20 The Heart

Learning Outcomes

These Learning Outcomes correspond by number to this chapter's sections and indicate what you should be able to do after completing the chapter.

20-1 Describe the **anatomy of the heart**, including vascular supply and pericardium structure, and trace **the flow of blood through the heart**, identifying the major **blood vessels, chambers, and heart valves**.

20-2 Explain the events of an **action potential in cardiac muscle**, indicate the importance of **calcium ions** to the contractile process, describe the **conducting system of the heart**, and identify the electrical events associated with a **normal electrocardiogram**.

20-3 Explain the events of the **cardiac cycle**, including atrial and ventricular systole and diastole, and relate the **heart sounds** to specific events in the cycle.

20-4 Define **cardiac output**, describe the factors that influence **heart rate and stroke volume**, and explain how adjustments in stroke volume and cardiac output are coordinated at different **levels of physical activity**.

Clinical Note

Abnormal Conditions Affecting Cardiac Output p. 697

Spotlights

Heart Disease and Heart Attacks pp. 682–683
Cardiac Arrhythmias p. 689

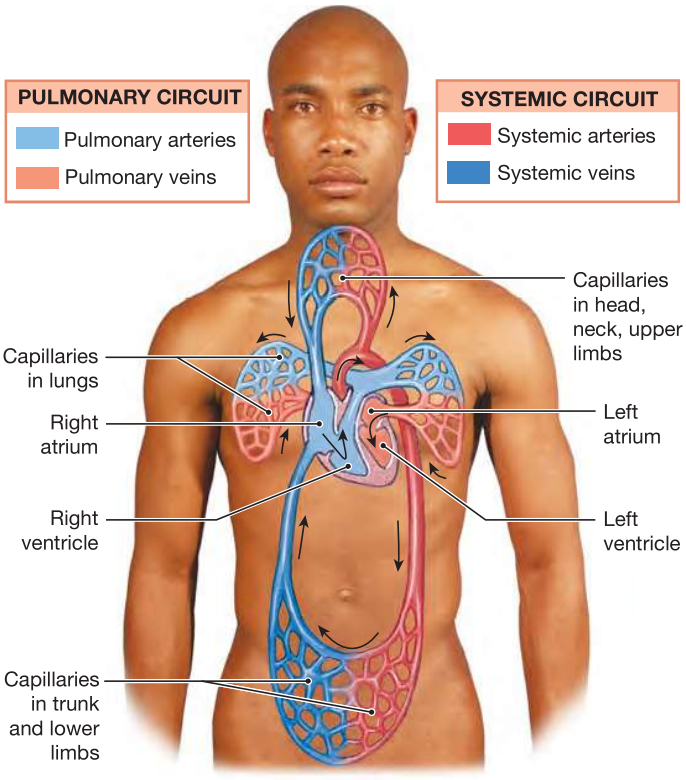
An Introduction to the Cardiovascular System

In this chapter we consider the structure and function of the heart. This extraordinary organ beats approximately 100,000 times each day. Unlike most other muscles, the heart never rests.

Blood flows through a network of blood vessels that extend between the heart and peripheral tissues. Those blood vessels make up a **pulmonary circuit,** which carries blood to and from the gas exchange surfaces of the lungs, and a **systemic circuit,** which transports blood to and from the rest of the body (**Figure 20–1**). Each circuit begins and ends at the heart, and blood travels through these circuits in sequence. Thus, blood returning to the heart from the systemic circuit must complete the pulmonary circuit before reentering the systemic circuit.

Arteries, or *efferent vessels*, carry blood away from the heart, and **veins,** or *afferent vessels,* return blood to the heart. Microscopic thin-walled vessels called **capillaries** interconnect the smallest arteries and the smallest veins. Capillaries are called **exchange vessels,** because their thin walls permit the exchange of nutrients, dissolved gases, and waste products between the blood and surrounding tissues.

Figure 20–1 An Overview of the Cardiovascular System. Driven by the pumping of the heart, blood flows through the pulmonary and systemic circuits in sequence. Each circuit begins and ends at the heart and contains arteries, capillaries, and veins.



Each day the heart pumps about 8000 liters of blood—enough to fill forty 55-gallon drums, or 8800 quart-sized milk cartons. Try transferring a gallon of water by using a squeeze pump, and you'll appreciate just how hard the heart has to work to keep you alive. Despite its impressive workload, the heart is a small organ, roughly the size of a clenched fist.

The heart has four muscular chambers, two associated with each circuit. The **right atrium** (Ā-trē-um; entry chamber; plural, *atria*) receives blood from the systemic circuit and passes it to the **right ventricle** (VEN-tri-kl; little belly), which then pumps blood into the pulmonary circuit. The **left atrium** collects blood from the pulmonary circuit and empties it into the **left ventricle,** which pumps blood into the systemic circuit. When the heart beats, first the atria contract, and then the ventricles contract. The two ventricles contract at the same time and eject equal volumes of blood into the pulmonary and systemic circuits.

20-1 The heart is a four-chambered organ, supplied by the coronary circulation, that pumps oxygen-poor blood to the lungs and oxygen-rich blood to the rest of the body

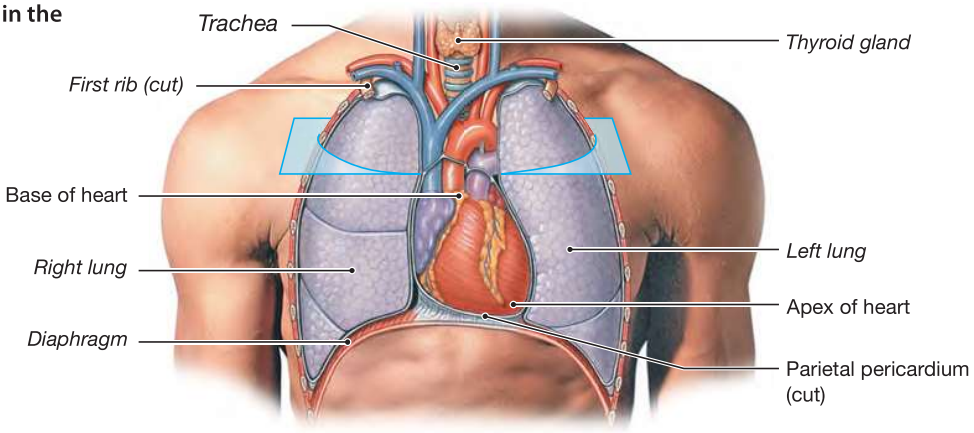
The heart is located near the anterior chest wall, directly posterior to the sternum (**Figure 20–2a**). The great veins and arteries are connected to the superior end of the heart at its base. The base sits posterior to the sternum at the level of the third costal cartilage, centered about 1.2 cm (0.5 in.) to the left side. The inferior, pointed tip of the heart is the **apex** (Ā-peks). A typical adult heart measures approximately 12.5 cm (5 in.) from the base to the apex, which reaches the fifth intercostal space approximately 7.5 cm (3 in.) to the left of the midline. A midsagittal section through the trunk does not divide the heart into two equal halves. Note that (1) the center of the base lies slightly to the left of the midline, (2) a line drawn between the center of the base and the apex points further to the left, and (3) the entire heart is rotated to the left around this line, so that the right atrium and right ventricle dominate an anterior view of the heart.

The heart sits in the anterior portion of the mediastinum. The **mediastinum** is the region between the two pleural cavities. It also contains the *great vessels* (the largest veins and arteries in the body), thymus, esophagus, and trachea. **Figure 20–2b** is a sectional view that shows the position of the heart relative to other structures in the mediastinum.

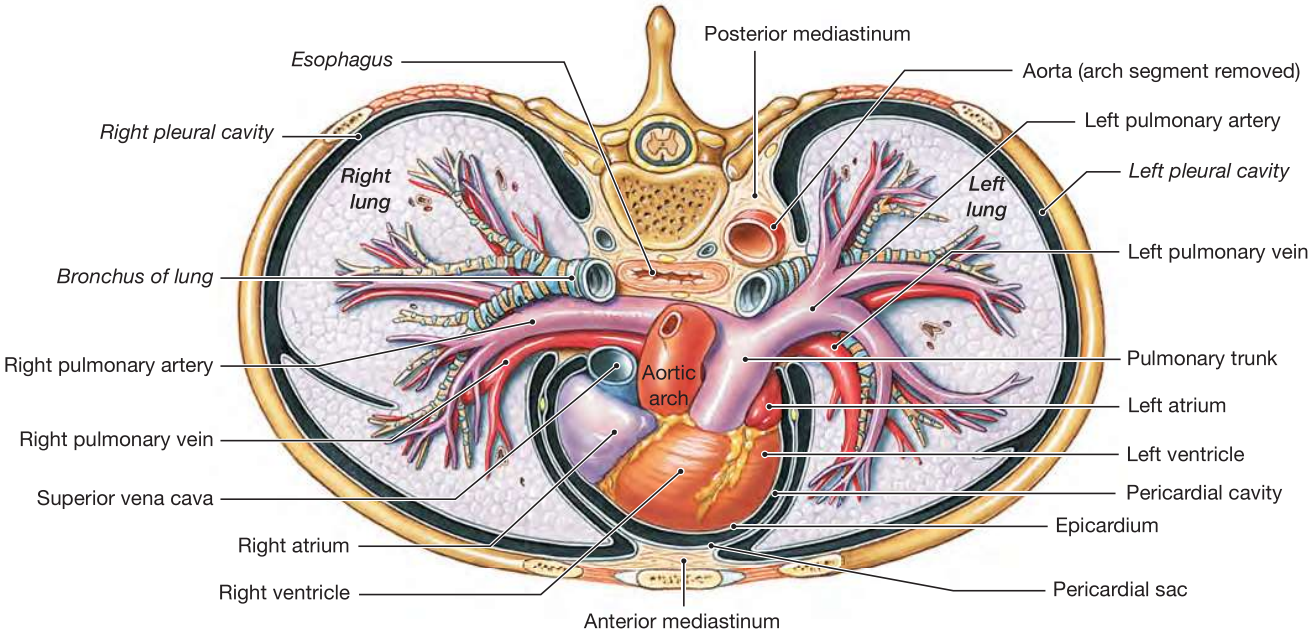
The Pericardium

The **pericardial** (per-i-KAR-dē-al) **sac,** or *fibrous pericardium*, surrounds the heart. The pericardial sac consists of a dense network

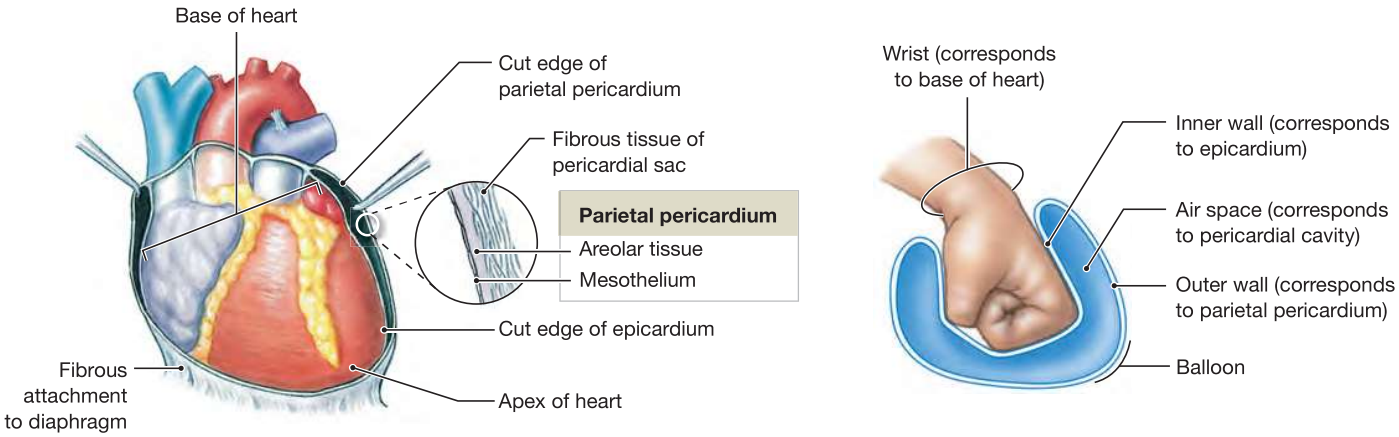
Figure 20–2 The Location of the Heart in the Thoracic Cavity. ATLAS: Plate 47a,b



a An anterior view of the chest, showing the position of the heart and major blood vessels relative to the ribs, lungs, and diaphragm.



b A superior view of the organs in the mediastinum; portions of the lungs have been removed to reveal blood vessels and airways. The heart is situated in the anterior part of the mediastinum, immediately posterior to the sternum.



c The relationship between the heart and the pericardial cavity; compare with the fist-and-balloon example.

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of collagen fibers. It stabilizes the position of the heart and associated vessels within the mediastinum.

The lining of the pericardial cavity is called the **pericardium.** To visualize the relationship between the heart and the pericardial cavity, imagine pushing your fist toward the center of a large, partially inflated balloon (**Figure 20–2c**). The balloon represents the pericardium, and your fist is the heart. Your wrist, where the balloon folds back on itself, corresponds to the **base** of the heart, where the great vessels are attached. The air space inside the balloon corresponds to the pericardial cavity.

The pericardium is lined by a delicate serous membrane that can be subdivided into two parts. The **visceral pericardium,** or *epicardium*, covers and adheres closely to the outer surface of the heart. The **parietal pericardium** lines the inner surface of the tough pericardial sac surrounding the heart (**Figure 20–2c**).

The small space between the parietal and visceral surfaces is the pericardial cavity. It normally contains 15–50 mL of **pericardial fluid,** secreted by the pericardial membranes. This fluid acts as a lubricant, reducing friction between the opposing surfaces as the heart beats. Pathogens can infect the pericardium, producing inflammation and the condition **pericarditis.** The inflamed pericardial surfaces rub against one another, making a distinctive scratching sound that can be heard through a stethoscope. The pericardial inflammation also commonly results in increased production of pericardial fluid. Fluid then collects in the pericardial cavity, restricting the movement of the heart. This condition, called *cardiac tamponade* (tam-po-NĀD; *tampon*, plug), can also result from traumatic injuries (such as stab wounds) that produce bleeding into the pericardial cavity.

20

Superficial Anatomy of the Heart

You can easily identify the four chambers of the heart in a superficial view (**Figure 20–3**). The two atria have relatively thin muscular walls and are highly expandable. When not filled with blood, the outer portion of each atrium deflates and becomes a lumpy, wrinkled flap. This expandable extension of an atrium is called an *atrial appendage*, or an **auricle** (AW-ri-kl; *auris*, ear), because it reminded early anatomists of the external ear (**Figure 20–3a**). The **coronary sulcus,** a deep groove, marks the border between the atria and the ventricles. The **anterior interventricular sulcus** and the **posterior interventricular sulcus** are shallower depressions that mark the boundary between the left and right ventricles (**Figure 20–3a,b**).

Substantial amounts of fat generally lie in the coronary and interventricular sulci. In fresh or preserved hearts, this fat must be stripped away to expose the underlying grooves. These sulci also contain the arteries and veins that carry blood to and from the cardiac muscle.

The Heart Wall

A section through the wall of the heart reveals three distinct layers: an outer epicardium, a middle myocardium, and an inner endocardium. **Figure 20–4a** illustrates these three layers:

1. The **epicardium** is the visceral pericardium that covers the outer surface of the heart. This serous membrane consists of an exposed mesothelium and an underlying layer of loose areolar connective tissue that is attached to the myocardium.
2. The **myocardium,** or muscular wall of the heart, forms the atria and ventricles. This layer contains cardiac muscle tissue, blood vessels, and nerves. The myocardium consists of concentric layers of cardiac muscle tissue. The atrial myocardium contains muscle bundles that wrap around the atria and form figure eights that encircle the great vessels (**Figure 20–4b**). Superficial ventricular muscles wrap around both ventricles, and deeper muscle layers spiral around and between the ventricles toward the apex in a figure-eight pattern.
3. The **endocardium** covers the inner surfaces of the heart, including those of the heart valves. This simple squamous epithelium is continuous with the endothelium of the attached great vessels.

Cardiac Muscle Tissue

As noted in Chapter 10, **cardiac muscle cells** are interconnected by **intercalated discs** (**Figure 20–5a,c**). At an intercalated disc, the interlocking membranes of adjacent cells are held together by desmosomes and linked by gap junctions (**Figure 20–5b**). Intercalated discs transfer the force of contraction from cell to cell and propagate action potentials. **Table 20–1** provides a quick review of the structural and functional differences between cardiac muscle cells and skeletal muscle fibers. Histological characteristics that distinguish cardiac muscle cells from skeletal muscle fibers include (1) small size; (2) a single, centrally located nucleus; (3) branching interconnections between cells; and (4) the presence of intercalated discs.

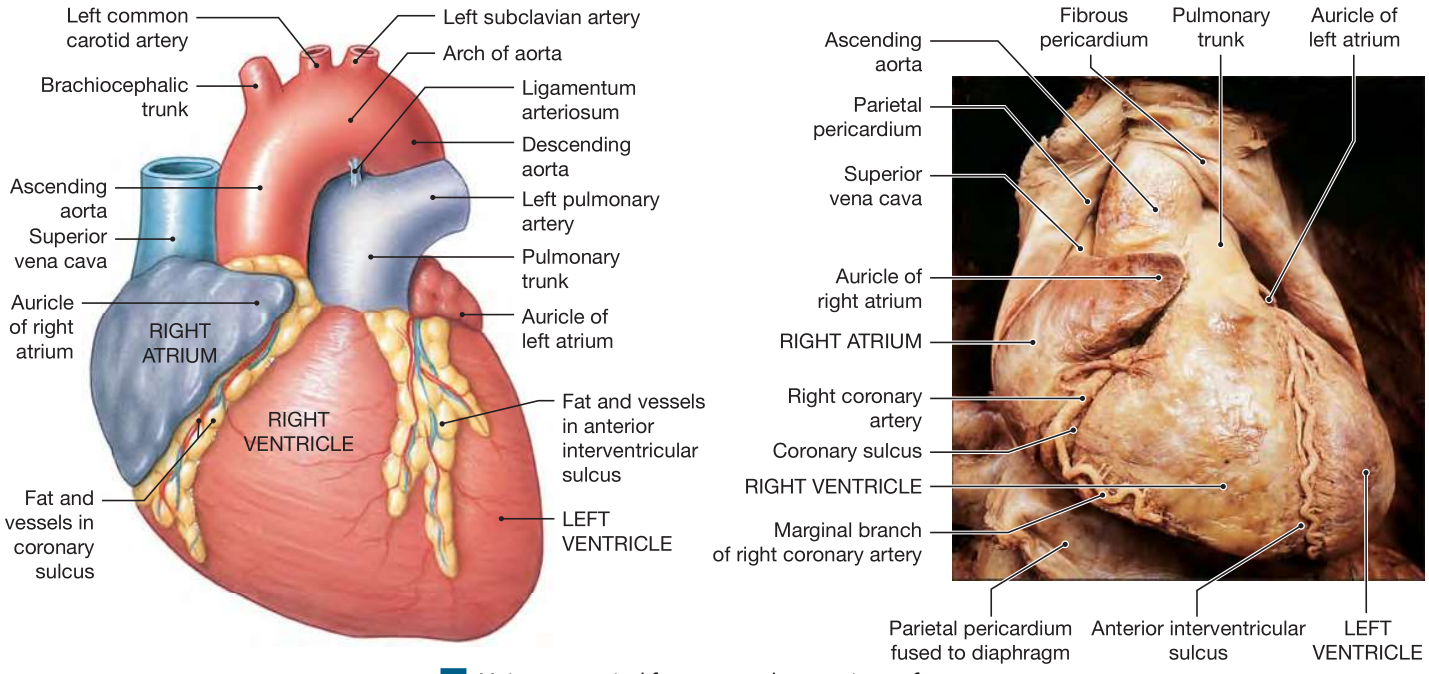
Tips & Tricks

The term *intercalated* means "inserted between other elements." Thus, intercalated discs appear to have been inserted between cardiac muscle cells.

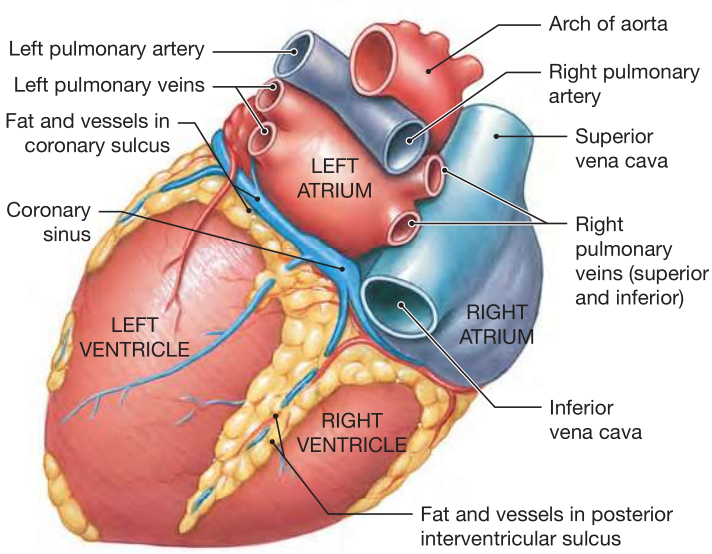
Internal Anatomy and Organization

Next let's examine the major landmarks and structures visible on the interior surface of the heart. In a sectional view, you can see that the right atrium communicates with the right ventricle, and the left atrium with the left ventricle (**Figure 20–6a,c**). The atria are separated by the **interatrial septum** (*septum*, wall), and the ventricles are separated by the much thicker

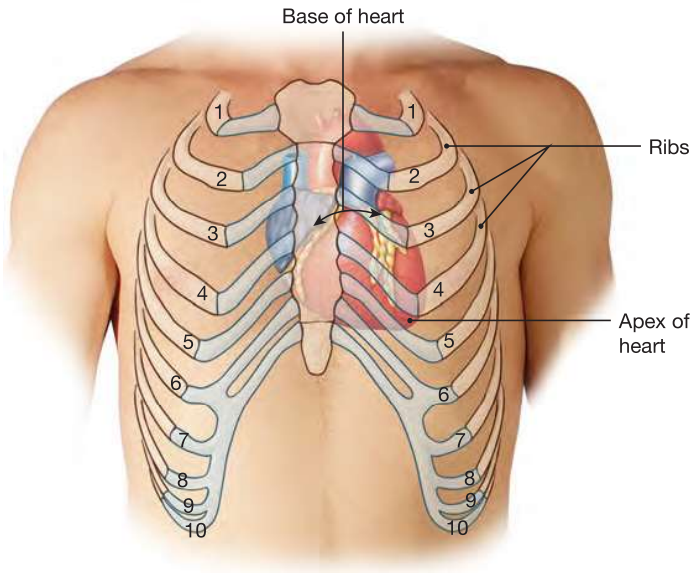
Figure 20–3 The Superficial Anatomy of the Heart.



a Major anatomical features on the anterior surface.



b Major landmarks on the posterior surface. Coronary arteries (which supply the heart itself) are shown in red; coronary veins are shown in blue.



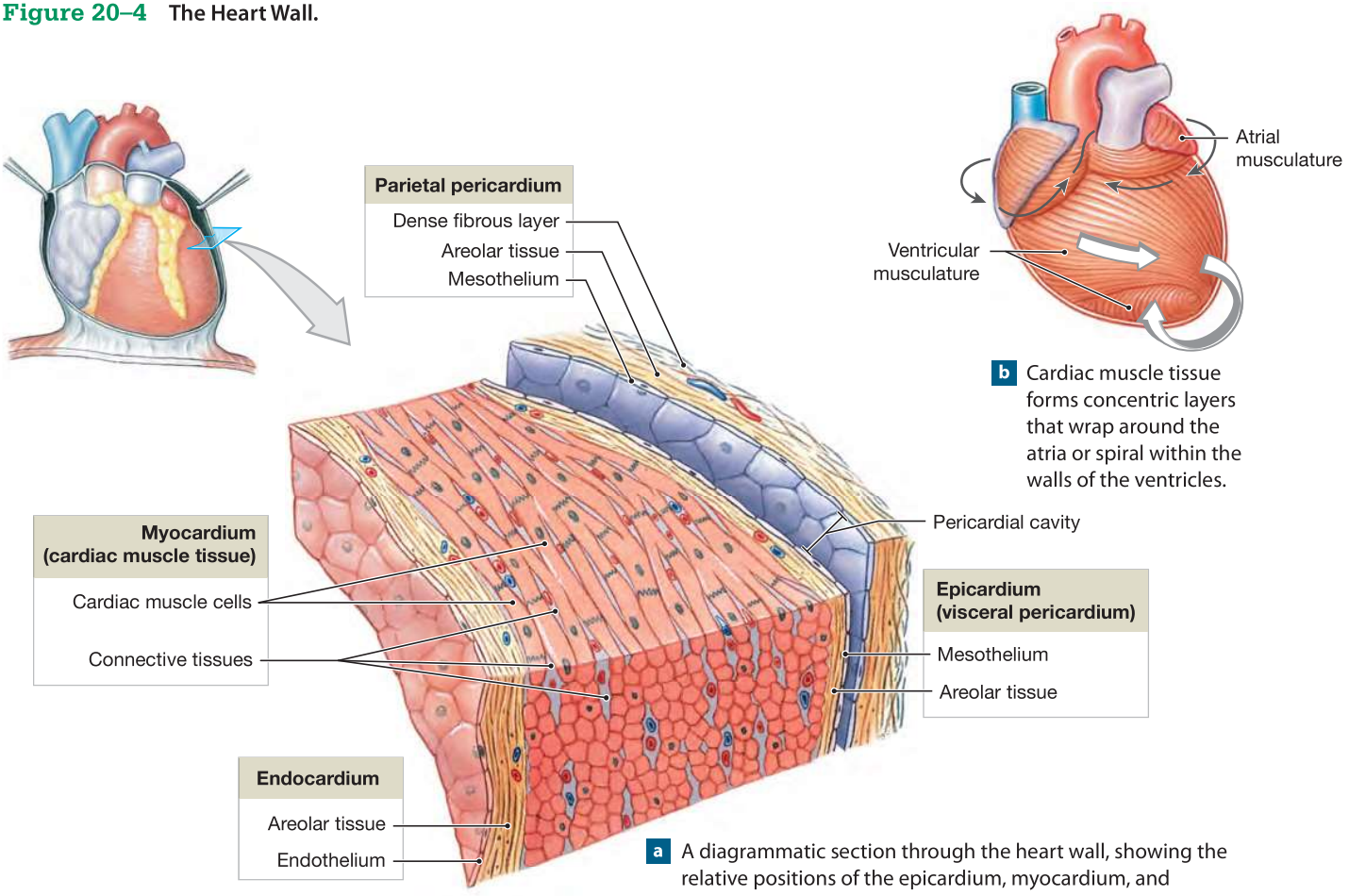
c Heart position relative to the rib cage.

interventricular septum. Each septum is a muscular partition. **Atrioventricular (AV) valves** are folds of fibrous tissue that extend into the openings between the atria and ventricles. These valves permit blood to flow only in one direction: from the atria to the ventricles.

The Right Atrium

The right atrium receives blood from the systemic circuit through the two great veins: the **superior vena cava** (VĒ-na KĀ-vuh; *venae cavae,* plural) and the **inferior vena cava.** The superior vena cava opens into the posterior and superior portion of the right

Figure 20–4 The Heart Wall.



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atrium. It delivers blood to the right atrium from the head, neck, upper limbs, and chest. The inferior vena cava opens into the posterior and inferior portion of the right atrium. It carries blood to the right atrium from the rest of the trunk, the viscera, and the lower limbs. The *cardiac veins* draining the myocardium return blood to the **coronary sinus,** a large, thin-walled vein that opens into the right atrium inferior to the connection with the superior vena cava.

The opening of the coronary sinus lies near the posterior edge of the interatrial septum. From the fifth week of embryonic development until birth, an oval opening called the **foramen ovale** penetrates the interatrial septum and connects the two atria of the fetal heart. Before birth, the foramen ovale permits blood to flow from the right atrium to the left atrium while the lungs are developing. At birth, the foramen ovale closes, and the opening is permanently sealed off within three months of delivery. (If the foramen ovale does not close, serious cardiovascular problems may result. We consider these in Chapter 21.) A small, shallow depression called the **fossa ovalis** remains at this site in the adult heart (**Figure 20–6a,c**).

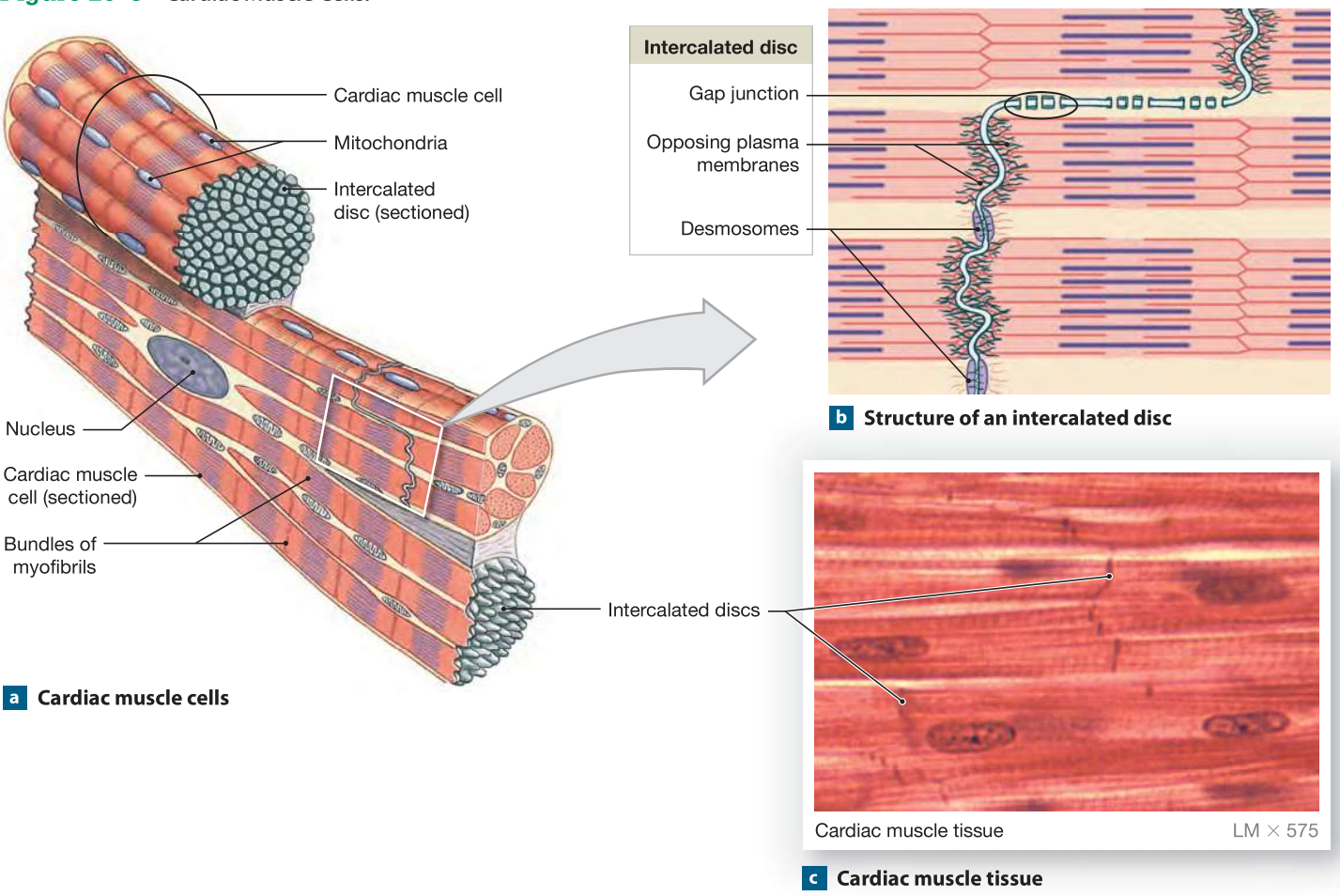
ATLAS: Embryology Summary 15: The Development of the Heart

The posterior wall of the right atrium and the interatrial septum have smooth surfaces. In contrast, the anterior atrial wall and the inner surface of the auricle contain prominent muscular ridges called the **pectinate muscles** (*pectin*, comb), or *musculi pectinati* (**Figure 20–6a,c**).

The Right Ventricle

Blood travels from the right atrium into the right ventricle through a broad opening bordered by three fibrous flaps. These flaps, called **cusps,** are part of the **right atrioventricular (AV) valve,** also known as the **tricuspid** (trī-KUS-pid; *tri*, three) **valve.** The free edge of each cusp is attached to connective tissue fibers called the **chordae tendineae** (KOR-dē TEN-di-nē-ē; tendinous cords). The fibers originate at the **papillary** (PAP-i-ler-ē) **muscles,** conical muscular projections that arise from the inner surface of the right ventricle (**Figure 20–6a,b**). The right AV valve closes when the right ventricle contracts, preventing the backflow of blood into the right atrium. Without the chordae tendineae to anchor their free edges, the cusps would be like swinging doors that permit blood flow in both directions.

