UNIT
Four

Alterations in the Cardiovascular System

CHAPTER
14

Structure and Function of the Cardiovascular System

The main function of the *circulatory system*, which consists of the heart and blood vessels, is transport. The circulatory system delivers oxygen and nutrients needed for metabolic processes to the tissues, carries waste products from cellular metabolism to the kidneys and other excretory organs for elimination, and circulates electrolytes and hormones

KEY CONCEPTS

FUNCTIONAL ORGANIZATION OF THE CIRCULATORY SYSTEM

- The circulatory system consists of the heart, which pumps blood; the arterial system, which distributes oxygenated blood to the tissues; the venous system, which collects deoxygenated blood from the tissues and returns it to the heart; and the capillaries, where exchange of gases, nutrients, and wastes occurs.
- The circulatory system is divided into two parts: the low-pressure pulmonary circulation, linking the transport function of the circulation with the gas exchange function of the lungs; and the high-pressure systemic circulation, providing oxygen and nutrients to the tissues.
- The circulation is a closed system, so the output of the right and left heart must be equal over time for effective functioning of the circulation.

needed to regulate body function. This process of nutrient delivery is carried out with exquisite precision so that the blood flow to each tissue of the body is exactly matched to tissue need.

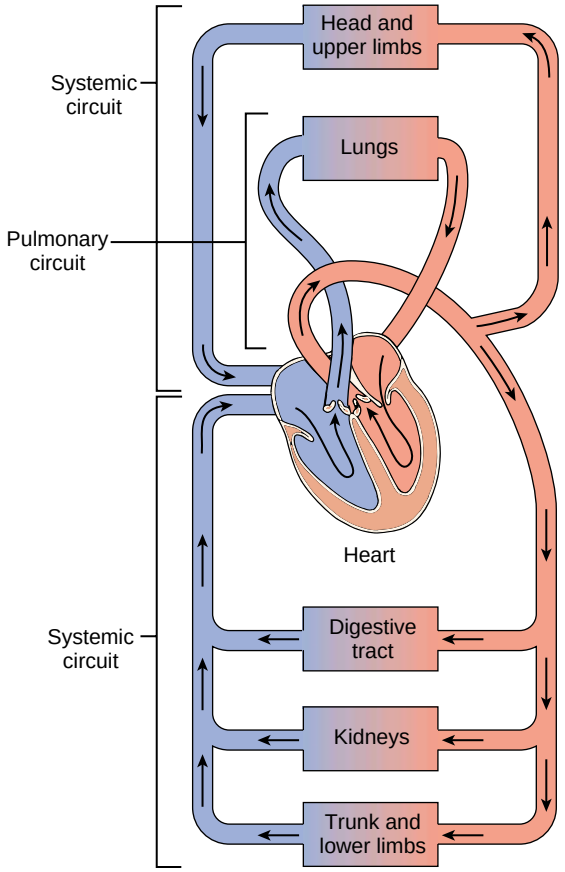
ORGANIZATION OF THE CIRCULATORY SYSTEM

Pulmonary and Systemic Circulations

The circulatory system can be divided into two parts: the *pulmonary circulation,* which moves blood through the lungs and creates a link with the gas exchange function of the respiratory system, and the *systemic circulation,* which moves blood throughout all the other tissues of the body (Fig. 14-1). The blood that is in the heart and pulmonary circulation is sometimes referred to as the *central circulation,* and that outside the central circulation as the *peripheral circulation.*

The pulmonary circulation consists of the right heart, the pulmonary artery, the pulmonary capillaries, and the pulmonary veins. The large pulmonary vessels are unique in that the pulmonary artery is the only artery that carries deoxygenated venous blood and the pulmonary veins, the only veins that carry oxygenated arterial blood. The systemic circulation consists of the left heart, the aorta and its branches, the capillaries that supply the brain and peripheral tissues, and the systemic venous system and the vena cava. The veins from the lower portion of the body empty into the inferior vena cava and those from the head and upper extremities into the superior vena cava. Blood from both the inferior and superior vena cava empties into the right heart.

Although the pulmonary and systemic systems function similarly, they have some important differences. The pulmonary circulation is the smaller of the two and functions with a much lower pressure. Because the pulmonary circulation is located in the chest near to the heart, it functions as a low-pressure system with a mean arterial pressure of approximately 12 mm Hg. The low pressure of the pulmonary circulation allows blood to move through the lungs more slowly, which is important for gas exchange. Because the systemic circulation must transport blood to distant parts of the body, often against the effects of gravity, it functions as a high-pressure system, with a mean arterial pressure of 90 to 100 mm Hg.

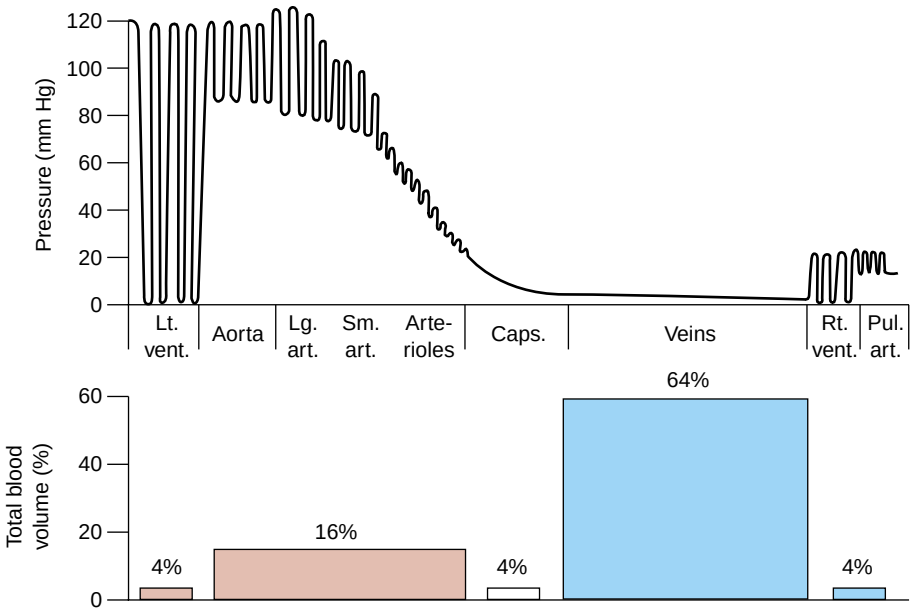


■ **FIGURE 14-1** ■ Systemic and pulmonary circulations. The right side of the heart pumps blood to the lungs, and the left side of the heart pumps blood to the systemic circulation.

The heart, which propels the blood through the circulation, consists of two pumps in series—the right heart which propels blood through the lungs and the left heart which propels blood to all other tissues of the body. The effective function of the circulatory system requires that the outputs of both sides of the heart pump the same amount of blood over time. If the output of the left heart were to fall below that of the right heart, blood would accumulate in the pulmonary circulation. Likewise, if the right heart were to pump less effectively than the left heart, blood would accumulate in the systemic circulation.

Volume and Pressure Distribution

Blood flow in the circulatory system depends on a blood volume that is sufficient to fill the blood vessels and a pressure difference across the system that provides the force that is needed to move blood forward. As shown in Figure 14-2, approximately 4% of the blood at any given time is in the left heart,



■ **FIGURE 14-2** ■ Pressure and volume distribution in the systemic circulation. The graphs show the inverse relation between internal pressure and volume in different portions of the circulatory system. (Smith J.J., Kampine J.P. [1990]. *Circulatory physiology: The essentials* [3rd ed.]. Baltimore: Williams & Wilkins)

16% is in the arteries and arterioles, 4% is in the capillaries, 64% is in the venules and veins, and 4% is in the right heart. The arteries and arterioles, which have thick, elastic walls and function as a distribution system, have the highest pressure. The capillaries are small, thin-walled vessels that link the arterial and venous sides of the circulation. They serve as an exchange system where transfer of gases, nutrients, and wastes take place. Because of their small size and large surface area, the capillaries contain the smallest amount of blood. The venules and veins, which contain the largest amount of blood, are thin-walled, distensible vessels that function as a reservoir to collect blood from the capillaries and return it to the right heart.

Blood moves from the arterial to the venous side of the circulation along a pressure difference, moving from an area of higher pressure to one of lower pressure. The pressure distribution in the different parts of the circulation is almost an inverse of the volume distribution (see Fig. 14-2). The pressure in the arterial side of the circulation, which contains only approximately one sixth of the blood volume, is much greater than the pressure on the venous side of the circulation, which contains approximately two thirds of the blood. This pressure and volume distribution is due in large part to the structure and relative elasticity of the arteries and veins. It is the pressure difference between the arterial and venous sides of the circulation (approximately 84 mm Hg) that provides the driving force for flow of blood in the systemic circulation. The pulmonary circulation has a similar arterial-venous pressure difference, albeit of a lesser magnitude, that facilitates blood flow.

Because the pulmonary and systemic circulations are connected and function as a closed system, blood can be shifted from one circulation to the other. In the pulmonary circulation, the blood volume (approximately 450 mL in the adult) can vary from as low as 50% of normal to as high as 200% of normal. An increase in intrathoracic pressure, such as occurs when exhaling against a closed glottis, impedes venous return to the right heart. This can produce a transient shift from the central to the systemic circulation of as much as 250 mL of blood. Body position also affects the distribution of blood volume. In the recumbent position, approximately 25% to 30% of the total blood volume is in the central circulation. On standing, this blood is rapidly displaced to the lower part of the body because of the forces of gravity. Because the volume of the systemic circulation is approximately seven times that of the pulmonary circulation, a shift of blood from one system to the other has a much greater effect in the pulmonary than in the systemic circulation.

In summary, the circulatory system functions as a transport system that circulates nutrients and other materials to the tissues and removes waste products. The circulatory system can be divided into two parts: the systemic and the pulmonary circulation. The heart pumps blood throughout the system, and the blood vessels serve as tubes through which blood flows. The arterial system carries blood from the heart to the tissues, and the veins carry it back to the heart. The cardiovascular system is a closed system with a right and left heart connected in series. The systemic circulation, which is served by the left heart, supplies all the tissues except the lungs, which are served by the right heart and the pulmonary circulation. Blood moves throughout the circulation along a pressure gradient, moving from the high-pressure arterial system to the low-pressure venous system. In the circulatory system, pressure is inversely related to volume. The pressure on the arterial side of the circulation, which contains only approximately one sixth of the blood volume, is much greater than the pressure on the venous side of the circulation, which contains approximately two thirds of the blood.

PRINCIPLES OF BLOOD FLOW

The term *hemodynamics* describes the physical principles governing pressure, flow, and resistance as they relate to the circulatory system. The hemodynamics of the circulatory system are

complex. The heart is an intermittent pump, and as a result, blood flow in the arterial circulation is pulsatile. The blood vessels are branched, distensible tubes of various dimensions. The blood is a suspension of blood cells, platelets, lipid globules, and plasma proteins. Despite this complexity, the function of the circulatory system can be explained by the principles of basic fluid mechanics that apply to nonbiologic systems, such as household plumbing systems.

Pressure, Flow, and Resistance

The most important factors governing the function of the circulatory system are *volume*, *pressure*, *resistance*, and *flow*. Optimal function requires a volume that is sufficient to fill the vascular compartment and a pressure that is sufficient to ensure blood flow to all body tissues.

Blood flow is determined by two factors: (1) a pressure difference between the two ends of a vessel or group of vessels and (2) the resistance that blood must overcome as it moves through the vessel or vessels (Fig. 14-3). The relation between pressure, resistance, and flow is expressed by the equation $F = P/R$, in which F is the blood flow, P is the difference in pressure between the two ends of the system, and R is the resistance to flow through the system. In the circulatory system, blood flow is represented by the cardiac output (CO).

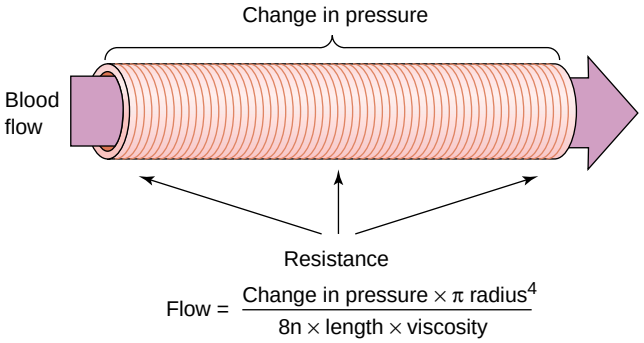
The resistance that blood encounters as it flows through the peripheral circulation is referred to as the *peripheral vascular resistance* (PVR) or, sometimes, as the systemic vascular resistance. A helpful equation for understanding factors that affect blood flow ($F = \Delta P \times \pi \times r^4/8n \times L \times \text{viscosity}$) was derived by the French physician Poiseuille more than a century ago (see Fig. 14-3). It expands the previous equation, $F = P/R$, by relating flow to several determinants of resistance—radius, length, and viscosity. According to this equation, the two most important determinants of flow in the circulatory system are a difference in pressure (ΔP) and the vessel radius to the fourth power (r^4). Because flow is directly related to the fourth power of the radius, small changes in vessel radius can produce large changes in flow to an organ or tissue. For example, if the pressure remains constant, the rate of flow is 16 times greater in a vessel with a radius of 2 mm ($2 \times 2 \times 2 \times 2$) than in a vessel with a radius of 1 mm.

Blood flow is also affected by the viscosity of blood. Viscosity is the resistance to flow caused by the friction of molecules in a fluid. The viscosity of a fluid is largely related to its thickness. The more particles that are present in a solution, the greater the frictional forces that develop between the molecules. Unlike water that flows through plumbing pipes, blood is a nonhomogeneous liquid. It contains blood cells, platelets, fat globules, and plasma proteins that increase its viscosity. The red blood cells, which constitute 40% to 45% of the formed elements of the blood, largely determine the viscosity of the blood. Under special conditions, temperature may affect viscosity. There is a 2% rise in viscosity for each 1°C decrease in body temperature, a fact that helps explain the sluggish blood flow seen in persons with hypothermia. The length (L) of vessels does not usually change, and 8n is a constant that does not change.

