of the ventricle). The diastolic pressure is the minimum pressure between heartbeats (repolarization of the ventricles). The blood pressure is written as a ratio of systolic over diastolic pressure, and for a healthy person in his or her twenties, a typical blood pressure is 120/75 (measurement in mm of mercury). A condition called *hypertension* (high blood pressure) occurs when the ventricles experience very strong contractions, and the blood pressure is elevated, either systolic pressure greater than 150 or diastolic pressures greater than 90.

The cardiac cycle consists of systole and diastole; the ventricles contract at systole and relax at diastole.

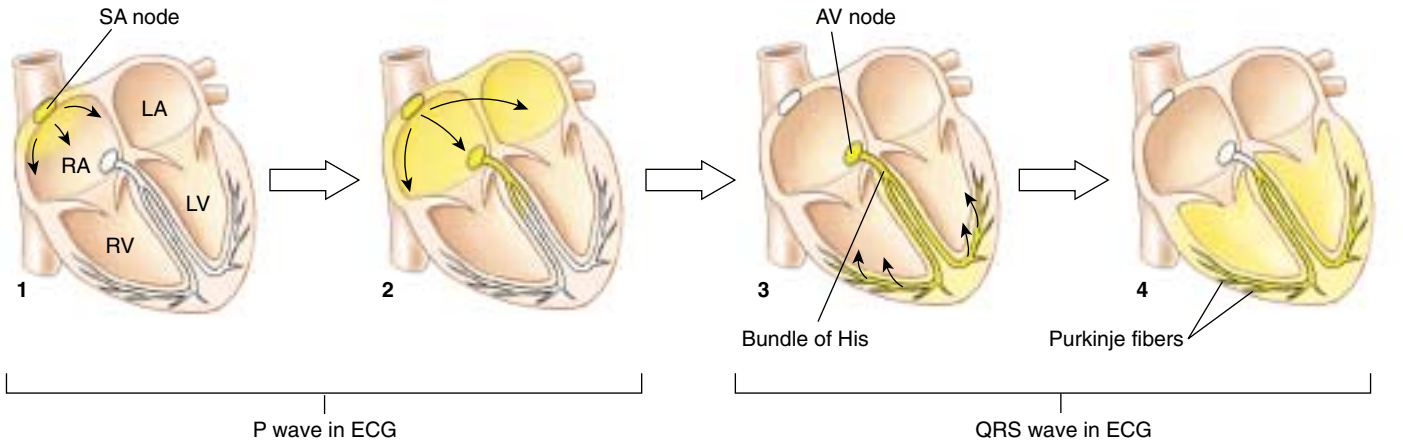
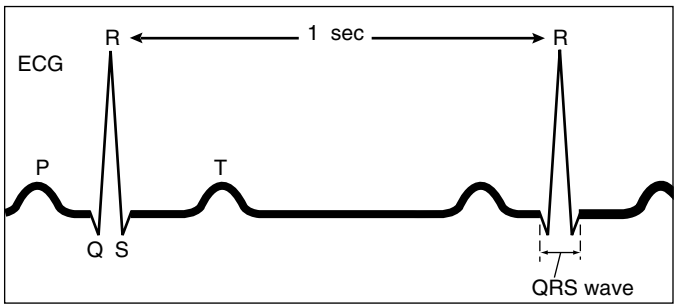


FIGURE 52.16
The path of electrical excitation in the heart. A wave of depolarization begins at the sinoatrial (SA) node. After passing over the atria and causing them to contract (forming the P wave on the ECG), the depolarization reaches the atrioventricular (AV) node, from which it passes to the ventricles along the septum by the bundle of His. Finer Purkinje fibers carry the depolarization into the right and left ventricular muscles (forming the QRS wave on the ECG). The T wave on the ECG corresponds to the repolarization of the ventricles.



Electrical Excitation and Contraction of the Heart

As in other types of muscle, contraction of heart muscle is stimulated by membrane **depolarization,** a reversal of the electrical polarity that normally exists across the plasma membrane (see chapter 50). In skeletal muscles, the nervous system initiates depolarization. However, in the heart, the depolarization is triggered by the **sinoatrial (SA) node** (figure 52.16), the small cluster of cardiac muscle cells derived from the sinus venosus. The SA node acts as a **pacemaker** for the rest of the heart by producing depolarization impulses spontaneously at a particular rate. Each depolarization initiated within this pacemaker region passes quickly from one cardiac muscle cell to another in a wave that envelops the right and left atria nearly simultaneously. The spread of depolarization is possible because the cardiac muscle cells are electrically coupled by gap junctions.

