Chapter Outline and Objectives

Functions of the Heart (p. 324)

1. List the major functions of the heart.

Size, Form, and Location of the Heart (p. 324)

2. Describe the size, shape, and location of the heart, and explain why knowledge of its location is important.

Anatomy of the Heart (p. 326)

3. Describe the structure of the pericardium.
4. Give the location and function of the coronary arteries.
5. Describe the chambers of the heart.
6. Name the valves of the heart and state their locations and functions.
7. Describe the flow of blood through the heart and name each of the chambers and structures through which the blood passes.

Histology of the Heart (p. 333)

8. List the components of the heart wall and describe the structure and function of each.
9. Describe the structural and functional characteristics of cardiac muscle cells.

Electrical Activity of the Heart (p. 335)

10. Describe the characteristics of action potentials in cardiac muscle.
11. Explain the structure and function of the conduction system of the heart.
12. Define each wave of the electrocardiogram and relate each of them to contractions of the heart.

Cardiac Cycle (p. 338)

13. Describe the cardiac cycle and the relationship between contraction of each of the chambers, the pressure in each of the chambers, the phases of the electrocardiogram, and the heart sounds.

Heart Sounds (p. 341)

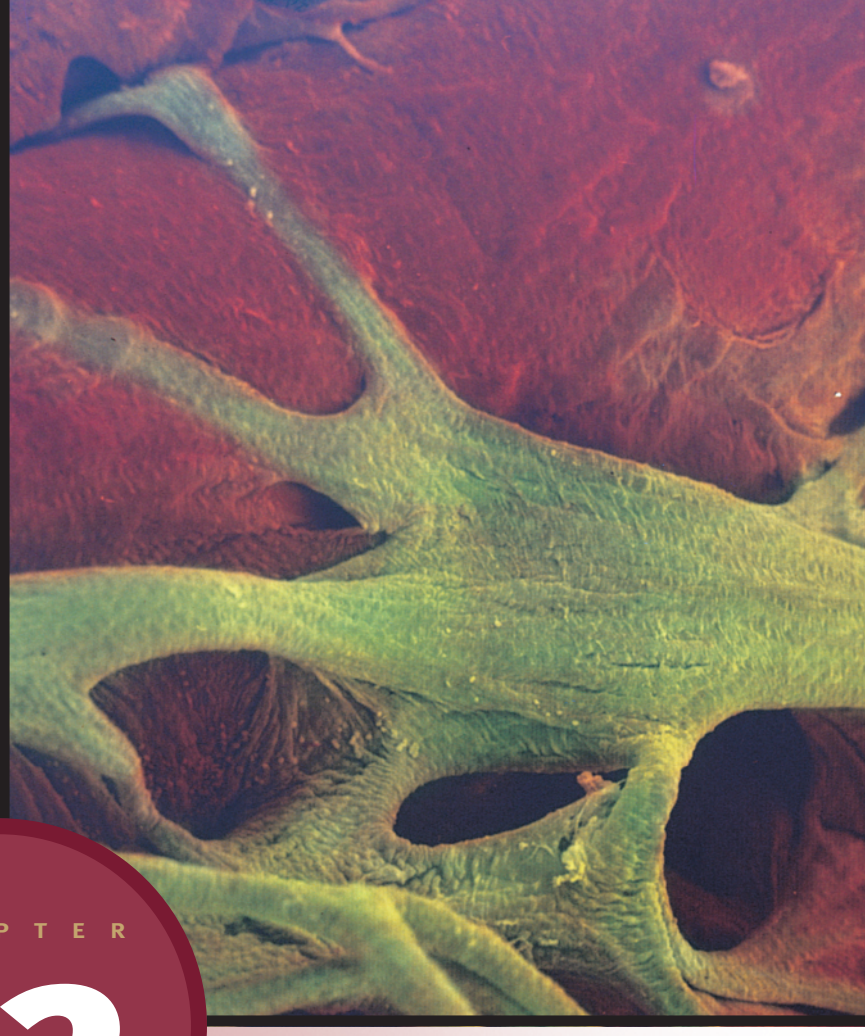
14. Describe the heart sounds and their significance.

Regulation of Heart Function (p. 342)

15. Describe intrinsic and extrinsic regulation of the heart.
16. Give the conditions for which the major heart medications and treatments are administered.

Effects of Aging on the Heart (p. 347)

17. List the major age-related changes that affect the heart.



CHAPTER

12

This is a colorized scanning electron micrograph of Purkinje fibers of the heart, which are specialized cardiac muscle cells that conduct action potentials more rapidly than other cardiac muscle fibers and have a reduced ability to contract. Purkinje fibers make up much of the conducting system of the heart.

Heart

People often refer to the heart as if it were the seat of certain strong emotions. A very determined person may be described as having "a lot of heart," and a person who has been disappointed romantically can be described as having a "broken heart." A popular holiday in February not only dramatically distorts the heart's anatomy, it also attaches romantic emotions to it. The heart is a muscular organ that is essential for life because it pumps blood through the body. Emotions are a product of brain function, not heart function.

Fluids flow through a pipe only if they are forced to do so. The force is commonly produced by a pump, which increases the pressure of the liquid at the pump above the pressure in the pipe. Thus, the liquid flows from the pump through the pipe from an area of higher pressure to an area of lower pressure. If the pressure produced by the pump increases, flow of liquid through the pipe increases. If the pressure produced by the pump decreases, flow of liquid through the pipe decreases.

Like a pump that forces water to flow through a pipe, the heart contracts forcefully to pump blood through the blood vessels of the body (figure 12.1). The heart of a healthy adult, at rest, pumps approximately 5 liters (L) of blood per minute. For most people, the heart continues to pump at approximately that rate for more than 75 years; and, during short periods of vigorous exercise, the amount of blood pumped per minute increases several fold. If the heart loses its pumping ability for even a few minutes, however, blood flow through the blood vessels stops, and the life of the individual is in danger.

The heart is actually two pumps in one. The right side of the heart pumps blood to the lungs and back to the left side of the heart through vessels of the **pulmonary circulation** (figure 12.2). The left side of the heart pumps blood to all other tissues of the body and back to the right side of the heart through vessels of the **systemic circulation.**

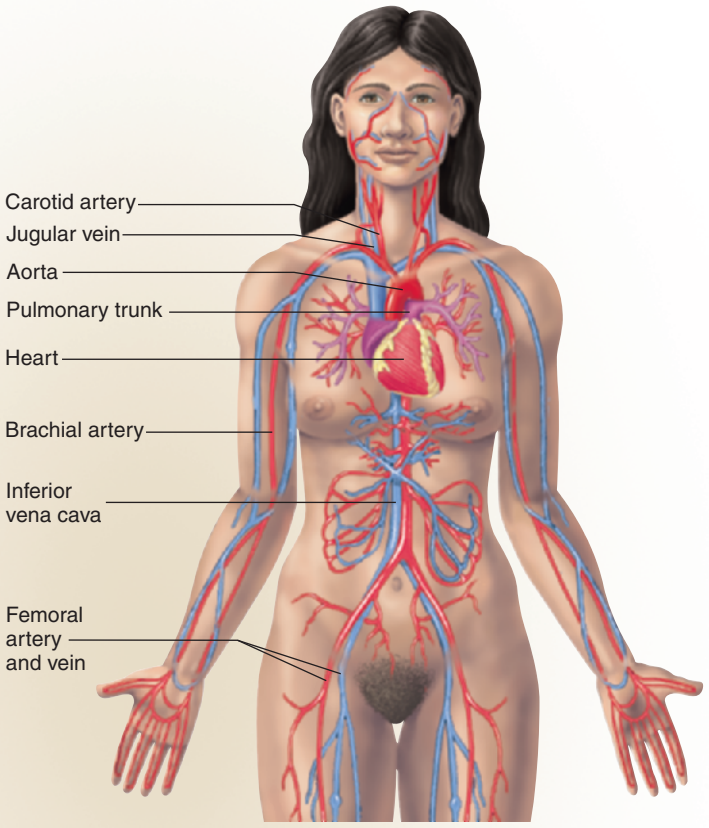


Figure 12.1 The Cardiovascular System

The heart, blood, and blood vessels are the major components of the cardiovascular system.

Functions of the Heart

Functions of the heart include:

1. *Generating blood pressure.* Contractions of the heart generate blood pressure, which is responsible for blood movement through the blood vessels.

2. *Routing blood.* The heart separates the pulmonary and systemic circulations, which ensures the flow of oxygenated blood to tissues.

3. *Ensuring one-way blood flow.* The valves of the heart ensure a one-way flow of blood through the heart and blood vessels.

4. *Regulating blood supply.* Changes in the rate and force of heart contraction match blood delivery to the changing metabolic needs of the tissues, such as during rest, exercise, and changes in body position.

Size, Form, and Location of the Heart

The heart is located in the thoracic cavity between the lungs. The heart, trachea, esophagus, and associated structures form a midline partition called the **mediastinum** (mē′dē-astī′nŭm, middle wall) (figure 12.3). The adult heart has the shape of a blunt cone and is slightly larger than a closed fist. The blunt, rounded point of the cone is the **apex** (ā′peks, tip); and the larger, flat portion at the opposite end of the cone is the **base.** The apex is the most inferior part of the heart and it is directed anteriorly and to the left. It is deep to the fifth intercostal (between the ribs) space. The base is superior and slightly posterior. The most superior portion of the base is deep to the second intercostal space.

It is important to know the location of the heart. Placing a stethoscope to hear the heart sounds, placing electrodes on the chest to record an electrocardiogram (ECG), and performing cardiopulmonary resuscitation (CPR) depend on accurate knowledge of the heart's position.

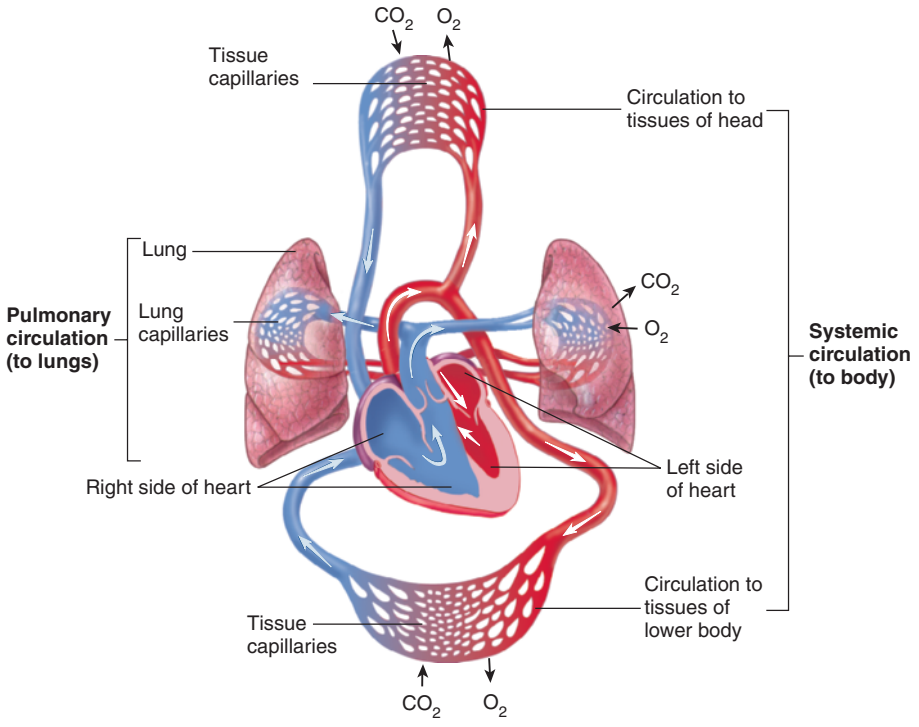


Figure 12.2 Overview of the Circulatory System

The circulatory system consists of the pulmonary and systemic circulations. The right side of the heart pumps blood through vessels to the lungs and back to the left side of the heart through the pulmonary circulation. The left side of the heart pumps blood through vessels to the tissues of the body and back to the right side of the heart through the systemic circulation.

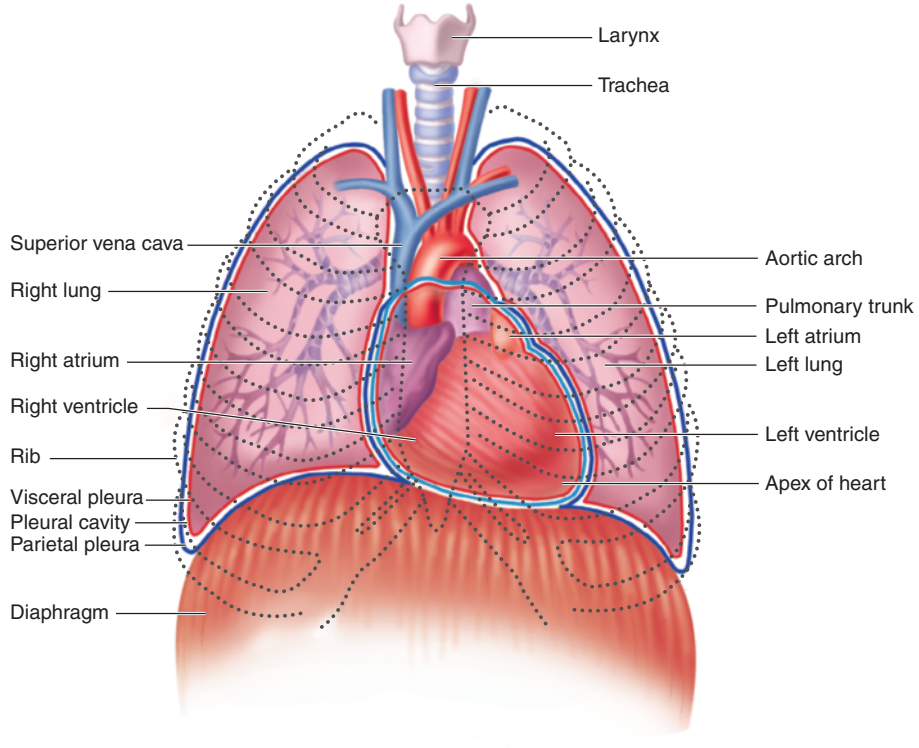


Figure 12.3 Location of the Heart in the Thorax

The heart is deep to the sternum and angled to the left. The base of the heart is deep to the sternum and extends to the second intercostal space. The apex of the heart is at the level of the fifth intercostal space, approximately 9 cm to the left of the midline.

Anatomy of the Heart

Pericardium

The heart is surrounded by a space called the **pericardial** (per-i-kar′dē-ăl, surrounding the heart) **cavity** (see chapter 1). The pericardial cavity is formed by the **pericardium** (per-i-kar′dē-ŭm), or **pericardial sac,** which is a double-layered, closed sac that surrounds the heart and anchors it within the mediastinum (see figures 12.3 and 12.4). The pericardium consists of a tough, fibrous connective tissue outer layer called the **fibrous pericardium** and an inner layer of flat epithelial cells and a thin layer of connective tissue called the **serous pericardium.** The portion of the serous pericardium lining the fibrous pericardium is the **parietal pericardium,** whereas the portion covering the heart surface is the **visceral pericardium,** or **epicardium** (ep-i-kar′dē-ŭm, upon the heart). The parietal and visceral pericardia are continuous with each other where the great vessels enter or leave the heart. The pericardial cavity, located between the visceral and parietal pericardia, is filled with a thin layer of **pericardial fluid** produced by the serous pericardium. The pericardial fluid helps reduce friction as the heart moves within the pericardial sac.

Disorders of the Pericardium

Pericarditis (per′i-kar-dī′tis) is an inflammation of the serous pericardium. The cause is frequently unknown, but it can result from infection, diseases of connective tissue, or damage due to radiation treatment for cancer. It can be extremely painful, with sensations of pain referred to the back and to the chest, which can be confused with the pain of a myocardial infarction (heart attack). Pericarditis can result in a small amount of fluid accumulation within the pericardial sac.

Cardiac tamponade (tam-pŏ-nād′, a pack or plug) is a potentially fatal condition in which fluid or blood accumulates in the pericardial sac. The fluid compresses the heart from the outside. The heart is a powerful muscle, but it relaxes passively. When it is compressed by fluid within the pericardial sac, it cannot dilate when the cardiac muscle relaxes. Consequently, the heart cannot fill with blood during relaxation, which makes it impossible for it to pump. Cardiac tamponade can cause a person to die quickly unless the fluid is removed. Causes of cardiac tamponade include rupture of the heart wall following a myocardial infarction, rupture of blood vessels in the pericardium after a malignant tumor invades the area, damage to the pericardium resulting from radiation therapy, and trauma such as occurs in a traffic accident.

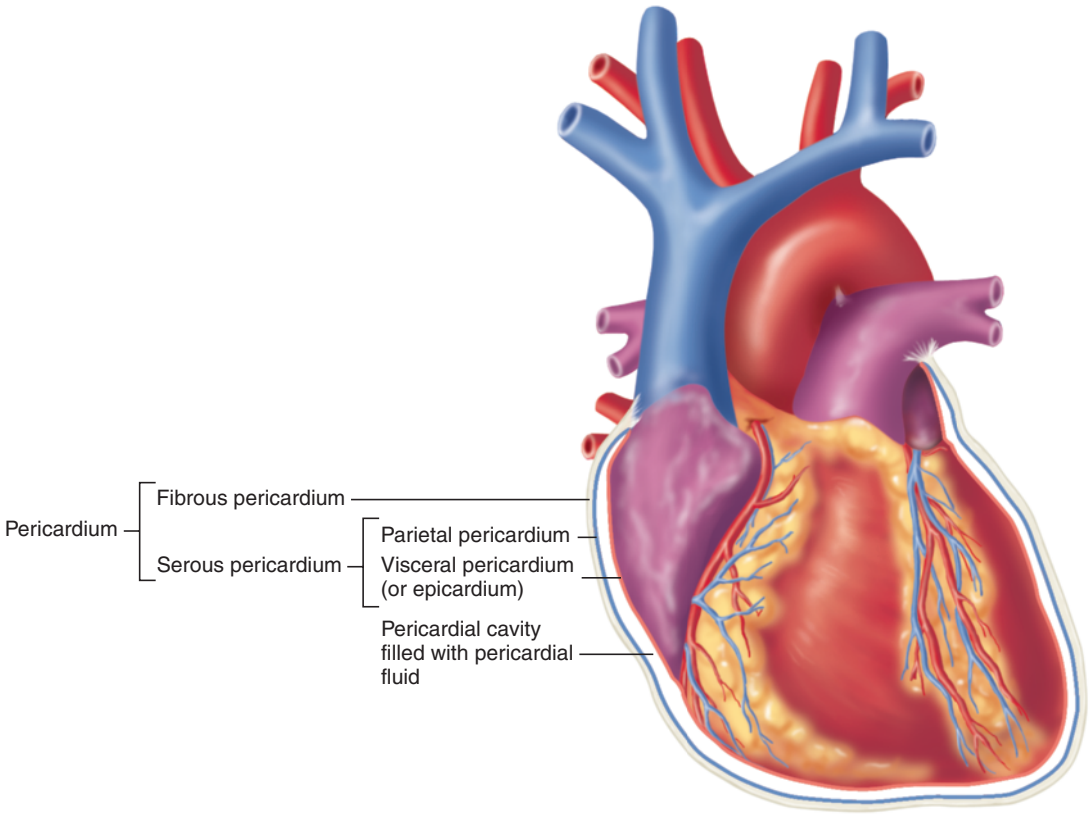


Figure 12.4 The Heart in the Pericardium

The heart is located in the pericardium, which consists of an outer fibrous pericardium and an inner serous pericardium. The serous pericardium has two parts: the parietal pericardium lines the fibrous pericardium, and the visceral pericardium (epicardium) covers the surface of the heart. The pericardial cavity, between the parietal and visceral pericardium, is filled with a small amount of pericardial fluid.