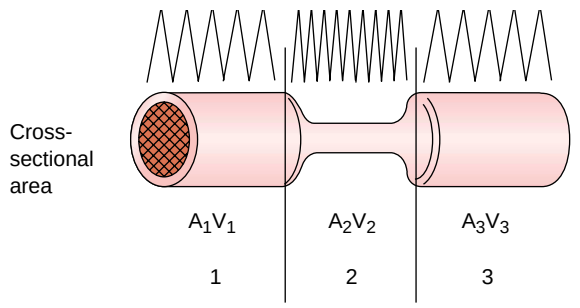
Cross-sectional Area and Velocity of Flow

Velocity is a distance measurement; it refers to the speed or linear movement with time (centimeters per second) with which blood flows through a vessel. *Flow* is a volume measurement (mL/second); it is determined by the cross-sectional area of a vessel and the velocity of flow (Fig. 14-4). When the flow through a given segment of the circulatory system is constant—as it must be for continuous flow—the velocity is inversely proportional to the cross-sectional area of the vessel (*i.e.*, the smaller the cross-sectional area, the greater the velocity of flow). This phenomenon can be compared with cars moving from a two-lane to a single-lane section of a highway. To keep traffic moving at its original pace, cars would have to double their speed in the single-lane section of the highway. So it is with flow in the circulatory system.

The linear velocity of blood flow in the circulatory system varies widely from 30 to 35 cm/second in the aorta to 0.2 to 0.3 mm/second in the capillaries. This is because even though each individual capillary is very small, the total cross-sectional area of all the systemic capillaries greatly exceeds the cross-sectional area of other parts of the circulation. As a result of this large surface area, the slower movement of blood allows ample



■ **FIGURE 14-3** ■ Factors that affect blood flow (Poiseuille's law). Increasing the pressure difference between the two ends of the vessel increases flow. Flow diminishes as resistance increases. Resistance is directly proportional to blood viscosity and the length of the vessel and inversely proportional to the fourth power of the radius.



■ **FIGURE 14-4** ■ Effect of cross-sectional area (A) on velocity (V) of flow. In section 1, velocity is low because of an increase in cross-sectional area. In section 2, velocity is increased because of a decrease in cross-sectional area. In section 3, velocity is again reduced because of an increase in cross-sectional area. Flow is assumed to be constant.

time for exchange of nutrients, gases, and metabolites between the tissues and the blood.

Laminar and Turbulent Flow

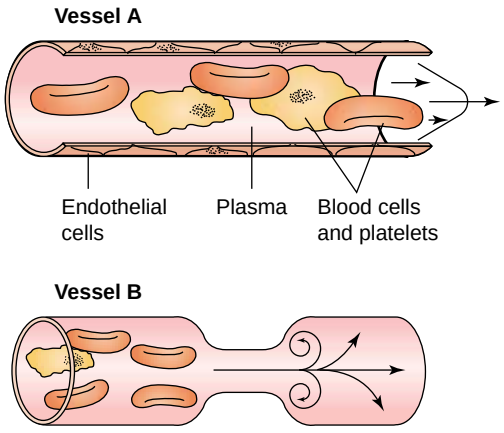
Blood flow normally is *laminar*, with the blood components arranged in layers so that the plasma is adjacent to the smooth, slippery endothelial surface of the blood vessel, and the blood cells, including the platelets, are in the center or *axis* of the bloodstream (Fig. 14-5). This arrangement reduces friction by allowing the blood layers to slide smoothly over one another, with the axial layer having the most rapid rate of flow.

Under certain conditions, blood flow switches from laminar to turbulent flow (see Fig. 14-5). Turbulent flow can be caused by a number of factors, including high velocity of flow, change in vessel diameter, and low blood viscosity. The tendency for turbulence to occur increases in direct proportion to the velocity of flow. Imagine the chaos as cars from a two- or three-lane highway converge on a single-lane section of the highway. The same type of thing happens in blood vessels that have been narrowed by disease processes, such as atherosclerosis. Low blood viscosity allows the blood to move faster and accounts for the transient occurrence of heart murmurs in some persons who are severely anemic. Turbulent flow may predispose to clot formation as platelets and other coagulation factors come in contact with the endothelial lining of the vessel. Turbulent flow often produces sounds that can be heard through the use of a stethoscope. For example, a heart murmur results from turbulent flow through a diseased heart valve.

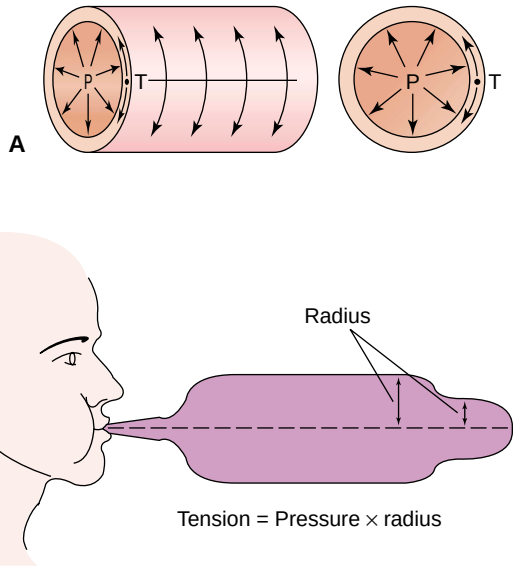
Wall Tension, Radius, and Pressure

In a blood vessel, *wall tension* is the force in the vessel wall that opposes the distending pressure inside the vessel. The French astronomer and mathematician Pierre de Laplace described the relationship between wall tension, pressure, and the radius of a vessel or sphere more than 200 years ago. This relationship, which has come to be known as *Laplace's law*, can be expressed by the equation, P = T/r, in which *T* is wall tension, *P* is the intraluminal pressure, and *r* is vessel radius (Fig. 14-6A). Accordingly, the internal pressure expands the vessel until it is exactly balanced by the tension in the vessel wall. The smaller the radius, the greater the pressure needed to balance the wall tension. Laplace's law can also be used to express the effect of the radius on wall tension (T = Pr). This correlation can be compared with a partially inflated balloon (Fig. 14-6B). Because the pressure is equal throughout, the tension in the part of the balloon with the smaller radius is less than the tension in the section with the larger radius (Fig. 14-6B). The same holds true for an arterial aneurysm in which the tension and risk of rupture increase as the aneurysm grows in size (see Chapter 16).

Laplace's law was later expanded to include wall thickness ($T = P \times r/wall\ thickness$). Wall tension is inversely related to wall thickness, such that the thicker the vessel wall, the lower the tension, and vice versa. In hypertension, arterial vessel walls hypertrophy and become thicker, thereby reducing the tension and minimizing wall stress. Laplace's law can also be applied to the pressure required to maintain the patency of small blood vessels. Providing that the thickness of a vessel wall remains constant, it takes more pressure to overcome wall tension and keep a vessel open as its radius decreases in size. The critical closing pressure refers to the point at which vessels collapse so that blood can no longer flow through them. For example, in circulatory shock there is a decrease in blood volume and vessel radii, along with a drop in blood pressure. As a result, many of the small vessels collapse as blood pressure drops to the point where it can no longer overcome the wall tension. The collapse of peripheral veins often makes it difficult



■ **FIGURE 14-5** ■ Laminar and turbulent flow in blood vessels. Vessel A shows streamlined or laminar flow in which the plasma layer is adjacent to the vessel endothelial layer and blood cells are in the center of the bloodstream. Vessel B shows turbulent flow in which the axial location of the platelets and other blood cells is disturbed.



■ **FIGURE 14-6** ■ Laplace's law relates pressure (P), tension (T), and radius in a cylindrical blood vessel (**A**). The pressure expanding the vessel is equal to the wall tension multiplied by the vessel radius. (**B**) Effect of the radius of a cylinder on tension. In a balloon, the tension in the wall is proportional to the radius because the pressure is the same everywhere inside the balloon. The tension is lower in the portion of the balloon with the smaller radius. (Rhoades R.A., Tanner G.A. [1996]. *Medical physiology* [p. 627]. Boston: Little, Brown)

to insert venous lines that are needed for fluid and blood replacement.

Distention and Compliance

Compliance refers to the total quantity of blood that can be stored in a given portion of the circulation for each millimeter rise in pressure. Compliance reflects the *distensibility* of the blood vessel. The distensibility of the aorta and large arteries allows them to accommodate the pulsatile output of the heart. The most distensible of all vessels are the veins, which can increase their volume with only slight changes in pressure, allowing them to function as a reservoir for storing large quantities of blood that can be returned to the circulation when it is needed. The compliance of a vein is approximately 24 times that of its corresponding artery, because it is eight times as distensible and has a volume three times as great.

In summary, blood flow is controlled by many of the same mechanisms that control fluid flow in nonbiologic systems. It is influenced by vessel length, pressure differences, vessel radius, blood viscosity, cross-sectional area, and wall tension. The rate of flow is directly related to the pressure difference between the two ends of the vessel and the vessel radius and inversely related to vessel length and blood viscosity. The cross-sectional area of a vessel influences the velocity of flow; as the cross-sectional area decreases, the velocity is increased, and vice versa. Laminar blood flow is flow in which there is layering of blood components in the center of the bloodstream. This reduces frictional forces and prevents clotting factors from coming in contact with the vessel wall. In contrast to laminar flow, turbulent flow is disordered flow, in which the blood moves crosswise and lengthwise in blood vessels. The relation between wall tension, transmural pressure, and radius is described by Laplace's law, which states the pressure needed to overcome wall tension becomes greater as the radius decreases. Wall tension is also affected by wall thickness; it increases as the wall becomes thinner and decreases as the wall becomes thicker.

THE HEART AS A PUMP

The heart is a four-chambered muscular pump approximately the size of a man's fist that beats an average of 70 times each minute, 24 hours each day, 365 days each year for a lifetime. In 1 day, this pump moves more than 1800 gallons of blood throughout the body, and the work performed by the heart over a lifetime would lift 30 tons to a height of 30,000 ft.

Functional Anatomy of the Heart

The heart is located between the lungs in the mediastinal space of the intrathoracic cavity in a loose-fitting sac called the *pericardium.* It is suspended by the great vessels, with its broader side (*i.e.,* base) facing upward and its tip (*i.e.,* apex) pointing downward, forward, and to the left (Fig.14-7).

The wall of the heart is composed of an outer epicardium, which lines the pericardial cavity; the myocardium or muscle layer; and the smooth endocardium, which lines the chambers of the heart. A fibrous skeleton supports the valvular structures of the heart. The interatrial and interventricular septa divide the heart into a right and a left pump, each composed of two muscular chambers: a thin-walled atrium, which serves as a reservoir for blood coming into the heart, and a thick-walled ventricle, which pumps blood out of the heart. The increased thickness of the left ventricular wall results from the additional work this ventricle is required to perform.

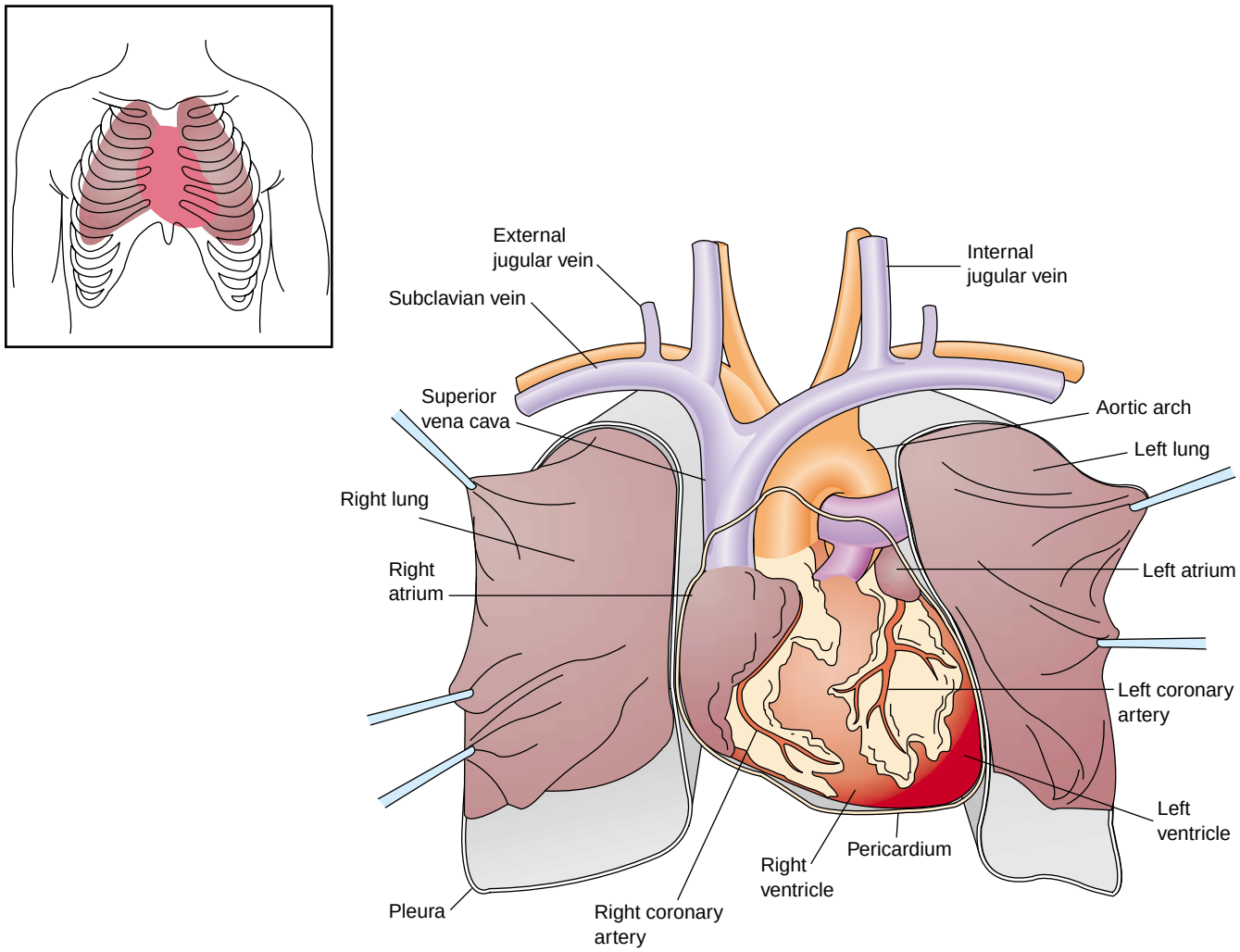
Pericardium

The pericardium forms a fibrous covering around the heart, holding it in a fixed position in the thorax and providing physical protection and a barrier to infection. The pericardium consists of a tough outer fibrous layer and a thin inner serous layer. The outer fibrous layer is attached to the great vessels that enter and leave the heart, the sternum, and the diaphragm. The fibrous pericardium is highly resistant to distention; it prevents acute dilatation of the heart chambers and exerts a restraining effect on the left ventricle. The inner serous layer consists of a visceral layer and a parietal layer. The visceral layer, also known as the *epicardium,* covers the entire heart and great vessels and then folds over to form the parietal layer that lines the fibrous pericardium (Fig. 14-8). Between the visceral and parietal layers is the *pericardial cavity,* a potential space that contains 30 to 50 mL of serous fluid. This fluid acts as a lubricant to minimize friction as the heart contracts and relaxes.