Figure 20–5 Cardiac Muscle Cells.



a Cardiac muscle cells

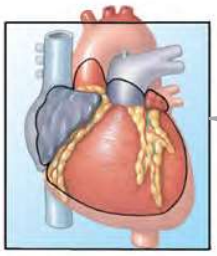
b Structure of an intercalated disc

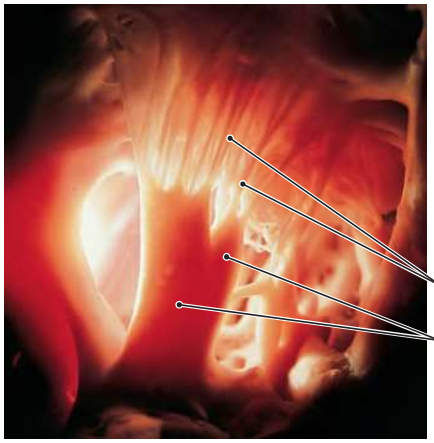
c Cardiac muscle tissue

Table 20–1 Structural and Functional Differences between Cardiac Muscle Cells and Skeletal Muscle Fibers

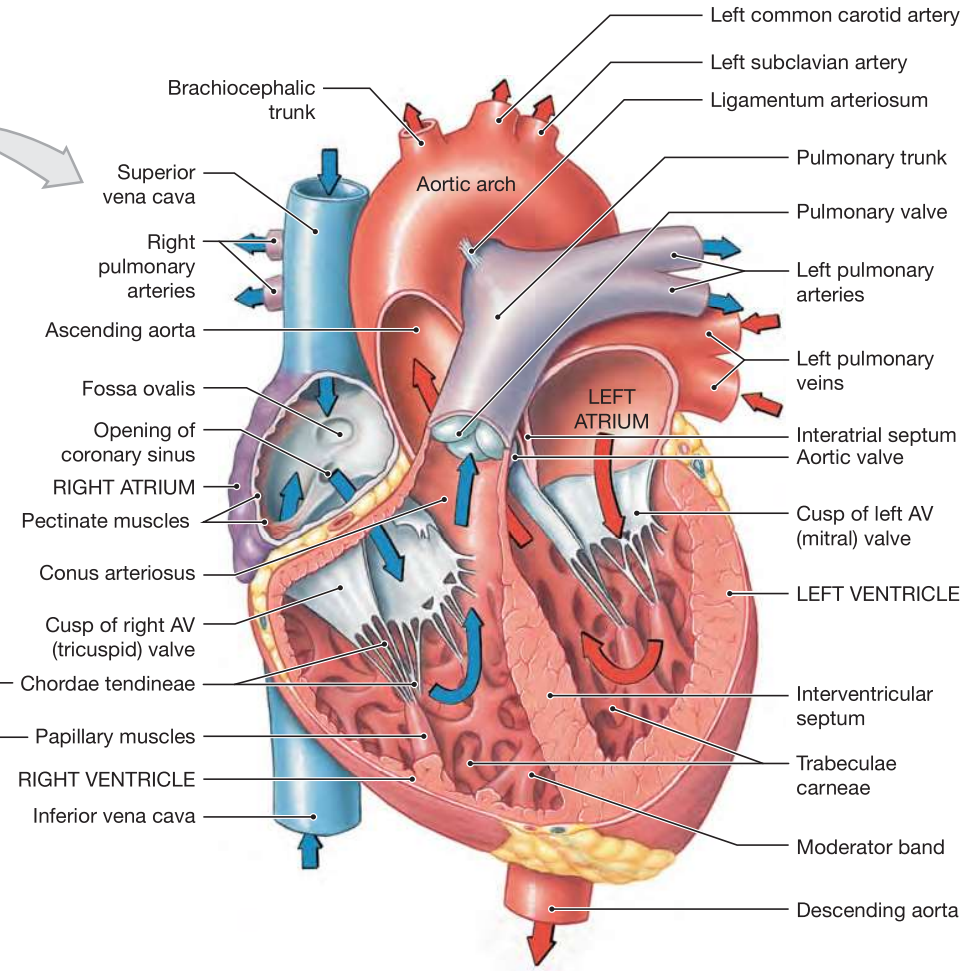
Feature	Cardiac Muscle Cells	Skeletal Muscle Fibers
Size	10–20 μm × 50–100 μm	100 μm × up to 40 cm
Nuclei	Typically 1 (rarely 2–5)	Multiple (hundreds)
Contractile proteins	Sarcomeres along myofibrils	Sarcomeres along myofibrils
Internal membranes	Short T tubules; no triads formed with sarcoplasmic reticulum	Long T tubules form triads with cisternae of the sarcoplasmic reticulum
Mitochondria	Abundant (25% of cell volume)	Much less abundant
Inclusions	Myoglobin, lipids, glycogen	Little myoglobin, few lipids, but extensive glycogen reserves
Blood supply	Very extensive	More extensive than in most connective tissues, but sparse compared with supply to cardiac muscle cells
Metabolism (resting)	Not applicable	Aerobic, primarily lipid-based
Metabolism (active)	Aerobic, primarily using lipids and carbohydrates	Anaerobic, through breakdown of glycogen reserves
Contractions	Twitches with brief relaxation periods; long refractory period prevents tetanic contractions	Usually sustained contractions
Stimulus for contraction	Autorhythmicity of pacemaker cells generates action potentials	Activity of somatic motor neuron generates action potentials in sarcolemma
Trigger for contraction	Calcium entry from the ECF and calcium release from the sarcoplasmic reticulum	Calcium release from the sarcoplasmic reticulum
Intercellular connections	Branching network with plasma membranes locked together at intercalated discs; connective tissue fibers tie adjacent layers together	Adjacent fibers tied together by connective tissue fibers

Figure 20–6 The Sectional Anatomy of the Heart.

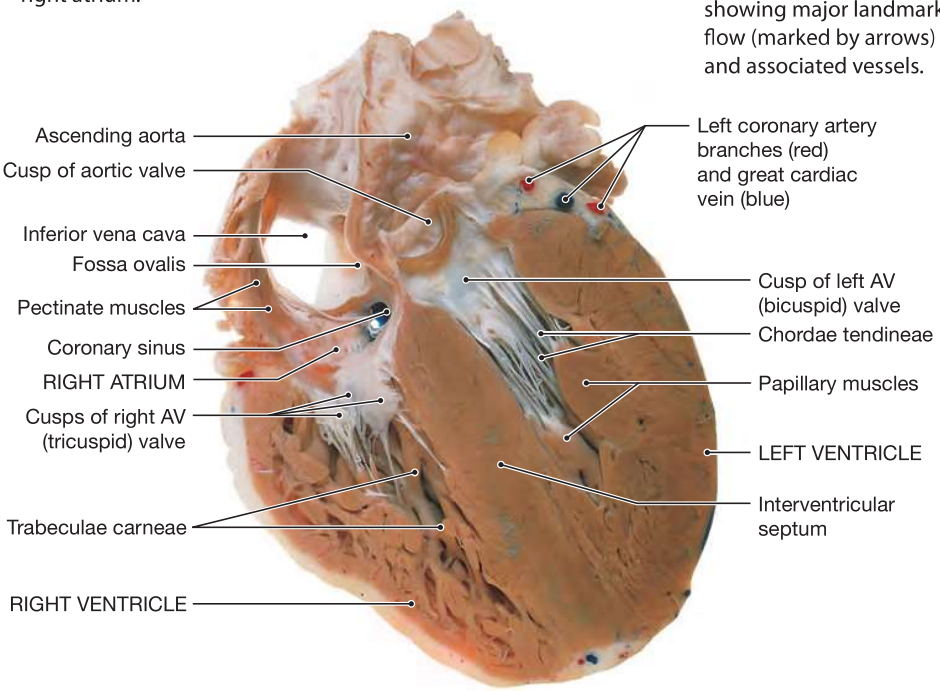




b The papillary muscles and chordae tendinae supporting the right AV (tricuspid) valve. The photograph was taken from inside the right ventricle, looking toward a light shining from the right atrium.



a A diagrammatic frontal section through the heart, showing major landmarks and the path of blood flow (marked by arrows) through the atria, ventricles, and associated vessels.



c A frontal section, anterior view.

The internal surface of the ventricle also contains a series of muscular ridges: the **trabeculae carneae** (tra-BEK-ū-lē KAR-nē-ē; *carneus*, fleshy). The *moderator band* is a muscular ridge that extends horizontally from the inferior portion of the interventricular septum and connects to the anterior papillary muscle. This ridge contains part of the *conducting system*, an internal network that coordinates the contractions of cardiac muscle cells. The moderator band delivers the stimulus for contraction to the papillary muscles. As a result, they begin tensing the chordae tendineae before the rest of the ventricle contracts.

Tips & Tricks

The saying "To tug on your heartstrings" may help you remember the functions of the papillary muscles and the chordae tendineae: Contractions of the papillary muscles pull on the chordae tendineae, which "tug" on your heart's valves.

The superior end of the right ventricle tapers to the **conus arteriosus,** a conical pouch that ends at the **pulmonary valve,** or *pulmonary semilunar valve*. The pulmonary valve consists of three semilunar (half-moon-shaped) cusps of thick connective tissue. Blood flowing from the right ventricle passes through this valve into the **pulmonary trunk,** the start of the pulmonary circuit. The cusps prevent backflow as the right ventricle relaxes. Once in the pulmonary trunk, blood flows into the **left pulmonary arteries** and the **right pulmonary arteries.** These vessels branch repeatedly within the lungs before supplying the capillaries, where gas exchange occurs.

The Left Atrium

From the respiratory capillaries, blood collects into small veins that ultimately unite to form the four pulmonary veins. The posterior wall of the left atrium receives blood from two **left** and two **right pulmonary veins.** Like the right atrium, the left atrium has an auricle. A valve, the **left atrioventricular (AV) valve,** or **bicuspid** (bī-KUS-pid) **valve,** guards the entrance to the left ventricle (**Figure 20–6a,c**). As the name *bicuspid* implies, the left AV valve contains two cusps, not three. Clinicians often call this valve the **mitral** (MĪ-tral; *mitre*, a bishop's hat) **valve.** The left AV valve permits blood to flow from the left atrium into the left ventricle, but it prevents backflow when the left ventricle contracts.

Tips & Tricks

To remember the locations of the tricuspid and bicuspid (mitral) valves, think **"try** to be **right"** for the ***tri***cuspid, and associate the ***l*** in mitra***l*** with the ***l*** in ***l***eft.

The Left Ventricle

Even though the two ventricles hold and pump equal amounts of blood, the left ventricle is much larger than the right ventricle. What's the reason? It has thicker walls. These thick, muscular walls enable the left ventricle to push blood through the large systemic circuit. In contrast, the right ventricle needs to pump blood, at lower pressure, only about 15 cm (6 in.) to and from the lungs.

The internal organization of the left ventricle resembles that of the right ventricle, but it has no moderator band (**Figure 20–6a,c**). The trabeculae carneae are prominent. A pair of large papillary muscles tenses the chordae tendineae that anchor the cusps of the AV valve and prevent blood from flowing back into the left atrium.

Blood leaves the left ventricle through the **aortic valve,** or *aortic semilunar valve*, and goes into the **ascending aorta.** The arrangement of cusps in the aortic valve is the same as that in the pulmonary valve. Once the blood has been pumped out of the heart and into the systemic circuit, the aortic valve prevents backflow into the left ventricle. From the ascending aorta, blood flows through the **aortic arch** and into the **descending aorta** (**Figure 20–6a**). The pulmonary trunk is attached to the aortic arch by the *ligamentum arteriosum*, a fibrous band left over from an important fetal blood vessel that once linked the pulmonary and systemic circuits.

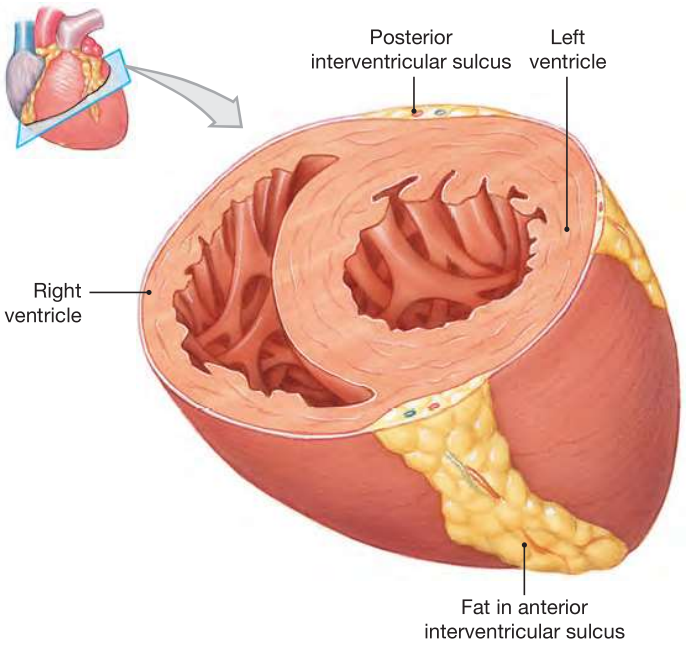
Structural Differences between the Left and Right Ventricles

The function of the atria is to collect blood that is returning to the heart and to convey it to the ventricles. The demands on the right and left atria are similar, and the two chambers look almost identical. The demands on the right and left ventricles, however, are very different, and the two have significant structural differences.

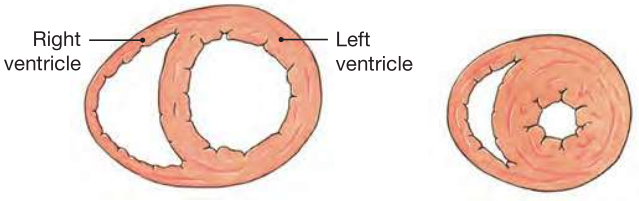
Anatomical differences between the left and right ventricles are easiest to see in a three-dimensional view (**Figure 20–7a**). The lungs are close to the heart, and the pulmonary blood vessels are relatively short and wide. For these reasons, the right ventricle normally does not need to work very hard to push blood through the pulmonary circuit. Accordingly, the muscular wall of the right ventricle is relatively thin. In sectional view, it resembles a pouch attached to the massive wall of the left ventricle. When the right ventricle contracts, it acts like a bellows, squeezing the blood against the thick wall of the left ventricle. This action moves blood very efficiently with minimal effort, but it develops relatively low pressures.

A comparable pumping arrangement would not work well for the left ventricle. Four to six times as much pressure must be exerted to push blood around the systemic circuit as around the pulmonary circuit. The left ventricle has an extremely thick muscular wall and is round in cross section (**Figure 20–7a**). When this ventricle contracts, it shortens and narrows. In other words, (1) the distance between the base and apex decreases, and (2) the diameter of the ventricular chamber decreases. The effect is similar to simultaneously squeezing and rolling up the end of a

Figure 20–7 Structural Differences between the Left and Right Ventricles. ATLAS: Plate 45d



a A diagrammatic sectional view through the heart, showing the relative thicknesses of the two ventricles. Notice the pouchlike shape of the right ventricle and the greater thickness of the left ventricle.



b Diagrammatic views of the ventricles just before a contraction (dilated) and just after a contraction (contracted).

toothpaste tube. The pressure generated is more than enough to open the aortic valve and eject blood into the ascending aorta.

As the powerful left ventricle contracts, it bulges into the right ventricular cavity (**Figure 20–7b**). This action makes the right ventricle more efficient. Individuals with severe damage to the right ventricle may survive, because the contraction of the left ventricle helps push blood into the pulmonary circuit. We return to this topic in Chapter 21, where we consider the integrated functioning of the cardiovascular system.

The Heart Valves

As we have seen, the heart has two pairs of one-way valves that prevent the backflow of blood as the chambers contract. Let's look at the structure and function of these heart valves.

The Atrioventricular Valves. The atrioventricular (AV) valves prevent the backflow of blood from the ventricles to the atria when the ventricles are contracting. The chordae tendineae and papillary muscles play important roles in the normal function of the AV valves. When the ventricles are relaxed, the chordae tendineae are loose, and the AV valves offer no resistance as blood flows from the atria into the ventricles (**Figure 20–8a**). When the ventricles contract, blood moving back toward the atria swings the cusps together, closing the valves (**Figure 20–8b**). At the same time, the contraction of the papillary muscles tenses the chordae tendineae, stopping the cusps before they swing into the atria. If the chordae tendineae were cut or the papillary muscles were damaged, backflow, called **regurgitation,** of blood into the atria would occur each time the ventricles contracted.

The Semilunar Valves. The pulmonary and aortic valves prevent the backflow of blood from the pulmonary trunk and aorta into the right and left ventricles, respectively. Unlike the AV valves, the semilunar valves do not need muscular braces, because the arterial walls do not contract and the relative positions of the cusps are stable. When the semilunar valves close, the three symmetrical cusps support one another like the legs of a tripod (**Figure 20–8a**).

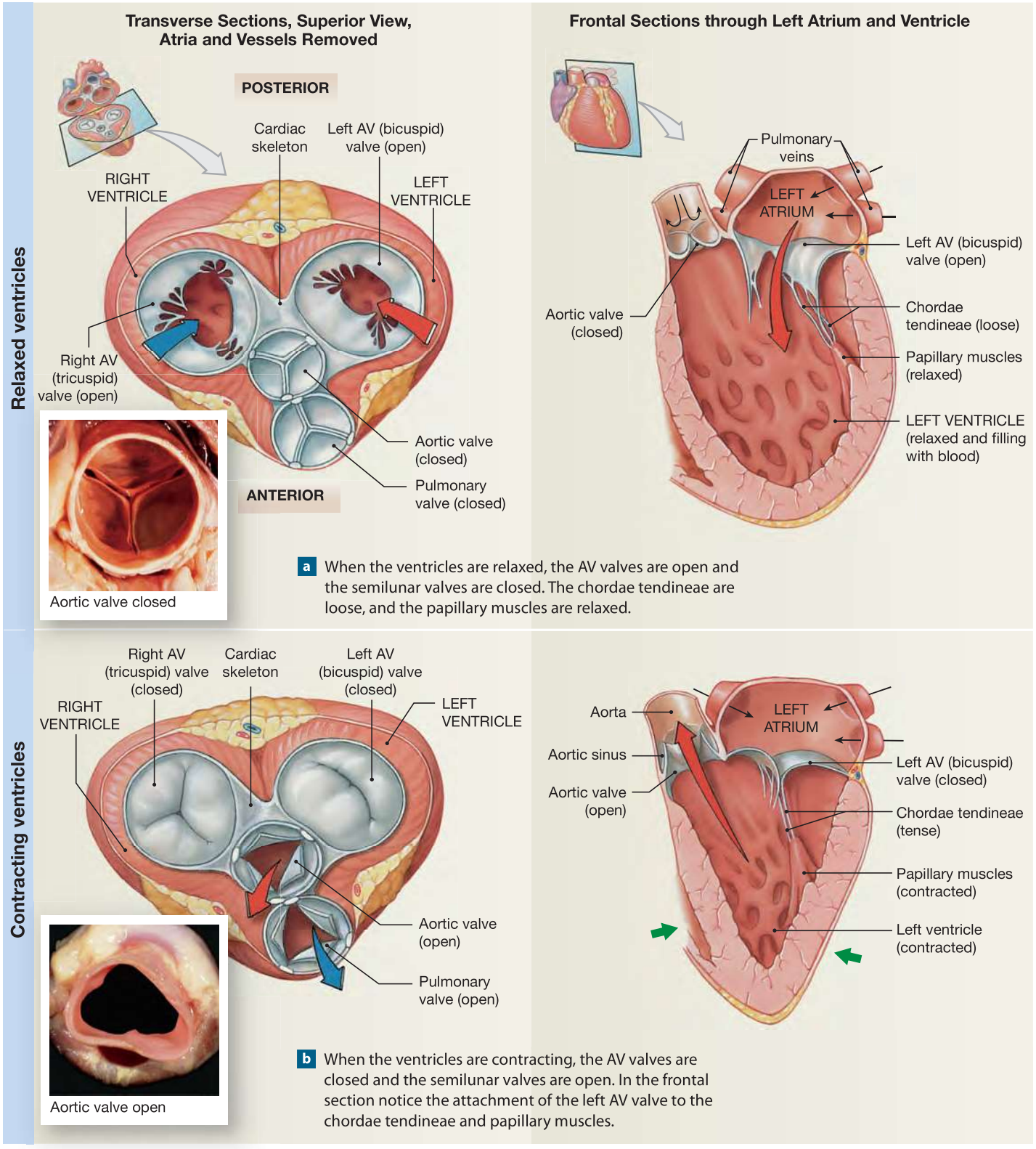
Adjacent to each cusp of the aortic valve are saclike dilations of the base of the ascending aorta. These sacs, called **aortic sinuses,** prevent the individual cusps from sticking to the wall of the aorta when the valve opens. The *right* and *left coronary arteries*, which deliver blood to the myocardium, originate at the right and left aortic sinuses. (The posterior aortic sinus does not give rise to any blood vessel.)

Serious valve problems can interfere with the working of the heart. If valve function deteriorates to the point at which the heart cannot maintain adequate circulatory flow, symptoms of **valvular heart disease (VHD)** appear. Congenital malformations may be responsible, but in many cases the condition develops after **carditis,** an inflammation of the heart, occurs. One important cause of carditis is **rheumatic** (roo-MAT-ik) **fever,** an inflammatory autoimmune response to an infection by streptococcal bacteria. It most often occurs in children.

Connective Tissues and the Cardiac Skeleton

The connective tissues of the heart include large numbers of collagen and elastic fibers. Each cardiac muscle cell is wrapped in a strong, but elastic, sheath. Adjacent cells are tied together by fibrous cross-links, or "struts." These fibers are, in turn, interwoven into sheets that separate the superficial and deep muscle layers. The connective tissue fibers (1) provide physical support for the cardiac muscle fibers, blood vessels, and nerves

Figure 20–8 Valves of the Heart. Red (oxygenated) and blue (deoxygenated) arrows indicate blood flow into or out of a ventricle; black arrows, blood flow into an atrium; and green arrows, ventricular contraction.



of the myocardium; (2) help distribute the forces of contraction; (3) add strength and prevent overexpansion of the heart; and (4) provide elasticity that helps return the heart to its original size and shape after a contraction.

The **cardiac skeleton** (sometimes called the *fibrous skeleton*) of the heart consists of four dense bands of tough elastic tissue that encircle the heart valves and the bases of the pulmonary trunk and aorta (**Figure 20–8**). These bands stabilize the positions of the heart valves and ventricular muscle cells. They also electrically insulate the ventricular cells from the atrial cells.

The Blood Supply to the Heart

The heart works continuously, so cardiac muscle cells need reliable supplies of oxygen and nutrients. A great volume of blood flows through the chambers of the heart, but the myocardium has its own, separate blood supply. The **coronary circulation** supplies blood to the muscle tissue of the heart. During maximum exertion, the heart's demand for oxygen rises considerably. The blood flow to the myocardium may then increase to nine times that of resting levels. The coronary circulation includes an extensive network of coronary blood vessels (**Figure 20–9**).

The Coronary Arteries

The left and right **coronary arteries** originate at the base of the ascending aorta, at the aortic sinuses (**Figure 20–9a**). Blood pressure here is the highest in the systemic circuit. Each time the left ventricle contracts, it forces blood into the aorta. The arrival of this blood at high pressures stretches the elastic walls of the aorta. When the left ventricle relaxes, blood no longer flows into the aorta, pressure declines, and the walls of the aorta recoil. This recoil, called *elastic rebound*, pushes blood both forward, into the systemic circuit, and backward, through the left and right aortic sinuses and then into the respective coronary arteries. In this way, the combination of elevated blood pressure and elastic rebound ensures a continuous flow of blood to meet the demands of active cardiac muscle tissue. Yet myocardial blood flow is not steady. It peaks while the heart muscle is relaxed, and almost ceases while it contracts.

The **right coronary artery** follows the coronary sulcus around the heart. It supplies blood to (1) the right atrium, (2) portions of both ventricles, and (3) portions of the conducting system of the heart, including the *sinoatrial (SA) node* and the *atrioventricular (AV) node*. The cells of these nodes are essential to establishing the normal heart rate. We focus on them in a later section.

Inferior to the right atrium, the right coronary artery generally gives rise to one or more **marginal arteries,** which extend across the surface of the right ventricle (**Figure 20–9a,b**). The right coronary artery then continues across the posterior surface of the heart. It supplies the **posterior interventricular artery,** or *posterior descending artery*, which runs toward the apex within the posterior interventricular sulcus (**Figure 20–9b,c**). The posterior interventricular artery supplies blood to the interventricular septum and adjacent portions of the ventricles.

The **left coronary artery** supplies blood to the left ventricle, left atrium, and interventricular septum. As it reaches the anterior surface of the heart, it gives rise to a circumflex branch and an anterior interventricular branch. The **circumflex artery** curves to the left around the coronary sulcus. It eventually meets and fuses with small branches of the **right coronary artery** (**Figure 20–9a–c**). The much larger **anterior interventricular artery,** or *left anterior descending artery (LAD)*, swings around the pulmonary trunk and runs along the surface within the anterior interventricular sulcus (**Figure 20–9a**).

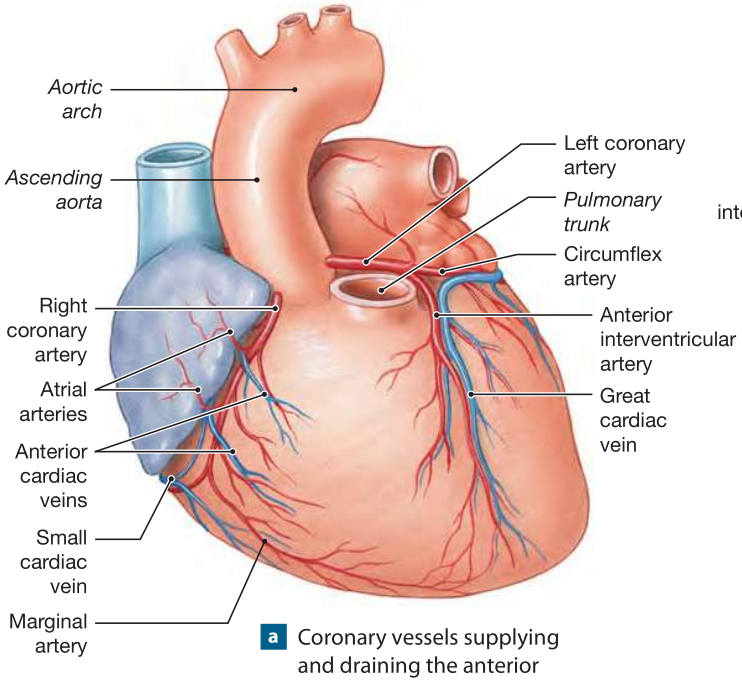
The anterior interventricular artery supplies small tributaries continuous with those of the posterior interventricular artery. Such interconnections between arteries are called **arterial anastomoses** (a-nas-tō-MŌ-sēz; *anastomosis*, outlet). Because the arteries are interconnected in this way, the blood supply to the cardiac muscle remains relatively constant despite pressure fluctuations in the left and right coronary arteries as the heart beats.

The Cardiac Veins

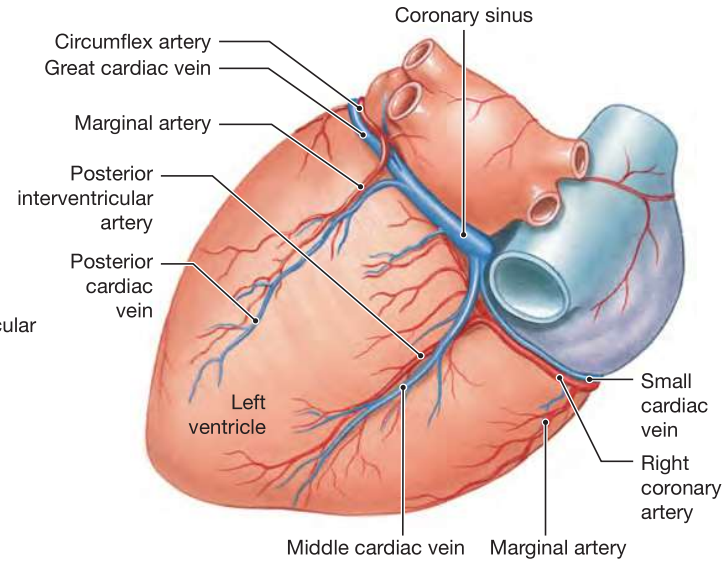
The various cardiac veins are shown in **Figure 20–9**. The **great cardiac vein** begins on the anterior surface of the ventricles, along the interventricular sulcus. This vein drains blood from the region supplied by the anterior interventricular artery, a branch of the left coronary artery. The great cardiac vein reaches the level of the atria and then curves around the left side of the heart within the coronary sulcus. The vein empties into the coronary sinus, which lies in the posterior portion of the coronary sulcus. The coronary sinus opens into the right atrium near the base of the inferior vena cava.

Other cardiac veins empty into the great cardiac vein or the coronary sinus. These veins include (1) the **posterior cardiac vein,** draining the area served by the circumflex artery; (2) the **middle cardiac vein,** draining the area supplied by the posterior interventricular artery; and (3) the **small cardiac vein,** which receives blood from the posterior surfaces of the right atrium and ventricle. The **anterior cardiac veins,** which drain

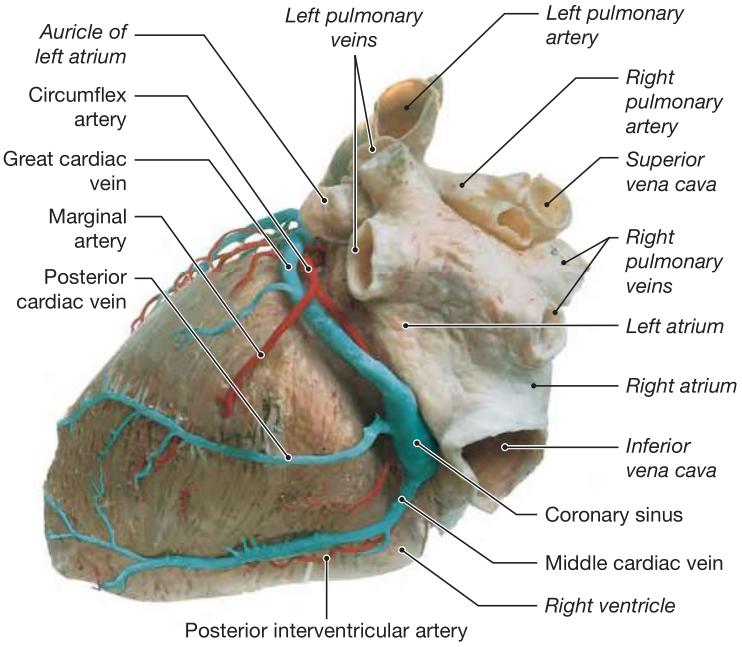
Figure 20–9 Coronary Circulation. ATLAS: Plate 45b,c



a Coronary vessels supplying and draining the anterior surface of the heart.



b Coronary vessels supplying and draining the posterior surface of the heart.



c A posterior view of the heart; the vessels have been injected with colored latex (liquid rubber).

the anterior surface of the right ventricle, empty directly into the right atrium.

Coronary artery disease is characterized by interrupted blood flow to the myocardium. **Spotlight Figure 20–10** describes this condition, along with myocardial infarction.

Checkpoint

1. **Damage to the semilunar valve of the right ventricle would affect blood flow into which vessel?**
2. **What prevents the AV valves from swinging into the atria?**
3. **Why is the left ventricle more muscular than the right ventricle?**

See the blue Answers tab at the back of the book.

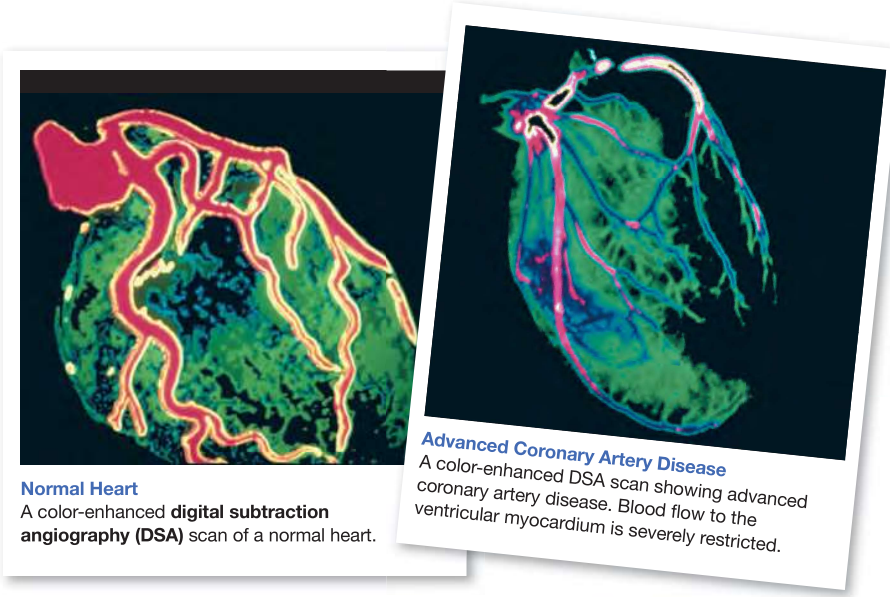
Spotlight

Figure 20–10
Heart Disease and Heart Attacks

Coronary Artery Disease

HEART DISEASE

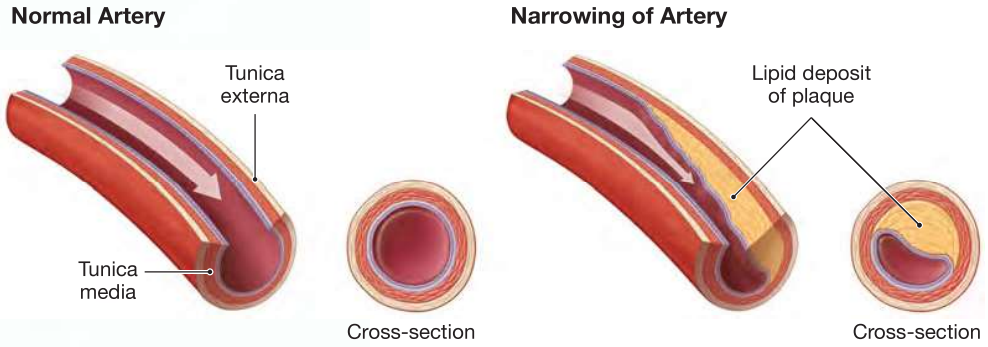
The term **coronary artery disease (CAD)** refers to areas of partial or complete blockage of coronary circulation. Cardiac muscle cells need a constant supply of oxygen and nutrients, so any reduction in blood flow to the heart muscle produces a corresponding reduction in cardiac performance. Such reduced circulatory supply, known as **coronary ischemia** (is-KĒ-mē-uh), generally results from partial or complete blockage of the coronary arteries. The usual cause is the formation of a fatty deposit, or *atherosclerotic plaque*, in the wall of a coronary vessel. The plaque, or an associated *thrombus* (clot), then narrows the passageway and reduces blood flow. Spasms in the smooth muscles of the vessel wall can further decrease or even stop blood flow. One of the first symptoms of CAD is commonly **angina pectoris** (an-JĪ-nuh PEK-tor-is; *angina*, pain spasm + *pectoris*, of the chest). In its most common form, a temporary ischemia develops when the workload of the heart increases. Although the individual may feel comfortable at rest, exertion or emotional stress can produce a sensation of pressure, chest constriction, and pain that may radiate from the sternal area to the arms, back, and neck.