External Anatomy

The right and left **atria** (a′trē-ă, entrance chambers; sing. atrium) are located at the base of the heart, and the right and left **ventricles** (ven′tri-klz, a cavity) extend from the base of the heart toward the apex (figure 12.5). A **coronary** (kōr′o-nār-ē, circling like a crown) **sulcus** (sul′kus, ditch) extends around the heart, separating the atria from the ventricles. In addition, two sulci, which indicate the division between the right and left ventricles, extend inferiorly from the coronary sulcus. One extends inferiorly from the coronary sulcus on the anterior surface of the heart, and the other extends inferiorly from the coronary sulcus on the posterior surface of the heart (see figure 12.5).

Six large veins carry blood to the heart (see figure 12.5*a* and *c*): the **superior vena cava** and **inferior vena cava** carry blood from the body to the right atrium, and four **pulmonary** (pŭl′mō-nār-ē, lung) **veins** carry blood from the lungs to the left atrium. Two arteries, the **pulmonary trunk** and the **aorta** (ā-ōr′tă), exit the heart. The pulmonary trunk, arising from the right ventricle, splits into the right and left **pulmonary arteries,** which carry blood to the lungs. The aorta carries blood from the left ventricle to the body.

Blood Supply to the Heart

Coronary Arteries

Cardiac muscle in the wall of the heart is thick and metabolically very active. The coronary arteries supply blood to the wall of the heart (figure 12.6*a*). Two **coronary arteries** originate from the base of the aorta, just above the aortic semilunar valves. The **left coronary artery** originates on the left side of the aorta. Its branches supply much of the anterior wall of the heart and most of the left ventricle. The **right coronary artery** originates on the right side of the heart and supplies most of the wall of the right ventricle. Both the right and left coronary arteries lie within the coronary sulcus.

In a resting person, blood flowing through the coronary arteries of the heart gives up approximately 70% of its oxygen. In comparison, blood flowing through arteries to skeletal muscle gives up only about 25% of its oxygen. The percentage of oxygen the blood releases to skeletal muscle increases to 70% or more during exercise. The percentage of oxygen the blood releases to cardiac muscle cannot increase substantially during exercise. Cardiac muscle is therefore very dependent on an increased rate of blood flow through the coronary arteries above its resting level to provide an adequate oxygen supply during exercise.

P R E D I C T 1

Predict the effect on the heart if blood flow through the anterior interventricular artery is restricted or completely blocked (*Hint:* See figure 12.6*a*).

Disorders of Coronary Arteries

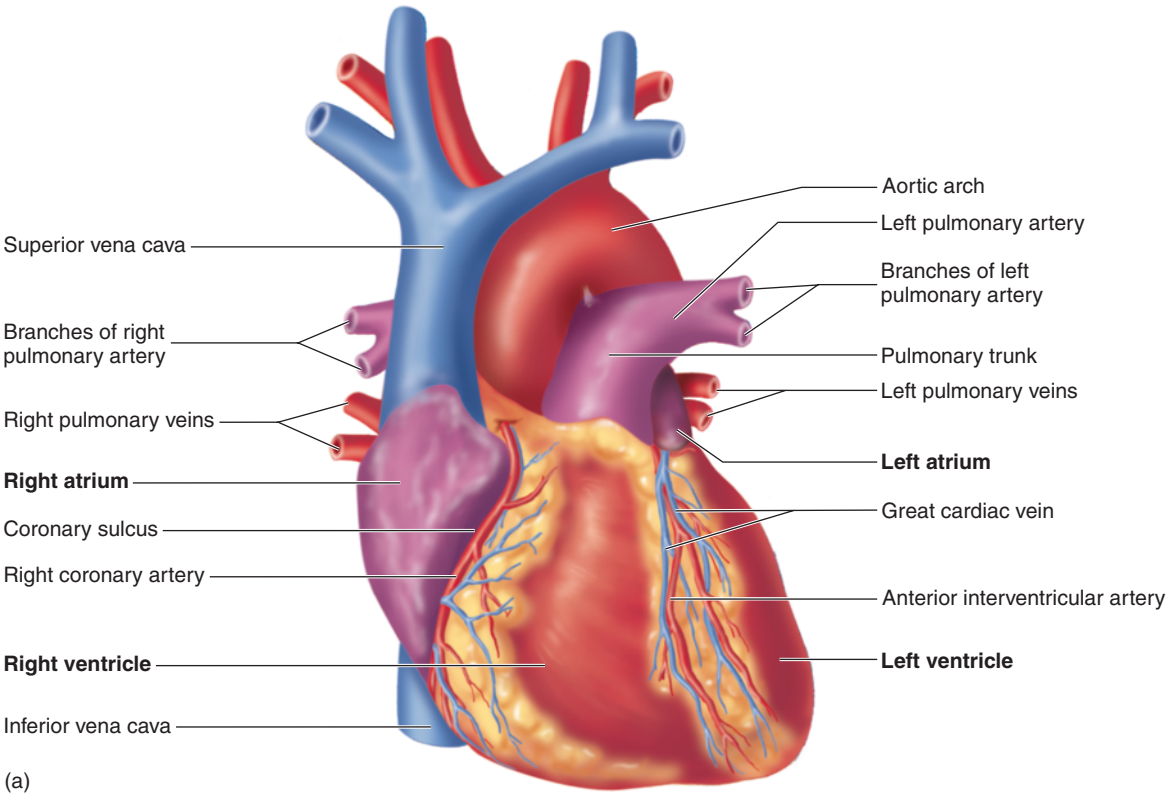
When a blood clot, or **thrombus** (throm′bŭs, a clot), suddenly blocks a coronary blood vessel, a **heart attack,** or **coronary thrombosis** (throm′bō-sis), occurs. The area that has been cut off from its blood supply suffers from a lack of oxygen and nutrients and dies if the blood supply is not quickly reestablished. The region of dead heart tissue is called an **infarct** (in′farkt). If the infarct is large enough, the heart may be unable to pump enough blood to keep the person alive. People who are at risk can reduce the likelihood of heart attack by taking small amounts of aspirin daily (see chapter 11).

Aspirin is also administered to many people who are exhibiting clear symptoms of a heart attack. In some cases, it is possible to treat heart attacks with enzymes such as **streptokinase** (strep-tō-kī′nās) or **tissue plasminogen** (plaz-min′o-jen) **activator (t-PA),** which break down blood clots. One of the enzymes is injected into the circulatory system of a heart attack patient, where it reduces or removes the blockage in the coronary artery. If the clot is broken down quickly, the blood supply to cardiac muscle is reestablished, and the heart may suffer little permanent damage.

Coronary arteries can become blocked more gradually by **atherosclerotic** (ath′er-ō-skler-ot′ik, *athero,* pasty material + *sclerosis,* hardness) **lesions.** These thickenings in the walls of arteries can contain deposits that are high in cholesterol and other lipids. The lesions protrude into the lumen (opening) of the arteries, thus restricting blood flow. The ability of cardiac muscle to function is reduced when it is deprived of an adequate blood supply. The person suffers from fatigue and often pain in the area of the chest and usually in the left arm with the slightest exertion. The pain is called **angina pectoris** (an-jī′nă, pain; pek′tō-ris, in the chest).

Angioplasty (an′jē-ō-plas-tē) is a surgical procedure in which a small balloon is threaded through the aorta and into a coronary artery. After the balloon has entered a partially blocked coronary artery, it is inflated, flattening the atherosclerotic deposits against the vessel walls and opening the blocked blood vessel. This technique improves the function of cardiac muscle in patients suffering from an inadequate blood flow to the cardiac through the coronary arteries. Some controversy exists about its effectiveness, at least in some patients, because dilation of the coronary arteries can be reversed within a few weeks or months and because blood clots can form in coronary arteries following angioplasty. Small rotating blades and lasers are also used to remove lesions from coronary vessels, or a small coil device, called a **stent,** is placed in the vessels to hold them open following angioplasty.

A **coronary bypass** is a surgical procedure that relieves the effects of obstructions in the coronary arteries. The technique involves taking healthy segments of blood vessels from other parts of the patient's body and using them to bypass, or create an alternative path around, obstructions in the coronary arteries. The technique is common for those who suffer from severe blockage of parts of the coronary arteries.



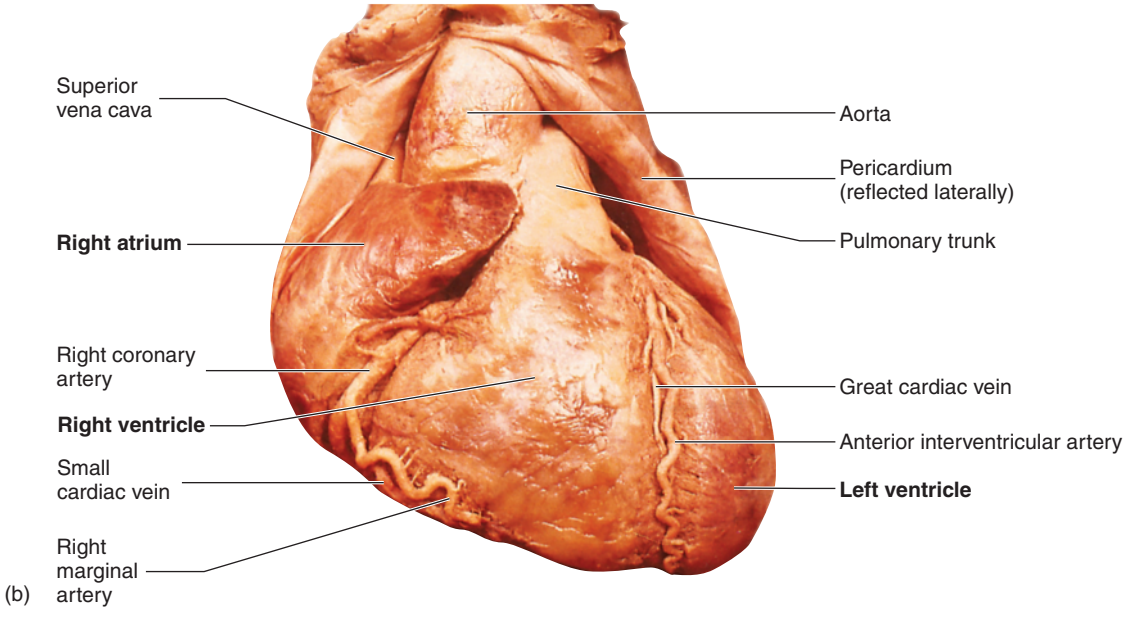


Figure 12.5 Anterior Surface View of the Heart

(*a*) The anterior view of the heart. The two atria (right and left) are located superiorly, and the two ventricles (right and left) are located inferiorly. The superior and inferior venae cava enter the right atrium. The pulmonary veins enter the left atrium. The pulmonary trunk exits the right ventricle, and the aorta exits the left ventricle. (*b*) Photograph of the anterior surface of the heart.

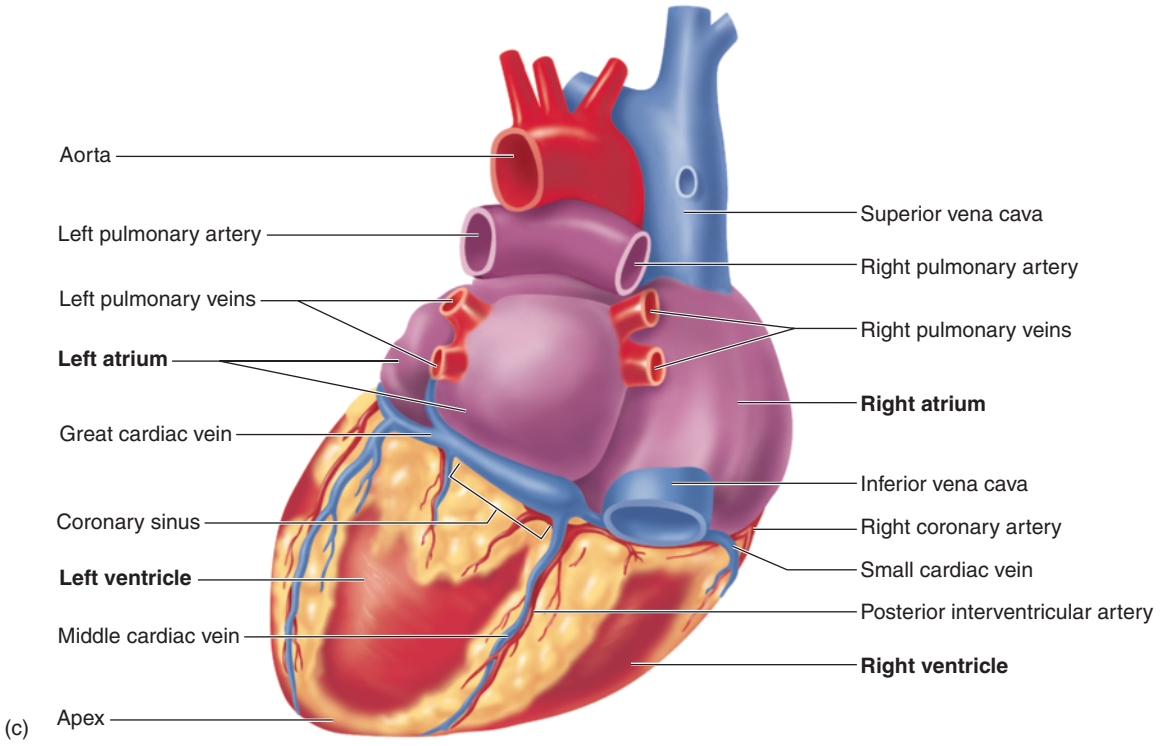


Figure 12.5 *continued*

(*c*) The posterior surface view of the heart. The two atria (right and left) are located superiorly, and the two ventricles (right and left) are located inferiorly. The superior and inferior venae cava enter the right atrium, and the four pulmonary veins enter the left atrium.

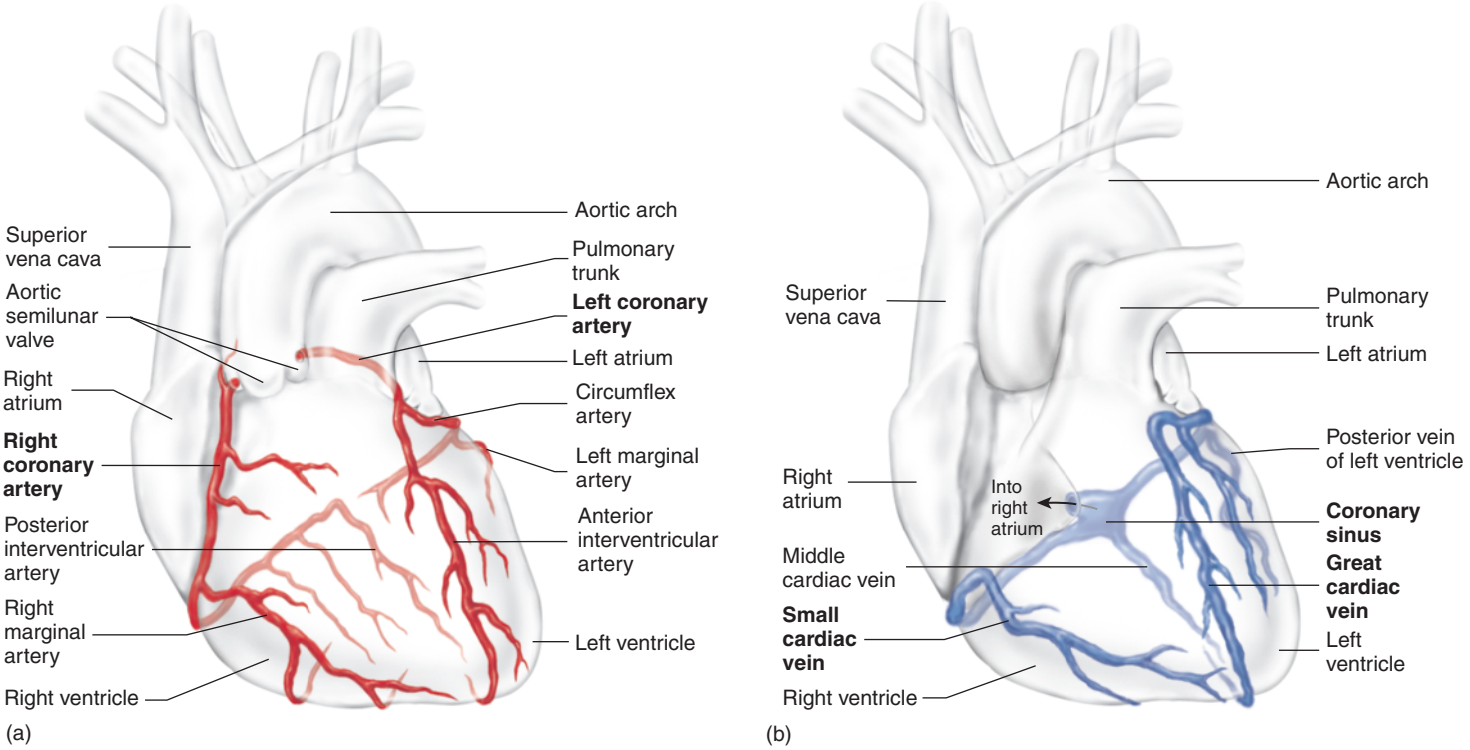


Figure 12.6 Blood Supply to the Heart

The vessels of the anterior surface of the heart are seen directly and are a darker color, whereas the vessels of the posterior surface are seen through the heart and are a lighter color. (*a*) Coronary arteries supply blood to the wall of the heart. (*b*) Cardiac veins carry blood from the wall of the heart back to the right atrium.

Cardiac Veins

The **cardiac veins** drain blood from the cardiac muscle. They are nearly parallel to the coronary arteries and most carry blood from cardiac muscle to the **coronary sinus,** a large vein located within the coronary sulcus on the posterior aspect of the heart. Blood flows from the coronary sinus into the right atrium (see figure 12.6*b*). Some small cardiac veins drain directly into the right atrium.

Heart Chambers and Internal Anatomy

The heart is a muscular pump consisting of four chambers: the two atria and two ventricles (figure 12.7).

Right and Left Atria

The atria of the heart receive blood from veins. The atria function primarily as reservoirs, where blood returning from veins collects before it enters the ventricles. Contraction of the atria forces blood into the ventricles to complete ventricular filling. The right atrium has two major openings, where large veins enter the heart from various parts of the body: the superior vena cava and the inferior vena cava (see figure 12.7). In addition, a smaller coronary sinus enters the right atrium from the wall of the heart (see figure 12.6*b*). The left atrium has four openings that receive the four pulmonary veins from the lungs (see figure 12.7). The two atria are separated from each other by a partition consisting of cardiac muscle called the **interatrial** (between the atria) **septum.**

Right and Left Ventricles

The ventricles of the heart are its major pumping chambers. They eject blood into the arteries and force it to flow through the circulatory system. The atria open into the ventricles, and each ventricle has one large outflow route located superiorly near the midline of the heart. The right ventricle opens into the pulmonary trunk, and the left ventricle opens into the aorta. The two ventricles are separated from each other by the muscular **interventricular** (between the ventricles) **septum** (see figure 12.7).

The wall of the left ventricle is thicker than the wall of the right ventricle because it generates a greater pressure than the right ventricle. When the left ventricle contracts, the pressure increases to approximately 120 mm Hg. When the right ventricle contracts, the pressure increases to approximately one-fifth of the pressure in the left ventricle, even though the left and right ventricles pump nearly the same volume of blood.