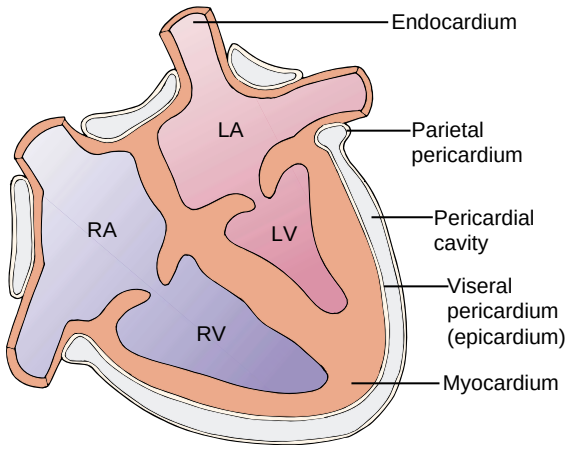
KEY CONCEPTS

THE HEART

- The heart is a four-chambered pump consisting of two atria (the right atrium, which receives blood returning to the heart from the systemic circulation, and the left atrium, which receives oxygenated blood from the lungs) and two ventricles (a right ventricle, which pumps blood to the lungs, and a left ventricle, which pumps blood into the systemic circulation).
- Heart valves control the direction of blood flow from the atria to the ventricles (the atrioventricular valves), from the right side of the heart to the lungs (pulmonic valve), and from the left side of the heart to the systemic circulation (aortic valve).
- The cardiac cycle is divided into two major periods: systole, when the ventricles are contracting, and diastole, when the ventricles are relaxed and filling.
- The work and efficiency of the heart is determined by the volume of blood it pumps out (preload), the pressure that it must generate to pump the blood out of the heart (afterload), and the rate at which it performs these functions (heart rate).



■ **FIGURE 14-7** ■ Anterior view of the heart and great vessels and their relationship to lungs and skeletal structures of the chest cage (*upper left box*).

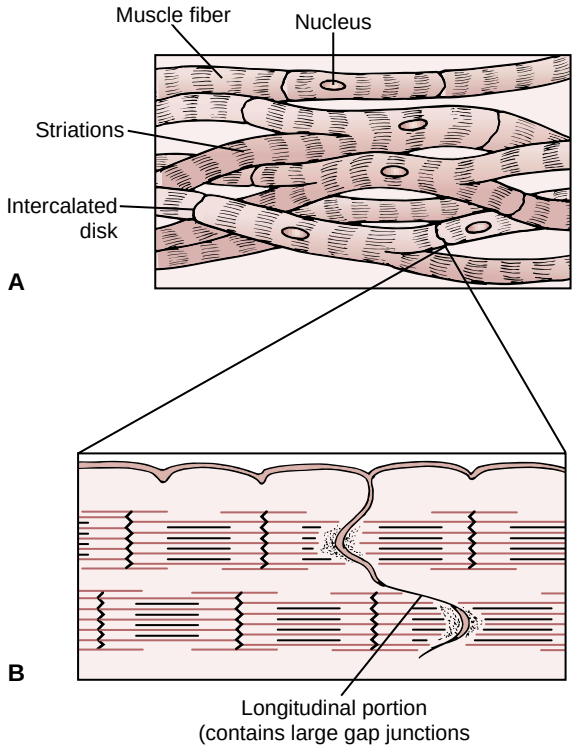


■ **FIGURE 14-8** ■ Layers of the heart, showing the visceral pericardium, pericardial cavity, parietal pericardium, myocardium, and endocardium. RA, right atrium; LA, left atrium; RV, right ventricle; LV, left ventricle.

Myocardium

The myocardium, or muscular portion of the heart, forms the wall of the atria and ventricles. Cardiac muscle cells, like skeletal muscle, are striated and composed of *sarcomeres* that contain actin and myosin filaments (see Chapter 1). They are smaller and more compact than skeletal muscle cells and contain many large mitochondria, reflecting their continuous energy needs.

Cardiac muscle contracts much like skeletal muscle, except the contractions are involuntary and the duration of contraction is much longer. Unlike the orderly longitudinal arrangement of skeletal muscle fibers, cardiac muscle cells are arranged as an interconnecting latticework, with their fibers dividing, recombining, and then dividing again (Fig. 14-9). The fibers are separated from neighboring cardiac muscle cells by dense structures called *intercalated disks*. The intercalated disks, which are unique to cardiac muscle, contain gap junctions that serve as low-resistance pathways for passage of ions and electrical impulses from one cardiac cell to another (Fig. 14-9). Thus, the myocardium behaves as a single unit, or *syncytium*, rather than



■ **FIGURE 14-9** ■ (**A**) Cardiac muscle fibers showing the branching structure. (**B**) Area indicated where cell junctions lie in the intercalated disks.

as a group of isolated units, as does skeletal muscle. When one myocardial cell becomes excited, the impulse travels rapidly so the heart can beat as a unit.

As in skeletal muscle, cardiac muscle contraction involves actin and myosin filaments, which interact and slide along one another during muscle contraction. However, compared with skeletal muscle cells, cardiac muscle cells have less well-defined sarcoplasmic reticulum for storing calcium, and the distance from the cell membrane to the myofibrils is shorter. Because less calcium can be stored in the muscle cells, cardiac muscle relies more heavily than skeletal muscle on an influx of extracellular calcium ions for contraction.

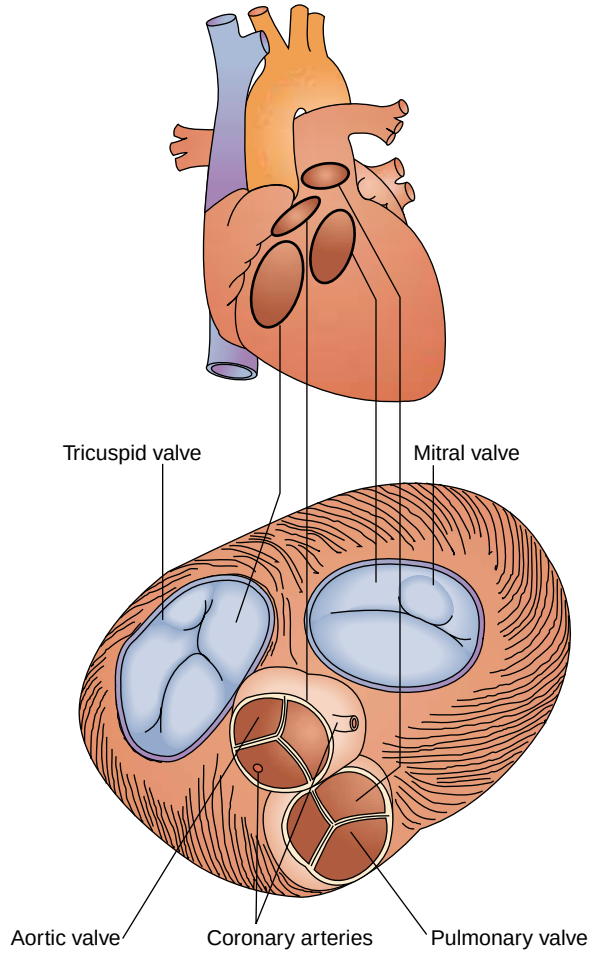
Endocardium

The endocardium is a thin, three-layered membrane that lines the heart and covers the valves. The innermost layer consists of smooth endothelial cells supported by a thin layer of connective tissue. The endothelial lining of the endocardium is continuous with the lining of the blood vessels that enter and leave the heart. The middle layer consists of dense connective tissue with elastic fibers. The outer layer, composed of irregularly arranged connective tissue cells, contains blood vessels and branches of the conduction system and is continuous with the myocardium.

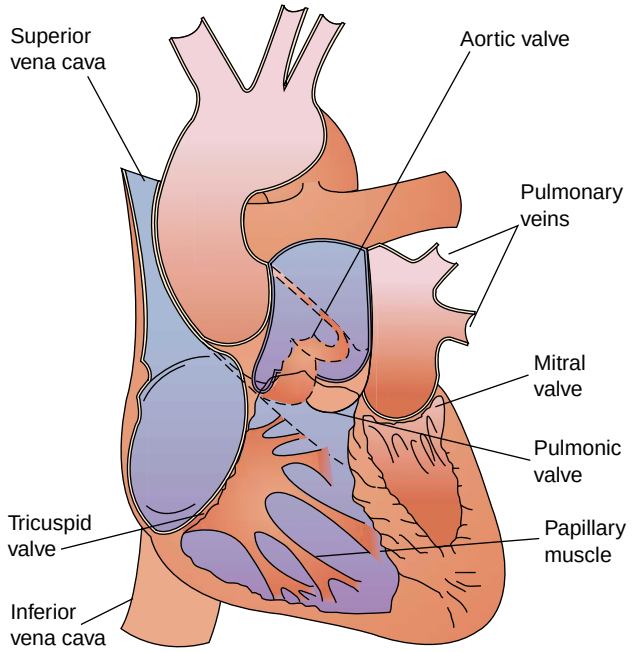
Heart Valves and Fibrous Skeleton

An important structural feature of the heart is its fibrous skeleton, which consists of four interconnecting valve rings and surrounding connective tissue. The fibrous skeleton separates the atria and ventricles and forms a rigid support for attachment of the valves and insertion of the cardiac muscle (Fig. 14-10). The tops of the valve rings are attached to the muscle tissue of the atria, pulmonary trunks, aorta, and valve rings. The bottoms are attached to the ventricular walls. For the heart to function effectively, blood flow must occur in a one-way direction, moving forward through the chambers of the right heart to the lungs and then through the chambers of the left heart to the systemic circulation. This unidirectional flow is provided by the heart's two atrioventricular (*i.e.*, tricuspid and mitral) valves and two semilunar (*i.e.*, pulmonic and aortic) valves (Fig. 14-11).

The atrioventricular (AV) valves control the flow of blood between the atria and the ventricles (Fig. 14-12). The thin edges of the AV valves form cusps, two on the left side of the heart (*i.e.*, *bicuspid* or *mitral valve*) and three on the right side (*i.e.*, *tricuspid valve*). The AV valves are supported by the papillary muscles, which project from the wall of the ventricles, and the chordae tendineae, which attach to the valve. Contraction of the papillary muscles at the onset of systole ensures closure by producing tension on the leaflets of the AV valves before the full force of ventricular contraction pushes against them. The chordae tendineae are cordlike structures that support the



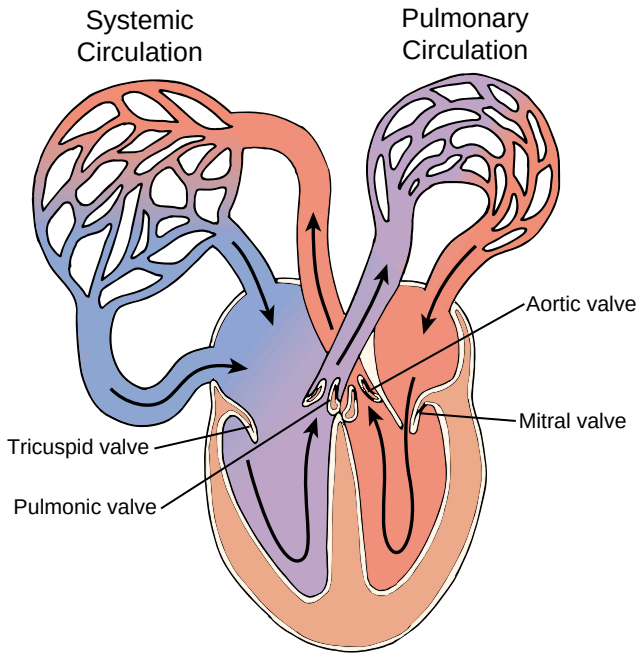
■ **FIGURE 14-10** ■ Fibrous skeleton of the heart, which forms the four interconnecting valve rings and support for attachment of the valves and insertion of cardiac muscle.



■ **FIGURE 14-11** ■ Valvular structures of the heart. The atrioventricular valves are in an open position, and the semilunar valves are closed. There are no valves to control the flow of blood at the inflow channels (*i.e.*, vena cava and pulmonary veins) to the heart.

AV valves and prevent them from everting into the atria during systole.

The *aortic* and *pulmonic* valves control the movement of blood out of the ventricles (Fig.14-12). Because of their half-moon shape, they often are referred to as the semilunar valves.



■ **FIGURE 14-12** ■ Unidirectional blood flow through the valvular structures of the heart.

The semilunar valves have three little teacup-shaped leaflets. These cuplike structures collect the *retrograde*, or backward, flow of blood that occurs toward the end of systole, enhancing closure. For the development of a perfect seal along the free edges of the semilunar valves, each valve cusp must have a triangular shape, which is facilitated by a nodular thickening at the apex of each leaflet (Fig. 14-13). The openings for the coronary arteries are located in the aorta just above the aortic valve.

There are no valves at the atrial sites (*i.e.*, venae cavae and pulmonary veins) where blood enters the heart. This means that excess blood is pushed back into the veins when the atria become distended. For example, the jugular veins typically become prominent in severe right-sided heart failure, whereas normally they are flat or collapsed. Likewise, the pulmonary venous system becomes congested when outflow from the left atrium is impeded.

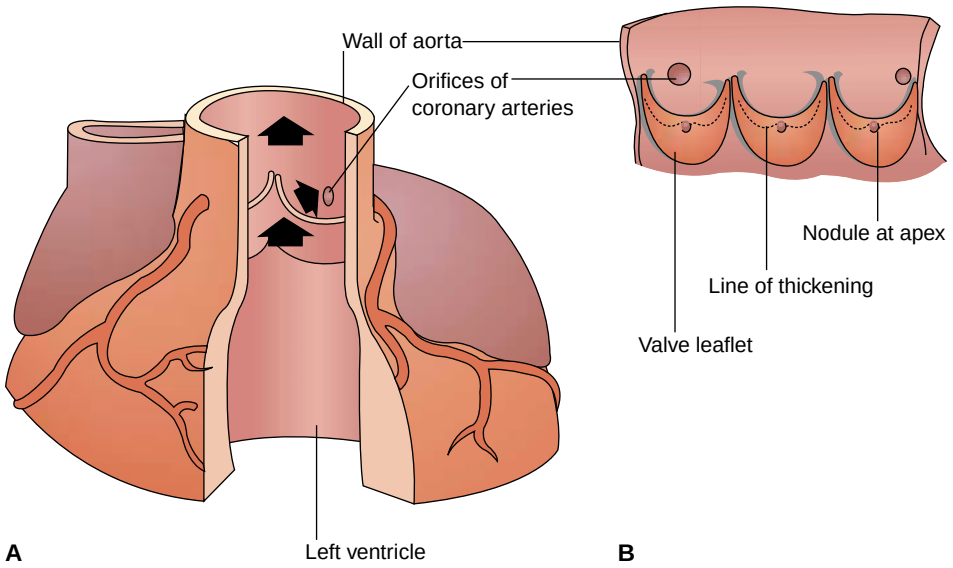
Cardiac Conduction System

Heart muscle is unique among other muscles in that it is capable of generating and rapidly conducting its own action potentials (*i.e.*, electrical impulses). These action potentials result in excitation of muscle fibers throughout the myocardium. Impulse formation and conduction result in weak electrical currents that spread through the entire body. When electrodes are applied to various positions on the body and connected to an electrocardiograph machine, an electrocardiogram (ECG) can be recorded.