Normal Heart
A color-enhanced **digital subtraction angiography (DSA)** scan of a normal heart.

Advanced Coronary Artery Disease
A color-enhanced DSA scan showing advanced coronary artery disease. Blood flow to the ventricular myocardium is severely restricted.

*Plaques may be visible by **angiography** or high-resolution ultrasound, and the effects on coronary blood flow can be detected in digital subtraction angiography (DSA) scans of the heart as shown above.*



Left: *Chest pain or discomfort is a common symptom of angina pectoris. Although similar symptoms may accompany a heart attack, the pain is also frequently felt in the left arm.*

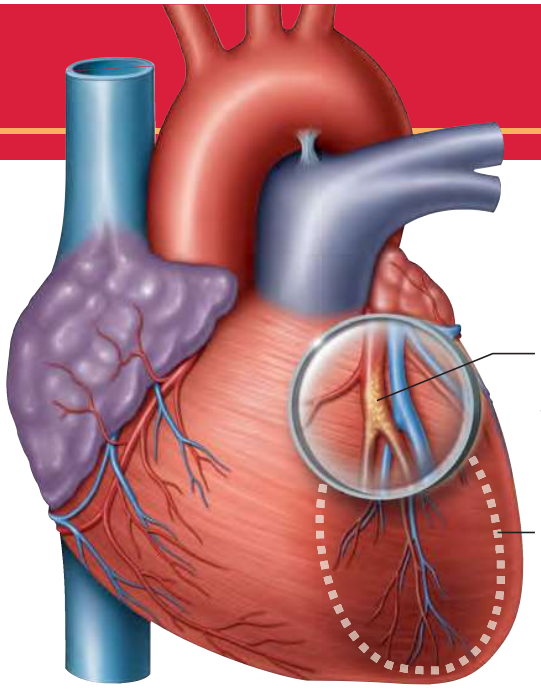
Below: *The presence of any two of these coronary risk factors more than doubles the risk of heart attack. It has been estimated that their reduction could prevent 150,000 deaths each year in the United States alone.*

Risk Factors for CAD and Myocardial Infarction

MOKING • HIGH BLOOD PRESSURE • HIGH CHOLESTEROL •
• MALE OVER AGE 70 • SEVERE EMOTIONAL STRESS • OE

Myocardial Infarction

HEART ATTACK



In a **myocardial** (mī-ō-KAR-dē-al) **infarction (MI)**, or *heart attack*, part of the coronary circulation becomes blocked, and cardiac muscle cells die from lack of oxygen. The death of affected tissue creates a nonfunctional area known as an *infarct*. Heart attacks most commonly result from severe coronary artery disease (CAD). The consequences depend on the site and nature of the circulatory blockage. If it occurs near the start of one of the coronary arteries, the damage will be widespread and the heart may stop beating. If the blockage involves one of the smaller arterial branches, the individual may survive the immediate crisis but may have many complications such as reduced contractility and cardiac arrhythmias.

A crisis often develops as a result of thrombus formation at a plaque (the most common cause of an MI), a condition called **coronary thrombosis**. A vessel already narrowed by plaque formation may also become blocked by a sudden spasm in the smooth muscles of the vascular wall.

Individuals having an MI experience intense pain, similar to that felt in angina, but persisting even at rest. However, pain does not always accompany a heart attack, and silent heart attacks may be even more dangerous than more apparent attacks, because the condition may go undiagnosed and may not be treated before a fatal MI occurs.

A myocardial infarction can usually be diagnosed with an ECG and blood studies. Damaged myocardial cells release enzymes into the circulation, and these elevated enzymes can be measured in diagnostic blood tests. The enzymes include **cardiac troponin T**, **cardiac troponin I**, and a special form of creatinine phosphokinase, **CK-MB**.

Treatment of CAD and Myocardial Infarction

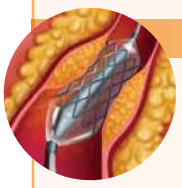
About 25% of MI patients die before obtaining medical assistance, and 65% of MI deaths among those under age 50 occur within an hour after the initial infarction.

Risk Factor Modification

Stop smoking, high blood pressure treatment, dietary modification to lower cholesterol and promote weight loss, stress reduction, and increased physical activity (where appropriate)

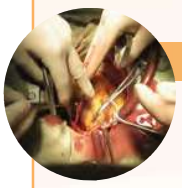
Drug Treatment

- Drugs that reduce coagulation and therefore the risk of thrombosis, such as aspirin and coumadin
- Drugs that block sympathetic stimulation (*propranolol* or *metoprolol*)
- Drugs that cause vasodilation, such as **nitroglycerin** (nī-trō-GLIS-er-in)
- Drugs that block calcium movement into the cardiac and vascular smooth muscle cells (calcium channel blockers)
- In a myocardial infarction, drugs to relieve pain, fibrinolytic agents to help dissolve clots, and oxygen



Noninvasive Surgery

- **Atherectomy**. Blockage by a single, soft plaque may be reduced with the aid of a long, slender **catheter** (KATH-e-ter) inserted into a coronary artery to the plaque. A variety of surgical tools can be slid into the catheter, and the plaque can then be removed.
- **Balloon angioplasty** (AN-jē-ō-plas-tē; *angeion*, vessel). In balloon angioplasty, the tip of the catheter contains an inflatable balloon. Once in position, the balloon is inflated, pressing the plaque against the vessel walls. Because plaques commonly redevelop after angioplasty, a fine tubular wire mesh called a stent may be inserted into the vessel, holding it open.



Coronary Artery Bypass Surgery (CABG)

In a coronary artery bypass graft, a small section is removed from either a small artery or a peripheral vein and is used to create a detour around the obstructed portion of a coronary artery. As many as four coronary arteries can be rerouted this way during a single operation. The procedures are named according to the number of vessels repaired, so we speak of single, double, triple, or quadruple coronary bypasses.

IABETES • HIGH CIRCULATING LOW-DENSITY LIPOPROTEIN
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20-2 The conducting system distributes electrical impulses through the heart, and an electrocardiogram records the associated electrical events

Next we look at several aspects of the contraction of the heart. We begin with an overview of how the heart works—cardiac physiology. Then we examine the structure and function of the conducting system, the electrical events as recorded in an electrocardiogram, and the functioning of contractile cells.

Cardiac Physiology

In a single cardiac contraction, or heartbeat, the entire heart contracts in series—first the atria and then the ventricles. Two types of cardiac muscle cells are involved in a normal heartbeat. (1) Specialized muscle cells of the *conducting system* control and coordinate the heartbeat, and (2) *contractile cells* produce the powerful contractions that propel blood.

Each heartbeat begins with an action potential generated at a pacemaker called the *SA node*, which is part of the conducting system. The conducting system then propagates and distributes this electrical impulse to stimulate contractile cells to push blood in the right direction at the proper time. A procedure known as *electrocardiography* can monitor the electrical events of the conducting system from the surface of the body. The printed record of the result is called an *electrocardiogram* (*ECG* or *EKG*).

The arrival of an electrical impulse at a cardiac muscle cell's plasma membrane produces an action potential that is comparable to an action potential in a skeletal muscle fiber. As in a skeletal muscle fiber, this action potential triggers the contraction of the cardiac muscle cell. Thanks to the coordination provided by the conducting system, the atria contract first, driving blood into the ventricles through the AV valves, and the ventricles contract next, driving blood out of the heart through the semilunar valves.

The SA node generates impulses at regular intervals, and one heartbeat follows another throughout your life. After each heartbeat comes a brief pause—less than half a second—before the next heartbeat begins. The period from the start of one heartbeat to the start of the next is called the *cardiac cycle*.

A heartbeat lasts only about 370 msec. Although brief, it is a very busy period! Let's follow the steps that produce a single heartbeat, from the generation of an action potential at the SA node through the contractions of the atria and ventricles.

The Conducting System

Unlike skeletal muscle, cardiac muscle tissue contracts on its own, without neural or hormonal stimulation. This property is called **automaticity,** or *autorhythmicity*. The cells that initiate and distribute the stimulus to contract are part of the heart's **conducting system,** also known as the *cardiac conduction system* or the *nodal system*. This system is a network of specialized cardiac muscle cells that initiates and distributes electrical impulses. The actual contraction lags behind the beginning of an electrical impulse (the action potential). The delay comes from the time it takes for calcium ions to enter the sarcoplasm and activate the contraction process, as described in Chapter 10. p. 299

The conducting system includes the following elements (**Figure 20–11a**):

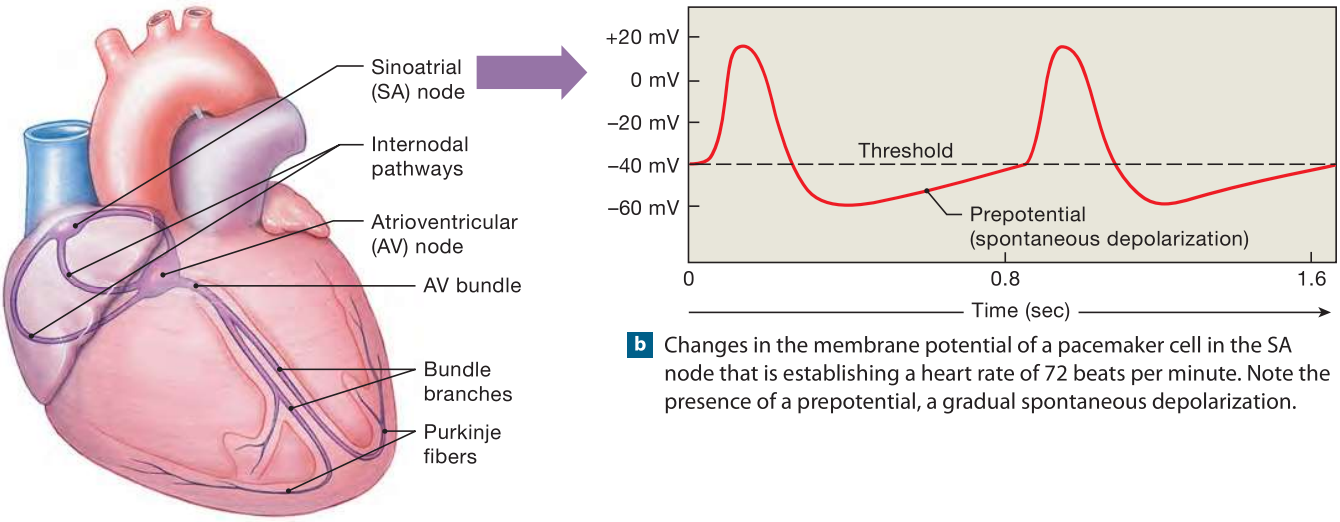
- The *sinoatrial (SA) node*, located in the wall of the right atrium.
- The *atrioventricular (AV) node*, located at the junction between the atria and ventricles.
- *Conducting cells* interconnect the two nodes and distribute the contractile stimulus throughout the myocardium. In the atria, conducting cells are found in **internodal pathways,** which distribute the contractile stimulus to atrial muscle cells as this electrical impulse travels from the SA node to the AV node. (The importance of these pathways in relaying the signal to the AV node remains in dispute, because an impulse can also spread from contractile cell to contractile cell, reaching the AV node at about the same time as an impulse that travels an internodal pathway.) In the ventricles, conducting cells include those in the *AV bundle* and the *bundle branches*, as well as the *Purkinje* (pur-KIN-jē) *fibers*, which distribute the stimulus to the ventricular myocardium.

Most of the cells of the conducting system are smaller than the contractile cells of the myocardium and contain very few myofibrils. Purkinje cells, however, are much larger in diameter than the contractile cells. As a result, they conduct action potentials more quickly than other conducting cells.

Conducting cells of the SA and AV nodes share a special characteristic. Their excitable membranes do not have a stable resting potential. Each time it repolarizes, the membrane then drifts toward threshold. This gradual depolarization is called a **prepotential** or *pacemaker potential* (**Figure 20–11b**). The prepotential results from a slow inflow of Na^+ without a compensating outflow of K^+.

The rate of spontaneous depolarization differs in various parts of the conducting system. It is fastest at the SA node. Without neural or hormonal stimulation, the SA node generates action potentials at a rate of 80–100 per minute. Isolated cells of the AV node depolarize more slowly, generating 40–60 action potentials per minute. Because the SA node reaches threshold first, it establishes the heart rate. In other words, the impulse generated by the SA node brings the AV nodal cells to threshold faster than does the prepotential of

Figure 20–11 The Conducting System of the Heart.



a Components of the conducting system.

b Changes in the membrane potential of a pacemaker cell in the SA node that is establishing a heart rate of 72 beats per minute. Note the presence of a prepotential, a gradual spontaneous depolarization.

the AV nodal cells. The normal resting heart rate is somewhat slower than 80–100 beats per minute, however, due to the effects of parasympathetic innervation. (We discuss the influence of autonomic innervation on heart rate in a later section.)

If the SA node or any of the atrial pathways becomes damaged, the heart continues to beat, but at a slower rate, usually 40–60 beats per minute, as dictated by the AV node. Certain cells in the Purkinje fiber network depolarize spontaneously at an even slower rate. If the rest of the conducting system is damaged, these cells can stimulate a heart rate of 20–40 beats per minute. Under normal conditions, cells of the AV bundle, the bundle branches, and most Purkinje fibers do not depolarize spontaneously. If, due to damage or disease, these cells *do* begin depolarizing spontaneously, the heart may no longer pump blood effectively. Death can result if the problem persists.

Now let's trace the path of an impulse from its initiation at the SA node, examining its effects on the surrounding myocardium as we proceed.

The Sinoatrial (SA) Node

The **sinoatrial** (sī-nō-Ā-trē-al) **node (SA node)** is embedded in the posterior wall of the right atrium, near the entrance of the superior vena cava (**Figure 20–12** 1). The SA node contains **pacemaker cells,** which establish the heart rate. As a result, the SA node is also known as the *cardiac pacemaker* or the *natural pacemaker*.

The SA node is connected to the larger AV node by the internodal pathways in the atrial walls. An action potential takes approximately 50 msec to travel from the SA node to the AV node along these pathways. Along the way, the conducting cells pass the stimulus to contractile cells of both atria. The action potential then spreads across the atrial surfaces by cell-to-cell contact (**Figure 20–12** 2). The stimulus affects only the atria, because the cardiac skeleton isolates the atrial myocardium from the ventricular myocardium.

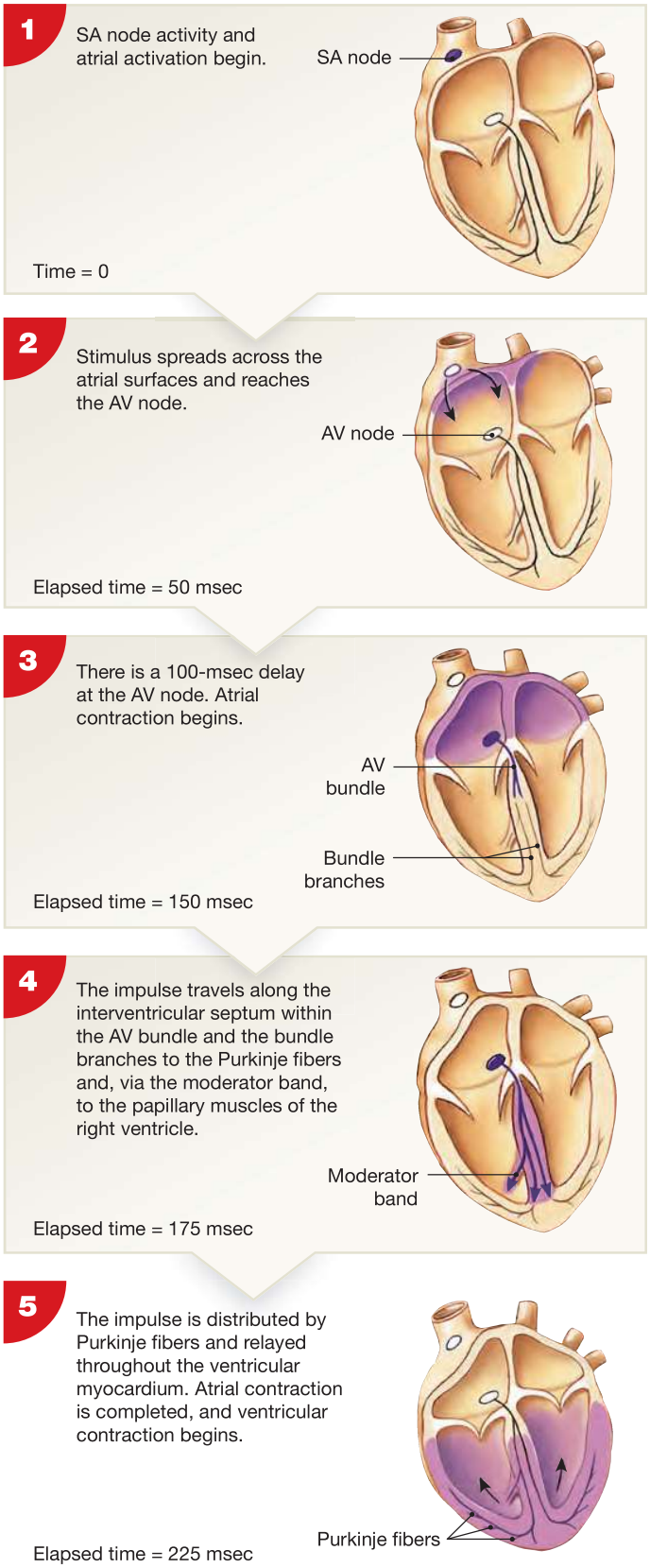
The Atrioventricular (AV) Node

The relatively large **atrioventricular (AV) node** (**Figure 20–12** 2) sits within the floor of the right atrium near the opening of the coronary sinus. The impulse slows as it leaves the internodal pathways and enters the AV node, because the nodal cells are smaller in diameter than the conducting cells. (Chapter 12 discussed the relationship between diameter and propagation speed. ↩ p. 400) In addition, the connections between nodal cells are less efficient than those between conducting cells at relaying the impulse from one cell to another. As a result, the impulse takes about 100 msec to pass through the AV node (**Figure 20–12** 3). This delay is important because it allows the atria to contract before the ventricles do. Otherwise, contraction of the powerful ventricles would close the AV valves and prevent blood flow from the atria into the ventricles.

After this brief delay, the impulse is conducted along the atrioventricular bundle and the bundle branches to the Purkinje fibers and the papillary muscles (**Figure 20–12** 4). The Purkinje fibers then distribute the impulse to the ventricular myocardium, and ventricular contraction begins (**Figure 20–12** 5).

The cells of the AV node can conduct impulses at a maximum rate of 230 per minute. Because each impulse results in a ventricular contraction, this value is the maximum normal heart rate. Even if the SA node generates impulses at a faster rate, the ventricles will still contract at 230 beats per minute (bpm). This limitation is important, because mechanical factors (discussed later) begin to decrease the pumping efficiency of the heart at

Figure 20–12 **Impulse Conduction through the Heart.**



rates above approximately 180 bpm. Rates above 230 bpm occur only when the heart or the conducting system has been damaged or stimulated by drugs. As ventricular rates increase toward their theoretical maximum limit of 300–400 bpm, pumping effectiveness becomes dangerously, if not fatally, reduced.

A number of clinical problems result from abnormal pacemaker function. **Bradycardia** (brād-ē-KAR-dē-uh; *bradys*, slow) is a condition in which the heart rate is slower than normal. **Tachycardia** (tak-ē-KAR-dē-uh; *tachys*, swift) is a faster-than-normal heart rate. These terms are relative, and in clinical practice the definitions vary with the normal resting heart rate of the individual.

The AV Bundle, Bundle Branches, and Purkinje Fibers

The connection between the AV node and the **AV bundle,** also called the *bundle of His* (hiss), is normally the only electrical connection between the atria and the ventricles. Once an impulse enters the AV bundle, it travels to the interventricular septum and enters the **right** and **left bundle branches.** The left bundle branch, which supplies the massive left ventricle, is much larger than the right bundle branch. Both branches extend toward the apex of the heart, turn, and fan out deep to the endocardial surface. As the branches diverge, they conduct the impulse to **Purkinje fibers** and, through the moderator band, to the papillary muscles of the right ventricle.

Purkinje fibers conduct action potentials very rapidly—as fast as small myelinated axons. Within about 75 msec, the signal to begin a contraction has reached all the ventricular cardiac muscle cells. By this time, the atria have completed their contractions and ventricular contraction can safely occur. The entire process, from the generation of an impulse at the SA node to the complete depolarization of the ventricular myocardium, normally takes around 225 msec.

Because the bundle branches deliver the impulse across the moderator band to the papillary muscles directly, rather than by way of Purkinje fibers, the papillary muscles begin contracting before the rest of the ventricular musculature does. Contraction of the papillary muscles applies tension to the chordae tendineae, bracing the AV valves. By limiting the movement of the cusps, tension in the chordae tendineae prevents the backflow of blood into the atria when the ventricles contract.

The Purkinje fibers radiate from the apex toward the base of the heart. As a result, the ventricles contract in a wave that begins at the apex and spreads toward the base. The contraction pushes blood toward the base of the heart, into the aorta and pulmonary trunk.

Damage to the conducting pathways disturbs the normal rhythm of the heart. The resulting problems are called *conduction deficits*. If the SA node or internodal pathways are damaged, the AV node assumes command. The heart continues beating normally, but at a slower rate.

If an abnormal conducting cell or ventricular muscle cell begins generating action potentials at a higher rate, the impulses

can override those of the SA or AV node. The origin of these abnormal signals is called an **ectopic** (ek-TOP-ik; out of place) **pacemaker**. The activity of an ectopic pacemaker partially or completely bypasses the conducting system, disrupting the timing of ventricular contraction. The result may be a dangerous reduction in the pumping efficiency of the heart. Such conditions are commonly diagnosed with the aid of an *electrocardiogram*.

The Electrocardiogram

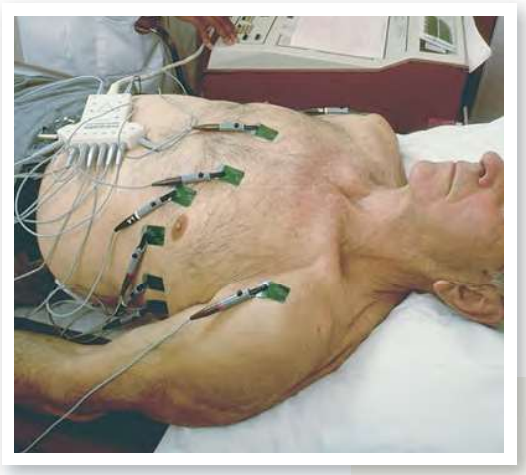
The electrical events in the heart are powerful enough to be detected by electrodes on the surface of the body. A recording of these events is an **electrocardiogram** (ē-lek-trō-KAR-dē-ō-gram), also called an **ECG** or **EKG.** Each time the heart beats, a wave of depolarization spreads through the atria, pauses at the AV node, then travels down the interventricular septum to the apex, turns, and spreads through the ventricular myocardium toward the base (**Figure 20–12**).

An ECG integrates electrical information from electrodes placed at different locations on the body surface. Clinicians can use an ECG to assess the performance of specific nodal, conducting, and contractile components. When a portion of the heart has been damaged by a heart attack, for example, the ECG reveals an abnormal pattern of impulse conduction.

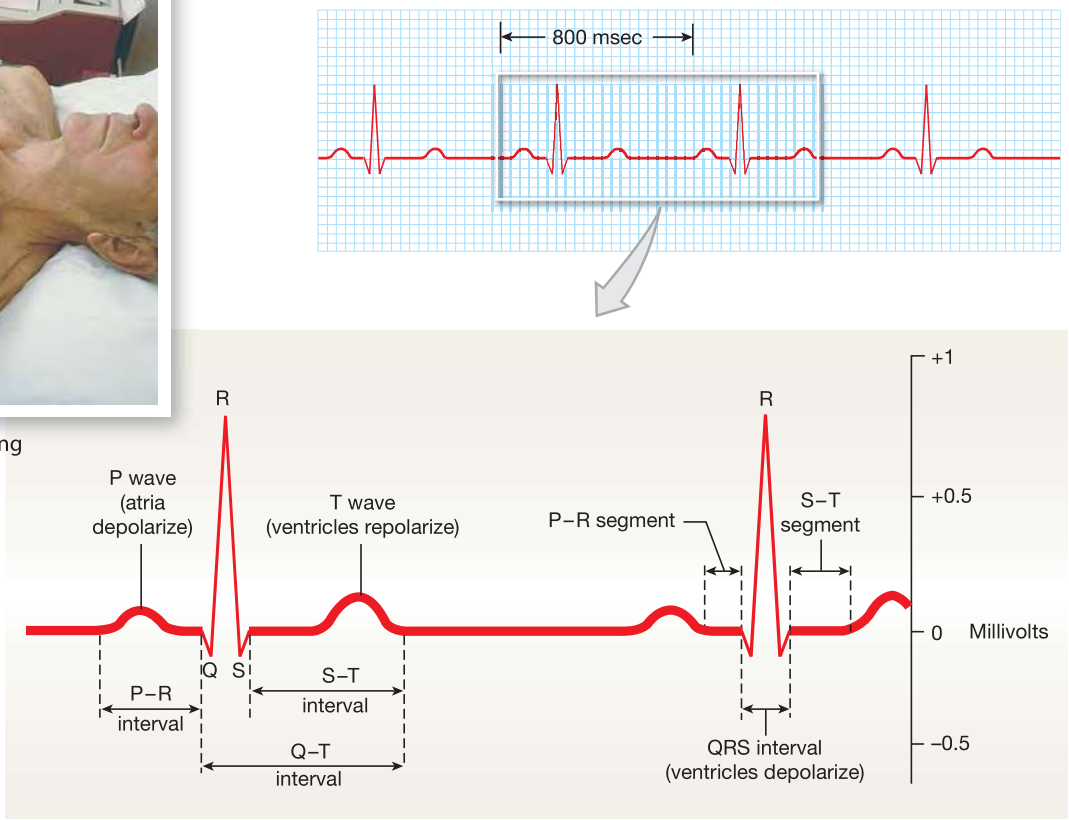
The appearance of the ECG varies with the placement of the monitoring electrodes, or *leads*. **Figure 20–13a** shows the leads in one of the standard configurations. **Figure 20–13b** depicts the important features of an ECG recorded with that configuration. Note the following ECG features:

- The small **P wave,** which accompanies the depolarization of the atria. The atria begin contracting about 25 msec after the start of the P wave.
- The **QRS complex,** which appears as the ventricles depolarize. This electrical signal is relatively strong, because the ventricular muscle is much more massive than that of the atria. It is also a complex signal, largely because of the

Figure 20–13 An Electrocardiogram.



a Electrode placement for recording a standard ECG.



b An ECG printout is a strip of graph paper containing a record of the electrical events monitored by the electrodes. The placement of electrodes on the body surface affects the size and shape of the waves recorded. The example is a normal ECG; the enlarged section indicates the major components of the ECG and the measurements most often taken during clinical analysis.

complex pathway that the spread of depolarization takes through the ventricles. The ventricles begin contracting shortly after the peak of the **R wave.**

- The smaller **T wave,** which indicates ventricular repolarization. Atrial repolarization is not apparent, because it takes place while the ventricles are depolarizing, and the QRS complex masks the electrical events.

To analyze an ECG, you must measure the size of the voltage changes and determine the durations and temporal (time) relationships of the various components. The amount of depolarization during the P wave and the QRS complex is particularly important in making a diagnosis. For example, an excessively large QRS complex often indicates that the heart has become enlarged. A smaller-than-normal electrical signal may mean that the mass of the heart muscle has decreased (although monitoring problems are more often responsible). The size and shape of the T wave may also be affected by any condition that slows ventricular repolarization. For example, starvation and low cardiac energy reserves, coronary ischemia, or abnormal ion concentrations reduce the size of the T wave.

The times between waves are reported as *segments* and *intervals*. Segments generally extend from the end of one wave to the start of another. Intervals are more variable, but always include at least one entire wave. Commonly used segments and intervals are labeled in **Figure 20–13b**. The names, however, can be somewhat misleading. For example:

- The **P–R interval** extends from the start of atrial depolarization to the start of the QRS complex (ventricular depolarization) rather than to R, because in abnormal ECGs the peak at R can be difficult to determine. Extension of the P–R interval to more than 200 msec can indicate damage to the conducting pathways or AV node.
- The **Q–T interval** indicates the time required for the ventricles to undergo a single cycle of depolarization and repolarization. It is usually measured from the end of the P–R interval rather than from the bottom of the Q wave. The Q–T interval can be lengthened by electrolyte disturbances, some medications, conduction problems, coronary ischemia, or myocardial damage. A congenital heart defect that can cause sudden death without warning may be detectable as a prolonged Q–T interval.

An *arrhythmia* (ā-RITH-mē-uh) is an irregularity in the normal rhythm or force of the heartbeat. Serious arrhythmias may indicate damage to the myocardium, injuries to the pacemakers or conduction pathways, exposure to drugs, or abnormalities in the electrolyte composition of extracellular fluids. **Spotlight Figure 20–14** describes cardiac arrhythmias.

Contractile Cells

The Purkinje fibers distribute the stimulus to the **contractile cells,** which form the bulk of the atrial and ventricular walls. These cells account for roughly 99 percent of the muscle cells in the heart. In both cardiac muscle cells and skeletal muscle fibers, (1) an action potential leads to the appearance of Ca^{2+} among the myofibrils, and (2) the binding of Ca^{2+} to troponin on the thin filaments initiates the contraction. But skeletal and cardiac muscle cells differ in terms of the nature of the action potential, the source of the Ca^{2+}, and the duration of the resulting contraction. ↩ p. 316

The Action Potential in Cardiac Muscle Cells

The resting potential of a ventricular contractile cell is approximately −90 mV, comparable to that of a resting skeletal muscle fiber (−85 mV). (The resting potential of an atrial contractile cell is about −80 mV, but the basic principles described here apply to atrial cells as well.) An action potential begins when the membrane of the ventricular muscle cell reaches threshold, usually at about −75 mV. Threshold is normally reached in a portion of the membrane next to an intercalated disc. The typical stimulus is the excitation of an adjacent muscle cell. Once threshold has been reached, the action potential proceeds in three basic steps (**Figure 20–15a**):

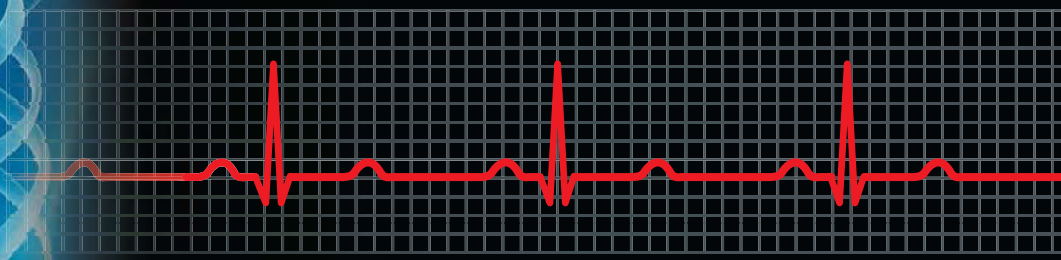
1 ***Rapid Depolarization.*** The stage of *rapid depolarization* in a cardiac muscle cell resembles that in a skeletal muscle fiber. At threshold, voltage-gated sodium channels open, and the membrane suddenly becomes permeable to Na^+. A massive influx of sodium ions rapidly depolarizes the sarcolemma. The channels involved are called **fast sodium channels,** because they open quickly and remain open for only a few milliseconds.