Heart Valves

Valves called **atrioventricular valves (AV)** are located between the right atrium and the right ventricle and between the left

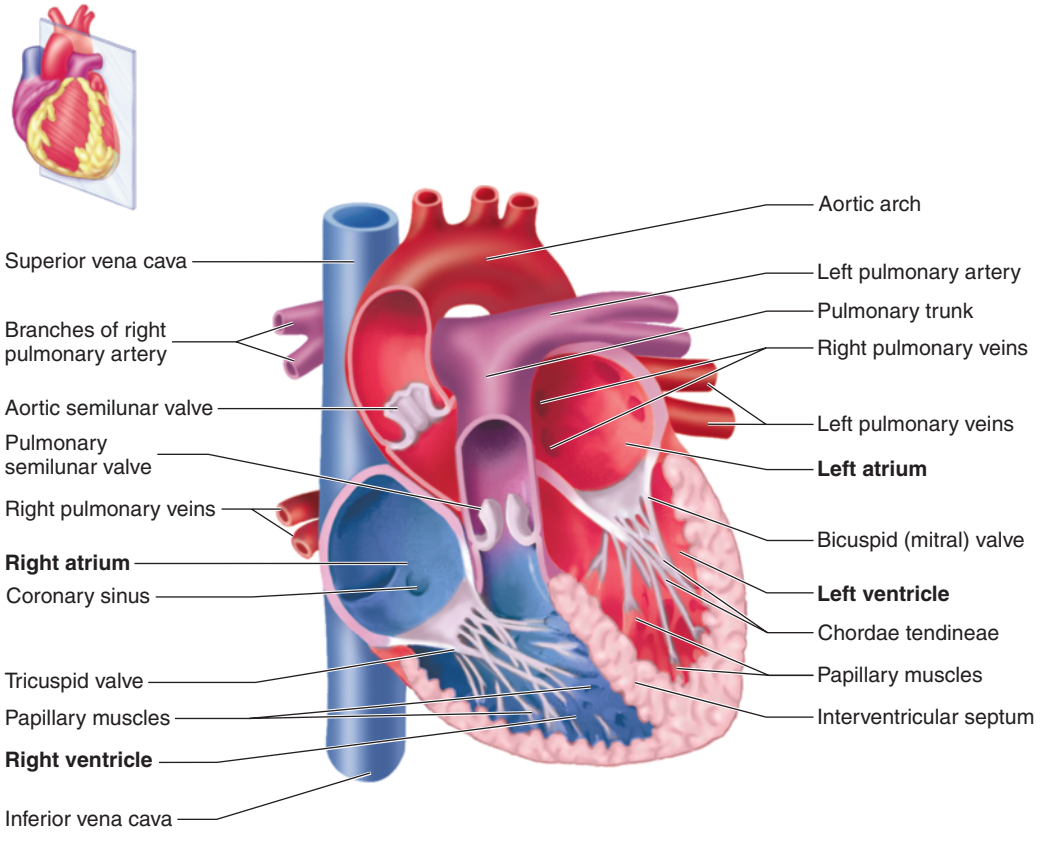
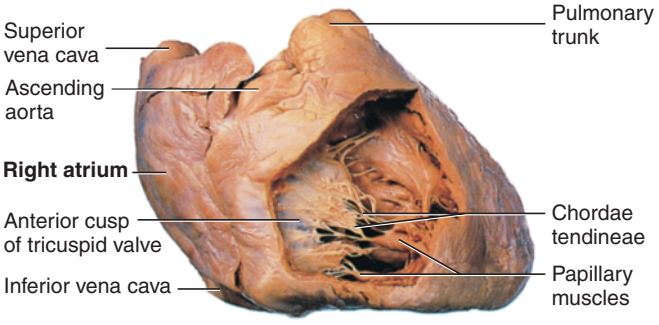


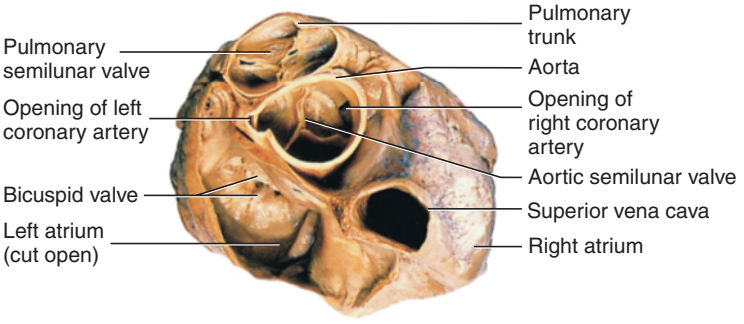
Figure 12.7 Internal Anatomy of the Heart

The heart is cut in a frontal plane to show the internal anatomy.

atrium and left ventricle. The AV between the right atrium and the right ventricle has three cusps and is called the **tricuspid valve** (see figure 12.7 and 12.8*a*). The AV between the left atrium and left ventricle has two cusps and is called the **bicuspid,** or **mitral** (resembling a bishop's miter, a two-pointed hat) **valve** (see figure 12.7 and 12.8*b*). These valves allow blood to flow from the atria into the ventricles but prevent it from flowing back into the atria. When the ventricles relax, blood flows from the atria into the ventricles and the valves are pushed open into the ventricles (figure 12.9*a*). In contrast, when the ventricles contract, blood pushes the valves back toward the atria, and the atrioventricular openings close as the valve cusps meet (figure 12.9*b*).

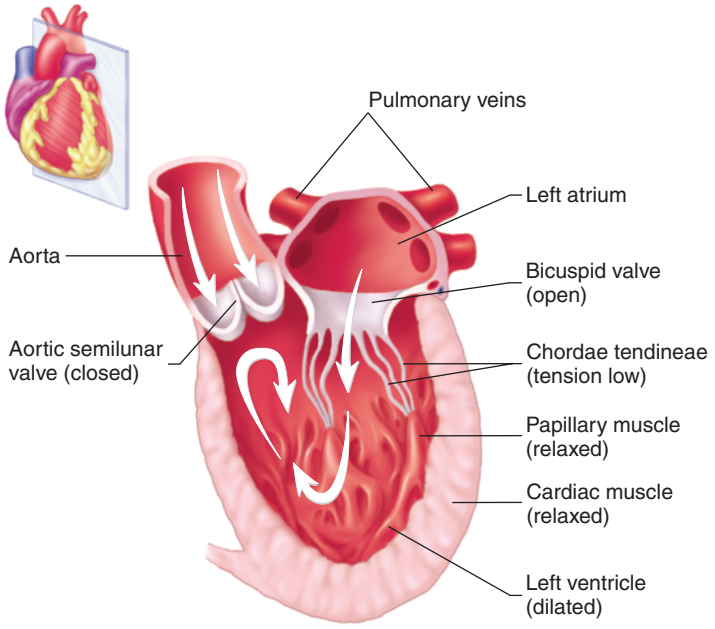


(a) View of the tricuspid valve, the chordae tendineae, and the papillary muscles.

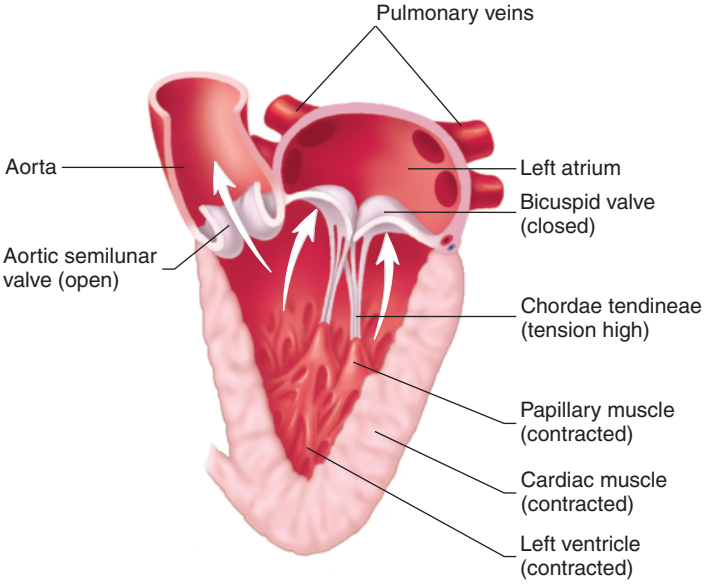


(b) A superior view of the heart valves. Note the three cusps of each semilunar valve meeting to prevent the backflow of blood.

Figure 12.8 Heart Valves



(a) When the bicuspid valve is open, the cusps of the valve are pushed by blood into the ventricle. Papillary muscles are relaxed and tension on the chordae tendineae is low. Blood flows from the left atrium into the left ventricle. When the aortic semilunar valve is closed, the cusps of the valve overlap as they are pushed by the blood in the aorta toward the ventricle. There is no blood flow from the aorta into the ventricle.



(b) When the bicuspid valve is closed, the cusps of the valves overlap as they are pushed by the blood toward the left atrium. There is no blood flow from the ventricle into the atrium. Papillary muscles are contracted and tension on the chordae tendineae is increased, which prevents the bicuspid valve from opening into the left atrium. When the aortic semilunar valve is open, the cusps of the valve are pushed by the blood toward the aorta. Blood then flows from the left ventricle into the aorta.

Figure 12.9 Function of the Heart Valves

Each ventricle contains cone-shaped muscular pillars called **papillary** (pap′ĭ-lār-ē, nipple- or pimple-shaped) **muscles.** These muscles are attached by thin, strong connective tissue strings called **chordae tendineae** (kōr′dē ten′di-nē-ē, heart strings) to the free margins of the cusps of the atrioventricular valves. When the ventricles contract, the papillary muscles contract and prevent the valves from opening into the atria by pulling on the chordae tendineae attached to the valve cusps (see figures 12.8*a* and 12.9).

The aorta and pulmonary trunk possess **aortic** and **pulmonary semilunar** (halfmoon-shaped) **valves,** respectively (see figure 12.7). Each valve consists of three pocketlike semilunar cusps (figures 12.8*b* and 12.9). When the ventricles contract, blood flowing out of the ventricles pushes against each valve, forcing the cusp to open (see figure 12.9*b*). When the ventricles relax, blood flows back from the aorta or pulmonary trunk toward the ventricle, it enters the pockets of the cusps, causing them to bulge toward and meet in the center of the aorta or pulmonary trunk, thus closing the vessels and keeping blood from flowing back into the ventricles (see figure 12.9*a*).

A plate of fibrous connective tissue, sometimes called the **skeleton of the heart,** consisting mainly of fibrous rings around the atrioventricular and semilunar valves, provides a solid support for the valves (figure 12.10). This connective tissue plate also serves as electrical insulation between the atria and the ventricles and provides a rigid site of attachment for the cardiac muscle.

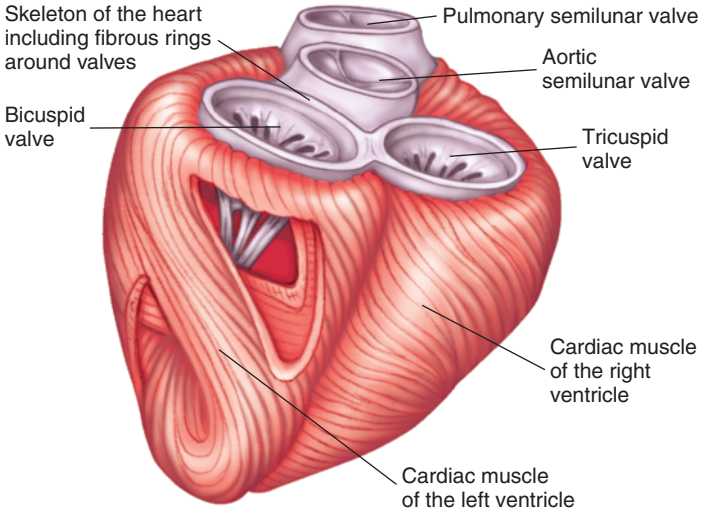


Figure 12.10 Skeleton of the Heart

The skeleton of the heart consists of fibrous connective tissue rings that surround the heart valves and separate the atria from the ventricles. Cardiac muscle attaches to the fibrous connective tissue. The muscle fibers are arranged so that when the ventricles contract a wringing motion is produced and the distance between the apex and base of the heart shortens.

Route of Blood Flow Through the Heart

Blood flow through the heart is depicted in figure 12.11. Even though blood flow through the heart is described for the right and then the left side of the heart, it is important to understand that both atria contract at the same time, and both ventricles contract at the same time. This concept is most important when the electrical activity, pressure changes, and heart sounds are considered.

Blood enters the right atrium from the systemic circulation through the superior and inferior venae cava, and from heart muscle through the coronary sinus (see figure 12.11*a* and *b*). Most of the blood flowing into the right atrium flows into the right ventricle while the right ventricle relaxes following the previous contraction. The right atrium then contracts, and enough blood is pushed from the right atrium into the right ventricle to complete right ventricular filling.

Following right atrial contraction, the right ventricle begins to contract. Contraction of the right ventricle pushes blood against the tricuspid valve, forcing it closed. After pressure within the right ventricle increases, the pulmonary semilunar valve is forced open, and blood flows into the pulmonary trunk. As the right ventricle relaxes, pressure in the pulmonary trunk is greater than in the right ventricle, and the back-flow of blood forces the pulmonary semilunar valve to close.

The pulmonary trunk branches to form the pulmonary arteries, which carry blood to the lungs, where carbon dioxide is released and oxygen is picked up. Blood returning from the lungs enters the left atrium through the four pulmonary veins (see figure 12.11*a* and *b*). Most of the blood flowing into the left atrium passes into the left ventricle while the left ventricle relaxes following the previous contraction. The left atrium then contracts, and enough blood is pushed from the left atrium into the left ventricle to complete left ventricular filling.

Following left atrial contraction, the left ventricle begins to contract. Contraction of the left ventricle pushes blood against the bicuspid valve, forcing it closed. After pressure within the left ventricle increases, the aortic semilunar valve is forced open, and blood flows into the aorta (see figure 12.11*a* and *b*). Blood flowing through the aorta is distributed to all parts of the body, except to that part of the lung supplied by the pulmonary blood vessels. As the left ventricle relaxes, pressure in the aorta is greater than in the left ventricle, and the back-flow of blood forces the aortic semilunar valve to close.

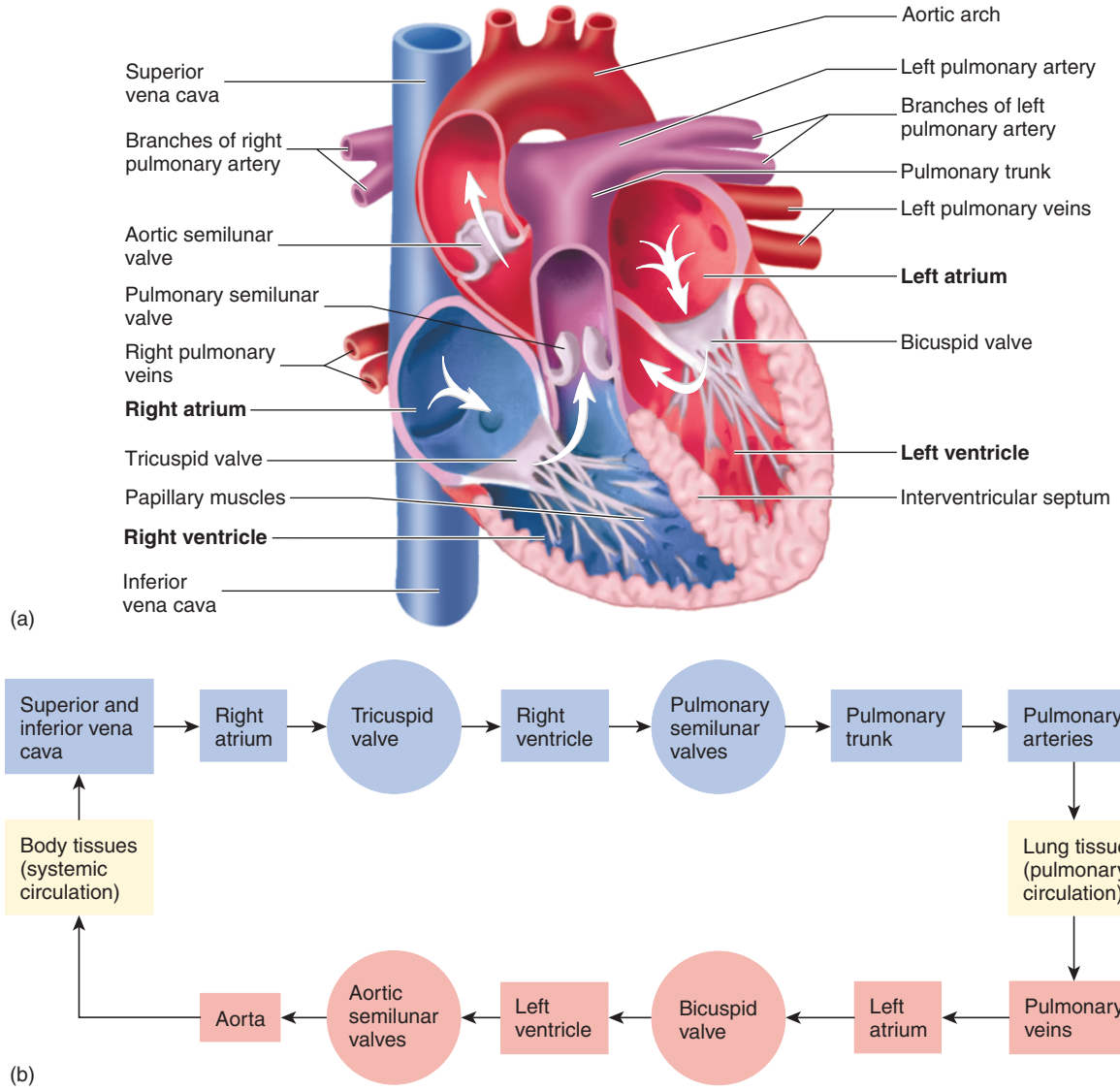


Figure 12.11 Blood Flow Through the Heart

(*a*) Frontal section of the heart revealing the four chambers and the direction of blood flow through the heart. (*b*) Diagram listing in order the structures through which blood flows in the systemic and pulmonary circulations. The heart valves are indicated by *circles;* deoxygenated blood (*blue*); oxygenated blood (*red*).

Histology of the Heart

Heart Wall

The heart wall is composed of three layers of tissue: the epicardium, the myocardium, and the endocardium (figure 12.12). The **epicardium** (ep-i-kar′dē-ŭm), also called the **visceral pericardium,** is a thin serous membrane forming the smooth outer surface of the heart. It consists of simple squamous epithelium overlying a layer of loose connective tissue and fat. The thick middle layer of the heart, the **myocardium** (mī-ō-kar′dē-ŭm), is composed of cardiac muscle cells and is responsible for the ability of the heart to contract. The smooth inner surface of the heart chambers is the **endocardium** (en-dō-kar′dē-ŭm), which consists of simple squamous epithelium over a layer of connective tissue. The endocardium allows blood to move easily through the heart. Each heart valve is formed by a fold of endocardium with connective tissue between the two layers.

The surfaces of the interior walls of the ventricles are modified by ridges and columns of cardiac muscle. Smaller muscular ridges are also found in portions of the atria.

Cardiac Muscle

Cardiac muscle cells are elongated, branching cells that contain one, or occasionally two, centrally located nuclei (figure 12.13). The cardiac muscle cells contain actin and myosin myofilaments organized to form sarcomeres, which are joined end-to-end to form myofibrils (see chapter 7). The actin and myosin myofilaments are responsible for muscle contraction, and their organization gives cardiac muscle a striated (banded) appearance. The striations are less regularly arranged and less numerous than is the case in skeletal muscle.

Adenosine triphosphate (ATP) provides the energy for cardiac muscle contraction, and, as in other tissues, ATP production depends on oxygen availability. Cardiac muscle cells are rich in mitochondria, which produce ATP at a rate rapid enough to sustain the normal energy requirements of cardiac muscle. An extensive capillary network provides an adequate oxygen supply to the cardiac muscle cells. Unlike skeletal muscle, however, cardiac muscle cannot develop a significant oxygen debt. Development of a large oxygen debt could result in muscular fatigue and cessation of cardiac muscle contraction.