In certain areas of the heart, the myocardial cells have been modified to form the specialized cells of the conduction system (Fig. 14-14). Although most myocardial cells are capable of initiating and conducting impulses, it is this specialized conduction system that maintains the pumping efficiency of the heart. Specialized pacemaker cells generate impulses at a faster rate than do other types of heart tissue, and the conduction tissue transmits impulses at a faster rate than do other types of heart tissue. Because of these properties, the conduction system usually controls the rhythm of the heart.

The conduction system consists of the sinoatrial node (SA node), where the rhythmic impulse is generated; the internodal pathways, which conduct the impulse from the SA node to the atrioventricular (AV) node; the AV node, in which the impulse from the atria is delayed before passing to the ventricles; the AV bundle, which conducts the impulse from the atria to the ventricles; and the left and right bundles of the Purkinje system, which conduct the cardiac impulses to all parts of the ventricles.

The *sinoatrial (SA) node* has the fastest intrinsic rate of firing (60 to 100 beats per minute) and is normally the pacemaker of the heart. The heart essentially has two conduction systems: one that controls atrial activity and one that controls ventricular activity. The *AV node* connects the two conduction systems and provides one-way conduction between the atria and ventricles. Within the AV node, atrial fibers connect with very small junctional fibers of the node itself. The velocity of conduction through these fibers is very slow (approximately one half that of normal cardiac muscle), which greatly delays transmission of the impulse into the AV node. A further delay occurs as the impulse travels through the AV node into the transitional fibers and into the AV bundle, also called the *bundle of His*. This delay provides a mechanical advantage whereby the atria complete



■ **FIGURE 14-13** ■ Diagram of the aortic valve. (**A**) The position of the aorta at the base of the ascending aorta is indicated. (**B**) The appearance of the three leaflets of the aortic valve when the aorta is cut open and spread out, flat. (Cormack D.H. [1987]. *Ham's histology* [9th ed.]. Philadelphia: J.B. Lippincott)

their ejection of blood before ventricular contraction begins. Under normal circumstances, the AV node provides the only connection between the two conduction systems. The atria and ventricles would beat independently of each other if the transmission of impulses through the AV node were blocked.

The Purkinje fibers lead from the AV node through the AV bundle into the ventricles where they divide to form the *right and left bundle branches* that straddle the interventricular septum. The main trunk of the left bundle branch extends for approximately 1 to 2 cm before fanning out as it enters the septal area and divides further into two segments: the *left posterior* and *anterior fascicles*. The Purkinje system has very large fibers that allow for rapid conduction and almost simultaneous excitation of the entire right and left ventricles. This rapid rate of conduction is necessary for the swift and efficient ejection of blood from the heart.

KEY CONCEPTS

CARDIAC CONDUCTION SYSTEM

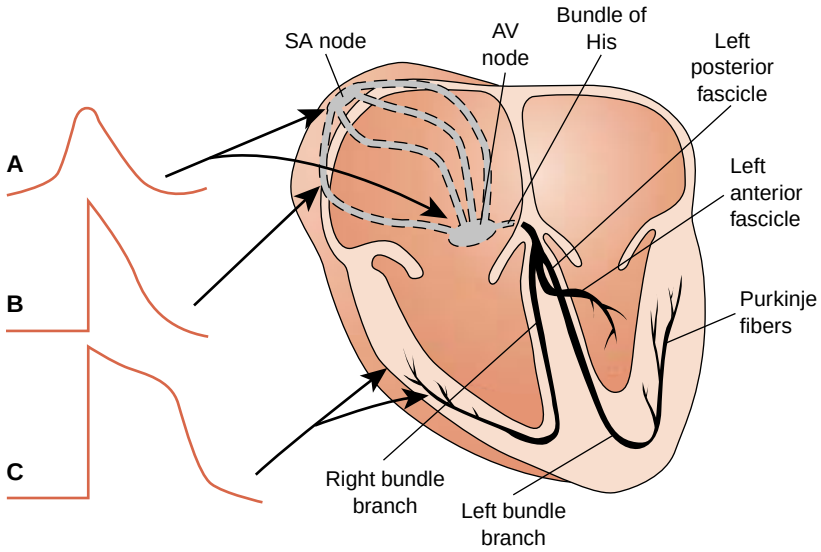
- The cardiac conduction system consists of the SA node, which functions as the pacemaker of the heart; the AV node, which connects the atrial and ventricular conduction systems; and the AV bundle and large Purkinje fibers, which provide for rapid depolarization of the ventricles.
- Cardiac action potentials are controlled by three types of ion channels—the fast sodium channels, which are responsible for the spikelike onset of the action potential; the slower calcium-sodium channels, which are responsible for the plateau; and the potassium channels, which are responsible for the repolarization phase and return of the membrane to the resting potential.
- There are two types of cardiac action potentials: the fast response, which occurs in atrial and ventricular muscle cells and the Purkinje conduction system and uses the fast sodium channels; and the slow response of the SA and AV nodes, which uses the slow calcium channels.

Action Potentials

A stimulus delivered to excitable tissues evokes an action potential that is characterized by a sudden change in voltage resulting from transient depolarization and subsequent repolarization. These action potentials are electrical currents involving the movement or flow of electrically charged ions at the level of the cell membrane (see Chapter 1).

The action potential of cardiac muscle is divided into five phases: phase 0—the upstroke or rapid depolarization; *phase 1*—early repolarization; *phase 2*—the plateau; *phase 3*—rapid repolarization; and *phase 4*—the resting membrane potential (Fig. 14-15). Cardiac muscle has three types of membrane ion channels that contribute to the voltage changes that occur during these phases of the action potential. They are the (1) fast sodium channels, (2) slow calcium-sodium channels, and (3) potassium channels. During *phase 0* in atrial and ventricular muscle and in the Purkinje system, opening of the fast sodium channels for a few ten-thousandths of a second is responsible for the spikelike onset of the action potential. The point at which the sodium gates open is called the *depolarization threshold*. When the cell has reached this threshold, a rapid influx of sodium ions to the interior of the membrane causes the membrane potential to shift from a resting membrane potential of approximately –90 mV to +20 mV.

Phase 1 occurs at the peak of the action potential and signifies inactivation of the fast sodium channels with an abrupt decrease in sodium permeability. *Phase 2* represents the plateau of the action potential. It is caused primarily by the slower opening of the calcium-sodium channels, which lasts for a few tenths of a second. Calcium ions entering the muscle during this phase of the action potential play a key role in the contractile process of the cardiac muscle fibers. These



■ **FIGURE 14-14** ■ Conduction system of the heart and action potentials. (**A**) Action potential of sinoatrial (SA) and atrioventricular (AV) nodes; (**B**) atrial muscle action potential; (**C**) action potential of ventricular muscle and Purkinje fibers.

unique features of the phase 2 plateau cause the action potential of cardiac muscle to last 3 to 15 times longer than that of skeletal muscle and cause a corresponding increased period of contraction.

Phase 3 reflects final rapid repolarization and begins with the downslope of the action potential. During the phase 3 repolarization period, the slow channels close and the influx of calcium and sodium ceases. There is a sharp rise in potassium permeability, contributing to the rapid outward movement of potassium during this phase and facilitating the reestablishment of the resting membrane potential (−90 mV). At the conclusion of phase 3, distribution of sodium and potassium returns to the normal resting state. *Phase 4* is the resting membrane potential. During phase 4, the sodium-potassium pump is activated, transporting sodium out of the cell and moving potassium back into the cell.

There are two main types of action potentials in the heart—the slow response and the fast response. The *slow response*, which is initiated by the slow calcium-sodium channels, is found in the SA node, which is the natural pacemaker of the heart, and the conduction fibers of the AV node (see Fig. 14-15). The *fast response*, which is characterized by opening of the fast sodium channels, occurs in the normal myocardial cells of the atria, the ventricles, and the Purkinje fibers. The fast-response cardiac cells do not normally initiate cardiac action potentials. Instead, these impulses originate in the specialized slow-response cells of the SA node and are conducted to the fast-response myocardial cells in the atria and ventricles, where they effect a change in membrane potential to the threshold level. On reaching threshold, the voltage-dependent sodium channels open to initiate the rapid upstroke of the phase 1 action potential. The amplitude and the rate of rise of phase 1 are important to the conduction velocity of the fast response.

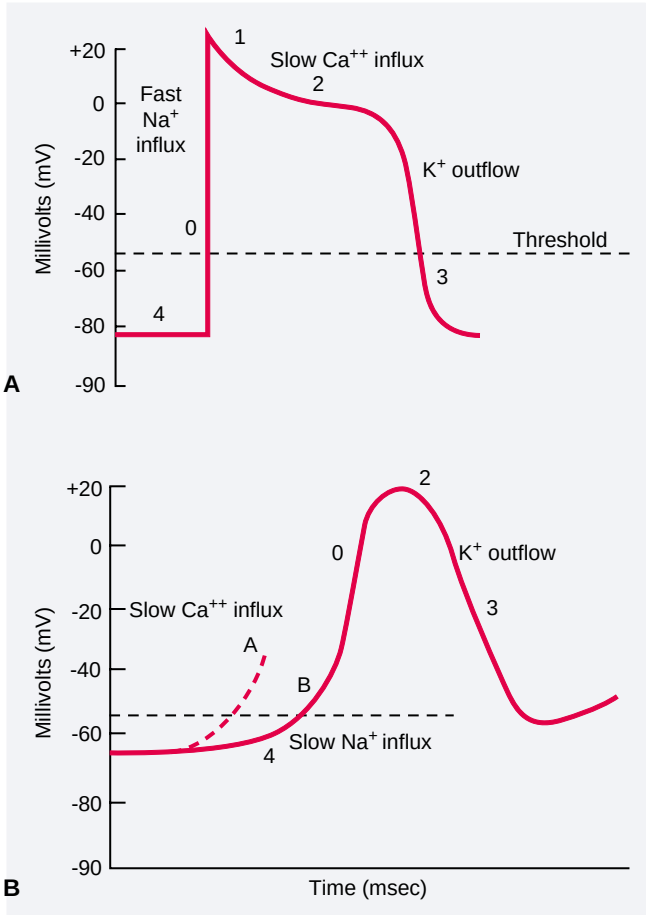
The hallmark of the pacemaker cells in the SA and AV nodes is a spontaneous phase 4 depolarization. The membrane permeability of these cells allows a slow inward leak of current to occur through the slow channels during phase 4. This leak continues until the threshold for firing is reached, at which point the cell spontaneously depolarizes. The rate of pacemaker cell discharge varies with the resting membrane potential and the slope of phase 4 depolarization (see Fig. 14-15). Catecholamines (*i.e.*, epinephrine and norepinephrine) increase the heart rate by increasing the slope or rate of phase 4 depolarization. Acetylcholine, which is released during vagal stimulation of the heart, slows the heart rate by decreasing the slope of phase 4.

Absolute and Relative Refractory Periods

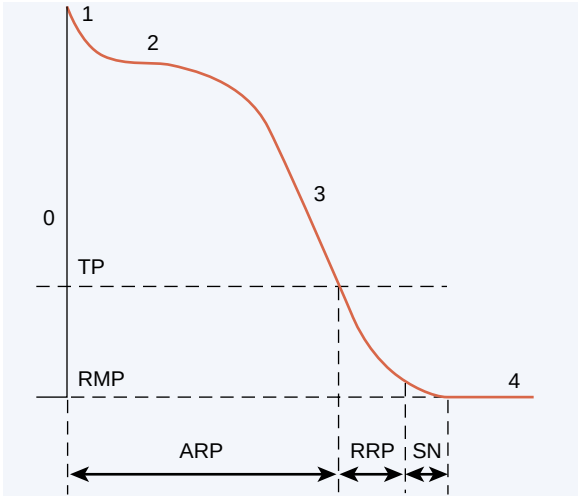
The pumping action of the heart requires alternating contraction and relaxation. There is a period in the action potential curve during which no stimuli can generate another action potential (Fig. 14-16). This period, which is known as the *absolute refractory period*, includes phases 0, 1, 2, and part of phase 3. During this time, the cell cannot depolarize again under any circumstances. In skeletal muscle, the refractory period is very short compared with the duration of contraction, such that a second contraction can be initiated before the first is over, resulting in a summated tetanized contraction. In cardiac muscle, the absolute refractory period is almost as long as the contraction, and a second contraction cannot be stimulated until the first is over. The longer length of the absolute refractory period of cardiac muscle is important in maintaining the alternating contraction and relaxation that is essential to the pumping action of the heart and for the prevention of fatal dysrhythmias. When repolarization has returned the membrane potential to below the threshold potential, but not to the resting membrane potential, the cell is capable of responding to a greater-than-normal stimulus. This condition is referred to as the *relative refractory period*. After the relative refractory period there is a short period of time, called the *supernormal excitatory period*, during which a weak stimulus can evoke a response. It is during this period that many cardiac dysrhythmias develop.

Dysrhythmias and Conduction Disorders

Dysrhythmias represent disorders of cardiac rhythm. Cardiac dysrhythmias are commonly divided into two categories: supraventricular and ventricular dysrhythmias. The supraventricular dysrhythmias include those that are generated in the SA



■ **FIGURE 14-15** ■ Changes in action potential recorded from a fast response in cardiac muscle cell (**A**) and from a slow response recorded in the sinoatrial and atrioventricular nodes (**B**). The phases of the action potential are identified by numbers: phase 4, resting membrane potential; phase 0, depolarization; phase 1, brief period of repolarization; phase 2, plateau; phase 3, repolarization. The slow response is characterized by a slow, spontaneous rise in the phase 4 membrane potential to threshold levels; it has a lesser amplitude and shorter duration than the fast response. Increased automaticity (*A*) occurs when the rate of phase 4 depolarization is increased.