2 ***The Plateau.*** As the transmembrane potential approaches +30 mV, the voltage-gated sodium channels close. They remain closed and inactivated until the transmembrane potential drops to −60 mV. The cell now begins actively pumping Na^+ out of the cell. However, a net loss of positive charges does not continue, because as the sodium channels are closing, voltage-gated calcium channels are opening. These channels are called **slow calcium channels,** because they open slowly and remain open for a relatively long period—roughly 175 msec. While the slow calcium channels are open, calcium ions enter the sarcoplasm. The entry of positive charges through the calcium channels, in the form of Ca^{2+}, roughly balances the loss of positive ions through the active transport of Na^+, and the transmembrane potential remains near 0 mV for an extended period. This portion of the action potential curve is called the *plateau*. The presence of a plateau is the major difference between action potentials in cardiac muscle cells and in skeletal muscle fibers. In a skeletal muscle fiber, rapid depolarization is immediately followed by rapid repolarization.

Spotlight

Figure 20–14
Cardiac Arrhythmias

Despite the variety of sophisticated equipment available to assess or visualize cardiac function, in the majority of cases the ECG provides the most important diagnostic information. ECG analysis is especially useful in detecting and diagnosing **cardiac arrhythmias** (ā-RITH-mē-az)—abnormal patterns of cardiac electrical activity. Momentary arrhythmias are not inherently dangerous, but clinical problems appear when arrhythmias reduce the pumping efficiency of the heart.



Premature Atrial Contractions (PACs)

Premature atrial contractions (PACs) often occur in healthy individuals. In a PAC, the normal atrial rhythm is momentarily interrupted by a "surprise" atrial contraction. Stress, caffeine, and various drugs may increase the incidence of PACs, presumably by increasing the permeabilities of the SA pacemakers. The impulse spreads along the conduction pathway, and a normal ventricular contraction follows the atrial beat.

Paroxysmal Atrial Tachycardia (PAT)

In **paroxysmal** (par-ok-SIZ-mal) **atrial tachycardia**, or **PAT**, a premature atrial contraction triggers a flurry of atrial activity. The ventricles are still able to keep pace, and the heart rate jumps to about 180 beats per minute.

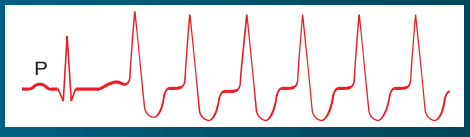
Atrial Fibrillation (AF)

During **atrial fibrillation** (fib-ri-LĀ-shun), the impulses move over the atrial surface at rates of perhaps 500 beats per minute. The atrial wall quivers instead of producing an organized contraction. The ventricular rate cannot follow the atrial rate and may remain within normal limits. Even though the atria are now nonfunctional, their contribution to ventricular end-diastolic volume (the maximum amount of blood the ventricles can hold at the end of atrial contraction) is so small that the condition may go unnoticed in older individuals.

Premature Ventricular Contractions (PVCs)

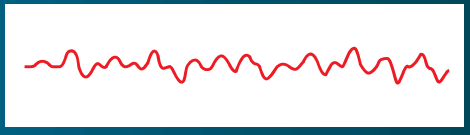
Premature ventricular contractions (PVCs) occur when a Purkinje cell or ventricular myocardial cell depolarizes to threshold and triggers a premature contraction. Single PVCs are common and not dangerous. The cell responsible is called an **ectopic pacemaker.** The frequency of PVCs can be increased by exposure to epinephrine, to other stimulatory drugs, or to ionic changes that depolarize cardiac muscle cell membranes.

Ventricular Tachycardia (VT)



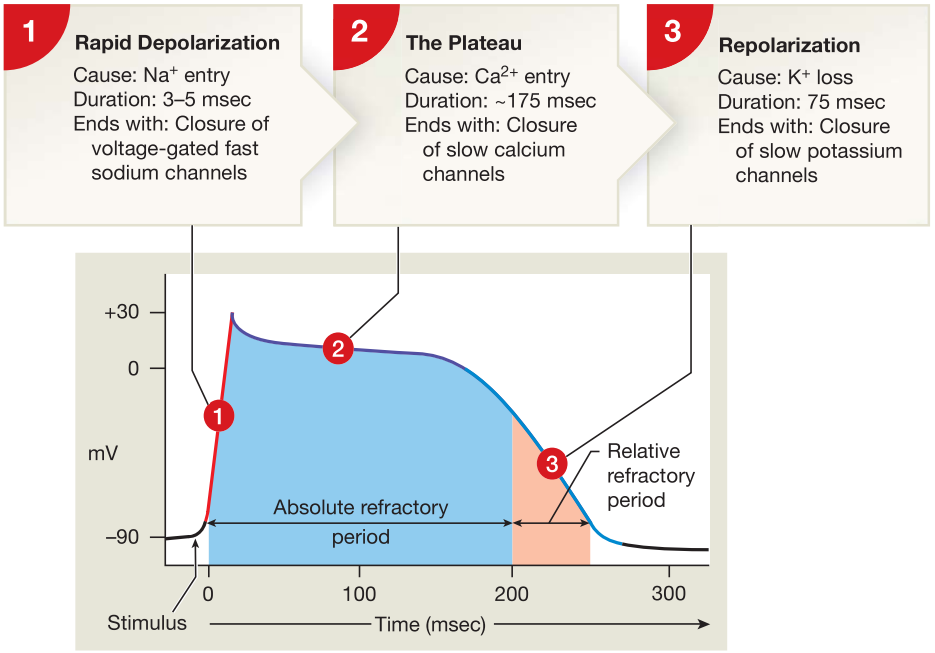
Ventricular tachycardia is defined as four or more PVCs without intervening normal beats. It is also known as **VT** or **V-tach**. Multiple PVCs and VT may indicate that serious cardiac problems exist.

Ventricular Fibrillation (VF)

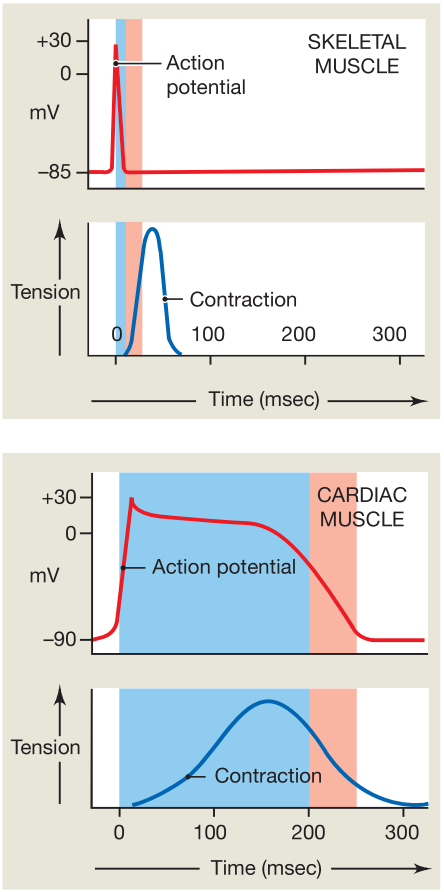


Ventricular fibrillation (VF) is responsible for the condition known as **cardiac arrest**. VF is rapidly fatal, because the ventricles quiver and stop pumping blood.

Figure 20–15 The Action Potential in Skeletal and Cardiac Muscle.



a Events in an action potential in a ventricular muscle cell.



b Action potentials and twitch contractions in a skeletal muscle (above) and cardiac muscle (below). The shaded areas indicate the durations of the absolute (blue) and relative (beige) refractory periods.

Absolute refractory period

Relative refractory period

3 ***Repolarization.*** As the plateau continues, slow calcium channels begin closing, and **slow potassium channels** begin opening. As these channels open, potassium ions (K^+) rush out of the cell, and the net result is a period of rapid repolarization that restores the resting potential.

The Refractory Period. As with skeletal muscle contractions, the membrane will not respond normally to a second stimulus for some time after an action potential begins. This time is called the refractory period. Initially, in the absolute refractory period, the membrane cannot respond at all, because the sodium channels either are already open or are closed and inactivated. In a ventricular muscle cell, the absolute refractory period lasts approximately 200 msec. It includes the plateau and the initial period of rapid repolarization.

The absolute refractory period is followed by a shorter (50 msec) relative refractory period. During this period, the voltage-gated sodium channels are closed, but can open. The membrane will respond to a stronger-than-normal stimulus by initiating another action potential.

In total, an action potential in a ventricular contractile cell lasts 250–300 msec, about 30 times as long as a typical action potential in a skeletal muscle fiber.

The Role of Calcium Ions in Cardiac Contractions

The appearance of an action potential in the cardiac muscle plasma membrane produces a contraction by causing an increase in the concentration of Ca^{2+} around the myofibrils. This process takes place in two steps:

1. Calcium ions crossing the plasma membrane during the plateau phase of the action potential provide roughly 20 percent of the Ca^{2+} required for a contraction.
2. The arrival of this extracellular Ca^{2+} triggers the release of additional Ca^{2+} from reserves in the sarcoplasmic reticulum (SR).

Extracellular calcium ions thus have both direct and indirect effects on cardiac muscle cell contraction. For this reason, cardiac muscle tissue is highly sensitive to changes in the Ca^{2+} concentration of the extracellular fluid.

In a skeletal muscle fiber, the action potential is relatively brief and ends as the resulting twitch contraction begins (**Figure 20–15b**). The twitch contraction is short and ends as the SR reclaims the Ca^{2+} it released. In a cardiac muscle cell, as

we have seen, the action potential is prolonged, and calcium ions continue to enter the cell throughout the plateau. As a result, the muscle cell actively contracts until the plateau ends. As the slow calcium channels close, the intracellular calcium ions are absorbed by the SR or are pumped out of the cell, and the muscle cell relaxes.

In skeletal muscle fibers, the refractory period ends before peak tension develops. As a result, twitches can summate and tetanus can occur. In cardiac muscle cells, the absolute refractory period continues until relaxation is under way. Because summation is not possible, tetanic contractions cannot occur in a normal cardiac muscle cell, regardless of the frequency or intensity of stimulation. This feature is vital: A heart in tetany could not pump blood. With a single twitch lasting 250 msec or longer, a normal cardiac muscle cell could reach 300–400 contractions per minute under maximum stimulation. This rate is not reached in a normal heart, due to limitations imposed by the conducting system.

The Energy for Cardiac Contractions

When a normal heart is beating, it gets energy as the mitochondria break down fatty acids (stored as lipid droplets) and glucose (stored as glycogen). These aerobic reactions can occur only when oxygen is readily available. ↩ p. 306

In addition to obtaining oxygen from the coronary circulation, cardiac muscle cells maintain their own sizable reserves of oxygen. In these cells, oxygen molecules are bound to the heme units of myoglobin molecules. (We discussed this globular protein, which reversibly binds oxygen molecules, and its function in muscle fibers in Chapter 10.) ↩ p. 309 Normally, the combination of circulatory supplies plus myoglobin reserves is enough to meet the oxygen demands of the heart, even when it is working at maximum capacity.

Checkpoint

4. **Define automaticity.**
5. **Which structure of the heart is known as the cardiac pacemaker or the natural pacemaker?**
6. **If the cells of the SA node did not function, how would the heart rate be affected?**
7. **Why is it important for impulses from the atria to be delayed at the AV node before they pass into the ventricles?**

See the blue Answers tab at the back of the book.

20-3 ◗ Events during a complete heartbeat constitute a cardiac cycle

A brief resting phase follows each heartbeat, allowing time for the chambers to relax and prepare for the next heartbeat. The period between the start of one heartbeat and the beginning of the next is a single **cardiac cycle.** It includes alternating periods of contraction and relaxation. For any one chamber in the heart, the cardiac cycle can be divided into two phases: (1) systole and (2) diastole. During **systole** (SIS-tō-lē), or contraction, the chamber contracts and pushes blood into an adjacent chamber or into an arterial trunk. Systole is followed by **diastole** (dī-AS-tō-lē), or relaxation. During diastole, the chamber fills with blood and prepares for the next cardiac cycle.

Tips & Tricks

To remember that systole is contraction, relate "***syst***" to "***syst***em," as in during systole, a contraction sends blood out of the heart and into the circulatory system. The word part "***di***" can mean two, so during ***di***astole, the heart "puts two feet up" and relaxes.

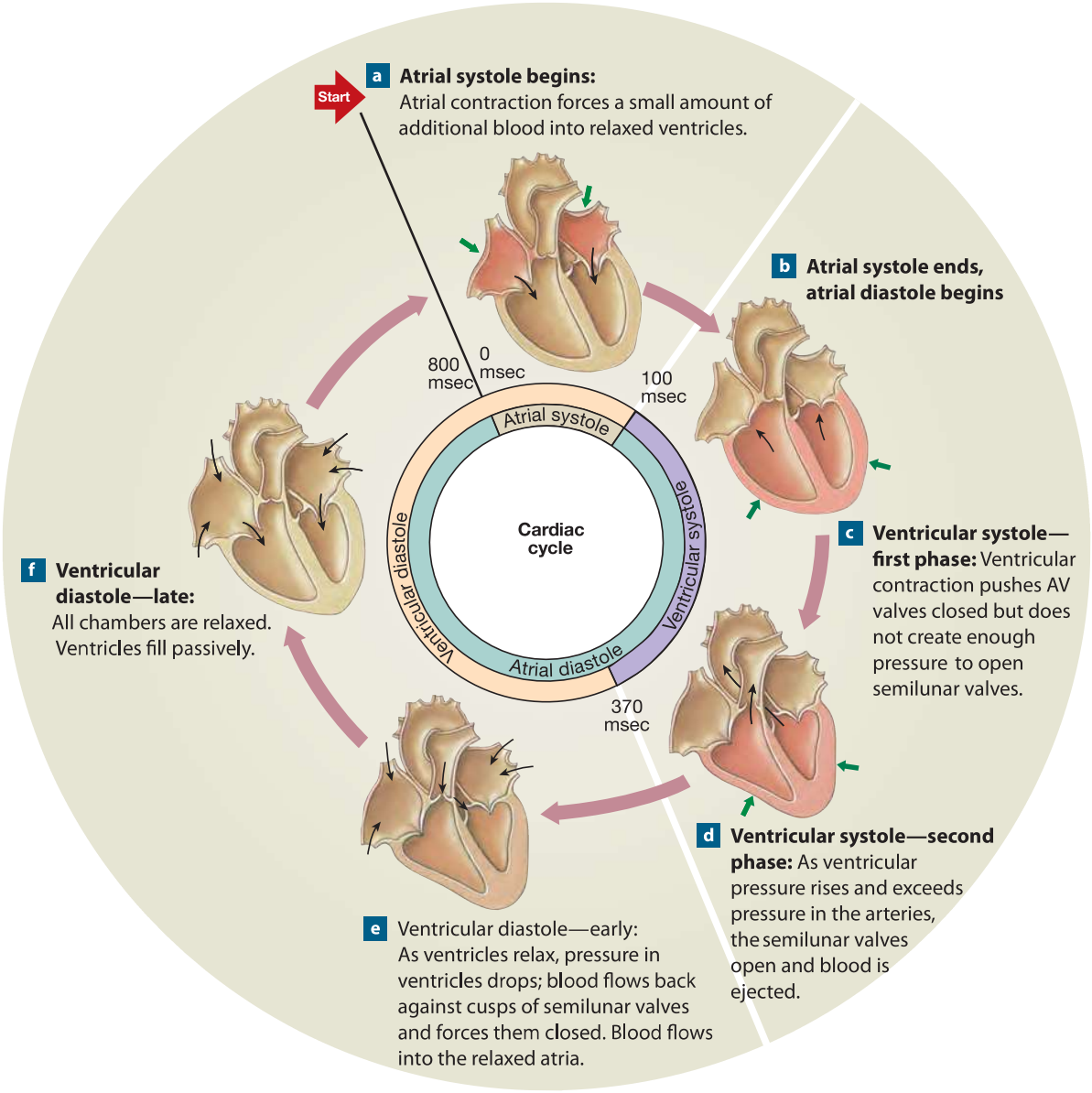
Fluids move from an area of higher pressure to an area of lower pressure. In the cardiac cycle, the pressure within each chamber rises during systole and falls during diastole. Valves between adjacent chambers help ensure that blood flows in the required direction, but blood flows from one chamber to another only if the pressure in the first chamber exceeds that in the second. This basic principle governs the movement of blood between atria and ventricles, between ventricles and arterial trunks, and between major veins and atria.

The correct pressure relationships depend on the careful timing of contractions. For example, blood could not move in the proper direction if an atrium and its attached ventricle contracted at precisely the same moment. The heart's elaborate pacemaking and conducting systems normally provide the required spacing between atrial and ventricular systoles. At a representative heart rate of 75 bpm, a sequence of systole and diastole in either the atria or the ventricles lasts 800 msec.

Phases of the Cardiac Cycle

The phases of the cardiac cycle—atrial systole, atrial diastole, ventricular systole, and ventricular diastole—are diagrammed in **Figure 20–16** for a heart rate of 75 bpm. When the cardiac cycle begins, all four chambers are relaxed, and the ventricles are partially filled with blood. Let's start by focusing on the atria. During atrial systole, the atria contract, filling the ventricles completely with blood (**Figure 20–16a,b**). Atrial systole lasts 100 msec. Over this period, blood cannot flow into the atria because atrial pressure exceeds venous pressure. Yet there is very little backflow into the veins, even though the connections with the venous system lack valves. The reason is that blood takes the path of least resistance. Resistance to blood flow through the broad AV connections and into the ventricles is less than that through the smaller, angled openings of the large veins.

Figure 20–16 Phases of the Cardiac Cycle. Thin black arrows indicate blood flow, and green arrows indicate contractions.



The atria next enter atrial diastole, which continues until the start of the next cardiac cycle. Atrial diastole and ventricular systole begin at the same time. Ventricular systole lasts 270 msec. During this period, the ventricles push blood through the systemic and pulmonary circuits and toward the atria (**Figure 20–16c,d**). The heart then enters ventricular diastole (**Figure 20–16e,f**), which lasts 530 msec (the 430 msec remaining in this cardiac cycle, plus the first 100 msec of the next, when the atria are again contracting). For the rest of this cycle, filling occurs passively, and both the atria and the ventricles are relaxed. The next cardiac cycle begins with atrial systole, which completes the filling of the ventricles.

When the heart rate increases, all the phases of the cardiac cycle are shortened. The greatest reduction occurs in the length of time spent in diastole. When the heart rate climbs from 75 bpm to 200 bpm, the time spent in systole drops by less than 40 percent, but the duration of diastole is reduced by almost 75 percent.

Pressure and Volume Changes in the Cardiac Cycle

Figure 20–17 plots the pressure and volume changes during the cardiac cycle. It also shows an ECG for the cardiac cycle. The circled numbers in the figure correspond to numbered paragraphs in the text. The figure shows pressure and volume within the left atrium and left ventricle, but our discussion applies to

both sides of the heart. Although pressures are lower in the right atrium and right ventricle, both sides of the heart contract at the same time, and they eject equal volumes of blood.

Atrial Systole

The cardiac cycle begins with atrial systole, which lasts about 100 msec in a resting adult:

1 As the atria contract, rising atrial pressures push blood into the ventricles through the open right and left AV valves.

2 At the start of atrial systole, the ventricles are already filled to about 70 percent of their normal capacity, due to passive blood flow during the end of the previous cardiac cycle. As the atria contract, rising atrial pressures provide the remaining 30 percent by pushing blood through the open AV valves. Atrial systole essentially "tops off" the ventricles.

3 At the end of atrial systole, each ventricle contains the maximum amount of blood that it will hold in this cardiac cycle. That quantity is called the **end-diastolic volume (EDV).** In an adult who is standing at rest, the end-diastolic volume is typically about 130 mL (about 4.4 oz).

Ventricular Systole

As atrial systole ends, ventricular systole begins. It lasts approximately 270 msec in a resting adult. As the pressures in the ventricles rise above those in the atria, the AV valves are pushed closed.

4 During the early stage of ventricular systole, the ventricles are contracting, but blood flow has yet to occur. Ventricular pressures are not yet high enough to force open the semilunar valves and push blood into the pulmonary or aortic trunk. Over this period, the ventricles contract isometrically. They generate tension and pressures rise inside them, but blood does not flow out. The ventricles are in **isovolumetric contraction:** All the heart valves are closed, the volumes of the ventricles do not change, and ventricular pressures are rising.

5 Once pressure in the ventricles exceeds that in the arterial trunks, the semilunar valves open and blood flows into the pulmonary and aortic trunks. This point marks the beginning of **ventricular ejection.** The ventricles now contract isotonically: The muscle cells shorten, and tension production remains relatively constant. (To review isotonic versus isometric contractions, see **Figure 10–18**, p. 303.)

After reaching a peak, ventricular pressures gradually decline near the end of ventricular systole. **Figure 20–17** shows values for the left ventricle and aorta. The right ventricle also goes through periods of isovolumetric contraction and ventricular ejection, but pressures in the right ventricle and pulmonary trunk are much lower.

During ventricular ejection, each ventricle ejects 70–80 mL of blood, the **stroke volume (SV)** of the heart. The stroke volume at rest is roughly 60 percent of the end-diastolic volume. This percentage, known as the *ejection fraction*, varies in response to changing demands on the heart. (We discuss the regulatory mechanisms involved in the next section.)

6 As the end of ventricular systole approaches, ventricular pressures fall rapidly. Blood in the aorta and pulmonary trunk now starts to flow back toward the ventricles, and this movement closes the semilunar valves. As the backflow begins, pressure decreases in the aorta. When the semilunar valves close, pressure rises again as the elastic arterial walls recoil. This small, temporary rise produces a valley in the pressure tracing, called a *dicrotic* (dī-KROT-ik; *dikrotos*, double beating) *notch*. The amount of blood remaining in the ventricle when the semilunar valve closes is the **end-systolic volume (ESV).** At rest, the end-systolic volume is 50 mL, about 40 percent of the end-diastolic volume.

Ventricular Diastole

The period of ventricular diastole lasts for the 430 msec remaining in the current cardiac cycle and continues through atrial systole in the next cycle.

7 All the heart valves are now closed, and the ventricular myocardium is relaxing. Because ventricular pressures are still higher than atrial pressures, blood cannot flow into the ventricles. This is **isovolumetric relaxation.** Ventricular pressures drop rapidly over this period, because the elasticity of the connective tissues of the heart and cardiac skeleton helps reexpand the ventricles toward their resting dimensions.

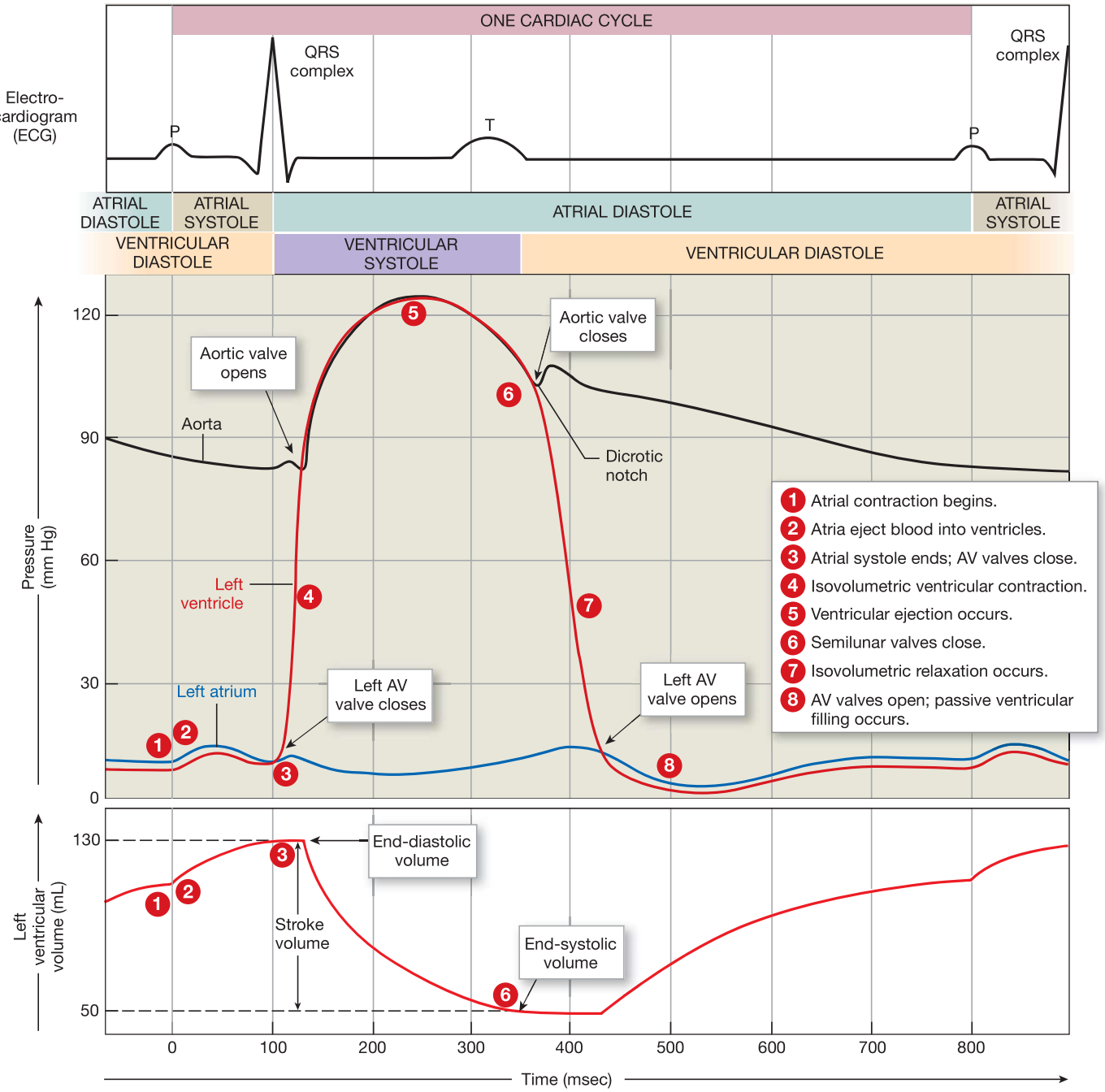
8 When ventricular pressures fall below those of the atria, the atrial pressures force the AV valves open. Blood now flows from the atria into the ventricles. Both the atria and the ventricles are in diastole, but the ventricular pressures continue to fall as the ventricular chambers expand. Throughout this period, pressures in the ventricles are so far below those in the major veins that blood pours through the relaxed atria and on through the open AV valves into the ventricles. This passive mechanism is the primary method of ventricular filling. The ventricles become nearly three-quarters full before the cardiac cycle ends.

The relatively minor contribution that atrial systole makes to ventricular volume explains why individuals can survive quite normally when their atria have been so severely damaged that they can no longer function. In contrast, damage to one or both ventricles can leave the heart unable to pump enough blood through peripheral tissues and organs. A condition of **heart failure** then exists.

Heart Sounds

Listening to the heart, a technique called *auscultation*, is a simple and effective method of cardiac assessment. Clinicians use an instrument called a **stethoscope** to listen for normal and

Figure 20–17 Pressure and Volume Relationships in the Cardiac Cycle. Major features of the cardiac cycle are shown for a heart rate of 75 bpm. The circled numbers correspond to those in the associated box; for further details, see the numbered list in the text.

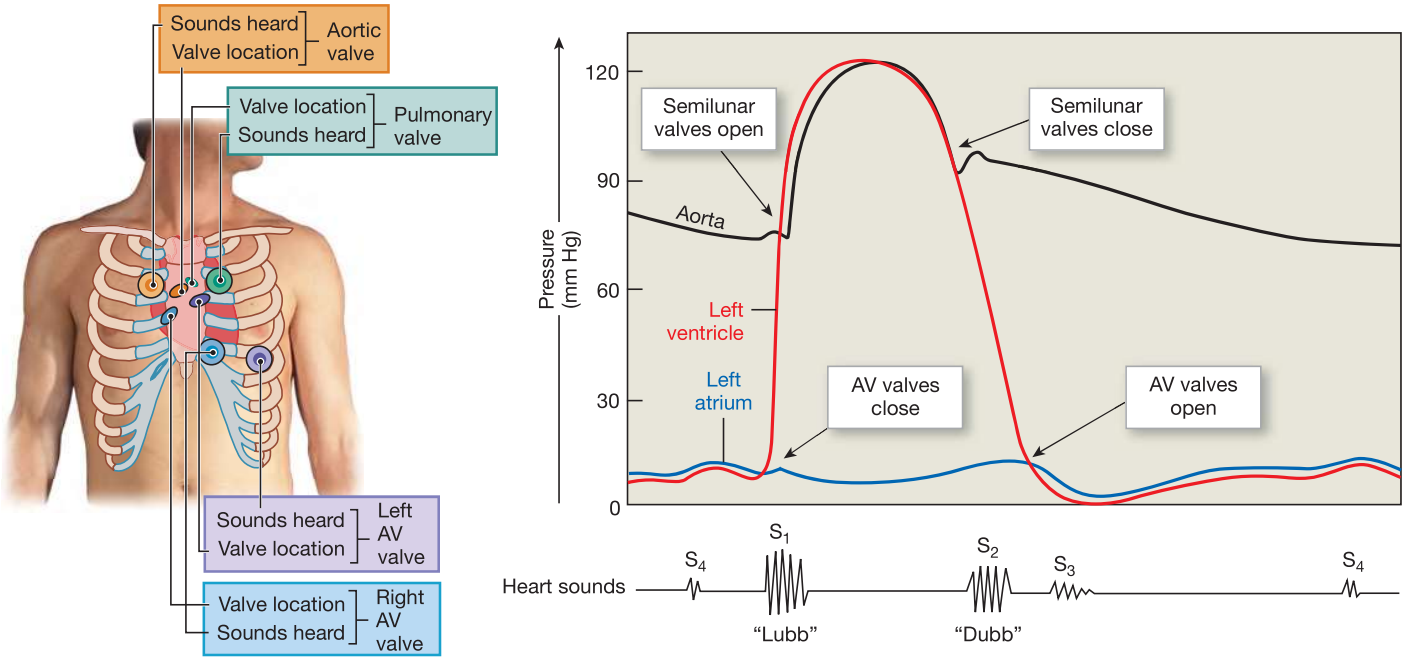


abnormal heart sounds. Where the stethoscope is placed depends on which valve is under examination (**Figure 20–18a**). Valve sounds must pass through the pericardium, surrounding tissues, and the chest wall, and some tissues muffle sounds more than others. For this reason, the placement of the stethoscope differs somewhat from the position of the valve under review.

There are four heart sounds, named S_1 through S_4 (**Figure 20–18b**). If you listen to your own heart with a stethoscope, you will clearly hear the *first* and *second heart sounds*. These sounds accompany the closing of your heart valves. The first heart sound, known as "lubb" (S_1), lasts a little longer than the second, called "dubb" or "dupp" (S_2). S_1 marks the start of ventricular contraction, when the AV valves close. S_2 occurs at the beginning of ventricular filling, when the semilunar valves close.

Third and *fourth heart sounds* are usually very faint and are seldom audible in healthy adults. These sounds are associated

Figure 20–18 Heart Sounds.



a Placements of a stethoscope for listening to the different sounds produced by individual valves

b The relationship between heart sounds and key events in the cardiac cycle

with blood flowing into the ventricles (S_3) and atrial contraction (S_4), rather than with valve action.

If the valve cusps are malformed or there are problems with the papillary muscles or chordae tendineae, the heart valves may not close properly. AV valve regurgitation then occurs during ventricular systole. The surges, swirls, and eddies that accompany regurgitation create a rushing, gurgling sound known as a **heart murmur.** Minor heart murmurs are common and inconsequential.

Checkpoint

8. **Provide the technical terms for heart contraction and heart relaxation.**
9. **List the phases of the cardiac cycle.**
10. **Is the heart always pumping blood when pressure in the left ventricle is rising? Explain.**
11. **What factor could cause an increase in the size of the QRS complex in an electrocardiogram?**

See the blue Answers tab at the back of the book.