Cardiac muscle cells are organized into spiral bundles or sheets. The cells are bound end-to-end and laterally to adjacent cells by specialized cell-to-cell contacts called **intercalated** (in-ter′kă-lā-ted, insertion between two others) **disks** (see figure 12.13). The membranes of the intercalated disks are highly folded, and the adjacent cells fit together, greatly increasing contact between them. Specialized cell membrane structures in the intercalated disks called **gap junctions** (see chapter 4) reduce electrical resistance between the cells, allowing action potentials to pass easily from one cell to adjacent cells. The cardiac muscle cells of the atria or ventricles, therefore, contract at nearly the same time. The highly coordinated contractions of the heart depend on this characteristic.

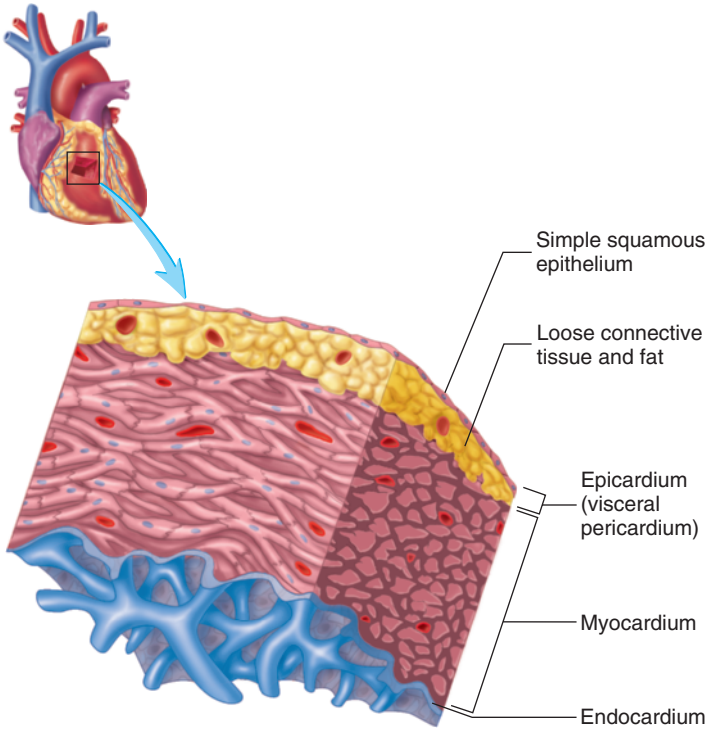


Figure 12.12 Heart Wall

Part of the wall of the heart has been removed, enlarged, and rotated so that the inner surface is visible. The enlarged section illustrates the epicardium (visceral pericardium), the myocardium, and the endocardium.

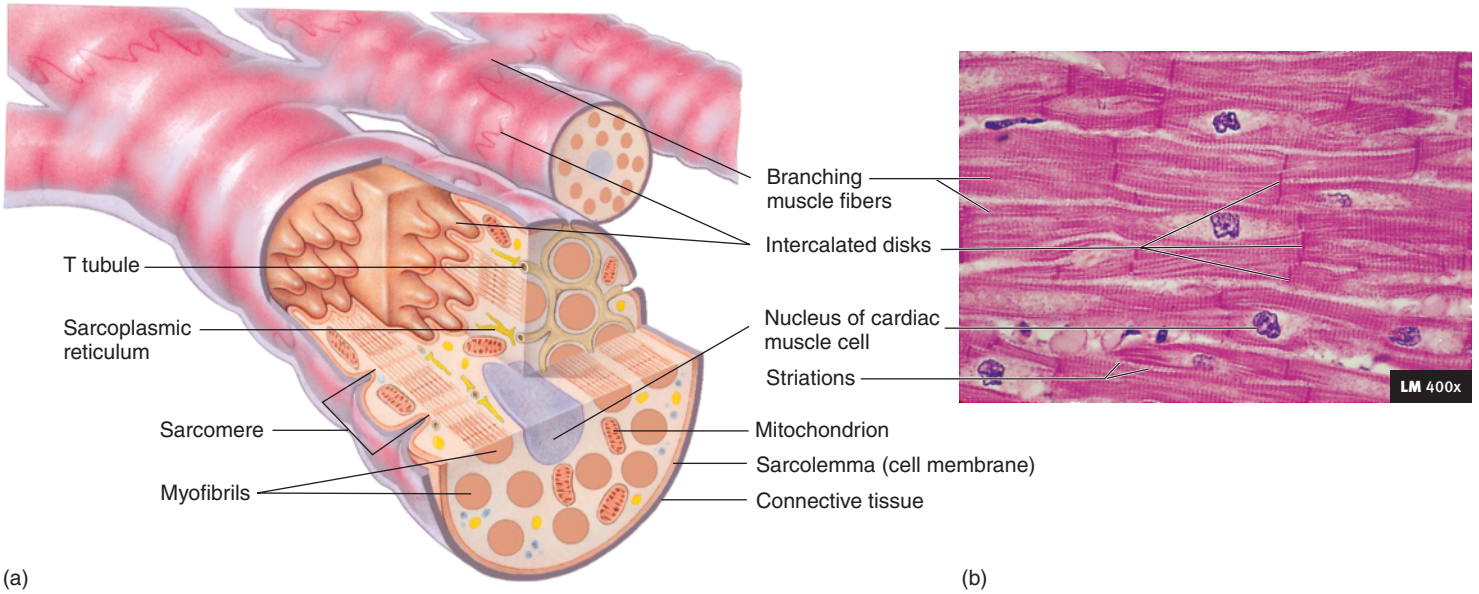


Figure 12.13 Cardiac Muscle Cells

(*a*) Cardiac muscle cells are branching cells with centrally located nuclei. As in skeletal muscle, sarcomeres join end-to-end to form myofibrils, and mitochondria provide ATP for contraction. The cells are joined to one another by intercalated disks, which allow action potentials to pass from one cardiac muscle cell to the next. Sarcoplasmic reticulum and T tubules are visible but are not as numerous as they are in skeletal muscle. (*b*) A light micrograph of cardiac muscle tissue. The cardiac muscle fibers appear to be striated because of the arrangement of the individual myofilaments.

Electrical Activity of the Heart

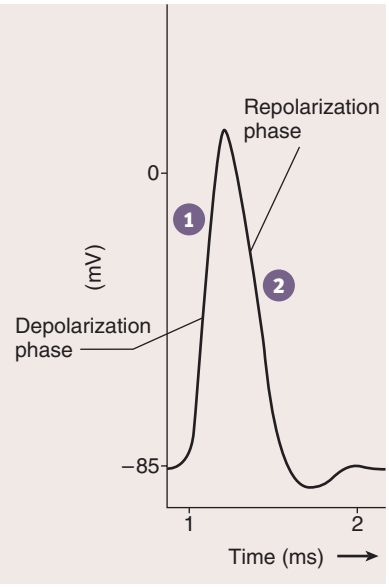
Action Potentials in Cardiac Muscle

Like action potentials in skeletal muscle and neurons, those in cardiac muscle exhibit depolarization followed by repolarization of the resting membrane potential. In cardiac muscle, however, the **plateau phase,** which is a period of slow repolarization, greatly prolongs the action potential (figure 12.14). In contrast to action potentials in skeletal muscle, which take less than 2 milliseconds (ms) to complete, action potentials in cardiac muscle take approximately 200 to 500 ms to complete.

Unlike in skeletal muscle, action potentials in cardiac muscle are conducted from cell to cell. Not only does the action potential take longer, but the rate of conduction in cardiac muscle cells is slower than the rate of conduction of action potentials in skeletal muscle cells and neurons.

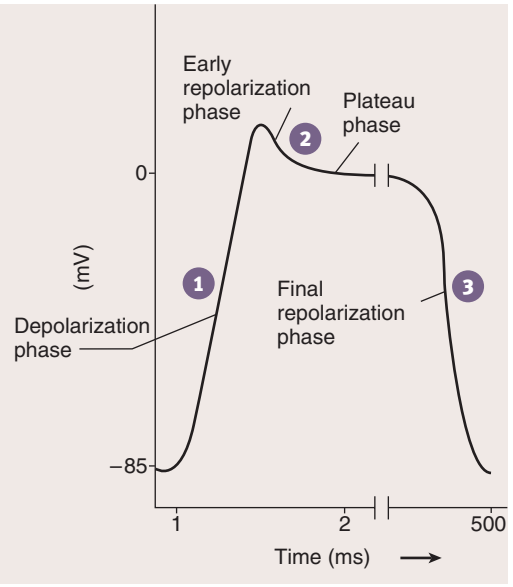
In cardiac muscle each action potential consists of a rapid **depolarization phase** followed by a rapid, but partial early **repolarization phase.** Then a longer period of slow repolarization, called the **plateau phase,** occurs. At the end of the plateau phase, a more rapid **final repolarization phase** takes place. During the final repolarization phase the membrane potential returns to its resting level (see figure 12.14).

Changes in membrane channels are responsible for the changes in the permeability of the cell membrane that produce action potentials. The depolarization phase of the action potential results from three permeability changes. **Voltage-gated Na^+ channels** open, increasing the permeability of the cell membrane to Na^+. Sodium ions then diffuse into the cell, causing depolarization. Voltage-gated K^+ channels quickly close, decreasing the permeability of the cell membrane to K^+. The decreased diffusion of K^+ out of the cell also causes depolarization. **Voltage-gated Ca^{2+} channels** slowly open, increasing the permeability of the cell membrane to Ca^{2+}. Calcium ions then diffuse into the cell and cause depolarization. It is not until the plateau phase that most of the voltage-gated Ca^{2+} channels are opened.



(a) Permeability changes due to voltage-gated channels opening and closing during an action potential in skeletal muscle:

1. **Depolarization phase**
   - Na^+ channels open.
   - K^+ channels begin to open.
2. **Repolarization phase**
   - Na^+ channels close.
   - K^+ channels continue to open causing repolarization.
   - K^+ channels close at the end of repolarization and return the membrane potential to its resting value.



(a) Permeability changes due to voltage-gated channels opening and closing during an action potential in cardiac muscle:

1. **Depolarization phase**
   - Na^+ channels open.
   - K^+ channels close.
   - Ca^{2+} channels begin to open.
2. **Early repolarization and plateau phases**
   - Na^+ channels close.
   - Some K^+ channels open, causing early repolarization.
   - Ca^{2+} channels are open, producing the plateau by slowing further repolarization.
3. **Final repolarization phase**
   - Ca^{2+} channels close.
   - Many K^+ channels open.

Process Figure 12.14 Comparison of Action Potentials in Skeletal and Cardiac Muscle

(*a*) An action potential in skeletal muscle consists of depolarization and repolarization phases. (*b*) An action potential in cardiac muscle consists of depolarization, early repolarization, plateau, and final repolarization phases. Cardiac muscle does not repolarize as rapidly as skeletal muscle (*indicated by the break in the curve*) because of the plateau phase.

Early repolarization occurs when the voltage-gated Na^+ channels close and a small number of **voltage-gated K^+ channels** open. Diffusion of Na^+ into the cell stops, and there is some movement of K^+ out of the cell. These changes in ion movement result in an early, but small repolarization.

The plateau phase occurs as voltage-gated Ca^{2+} channels continue to open, and the diffusion of Ca^{2+} into the cell counteracts the potential change produced by the diffusion of K^+ out of the cell. The plateau phase ends and final repolarization begins as the voltage-gated Ca^{2+} channels close, and many voltage-gated K^+ channels open. Diffusion of Ca^{2+} into the cell decreases and diffusion of K^+ out of the cell increases. These changes cause the membrane potential to return to its resting level.

Action potentials in cardiac muscle exhibit a **refractory period,** like that of action potentials in skeletal muscle and in neurons. The refractory period lasts about the same length of time as the prolonged action potential in cardiac muscle. The prolonged action potential and refractory period allow cardiac muscle to contract and almost complete relaxation to take place before another action potential can be produced. Also, the long refractory period in cardiac muscle prevents tetanic contractions from occurring, thus ensuring a rhythm of contraction and relaxation for cardiac muscle. Therefore, action potentials in cardiac muscle are different from those in skeletal muscle because of the plateau phase, which makes the action potential and its refractory period last longer.

P R E D I C T 2

Why is it important to prevent tetanic contractions in cardiac muscle but not in skeletal muscle?

The **sinoatrial (SA)** (sī′nō-a′trē′-ăl) **node,** which functions as the pacemaker of the heart, is located in the superior wall of the right atrium and initiates the contraction of the heart. The SA node is the pacemaker because it produces action potentials at a faster rate than other areas of the heart. The action potential of the SA node acts as a stimulus to adjacent areas of the heart. Also, the SA node action potentials have characteristics that are somewhat different from action potentials in the rest of the cardiac muscle. The SA node has a larger number of voltage-gated Ca^{2+} channels than other areas of the heart. As soon as the resting membrane potential is reestablished after an action potential, some of the voltage-gated Ca^{2+} channels open spontaneously. As they open, Ca^{2+} begin to diffuse into the cell and cause depolarization. The depolarization stimulates additional voltage-gated Ca^{2+} channels to open and voltage-gated Na^+ channels to open. Thus, additional Ca^{2+} and Na^+ diffuse into the cell and cause further depolarization. Quickly, threshold is reached and another action potential is produced. Drugs called Ca^{2+} channel blocking agents are used to treat some types of tachycardia (rapid heart rate) and arrhythmia (abnormal rhythm) because they block Ca^{2+} channels and slow the rate of action potential production.

Conduction System of the Heart

Contraction of the atria and ventricles is coordinated by specialized cardiac muscle cells in the wall of the heart that form the **conduction system of the heart** (figure 12.15). Action potentials originate in the SA node and spread over the right and left atria, causing them to contract.

A second area of the heart, called the **atrioventricular (AV)** (ā-trē-ō-ven′trik′-ū′lăr) **node,** is located in the lower portion of the right atrium. When action potentials reach the AV node, they spread slowly through it and then into a bundle of specialized cardiac muscle called the **atrioventricular bundle.** The slow rate of action potential conduction in the AV node allows the atria to complete their contraction before action potentials are delivered to the ventricles.

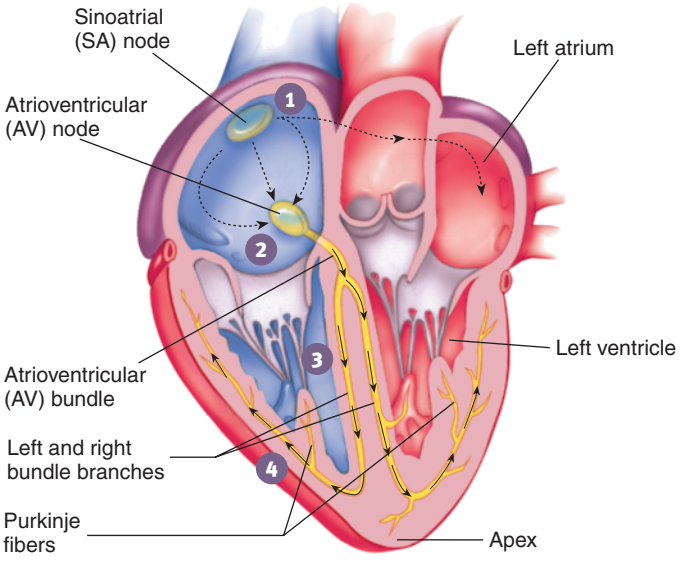
After action potentials pass through the AV node, they are transmitted through the AV bundle, which projects through the fibrous connective tissue plate that separates the atria from the ventricles (see figure 12.10). The AV bundle then divides into two branches of conducting tissue called the **left** and **right**

1. Action potentials originate in the sinoatrial (SA) node and travel across the wall of the atrium (*arrows*) from the SA node to the atrioventricular (AV) node.

2. Action potentials pass through the AV node and along the atrioventricular (AV) bundle, which extends from the AV node, through the fibrous skeleton, into the interventricular septum.

3. The AV bundle divides into right and left bundle branches, and action potentials descend to the apex of each ventricle along the bundle branches.

4. Action potentials are carried by the Purkinje fibers from the bundle branches to the ventricular walls.



Process Figure 12.15 Conduction System of the Heart

bundle branches (see figure 12.15). At the tips of the left and right bundle branches, the conducting tissue forms many small bundles of **Purkinje** (pŭr-kĭn′jē, Johannes von Purkinje, Bohemian anatomist, 1787–1869) **fibers.** These Purkinje fibers pass to the apex of the heart and then extend to the cardiac muscle of the ventricle walls. The AV bundle, the bundle branches, and the Purkinje fibers are composed of specialized cardiac muscle fibers that conduct action potentials more rapidly than do other cardiac muscle fibers. Consequently, action potentials are rapidly delivered to all the cardiac muscle of the ventricles. The coordinated contraction of the ventricles depends on the conduction of action potentials by the conduction system.

PREDICT 3

If blood supply is reduced in a small area of the heart through which the left bundle branch passed, predict the effect on ventricular contractions.

Following their contraction, the ventricles begin to relax. After the ventricles have completely relaxed, another action potential originates in the SA node to begin the next cycle of contractions.

The SA node is the pacemaker of the heart, but other cardiac muscle cells also are capable of producing action potentials spontaneously. For example, if the SA node is unable to function, another area of the heart, such as the AV node, becomes the pacemaker. The resulting heart rate is much slower than normal. When action potentials originate in an area of the heart other than the SA node, the result is called an **ectopic** (ek-top′ik) **beat.**

Fibrillation of the Heart

Cardiac muscle can also act as if there are thousands of pacemakers, each making a very small portion of the heart contract rapidly and independently of all other areas. This condition is called **fibrillation** (fī-bri-lā′shŭn), and it reduces the output of the heart to only a few milliliters of blood per minute when it occurs in the ventricles. Death of the individual results in a few minutes unless fibrillation of the ventricles is stopped.

To stop the process of fibrillation, defibrillation is used, in which a strong electrical shock is applied to the chest region. The electrical shock causes simultaneous depolarization of all cardiac muscle fibers. Following depolarization, the SA node can recover and produce action potentials before any other area of the heart. Consequently, the normal pattern of action potential generation and the normal rhythm of contraction can be reestablished.

Fibrillation of the heart is more likely to occur when action potentials originate at ectopic sites in the heart. For example, people who have ectopic beats that originate from one of their ventricles are more likely to develop fibrillation of the heart than people who have normal heart beats.

Electrocardiogram

Action potentials conducted through the heart during the cardiac cycle produce electrical currents that can be measured at the surface of the body. Electrodes placed on the surface of the body and attached to a recording device can detect the small electrical changes resulting from the action potentials in all of the cardiac muscle cells. The record of these electrical events is an **electrocardiogram** (**ECG** or **EKG**) (figure 12.16).

The normal ECG consists of a P wave, a QRS complex, and a T wave. The **P wave** results from depolarization of the atrial myocardium, and the beginning of the P wave precedes the onset of atrial contraction. The **QRS complex** consists of three individual waves: the Q, R, and S waves. The QRS complex results from depolarization of the ventricles, and the beginning of the QRS complex precedes ventricular contraction. The **T wave** represents repolarization of the ventricles, and the beginning of the T wave precedes ventricular relaxation. A wave representing repolarization of the atria cannot be seen because it occurs during the QRS complex.

The time between the beginning of the P wave and the beginning of the QRS complex is the **PQ interval,** commonly called the **PR interval** because the Q wave is very small. During the PQ interval the atria contract and begin to relax. At the end of the PQ interval the ventricles begin to depolarize.

The **QT interval** extends from the beginning of the QRS complex to the end of the T wave and represents the length of time required for ventricular depolarization and repolarization. Table 12.1 describes several conditions associated with abnormal heart rhythms.

PREDICT 4

Explain how the ECGs appear for a person who has a damaged left bundle branch (see Predict 3) and for a person who has many ectopic beats originating from her atria.