■ **FIGURE 14-16** ■ Diagram of an action potential of a ventricular muscle cell, showing the threshold potential (TP), resting membrane potential (RMP), absolute refractory period (ARP), relative refractory period (RRP), and supernormal (SN) period.

node, atria, AV node, and junctional tissues. The ventricular dysrhythmias include those that are generated in the ventricular conduction system and the ventricular muscle. Because the ventricles are the pumping chambers of the heart, ventricular dysrhythmias (*e.g.*, ventricular tachycardia and fibrillation) are the most serious in terms of immediate life-threatening events.

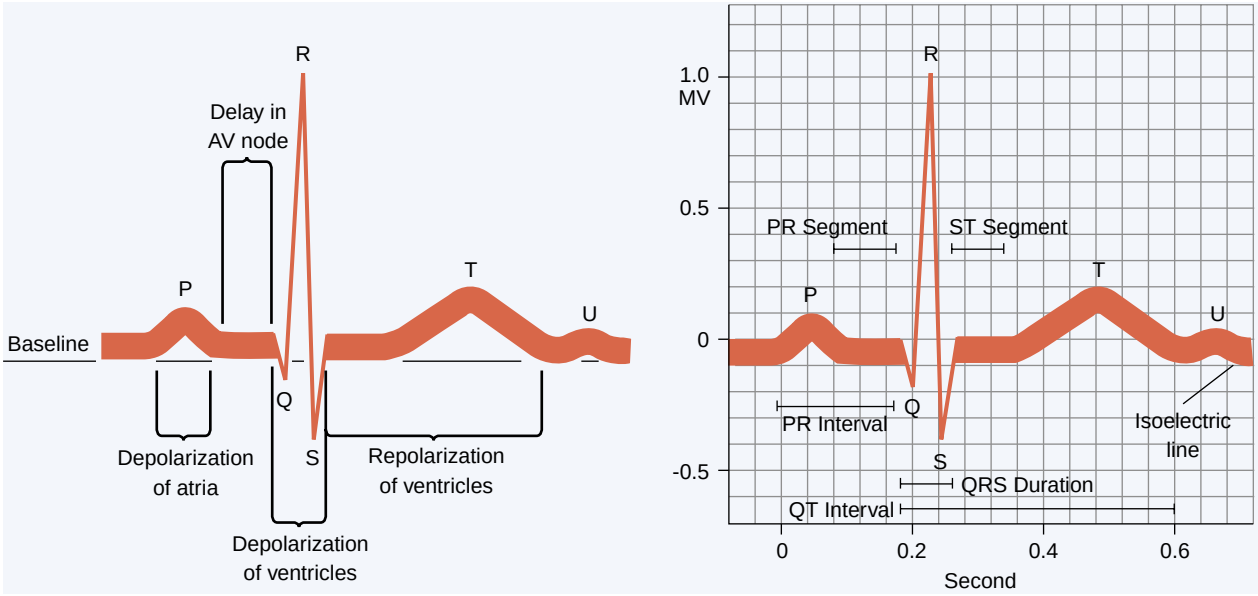
Disorders of cardiac rhythm can range from excessively rapid heart rate (tachyarrhythmias) to an extremely slow heart rate (bradyarrhythmias). Conduction disorders disrupt the flow of impulses through the conduction system of the heart. *Heart block* occurs when the conduction of impulses is blocked, often in the AV node. Under normal conditions, the AV junction provides the only connection for transmission of impulses between the atrial and ventricular conduction systems; in complete heart block, the atria and ventricles beat independently of each other. The most serious effect of some forms of AV block is a slowing of heart rate to the extent that circulation to the brain is compromised. An *ectopic pacemaker* is an excitable focus outside the normally functioning SA node. A *premature ventricular contraction* (PVC) occurs when an ectopic pacemaker initiates a beat. The occurrence of frequent PVCs in the diseased heart predisposes one to the development of other, more serious dysrhythmias, including ventricular tachycardia and ventricular fibrillation.

Fibrillation is the result of disorganized current flow within the atria (atrial fibrillation) or ventricle (ventricular fibrillation). Fibrillation interrupts the normal contraction of the atria or ventricles. In ventricular fibrillation, the ventricle quivers but does not contract. When the ventricle does not contract, there is no cardiac output, and there are no palpable or audible pulses. Ventricular fibrillation is a fatal event unless treated with immediate defibrillation.

Electrocardiography

The ECG is a recording of the electrical activity of the heart. The electrical currents generated by the heart spread through the body to the skin, where they can be sensed by appropriately placed electrodes, amplified, and viewed on an oscilloscope or chart recorder. The deflection points of an ECG are designated by the letters P, Q, R, S, and T. Figure 14-17 depicts the electrical activity of the conduction system on an ECG tracing. The P wave represents the SA node and atrial depolarization; the QRS complex (*i.e.*, beginning of the Q wave to the end of the S wave) depicts ventricular depolarization; and the T wave portrays ventricular repolarization. The isoelectric line between the P wave and the Q wave represents depolarization of the AV node, bundle branches, and Purkinje system (Fig. 14-17). Atrial repolarization occurs during ventricular depolarization and is hidden in the QRS complex.

The horizontal axis of the ECG measures time in seconds, and the vertical axis measures the amplitude of the impulse in



■ **FIGURE 14-17** ■ Diagram of the electrocardiogram (lead II) and representative depolarization and repolarization of the atria and ventricle. The P wave represents atrial depolarization, the QRS complex ventricular depolarization, and the T wave ventricular repolarization. Atrial repolarization occurs during ventricular depolarization and is hidden under the QRS complex.

millivolts (mV). Each heavy vertical line represents 0.2 second, and each thin line represents 0.04 second (see Fig. 14-17). The widths of ECG complexes are commonly referred to in terms of duration of time. On the vertical axis, each heavy horizontal line represents 0.5 mV. The connections of the ECG are arranged such that an upright deflection indicates a positive potential and a downward deflection indicates a negative potential.

The ECG records the potential difference in charge between two electrodes as the depolarization and repolarization waves move through the heart and are conducted to the skin surface. The shape of the recorder tracing is determined by the direction in which the impulse spreads through the heart muscle in relation to electrode placement. A depolarization wave that moves toward the recording electrode registers as a positive, or upward, deflection. Conversely, if the impulse moves away from the recording electrode, the deflection is downward, or negative. When there is no flow of charge between electrodes, the potential is zero, and a straight line is recorded at the baseline of the chart.

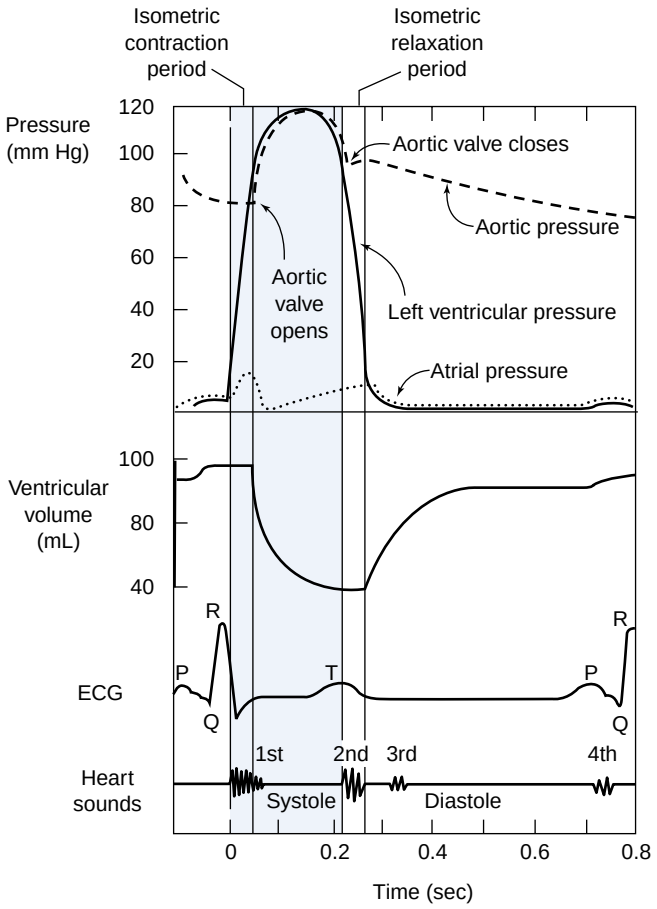
Conventionally, 12 leads are recorded for a diagnostic ECG, each providing a unique view of the electrical forces of the heart from a different position on the body's surface. Six limb leads view the electrical forces as they pass through the heart on the frontal or vertical plane. The electrodes for the limb leads are attached to the four extremities or representative areas on the body near the shoulders and lower chest or abdomen. Chest electrodes provide a view of the electrical forces as they pass through the heart on the horizontal plane. They are moved to different positions on the chest, including the right and left sternal borders and the left anterior surface. The right lower extremity lead is used as a ground electrode. When indicated, additional electrodes may be applied to other areas of the body, such as the back or right anterior chest.

Cardiac Cycle

The term *cardiac cycle* is used to describe the rhythmic pumping action of the heart. The cardiac cycle is divided into two parts: *systole,* the period during which the ventricles are contracting, and *diastole,* the period during which the ventricles are relaxed and filling with blood. Simultaneous changes occur in atrial pressure, ventricular pressure, aortic or pulmonary artery pressure, ventricular volume, the electrocardiogram (ECG), and heart sounds during the cardiac cycle (Fig. 14-18).

Ventricular Systole and Diastole

Ventricular systole is divided into two periods: the isovolumetric contraction period and the ejection period. The *isovolumetric contraction period,* which begins with the closure of the AV valves and occurrence of the first heart sound, heralds the onset of systole. Immediately after closure of the AV valves, there is an additional 0.02 to 0.03 second during which the semilunar outlet (pulmonic and aortic) valves remain closed. During this period, the ventricular volume remains the same while the ventricles contract, producing an abrupt increase in pressure. The ventricles continue to contract until left ventricular pressure is slightly higher than aortic pressure, and right ventricular pressure is higher than pulmonary artery pressure. At this point, the semilunar valves open, signaling the onset of the *ejection period.* Approximately 60% of the stroke volume is ejected during the first quarter of systole, and the remaining 40% is ejected during the next two quarters of systole. Little blood is ejected from the heart during the last quarter of systole, although the ventricle remains contracted. At the end of systole, the ventricles relax, causing a precipitous fall in intraventricular pressures. As this occurs, blood from the large arteries flows back toward the ventricles, causing the aortic and



■ **FIGURE 14-18** ■ Events in the cardiac cycle, showing changes in aortic pressure, left ventricular pressure, atrial pressure, left ventricular volume, the electrocardiogram (ECG), and heart sounds.

pulmonic valves to snap shut—an event that is marked by the second heart sound.

The aortic pressure reflects changes in the ejection of blood from the left ventricle. There is a rise in pressure and stretching of the elastic fibers in the aorta as blood is ejected into the aorta at the onset of the ejection period. The aortic pressure continues to rise and then begins to fall during the last quarter of systole as blood flows out of the aorta into the peripheral vessels. The incisura, or notch, in the aortic pressure tracing represents closure of the aortic valve. The aorta is highly elastic and as such stretches during systole to accommodate the blood that is being ejected from the left heart during systole. During diastole, recoil of the elastic fibers in the aorta serves to maintain the arterial pressure.

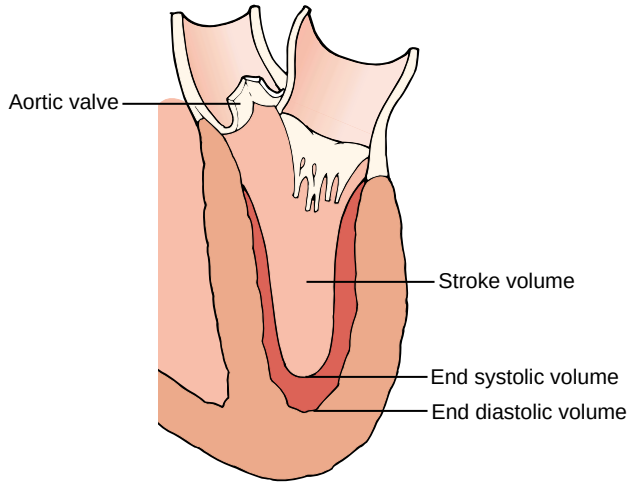
Diastole is marked by ventricular relaxation and filling. After closure of the semilunar valves, the ventricles continue to relax for another 0.03 to 0.06 second. During this time, which is called the *isovolumetric relaxation period,* ventricular volume remains the same but ventricular pressure drops until it becomes less than atrial pressure. As this happens, the AV valves open, and the blood that has been accumulating in the atria during systole flows into the ventricles. Most of ventricular filling occurs during the first third of diastole, which is called the *rapid filling period.* During the middle third of diastole, inflow into the ventricles is almost at a standstill. The last third of diastole is marked by atrial contraction, which gives an additional thrust to ventricular filling. When audible, the third heart sound is heard during the rapid filling period of diastole as blood flows into a distended or noncompliant ventricle. A fourth heart sound, when present, occurs during the last third of diastole as the atria contract.

During diastole, the ventricles increase their volume to approximately 120 mL (*i.e.,* the *end-diastolic volume*), and at the end of systole, approximately 50 mL of blood (*i.e.,* the *end-systolic volume*) remains in the ventricles (Fig. 14-19). The difference between the end-diastolic and end-systolic volumes (approximately 70 mL) is called the *stroke volume.* The *ejection fraction,* which is the stroke volume divided by the end-diastolic volume, represents the fraction or percentage of the diastolic volume that is ejected from the heart during systole.

Atrial Filling and Contraction

Because there are no valves between the junctions of the central veins (*i.e.,* venae cavae and pulmonary veins) and the atria, atrial filling occurs during both systole and diastole. During normal quiet breathing, right atrial pressure usually varies between −2 and +2 mm Hg. It is this low atrial pressure that maintains the movement of blood from the systemic veins into the right atrium and from the pulmonary veins into the left atrium.

Right atrial pressure is regulated by a balance between the ability of the right ventricle to move blood out of the right heart and the pressures that move blood from the venous circulation into the right atrium (venous return). When the heart pumps strongly, right atrial pressure is decreased and atrial filling is enhanced. Right atrial pressure is also affected by changes in intrathoracic pressure. It is decreased during inspiration when intrathoracic pressure becomes more negative, and it is increased during coughing or forced expiration when intrathoracic pressure becomes more positive. Venous return is a reflection of the amount of blood in the systemic circulation that is available for return to the right heart and the forces that move blood back to the right heart. Venous return is in-



■ **FIGURE 14-19** ■ The ejection fraction, which represents the difference between left ventricular end-diastolic and end-systolic volumes.

creased when the blood volume is expanded or when right atrial pressure falls and is decreased in hypovolemic shock or when right atrial pressure rises.