After a delay of almost 0.1 second, the wave of depolarization spreads to the ventricles. The reason for this delay is that connective tissue separates the atria from the ventricles, and connective tissue cannot transmit depolarization. The depolarization would not pass to the ventricles at all, were it not for a group of specialized cardiac muscle cells known as the **atrioventricular (AV) node.** The cells in the AV node transmit the depolarization slowly, causing the delay. This delay permits the atria to finish contracting and emptying their blood into the ventricles before the ventricles contract.

From the AV node, the wave of depolarization is conducted rapidly over both ventricles by a network of fibers called the **atrioventricular bundle** or **bundle of His.** It is then transmitted by **Purkinje fibers,** which directly stimulate the myocardial cells of the ventricles. The rapid conduction of the depolarization along the bundle of His and the Purkinje fibers causes the almost simultaneous contraction of the left and right ventricles. The rate can be increased or decreased by neural regulation or increased by the hormone epinephrine.

The spread of electrical activity through the heart creates currents that can be recorded from the surface of the body with electrodes placed on the limbs and chest. The recording, called an **electrocardiogram** (**ECG** or **EKG**), shows how the cells of the heart depolarize and repolarize during the cardiac cycle (see figure 52.16). As was explained in chapter 50, depolarization causes contraction of a muscle (including the heart), while repolarization causes relaxation. The first peak in the recording, P, is produced by the depolarization of the atria, and thus is associated with atrial systole. The second, larger peak, QRS, is produced by ventricular depolarization; during this time, the ventricles contract (ventricular systole) and eject blood into the arteries. The last peak, T, is produced by ventricular repolarization; at this time the ventricles begin diastole.

The SA node in the right atrium initiates waves of depolarization that stimulate first the atria and then the ventricles to contract.

Blood Flow and Blood Pressure

Cardiac Output

Cardiac output is the volume of blood pumped by each ventricle per minute. Because humans (like all vertebrates) have a closed circulation, the cardiac output is the same as the volume of blood that traverses the systemic or pulmonary circulations per minute. It is calculated by multiplying the heart rate by the *stroke volume*, which is the volume of blood ejected by each ventricle per beat. For example, if the heart rate is 72 beats per minute and the stroke volume is 70 milliliters, the cardiac output is 5 liters per minute, which is about average in a resting person.

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

During exercise, the cardiac output increases to a maximum of about 25 liters per minute in an average young adult. Although the cardiac output has increased five times, not all organs receive five times the blood flow; some receive more, others less. This is because the arterioles in some organs, such as in the digestive system, constrict, while the arterioles in the exercising muscles and heart dilate. As previously mentioned, the resistance to flow decreases as the radius of the vessel increases. As a consequence, vasodilation greatly increases and vasoconstriction greatly decreases blood flow.

Blood Pressure and the Baroreceptor Reflex

The arterial blood pressure depends on two factors: how much blood the ventricles pump (the cardiac output) and how great a resistance to flow the blood encounters in the entire arterial system. An increased blood pressure, therefore, could be produced by an increased heart rate or an increased blood volume (because both increase the cardiac output) or by vasoconstriction, which increases the resistance to blood flow. Conversely, blood pressure will fall if the heart rate slows or if the blood volume is reduced, for example by dehydration or excessive bleeding (hemorrhage).

Changes in the arterial blood pressure are detected by **baroreceptors** located in the arch of the aorta and in the carotid arteries. These receptors activate sensory neurons that relay information to *cardiovascular control centers* in the medulla oblongata, a region of the brain stem. When the baroreceptors detect a fall in blood pressure, they stimulate neurons that go to blood vessels in the skin and viscera, causing arterioles in these organs to constrict and raise the blood pressure. This baroreceptor reflex therefore completes a negative feedback loop that acts to correct the fall in blood pressure and restore homeostasis.

Blood Volume Reflexes

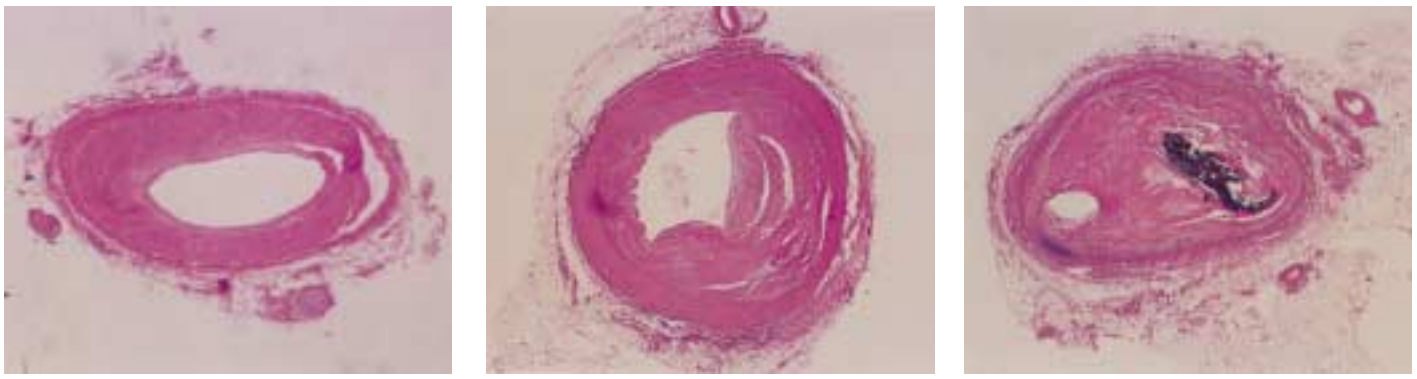
Blood pressure depends in part on the total blood volume. A decrease in blood volume, therefore, will decrease blood pressure, if all else remains equal. Blood volume regulation involves the effects of four hormones: (1) antidiuretic hormone; (2) aldosterone; (3) atrial natriuretic hormone; and (4) nitric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