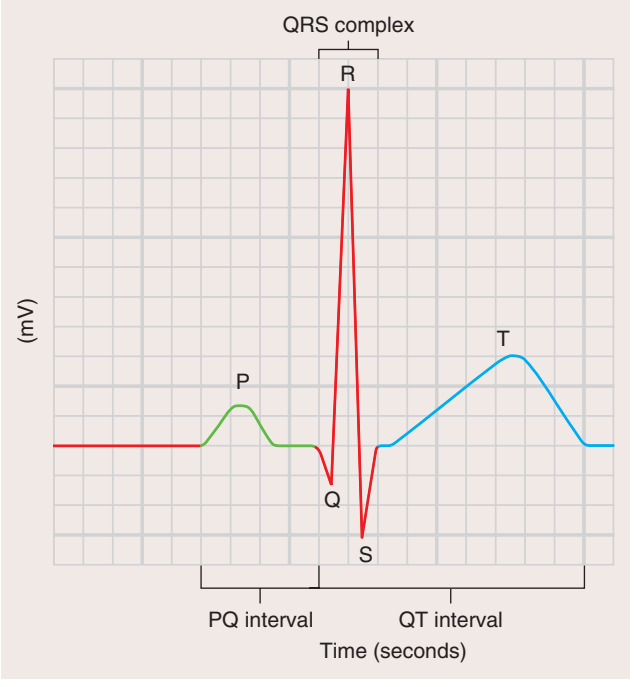


Figure 12.16 Electrocardiogram

The major waves and intervals of an electrocardiogram are labeled. Each thin horizontal line on the ECG recording represents 1 mV, and each thin vertical line represents 0.04 second.

Table 12.1 Major Cardiac Arrhythmias

Condition	Symptoms	Possible Causes
Abnormal Heart Rhythms		
Tachycardia	Heart rate in excess of 100 bpm	Elevated body temperature, excessive sympathetic stimulation, toxic conditions
Bradycardia	Heart rate less than 60 bpm	Increased stroke volume in athletes, excessive vagus nerve stimulation, nonfunctional SA node, carotid sinus syndrome
Sinus arrhythmia	Heart rate varies as much as 5% during respiratory cycle and up to 30% during deep respiration	Cause not always known; occasionally caused by ischemia, inflammation, or cardiac failure
Paroxysmal atrial tachycardia	Sudden increase in heart rate to 95–150 bpm for a few seconds or even for several hours; P waves precede every QRS complex; P wave inverted and superimposed on T wave	Excessive sympathetic stimulation, abnormally elevated permeability of cardiac muscle to Ca^{2+}
Atrial flutter	As many as 300 P waves/min and 125 QRS complexes/min; resulting in two or three P waves (atrial contractions) for every QRS complex (ventricular contraction)	Ectopic beats in the atria
Atrial fibrillation	No P waves, normal QRS and T waves, irregular timing, ventricles are constantly stimulated by atria, reduced ventricle filling; increased chance of fibrillation	Ectopic beats in the atria
Ventricular tachycardia	Frequently causes fibrillation	Often associated with damage to AV node or ventricular muscle
Heart Blocks		
SA node block	No P waves, low heart rate resulting from AV node acting as the pacemaker, normal QRS complexes and T waves	Ischemia, tissue damage resulting from infarction; cause sometimes is unknown
AV node blocks		
First-degree	PQ interval greater than 0.2 s	Inflammation of AV bundle
Second-degree	PQ interval 0.25–0.45 s; some P waves trigger QRS complexes and others do not; examples of 2:1, 3:1, and 3:2 P wave/QRS complex ratios	Excessive vagus nerve stimulation, AV node damage
Complete heart block	P wave dissociated from QRS complex, atrial rhythm about 100 bpm, ventricular rhythm less than 40 bpm	Ischemia of AV node or compression of AV bundle
Premature Contractions		
Premature atrial contractions	Occasional shortened intervals between one contraction and the succeeding contraction; frequently occurs in healthy people	Excessive smoking, lack of sleep, or too much caffeine
Premature ventricular contractions (PVCs)	Prolonged QRS complex, exaggerated voltage because only one ventricle may depolarize, possible inverted T wave, increased probability of fibrillation	Ectopic beat in ventricles, lack of sleep, too much coffee, irritability; occasionally occurs with coronary thrombosis

The ECG as a Diagnostic Tool

The ECG is not a direct measurement of mechanical events in the heart, and neither the force of contraction nor the blood pressure can be determined from it. Each deflection in the ECG record, however, indicates an electrical event within the heart and correlates with a subsequent mechanical event. Consequently, it is an extremely valuable diagnostic tool in identifying a number of cardiac abnormalities, particularly because it is painless, easy to record, and does not require surgical procedures. Abnormal heart rates or rhythms, abnormal conduction pathways such as blockages in the conduction pathways, hypertrophy or atrophy of portions of the heart, and the approximate location of damaged cardiac muscle can be determined from analysis of an ECG.

Cardiac Cycle

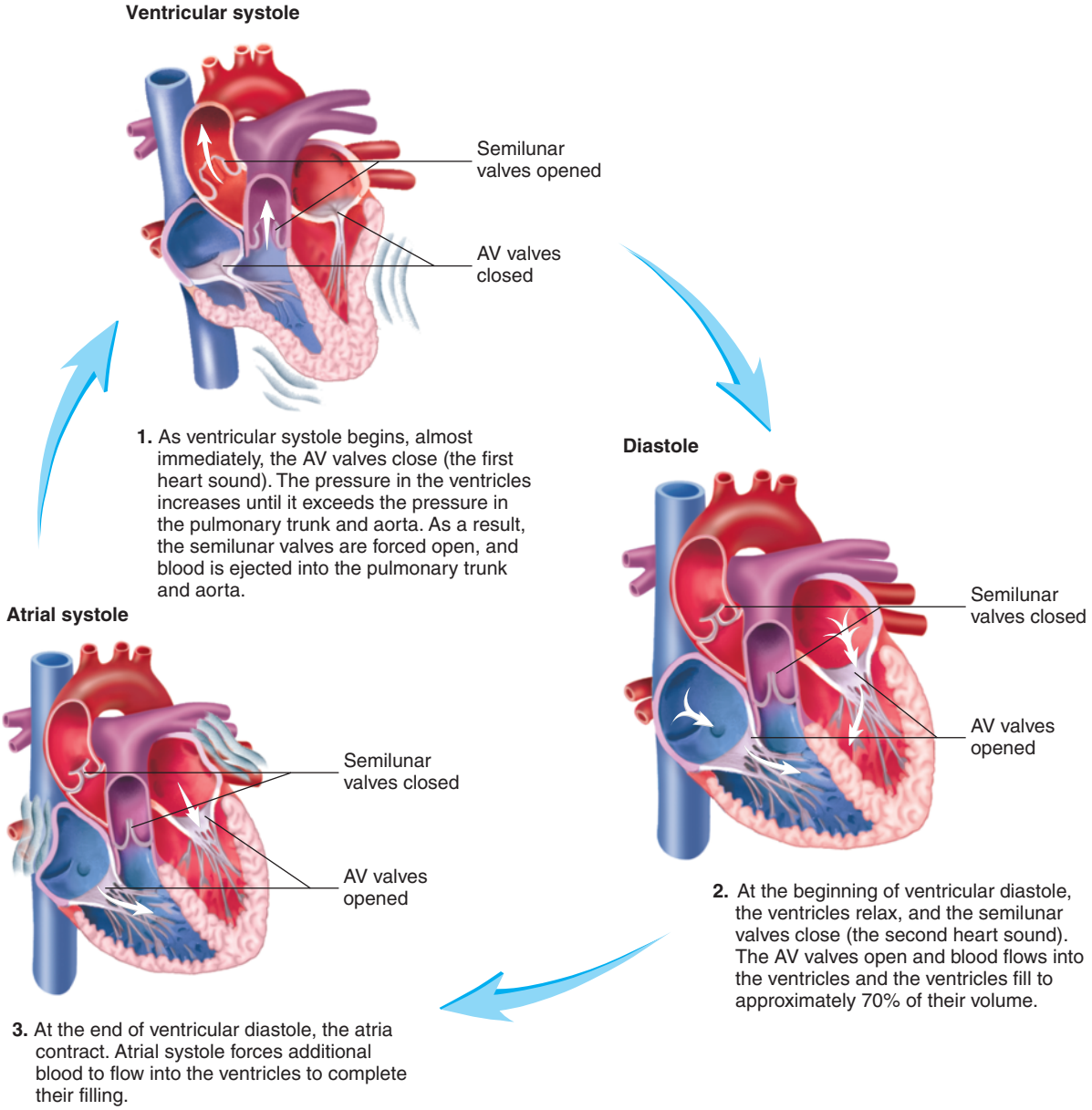
The heart can be viewed as two separate pumps represented by the right and left halves of the heart. Each pump consists of a primer pump—the atrium—and a power pump—the ventricle. The atria act as primer pumps because they complete the

filling of the ventricles with blood, and the ventricles act as power pumps because they produce the major force that causes blood to flow through the pulmonary and systemic circulations. The term **cardiac cycle** refers to the repetitive pumping process that begins with the onset of cardiac muscle contraction and ends with the beginning of the next contraction (figure 12.17). Pressure changes produced within the heart chambers as a result of cardiac muscle contraction are responsible for blood movement because blood moves from areas of higher pressure to areas of lower pressure.

Atrial systole (sis′tō-lē, a contracting) refers to contraction of the two atria. **Ventricular systole** refers to contraction of the two ventricles. **Atrial diastole** (dī-as′tō-lē, dilation) refers to relaxation of the two atria, and **ventricular diastole** refers to relaxation of the two ventricles. When the terms **systole** and **diastole** are used without reference to the atria or ventricles, they refer to ventricular contraction or relaxation. The ventricles contain more cardiac muscle than the atria and produce a far greater pressure, which forces blood to circulate throughout the vessels of the body.

The major events of the cardiac cycle are

1. As systole begins, contraction of the ventricles pushes blood toward the atria, causing the AV valves to close. When the pressure in the ventricles exceeds the pressure in the pulmonary trunk and aorta, the semilunar valves are forced open, and blood is ejected into the pulmonary trunk and aorta (see figure 12.17 step 1).
2. At the beginning of ventricular diastole, the pressure in the ventricles decreases. The semilunar valves close and prevent blood from flowing back into the ventricles. The



Process Figure 12.17 The Cardiac Cycle

pressure continues to decline in the ventricles until finally the AV valves open and blood flows directly from the atria into the relaxed ventricles. During the previous ventricular systole, the atria were relaxed and blood collected in them. When the ventricles relax and the AV valves open, blood flows into the ventricles (see figure 12.17 step 2) and fills them to approximately 70% of their volume.

3. At the end of ventricular diastole, the atria contract and then relax. Atrial systole forces additional blood to flow into the ventricles to complete their filling (see figure 12.17 step 3). The semilunar valves remain closed.

Figure 12.18 displays the main events of the cardiac cycle in graphic form and should be examined from top to bottom for each period of the cardiac cycle. The ECG indicates the electrical

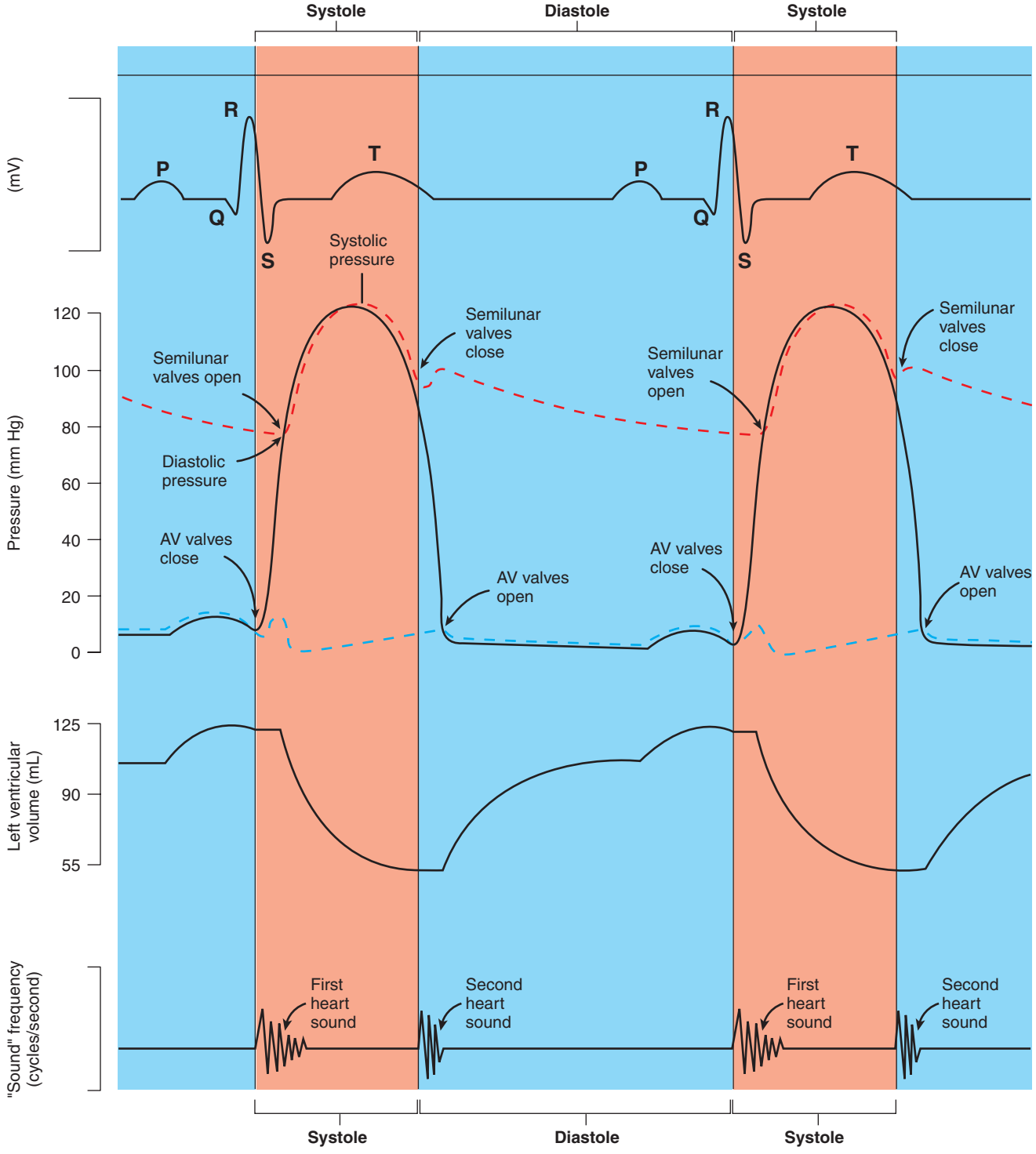


Figure 12.18 Events Occurring During the Cardiac Cycle (see Table 12.2)

The cardiac cycle is divided into systole and diastole (*see top of figure*). Within systole and diastole, four graphs are presented. From *top* to *bottom,* the electrocardiogram; pressure changes for the left atrium (*blue line*), left ventricle (*black line*), and aorta (*red line*); left ventricular volume curve; and heart sounds are illustrated.

events that cause contraction and relaxation of the atria and ventricles. The pressure graph shows the pressure changes within the left atrium, left ventricle, and aorta resulting from atrial and ventricular contraction and relaxation. The pressure changes on the right side of the heart are not shown here, but they are similar to those in the left side, only lower. The volume graph presents the changes in left ventricular volume as blood flows into and out of the left ventricle as a result of the pressure changes. The sound graph records the closing of valves caused by blood flow. See figure 12.17 for illustration of the valves and blood flow and table 12.2 for a summary of the events occurring during each period.

The Consequences of an Incompetent Bicuspid Valve

Incompetent valves do not close completely and therefore they leak when they are supposed to be closed. Incompetent valves allow blood to flow in the reverse direction. For example, an incomepetent bicuspid valve allows blood to flow from the left ventrical to the left atrium during ventricular systole. This reduces the amount of blood pumped into the aorta. It also dramatically increases the blood pressure in the left atrium and in the pulmonary veins during ventricular systole. During diastole, the excess blood pumped into the atrium once again flows into the ventricle along with the blood that normally flows from the lungs to the left atrium. Therefore, the volume of blood entering the left ventricle is greater than normal. The increased filling of the left ventricle gradually causes it to hypertrophy and can lead to heart failure. The increased pressure in the pulmonary veins can cause edema in the lungs.

PREDICT 5

Predict the effect of a leaky (incompetent) aortic semilunar valve on the volume of blood in the left ventricle just before ventricular contraction. Predict the effect of a severely narrowed opening through the aortic semilunar valves on the amount of work the heart must do to pump the normal volume of blood into the aorta during each beat of the heart.

Heart Sounds

A **stethoscope** (steth′ō-skōp, *stetho,* the chest) was originally developed to listen to the sounds of the lungs and heart and is now used to listen to other sounds of the body (figure 12.19). There are two main heart sounds. The **first heart sound** can be represented by the syllable **lubb,** and the **second heart sound** can be

Table 12.2 Summary of Events of the Cardiac Cycle for the Left Atrium and Ventricle (see figure 12.18)

	Ventricular Systole	Ventricular Diastole
ECG	The QRS complex is completed and the ventricles are stimulated to contract. The T wave begins.	The T wave is completed and the ventricles relax. Then the P wave stimulates the atria to contract, after which they relax.
Ventricular pressure curve (*black*)	Pressure increases rapidly as a result of left ventricular contraction. When left ventricular pressure exceeds aortic pressure, blood pushes the aortic semilunar valve open. Continued contraction increases ventricular pressure to a peak value of 120 mm Hg. Ventricular pressure then decreases as blood flows out of the left ventricle into the aorta.	Ventricular pressure decreases rapidly to nearly zero as the left ventricle relaxes.
Aortic pressure curve (*red*)	As ventricular contraction forces blood into the aorta, pressure in the aorta increases to its highest value (120 mm Hg), called the systolic pressure.	Ventricular pressure decreases below aortic pressure. Blood flows back toward the left ventricle and the aortic semilunar valve closes. As blood flows out of the aorta toward the body, elastic recoil of the aorta prevents a sudden decrease in pressure. Just before the aortic semilunar valve opens, pressure in the aorta decreases to its lowest value (80 mm Hg), called the diastolic pressure.
Atrial pressure curve (*blue*)	Atrial pressure increases slightly as contraction of the left ventricle pushes blood toward the left atrium. After closure of the bicuspid valve, pressure drops as the left atrium relaxes, then increases as blood flows into the atrium from the inferior vena cava and superior vena cava.	After the bicuspid valve opens, pressure decreases slightly as blood flows into the left ventricle. At the end of ventricular diastole, contraction of the left atrium increases the pressure.
Volume graph	Blood pushes the aortic semilunar valve opens, blood is ejected from the left ventricle, and ventricular volume decreases.	Blood flows from the left atrium into the left ventricle, accounting for 70% of ventricular filling. Near the end of ventricular diastole, contraction of the left atrium pushes blood into the left ventricle, completing ventricular filling.
Sound graph	As contraction of the ventricles pushes blood toward the atria, the AV valves close, preventing the flow of blood into the atria and producing the first heart sound.	As blood flows back toward the heart, the semilunar valves close, preventing the flow of blood into the ventricles and producing the second heart sound.