20-4 Cardiodynamics examines the factors that affect cardiac output

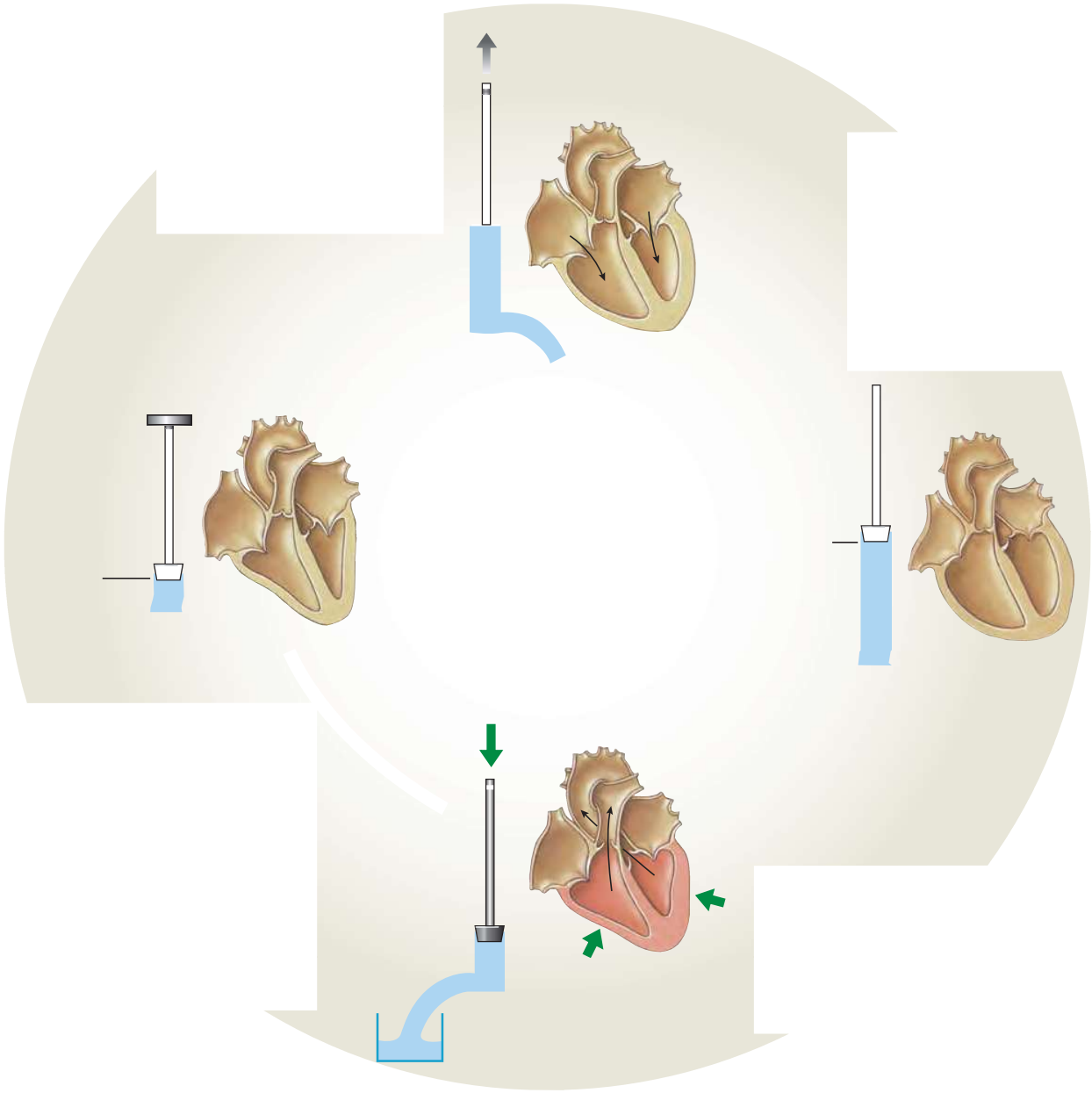
The term **cardiodynamics** refers to the movements and forces generated during cardiac contractions. Each time the heart beats, the two ventricles eject equal amounts of blood. Earlier we introduced these terms:

- *End-Diastolic Volume (EDV):* The amount of blood in each ventricle at the end of ventricular diastole (the start of ventricular systole).
- *End-Systolic Volume (ESV):* The amount of blood remaining in each ventricle at the end of ventricular systole (the start of ventricular diastole).
- *Stroke Volume (SV):* The amount of blood pumped out of each ventricle during a single beat. It can be expressed as SV = EDV − ESV.
- *Ejection Fraction:* The percentage of the EDV represented by the SV.

Stroke volume is the most important factor in an examination of a single cardiac cycle. If the heart were an old-fashioned bicycle pump, the stroke volume would be the amount of air pumped in one up–down cycle of the handle (**Figure 20–19**). Where you stop when you lift the handle determines how much air the pump contains—the end-diastolic volume. How far down you push the handle determines how much air remains in the pump at the end of the cycle—the end-systolic volume. You pump the maximum amount of air when you pull the handle all the way to the top and then push it all the way to the bottom. In other words, you get the largest stroke volume when the EDV is as large as it can be and the ESV is as small as it can be.

When considering cardiac function over time, physicians generally are most interested in the **cardiac output (CO),** the amount of blood pumped by the left ventricle in one minute. In essence, cardiac output is an indication of the blood flow through peripheral tissues—and without adequate blood flow, homeostasis cannot be maintained. The cardiac output provides a useful indication of ventricular efficiency over time. We can calculate it by multiplying the heart rate (HR) by the average stroke volume (SV):

CO	=	HR	×	SV
cardiac output (mL/min)		heart rate (beats/min)		stroke volume (mL/beat)



For example, if the heart rate is 75 bpm and the stroke volume is 80 mL per beat, the cardiac output is

$$CO = 75 \text{ bpm} \times 80 \text{ mL/beat} = 6000 \text{ mL/min (6 L/min)}$$

The body precisely adjusts cardiac output to supply peripheral tissues with enough blood as conditions change. When necessary, the heart rate can increase by 250 percent, and stroke volume in a normal heart can almost double.

Overview: Factors Affecting Cardiac Output

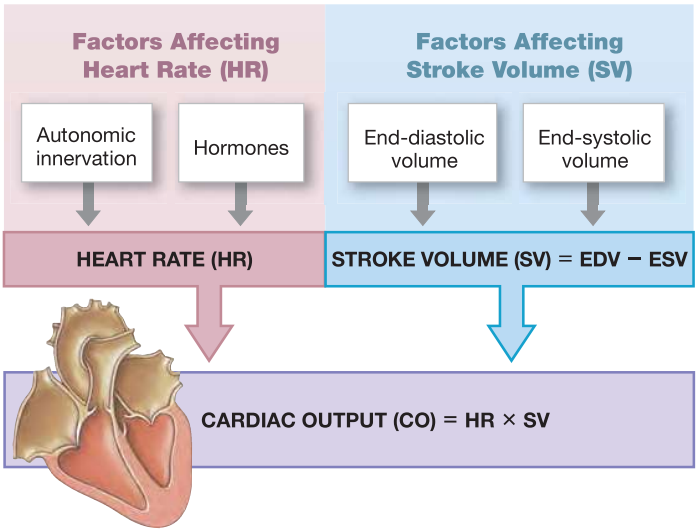
Figure 20–20 summarizes the factors involved in the normal regulation of cardiac output. Cardiac output can be adjusted by changes in either heart rate or stroke volume. For convenience, we will consider these independently as we discuss the individual factors involved. However, changes in cardiac output generally reflect changes in both heart rate and stroke volume.

The heart rate can be adjusted by the activities of the autonomic nervous system or by circulating hormones. The stroke volume can be adjusted by changes in the end-diastolic volume (how full the ventricles are when they start to contract), the end-systolic volume (how much blood remains in the ventricle after it contracts), or both. As we saw in **Figure 20–19**, stroke volume peaks when EDV is highest and ESV is lowest. A variety of other factors can influence cardiac output under abnormal circumstances, and we consider several examples in the Clinical Note.

Factors Affecting the Heart Rate

Under normal circumstances, autonomic activity and circulating hormones make homeostatic adjustments to the heart rate as cardiovascular demands change. These factors act by modifying the natural rhythm of the heart. Even a heart removed for a heart transplant continues to beat unless steps are taken to prevent it from doing so.

Figure 20–20 Factors Affecting Cardiac Output.



Clinical Note

Abnormal Conditions Affecting Cardiac Output Various drugs, abnormal variations in extracellular ion concentrations, and changes in body temperature can alter the basic rhythm of contraction established by the SA node. In Chapter 12, we noted that several drugs, including caffeine and nicotine, have a stimulatory effect on the excitable membranes in the nervous system. ↩ p. 409 These drugs also cause an increase in heart rate. Caffeine acts directly on the conducting system and increases the rate of depolarization at the SA node. Nicotine directly stimulates the activity of sympathetic neurons that innervate the heart.

Disorders affecting ion concentrations or body temperature can have direct effects on cardiac output by changing the stroke volume, the heart rate, or both. Abnormal ion concentrations can change both the contractility of the heart (the strength of contractions), by affecting the cardiac muscle cells, and the heart rate, by affecting the SA nodal cells. The most obvious and clinically important examples of problems with ion concentrations involve K^+ and Ca^{2+}.

Temperature changes also affect metabolic operations throughout the body. For example, a reduction in temperature slows the rate of depolarization at the SA node, lowers the heart rate, and reduces the strength of cardiac contractions. (In open-heart surgery, the exposed heart may be deliberately chilled until it stops beating.) An elevated body temperature accelerates the heart rate and the contractile force. That is one reason your heart may seem to race and pound when you have a fever.

Autonomic Innervation

The sympathetic and parasympathetic divisions of the autonomic nervous system innervate the heart by means of the nerve network known as the *cardiac plexus* (**Figure 16–10**, p. 533, and **Figure 20–21**). Postganglionic sympathetic neurons are located in the cervical and upper thoracic ganglia. The vagus nerves (N X) carry parasympathetic preganglionic fibers to small ganglia in the cardiac plexus. Both ANS divisions innervate the SA and AV nodes and the atrial muscle cells. Both divisions also innervate ventricular muscle cells, but sympathetic fibers far outnumber parasympathetic fibers there.

The *cardiac centers* of the medulla oblongata contain the autonomic headquarters for cardiac control. ↩ p. 458 The

cardioacceleratory center controls sympathetic neurons that increase the heart rate. The adjacent **cardioinhibitory center** controls the parasympathetic neurons that slow the heart rate. Reflex pathways regulate the cardiac centers. They also receive input from higher centers, especially from the parasympathetic and sympathetic headquarters in the hypothalamus.

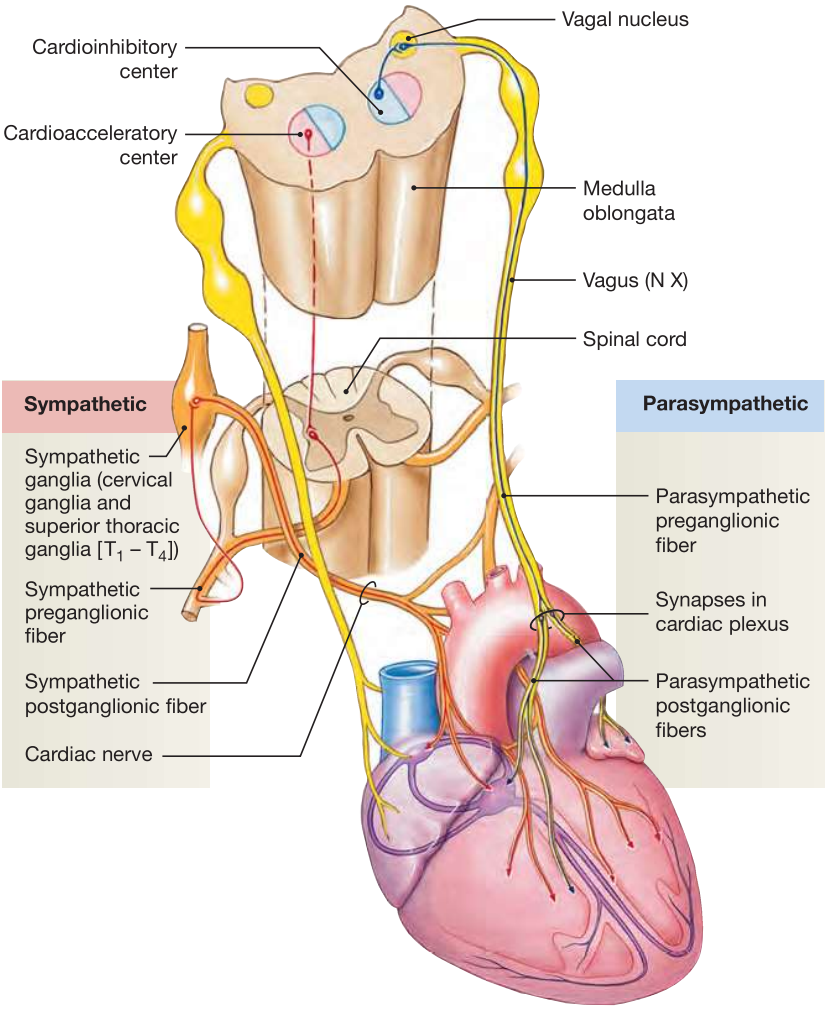
Tips & Tricks

To remember the effect of the sympathetic nervous system on cardiac performance, remember that ***s***ympathetic input ***s***peeds and ***s***trengthens the heartbeat.

Cardiac Reflexes. Information about the status of the cardiovascular system arrives over visceral sensory fibers accompanying the vagus nerve and the sympathetic nerves of the cardiac plexus. The cardiac centers monitor baroreceptors and chemoreceptors innervated by the glossopharyngeal (N IX) and vagus (N X) nerves. ↩ pp. 485, 486 On the basis of the information received, the cardiac centers adjust the heart's activity to maintain adequate circulation to vital organs, such as the brain.

The cardiac centers respond to changes in blood pressure as reported by baroreceptors, and to changes in arterial concentrations of dissolved oxygen and carbon dioxide as reported by chemoreceptors. For example, a decline in blood pressure or oxygen concentrations or an increase in carbon dioxide levels generally means that the heart must work harder to meet the demands of peripheral tissues. The cardiac centers then call for an increase in cardiac activity. We detail these reflexes and their effects on the heart and peripheral vessels in Chapter 21.

Figure 20–21 Autonomic Innervation of the Heart.



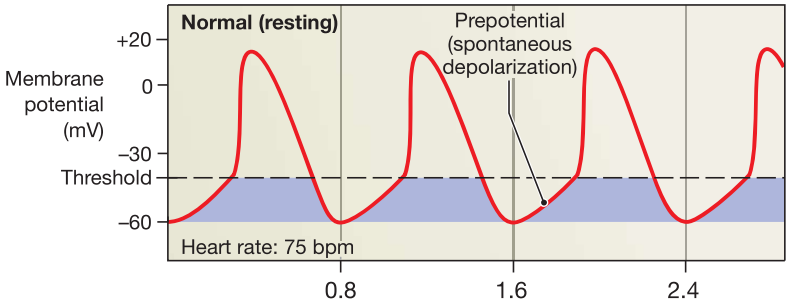
Autonomic Tone. Like other organs with dual innervation, the heart has a resting autonomic tone. Both autonomic divisions are normally active at a steady background level, releasing ACh and NE at the nodes and into the myocardium. For this reason, cutting the vagus nerves increases the heart rate, and sympathetic blocking agents slow the heart rate.

Parasympathetic effects dominate in a healthy, resting individual. Without autonomic innervation, the pacemaker cells of the SA node establish the heart rate. Such a heart beats at a rate of 80–100 bpm. At rest, a typical adult heart with normal innervation beats more slowly, at 70–80 bpm, due to activity in the parasympathetic nerves innervating the SA node. If parasympathetic activity increases, the heart rate declines further. Conversely, the heart rate increases if parasympathetic activity decreases, or if sympathetic activation occurs. Through dual innervation and adjustments in autonomic tone, the ANS can make very delicate adjustments in cardiovascular function to meet the demands of other systems.

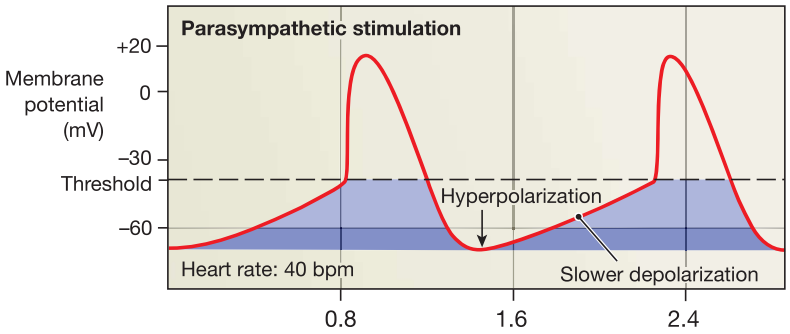
Effects on the SA Node. How do the sympathetic and parasympathetic divisions alter the heart rate? They do so by changing the ionic permeabilities of cells in the conducting system. The most dramatic effects take place at the SA node, which affects the heart rate through changes in the rate at which impulses are generated.

Consider the SA node of a resting individual whose heart is beating at 75 bpm (**Figure 20–22a**). Any factor that changes the rate of spontaneous depolarization or the duration of repolarization in nodal cells will alter the heart rate by changing the time required for these cells to reach threshold. Acetylcholine released by parasympathetic neurons opens chemically gated K^+ channels in the plasma membrane. Then K^+ leaves the nodal cells, dramatically slowing their rate of spontaneous de-

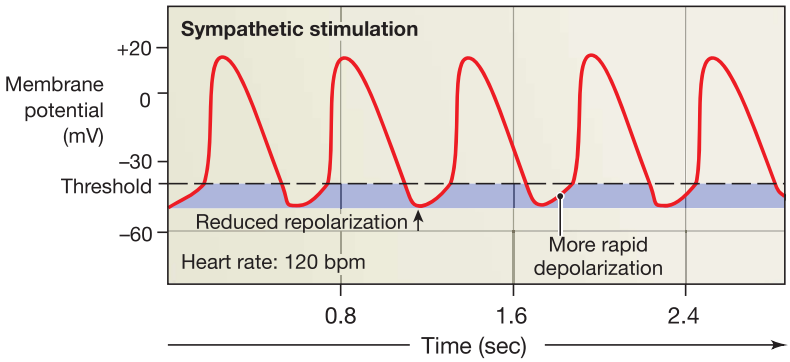
Figure 20–22 Autonomic Regulation of Pacemaker Function.



a Pacemaker cells have membrane potentials closer to threshold than those of other cardiac muscle cells (–60 mV versus –90 mV). Their plasma membranes undergo spontaneous depolarization to threshold, producing action potentials at a frequency determined by (1) the resting-membrane potential and (2) the rate of depolarization.



b Parasympathetic stimulation releases ACh, which extends repolarization and decreases the rate of spontaneous depolarization. The heart rate slows.



c Sympathetic stimulation releases NE, which shortens repolarization and accelerates the rate of spontaneous depolarization. As a result, the heart rate increases.

polarization and also slightly extending their duration of repolarization (**Figure 20–22b**). As a result, heart rate declines.

Norepinephrine released by sympathetic neurons binds to beta-1 receptors, leading to the opening of sodium-calcium ion channels. Then an influx of positively charged ions increases the rate of depolarization and shortens the period of repolarization. The nodal cells reach threshold more quickly, and the heart rate increases (**Figure 20–22c**).

The Atrial Reflex. The **atrial reflex,** or *Bainbridge reflex,* involves adjustments in heart rate in response to an increase in the **venous return** (the amount of blood returning to the heart through veins). When the walls of the right atrium are stretched, stretch receptors there trigger a reflexive increase in heart rate by stimulating sympathetic activity (**Figure 20–22**). Thus, when the rate of venous return to the heart increases, so does the heart rate, and for this reason the cardiac output rises as well.

Hormones

Epinephrine, norepinephrine, and thyroid hormone increase heart rate by their effect on the SA node. The effects of epinephrine on the SA node are similar to those of norepinephrine. Epinephrine also affects the contractile cells. After massive sympathetic stimulation of the adrenal medullae, the myocardium may become so excitable that abnormal contractions occur.

Venous Return

In addition to its indirect effect on heart rate via the atrial reflex, venous return also directly affects nodal cells. When venous return increases, the atria receive more blood and the walls are stretched. Stretching of the cells of the SA node leads to more rapid depolarization and an increase in the heart rate.

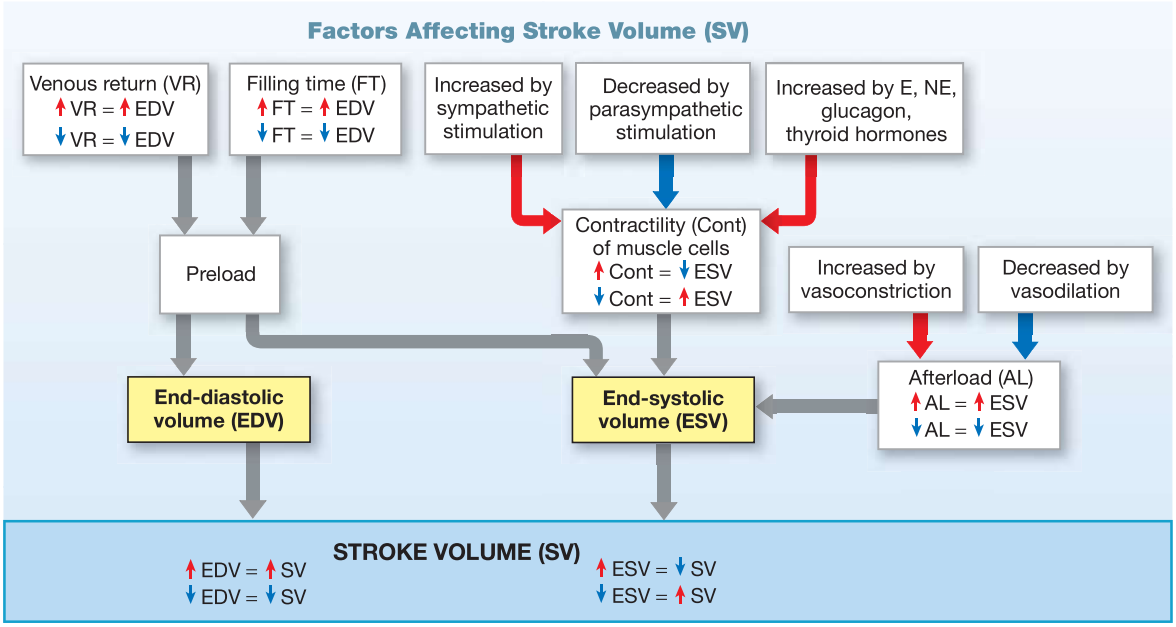
Factors Affecting the Stroke Volume

The stroke volume is the difference between the end-diastolic volume and the end-systolic volume. Changes in either EDV or ESV can change the stroke volume, and thus cardiac output. The factors involved in the regulation of stroke volume are indicated in **Figure 20–23**.

The EDV

Recall that the EDV is the amount of blood in a ventricle at the end of diastole, just before a contraction begins. Two factors affect this volume: the filling time and the venous return. **Filling time** is the duration of ventricular diastole. It depends entirely on the heart rate: The faster the heart rate, the shorter is the time available for filling. Venous return is variable over this period. It varies in response to changes in cardiac output, blood volume, patterns of peripheral circulation, skeletal muscle activity, and other factors that affect

Figure 20–23 Factors Affecting Stroke Volume. The arrows indicate the nature of the effects: ↑ = increases, ↓ = decreases.



the rate of blood flow back to the heart. (We explore these factors in Chapter 21.)

Preload. The degree of stretching in ventricular muscle cells during ventricular diastole is called the **preload.** The preload is directly proportional to the EDV: The greater the EDV, the larger the preload. Preload matters because it affects the ability of muscle cells to produce tension. As sarcomere length increases past resting length, the amount of force produced during systole increases.

The amount of preload, and hence the degree of myocardial stretching, varies with the demands on the heart. When you are standing at rest, your EDV is low. The ventricular muscle is stretched very little, and the sarcomeres are relatively short. During ventricular systole, the cardiac muscle cells develop little power, and the ESV (the amount of blood in the ventricle after contraction) is relatively high because the muscle cells contracted only a short distance. If you begin exercising, venous return increases and more blood flows into your heart. Your EDV increases, and the myocardium stretches further. As the sarcomeres approach optimal lengths, the ventricular muscle cells can contract more efficiently and produce more forceful contractions. They also shorten more, and more blood is pumped out of your heart.

The EDV and Stroke Volume. In general, the greater the EDV, the larger the stroke volume. Stretching the cardiac muscle cells *past* their optimal length would *reduce* the force of contraction, but this degree of stretching does not normally take place. Myocardial connective tissues, the cardiac skeleton, and the pericardial sac all limit the expansion of the ventricles.

The relationship between the amount of ventricular stretching and the contractile force means that, within normal physiological limits, increasing the EDV results in a corresponding increase in the stroke volume. This general rule of "more in = more out" was first proposed by Ernest H. Starling based on his studies and research by Otto Frank. The relationship is known as the **Frank–Starling principle,** or *Starling's law of the heart*.

Autonomic adjustments to cardiac output normally make the effects of the Frank–Starling principle difficult to see. However, we can see the effects more clearly in individuals who have received a heart transplant, because the implanted heart is not innervated by the ANS. The most obvious effect of the Frank–Starling principle in these hearts is that the outputs of the left and right ventricles remain balanced under a variety of conditions.

Consider, for example, an individual at rest, with the two ventricles ejecting equal volumes of blood. Although the ventricles contract together, they work in series: When the heart contracts, blood leaving the right ventricle heads to the lungs. During the next ventricular diastole, that volume of blood passes through the left atrium, to be ejected by the left ventricle at the next contraction. If the venous return decreases, the EDV of the right ventricle will decline. During ventricular systole, the right ventricle will then pump less blood to the lungs. In the next cardiac cycle, the EDV of the left ventricle will be reduced, and that ventricle will eject a smaller volume of blood. The output of the two ventricles will again be in balance, but both will have smaller stroke volumes than they did initially.

The ESV

After the ventricle has contracted and ejected the stroke volume, the amount of blood that remains in the ventricle at the end of ventricular systole is the ESV. Three factors that influence the ESV are the *preload* (discussed earlier), the *contractility* of the ventricle, and the *afterload*.

Contractility. **Contractility** is the amount of force produced during a contraction, at a given preload. Under normal circumstances, autonomic innervation or circulating hormones can alter contractility. Under special circumstances, drugs or abnormal ion concentrations in the extracellular fluid can alter contractility.

Factors that increase contractility are said to have a *positive inotropic action* (*ino-*, fiber). Factors that decrease contractility have a *negative inotropic action*. Positive inotropic agents typically stimulate Ca^{2+} entry into cardiac muscle cells, thus increasing the force and duration of ventricular contractions. Negative inotropic agents may block Ca^{2+} movement or depress cardiac muscle metabolism. Positive and negative inotropic factors include ANS activity, hormones, and changes in extracellular ion concentrations.

Effects of Autonomic Activity on Contractility. Autonomic activity alters the degree of contraction and changes the ESV in the following ways:

- Sympathetic stimulation has a positive inotropic effect. It causes the release of norepinephrine (NE) by postganglionic fibers of the cardiac nerves and the secretion of epinephrine (E) and NE by the adrenal medullae. These hormones affect heart rate, as we will discuss shortly. They also stimulate alpha and beta receptors in cardiac muscle plasma membranes. This stimulation increases cardiac muscle cell metabolism and the force and degree of contraction. The net effect is that the ventricles contract more forcefully, increasing the ejection fraction and decreasing the ESV.
- Parasympathetic stimulation from the vagus nerves has a negative inotropic effect. The primary effect of acetylcholine (ACh) is at the membrane surface, where it produces hyperpolarization and inhibition. As a result, the force of cardiac contractions is reduced. The atria show the greatest changes in contractile force because the ventricles are not extensively innervated by the parasympathetic division. However, under strong parasympathetic stimulation or after the administration of drugs that mimic the actions of ACh, the ventricles contract less forcefully, the ejection fraction decreases, and the ESV becomes larger.

Hormones. Many hormones affect the contractility of the heart. For example, epinephrine, norepinephrine, and thyroid hormones all have positive inotropic effects. Glucagon also has a positive inotropic effect. Before synthetic inotropic agents were available, glucagon was widely used to stimulate cardiac function. It is still used in cardiac emergencies and to treat some forms of heart disease.

The drugs *isoproterenol*, *dopamine*, and *dobutamine* mimic the action of E and NE by stimulating beta-1 receptors on cardiac muscle cells. ↩ p. 525 Dopamine (at high doses) and dobutamine also stimulate Ca^{2+} entry through alpha-1 receptor stimulation. *Digitalis* and related drugs elevate intracellular Ca^{2+} concentrations, but by a different mechanism. They interfere with the removal of Ca^{2+} from the sarcoplasm of cardiac muscle cells.

Many of the drugs used to treat hypertension (high blood pressure) have a negative inotropic action. Beta-blocking drugs such as *propranolol*, *timolol*, *metoprolol*, *atenolol*, and *labetalol* block beta receptors, alpha receptors, or both, and prevent sympathetic stimulation of the heart. Calcium channel blockers such as *nifedipine* or *verapamil* also have a negative inotropic effect.

Afterload. The **afterload** is the amount of tension that the contracting ventricle must produce to force open the semilunar valve and eject blood. Afterload increases with increased resistance to blood flow out of the ventricle. The greater the afterload, the longer the period of isovolumetric contraction, the shorter the duration of ventricular ejection, and the larger the ESV. In other words, as the afterload increases, the stroke volume decreases.

Any factor that restricts blood flow through the arterial system increases afterload. For example, either the constriction of peripheral blood vessels or a circulatory blockage elevates arterial blood pressure and increases the afterload. If the afterload is too great, the ventricle cannot eject blood. Such a high afterload is rare in a normal heart. However, damage to the heart muscle can weaken the myocardium enough that even a modest rise in arterial blood pressure can reduce stroke volume to dangerously low levels, producing symptoms of heart failure. Damage to the semilunar valve that restricts blood flow will also increase afterload.

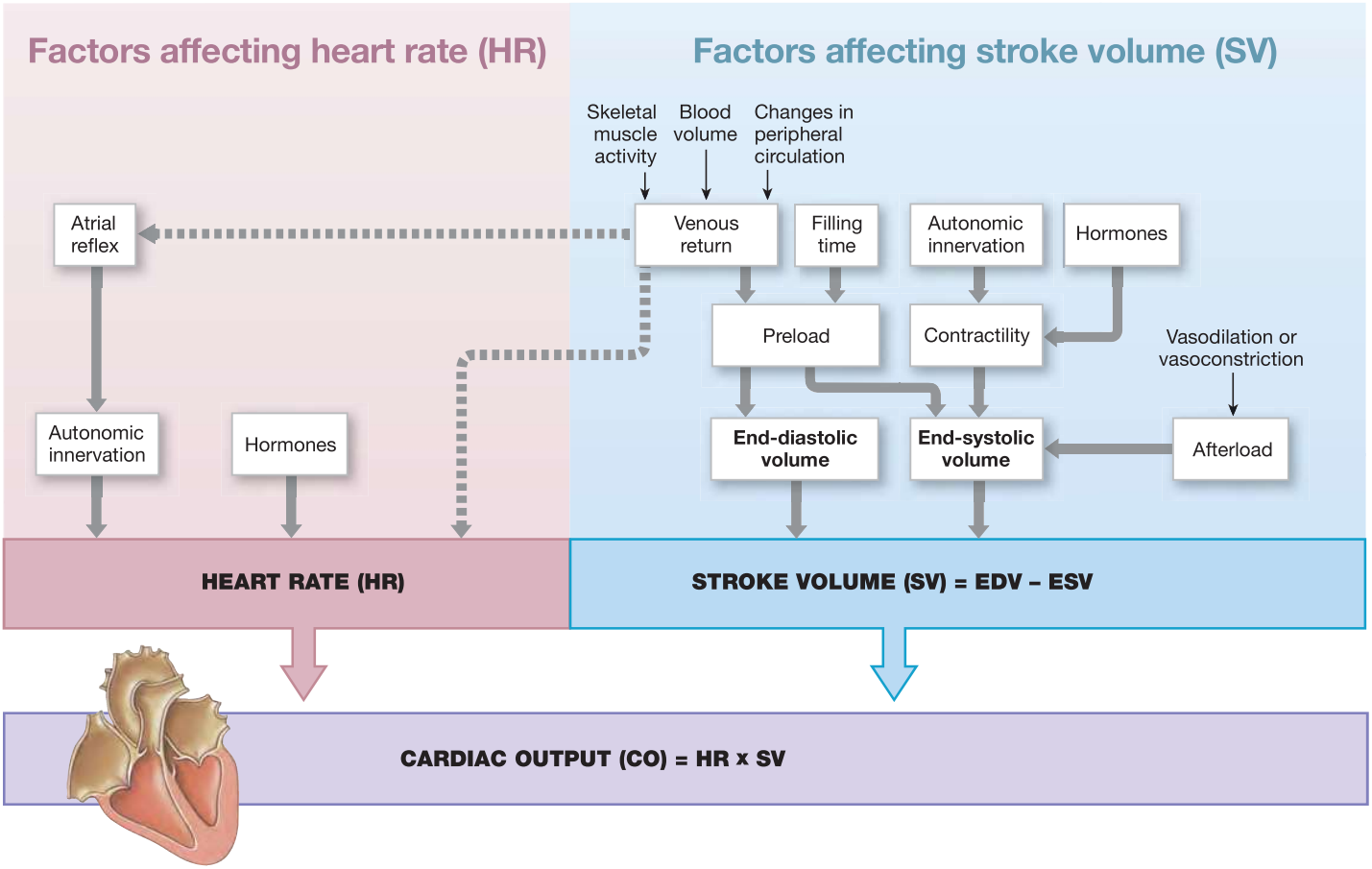
Summary: The Control of Cardiac Output

Figure 20–24 summarizes the factors that regulate heart rate and stroke volume, which interact to determine cardiac output under normal conditions.

The heart rate is influenced by the autonomic nervous system, circulating hormones, and the venous return.

- Sympathetic stimulation increases the heart rate, and parasympathetic stimulation decreases it. Under resting conditions, parasympathetic tone dominates, and the heart rate is slightly slower than the intrinsic heart rate. When activity levels rise, venous return increases and triggers the atrial reflex. The result is an increase in sympathetic tone and an increase in heart rate.

Figure 20–24 A Summary of the Factors Affecting Cardiac Output.