Although the main function of the atria is to store blood as it enters the heart, these chambers also act as pumps that aid in ventricular filling. Atrial contraction occurs during the last third of diastole. Atrial contraction becomes more important during periods of increased activity when the diastolic filling time is decreased because of an increase in heart rate or when heart disease impairs ventricular filling. In these two situations, the cardiac output would fall drastically were it not for the action of the atria. It has been estimated that atrial contraction can contribute as much as 30% to cardiac reserve during periods of increased need, while having little or no effect on cardiac output during rest.

Regulation of Cardiac Performance

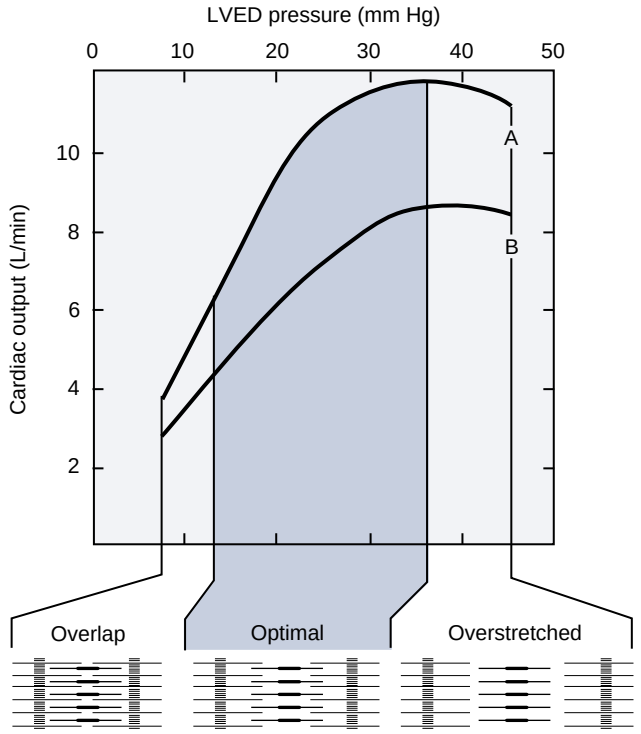
The efficiency and work of the heart as a pump often is measured in terms of *cardiac output* or the amount of blood the heart pumps each minute. The cardiac output (CO) is the product of the *stroke volume* (SV) and the *heart rate* (HR) and can be expressed by the equation: $CO = SV \times HR$. The cardiac output varies with body size and the metabolic needs of the tissues. It increases with physical activity and decreases during rest and sleep. The average cardiac output in normal adults ranges from 3.5 to 8.0 L/minute. In the highly trained athlete, this value can increase to levels as high as 32 L/minute during maximum exercise.

The *cardiac reserve* refers to the maximum percentage of increase in cardiac output that can be achieved above the normal resting level. The normal young adult has a cardiac reserve of approximately 300% to 400%. The heart's ability to increase its output according to body needs mainly depends on four factors: the *preload,* or ventricular filling; the *afterload,* or resistance to ejection of blood from the heart; *cardiac contractility;* and the *heart rate.* Cardiac performance is influenced by the work demands of the heart and the ability of the coronary circulation to meet its metabolic needs.

Preload

The preload represents the volume work of the heart. It is called the *preload* because it is the work imposed on the heart before the contraction begins. Preload represents the amount of blood that the heart must pump with each beat and is largely determined by the venous return to the heart and the accompanying stretch of the muscle fibers.

The increased force of contraction that accompanies an increase in ventricular end-diastolic volume is referred to as the *Frank-Starling mechanism* or Starling's law of the heart (Fig. 14-20). The anatomic arrangement of the actin and myosin filaments in the myocardial muscle fibers is such that the tension or force of contraction is greatest when the muscle fibers are stretched just before the heart begins to contract. The maximum force of contraction and cardiac output is achieved when venous return produces an increase in left ventricular end-diastolic filling (*i.e.*, preload) such that the muscle fibers are stretched about two and one-half times their normal resting length (Fig. 14-20, *curve B*). When the muscle fibers are stretched to this degree, there is optimal overlap of the actin and myosin filaments needed for maximal contraction.



■ **FIGURE 14-20** ■ (**Top**) Starling ventricular function curve in normal heart. An increase in left ventricular end-diastolic (LVED) pressure produces an increase in cardiac output (*curve B*) by means of the Frank-Starling mechanism. The maximum force of contraction and increased stroke volume are achieved when diastolic filling causes the muscle fibers to be stretched about two and one half times their resting length. In *curve A,* an increase in cardiac contractility produces an increase in cardiac output without a change in LVED volume and pressure. (**Bottom**) Stretching of the actin and myosin filaments at the different LVED filling pressures.

The Frank-Starling mechanism allows the heart to adjust its pumping ability to accommodate various levels of venous return. Cardiac output is less when decreased filling causes excessive overlap of the actin and myosin filaments or when excessive filling causes the filaments to be pulled too far apart.

Afterload

The afterload is the pressure or tension work of the heart. It is the pressure that the heart must generate to move blood into the aorta. It is called the *afterload* because it is the work presented to the heart after the contraction has commenced. The systemic arterial blood pressure is the main source of afterload work on the left heart and the pulmonary arterial pressure is the main source of afterload work for the right heart. The afterload work of the left ventricle is also increased with narrowing (*i.e.*, stenosis) of the aortic valve. For example, in the late stages of aortic stenosis, the left ventricle may need to generate systolic pressures as great as 300 mm Hg to move blood through the diseased valve.

Cardiac Contractility

Cardiac contractility refers to the ability of the heart to change its force of contraction without changing its resting (*i.e.*, diastolic) length. The contractile state of the myocardial muscle is

determined by biochemical and biophysical properties that govern the actin and myosin interactions in the myocardial cells. It is strongly influenced by the number of calcium ions that are available to participate in the contractile process.

An *inotropic* influence is one that modifies the contractile state of the myocardium independent of the Frank-Starling mechanism (see Fig. 14-20, *curve A*). For instance, sympathetic stimulation produces a positive inotropic effect by increasing the calcium that is available for interaction between the actin and myosin filaments. Hypoxia exerts a negative inotropic effect by interfering with the generation of adenosine triphosphate (ATP), which is needed for muscle contraction.

Heart Rate

The heart rate influences cardiac output and the work of the heart by determining the frequency with which the ventricle contracts and blood is ejected from the heart. Heart rate also determines the time spent in diastolic filling. While systole and the ejection period remain fairly constant across heart rates, the time spent in diastolic and filling of the ventricles becomes shorter as the heart rate increases. This leads to a decrease in stroke volume, and at high heart rates, may produce a decrease in cardiac output. One of the dangers of ventricular tachycardia is a reduction in cardiac output because the heart does not have time to fill adequately.

The cardiac cycle describes the pumping action of the heart. It is divided into two parts: systole, during which the ventricles contract and blood is ejected from the heart, and diastole, during which the ventricles are relaxed and blood is filling the heart. The stroke volume (approximately 70 mL) represents the difference between the end-diastolic volume (approximately 120 mL) and the end-systolic volume (approximately 50 mL). Atrial contraction occurs during the last third of diastole. Although the main function of the atria is to store blood as it enters the heart, atrial contraction acts to increase cardiac output during periods of increased activity when the filling time is reduced or in disease conditions in which ventricular filling is impaired.

The heart's ability to increase its output according to body needs depends on the preload, or filling of the ventricles (*i.e.,* end-diastolic volume); the afterload, or resistance to ejection of blood from the heart; cardiac contractility, which is determined by the interaction of the actin and myosin filaments of cardiac muscle fibers; and the heart rate, which determines the frequency with which blood is ejected from the heart. The maximum force of cardiac contraction occurs when an increase in preload stretches muscle fibers of the heart to approximately two and one-half times their resting length (*i.e.,* Frank-Starling mechanism).

In summary, the heart is a four-chambered muscular pump that lies in the pericardial sac within the mediastinal space of the intrathoracic cavity. The wall of the heart is composed of an outer epicardium, which lines the pericardial cavity; a fibrous skeleton; the myocardium, or muscle layer; and the smooth endocardium, which lines the chambers of the heart. The four heart valves control the direction of blood flow.

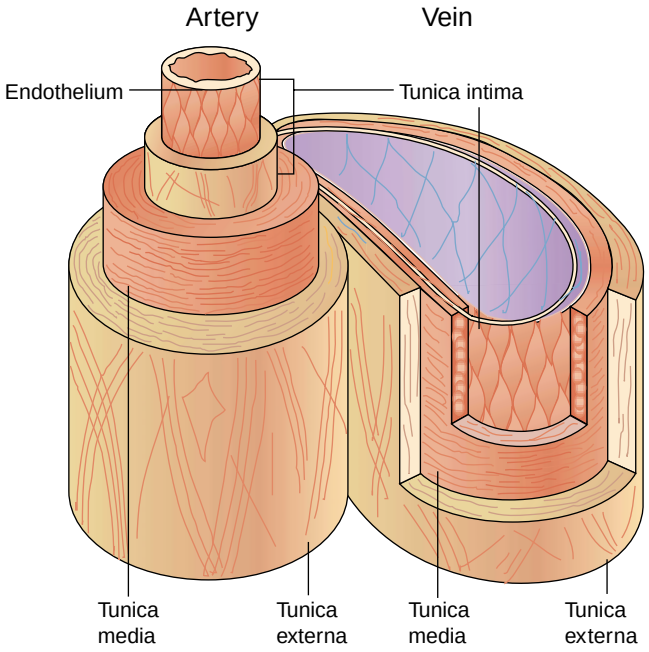
The specialized cells of the heart's conduction system control the rhythmic contraction and relaxation of the heart. The SA node has the fastest inherent rate of impulse generation and acts as the pacemaker of the heart. Impulses from the SA node travel through the atria to the AV node and then to the AV bundle and the ventricular Purkinje system. The AV node provides the only connection between the atrial and ventricular conduction systems. The action potential of cardiac muscle is controlled by the (1) fast sodium channels, (2) slow calcium-sodium channels, and (3) potassium channels. Opening of the fast sodium channels is responsible for the rapid spikelike onset of the ventricular action potential; the slower opening calcium-sodium channels for the plateau of the action potential, and potassium channels for repolarization and return to the resting membrane potential. The absolute refractory period, which represents the time during which a normal cardiac impulse cannot re-excite an already excited area of cardiac muscle, is important in preventing disorders of cardiac rhythm that would disrupt the normal pumping ability of the heart. Disorders of the cardiac conduction system include dysrhythmias and conduction defects. Ventricular dysrhythmias are generally more serious than atrial dysrhythmias because they afford the potential for disrupting the pumping ability of the heart.

BLOOD VESSELS AND THE PERIPHERAL CIRCULATION

The vascular system functions in the delivery of oxygen and nutrients and removal of wastes from the tissues. It consists of arteries and arterioles, the capillaries, and the venules and veins. Blood vessels are dynamic structures that constrict and relax to adjust blood pressure and flow to meet the varying needs of the many different tissue types and organ systems. Structures such as the heart, brain, liver, and kidneys require a large and continuous flow to carry out their vital functions. In other tissues, such as the skin and skeletal muscle, the need for blood flow varies with the level of function. For example, there is a need for increased blood flow to the skin during fever and for increased skeletal muscle blood flow during exercise.

Blood Vessels

All blood vessels, except the capillaries, have walls composed of three layers, or coats, called *tunicae* (Fig. 14-21). The *tunica externa,* or *tunica adventitia,* is the outermost covering of the vessel. This layer is composed of fibrous and connective tissues that support the vessel. The *tunica media,* or middle layer, is largely a smooth muscle layer that constricts to regulate and control the diameter of the vessel. The *tunica intima,* or inner layer, has an elastic layer that joins the media and a thin layer of endothelial cells that lie adjacent to the blood. The endothelial layer provides a smooth and slippery inner surface for the vessel. This smooth inner lining, as long as it remains intact, prevents platelet adherence and blood clotting. The layers of the different types of blood vessels vary with vessel function.



■ **FIGURE 14-21** ■ Medium-sized artery and vein, showing the relative thickness of the three layers.

The walls of the arterioles, which control blood pressure, have large amounts of smooth muscle. Veins are thin-walled, distensible, and collapsible vessels. Capillaries are single-cell–thick vessels designed for the exchange of gases, nutrients, and waste materials.

Vascular Smooth Muscle

Smooth muscle contracts slowly and generates high forces for long periods with low energy requirements; it uses only 1/10 to 1/300 the energy of skeletal muscle. These characteristics are important in structures, such as blood vessels, that must maintain their tone day in and day out.

Although vascular smooth muscle contains actin and myosin filaments, these contractile filaments are not arranged in striations as they are in skeletal and cardiac muscle. The smooth muscle fibers are instead linked together in a strong cablelike system that generates a circular pull as it contracts. In addition, smooth muscle has less well developed sarcoplasmic reticulum for storing intracellular calcium than do skeletal and cardiac muscle, and it has very few fast sodium channels. Instead, depolarization of smooth muscle relies largely on extracellular calcium, which enters through calcium channels in the muscle membrane. These channels respond to changes in membrane potential or receptor-activated responses to chemical mediators such as norepinephrine. Sympathetic nervous system control of vascular smooth muscle tone occurs by way of receptor-activated channels. In general, α-adrenergic receptors are excitatory and produce vasoconstriction, and β-adrenergic receptors are inhibitory and produce vasodilation. Calcium-channel blocking drugs cause vasodilation by blocking calcium entry through the calcium channels.

Arterial System

The arterial system consists of the large and medium-sized arteries and the arterioles. Arteries are thick-walled vessels with large amounts of elastic fibers. The elasticity of these vessels allows them to stretch during cardiac systole, when the heart contracts and blood is ejected into the circulation, and to recoil during diastole, when the heart relaxes. The arterioles, which are predominantly smooth muscle, serve as resistance vessels for the circulatory system. They act as control valves through which blood is released as it moves into the capillaries. Changes in the activity of sympathetic fibers that innervate these vessels cause them to constrict or to relax as needed to maintain blood pressure. The regulation of arterial blood pressure is discussed further in Chapter 16.