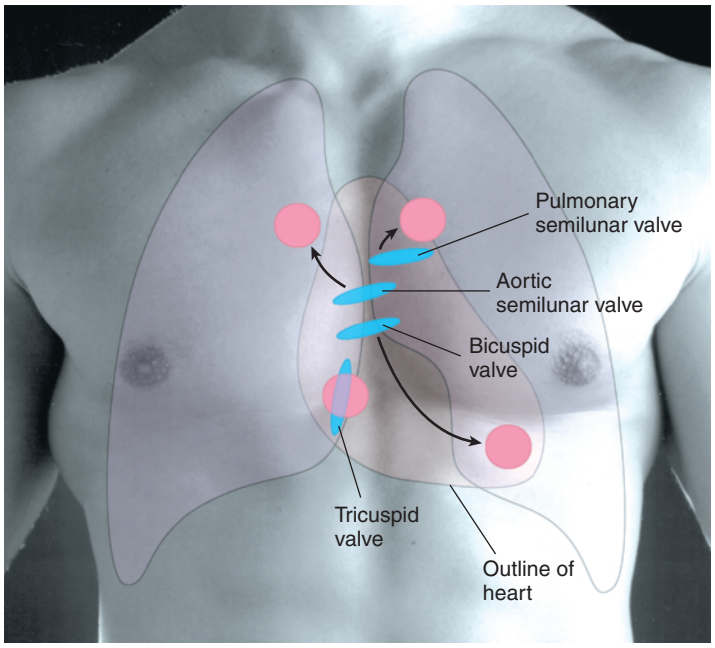


Figure 12.19 Location of the Heart Valves in the Thorax

Surface markings of the heart in the male. The positions of the four heart valves are indicated by *blue ellipses,* and the sites where the sounds of the valves are best heard with the stethoscope are indicated by *pink circles*.

represented by **dupp.** The first heart sound has a lower pitch than the second. The first heart sound occurs at the beginning of ventricular systole and results from closure of the AV valves (see figure 12.17 step 1 and 12.18). The second heart sound occurs at the beginning of ventricular diastole and results from closure of the semilunar valves (see figure 12.17 step 2 and 12.18). The valves usually do not make sounds when they open.

Clinically, ventricular systole occurs between the first and second heart sounds. Ventricular diastole occurs between the second heart sound and the first heart sound of the next beat. Because ventricular diastole lasts longer than ventricular systole, there is less time between the first and second heart sounds than between the second heart sound and the first heart sound of the next beat.

P R E D I C T 6

Compare the rate of blood flow out of the ventricles between the first and second heart sounds of the same beat with the rate of blood flow out of the ventricles between the second heart sound of one beat and the first heart sound of the next beat.

Abnormal heart sounds called **murmurs** are usually a result of faulty valves. For example, an **incompetent valve** fails to close tightly and blood leaks through the valve when it is closed. A murmur caused by an incompetent valve makes a swishing sound immediately after closure of the valve. For example, an incompetent bicuspid valve results in a swishing sound immediately after the first heart sound.

When the opening of a valve is narrowed, or **stenosed** (sten′ozd, a narrowing), a swishing sound precedes closure of the stenosed valve. For example, when the bicuspid valve is stenosed, a swishing sound precedes the first heart sound.

P R E D I C T 7

If normal heart sounds are represented by lubb–dupp, lubb–dupp, what does a heart sound represented by lubb–duppshhh, lubb–duppshhh represent? What does lubb–shhhdupp, lubb–shhhdupp represent (assume that shhh represents a swishing sound)?

Regulation of Heart Function

Cardiac output (CO) is the volume of blood pumped by either ventricle of the heart each minute. Cardiac output can be calculated by multiplying the stroke volume times the heart rate. **Stroke volume (SV)** is the volume of blood pumped per ventricle each time the heart contracts, and the **heart rate (HR)** is the number of times the heart contracts each minute.

$$\underset{\text{(mL/min)}}{\text{CO}} = \underset{\text{(mL/beat)}}{\text{SV}} \times \underset{\text{(beats/min)}}{\text{HR}}$$

Under resting conditions, the heart rate is approximately 72 beats/min (or bpm) and the stroke volume is approximately 70 mL/beat. Consequently, the cardiac output is slightly more than 5 L/min:

$$\begin{aligned}\text{CO} &= \text{SV} \times \text{HR}\\ &= 70\ \text{mL/beat} \times 72\ \text{bpm}\\ &= 5040\ \text{mL/min (approximately 5 L/min)}\end{aligned}$$

The heart rate and the stroke volume vary considerably among people. Athletes tend to have a larger stroke volume and lower heart rate at rest because exercise has increased the size of their hearts. Nonathletes are more likely to have a higher heart rate and lower stroke volume. During exercise the heart in a nonathlete can increase to 190 bpm and the stroke volume can increase to 115 mL/beat. Therefore, the cardiac output increases to approximately 22 L/min:

$$\begin{aligned}\text{CO} &= \text{SV} \times \text{HR}\\ &= 115\ \text{mL/beat} \times 190\ \text{bpm}\\ &= 21{,}850\ \text{mL/min (approximately 22 L/min)}\end{aligned}$$

This produces a cardiac output that is several times greater than the cardiac output under resting conditions. Athletes can increase their cardiac output to a greater degree than nonathletes.

The control mechanisms that modify the stroke volume and the heart rate are classified as intrinsic and extrinsic mechanisms.

Intrinsic Regulation of the Heart

Intrinsic regulation of the heart refers to mechanisms contained within the heart itself. The force of contraction produced by cardiac muscle is related to the degree of stretch of cardiac muscle fibers. The amount of blood in the ventricles at the end of ventricular diastole determines the degree to which cardiac muscle fibers are stretched. **Venous return** is the amount of blood that returns to the heart, and the degree to which the ventricular walls are stretched at the end of diastole is called **preload.** If venous return increases, the heart fills to a greater volume and stretches

Clinical Focus Conditions and Diseases Affecting the Heart

Heart Diseases

Inflammation of Heart Tissues

Endocarditis (en′dō-kar-dī′tis) is inflammation of the endocardium. It affects the valves more severely than other areas of the heart and may lead to deposition of scar tissue, causing valves to become stenosed or incompetent.

Myocarditis (mī′ō-kar-dī′tis) is inflammation of the myocardium and can lead to heart failure.

Pericarditis (per′i-kar-dī′tis) is inflammation of the pericardium. Pericarditis can result from bacterial or viral infections and can be extremely painful.

Rheumatic (roo-mat′ik) **heart disease** can result from a **streptococcal** (strep′tō-kok′ăl) **infection** in young people. Toxin produced by the bacteria can cause an immune reaction called rheumatic fever approximately 2–4 weeks after the infection. The immune reaction can cause inflammation of the endocardium, called **rheumatic endocarditis.** The inflamed valves, especially the bicuspid valve, can become stenosed or incompetent. The effective treatment of streptococcal infections with antibiotics has reduced the frequency of rheumatic heart disease.

Reduced Blood Flow to Cardiac Muscle

Coronary heart disease reduces the amount of blood that the coronary arteries are able to deliver to the myocardium. The reduction in blood flow can damage the myocardium. The degree of damage depends on the size of the arteries involved, whether occlusion (blockage) is partial or complete, and whether occlusion is gradual or sudden. As the walls of the arteries thicken and harden with age, the volume of blood they can supply to the heart muscle declines, and the ability of the heart to pump blood decreases. Inadequate blood flow to the heart muscle can result in **angina pectoris,** which is a poorly localized sensation of pain in the region of the chest, left arm, and left shoulder.

Degenerative changes in the artery wall can cause the inside surface of the artery to become roughened. The chance of platelet aggregation increases at the rough surface, which increases the chance of **coronary thrombosis** (throm-bō′sis), the formation of a blood clot in a coronary vessel. Inadequate blood flow can cause an **infarct** (in′farkt), an area of damaged cardiac tissue. A heart attack is often referred to as a coronary thrombosis or a **myocardial infarction.** The outcome of coronary thrombosis depends on the extent of the damage to heart muscle caused by inadequate blood flow and whether other blood vessels can supply enough blood to maintain the function of the heart. Death can occur swiftly if the infarct is large; if the infarct is small, the heart can continue to function. In some cases, the infarct weakens the wall of the heart, and the wall ruptures; but in most cases scar tissue replaces damaged cardiac muscle in the area of the infarct.

People who survive infarctions often lead fairly normal lives if they take precautions. Most cases call for moderate exercise, adequate rest, a disciplined diet, and reduced stress. Small doses of aspirin and treatments, including drugs, to reduce elevated blood pressure appear to provide protection against the development of myocardial infarcts.

Congenital Conditions Affecting the Heart

Congenital (occuring at birth) **heart disease** is heart disease present at birth and is the result of abnormal development of the heart. The following are common congenital defects:

A **septal defect** is a hole in a septum between the left and right sides of the heart. The hole may be in the interatrial or interventricular septum. These defects allow blood to flow from one side of the heart to the other and, as a consequence, greatly reduce the pumping effectiveness of the heart.

Patent (to lie open) **ductus arteriosus** (dŭk′tŭs artēr′ē-ō-sŭs) results when a blood vessel called the **ductus arteriosus,** which is present in the fetus, fails to close after birth. The ductus arteriosus extends between the pulmonary trunk and the aorta. It allows blood to pass from the pulmonary trunk to the aorta, thus bypassing the lungs. This is normal before birth because the lungs are not functioning. If the ductus arteriosus fails to close after birth, however, blood flows in the opposite direction, from the aorta to the pulmonary trunk. As a consequence, blood flows through the lungs under a higher pressure and damages them. In addition, the amount of work required of the left ventricle to maintain an adequate systemic blood pressure increases.

Stenosis (ste-nō′sis) **of the heart valves** is a narrowed opening through one or more of the heart valves. In aortic or pulmonary semilunar valve stenosis, the workload of the heart is increased because the ventricles must contract with a much greater force to pump blood from the ventricles. Stenosis of the bicuspid valve prevents the flow of blood into the left ventricle, causing blood to back up in the left atrium and the lungs, resulting in edema in the lungs. Stenosis of the tricuspid valve causes blood to back up in the right atrium and systemic veins, causing edema in the periphery.

Cyanosis (sī-ă-nō′sis, *cyan,* blue + *osis,* condition of) is a symptom of inadequate heart function in babies suffering from congenital heart disease. The term “blue baby” is sometimes used to refer to infants with cyanosis. The blueness of the skin is caused by low oxygen levels in the blood in peripheral blood vessels.

the cardiac muscle fibers, producing an increased preload. In response to the increased preload, cardiac muscle fibers contract with a greater force. The greater force of contraction causes an increased volume of blood to be ejected from the heart, resulting in an increased stroke volume. As venous return increases, resulting in an increased preload, cardiac output increases. Conversely, if venous return decreases, resulting in a decreased preload, the cardiac output decreases. The relationship between preload and stroke volume is called **Starling's law of the heart.**

Because venous return is influenced by many conditions, Starling's law of the heart has a major influence on cardiac output. For example, muscular activity during exercise causes increased venous return, resulting in an increased preload, stroke volume, and cardiac output. This is beneficial because an increased cardiac output is needed during exercise to supply oxygen to exercising skeletal muscles.

Afterload refers to the pressure against which the ventricles must pump blood. People suffering from hypertension have an increased afterload because they have an elevated aortic pressure during contraction of the ventricles. The heart must do more work to pump blood from the left ventricle into the aorta, which increases the workload on the heart and can eventually lead to heart failure. A reduced afterload decreases the work the heart must do. People who have a lower blood pressure have a reduced afterload and develop heart failure less often than people who have hypertension. The afterload, however, influences cardiac output less than preload influences it. The afterload must increase substantially before it decreases the volume of blood pumped by a healthy heart.

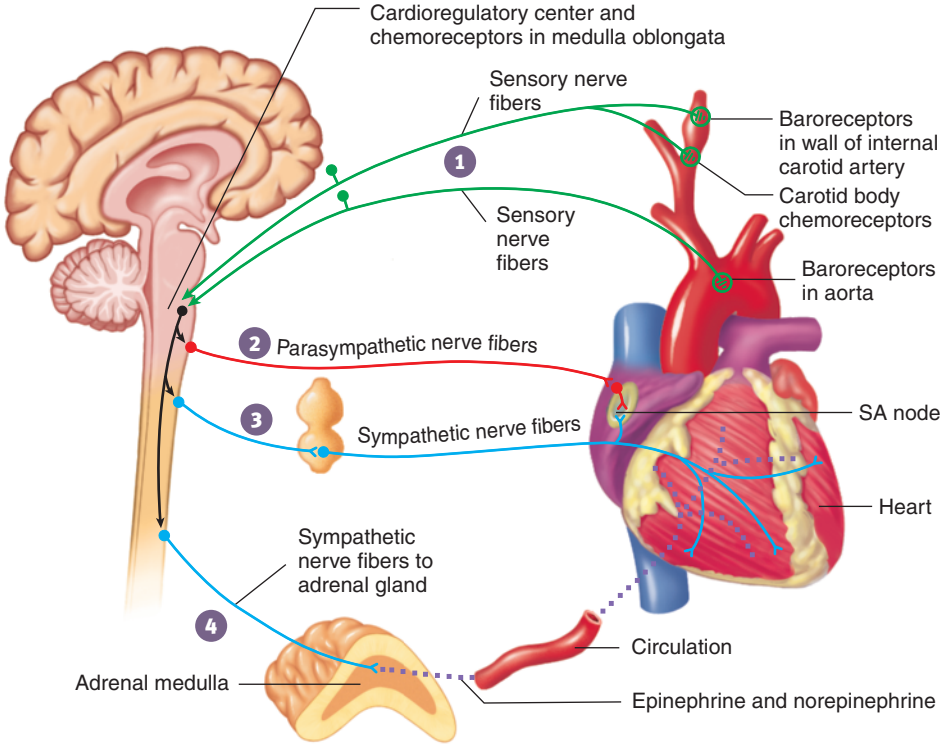
Consequences of Heart Failure

Although heart failure can occur in young people, it usually results from a progressive weakening of the heart muscle in elderly people. A failing heart gradually enlarges and eventually fails. In heart failure, the heart is not capable of pumping all the blood that is returned to it because further stretching of the cardiac muscle fibers does not increase the stroke volume of the heart. Consequently, blood backs up in the veins. For example, heart failure that affects the right ventricle is called **right heart failure** and causes blood to back up in the veins that return blood from systemic vessels to the heart. Filling of the veins with blood causes edema, especially in the legs and feet. Edema results from the accumulation of fluid in tissues outside of blood vessels. Heart failure that affects the left ventricle is called **left heart failure** and causes blood to back up in the veins that return blood from the lungs to the heart. Filling of these veins causes edema in the lungs, which makes breathing difficult.

Extrinsic Regulation of the Heart

Extrinsic regulation refers to mechanisms external to the heart, such as either hormonal or nervous regulation (figure 12.20). Nervous influences are carried through the autonomic nervous system. Both sympathetic and parasympathetic nerve fibers innervate the heart, and have a major effect on the SA node.

1. Sensory (*green*) neurons carry action potentials from baroreceptors to the cardioregulatory center. Chemoreceptors in the medulla oblongata influence the cardioregulatory center.
2. The cardioregulatory center controls the frequency of action potentials in the parasympathetic (*red*) neurons extending to the heart. The parasympathetic neurons decrease the heart rate.
3. The cardioregulatory center controls the frequency of action potential in the sympathetic (*blue*) neurons extending to the heart. The sympathetic neurons increase the heart rate and the stroke volume.
4. The cardioregulatory center influences the frequency of action potentials in the sympathetic (*blue*) neurons extending to the adrenal medulla. The sympathetic neurons increase the secretion of epinephrine and some norepinephrine into the general circulation. Epinephrine and norepinephrine increase the heart rate and stroke volume.



Process Figure 12.20 Baroreceptor and Chemoreceptor Reflexes

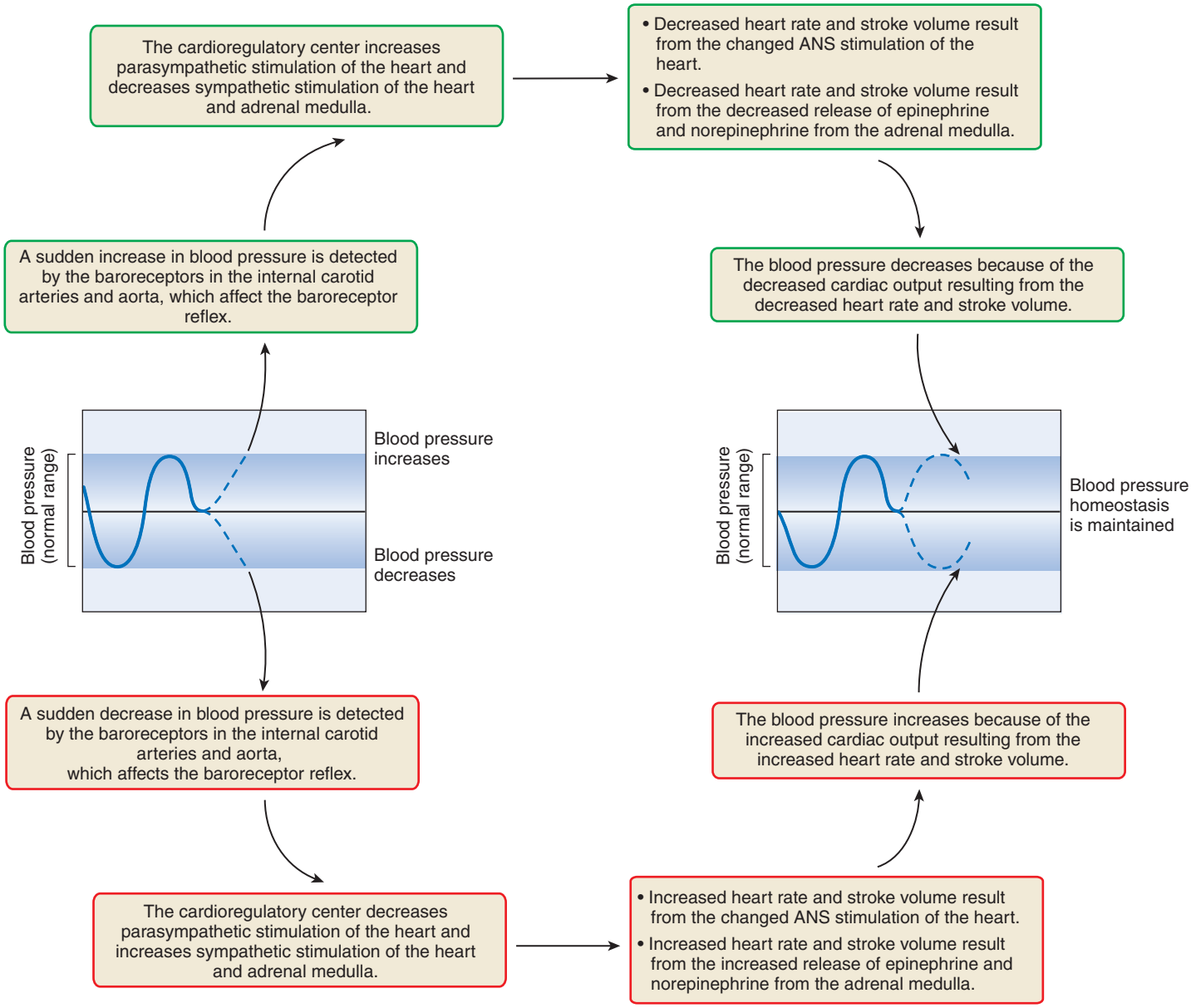
Sensory (*green*) nerves carry action potentials from sensory receptors to the medulla oblongata. Sympathetic (*blue*) and parasympathetic (*red*) nerves exit the spinal cord or medulla oblongata and extend to the heart to regulate its function. Epinephrine and norepinephrine from the adrenal gland also help regulate the heart's action. (SA = sinoatrial)

Stimulation by sympathetic nerve fibers causes the heart rate and the stroke volume to increase, whereas stimulation by parasympathetic nerve fibers causes the heart rate to decrease.

The **baroreceptor** (bar′ō-rē-sep′ter, *baro,* pressure) **reflex** plays an important role in regulating the function of the heart. **Baroreceptors** are stretch receptors that monitor blood pressure in the aorta and in the wall of the internal carotid arteries, which carry blood to the brain (see figure 12.20). Changes in blood pressure result in changes in the stretch of the walls of these blood vessels. Thus, changes in blood pressure cause changes in the frequency of action potentials produced by the baroreceptors. The action potentials are transmitted along nerve fibers from the stretch receptors to the medulla oblongata of the brain.