20

- Circulating hormones, specifically E, NE, and T_3, accelerate heart rate.
- An increase in venous return stretches the nodal cells and increases heart rate.
- The stroke volume is the difference between the end-diastolic volume (EDV) and the end-systolic volume (ESV).
- The EDV is determined by the available filling time and the rate of venous return.
- The ESV is determined by the amount of preload (the degree of myocardial stretching), the degree of contractility (adjusted by hormones and autonomic innervation), and the afterload (the arterial resistance to blood flow out of the heart).

In most healthy people, increasing both the stroke volume and the heart rate, such as occurs during heavy exercise, can raise the cardiac output by 300–500 percent, to 18–30 L/min. The difference between resting and maximal cardiac outputs is the **cardiac reserve.** Trained athletes exercising at maximal levels may increase cardiac output by nearly 700 percent, to 40 L/min.

Cardiac output cannot increase indefinitely, primarily because the available filling time shortens as the heart rate increases. At heart rates up to 160–180 bpm, the combination of increased rate of venous return and increased contractility compensates for the reduction in filling time. Over this range, cardiac output and heart rate increase together. But if the heart rate continues to climb, the stroke volume begins to drop. Cardiac output first plateaus and then declines.

The Heart and the Cardiovascular System

The purpose of cardiovascular regulation is to maintain adequate blood flow to all body tissues. The heart cannot accomplish this by itself, and it does not work in isolation. For example, when blood pressure changes, the cardiovascular centers adjust not only the heart rate but also the diameters of peripheral blood vessels. These adjustments work together to keep the blood pressure within normal limits and to maintain circulation to vital tissues and organs. In Chapter 21 we complete this story by detailing the cardiovascular responses to changing activity patterns and circulatory emergencies. We then conclude our discussion of the cardiovascular system by examining the anatomy of the pulmonary and systemic circuits.

Checkpoint

12. Define cardiac output.
13. Caffeine has effects on conducting cells and contractile cells that are similar to those of NE. What effect would drinking large amounts of caffeinated drinks have on the heart?
14. If the cardioinhibitory center of the medulla oblongata were damaged, which part of the autonomic nervous system would be affected, and how would the heart be influenced?
15. How does a drug that increases the length of time required for the repolarization of pacemaker cells affect the heart rate?
16. Why is it a potential problem if the heart beats too rapidly?
17. What effect would stimulating the acetylcholine receptors of the heart have on cardiac output?
18. What effect would an increase in venous return have on the stroke volume?
19. How would an increase in sympathetic stimulation of the heart affect the end-systolic volume?
20. Joe's end-systolic volume is 40 mL, and his end-diastolic volume is 125 mL. What is Joe's stroke volume?

See the blue Answers tab at the back of the book.

Related Clinical Terms

artificial pacemaker: A small, battery-operated device that keeps one's heart beating in a regular rhythm. It may be permanently implanted internally or for temporary usage it may be an external device.

asystole: The absence of cardiac activity with no contraction and no output.

automated external defibrillator (AED): A device that, when applied, automatically checks the function of the heart. Upon detecting a condition that may respond to an electric shock, it delivers a shock to restore normal heartbeat rhythm.

automatic implantable cardioverter defibrillator (AICD): A surgically implanted battery-operated device that monitors the function of the heart. Upon detecting a condition that may respond to an electric shock, such as a disorganized heartbeat, the device delivers a shock to restore normal heartbeat rhythm.

cardiac arrest: Sudden stopping of the pumping action of the heart causing the loss of arterial blood pressure.

cardiology: The branch of medicine dealing with the diagnosis and treatment of heart disorders and related conditions.

cardiomegaly: An enlarged heart, which is a sign of some other condition such as stress, weakening of the heart muscle, coronary artery disease, heart valve problems, or abnormal heart rhythms.

cardiomyoplasty: A surgical procedure that uses stimulated latissimus dorsi muscle to assist with cardiac function. The latissimus dorsi muscle is relocated and wrapped around the left and right ventricles and stimulated to contract during cardiac systole by means of an implanted burst-stimulator.

commotio cordis: Sudden cardiac arrest as the result of a blunt hit or impact to the chest.

congestive heart failure: The heart condition of weakness, edema, and shortness of breath caused by the inability of the heart to maintain adequate blood circulation in the peripheral tissues and the lungs.

cor pulmonale: Weakness of the right ventricle of the heart due to prolonged high blood pressure in the pulmonary artery and right ventricle; or any disease or malfunction that affects the pulmonary circuit in the lungs.

echocardiography: A noninvasive diagnostic test that uses ultrasound to make images of the heart chambers, valves, and surrounding structures. This diagnostic tool can also measure cardiac output, detect inflammation around the heart, identify abnormal anatomy, and detect infections of the heart valves.

endocarditis: Inflammation or infection of the endocardium, the inner lining of the heart muscle.

fibrillation: Fast twitching of the heart muscle fibers with little or no movement of the muscle as a whole. Atrial fibrillation occurs in the atria of the heart and is characterized by chaotic quivers and irregular ventricular beating with both atria and ventricles being out of sync.

heart block: Delay in the normal electrical pulses that cause the heart to beat.

mitral valve prolapse: A condition in which the mitral (bicuspid) valve cusps do not close properly and are pushed back toward the left atrium.

myocarditis: Inflammation of the myocardium, the middle layer of the heart wall tissue.

palpitation: Irregular and rapid beating of the heart.

percutaneous transluminal coronary angioplasty (PTCA): The surgical use of a balloon-tipped catheter to enlarge a narrowed artery.

sick sinus syndrome: A group of heart rhythm disorders or problems in which the sinus node does not work properly to regulate the heart rhythms.

Chapter Review

Study Outline

An Introduction to the Cardiovascular System p. 670

1. The blood vessels can be subdivided into the **pulmonary circuit** (which carries blood to and from the lungs) and the **systemic circuit** (which transports blood to and from the rest of the body).
2. **Arteries** carry blood away from the heart; **veins** return blood to the heart. **Capillaries,** or *exchange vessels*, are thin-walled, narrow-diameter vessels that connect the smallest arteries and veins. *(Figure 20–1)*
3. The heart has four chambers: the **right atrium** and **right ventricle,** and the **left atrium** and **left ventricle.**

20-1 The heart is a four-chambered organ, supplied by the coronary circulation, that pumps oxygen-poor blood to the lungs and oxygen-rich blood to the rest of the body p. 670

4. The heart is surrounded by the **pericardial cavity** and lies within the anterior portion of the **mediastinum,** which separates the two pleural cavities. *(Figure 20–2)*
5. The pericardial cavity is lined by the **pericardium.** The **visceral pericardium (epicardium)** covers the heart's outer surface, and the **parietal pericardium** lines the inner surface of the **pericardial sac,** which surrounds the heart. *(Figure 20–2)*
6. The **coronary sulcus,** a deep groove, marks the boundary between the atria and the ventricles. Other surface markings also provide useful reference points in describing the heart and associated structures. *(Figure 20–3)*
7. The bulk of the heart consists of the muscular **myocardium.** The **endocardium** lines the inner surfaces of the heart, and the **epicardium** covers the outer surface. *(Figure 20–4)*
8. **Cardiac muscle cells** are interconnected by **intercalated discs,** which convey the force of contraction from cell to cell and conduct action potentials. *(Figure 20–5;Table 20–1)*
9. The atria are separated by the **interatrial septum,** and the ventricles are divided by the **interventricular septum.** The right atrium receives blood from the systemic circuit via two large veins, the **superior vena cava** and the **inferior vena cava.** (The atrial walls contain the **pectinate muscles,** prominent muscular ridges.) *(Figure 20–6)*
10. Blood flows from the right atrium into the right ventricle via the **right atrioventricular (AV) valve (tricuspid valve).** This opening is bounded by three **cusps** of fibrous tissue braced by the **chordae tendineae,** which are connected to **papillary muscles.** *(Figure 20–6)*
11. Blood leaving the right ventricle enters the **pulmonary trunk** after passing through the **pulmonary valve.** The pulmonary trunk divides to form the **left** and **right pulmonary arteries.** The **left** and **right pulmonary veins** return blood from the lungs to the left atrium. Blood leaving the left atrium flows into the left ventricle via the **left atrioventricular (AV) valve (bicuspid,** or **mitral, valve).** Blood leaving the left ventricle passes through the **aortic valve** and into the systemic circuit via the **ascending aorta.** *(Figure 20–6)*
12. Anatomical differences between the ventricles reflect the functional demands placed on them. The wall of the right ventricle is relatively thin, whereas the left ventricle has a massive muscular wall. *(Figure 20–7)*
13. Valves normally permit blood flow in only one direction, preventing the **regurgitation** (backflow) of blood. *(Figure 20–8)*
14. The connective tissues of the heart (mainly collagen and elastic fibers) and the **cardiac skeleton** support the heart's contractile cells and valves. *(Figure 20–8)*
15. The **coronary circulation** meets the high oxygen and nutrient demands of cardiac muscle cells. The **coronary arteries** originate at the base of the ascending aorta. Interconnections between arteries, called **arterial anastomoses,** ensure a constant blood supply. The **great, posterior, small, anterior,** and **middle cardiac veins** are epicardial vessels that carry blood from the coronary capillaries to the **coronary sinus.** *(Figure 20–9)*
16. In **coronary artery disease (CAD),** portions of the coronary circulation undergo partial or complete blockage. A **myocardial infarction (MI),** or heart attack, occurs when part of the coronary circulation becomes blocked and muscle tissue dies when it cannot be oxygenated *(Spotlight Figure 20–10)*

20-2 The conducting system distributes electrical impulses through the heart, and an electrocardiogram records the associated electrical events p. 684

17. Two general classes of cardiac muscle cells are involved in the normal **heartbeat: contractile cells** and cells of the **conducting system.**
18. The **conducting system** is composed of the *sinoatrial node*, the *atrioventricular node*, and *conducting cells*. The conducting system initiates and distributes electrical impulses within the heart. Nodal cells establish the rate of cardiac contraction, and conducting cells distribute the contractile stimulus from the SA node to the atrial myocardium and the AV node (along *internodal pathways*), and from the AV node to the ventricular myocardium. *(Figure 20–11)*
19. Unlike skeletal muscle, cardiac muscle contracts without neural or hormonal stimulation. **Pacemaker cells** in the **sinoatrial (SA) node** (*cardiac pacemaker*) normally establish the rate of contraction. From the SA node, the stimulus travels to the **atrioventricular (AV) node,** and then to the **AV bundle,** which divides into **bundle branches.** From there, **Purkinje fibers** convey the impulses to the ventricular myocardium. *(Figures 20–11,Figures 20–12)*
20. A recording of electrical activities in the heart is an **electrocardiogram (ECG** or **EKG).** Important landmarks of an ECG include the **P wave** (atrial depolarization), the **QRS complex** (ventricular depolarization), and the **T wave** (ventricular repolarization). *(Figure 20–13)*
21. **Cardiac arrhythmias** are abnormal patterns of electrical activity in the heart. *(Spotlight Figure 20–14)*
22. **Contractile cells** form the bulk of the atrial and ventricular walls. Cardiac muscle cells have a long refractory period, so rapid stimulation produces twitches rather than tetanic contractions. *(Figure 20–15)*

20-3 Events during a complete heartbeat constitute a cardiac cycle p. 691

23. The **cardiac cycle** contains periods of **atrial** and **ventricular systole** (contraction) and **atrial** and **ventricular diastole** (relaxation). *(Figure 20–16)*

24. When the heart beats, the two ventricles eject equal volumes of blood. *(Figure 20–17)*
25. The closing of valves and rushing of blood through the heart cause characteristic heart sounds, which can be heard during *auscultation*. *(Figure 20–18)*

20-4 Cardiodynamics examines the factors that affect cardiac output p. 695

26. The amount of blood ejected by a ventricle during a single beat is the **stroke volume (SV).** The amount of blood pumped by a ventricle each minute is the **cardiac output (CO).** *(Figure 20–19)*
27. Cardiac output can be adjusted by changes in either stroke volume or heart rate. *(Figure 20–20)*
28. The **cardioacceleratory center** in the medulla oblongata activates sympathetic neurons; the **cardioinhibitory center** controls the parasympathetic neurons that slow the heart rate. These cardiac centers receive inputs from higher centers and from receptors monitoring blood pressure and the concentrations of dissolved gases. *(Figure 20–21)*
29. The basic heart rate is established by the pacemaker cells of the SA node, but it can be modified by the autonomic nervous system. The **atrial reflex** accelerates the heart rate when the walls of the right atrium are stretched. *(Figure 20–22)*
30. Sympathetic activity produces more powerful contractions that reduce the ESV. Parasympathetic stimulation slows the heart rate, reduces the contractile strength, and raises the ESV.
31. Cardiac output is affected by various factors, including autonomic innervation and hormones. *(Figure 20–22)*
32. The stroke volume is the difference between the **end-diastolic volume (EDV)** and the **end-systolic volume (ESV)**. The **filling time** and **venous return** interact to determine the EDV. Normally, the greater the EDV, the more powerful is the succeeding contraction (the **Frank–Starling principle**). *(Figure 20–23)*
33. The difference between resting and maximal cardiac outputs is the **cardiac reserve.** *(Figure 20–24)*
34. The heart does not work in isolation in maintaining adequate blood flow to all tissues.

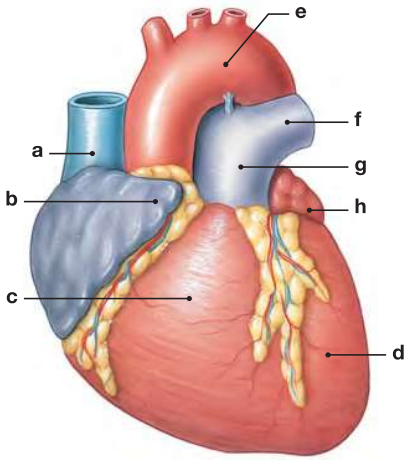
Review Questions

See the blue Answers tab at the back of the book.

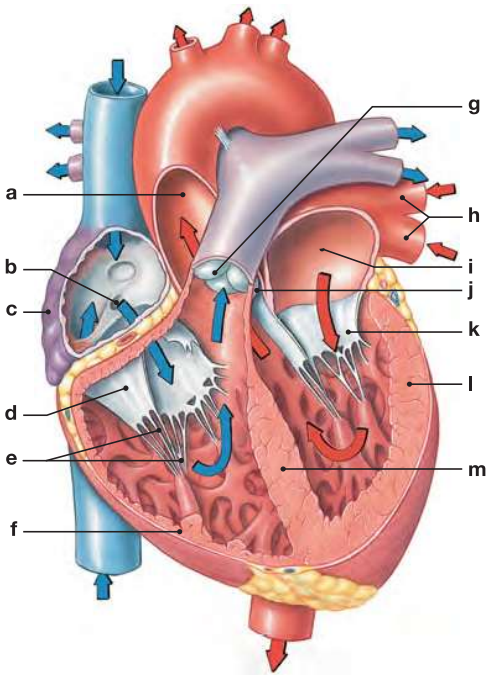
LEVEL 1 Reviewing Facts and Terms

1. Identify the superficial structures in the following diagram of the heart.

(a) _____
(b) _____
(c) _____
(d) _____
(e) _____
(f) _____
(g) _____
(h) _____



2. The great cardiac vein drains blood from the heart muscle to the
   (a) left ventricle. (b) right ventricle.
   (c) right atrium. (d) left atrium.
3. The autonomic centers for cardiac function are located in
   (a) the myocardial tissue of the heart.
   (b) the cardiac centers of the medulla oblongata.
   (c) the cerebral cortex.
   (d) all of these structures.
4. The serous membrane covering the outer surface of the heart is the
   (a) parietal pericardium. (b) endocardium.
   (c) myocardium. (d) visceral pericardium.
5. The simple squamous epithelium covering the valves of the heart constitutes the
   (a) epicardium. (b) endocardium.
   (c) myocardium. (d) cardiac skeleton.
6. The heart lies in the
   (a) pleural cavity. (b) peritoneal cavity.
   (c) abdominopelvic cavity. (d) mediastinum.
   (e) abdominal cavity.
7. Identify the structures in the following diagram of a sectional view of the heart.



(a) _____ (b) _____
(c) _____ (d) _____
(e) _____ (f) _____
(g) _____ (h) _____
(i) _____ (j) _____
(k) _____ (l) _____
(m) _____

8. The cardiac skeleton of the heart has which *two* of the following functions?
   (a) It physically isolates the muscle fibers of the atria from those of the ventricles.
   (b) It maintains the normal shape of the heart.
   (c) It helps distribute the forces of cardiac contraction.
   (d) It allows more rapid contraction of the ventricles.
   (e) It strengthens and helps prevent overexpansion of the heart.
9. Cardiac output is equal to the
   (a) difference between the end-diastolic volume and the end-systolic volume.
   (b) product of heart rate and stroke volume.
   (c) difference between the stroke volume at rest and the stroke volume during exercise.
   (d) stroke volume less the end-systolic volume.
   (e) product of heart rate and blood pressure.
10. During diastole, a chamber of the heart
   (a) relaxes and fills with blood.
   (b) contracts and pushes blood into an adjacent chamber.
   (c) experiences a sharp increase in pressure.
   (d) reaches a pressure of approximately 120 mm Hg.
11. During the cardiac cycle, the amount of blood ejected from the left ventricle when the semilunar valve opens is the
   (a) stroke volume (SV).
   (b) end-diastolic volume (EDV).
   (c) end-systolic volume (ESV).
   (d) cardiac output (CO).
12. What role do the chordae tendineae and papillary muscles play in the normal function of the AV valves?
13. Describe the three distinct layers that make up the heart wall.
14. What are the valves in the heart, and what is the function of each?
15. Trace the normal pathway of an electrical impulse through the conducting system of the heart.
16. What is the cardiac cycle? What phases and events are necessary to complete a cardiac cycle?
17. What three factors regulate stroke volume to ensure that the left and right ventricles pump equal volumes of blood?

LEVEL 2 Reviewing Concepts

18. The cells of the conducting system differ from the contractile cells of the heart in that
   (a) conducting cells are larger and contain more myofibrils.
   (b) contractile cells exhibit prepotentials.
   (c) contractile cells do not normally exhibit automaticity.
   (d) both a and b are correct.
19. Which of the following is *longer*?
   (a) the refractory period of cardiac muscle
   (b) the refractory period of skeletal muscle
20. If the papillary muscles fail to contract,
   (a) the ventricles will not pump blood.
   (b) the atria will not pump blood.
   (c) the semilunar valves will not open.
   (d) the AV valves will not close properly.
   (e) none of these happen.
21. Cardiac output cannot increase indefinitely because
   (a) the available filling time becomes shorter as the heart rate increases.
   (b) the cardiovascular centers adjust the heart rate.
   (c) the rate of spontaneous depolarization decreases.
   (d) the ion concentrations of pacemaker plasma membranes decrease.
22. Describe the function of the SA node in the cardiac cycle. How does this function differ from that of the AV node?
23. What are the sources and significance of the four heart sounds?
24. Differentiate between stroke volume and cardiac output. How is cardiac output calculated?
25. What factors influence cardiac output?
26. What effect does sympathetic stimulation have on the heart? What effect does parasympathetic stimulation have on the heart?
27. Describe the effects of epinephrine, norepinephrine, glucagon, and thyroid hormones on the contractility of the heart.

LEVEL 3 Critical Thinking and Clinical Applications

28. Vern is suffering from cardiac arrhythmias and is brought into the emergency room of a hospital. In the emergency room he begins to exhibit tachycardia and as a result loses consciousness. Explain why Vern lost consciousness.
29. Harvey has a heart murmur in his left ventricle that produces a loud "gurgling" sound at the beginning of systole. Which valve is probably faulty?
30. The following measurements were made on two individuals (the values recorded remained stable for one hour):
    Person 1: heart rate, 75 bpm; stroke volume, 60 mL
    Person 2: heart rate, 90 bpm; stroke volume, 95 mL
    Which person has the greater venous return? Which person has the longer ventricular filling time?
31. Karen is taking the medication verapamil, a drug that blocks the calcium channels in cardiac muscle cells. What effect should this medication have on Karen's stroke volume?

21

Blood Vessels and Circulation

Learning Outcomes

These Learning Outcomes correspond by number to this chapter's sections and indicate what you should be able to do after completing the chapter.

21-1 Distinguish among the types of **blood vessels** based on their structure and function, and describe how and where **fluid and dissolved materials** enter and leave the cardiovascular system.

21-2 Explain the mechanisms that regulate **blood flow through vessels**, describe the factors that influence **blood pressure**, and discuss the mechanisms that regulate **movement of fluids** between capillaries and interstitial spaces.

21-3 Describe the control mechanisms that regulate **blood flow and pressure in tissues**, and explain how the activities of the **cardiac, vasomotor, and respiratory centers** are coordinated to control blood flow through the tissues.

21-4 Explain the cardiovascular system's **homeostatic response** to exercise and hemorrhaging, and identify the principal blood vessels and functional characteristics of the special **circulation to the brain, heart, and lungs**.

21-5 Describe the three **general functional patterns** seen in the **pulmonary and systemic circuits** of the cardiovascular system.

21-6 Identify the major arteries and veins of the **pulmonary circuit**.

21-7 Identify the major arteries and veins of the **systemic circuit**.

21-8 Identify the differences between **fetal and adult circulation patterns**, and describe the changes in the patterns of blood flow that occur at birth.

21-9 Discuss the **effects of aging** on the cardiovascular system, and give examples of interactions between the cardiovascular system and other organ systems.

Clinical Notes

Spotlight

An Introduction to Blood Vessels and Circulation

Blood circulates throughout the body, moving from the heart through the tissues and back to the heart, in blood vessels. In this chapter we examine the organization of blood vessels and consider the integrated functions of the cardiovascular system as a whole. We begin with a description of the histological organization of arteries, capillaries, and veins. Then we explore the functions of these vessels, the basic principles of cardiovascular regulation, and the distribution of major blood vessels in the body. We will then be ready to consider the organization and function of the lymphatic system, the focus of Chapter 22.

21-1 Arteries, arterioles, capillaries, venules, and veins differ in size, structure, and functional properties

The cardiovascular system has five general classes of blood vessels. **Arteries** carry blood away from the heart. As they enter peripheral tissues, arteries branch repeatedly, and the branches decrease in diameter. The smallest arterial branches are called **arterioles** (ar-TĒR-ē-ōls). From the arterioles, blood moves into **capillaries,** where diffusion takes place between blood and interstitial fluid. From the capillaries, blood enters small **venules** (VEN-ūls), which unite to form larger **veins** that return blood to the heart.

Blood leaves the heart through the pulmonary trunk, which originates at the right ventricle, and the aorta, which originates at the left ventricle. Each of these arterial trunks has an internal diameter of about 2.5 cm (1 in.). The pulmonary arteries that branch from the pulmonary trunk carry blood to the lungs. The systemic arteries that branch from the aorta distribute blood to all other organs. Within these organs, the vessels branch into several hundred million tiny arterioles that provide blood to more than 10 billion capillaries within their own branching networks. These capillaries are barely the diameter of a single red blood cell. If all the capillaries in your body were placed end to end, their combined length would be more than 25,000 miles, enough to circle the planet.

The vital functions of the cardiovascular system depend entirely on events at the capillary level: All chemical and gaseous exchange between blood and interstitial fluid takes place across capillary walls. Cells rely on capillary diffusion to obtain nutrients and oxygen and to remove metabolic wastes, such as carbon dioxide and urea. Diffusion takes place very rapidly, because the distances involved are very short. Few cells lie farther than 125 μm (0.005 in.) from a capillary. As we will see, homeostatic mechanisms operating at the local, regional, and systemic levels adjust blood flow through the capillaries to meet the demands of peripheral tissues.

Blood vessels must be resilient enough to withstand changes in pressure, and flexible enough to move with underlying tissues and organs. The pressures inside vessels vary with distance from the heart, and the structures of different vessels reflect this fact. The arteries, veins, and capillaries also differ in function, and these functional differences are associated with distinctive anatomical features.

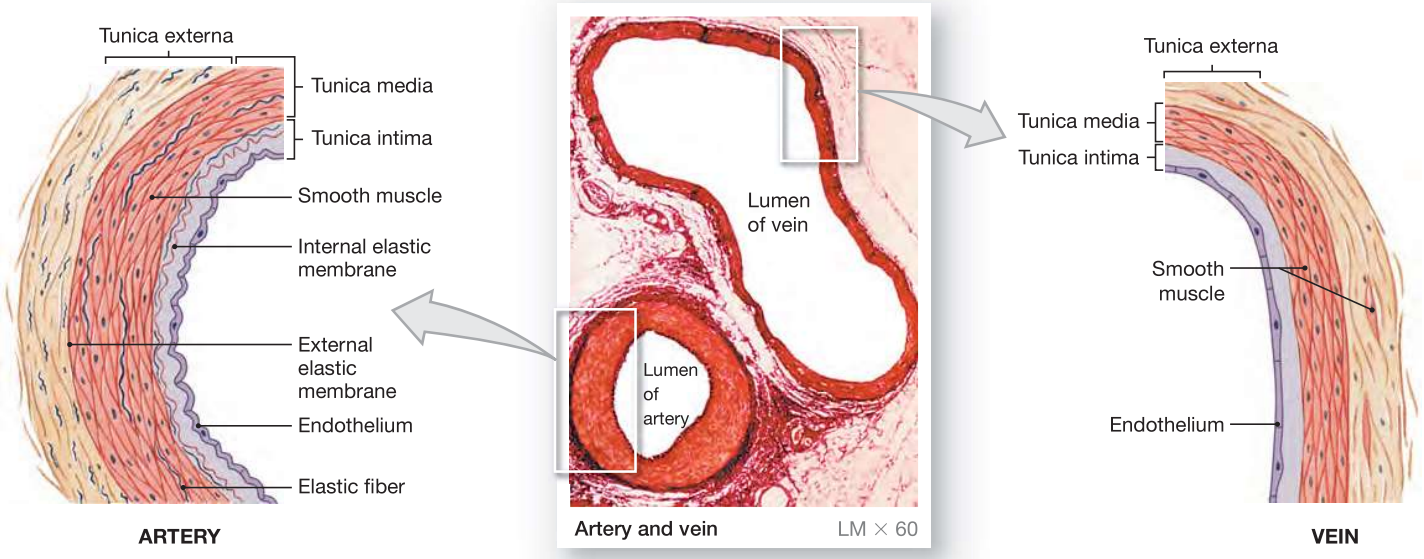
The Structure of Vessel Walls

The walls of arteries and veins have three distinct layers—the tunica intima, tunica media, and tunica externa (**Figure 21–1**):

1. The **tunica intima** (IN-ti-muh), or *tunica interna*, is the inner layer of a blood vessel. It includes the endothelial lining and a surrounding layer of connective tissue with a variable number of elastic fibers. In arteries, the outer margin of the tunica intima contains a thick layer of elastic fibers called the **internal elastic membrane.**
2. The **tunica media** is the middle layer of a blood vessel. It contains concentric sheets of smooth muscle tissue in a framework of loose connective tissue. The collagen fibers bind the tunica media to the tunica intima and tunica externa. The tunica media is commonly the thickest layer in a small artery. It is separated from the surrounding tunica externa by a thin band of elastic fibers called the **external elastic membrane.** The smooth muscle cells of the tunica media encircle the endothelium that lines the lumen of the blood vessel. When these smooth muscles contract, the vessel decreases in diameter, and when they relax, the diameter increases. Large arteries also contain layers of longitudinally arranged smooth muscle cells.
3. The **tunica externa** (eks-TER-nuh) or *tunica adventitia* (adven-TISH-a) is the outer layer of a blood vessel. It is a connective tissue sheath. In arteries, it contains collagen fibers with scattered bands of elastic fibers. In veins, it is generally thicker than the tunica media and contains networks of elastic fibers and bundles of smooth muscle cells. The connective tissue fibers of the tunica externa typically blend into those of adjacent tissues, stabilizing and anchoring the blood vessel.

Their layered walls give arteries and veins considerable strength. The muscular and elastic components also permit controlled changes in diameter as blood pressure or blood volume changes. However, the walls of arteries and veins are too thick to allow diffusion between the bloodstream and surrounding tissues, or even between the blood and the tissues of the vessel itself. For this reason, the walls of large vessels contain small arteries and veins that supply the smooth muscle cells and fibroblasts of the tunica media and tunica externa.

Figure 21–1 Comparisons of a Typical Artery and a Typical Vein.



Feature	Typical Artery	Typical Vein
GENERAL APPEARANCE IN SECTIONAL VIEW	Usually round, with relatively thick wall	Usually flattened or collapsed, with relatively thin wall
TUNICA INTIMA		
Endothelium	Usually rippled, due to vessel constriction	Often smooth
Internal elastic membrane	Present	Absent
TUNICA MEDIA	Thick, dominated by smooth muscle cells and elastic fibers	Thin, dominated by smooth muscle cells and collagen fibers
External elastic membrane	Present	Absent
TUNICA EXTERNA	Collagen and elastic fibers	Collagen and elastic fibers and smooth muscle cells

These blood vessels are called the *vasa vasorum* ("vessels of vessels").

Differences between Arteries and Veins

Arteries and veins supplying the same region lie side by side (**Figure 21–1**). In sectional view, you can distinguish arteries and veins by the following features:

- *Vessel walls* In general, the walls of arteries are thicker than those of veins. The tunica media of an artery contains more smooth muscle and elastic fibers than does that of a vein. These components help resist the arterial pressure generated by the heart as it pumps blood into the pulmonary trunk and aorta.
- *Vessel lumen* When not opposed by blood pressure, the elastic fibers in the arterial walls recoil, constricting the lumen. Thus, seen on dissection or in sectional view, the lumen of an artery often looks smaller than that of the corresponding vein. Because the walls of arteries are relatively thick and strong, they keep their circular shape in section. In contrast, cut veins tend to collapse. In section, these veins often look flattened or grossly distorted.
- *Vessel lining* The endothelial lining of an artery cannot contract, so when an artery constricts, its endothelium is thrown into folds that give sectioned arteries a pleated appearance. The lining of a vein lacks these folds.

In gross dissection, arteries and veins can generally be distinguished because:

- The thicker walls of arteries can be felt if the vessels are compressed.
- Arteries usually keep their cylindrical shape, but veins often collapse.
- Arteries are more resilient: When stretched, they keep their shape and elongate. When released, they snap back. A

small vein cannot tolerate as much distortion without collapsing or tearing.

- Veins typically contain *valves*—internal structures that prevent the backflow of blood toward the capillaries. In an intact vein, the location of each valve is marked by a slight distension of the vessel wall. (We consider valve structure in a later section.)

Arteries

Their relatively thick, muscular walls make arteries elastic and contractile. Elasticity permits the vessel diameter to change passively in response to changes in blood pressure. For example, it allows arteries to absorb the surging pressure waves that accompany the contractions of the ventricles.

The contractility of the arterial walls enables them to actively change diameter. This change takes place primarily under the control of the sympathetic division of the autonomic nervous system. When stimulated, arterial smooth muscles contract, constricting the artery—a process called **vasoconstriction.** When these smooth muscles relax, the diameter of the lumen increases—a process called **vasodilation.** Vasoconstriction and vasodilation affect (1) the afterload on the heart, (2) peripheral blood pressure, and (3) capillary blood flow. We explore these effects in a later section. Contractility is also important during the vascular phase of hemostasis, when the contraction of a damaged vessel wall helps reduce bleeding. ↩ p. 661

In traveling from the heart to peripheral capillaries, blood passes through *elastic arteries*, *muscular arteries*, and *arterioles* (**Figure 21–2**).

Elastic Arteries

Elastic arteries are also known as *conducting arteries* because they carry large volumes of blood away from the heart. They are large vessels with diameters up to 2.5 cm (1 in.) (**Figure 21–2**). The pulmonary trunk and aorta, as well as their major branches (the *pulmonary*, *common carotid*, *subclavian*, and *common iliac arteries*), are elastic arteries.

The walls of elastic arteries are extremely resilient because the tunica media contains a high density of elastic fibers and relatively few smooth muscle cells. As a result, elastic arteries can tolerate the pressure changes of the cardiac cycle. We have already seen that elastic rebound in the aorta helps to maintain blood flow in the coronary arteries. ↩ p. 680 Elastic rebound also occurs to some degree in all elastic arteries. During ventricular systole, pressures rise rapidly and the elastic arteries expand as the stroke volume is ejected. During ventricular diastole, blood pressure within the arterial system falls and the elastic fibers recoil to their original dimensions. Their expansion cushions the sudden rise in pressure during ventricular systole, and their recoil slows the drop in pressure during ventricular diastole. In this way, elastic arteries help to make blood flow continuous.

This function is important because blood pressure is the driving force behind blood flow: The greater the pressure oscillations, the greater the changes in blood flow. The elasticity of the arterial system dampens the pressure peaks and valleys that accompany the heartbeat. By the time blood reaches the arterioles, the pressure oscillations have disappeared, and blood flow is continuous.

Muscular Arteries

Muscular arteries, or *medium-sized arteries,* are also known as *distribution arteries* because they distribute blood to the body's skeletal muscles and internal organs. Most of the vessels of the arterial system are muscular arteries. They are characterized by a thick tunica media. It contains more smooth muscle cells than does the tunica media of elastic arteries (**Figures 21–1** and **21–2**). A typical muscular artery has a lumen diameter of approximately 4.0 mm (0.16 in.), but some have diameters as small as 0.5 mm. The *external carotid arteries* of the neck, the *brachial arteries* of the arms, the *mesenteric arteries* of the abdomen, and the *femoral arteries* of the thighs are examples of muscular arteries. Superficial muscular arteries are important as *pressure points*—places in the body where muscular arteries can be pressed against deeper bones to reduce blood flow and control severe bleeding. Major arterial pressure points are the common carotid, radial, brachial, femoral, popliteal, posterior tibial, and dorsal pedal.