Aortic Pressure Pulse

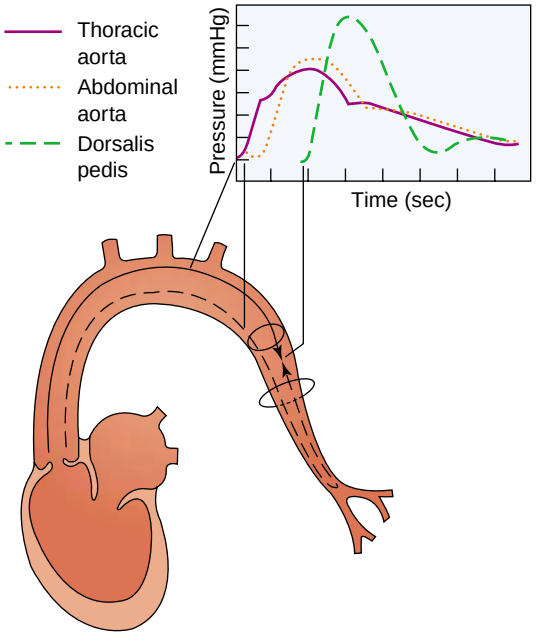
The delivery of blood to the tissues of the body is dependent on pressure pulsations or waves of pressure that are generated by the intermittent ejection of blood from the left ventricle into the distensible aorta and large arteries of the arterial system. The aortic pressure pulse represents the energy that is transmitted from molecule to molecule along the length of the vessel (Fig. 14-22). In the aorta, this pressure pulse is transmitted at a velocity of 4 to 6 meters/second, which is approximately 20 times faster than the flow of blood. Therefore, the pressure pulse has no direct relation to blood flow and could occur if there was no flow at all. When taking a pulse, it is the pressure pulses that are felt, and it is the pressure pulses that produce the Korotkoff sounds heard during blood pressure measurement. The tip or maximum deflection of the pressure pulsation coincides with the systolic blood pressure, and the minimum point of deflection coincides with the diastolic pressure.

Both the pressure values and the conformation of the pressure wave changes as it moves though the peripheral arteries (Fig. 14-22). As the pressure wave moves out through the aorta into the arteries, it changes as it collides with reflected waves from the periphery. This is why the systolic pressure is higher in the medium-sized arteries than in the aorta even though the diastolic pressure is lower. After its initial amplification, the pressure pulse becomes smaller and smaller as it moves through the smaller arteries and arterioles, until it disappears almost entirely in the capillaries. This allows for continuous, rather than pulsatile, flow in the capillary beds.

Although the pressure pulses usually are not transmitted to the capillaries, there are situations in which this does occur. For example, injury to a finger or other area of the body often results in a throbbing sensation. In this case, extreme dilatation of the small vessels in the injured area produces a reduction in the dampening of the pressure pulse. Capillary pulsations also occur in conditions that cause exaggeration of aortic pressure pulses, such as aortic regurgitation (see Chapter 17).

Venous System

The veins and venules are thin-walled, distensible, and collapsible vessels. The venules collect blood from the capillaries, and the veins transport blood back to the heart. The veins are capable of enlarging and storing large quantities of blood, which can be made available to the circulation as needed. Even though the veins are thin walled, they are muscular. This allows



■ **FIGURE 14-22** ■ Amplification of the arterial pressure wave as it moves forward in the peripheral arteries. This amplification occurs as a forward-moving pressure wave merges with a backward-moving reflected pressure wave. (**Inset**) The amplitude of the pressure pulse increases in the thoracic aorta, abdominal aorta, and dorsalis pedis.

them to contract or expand to accommodate varying amounts of blood. Veins are innervated by the sympathetic nervous system. When blood is lost from the circulation, the veins constrict as a means of maintaining intravascular volume.

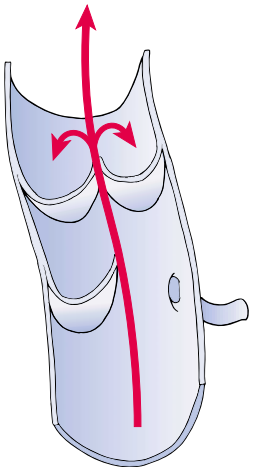
The venous system is a low-pressure system, and when a person is in the upright position, blood flow in the venous system must oppose the effects of gravity. Valves in the veins of extremities prevent retrograde flow (Fig. 14-23), and with the help of skeletal muscles that surround and intermittently compress the veins in a milking manner, blood is moved forward to the heart. Their pressure ranges from approximately 10 mm Hg at the end of the venules to approximately 0 mm Hg at the entrance of the vena cava into the heart. There are no valves in the abdominal or thoracic veins, and blood flow in these veins is heavily influenced by the pressure in the abdominal and thoracic cavities, respectively.

Lymphatic System

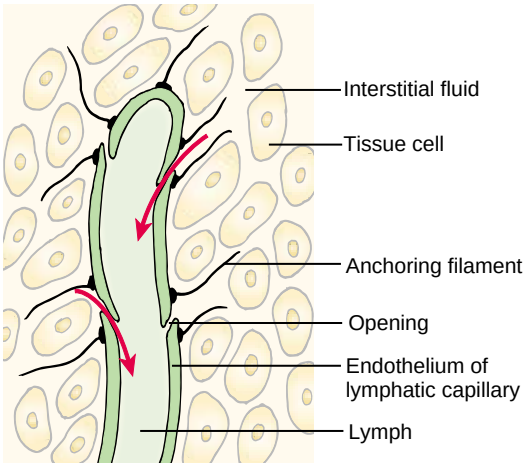
The lymphatic system, commonly called the *lymphatics*, serves almost all body tissues, except cartilage, bone, epithelial tissue, and tissues of the central nervous system. However, most of these tissues have prelymphatic channels that eventually flow into areas supplied by the lymphatics. Lymph is derived from interstitial fluids that flow through the lymph channels. It contains plasma proteins and other osmotically active particles that rely on the lymphatics for movement back into the circulatory system. The lymphatic system is also the main route for absorption of nutrients, particularly fats, from the gastrointestinal tract.

The lymphatic system is made up of vessels similar to those of the circulatory system. These vessels commonly travel along with an arteriole or venule or with its companion artery and vein. The terminal lymphatic vessels are made up of a single layer of connective tissue with an endothelial lining and resemble blood capillaries. The lymphatic vessels lack tight junctions and are loosely anchored to the surrounding tissues by fine filaments (Fig. 14-24). The loose junctions permit the entry of large particles, and the filaments hold the vessels open under conditions of edema, when the pressure of the surrounding tissues would otherwise cause them to collapse. The lymph capillaries drain into larger lymph vessels that ultimately empty into the right and left thoracic ducts (Fig. 14-25). The thoracic ducts empty into the circulation at the junctions of the subclavian and internal jugular veins.

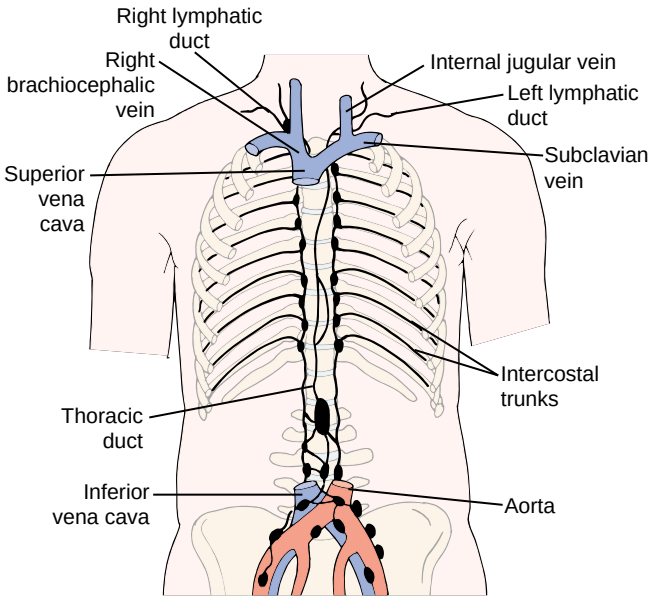
Although the divisions are not as distinct as in the circulatory system, the larger lymph vessels show evidence of having intimal, medial, and adventitial layers similar to those of blood vessels. Contraction of the smooth muscle in the medial layer



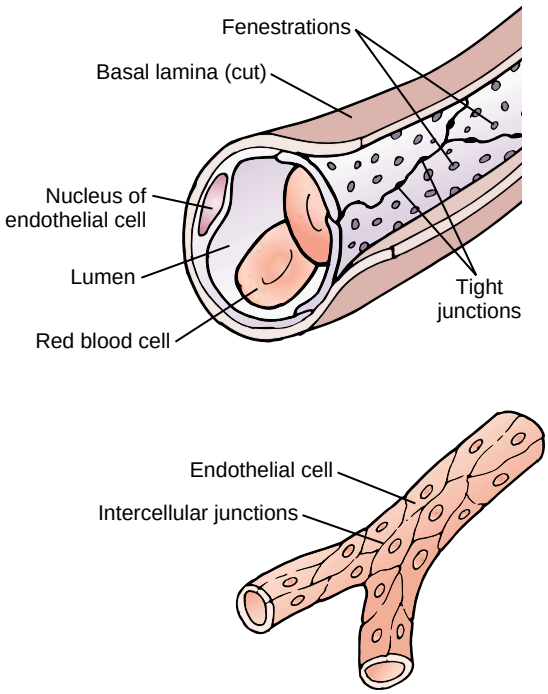
■ **FIGURE 14-23** ■ Portion of a femoral vein opened, to show the valves. The direction of flow is upward. Backward flow closes the valve.



■ **FIGURE 14-24** ■ Details of a lymphatic capillary.



■ **FIGURE 14-25** ■ Lymphatic system showing the thoracic duct and position of the left and right lymphatic ducts.



■ **FIGURE 14-26** ■ Endothelial cells and intercellular junctions in a section of capillary.

of the larger collecting lymph channels assists in propelling lymph fluid toward the thorax. External compression of the lymph channels by active and passive movements of body parts also aid in forward propulsion of lymph fluid. The rate of flow through the lymphatic system by way of all of the various lymph channels, approximately 120 mL per hour, is determined by the interstitial fluid pressure and the activity of lymph pumps.

The Microcirculation and Local Control of Blood Flow

The capillaries, venules, and arterioles of the circulatory system are collectively referred to as the *microcirculation*. It is here that exchange of gases, nutrients, and metabolites takes place between the tissues and the circulating blood. The lymphatic system represents an accessory system that removes excess fluid, proteins, and large particles from the interstitial spaces and returns them to the circulation. Because of their size, these particles cannot be reabsorbed into the capillaries.

Capillaries

Capillaries are microscopic, single-cell–thick vessels that connect the arterial and venous segments of the circulation. In each person, there are approximately 10 billion capillaries, with a total surface area of 500 to 700 m^2.

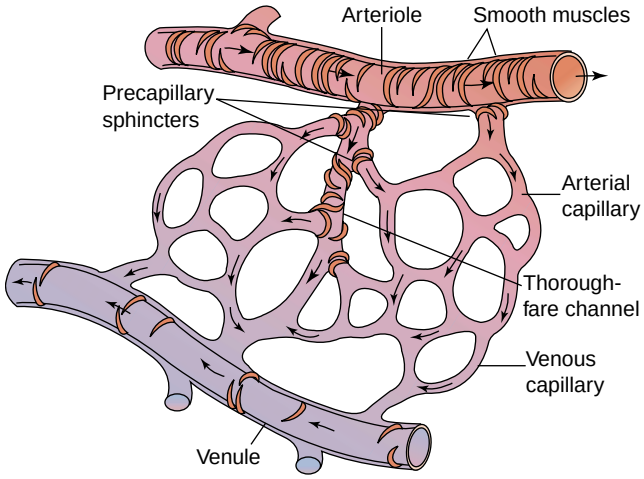
The capillary wall is composed of a single layer of endothelial cells surrounded by a basement membrane (Fig. 14-26). Intracellular junctions join the capillary endothelial cells; these are called the *capillary pores*. Lipid-soluble materials diffuse directly through the capillary cell membrane. Water and water-soluble materials leave and enter the capillary through the capillary pores. The size of the capillary pores varies with capillary function. In the brain, the endothelial cells are joined by tight junctions that form the blood-brain barrier. This prevents substances that would alter neural excitability from leaving the capillary. In organs that process blood contents, such as the liver, capillaries have large pores so that substances can pass easily through the capillary wall. In the kidneys, the glomerular capillaries have small openings called *fenestrations* that pass directly through the middle of the endothelial cells. Fenestrated capillary walls are consistent with the filtration function of the glomerulus.

Blood enters the microcirculation through an arteriole, passes through the capillaries, and leaves by way of a small venule. The metarterioles serve as thoroughfare channels that link arterioles and capillaries (Fig. 14-27). Small cuffs of smooth muscle, the precapillary sphincters, are positioned at the arterial end of the capillary. The smooth muscle tone of the arterioles, venules, and precapillary sphincters serves to control blood flow through the capillary bed. Depending on venous pressure, blood flows through the capillary channels when the precapillary sphincters are open.

Blood flow through capillary channels, designed for exchange of nutrients and metabolites, is called *nutrient flow*. In some parts of the microcirculation, blood flow bypasses the capillary bed, moving through a connection called an *arteriovenous shunt*, which directly connects an arteriole and a venule. This type of blood flow is called *non-nutrient flow* because it does not allow for nutrient exchange. Non-nutrient channels are common in the skin and are important in terms of heat exchange and temperature regulation.

Autoregulation

Tissue blood flow is regulated on a minute-to-minute basis in relation to tissue needs and on a longer-term basis through the development of collateral circulation. Neural mechanisms



■ **FIGURE 14-27** ■ **Capillary bed.** Precapillary sphincters control the flow of blood through the capillary network. Thoroughfare channels (*i.e.*, arteriovenous shunts) allow blood to move directly from the arteriole into the venule without moving through nutrient channels of the capillary.

regulate the cardiac output and blood pressure needed to support these local mechanisms.

Local control of blood flow is governed largely by the nutritional needs of the tissue. For example, blood flow to organs such as the heart, brain, and kidneys remains relatively constant, although blood pressure may vary throughout a range of 60 to 180 mm Hg. The ability of the tissues to regulate their own blood flow throughout a wide range of pressures is called *autoregulation.* Autoregulation of blood flow is mediated by changes in blood vessel tone caused by changes in flow through the vessel or by local tissue factors, such as lack of oxygen or accumulation of tissue metabolites (*i.e.*, potassium, lactic acid, or adenosine, which is a breakdown product of ATP). Local control is particularly important in tissues such as skeletal muscle, which has blood flow requirements that vary according to the level of activity.