Within the medulla oblongata of the brain is a **cardioregulatory center,** which receives and integrates action potentials from the baroreceptors. The cardioregulatory center controls the action potential frequency in sympathetic and parasympathetic nerve fibers that extend from the brain and spinal cord to the heart. The cardioregulatory center also influences sympathetic stimulation of the adrenal gland (see figure 12.20). Epinephrine and norepinephrine, released from the adrenal gland increase the stroke volume and heart rate.

When the blood pressure increases, the baroreceptors are stimulated. There is increased frequency of action potentials, sent along the nerve fibers to the medulla oblongata of the brain. This prompts the cardioregulatory center to increase parasympathetic stimulation and to decrease sympathetic stimulation of the heart. As a result, the heart rate and stroke volume decrease, causing blood pressure to decline (figure 12.21).



Homeostasis Figure 12.21 Baroreceptor Reflex

The baroreceptor reflex maintains homeostasis in response to changes in blood pressure. (ANS = autonomic nervous system)

Clinical Focus Treatment and Prevention of Heart Disease

Heart Medications

Digitalis

Digitalis (dij′i-tal′is, refers to fingerlike flowers), an extract of foxglove plants, slows and strengthens contractions of the heart muscle. This drug is frequently given to people who suffer from heart failure, although it can also be used to treat atrial tachycardia.

Nitroglycerin

During exercise, when the heart rate and stroke volume are increased, dilation of blood vessels in the exercising skeletal muscles and constriction in most other blood vessels results in an increased venous return to the heart and an increased preload. **Nitroglycerin** (nī-trō-glis′er-in) causes dilation of all of the veins and arteries without an increase in heart rate or stroke volume. When all blood vessels dilate, a greater volume of blood pools in the dilated blood vessels, causing a decrease in the venous return to the heart. The reduced preload causes cardiac output to decrease, resulting in a decreased amount of work performed by the heart. Nitroglycerin is frequently given to people who suffer from coronary artery disease, which restricts coronary blood flow. The decreased work performed by the heart reduces the amount of oxygen required by the cardiac muscle. In addition, dilation of coronary arteries can increase blood flow to cardiac muscle. Consequently, the heart does not suffer from a lack of oxygen, and angina pectoris does not develop.

Beta-Adrenergic Blocking Agents

Beta-adrenergic (bā-tă ad-rĕ-ner′jik) **blocking agents** reduce the rate and strength of cardiac muscle contractions, thus reducing the oxygen demand of the heart. They bind to receptors for norepinephrine and epinephrine and prevent these substances from having their normal effects. Beta-adrenergic blocking agents are often used to treat people who suffer from rapid heart rates, certain types of arrhythmias, and hypertension.

Calcium Channel Blockers

Calcium channel blockers reduce the rate at which Ca^{2+} diffuse into cardiac muscle cells and smooth muscle cells. Because the action potentials that produce cardiac muscle contractions depend in part on the flow of Ca^{2+} into the cardiac muscle cells, the Ca^{2+} channel blockers can be used to control the force of heart contractions and reduce arrhythmia, tachycardia, and hypertension. Because entry of Ca^{2+} to smooth muscle cells causes contraction, Ca^{2+} channel blockers cause dilation of blood vessels. They dilate coronary blood vessels and increase blood flow to cardiac muscle. Consequently, they can be used to treat angina pectoris.

Antihypertensive Agents

Several drugs are used specifically to treat hypertension. These drugs reduce blood pressure and therefore reduce the work required by the heart to pump blood. In addition, the reduction of blood pressure reduces the risk of heart attacks and strokes. Medications used to treat hypertension include drugs that reduce the activity of the sympathetic division, those that dilate arteries and veins, those that increase urine production (diuretics), and those that block the conversion of angiotensin I to angiotensin II (see chapter 13).

Anticoagulants

Anticoagulants (an′tē-kō-ag′ū-lants) prevent clot formation in persons with damage to heart valves or blood vessels or in persons who have had a myocardial infarction. Aspirin functions as a weak anticoagulant by inhibiting the synthesis of prostaglandins in platelets, which in turn reduces clot formation. Some data suggest that taking a small dose of aspirin regularly reduces the chance of a heart attack. One aspirin each day may benefit those who are likely to experience a coronary thrombosis.

Instruments

Artificial Pacemaker

An **artificial pacemaker** is an instrument placed beneath the skin that is equipped with an electrode that extends to the heart. An artificial pacemaker provides an electrical stimulus to the heart at a set frequency. Artificial pacemakers are used in patients in whom the natural pacemaker of the heart does not produce a heart rate high enough to sustain normal physical activity. Modern electronics has made it possible to design artificial pacemakers that can increase the heart rate as physical activity increases. In addition, special artificial pacemakers can defibrillate the heart if it becomes arrhythmic. It is likely that rapid development of electronics for artificial pacemakers will further increase the degree to which the pacemakers can regulate the heart.

Heart–Lung Machine

A **heart–lung machine** serves as a temporary substitute for the patient's heart and lungs. It pumps blood throughout the body and oxygenates and removes carbon dioxide from the blood. It has made possible many surgeries on the heart and lungs.

Surgical Procedures

Heart Valve Replacement or Repair

Heart valve replacement or repair is a surgical procedure performed on those who have diseased valves that are so deformed and scarred from conditions such as endocarditis that the valves are severely incompetent or stenosed. Substitute valves made of synthetic materials such as plastic or Dacron are effective; valves transplanted from pigs are also used.

Heart Transplants

Heart transplants are possible when the immune characteristics of a donor and the recipient are closely matched. The heart of a recently deceased donor is transplanted to the recipient, and the diseased heart of the recipient is removed. People who have received heart transplants must remain on drugs that suppress their immune responses for the rest of their lives. Unless they do so, their immune system rejects the transplanted heart.

Artificial Hearts

Artificial hearts have been used on an experimental basis to extend the lives of individuals until an acceptable transplant can be found or to replace the heart permanently. The technology currently available for artificial hearts has not yet reached the point at which a high quality of life can be achieved with a permanent artificial heart.

Prevention of Heart Disease

Proper nutrition is important in reducing the risk of heart disease. A recommended diet is low in fats, especially saturated fats and cholesterol, and low in refined sugar. Diets should be high in fiber, whole grains,

Clinical Focus (continued)

fruits, and vegetables. Total food intake should be limited to avoid obesity, and sodium chloride intake should be reduced.

Tobacco and excessive use of alcohol should be avoided. Smoking increases the risk of heart disease by at least 10-fold, and excessive use of alcohol also substantially increases the risk of heart disease. However, moderate use of alcohol may reduce the risk of heart disease.

Chronic stress, frequent emotional upsets, and a lack of physical exercise can increase the risk of cardiovascular disease. Remedies include relaxation techniques and aerobic exercise programs involving gradual increases in duration and difficulty in activities such as swimming, walking, jogging, or aerobic dancing.

Hypertension is an abnormally high systemic blood pressure. Hypertension affects approximately one-fifth of the population. Regular blood pressure measurements are important because hypertension does not produce obvious symptoms. If hypertension cannot be controlled by diet and exercise, it is important to treat the condition with prescribed drugs. The cause of hypertension in the majority of cases is unknown.

When the blood pressure decreases, there is less stimulation of the baroreceptors. A lower frequency of action potentials is sent to the medulla oblongata of the brain and this triggers a response in the cardioregulatory center. The cardioregulatory center responds by increasing sympathetic stimulation of the heart and decreasing parasympathetic stimulation. Consequently, the heart rate and stroke volume increase. If the decrease in blood pressure is large, sympathetic stimulation of the adrenal medulla also increases. The epinephrine and norepinephrine secreted by the adrenal medulla increase the heart rate and stroke volume, also causing the blood pressure to increase toward its normal value (see figure 12.21).

PREDICT 8

In response to a severe hemorrhage, blood pressure lowers, the heart rate increases dramatically, and the stroke volume lowers. If low blood pressure activates a reflex that increases sympathetic stimulation of the heart, why is the stroke volume low?

Emotions integrated in the cerebrum of the brain can influence the heart. Excitement, anxiety, or anger can affect the cardioregulatory center, resulting in increased sympathetic stimulation of the heart and an increased cardiac output. Depression, on the other hand, can increase parasympathetic stimulation of the heart, causing a slight reduction in cardiac output.

Epinephrine and small amounts of norepinephrine released from the adrenal medulla in response to exercise, emotional excitement, or stress also influence the heart's function (see figures 12.20 and 12.21). Epinephrine and norepinephrine bind to receptor molecules on cardiac muscle and cause increased heart rate and stroke volume.

Exercise and Cardiac Output

During exercise, the cardiac output of the heart increases, resulting in increased delivery of blood to skeletal muscles. Cardiac output increases because of the increased heart rate and stroke volume that result from increased sympathetic stimulation of the heart and from the effects of epinephrine and norepinephrine on cardiac muscle. Starling's law of the heart also contributes to the increase in stroke volume during exercise. Blood vessels in exercising skeletal muscles dilate, which increases blood flow to the muscle tissue. The dilation of the blood vessels also increases venous return to the heart because the rate of blood flow from exercising skeletal muscle through the veins is greatly increased. As venous return increases, preload increases, and cardiac muscle is stretched. Consequently, the muscle contracts more forcefully (Starling's law) and stroke volume increases.

The medulla oblongata of the brain also contains chemoreceptors that are sensitive to changes in pH and carbon dioxide levels (see figure 12.20). A decrease in pH, often caused by an increase in carbon dioxide, results in sympathetic stimulation of the heart (figure 12.22).

Changes in the extracellular concentration of K^+, Ca^{2+}, and Na^+, which influence other electrically excitable tissues, also affect cardiac muscle function. Excess extracellular K^+ cause the heart rate and stroke volume to decrease. If the extracellular K^+ concentration increases further, normal conduction of action potentials through cardiac muscle is blocked, and death can result. An excess of extracellular Ca^{2+} causes the heart to contract arrhythmically. Reduced extracellular Ca^{2+} cause both the heart rate and stroke volume to decrease.

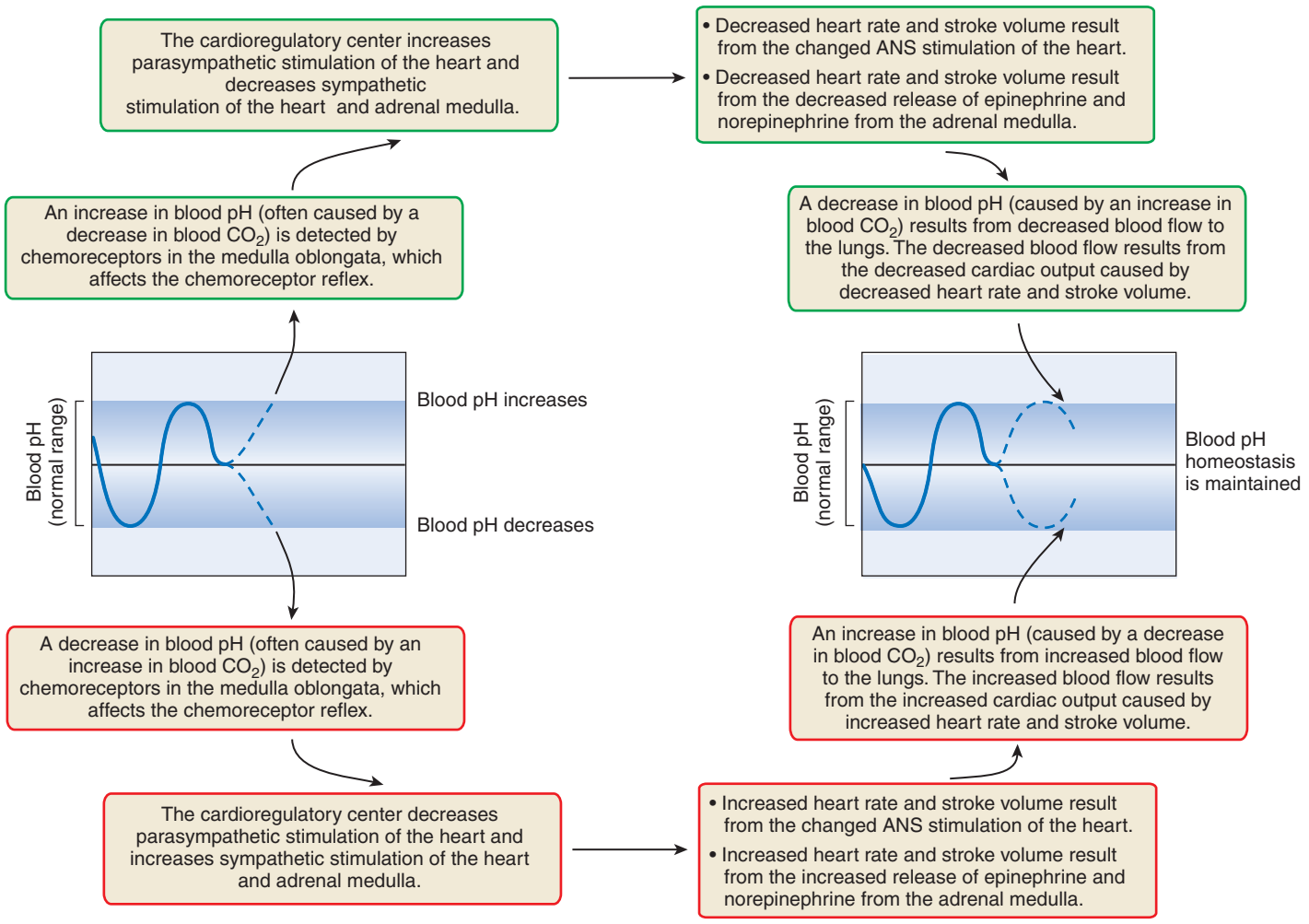
Body temperature affects metabolism in the heart like it affects other tissues. Elevated body temperature increases the heart rate, and reduced body temperature slows the heart rate. For example, during fever the heart rate is usually elevated. During heart surgery the body temperature is sometimes intentionally lowered to slow the heart rate and metabolism.

Effects of Aging on the Heart

Gradual changes in the function of the heart are associated with aging. These changes are minor under resting conditions, but become more obvious during exercise and in response to age-related diseases.

By age 70 cardiac output often decreases by approximately one-third. Because of the decrease in the reserve strength of the heart, many elderly people are limited in their ability to respond to emergencies, infections, blood loss, or stress.

Hypertrophy (enlargement) of the left ventricle is a common age-related change. This appears to result from a gradual increase in the pressure in the aorta (afterload) against which the left ventricle must pump. The increased aortic pressure results from a gradual decrease in the elasticity of the aorta, and there is an increased stiffness of the cardiac



Homeostasis Figure 12.22 Chemoreceptor Reflex—pH

The chemoreceptor reflex maintains homeostasis in response to changes in blood concentrations of CO_2 and H^+ (or pH). (ANS = autonomic nervous system)

muscle. The enlarged left ventricle has a reduced ability to pump blood out of the left ventricle. This can cause an increase in left atrial pressure, which can result in increased pulmonary edema. Consequently, there is an increased tendency for people to feel out of breath when they exercise strenuously.

Aging cardiac muscle requires a greater amount of time to contract and relax. Thus, there is a decrease in the maximum heart rate. Both the resting and maximum cardiac output slowly decrease as people age and, by 85 years of age, the cardiac output is decreased by 30–60%.

Age-related changes in the connective tissue of the heart valves occur. The connective tissue becomes less flexible, and calcium deposits develop in the valves. As a result, there is an increased tendency for the aortic semilunar valve to become stenosed or incompetent.

There is an age-related increase in cardiac arrhythmias as a consequence of a decrease in the number of cardiac cells in the SA node and because of the replacement of cells of the AV bundle.

The development of coronary artery disease and heart failure also are age-related. Approximately 10% of elderly people over age 80 have heart failure, and a major contributing factor is coronary heart disease. Advanced age, malnutrition, chronic infections, toxins, severe anemias, hyperthyroidism, and hereditary factors can lead to heart failure.

Exercise has many beneficial effects on the heart. Regular aerobic exercise improves the functional capacity of the heart at all ages, providing there are no conditions that cause the increased workload of the heart to be harmful.

Systems Pathology

Myocardial Infarction

Mr. P. was an overweight, out-of-shape executive who regularly consumed food with a high fat content and smoked. He viewed his job as frustrating because he was frequently confronted with stressful deadlines. He had not had a physical examination for several years so he was not aware that his blood pressure was high. One evening, Mr. P. was walking to his car after work when he began to feel pain in his chest that also radiated down his left arm. Shortly after the onset of pain he became out of breath, developed marked pallor, became dizzy, and had to lie down on the sidewalk. The pain in his chest and arm was poorly localized, but intense and he became anxious and then disoriented. Mr. P. lost consciousness, although he did not stop breathing. After a short delay, one of his coworkers noticed him and called for help. When paramedics arrived, they determined that Mr. P's blood pressure was low and he exhibited arrhythmia and tachycardia. The paramedics transmitted the electrocardiogram they took to a physician by way of their electronic communication system, and they discussed Mr. P.'s symptoms with the physician who was at the hospital. The paramedics were directed to administer oxygen and medication to control arrythmias and to transport him to the hospital. At the hospital, tissue plasminogen activator (t-PA) was administered, which improved blood flow to the damaged area of the heart by activating plasminogen which dissolves blood clots. Blood levels of enzymes such as creatine phosphokinase increased in Mr. P.'s blood over the next few days, which confirmed that damage to cardiac muscle resulted from an infarction.

In the hospital, Mr. P. began to experience shortness of breath because of pulmonary edema, and after a few days in the hospital he developed pneumonia. He was treated for pneumonia and gradually improved over the next few weeks. An **angiogram** (an′jē-ō-gram, *angeion,* a vessel + *gramma,* a writing) (figure A), which is an imaging technique used to visualize the coronary arteries, was performed several days after Mr. P.'s infarction. The angiogram indicated that Mr. P. suffered damage to a significant part of the lateral wall of his left ventricle and that neither angioplasty nor bypass surgery were necessary, although Mr. P. has some serious restrictions to blood flow in his coronary arteries.

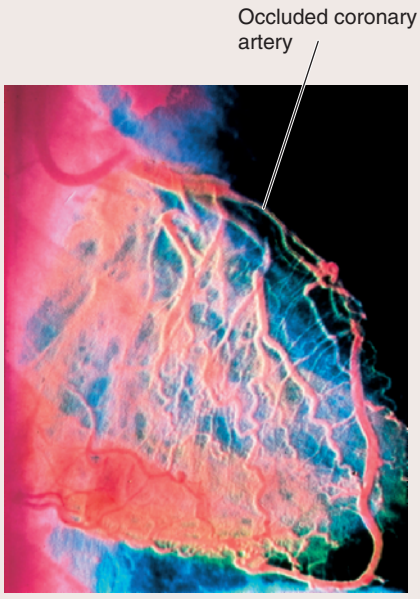


Figure A Angiogram

An angiogram is a picture of a blood vessel. It is usually obtained by placing a catheter into a blood vessel and injecting a dye that can be detected with x-rays. Note the occluded (blocked) coronary blood vessel in this angiogram, which has been computer-enhanced to show colors.

Background Information

Mr. P. experienced a myocardial infarction. A thrombosis in one of the branches of the left coronary artery reduced blood supply to the lateral wall of the left ventricle, resulting in ischemia of the left ventricle wall. That t-PA was an effective treatment is consistent with the conclusion that the infarction was due to a thrombosis. An ischemic area of the heart wall was not able to contract normally and, therefore, the pumping effectiveness of the heart was dramatically reduced. The reduced pumping capacity of the heart was responsible for the low blood pressure, which caused the blood flow to his brain to decrease resulting in confusion, disorientation, and possibly unconsciousness.

Low blood pressure, increasing blood carbon dioxide levels, pain, and anxiousness increased sympathetic stimulation of the heart and adrenal glands. Increased sympathetic stimulation of the adrenal medulla resulted in the release of epinephrine from the adrenal medulla. Increased parasympathetic stimulation of the heart resulted from pain sensations. The heart rate was periodically arrhythmic because of the combined effects of parasympathetic stimulation, epinephrine and norepinephrine from the adrenal gland, and sympathetic stimulation. In addition, ectopic beats were produced by the ischemic areas of the left ventricle.