Arterioles

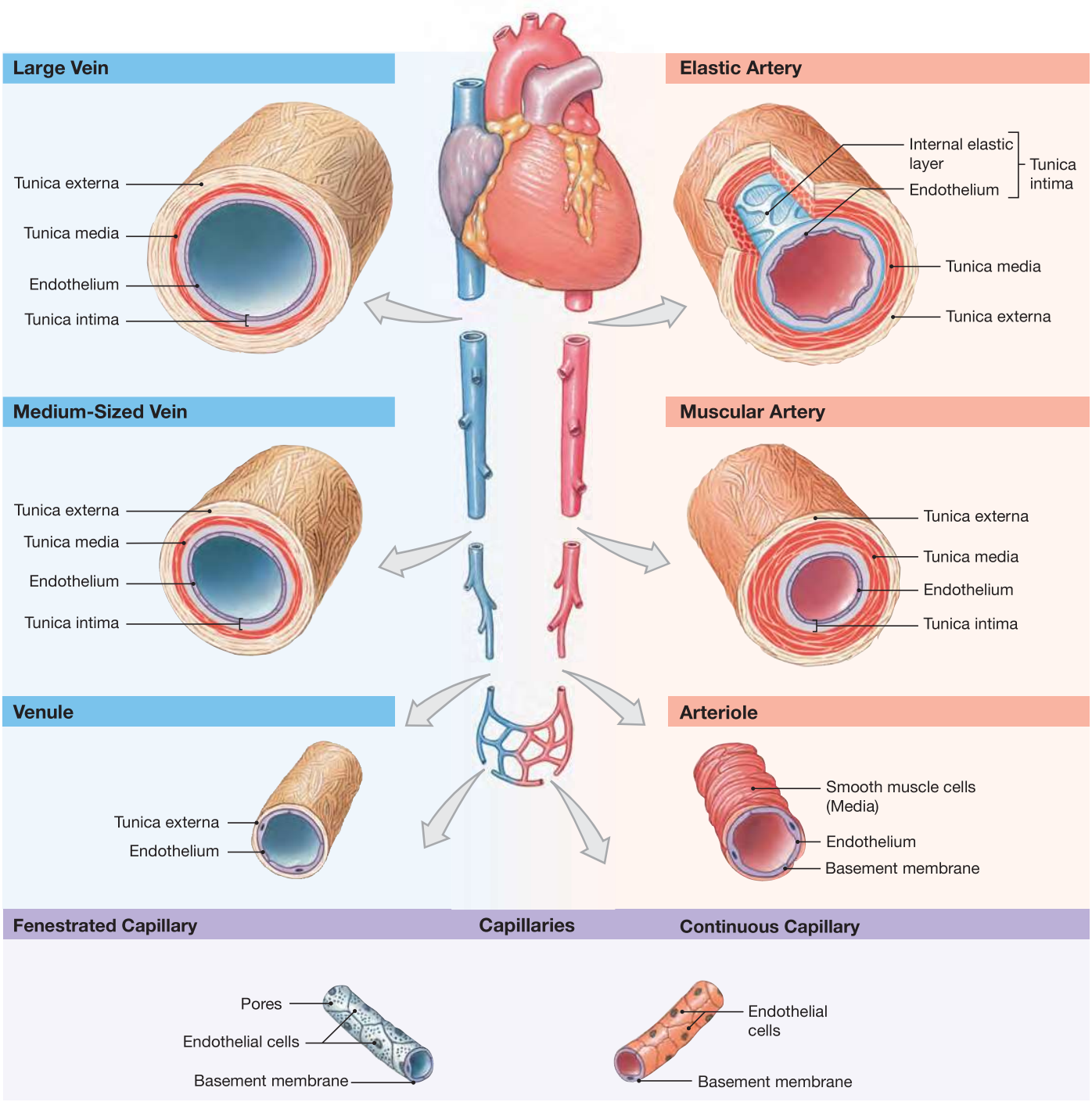
Arterioles, with an internal diameter of 30 μm or less, are considerably smaller than muscular arteries. Arterioles have a poorly defined tunica externa. In the larger arterioles, the tunica media consists of one or two layers of smooth muscle cells (**Figure 21–2**). In the smallest arterioles, the tunica media contains scattered smooth muscle cells that do not form a complete layer.

The diameters of smaller muscular arteries and arterioles change in response to local conditions or to sympathetic or endocrine stimulation. For example, arterioles in most tissues vasodilate when oxygen levels are low. Also, as we saw in Chapter 16, arterioles vasoconstrict under sympathetic stimulation. ↩ p. 525 Changes in their diameter affect the amount of force required to push blood around the cardiovascular system: More pressure is required to push blood through a constricted vessel than through a dilated one. The force opposing blood flow is called **resistance (R),** so arterioles are also called **resistance vessels.**

Vessel characteristics change gradually with distance from the heart. Each type of vessel described here actually represents the midpoint in a portion of a continuum. Thus, the largest muscular arteries contain a considerable amount of elastic tissue, and the smallest resemble heavily muscled arterioles.

Arteries carry blood under great pressure, and their walls are adapted to handle that pressure. Occasionally, local arterial pressure exceeds the capacity of the elastic components of the tunics.

Figure 21–2 Histological Structure of Blood Vessels. Representative diagrammatic cross-sectional views of the walls of arteries, capillaries, and veins. Notice the relative sizes of the layers in these vessels.



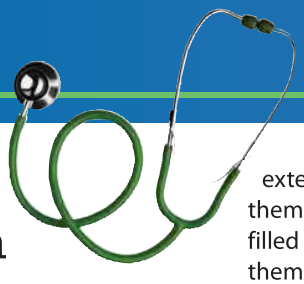
The result is an **aneurysm** (AN-ū-rizm), or bulge in the weakened wall of an artery. The bulge is like a bubble in the wall of a tire—and like a bad tire, the artery can suffer a catastrophic blowout. The most dangerous aneurysms occur in arteries of the brain (where they cause strokes) or in the aorta (where a rupture will cause fatal bleeding in a matter of minutes).

Capillaries

When we think of the cardiovascular system, we think first of the heart or the great blood vessels connected to it. But the microscopic capillaries that permeate most tissues do the real work of the cardiovascular system. These delicate vessels weave

Clinical Note

Arteriosclerosis



These aren't **plaques** you hang on the wall

Arteriosclerosis (ar-tēr-ē-ō-skler-Ō-sis; *arterio-*, artery + *sklerosis*, hardness) is a thickening and toughening of arterial walls. This condition may not sound life-threatening, but complications related to arteriosclerosis account for about half of all deaths in the United States. The effects of arteriosclerosis are varied. For example, arteriosclerosis of coronary vessels is responsible for *coronary artery disease (CAD)*, and arteriosclerosis of arteries supplying the brain can lead to strokes. ↩ p. 682 Arteriosclerosis takes two major forms:

1. **Focal calcification** is the deposition of calcium salts following the gradual degeneration of smooth muscle in the tunica media. Some focal calcification is a part of the aging process, and it may develop in association with atherosclerosis (described next). Rapid and severe calcification may take place as a complication of diabetes mellitus, an endocrine disorder. ↩ p. 622
2. **Atherosclerosis** (ath-er-ō-skler-Ō-sis; *athero-*, fatty degeneration) is the formation of lipid deposits in the tunica media associated with damage to the endothelial lining. It is the most common form of arteriosclerosis.

Many factors may be involved in the development of atherosclerosis. One major factor is lipid levels in the blood. Atherosclerosis tends to develop in people whose blood contains elevated levels of plasma lipids—specifically, cholesterol. Circulating cholesterol is transported to peripheral tissues in *lipoproteins*, which are protein–lipid complexes. (We will discuss the various types of lipoproteins in Chapter 25.)

When plasma cholesterol levels are chronically elevated, cholesterol-rich lipoproteins remain in circulation for an extended period. Circulating monocytes then begin removing them from the bloodstream. Eventually, the monocytes become filled with lipid droplets. Now called *foam cells*, they attach themselves to the endothelial walls of blood vessels, where they release cytokines. These growth factors stimulate smooth muscle cells near the tunica intima to divide, thickening the vessel wall.

Other monocytes then invade the area, migrating between the endothelial cells. As these changes take place, the monocytes, smooth muscle cells, and endothelial cells begin phagocytizing lipids as well. The result is an atherosclerotic **plaque,** a fatty mass of tissue that projects into the lumen of the vessel. At this point, the plaque has a relatively simple structure, and evidence suggests that the process can be reversed with appropriate dietary adjustments.

If the conditions persist, the endothelial cells become swollen with lipids, and gaps appear in the endothelial lining. Platelets now begin sticking to the exposed collagen fibers. The combination of platelet adhesion and aggregation leads to the formation of a localized blood clot, which further restricts blood flow through the artery. The structure of the plaque is now relatively complex.

A typical plaque is shown in **Figure 21–3**. Elderly individuals—especially elderly men—are most likely to develop atherosclerotic plaques. Estrogens may slow plaque formation, which may account for the lower incidence of CAD, myocardial infarctions (MIs), and strokes in women. After menopause, when estrogen production declines, the risks of CAD, MIs, and strokes in women increase markedly.

In addition to advanced age and male gender, other important risk factors for atherosclerosis include high blood cholesterol levels, high blood pressure, and cigarette smoking. Roughly 20 percent of middle-aged men have all three of these risk factors. These individuals are four times more likely to experience an MI or a cardiac arrest than other men in their age group. Fewer women develop atherosclerotic plaques, but

throughout active tissues, forming intricate networks that surround muscle fibers. Capillaries radiate through connective tissues, and branch beneath the basement membrane of epithelia.

Capillaries are the *only* blood vessels whose walls permit exchange between the blood and the surrounding interstitial fluids. Exchange can take place quickly because capillary walls are thin and diffusion distances are short. In addition, blood flows through capillaries relatively slowly, allowing sufficient time for the diffusion or active transport of materials across the capillary walls. In this way, the histological structure of capillaries permits a two-way exchange of substances between blood and interstitial fluid.

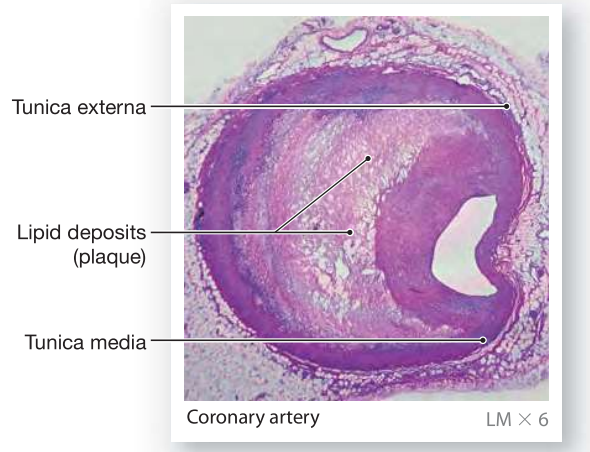
A typical capillary consists of an endothelial tube inside a thin basement membrane. Neither a tunica media nor a tunica externa is present (**Figure 21–2**). The average diameter of a capillary is a mere 8 μm, very close to that of a single red blood cell. The two major types of capillaries are *continuous capillaries* and *fenestrated capillaries*.

Continuous Capillaries

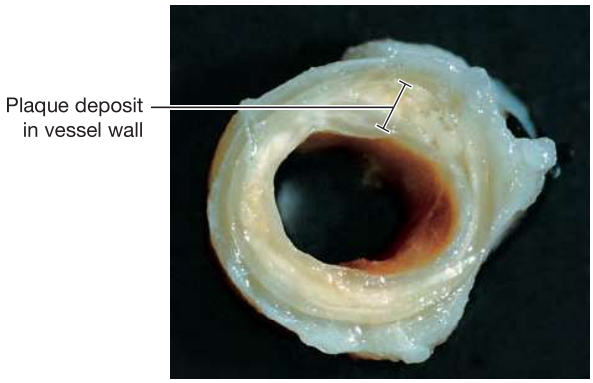
Most regions of the body are supplied by continuous capillaries. In a **continuous capillary,** the endothelium is a complete lining. A cross section through a large continuous capillary cuts across several endothelial cells (**Figure 21–4a**). In a small continuous capillary, a single endothelial cell may completely encircle the lumen.

Continuous capillaries are located in all tissues except epithelia and cartilage. Continuous capillaries permit the water, small solutes, and lipid-soluble materials to diffuse into the interstitial fluid. At the same time, they prevent the loss of blood

Figure 21–3 A Plaque within an Artery.



a A cross-sectional view of a large plaque



b A section of a coronary artery narrowed by plaque formation

elderly female smokers with high blood cholesterol and high blood pressure are at much greater risk than other women. Diabetes mellitus, obesity, and stress can promote the development of atherosclerosis in both men and women. Evidence also indicates that at least some forms of atherosclerosis may be linked to chronic infection with *Chlamydia pneumoniae*, a bacterium responsible for several types of respiratory infections, including some forms of pneumonia.

We discussed potential treatments for atherosclerotic plaques, such as catheterization with balloon angioplasty and stenting, and bypass surgery, in Chapter 20. ↩ p. 683 In the many cases where changes in diet do not lower circulating LDL levels sufficiently, drug therapies can bring them under control. Genetic engineering techniques have been used to treat an inherited form of *hypercholesterolemia* (high blood cholesterol) linked to extensive plaque formation. (Individuals with this condition are unable to absorb and recycle cholesterol in the liver.) In this experimental procedure, circulating cholesterol levels declined after copies of appropriate genes were inserted into some of the individual's liver cells.

Without question, the best approach to atherosclerosis is to avoid it by eliminating or reducing associated risk factors. Suggestions include (1) reducing your intake of dietary cholesterol, saturated fats, and trans fatty acids by restricting consumption of fatty meats (such as beef, lamb, and pork), egg yolks, and cream; (2) not smoking; (3) checking your blood pressure and taking steps to lower it if necessary; (4) having your blood cholesterol levels checked annually; (5) controlling your weight; and (6) exercising regularly.

cells and plasma proteins. In addition, some exchange may occur between blood and interstitial fluid by *bulk transport*—the movement of materials by endocytosis (via endosomes) or exocytosis at the inner endothelial surface. ↩ p. 92

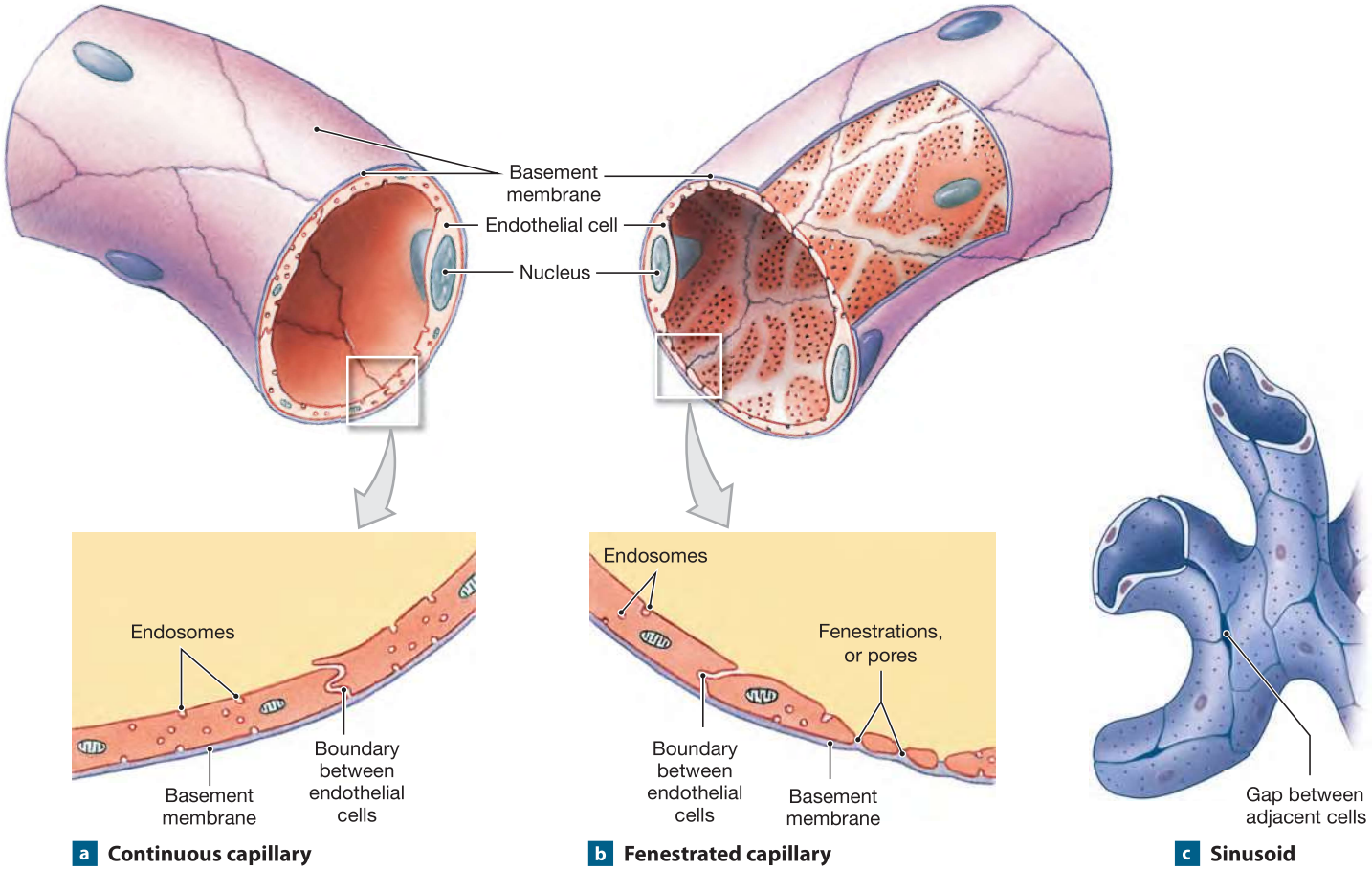
In specialized continuous capillaries in most of the central nervous system and in the thymus, the endothelial cells are bound together by tight junctions. These capillaries have very restricted permeability. We discussed one example—the capillaries responsible for the *blood–brain barrier*—in Chapters 12 and 14. ↩ pp. 381, 455

Fenestrated Capillaries

Fenestrated (FEN-es-trā-ted; *fenestra*, window) **capillaries** contain "windows," or pores, that penetrate the endothelial lining (**Figure 21–4b**). The pores allow rapid exchange of water and solutes between plasma and interstitial fluid. Examples of fenestrated capillaries include the *choroid plexus* of the brain and the blood vessels in a variety of endocrine organs, such as the hypothalamus and the pituitary, pineal, and thyroid glands. Fenestrated capillaries are also found along absorptive areas of the intestinal tract and at filtration sites in the kidneys. Both the number of pores and their permeability characteristics may vary from one region of the capillary to another.

Sinusoids (SĪ-nuh-soydz), also called **sinusoidal capillaries,** resemble fenestrated capillaries that are flattened and irregularly shaped (**Figure 21–4c**). In addition to being fenestrated, sinusoids commonly have gaps between adjacent endothelial cells, and the basement membrane is either thinner or absent. As a result, sinusoids permit the free exchange of water and solutes as large as plasma proteins between blood and interstitial fluid.

Figure 21–4 Capillary Structure.



Blood moves through sinusoids relatively slowly, maximizing the time available for exchange across the sinusoidal walls. Sinusoids occur in the liver, bone marrow, spleen, and many endocrine organs, including the pituitary and adrenal glands. At liver sinusoids, plasma proteins secreted by liver cells enter the bloodstream. Along sinusoids of the liver, spleen, and bone marrow, phagocytic cells monitor the passing blood, engulfing damaged red blood cells, pathogens, and cellular debris.

Capillary Beds

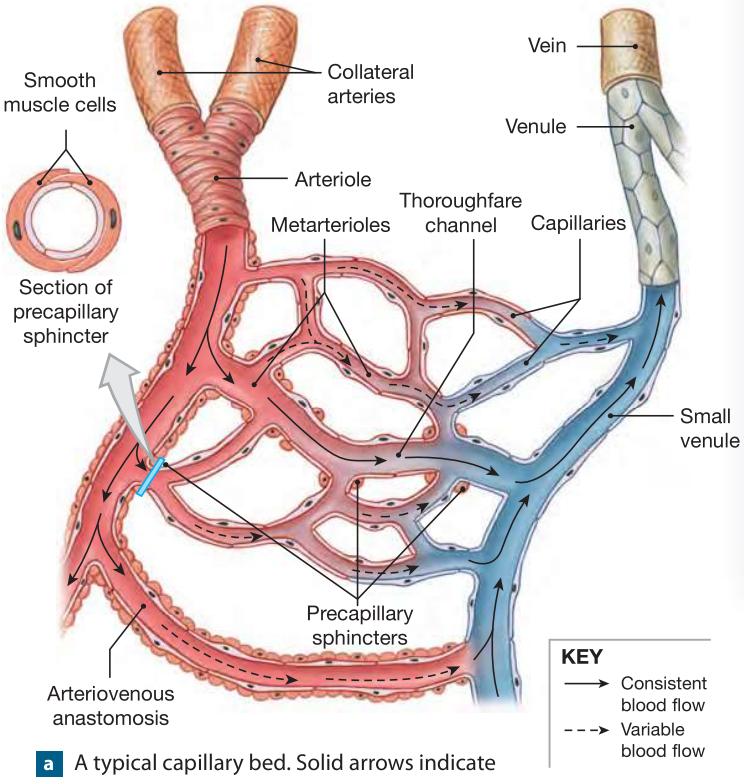
Capillaries function not as individual units, but rather, as part of an interconnected network called a **capillary bed,** or **capillary plexus** (Figure 21–5). A single arteriole generally gives rise to dozens of capillaries. They empty into several *venules*, the smallest vessels of the venous system. The entrance to each capillary is guarded by a **precapillary sphincter.** Contraction of the smooth muscle cells of this sphincter narrows the capillary entrance, reducing or stopping the flow of blood. When one precapillary sphincter constricts, blood is diverted into other branches of the network. When a precapillary sphincter relaxes, the entrance dilates, and blood flows into the capillary.

A capillary bed contains several direct connections between arterioles and venules. The wall in the first part of such a passageway contains smooth muscle that can change its diameter. This segment is called a **metarteriole** (met-ar-TĒR-ē-ōl) or **precapillary arteriole.** The rest of the passageway resembles a typical capillary in structure and is called a **thoroughfare channel.**

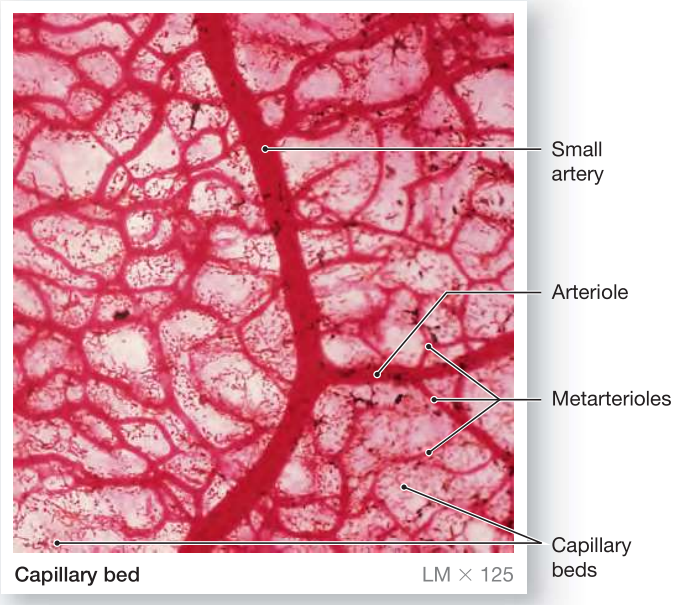
More than one artery may supply blood to a capillary bed. The multiple arteries are called **collaterals.** They fuse before giving rise to arterioles. The fusion of two collateral arteries that supply a capillary bed is an example of an **arterial anastomosis.** (An *anastomosis* is the joining of blood vessels.) The interconnections between the *anterior* and *posterior interventricular arteries* of the heart are arterial anastomoses. ↩ p. 680 An arterial anastomosis acts like an insurance policy: If one artery is compressed or blocked, capillary circulation will continue.

Arteriovenous (ar-tēr-ē-ō-VĒ-nus) **anastomoses** are direct connections between arterioles and venules. When an arteriovenous anastomosis is dilated, blood bypasses the capillary bed and flows directly into the venous circulation. The pattern of blood flow through an arteriovenous anastomosis is regu-

Figure 21–5 The Organization of a Capillary Bed.



a A typical capillary bed. Solid arrows indicate consistant blood flow; dashed arrows indicate variable or pulsating blood flow.



b A micrograph of a number of capillary beds.

lated primarily by sympathetic innervation under the control of the cardiovascular centers of the medulla oblongata.

Angiogenesis (an-jē-ō-JEN-e-sis; *angio-*, blood vessel + *genesis*, production) is the formation of new blood vessels and occurs under the direction of **vascular endothelial growth factor (VEGF).** Angiogenesis occurs in the embryo as tissues and organs develop. It may also occur at other times in any body tissue in response to factors released by cells that are *hypoxic*, or oxygen-starved. Clinically, angiogenesis is probably most important in cardiac muscle, where it takes place in response to a chronically constricted or occluded vessel.

Vasomotion

Although blood normally flows from arterioles to venules at a constant rate, the flow within each capillary varies. Each precapillary sphincter contracts and relaxes, perhaps a dozen times per minute. As a result, the blood flow within any capillary occurs in pulses rather than as a steady and constant stream. The net effect is that blood may reach the venules by one route now and by a different route later. The cycling of contraction and relaxation of smooth muscles that changes blood flow through capillary beds is called **vasomotion.**

Vasomotion is controlled locally by changes in the concentrations of chemicals and dissolved gases in the interstitial fluids. For example, when dissolved oxygen concentrations decline within a tissue, the capillary sphincters relax, so blood flow to the area increases. This process is an example of capillary *autoregulation*. We focus on it in a later section.

When you are at rest, blood flows through about 25 percent of the vessels within a typical capillary bed in your body. Your cardiovascular system does not contain enough blood to maintain adequate blood flow to all the capillaries in all the capillary beds in your body at the same time. As a result, when many tissues become active, the blood flow through capillary beds must be coordinated. We describe the mechanisms by which the cardiovascular centers perform this coordination later in the chapter.

Veins

Veins collect blood from all tissues and organs and return it to the heart. The walls of veins can be thinner than those of corresponding arteries because the blood pressure in veins is lower than that in arteries. We classify veins on the basis of their size.

Even though their walls are thinner, in general veins are larger in diameter than their corresponding arteries. (Review **Figure 21–2** to compare typical arteries and veins.)

Venules

Venules are the smallest venous vessels. They collect blood from capillary beds. They vary widely in size and structure. An average venule has an internal diameter of roughly 20 μm. Venules smaller than 50 μm lack a tunica media, and the smallest venules resemble expanded capillaries.

Medium-Sized Veins

Medium-sized veins are comparable in size to muscular arteries. They range from 2 to 9 mm in internal diameter. Their tunica media is thin and contains relatively few smooth muscle cells. The thickest layer of a medium-sized vein is the tunica externa, which contains longitudinal bundles of elastic and collagen fibers.

Large Veins

Large veins include the superior and inferior venae cavae and their tributaries within the abdominopelvic and thoracic cavities. All large veins have all three layers. The slender tunica media is surrounded by a thick tunica externa composed of a mixture of elastic and collagen fibers.

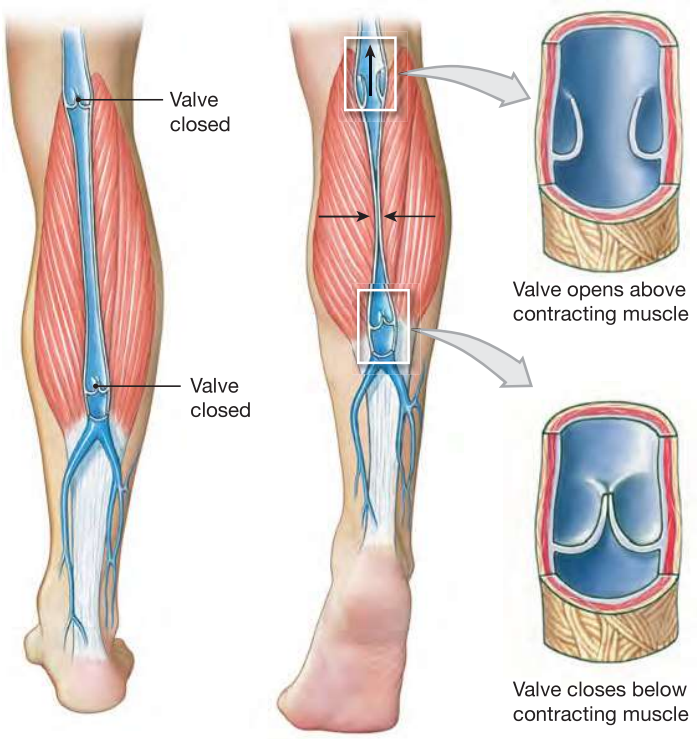
Venous Valves

The arterial system is a high-pressure system: Almost all the force developed by the heart is required to push blood along the network of arteries and through miles of capillaries. Blood pressure in a peripheral venule is only about 10 percent of that in the ascending aorta, and pressures continue to fall along the venous system.

The blood pressure in venules and medium-sized veins is so low that it cannot overcome the force of gravity. In the limbs, veins of this size contain **valves,** folds of the tunica intima that project from the vessel wall and point in the direction of blood flow. These valves, like those in the heart, permit blood flow in one direction only. Venous valves prevent blood from moving back toward the capillaries (**Figure 21–6**).

As long as the valves function normally, any movement that distorts or compresses a vein pushes blood toward the heart. This effect improves *venous return*, the rate of blood flow to the heart. ↩ p. 699 The mechanism is particularly important when you are standing, because blood returning from your feet must overcome gravity to ascend to the heart. Valves compartmentalize the blood within the veins, dividing the weight of the blood among the compartments. Any contraction of the surrounding skeletal muscles squeezes the blood toward the heart. Although you are probably not aware of it, when you stand, rapid cycles of contraction and relaxation occur within your leg muscles, helping to push blood toward the trunk. When you lie down, venous valves play a smaller part in venous return, because your heart and major vessels are at the same level.

Figure 21–6 The Function of Valves in the Venous System.



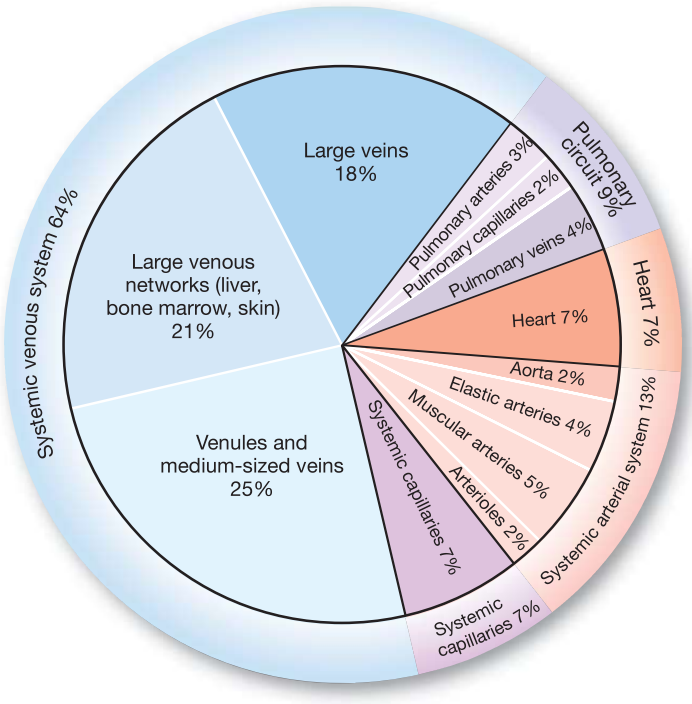
If the walls of the veins near the valves weaken or become stretched and distorted, the valves may not work properly. Blood then pools in the veins, and the vessels become grossly distended. The effects range from mild discomfort and a cosmetic problem, as in superficial **varicose veins** in the thighs and legs, to painful distortion of adjacent tissues, as in **hemorrhoids.**

The Distribution of Blood

Our total blood volume is unevenly distributed among arteries, veins, and capillaries (**Figure 21–7**). The heart, arteries, and capillaries in the pulmonary and systemic circuits normally contain 30–35 percent of the blood volume (roughly 1.5 liters of whole blood). The venous system contains the rest (65–70 percent, or about 3.5 liters). About one-third of the blood in the venous system (about a liter) is circulating within the liver, bone marrow, and skin. These organs have extensive venous networks that at any moment contain large volumes of blood.

Veins are much more *distensible,* or expandable, than arteries because their walls are thinner, with less smooth muscle. For a given rise in blood pressure, a typical vein stretches about eight times as much as a corresponding artery. The *capacitance* of a blood vessel is the relationship between the volume of blood it contains and the blood pressure. If a vessel behaves like

Figure 21–7 The Distribution of Blood in the Cardiovascular System.



a child's balloon, expanding easily at low pressures, it has high capacitance. If it behaves more like a truck tire, expanding only at high pressures, it has low capacitance. Veins, which expand easily, are called **capacitance vessels.** Because veins have high capacitance, they can accommodate large changes in blood volume. If the blood volume rises or falls, the elastic walls stretch or recoil, changing the volume of blood in the venous system.