Antidiuretic Hormone. *Antidiuretic hormone* (ADH), also called *vasopressin*, is secreted by the posterior pituitary gland in response to an increase in the osmotic concentration of the blood plasma. Dehydration, for example, causes the blood volume to decrease while the remaining plasma becomes more concentrated. This stimulates *osmoreceptors* in the hypothalamus of the brain, a region located immediately above the pituitary. The osmoreceptors promote thirst and stimulate ADH secretion from the posterior pituitary gland. ADH, in turn, stimulates the kidneys to retain more water in the blood, excreting less in the urine (urine is derived from blood plasma—see chapter 58). A dehydrated person thus drinks more and urinates less, helping to raise the blood volume and restore homeostasis.

Aldosterone. If a person's blood volume is lowered (by dehydration, for example), the flow of blood through the organs will be reduced if no compensation occurs. Whenever the kidneys experience a decreased blood flow, a group of kidney cells initiate the release of a short polypeptide known as *angiotensin II*. This is a very powerful molecule: it stimulates vasoconstriction throughout the body while it also stimulates the adrenal cortex (the outer region of the adrenal glands) to secrete the hormone *aldosterone*. This important steroid hormone is necessary for life; it acts on the kidneys to promote the retention of Na^+ and water in the blood. An animal that lacks aldosterone will die if untreated, because so much of the blood volume is lost in urine that the blood pressure falls too low to sustain life.

Atrial Natriuretic Hormone. When the body needs to eliminate excessive Na^+, less aldosterone is secreted by the adrenals, so that less Na^+ is retained by the kidneys. In recent years, scientists have learned that Na^+ excretion in the urine is promoted by another hormone. Surprisingly, this hormone is secreted by the right atrium of the heart—the heart is an endocrine gland! The right atrium secretes *atrial natriuretic hormone* in response to stretching of the atrium by an increased blood volume. The action of atrial natriuretic hormone completes a negative feedback loop, because it promotes the elimination of Na^+ and water, which will lower the blood volume and pressure.

Nitric Oxide. *Nitric oxide* (NO) is a gas that acts as a hormone in vertebrates, regulating blood pressure and blood flow. As described in chapter 7, nitric oxide gas is a paracrine hormone, is produced by one cell, penetrates through membranes, and alters the activities of other



(a) (b) (c)

FIGURE 52.17
Atherosclerosis. (*a*) The coronary artery shows only minor blockage. (*b*) The artery exhibits severe atherosclerosis—much of the passage is blocked by build-up on the interior walls of the artery. (*c*) The coronary artery is essentially completely blocked.

neighboring cells. In 1998 the Nobel Prize for Medicine was awarded for the discovery of this signal transmission activity. How does NO regulate blood pressure? Nitric oxide gas produced by the surface endothelial cells of blood vessels passes inward through the cell layers of the vessel, causing the smooth muscles that encase it to relax and the blood vessel to dilate (become wider). For over a century, heart patients have been prescribed nitroglycerin to relieve chest pain, but only now has it become clear that nitroglycerin acts by releasing nitric oxide gas.

Cardiovascular Diseases

Cardiovascular diseases are the leading cause of death in the United States; more than 42 million people have some form of cardiovascular disease. Heart attacks are the main cause of cardiovascular deaths in the United States, accounting for about a fifth of all deaths. They result from an insufficient supply of blood reaching one or more parts of the heart muscle, which causes myocardial cells in those parts to die. Heart attacks may be caused by a blood clot forming somewhere in the coronary arteries (the arteries that supply the heart muscle with blood) and blocking the passage of blood through those vessels. They may also result if an artery is blocked by atherosclerosis (see below). Recovery from a heart attack is possible if the portion of the heart that was damaged is small enough that the other blood vessels in the heart can enlarge their capacity and resupply the damaged tissues. **Angina pectoris,** which literally means "chest pain," occurs for reasons similar to those that cause heart attacks, but it is not as severe. The pain may occur in the heart and often also in the left arm and shoulder. Angina pectoris is a warning sign that the blood supply to the heart is inadequate but still sufficient to avoid myocardial cell death.