Pulmonary edema resulted from the increased pressure in the pulmonary veins because of the reduced ability of the left ventricle to pump blood. The edema allowed bacteria to infect the lungs and cause pneumonia.

Systems Interactions: Effects of Myocardial Infractions on Other Systems

System	Interactions
Integumentary	Pallor of the skin resulted from intense vasoconstriction of peripheral blood vessels, including those in the skin.
Muscular	Reduced skeletal muscle activity required for activities such as walking result because of the effect of a lack of blood flow to the brain and because blood is shunted from blood vessels that supply skeletal muscles to those that supply the heart and brain.
Nervous	Decreased blood flow to the brain, decreased blood pressure, and pain because of ischemia of heart muscle result in increased sympathetic and parasympathetic stimulation of the heart. Loss of consciousness occurs when the blood flow to the brain decreases enough to result in too little oxygen to maintain normal brain function, especially in the reticular activating system.
Endocrine	When blood pressure decreases to low values, antidiuretic hormone (ADH) is released from the posterior pituitary gland and renin, released from the kidney, activates the renin–angiotensin–aldosterone mechanism. ADH, secreted in large amounts, and angiotensin II cause vasoconstriction of peripheral blood vessels. ADH and aldosterone act on the kidneys to retain water and ions. An increased blood volume increases venous return, which results in an increased stroke volume of the heart and an increase in blood pressure unless damage to the heart is very severe.
Lymphatic or Immune	White blood cells, including macrophages, move to the area of cardiac muscle damage and phagocytize any dead cardiac muscle cells.
Respiratory	Decreased blood pressure results in a decreased blood flow to the lungs. The decrease in gas exchange results in increased blood carbon dioxide levels, acidosis, and decreased blood oxygen levels. Initially, respiration becomes deep and labored because of the elevated carbon dioxide levels, decreased blood pH, and depressed oxygen levels. If the blood oxygen levels decrease too much the person loses consciousness. Pulmonary edema can result when the pumping effectiveness of the left ventricle is substantially reduced.
Digestive	Intense sympathetic stimulation decreases blood flow to the digestive system to very low levels, which often results in increased nausea and vomiting.
Urinary	Blood flow to the kidney decreases dramatically in response to sympathetic stimulation. If the kidney becomes ischemic, damage to the kidney tubules can occur, resulting in the development of acute renal failure. Acute renal failure results in reduced urine production. Increased blood urea nitrogen, increased blood levels of K^+, and edema are indications that the kidneys cannot eliminate waste products and excess water. If damage is not too great, the period of reduced urine production may last up to 3 weeks, and then the rate of urine production slowly returns to normal as the kidney tubules heal.

The heart began to beat rhythmically in response to medication because the infarction did not damage the conducting system of the heart, which is an indication that there were no permanent arrhythmias. Permanent arrhythmias are indications of damage done to cardiac muscle cells specialized to conduct action potentials in the heart.

Analysis of the electrocardiogram, blood pressure measurements, and the angiogram indicated that the infarction, in this case, was located on the left side of Mr P.'s heart.

Mr. P.'s physician made it very clear to him that he was lucky to have survived a myocardial infarction and recommended a weight-loss program and a low-sodium and low-fat diet. Mr. P.'s physician also recommended that Mr. P. regularly take a small amount of aspirin and stop smoking. He explained that Mr. P. would have to take medication for high blood pressure if his blood pressure did not decrease in response to the recommended changes. After a period of recovery, the physician recommended an aerobic exercise program and suggested that Mr. P. seek ways to reduce the stress associated with his job. Mr. P. followed the doctor's recommendations, and after several months he began to feel better than he had in years and his blood pressure was normal.

PREDICT 9

Severe ischemia in the wall of a ventricle can result in the death of cardiac muscle cells. Inflammation around the necrotic tissue results and macrophages invade the necrotic tissue and phagocytize dead cells. At the same time, blood vessels and connective tissue grow into the necrotic area and begin to deposit connective tissue to replace the necrotic tissue. A person who entered the hospital at about the same time with a very similar condition to Mr. P.'s was recovering. After about a week, his blood pressure suddenly decreased to very low levels and he died within a very short time. Upon autopsy, a large amount of blood was found in the pericardial sac, and the wall of the left ventricle was ruptured. Explain.

SUMMARY

Functions of the Heart (p. 324)

The heart functions include

1. The heart generates blood pressure.
2. The heart routes blood through the systemic and pulmonary circulation.
3. The pumping action of the heart and the valves of the heart ensure a one-way flow of blood through the heart and blood vessels.
4. The heart helps regulate blood supply to tissues.

Size, Form, and Location of the Heart (p. 324)

The heart is approximately the size of a fist and is located in the pericardial cavity.

Anatomy of the Heart (p. 326)

Pericardium

1. The pericardial sac consists of a fibrous and serous pericardium. The fibrous pericardium is lined by the parietal pericardium.
2. The outer surface of the heart is lined by the visceral pericardium (epicardium).
3. Between the visceral and parietal pericardium is the pericardial cavity, which is filled with pericardial fluid.

External Anatomy

1. Atria are separated externally from the ventricles by the coronary sulcus. The right and left ventricles are separated externally by the interventricular sulci.
2. The inferior and superior venae cava enter the right atrium. The four pulmonary veins enter the left atrium.
3. The pulmonary trunk exits the right ventricle, and the aorta exits the left ventricle.

Blood Supply to the Heart

The left and right coronary arteries originate from the base of the aorta and supply the heart. Blood returns from heart tissue through cardiac veins to the coronary sinus and into the right atrium. Small cardiac veins also return blood directly to the right atrium.

Heart Chambers and Internal Anatomy

1. There are four chambers in the heart. The left and right atria receive blood from veins and function mainly as reservoirs. Contraction of the atria completes ventricular filling.
2. The atria are separated internally from each other by the interatrial septum.
3. The ventricles are the main pumping chambers of the heart. The right ventricle pumps blood into the pulmonary trunk and the left ventricle, which has a thicker wall, and pumps blood into the aorta.
4. The ventricles are separated internally by the interventricular septum.

Heart Valves

1. The heart valves ensure one-way flow of blood.
2. The tricuspid valve (three cusps) separates the right atrium and right ventricle, and the bicuspid valve (two cusps) separates the left atrium and left ventricle.
3. The papillary muscles attach by the chordae tendineae to the cusps of the tricuspid and bicuspid valves and adjust tension on the valves.
4. The aorta and pulmonary trunk are separated from the ventricles by the semilunar valves.
5. The skeleton of the heart is a plate of fibrous connective tissue that separates the atria from the ventricles, acts as an electrical barrier between the atria and ventricles, and supports the valves of the heart.

Route of Blood Flow Through the Heart

1. The left and right sides of the heart can be considered separate pumps.
2. Blood flows from the systemic vessels to the right atrium and from the right atrium to the right ventricle. From the right ventricle blood flows to the pulmonary trunk and from the pulmonary trunk to the lungs. From the lungs blood flows through the pulmonary veins to the left atrium, and from the left atrium blood flows to the left ventricle. From the left ventricle blood flows into the aorta and then through the systemic vessels.

Histology of the Heart (p. 333)

Heart Wall

The heart wall consists of the outer epicardium, the middle myocardium, and the inner endocardium.

Cardiac Muscle

1. Cardiac muscle is striated and depends on ATP for energy. It depends on aerobic metabolism.
2. Cardiac muscle cells are joined by intercalated disks that allow action potentials to be propagated throughout the heart.

Electrical Activity of the Heart (p. 335)

Action Potentials in Cardiac Muscle

1. Action potentials in cardiac muscle are prolonged compared with those in skeletal muscle and have a depolarization phase, a plateau phase, and a repolarization phase.
2. The depolarization is due mainly to opening of the voltage-gated Na^+ channels, and the plateau phase is due to opened voltage-gated Ca^{2+} channels. Repolarization at the end of the plateau phase is due to the opening of K^+ channels for a brief period.
3. The prolonged action potential in cardiac muscle ensures that contraction and relaxation occurs and prevents tetany in cardiac muscle.
4. The SA node located in the upper wall of the right atrium is the normal pacemaker of the heart and cells of the SA node have more voltage-gated Ca^{2+} channels than other areas of the heart.

Conduction System of the Heart

1. The conduction system of the heart is made up of specialized cardiac muscle cells.
2. The SA node produces action potentials that are propagated over the atria to the AV node.
3. The AV node and atrioventricular bundle conduct action potentials to the ventricles.
4. The right and left bundle branches conduct action potentials from the atrioventricular bundle through Purkinje fibers to the ventricular muscle.
5. An ectopic beat results from an action potential that originates in an area of the heart other than the SA node.

Electrocardiogram

1. The ECG is a record of electrical events within the heart.
2. The ECG can be used to detect abnormal heart rates or rhythms, conduction pathways, hypertrophy or atrophy of the heart, and the approximate location of damaged cardiac muscle.
3. The normal ECG consists of a P wave (atrial depolarization), a QRS complex (ventricular depolarization), and a T wave (ventricular repolarization).
4. Atrial contraction occurs during the PQ interval, and the ventricles contract and relax during the QT interval.

Cardiac Cycle (p. 338)

1. Atrial systole is contraction of the atria, and ventricular systole is contraction of the ventricles. Atrial diastole is relaxation of the atria, and ventricular diastole is relaxation of the ventricles.
2. During ventricular systole, the AV valves close, pressure increases in the ventricles, the semilunar valves are forced to open, and blood flows into the aorta and pulmonary trunk.
3. At the beginning of ventricular diastole, pressure in the ventricles decreases. The semilunar valves close to prevent backflow of blood from the aorta and pulmonary trunk into the ventricles.
4. When the pressure in the ventricles is low enough, the AV valves open and blood flows from the atria into the ventricles.
5. During atrial systole, the atria contract and complete filling of the ventricles.

Heart Sounds (p. 341)

1. The first heart sound results from closure of the AV valves. The second heart sound results from closure of the semilunar valves.
2. Abnormal heart sounds are called murmurs. They can result from incompetent (leaky) valves or stenosed (narrowed) valves.

Regulation of Heart Function (p. 342)

Cardiac output (volume of blood pumped per ventricle per minute) is equal to the stroke volume (volume of blood ejected per beat) times the heart rate (beats per minute).

Intrinsic Regulation of the Heart

1. Intrinsic regulation refers to regulation that is contained in the heart.
2. As venous return to the heart increases, the heart wall is stretched, and the increased stretch of the ventricular walls is called preload.
3. An increase in preload causes the stroke volume to increase (Starling's law of the heart) and heart rate to increase.
4. Afterload is the pressure against which the ventricles must pump blood.

Extrinsic Regulation of the Heart

1. Extrinsic regulation refers to nervous and hormonal mechanisms.
2. Sympathetic stimulation increases stroke volume and heart rate; parasympathetic stimulation decreases heart rate.
3. The baroreceptor reflex detects changes in blood pressure and causes a decrease in heart rate and stroke volume in response to a sudden increase in blood pressure or an increase in heart rate and stroke volume in response to a sudden decrease in blood pressure.
4. Emotions influence heart function by increasing sympathetic stimulation of the heart in response to exercise, excitement, anxiety, or anger and by increasing parasympathetic stimulation in response to depression.
5. Alterations in body fluid levels of carbon dioxide, pH, and ion concentrations, as well as changes in body temperature, influence heart function.

Effects of Aging on the Heart (p. 347)

The following age-related changes are common

1. By age 70 cardiac output often decreases by one-third.
2. Hypertrophy of the left ventricle can cause pulmonary edema.
3. Decrease in the maximum heart rate by 30–60% by age 85 leads to a decrease in cardiac output.
4. Aortic semilunar valves can become stenotic or incompetent.
5. Coronary artery disease and congestive heart failure can develop.
6. Aerobic exercise improves the functional capacity of the heart at all ages.

REVIEW AND COMPREHENSION

1. Describe the size and location of the heart, including its base and apex.
2. Describe the structure and function of the pericardium.
3. Describe the vessels that supply blood to the cardiac muscle.
4. Define coronary thrombosis and infarct. How do atherosclerotic lesions affect the heart?
5. What chambers make up the left and right side of the heart? What are their functions?
6. Describe the structure and location of the tricuspid, bicuspid, and semilunar valves. What is the function of these valves?
7. What are the functions of the atria and ventricles?
8. Starting in the right atrium, describe the flow of blood through the heart.
9. Describe the three layers of the heart. Which of the three layers is most important in causing contractions of the heart?
10. Describe the structure of cardiac muscle cells, including the structure and function of intercalated disks.
11. Describe the events that result in an action potential in cardiac muscle.
12. Explain how cardiac muscle cells in the SA node produce action potentials spontaneously and why the SA node is the pacemaker of the heart.
13. What is the function of the conduction system of the heart? Starting with the SA node, describe the route taken by an action potential as it goes through the conduction system of the heart.
14. Explain the electrical events that generate each portion of the electrocardiogram. How do they relate to contraction events?
15. What contraction and relaxation events occur during the P-Q interval and the Q-T interval of the electrocardiogram?
16. Define cardiac cycle, systole, and diastole.
17. Describe blood flow and the opening and closing of heart valves during the cardiac cycle.
18. Describe the pressure changes that occur in the left atrium, left ventricle, and aorta during ventricular systole and diastole (see figure 12.18).
19. What events cause the first and second heart sounds?
20. Define murmur. Describe how either an incompetent or a stenosed valve can cause a murmur.
21. Define cardiac output, stroke volume, and heart rate.
22. What is Starling's law of the heart? What effect does an increase or a decrease in venous return have on cardiac output?
23. Describe the effect of parasympathetic and sympathetic stimulation on heart rate and stroke volume.
24. How does the nervous system detect and respond to the following:
    a. A decrease in blood pressure
    b. An increase in blood pressure
25. What is the effect of epinephrine on the heart rate and stroke volume?
26. Explain how emotions affect heart function.

27. What effects do the following have on cardiac output:
    a. Decrease in blood pH
    b. Increase in blood carbon dioxide
28. How do changes in body temperature influence the heart rate?
29. List the common age-related heart diseases that develop in elderly people.

CRITICAL THINKING

1. A friend tells you that her son had an ECG, and it revealed that he has a slight heart murmur. Should you be convinced that he has a heart murmur? Explain.
2. Predict the effect on Starling's law of the heart if the parasympathetic (vagus) nerves to the heart are cut.
3. An experiment is performed on a dog in which the arterial blood pressure in the aorta is monitored before and after the common carotid arteries are clamped (at time A). Explain the change in arterial blood pressure (*Hint:* Baroreceptors are located in the internal carotid arteries, which are superior to the site of clamping of the common carotid arteries).
4. Predict the consequences on the heart if a person took a large dose of a drug that blocks all Ca^{2+} channels.
5. What happens to cardiac output following the ingestion of a large amount of fluid?
6. At rest, the cardiac output of athletes and nonathletes can be equal, but the heart rate of athletes is lower than that of nonathletes. At maximum exertion, the maximum heart rate of athletes and nonathletes can be equal, but the cardiac output of athletes is greater than that of nonathletes. Explain.
7. Explain why the walls of the ventricles are thicker than those of the atria.
8. Predict the effect of having an incompetent aortic semilunar valve on ventricular and aortic pressure during ventricular systole and diastole.

Answers in Appendix D

ANSWERS TO PREDICT QUESTIONS

1. The anterior interventricular artery supplies blood to the anterior wall of the heart and to much of the left ventricle. A blocked anterior interventricular artery reduces the oxygen supply to the portion of the heart that is supplied by that artery, and the cardiac muscle in that area is not able to contract effectively. Thus, the left ventricle on the anterior surface of the heart does not contract normally.
2. It is important to prevent tetanic contractions in cardiac muscle because the cycle of contraction and relaxation stops during tetanic contractions. This causes the pumping action of the heart to stop. In skeletal muscle, the cycle of contraction and relaxation is not important as a pump, but it is important to maintain a static contracted state. This is essential to maintaining posture or to holding a limb in a specific position.
3. If the normal blood supply is reduced in a small area of the heart through which the left bundle branch passes, conduction of action potentials through that side of the heart is reduced or blocked. As a consequence, the left side of the heart contracts more slowly. The right side of the heart contracts more normally. The reduced rate of contraction of the left ventricle reduces the pumping effectiveness of the left ventricle.
4. A person who has a damaged left bundle branch will exhibit the consequences outlined for predict question 3, but the electrocardiogram will also be altered. The QRS complex results from depolarization of the ventricles. Action potentials pass through the right bundle branch normally but conduction of action potentials through the left bundle branch is showed because of damage. The QRS complex has an abnormal shape and it is prolonged. If many ectopic action potentials arise in the atria, heart rate increases. Each ectopic action potential initiates a new heart beat. It is possible for some ectopic action potentials arising in the atria to occur while the ventricle is depolarized; but these action potentials do not initiate ventricular contractions. There can, therefore, be more P waves than QRS complexes in the electrocardiogram. If ectopic action potentials do not occur in a regular fashion, they can cause the heart to beat at an irregular rate, or arrhythmically.
5. A leaky aortic semilunar valve results in an increased left ventricular volume just before ventricular contraction. During ventricular relaxation, the aortic semilunar valve closes in a normal person, and blood flows out of the left ventricle into the aorta. When the aortic semilunar valve is incompetent, some blood leaks back into the left ventricle from the aorta during ventricular relaxation. When this blood is added to the blood that normally enters the left ventricle from the left atrium, there is a greater than normal volume of blood in the left ventricle just before ventricular contraction.

   A severely narrowed opening through the aortic semilunar valve increases the amount of work the heart must do to pump the normal volume of blood into the aorta. A greater pressure is required in the ventricle to force the same amount of blood through the narrowed opening during ventricular contraction.
6. Most of the ventricular contraction occurs between the first and second heart sounds of the same beat. Between the first and second heart sounds, blood therefore is ejected from the ventricles into the pulmonary trunk and the aorta. Between the second heart sound of one beat and the first heart sound of the next beat, the ventricles are relaxing. No blood passes from the ventricles into the aorta or pulmonary trunk during that period.
7. The shhh sound made after a heart sound is created by the backward flow of blood after closure of a leaky or incompetent valve. A swishing sound immediately after the second heart sound (lubb–duppshhh) represents a leaky aortic semilunar or pulmonary semilunar valve. The shhh sound before a heart sound is created by blood being forced through a narrowed, or stenosed, valve just before the valve closes. The lubb–shhhdupp suggests that there is a swishing sound immediately before the second heart sound; thus indicating a stenosed aortic or pulmonary semilunar valve.
8. In response to severe hemorrhage, blood pressure decreases, which is detected by baroreceptors. A reduced frequency of action potentials is sent from the baroreceptors to the medulla oblongata. This causes the cardioregulatory center to increase sympathetic stimulation of the heart and increase the heart rate. Sympathetic stimulation of the heart also increases stroke volume, as long as the volume of blood returned to the heart is adequate. Following hemorrhage, however, the blood volume in the body is reduced, and the venous return to the heart from the body is reduced. As a

consequence, the volume of blood in the heart is lower than normal. Because of Starling's law, the stroke volume is reduced. The heart rate is increased, but the volume of blood returning to the heart is decreased; thus the ventricle does not fill with blood. As a consequence, the stroke volume is low, and the heart rate is high.

9. Rupture of the left ventricle can occur several days after a myocardial infarction. As the necrotic tissues are being removed by macrophages, the wall of the ventricle becomes thinner and may bulge during systole. If the wall of the ventricle becomes very thin before new connective tissue is deposited, it can rupture. If the left ventricle ruptures, blood flows from the left ventricle into the pericardial sac, resulting in cardiac tamponade. As blood fills the pericardial sac, it compresses the ventricle from the outside. As a consequence, the ventricle is not able to fill with blood and its pumping ability is rapidly eliminated. Rupture of the left ventricular wall quickly results in death.