An increase in local blood flow is called *hyperemia.* The ability of tissues to increase blood flow in situations of increased activity, such as exercise, is called *functional hyperemia.* When the blood supply to an area has been occluded and then restored, local blood flow through the tissues increases within seconds to restore the metabolic equilibrium of the tissues. This increased flow is called *reactive hyperemia.* The transient redness seen on an arm after leaning on a hard surface is an example of reactive hyperemia. Local control mechanisms rely on a continuous flow from the main arteries; therefore, hyperemia cannot occur when the arteries that supply the capillary beds are narrowed. For example, if a major coronary artery becomes occluded, the opening of channels supplied by that vessel cannot restore blood flow.

Tissue Factors Contributing to Local Control of Blood Flow. Vasoactive substances, formed in tissues in response to a need for increased blood flow, also aid in the local control of blood flow. The most important of these are histamine, serotonin (*i.e.*, 5-hydroxytryptamine), the kinins, and the prostaglandins.

Histamine increases blood flow. Most blood vessels contain histamine in mast cells and nonmast cell stores; when these tissues are injured, histamine is released. In certain tissues, such as skeletal muscle, the activity of the mast cells is mediated by the sympathetic nervous system; when sympathetic control is withdrawn, the mast cells release histamine. Vasodilation then results from increased histamine and the withdrawal of vasoconstrictor activity.

Serotonin is liberated from aggregating platelets during the clotting process; it causes vasoconstriction and plays a major role in the control of bleeding. Serotonin is found in brain and lung tissues, and there is some speculation that it may be involved in the vascular spasm associated with some allergic pulmonary reactions and migraine headaches.

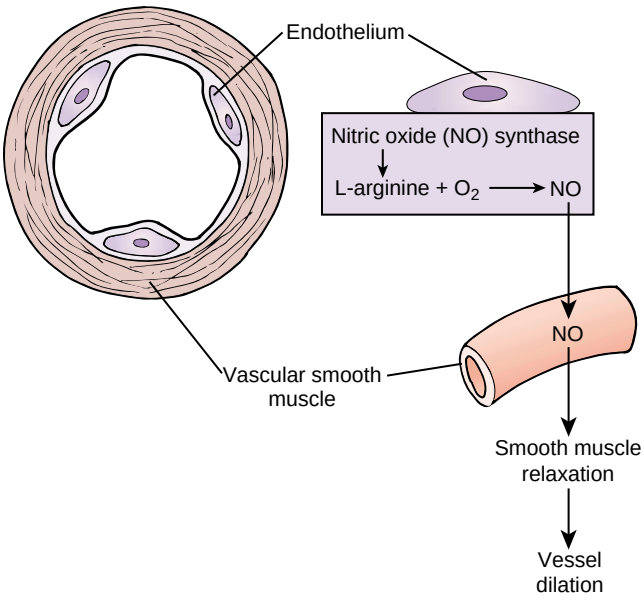
The *kinins* (*i.e.*, kallidins and bradykinin) are liberated from the globulin kininogen, which is present in body fluids. The kinins cause relaxation of arteriolar smooth muscle, increase capillary permeability, and constrict the venules. In exocrine glands, the formation of kinins contributes to the vasodilation needed for glandular secretion.

Prostaglandins are synthesized from constituents of the cell membrane (*i.e.*, the long-chain fatty acid *arachidonic acid*). Tissue injury incites the release of arachidonic acid from the cell membrane, which initiates prostaglandin synthesis. There are several prostaglandins (*e.g.*, E_2, F_2, D_2), which are subgrouped according to their solubility; some produce vasoconstriction and some produce vasodilation. As a rule of thumb, those in the E group are vasodilators, and those in the F group are vasoconstrictors. The adrenal glucocorticoid hormones produce an anti-inflammatory response by blocking the release of arachidonic acid, preventing prostaglandin synthesis.

Endothelial Control of Vasodilation and Vasoconstriction. The *endothelium,* which lies between the blood and the vascular smooth muscle, serves as a physical barrier for vasoactive substances that circulate in the blood. Once thought to be nothing more than a single layer of cells that line blood vessels, it is now known that the endothelium plays an active role in controlling vascular function. In capillaries, which are composed of a single layer of endothelial cells, the endothelium is active in transporting cell nutrients and wastes. In addition to its function in capillary transport, the vascular endothelium removes vasoactive agents such as norepinephrine from the blood, and it produces enzymes that convert precursor molecules to active products (*e.g.*, angiotensin I to angiotensin II in lung vessels).

One of the important functions of the endothelial cells in the small arteries and arterioles is to synthesize and release factors that control vessel dilation. Of particular importance was the discovery, first reported in the early 1980s, that the intact endothelium was able to produce a factor that caused relaxation of vascular smooth muscle. This factor was originally named *endothelium-derived relaxing factor* and is now known to be *nitric oxide.* Many other cell types produce nitric oxide. In these tissues, nitric oxide has other functions, including modulation of nerve activity in the nervous system.

The normal endothelium maintains a continuous release of nitric oxide, which is formed from L-arginine through the action of an enzyme called *nitric oxide synthase* (Fig. 14-28). The production of nitric oxide can be stimulated by a variety of



■ **FIGURE 14-28** ■ Function of nitric oxide in smooth muscle relaxation.

endothelial *agonists,* including acetylcholine, bradykinin, histamine, and thrombin. *Shear stress* on the endothelium, resulting from an increase in blood flow or blood pressure, also stimulates nitric oxide production and vessel relaxation. Nitric oxide also inhibits platelet aggregation and secretion of platelet contents, many of which cause vasoconstriction. The fact that nitric oxide is released into the vessel lumen (to inactivate platelets) and away from the lumen (to relax smooth muscle) suggests that it protects against both thrombosis and vasoconstriction. Nitroglycerin, which is used in treatment of angina, produces its effects by releasing nitric oxide in vascular smooth muscle of the target tissues.

The endothelium also produces a number of vasoconstrictor substances, including *angiotensin II,* vasoconstrictor prostaglandins, and a family of peptides called *endothelins.* There are at least three endothelins. Endothelin-1, made by human endothelial cells, is the most potent endogenous vasoconstrictor known. Receptors for endothelins also have been identified.

Collateral Circulation

Collateral circulation is a mechanism for the long-term regulation of local blood flow. In the heart and other vital structures, anastomotic channels exist between some of the smaller arteries. These channels permit perfusion of an area by more than one artery. When one artery becomes occluded, these anastomotic channels increase in size, allowing blood from a patent artery to perfuse the area supplied by the occluded vessel. For example, persons with extensive obstruction of a coronary blood vessel may rely on collateral circulation to meet the oxygen needs of the myocardial tissue normally supplied by that vessel. As with other long-term compensatory mechanisms, the recruitment of collateral circulation is most efficient when obstruction to flow is gradual, rather than sudden.

In summary, the walls of all blood vessels, except the capillaries, are composed of three layers: the tunica externa, tunica media, and tunica intima. The layers of the vessel vary with its function. Arteries are thick-walled vessels with large amounts of elastic fibers. The walls of the arterioles, which control blood pressure, have large amounts of smooth muscle. Veins are thin-walled, distensible, and collapsible vessels. Venous flow is designed to return blood to the heart. It is a low-pressure system and relies on venous valves and the action of muscle pumps to offset the effects of gravity. Capillaries are single-cell–thick vessels designed for the exchange of gases, nutrients, and waste materials.

The delivery of blood to the tissues of the body is dependent on pressure pulses that are generated by the intermittent ejection of blood from the left ventricle into the distensible aorta and large arteries of the arterial system. The combination of distensibility of the arteries and their resistance to flow reduces the pressure pulsations, therefore, blood flow is almost constant by the time blood reaches the capillaries. Two major factors affect the pressure pulsations: (1) the stroke volume output of the heart, and (2) and the compliance of the arterial system into which the blood is ejected. A large stroke volume and/or decrease in arterial compliance produce an increase in pulse pressure.

The mechanisms that control blood flow are designed to ensure adequate delivery of blood to the capillaries in the microcirculation, where the exchange of cellular nutrients and wastes occurs. Local control is governed largely by the needs of the tissues and is regulated by local tissue factors such as lack of oxygen and the accumulation of metabolites. Hyperemia is a local increase in blood flow that occurs after a temporary occlusion of blood flow. It is a compensatory mechanism that decreases the oxygen debt of the deprived tissues. Collateral circulation is a mechanism for long-term regulation of local blood flow that involves the development of collateral vessels.

NEURAL CONTROL OF CIRCULATORY FUNCTION

The neural control of the circulatory system occurs primarily through the *sympathetic* and *parasympathetic* divisions of the autonomic nervous system (ANS). The ANS contributes to the control of cardiovascular function through modulation of cardiac (*i.e.,* heart rate and cardiac contractility) and vascular (*i.e.,* peripheral vascular resistance) function.

The neural control centers for the integration and modulation of cardiac function and blood pressure are located bilaterally in the medulla oblongata. The medullary cardiovascular neurons are grouped into three distinct pools that lead to sympathetic innervation of the heart and blood vessels and parasympathetic innervation of the heart. The first two, which control sympathetic-mediated acceleration of heart rate and blood vessel tone, are called the vasomotor center. The third, which controls parasympathetic-mediated slowing of heart

rate, is called the *cardioinhibitory center.* These brain stem centers receive information from many areas of the nervous system, including the hypothalamus. The arterial baroreceptors and chemoreceptors provide the medullary cardiovascular center with continuous information regarding changes in blood pressure (see Chapter 16).

Autonomic Regulation of Cardiac Function

The heart is innervated by the parasympathetic and sympathetic nervous systems. Parasympathetic innervation of the heart is achieved by means of the *vagus nerve.* The parasympathetic outflow to the heart originates from the vagal nucleus in the medulla. The axons of these neurons pass to the heart in the cardiac branches of the vagus nerve. The effect of vagal stimulation on heart function is largely limited to heart rate, with increased vagal activity producing a slowing of the pulse. Sympathetic outflow to the heart and blood vessels arises from neurons located in the reticular formation of the brain stem. The axons of these neurons exit the thoracic segments of the spinal cord to synapse with the postganglionic neurons that innervate the heart. Cardiac sympathetic fibers are widely distributed to the SA and AV nodes and the myocardium. Increased sympathetic activity produces an increase in the heart rate and the velocity and force of cardiac contraction.

Autonomic Regulation of Vascular Function

The sympathetic nervous system serves as the final common pathway for controlling the smooth muscle tone of the blood vessels. Most of the sympathetic preganglionic fibers that control vessel function originate in the vasomotor center of the brain stem, travel down the spinal cord, and exit in the thoracic and lumbar (T1-L2) segments. The sympathetic neurons that supply the blood vessels maintain them in a state of tonic activity, so that even under resting conditions, the blood vessels are partially constricted. Vessel constriction and relaxation are accomplished by altering this basal input. Increasing sympathetic activity causes constriction of some vessels, such as those of the skin, the gastrointestinal tract, and the kidneys. Blood vessels in skeletal muscle are supplied by both vasoconstrictor and vasodilator fibers. Activation of sympathetic vasodilator fibers causes vessel relaxation and provides the muscles with increased blood flow during exercise. Although the parasympathetic nervous system contributes to the regulation of heart function, it has little or no control over blood vessels.

Autonomic Neurotransmitters

The actions of the ANS are mediated by chemical neurotransmitters. *Acetylcholine* is the postganglionic neurotransmitter for parasympathetic neurons and *norepinephrine* is the main neurotransmitter for postganglionic sympathetic neurons. Sympathetic neurons also respond to epinephrine, which is released into the bloodstream by the adrenal medulla. The neurotransmitter *dopamine* can also act as a neurotransmitter for some sympathetic neurons. The synthesis, release, and inactivation of the autonomic neurotransmitters are discussed in Chapter 36.

In summary, the neural control centers for the regulation of cardiac function and blood pressure are located in the reticular formation of the lower pons and medulla of the brain stem, where the integration and modulation of ANS responses occur. These brain stem centers receive information from many areas of the nervous system, including the hypothalamus. Both the parasympathetic and sympathetic nervous systems innervate the heart. The parasympathetic nervous system functions in regulating heart rate through the vagus nerve, with increased vagal activity producing a slowing of heart rate. The sympathetic nervous system has an excitatory influence on heart rate and contractility, and it serves as the final common pathway for controlling the smooth muscle tone of the blood vessels.

REVIEW QUESTIONS

- Compare the functions and distribution of blood flow and blood pressure in the systemic and pulmonary circulations.
- Use Laplace's law to explain the collapse of small blood vessels during shock caused by a loss of blood volume and to explain why atherosclerotic disease is usually a silent disorder until the disease has produced a 75% reduction in vessel radius.
- Describe the cardiac conduction system and relate it to the mechanical functioning of the heart.
- Characterize the four phases of a cardiac action potential and differentiate between the fast and slow responses.
- Draw a figure of the cardiac cycle, incorporating volume, pressure, phonocardiographic, and electrocardiographic changes that occur during atrial and ventricular systole and diastole.
- Explain the concepts of *preload* and *afterload* in terms of venous return to the heart, aortic valvular stenosis, and hypertension.
- State the formula for calculating the cardiac output and explain the effects that venous return, cardiac contractility, and heart rate have on cardiac output.
- Describe the cardiac reserve and relate it to the Frank-Starling mechanism.
- Compare the structure and function of arteries, arterioles, veins, and capillaries.
- Define autoregulation and characterize mechanisms responsible for short-term and long-term regulation of blood flow.
- Describe the distribution of the sympathetic and parasympathetic nervous system in innervation of the circulatory system and their effects on heart rate and cardiac contractility.

connection

Visit the Connection site at connection.lww.com/go/porth for links to chapter-related resources on the Internet.

BIBLIOGRAPHY

Berne R.M., Levy M.N. (2000). *Principles of physiology* (3rd ed., pp. 201–275). St. Louis: C.V. Mosby.

Berne R.M., Levy M.N. (2001). *Cardiovascular physiology* (8th ed.). St. Louis: C.V. Mosby.

Feletou M., Vanhoutte P.M. (1999). The alternative: EDHF. *Journal of Molecular and Cellular Cardiology* 31, 15–22.

Ganong W.F. (1999). *Review of medical physiology* (19th ed., 493–601). Stamford, CT: Appleton & Lange.

Guyton A.C., Hall J.E. (2000). *Medical physiology* (10th ed., pp. 144–222). Philadelphia: W.B. Saunders.

McCormack D.H. (1987). *Ham's histology* (9th ed., p. 448). Philadelphia: J.B. Lippincott.

Rhoades R.A, Tanner G.A. (1996). *Medical physiology* (pp. 207–301). Boston: Little, Brown.

Smith J.J., Kampine J.P. (1989). *Circulatory physiology* (3rd ed.). Baltimore: Williams & Wilkins.

Vanhoutte P.M. (1999). How to assess endothelial function in human blood vessels. *Journal of Hypertension* 17, 1047–1058.