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

Atherosclerosis is an accumulation within the arteries of fatty materials, abnormal amounts of smooth muscle, deposits of cholesterol or fibrin, or various kinds of cellular debris. These accumulations cause blood flow to be reduced (figure 52.17). The lumen (interior) of the artery may be further reduced in size by a clot that forms as a result of the atherosclerosis. In the severest cases, the artery may be blocked completely. Atherosclerosis is promoted by genetic factors, smoking, hypertension (high blood pressure), and high blood cholesterol levels. Diets low in cholesterol and saturated fats (from which cholesterol can be made) can help lower the level of blood cholesterol, and therapy for hypertension can reduce that risk factor. Stopping smoking, however, is the single most effective action a smoker can take to reduce the risk of atherosclerosis.

Arteriosclerosis, or hardening of the arteries, occurs when calcium is deposited in arterial walls. It tends to occur when atherosclerosis is severe. Not only do such arteries have restricted blood flow, but they also lack the ability to expand as normal arteries do to accommodate the volume of blood pumped out by the heart. This inflexibility forces the heart to work harder.

Cardiac output depends on the rate of the heart and how much blood is ejected per beat. Blood flow is regulated by the degree of constriction of the arteries, which affects the resistance to flow. Blood pressure is influenced by blood volume. The volume of water retained in the vascular system is regulated by hormones that act on the kidneys and blood vessels. Many cardiovascular diseases are associated with the accumulation of fatty materials on the inner surfaces of arteries.

Chapter 52

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Summary

Questions

Media Resources

52.1 The circulatory systems of animals may be open or closed.

- Vertebrates have a closed circulation, where the blood stays within vessels as it travels away from and back to the heart.
- The circulatory system serves a variety of functions, including transport, regulation, and protection.

1. What is the difference between a closed circulatory system and an open circulatory system? In what types of animals would you find each?

- Bioethics case study: Heart transplant

- Types of systems

52.2 A network of vessels transports blood through the body.

- Plasma is the liquid portion of the blood. A variety of plasma proteins, ions, metabolites, wastes, and hormones are dissolved in the plasma.
- Erythrocytes, or red blood cells, contain hemoglobin and function to transport oxygen; the leukocytes, or white blood cells, function in immunological defenses.
- The heart pumps blood into arteries, which branch into smaller arterioles.
- Blood from the arterial system empties into capillaries with thin walls; all exchanges between the blood and tissues pass across the walls of capillaries.
- Blood returns to the heart in veins, which have one-way valves to ensure that blood travels toward the heart only.
- Lymphatic vessels return interstitial fluid to the venous system.

2. What are the major components of blood plasma?

3. Describe the structure of arteries and veins, explaining their similarities and differences. Why do arteries differ in structure from veins?

4. What is the relationship between vessel diameter and the resistance to blood flow? How do the arterial trees adjust their resistance to flow?

5. What drives the flow of fluid within the lymphatic system, and in what direction does the fluid flow?

- Art Activities:
  Blood vessels
  Capillary bed anatomy
  Human circulatory system
  Lymphatic system
  Lymphoid organs

- Lymphatic system

- Vessels and pressure
- Blood
- Lymph system
- Plasma

52.3 The vertebrate heart has undergone progressive evolutionary change.

- The fish heart consists of four chambers in a row; the beat originates in the sinus venosus and spreads through the atrium, ventricle, and conus arteriosus.
- In the circulation of fishes, blood from the heart goes to the gills and then to the rest of the body before returning to the heart; in terrestrial vertebrates, blood returns from the lungs to the heart before it is pumped to the body.

6. Describe the pattern of circulation through a fish and an amphibian, and compare the structure of their hearts. What new circulatory pattern accompanies the evolution of lungs?

- On Science Article: Dinosaur hearts

- Art Activities:
  External heart anatomy
  Internal view of heart

- Cardiac cycle blood flow

52.4 The cardiac cycle drives the cardiovascular system.

- Electrical excitation of the heart is initiated by the SA (sinoatrial) node, spreads through gap junctions between myocardial cells in the atria, and then is conducted into the ventricles by specialized conducting tissue.
- The cardiac output is regulated by nerves that influence the cardiac rate and by factors that influence the stroke volume.

7. How does the baroreceptor reflex help to maintain blood pressure? How do ADH and aldosterone maintain blood volume and pressure? What causes their secretion?

- Art Activity: Plaque

- Blood flow
- Cardiac cycle
- Blood pressure