If serious hemorrhaging occurs, the *vasomotor center* of the medulla oblongata stimulates sympathetic nerves that innervate smooth muscle cells in the walls of medium-sized veins. This activity has two major effects:

1. *Systemic veins constrict.* This process, called **venoconstriction** (vē-nō-kon-STRIK-shun), reduces the amount of blood within the venous system, increasing the volume within the arterial system and capillaries. Venoconstriction can keep the blood volume within the arteries and capillaries at near-normal levels despite a significant blood loss.
2. *The constriction of veins in the liver, skin, and lungs redistributes a significant proportion of the total blood volume.* As a result, blood flow to delicate organs (such as the brain) and to active skeletal muscles can be increased or maintained after blood loss. The amount of blood that can be shifted from veins in the liver, skin, and lungs to the general circulation is called the **venous reserve.** It is normally about 20 percent of total blood volume.

Checkpoint

1. List the five general classes of blood vessels.
2. A cross section of tissue shows several small, thin-walled vessels with very little smooth muscle tissue in the tunica media. Which type of vessel are these?
3. Why are valves located in veins, but not in arteries?
4. Where in the body would you find fenestrated capillaries?

See the blue Answers tab at the back of the book.

21-2 Pressure and resistance determine blood flow and affect rates of capillary exchange

Figure 21–8 provides an overview of the discussion of cardiovascular physiology that follows. The purpose of cardiovascular regulation is the maintenance of adequate blood flow through the capillaries in peripheral tissues and organs. Under normal circumstances, blood flow is equal to cardiac output. When cardiac output goes up, so does the blood flow through capillary beds, and when cardiac output declines, capillary blood flow is reduced.

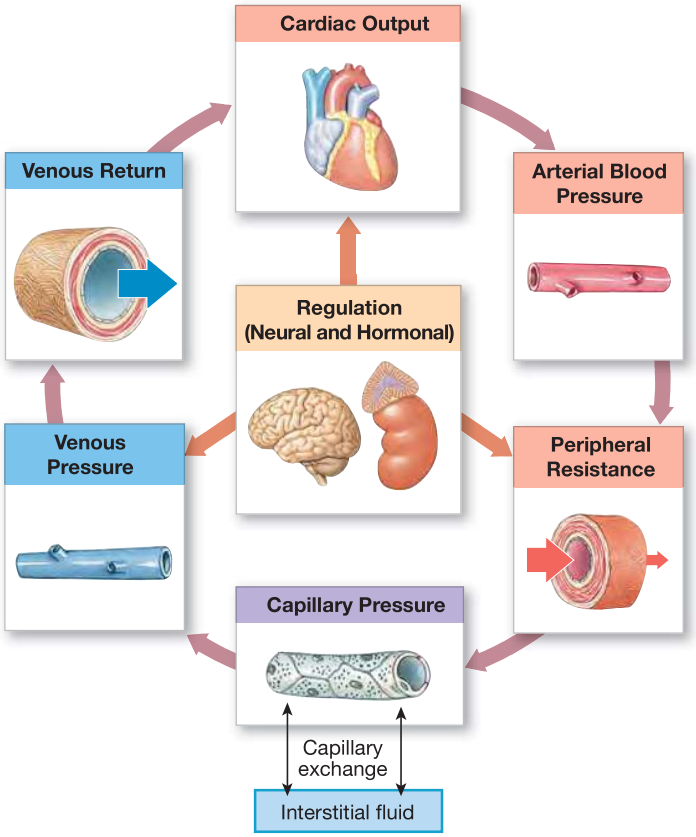
Capillary blood flow is determined by the interplay between *pressure (P)* and *resistance (R)* in the cardiovascular network. To keep blood moving, the heart must generate enough pressure to overcome the resistance to blood flow in the pulmonary and systemic circuits. In general terms, flow (*F*) is directly proportional to the pressure (increased pressure → increased flow), and inversely proportional to resistance (increased resistance → decreased flow). However, the absolute pressure is less important than the pressure *gradient*—the difference in pressure from one end of the vessel to the other. This relationship can be summarized as

$$F \propto \frac{\Delta P}{R}$$

where the symbol ∝ means "is proportional to" and Δ means "the difference in." The largest pressure gradient is found between the base of the aorta and the proximal ends of peripheral capillary beds. Cardiovascular control centers can alter this pressure gradient, and change the rate of capillary blood flow, by adjusting cardiac output and peripheral resistance.

Blood leaving the peripheral capillaries enters the venous system. The pressure gradient across the venous system is relatively small, but venous resistance is very low. The low venous blood pressure—aided by valves, skeletal muscle contraction, gravity, and other factors—is enough to return the blood to the heart. When necessary, cardiovascular control centers can raise venous pressure (through venoconstriction) to improve venous return and maintain adequate cardiac output.

Figure 21–8 An Overview of Cardiovascular Physiology. Neural and hormonal activities influence cardiac output, peripheral resistance, and venous pressure (through venoconstriction). Capillary pressure is the primary drive for exchange between blood and interstitial fluid.



We will begin this section by examining blood pressure and resistance more closely. We will then consider the mechanisms of *capillary exchange*, the transfer of liquid and solutes between the blood and interstitial fluid. Capillary exchange provides tissues with oxygen and nutrients and removes the carbon dioxide and waste products generated by active cells.

Active tissues need more blood flow than inactive ones. Even something as simple as a change in position—going from sitting to standing, for instance—triggers a number of cardiovascular changes. We will end this section with a discussion of what those changes are and how they are coordinated.

Pressure

When talking about cardiovascular pressures, three values are usually reported:

1. *Blood Pressure.* The term **blood pressure (BP)** refers to arterial pressure, usually reported in millimeters of mercury (mm Hg). Average systemic arterial pressures range from an average of 100 mm Hg at the entrance to the aorta to roughly 35 mm Hg at the start of a capillary network.
2. *Capillary Hydrostatic Pressure.* Hydrostatic pressure is the force exerted by a fluid pressing against a wall. **Capillary hydrostatic pressure (CHP),** or *capillary pressure*, is the pressure within capillary walls. Along the length of a typical capillary, pressures decline from roughly 35 mm Hg to about 18 mm Hg.
3. *Venous Pressure.* **Venous pressure** is the pressure within the venous system. Venous pressure is quite low: The pressure gradient from the venules to the right atrium is only about 18 mm Hg.

The difference in pressure (ΔP) across the entire systemic circuit, sometimes called the *circulatory pressure*, averages about 100 mm Hg. For circulation to occur, the circulatory pressure must overcome the **total peripheral resistance**—the resistance of the entire cardiovascular system. The arterial network has by far the largest pressure gradient (65 mm Hg), and this primarily reflects the relatively high resistance of the arterioles.

Total Peripheral Resistance

The total peripheral resistance of the cardiovascular system reflects a combination of factors: *vascular resistance*, *blood viscosity*, and *turbulence*.

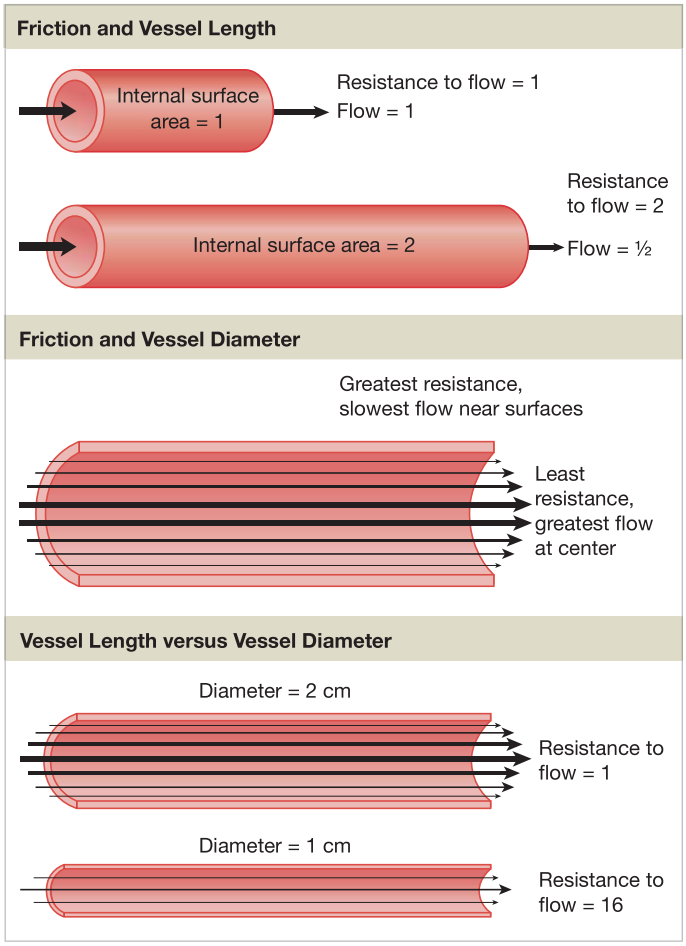
Vascular Resistance

Vascular resistance, the forces that oppose blood flow in the blood vessels, is the largest component. The most important factor in vascular resistance is friction between blood and the vessel walls. The amount of friction depends on two factors: vessel length and vessel diameter. **Figure 21–9** shows the factors affecting friction and vascular resistance.

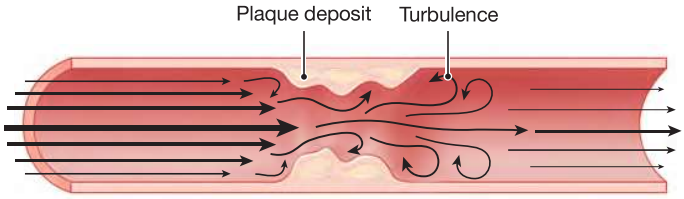
Vessel Length. Increasing the length of a blood vessel increases friction: The longer the vessel, the larger the surface area in contact with blood. You can easily blow the water out of a snorkel that is 2.5 cm (1 in.) in diameter and 25 cm (10 in.) long, but you cannot blow the water out of a 15 m-(16 yard) long garden hose, because the total friction is too great. The most dramatic changes in blood vessel length occur between birth and maturity, as individuals grow to adult size. In adults, vessel length can increase or decrease gradually when individuals gain or lose weight, but on a day-to-day basis this component of vascular resistance can be considered constant.

Vessel Diameter. The effects of friction on blood act in a narrow zone closest to the vessel wall. In a small-diameter vessel, friction with the walls slows nearly all the blood. Resistance is therefore relatively high. Blood near the center of a large-diameter vessel does not encounter friction with the walls, so the resistance in large vessels is fairly low.

Figure 21–9 Factors Affecting Friction and Vascular Resistance.



Factors Affecting Vascular Resistance



Turbulence

Differences in diameter have much more significant effects on resistance than do differences in length. If two vessels are equal in diameter but one is twice as long as the other, the longer vessel offers twice as much resistance to blood flow. But for two vessels of equal length, one twice the diameter of the other, the narrower one offers 16 times as much resistance to blood flow. This relationship, expressed in terms of the vessel radius r and resistance R, can be summarized as $R \propto 1/r^4$.

More significantly, there is no way to control vessel length, but vessel diameter can change quickly through vasoconstriction or vasodilation. Most of the peripheral resistance occurs in arterioles, the smallest vessels of the arterial system. As noted earlier in the chapter, arterioles are extremely muscular: The wall of an arteriole with an inner diameter of 30 μm can have a 20-µm-thick layer of smooth muscle. When these smooth muscles contract or relax, peripheral resistance increases or decreases. Because a small change in diameter produces a large change in resistance, mechanisms that alter the diameters of arterioles provide control over peripheral resistance and blood flow.

Blood Viscosity

Viscosity is the resistance to flow caused by interactions among molecules and suspended materials in a liquid. Liquids of low viscosity, such as water (viscosity 1.0), flow at low pressures. Thick, syrupy fluids, such as molasses (viscosity 300), flow only under higher pressures. Whole blood has a viscosity about five times that of water, due to its plasma proteins and blood cells. Under normal conditions, the viscosity of blood remains stable. Anemia, polycythemia, and other disorders that affect the hematocrit also change blood viscosity, and thus peripheral resistance.

Turbulence

High flow rates, irregular surfaces, and sudden changes in vessel diameter upset the smooth flow of blood, creating eddies and swirls. This phenomenon, called **turbulence,** increases resistance and slows blood flow.

Turbulence normally occurs when blood flows between the atria and the ventricles, and between the ventricles and the aortic and pulmonary trunks. It also develops in large arteries, such as the aorta, when cardiac output and arterial flow rates are very high. However, turbulence seldom occurs in smaller vessels unless their walls are damaged. For example, an atherosclerotic plaque creates abnormal turbulence and restricts blood flow. Because turbulence makes a distinctive sound, or *bruit* (broo-Ē), plaques in large blood vessels can often be detected with a stethoscope.

Table 21–1 provides a quick review of the terms and relationships discussed in this section.

An Overview of Cardiovascular Pressures

Look at the graphs in Figure 21–10 for an overview of the vessel diameters, cross-sectional areas, pressures, and velocity of blood flow in the systemic circuit.

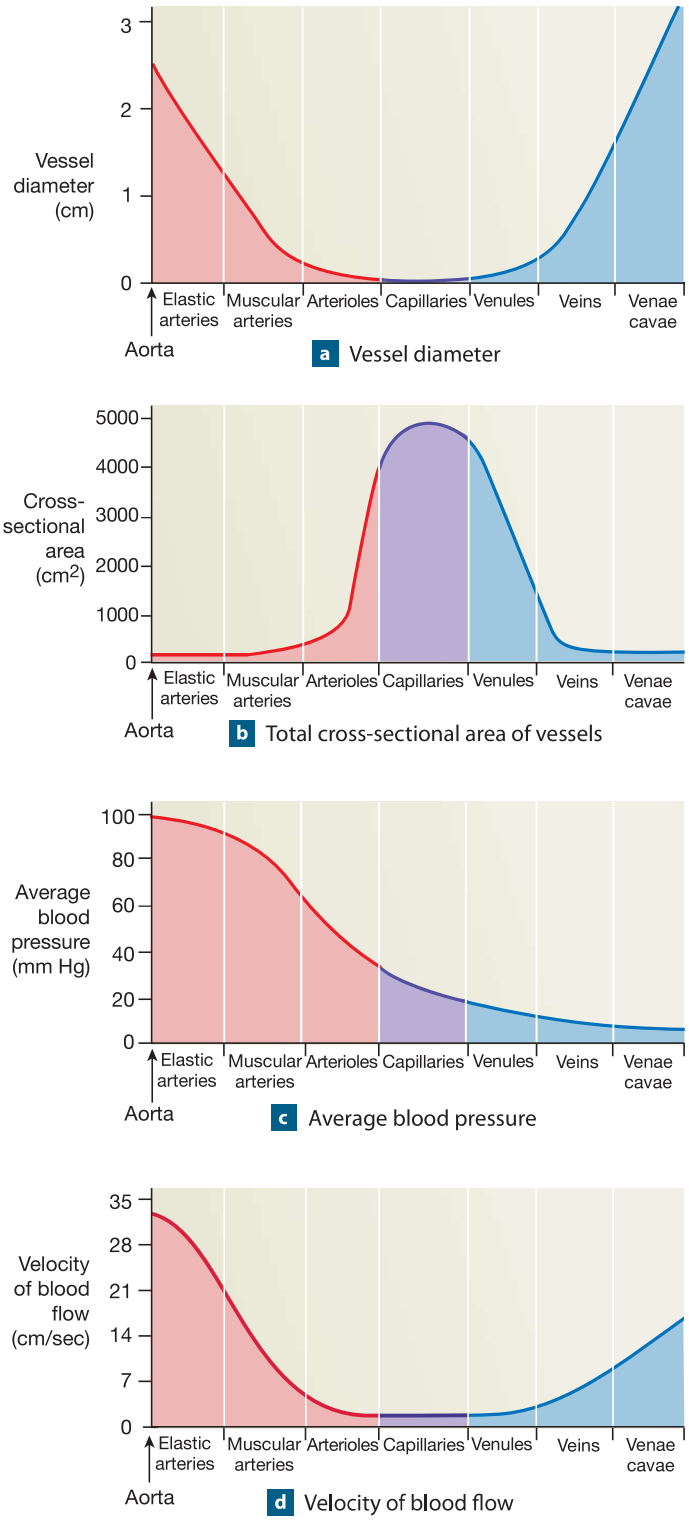
- *Vessel Diameters.* As blood proceeds from the aorta toward the capillaries, vessels diverge. The arteries branch repeatedly, and each branch is smaller in diameter than the preceding one (Figure 21–10a). As blood proceeds from the capillaries toward the venae cavae, vessels converge. Vessel diameters increase as venules combine to form small and medium-sized veins.

Table 21–1 Key Terms and Relationships Pertaining to Blood Circulation

Blood Flow *(F)*:	The volume of blood flowing per unit of time through a vessel or a group of vessels; may refer to circulation through a capillary, a tissue, an organ, or the entire vascular network. Total blood flow is equal to cardiac output.
Blood Pressure *(BP)*:	The hydrostatic pressure in the arterial system that pushes blood through capillary beds.
Circulatory Pressure:	The pressure difference between the base of the ascending aorta and the entrance to the right atrium.
Hydrostatic Pressure:	A pressure exerted by a liquid in response to an applied force.
Peripheral Resistance *(PR)*:	The resistance of the arterial system; affected by such factors as vascular resistance, viscosity, and turbulence.
Resistance *(R)*:	A force that opposes movement (in this case, blood flow).
Total Peripheral Resistance:	The resistance of the entire cardiovascular system.
Turbulence:	A resistance due to the irregular, swirling movement of blood at high flow rates or exposure to irregular surfaces.
Vascular Resistance:	A resistance due to friction within a blood vessel, primarily between the blood and the vessel walls. Increases with increasing length or decreasing diameter; vessel length is constant, but vessel diameter can change.
Venous Pressure:	The hydrostatic pressure in the venous system.
Viscosity:	A resistance to flow due to interactions among molecules within a liquid.
RELATIONSHIPS AMONG THE PRECEDING TERMS	
$F \propto P$	Flow is proportional to the pressure gradient.
$F \propto 1/R$	Flow is inversely proportional to resistance.
$F \propto P/R$	Flow is directly proportional to the pressure gradient, and inversely proportional to resistance.
$F \propto BP/PR$	Flow is directly proportional to blood pressure, and inversely proportional to peripheral resistance.
$R \propto 1/r^4$	Resistance is inversely proportional to the fourth power of the vessel radius.

- *Total Cross-Sectional Areas.* Although the arterioles, capillaries, and venules are small in diameter, the body has large numbers of them. All the blood flowing through the aorta also flows through peripheral capillaries. Blood pressure and the speed of blood flow are proportional to the cross-sectional area of the vessels involved. What is important is not the cross-sectional area of each individual vessel, but the *combined* cross-sectional area of *all* the vessels (**Figure 21–10b**). In effect, your blood moves from one big pipe (the aorta, with a cross-sectional area of 4.5 cm^2) into countless tiny ones (the peripheral capillaries, with a total cross-sectional area of 5000 cm^2), and then blood travels back to the heart through two large pipes (the venae cavae).

Figure 21–10 Relationships among Vessel Diameter, Cross-Sectional Area, Blood Pressure, and Blood Velocity within the Systemic Circuit.



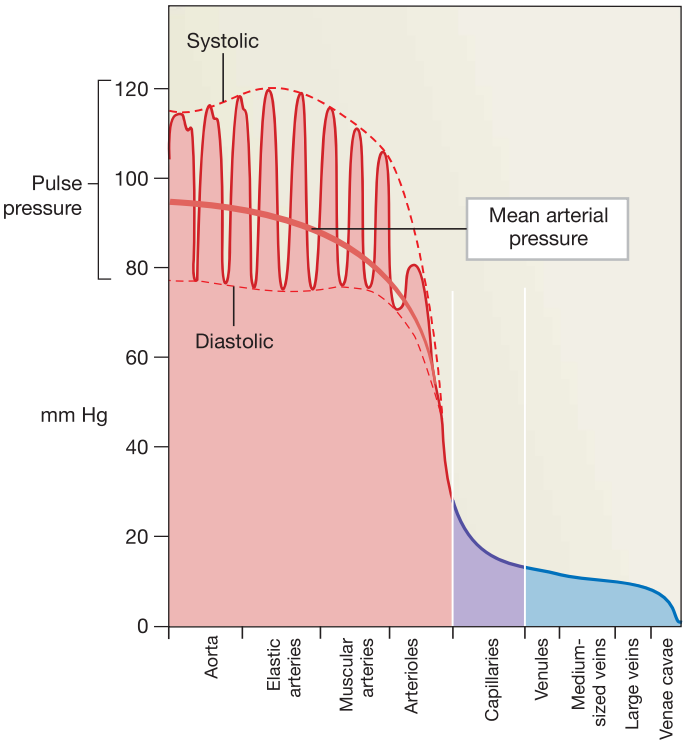
- *Pressures.* As arteries branch, their total cross-sectional area increases, and blood pressure falls rapidly (**Figure 21–10c**). Most of the decline takes place in the small arteries and arterioles. Venous pressures are relatively low.
- *Velocity of Blood Flow.* As the total cross-sectional area of the vessels increases from the aorta toward the capillaries, the velocity of blood flow decreases (**Figure 21–10d**). Blood flow velocity then increases as the total cross-sectional area drops from the capillaries toward the venae cavae.

Figure 21–11 graphs the blood pressure throughout the cardiovascular system. Systemic pressures are highest in the aorta, peaking at about 120 mm Hg. Pressures reach a minimum of 2 mm Hg at the entrance to the right atrium. Pressures in the pulmonary circuit are much lower than those in the systemic circuit. The right ventricle does not ordinarily develop high pressures because the pulmonary vessels are much shorter and more distensible than the systemic vessels, thus providing less resistance to blood flow.

Arterial Blood Pressure

Arterial pressure is important because it maintains blood flow through capillary beds. To do this, it must always be high enough to overcome the peripheral resistance. Arterial pressure is not constant. Rather, it rises during ventricular systole and falls during ventricular diastole. The peak blood pressure measured during ventricular systole is called **systolic pressure,** and the minimum blood pressure at the end of ventricular diastole is called **diastolic pressure.** In recording blood pressure, we separate systolic and diastolic pressures by a slash, as in "120/80" ("one-twenty over eighty") or "110/75."

Figure 21–11 **Pressures within the Systemic Circuit.** Notice the general reduction in circulatory pressure within the systemic circuit and the elimination of the pulse pressure within the arterioles.



A *pulse* is a rhythmic fluctuation in pressure that accompanies each heartbeat. The difference between the systolic and diastolic pressures is the **pulse pressure** (**Figure 21–11**). To report a single blood pressure value, we use the **mean arterial pressure (MAP).** It is calculated by adding one-third of the pulse pressure to the diastolic pressure:

$$\text{MAP} = \text{diastolic pressure} + \frac{\text{pulse pressure}}{3}$$

For a systolic pressure of 120 mm Hg and a diastolic pressure of 90 mm Hg, we calculate MAP as follows:

$$\text{MAP} = 90 + \frac{(120 - 90)}{3} = 90 + 10 = 100 \text{ mm Hg}$$

A normal range of systolic and diastolic pressures occurs in healthy individuals. When pressures shift outside of the normal range, clinical problems develop. Abnormally high blood pressure is termed **hypertension.** Abnormally low blood pressure is **hypotension.** Hypertension is much more common. In fact, many cases of hypotension result from overly aggressive drug treatment for hypertension.

The usual criterion established by the American Heart Association for hypertension in adults is a blood pressure greater than 140/90. Blood pressure at or below 120/80 is normal, and values between 121/81 and 139/89 indicate *pre-hypertension*. Cardiologists often recommend some combination of diet modification and drug therapy for people whose blood pressures are consistently pre-hypertensive.

Hypertension significantly increases the workload on the heart, and the left ventricle gradually enlarges. More muscle mass means a greater demand for oxygen. When the coronary circulation cannot keep pace, signs and symptoms of coronary ischemia appear. ↩ p. 682 Increased arterial pressures also place a physical stress on the walls of blood vessels throughout the body. This stress promotes or accelerates the development of arteriosclerosis. It also increases the risk of aneurysms, heart attacks, and strokes.

Elastic Rebound

As systolic pressure climbs, the arterial walls stretch, just as an extra puff of air expands a partially inflated balloon. This expansion allows the arterial system to accommodate some of the blood provided by ventricular systole. When diastole begins and blood pressures fall, the arteries recoil to their original dimensions. This phenomenon is called **elastic rebound.**

Some blood is forced back toward the left ventricle, closing the aortic valve and helping to drive additional blood into the coronary arteries. However, most of the push from elastic rebound forces blood toward the capillaries. This maintains blood flow along the arterial network while the left ventricle is in diastole.

Pressures in Small Arteries and Arterioles

The mean arterial pressure and the pulse pressure become smaller as the distance from the heart increases (**Figure 21–11**):

- The mean arterial pressure declines as the arterial branches become smaller and more numerous. In essence, blood pressure decreases as it overcomes friction and produces blood flow.
- The pulse pressure lessens due to the cumulative effects of elastic rebound along the arterial system. The effect can be likened to a series of ever-softer echoes following a loud shout. Each time an echo is produced, the reflecting surface absorbs some of the sound energy. Eventually, the echo disappears. The pressure surge accompanying ventricular ejection is like the shout, and it is reflected by the wall of the aorta, echoing down the arterial system until it finally disappears at the level of the small arterioles. By the time blood reaches a precapillary sphincter, no pressure fluctuations remain, and the blood pressure is steady at approximately 35 mm Hg.

Venous Pressure and Venous Return

Venous pressure, although low, determines venous return—the amount of blood arriving at the right atrium each minute. Venous return has a direct impact on cardiac output. ↩ p. 699 Blood pressure at the start of the venous system is only about one-tenth that at the start of the arterial system, but the blood must still travel through a vascular network as complex as the arterial system before returning to the heart.

Pressures at the entrance to the right atrium fluctuate, but they average about 2 mm Hg. Thus, the effective pressure in the venous system is roughly 16 mm Hg (from 18 mm Hg in the venules to 2 mm Hg in the venae cavae). This pressure compares with 65 mm Hg in the arterial system (from 100 mm Hg at the aorta to 35 mm Hg at the capillaries). Yet, although venous pressures are low, veins offer comparatively little resistance, so pressure declines very slowly as blood moves through the venous system. As blood moves toward the heart, the veins become larger, resistance drops, and the velocity of blood flow increases (**Figure 21–10**).

When you stand, the venous blood returning from your body inferior to the heart must overcome gravity as it travels up the inferior vena cava. Two factors assist the low venous pressures in propelling blood toward your heart: *muscular compression* of peripheral veins and the *respiratory pump*.

Muscular Compression. The contractions of skeletal muscles near a vein compress it, helping to push blood toward the heart. The valves in small and medium-sized veins ensure that blood flows in one direction only (**Figure 21–6**). When you are standing and walking, the cycles of contraction and relaxation that accompany your normal movements assist venous return. If you stand at attention, with knees locked and leg muscles immobilized, that assistance is lost. The reduction in venous return then leads to a fall in cardiac output, which reduces the blood supply to the brain. This decline is sometimes enough to cause **fainting,** a temporary loss of consciousness. You would then collapse, but while you were in the horizontal position, both venous return and cardiac output would return to normal.

The Respiratory Pump. As you inhale, your thoracic cavity expands, reducing the pressure within the pleural cavities. This drop in pressure pulls air into your lungs. At the same time, it also pulls blood into the inferior vena cava and right atrium from the smaller veins of your abdominal cavity and lower body. The effect on venous return through the superior vena cava is less pronounced, because blood in that vessel is normally assisted by gravity. As you exhale, your thoracic cavity decreases in size. Internal pressure then rises, forcing air out of your lungs and pushing venous blood into the right atrium. This mechanism is called the **respiratory pump.** Such pumping action becomes more important during heavy exercise, when respirations are deep and frequent.

Capillary Pressures and Capillary Exchange

Capillary exchange plays a key role in homeostasis. The most important processes that move materials across typical capillary walls are *diffusion*, *filtration*, and *reabsorption*.

Diffusion

As we saw in Chapter 3, *diffusion* is the net movement of ions or molecules from an area where their concentration is higher to an area where their concentration is lower. ↩ p. 86 The difference between the high and low concentrations represents a *concentration gradient*. Diffusion tends to eliminate that gradient. Diffusion occurs most rapidly when (1) the distances involved are short, (2) the concentration gradient is large, and (3) the ions or molecules involved are small.

Different substances diffuse across capillary walls by different routes:

1. *Water, ions, and small organic molecules, such as glucose, amino acids, and urea*, can usually enter or leave the bloodstream by diffusion between adjacent endothelial cells or through the pores of fenestrated capillaries.
2. *Many ions, including sodium, potassium, calcium, and chloride,* can diffuse across endothelial cells by passing through channels in plasma membranes.

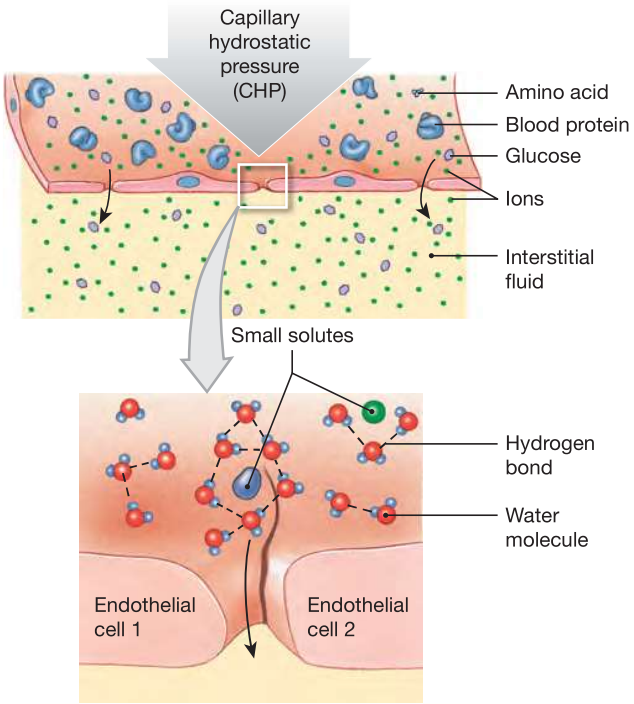
3. *Large water-soluble compounds* are unable to enter or leave the bloodstream except at fenestrated capillaries, such as those of the hypothalamus, the kidneys, many endocrine organs, and the intestinal tract.
4. *Lipids, such as fatty acids and steroids, and lipid-soluble materials, including soluble gases such as oxygen and carbon dioxide,* can cross capillary walls by diffusion through the endothelial plasma membranes.
5. *Plasma proteins* are normally unable to cross the endothelial lining anywhere except in sinusoids, such as those of the liver, where plasma proteins enter the bloodstream.

Filtration

Filtration is the removal of solutes as a solution flows across a porous membrane. Solutes too large to pass through the pores are filtered out of the solution. The driving force for filtration is hydrostatic pressure. As we saw earlier, it pushes water from an area of higher pressure to an area of lower pressure.

In *capillary filtration*, water and small solutes are forced across a capillary wall, leaving larger solutes and suspended proteins in the bloodstream (**Figure 21–12**). The solute molecules that leave the bloodstream are small enough to pass between adjacent endothelial cells or through the pores in a fenestrated capillary. Filtration takes place primarily at the arterial end of a capillary, where capillary hydrostatic pressure (CHP) is highest.

Figure 21–12 Capillary Filtration. Capillary hydrostatic pressure (CHP) forces water and solutes through the gaps between adjacent endothelial cells in continuous capillaries. The sizes of solutes that move across the capillary wall are determined primarily by the dimensions of the gaps.



Reabsorption

Reabsorption occurs as the result of osmosis. *Osmosis* is a special term for the diffusion of water across a selectively permeable membrane that separates two solutions of differing solute concentrations. Water molecules tend to diffuse across a membrane *toward* the solution containing the higher solute concentration (**Figure 3–16**, p. 86).

The **osmotic pressure (OP)** of a solution is an indication of the force of osmotic water movement. In other words, it represents the pressure that must be applied to prevent osmotic movement across a membrane. The higher the solute concentration of a solution, the greater is the solution's osmotic pressure. The presence of suspended proteins that cannot cross capillary walls creates an osmotic pressure called *blood colloid osmotic pressure (BCOP)*. Clinicians often use the term *oncotic pressure* (*onkos*, a swelling) when referring to the colloid osmotic pressure of body fluids. The two terms are equivalent. Osmotic water movement continues until either the solute concentrations are equalized or an opposing hydrostatic pressure prevents the movement.

Now let's look at the interplay between filtration and reabsorption along the length of a typical capillary. In this discussion, remember that hydrostatic pressure forces water *out of* a solution, and osmotic pressure draws water *into* a solution.

The Interplay between Filtration and Reabsorption

The continuous movement of water out of the capillaries, through peripheral tissues, and then back to the bloodstream by way of the lymphatic system has four important functions:

1. It ensures that plasma and interstitial fluid, two major components of extracellular fluid, are in constant communication and mutual exchange.
2. It accelerates the distribution of nutrients, hormones, and dissolved gases throughout tissues.
3. It assists in the transport of insoluble lipids and tissue proteins that cannot enter the bloodstream by crossing the capillary walls.
4. It has a flushing action that carries bacterial toxins and other chemical stimuli to lymphatic tissues and organs responsible for providing immunity to disease.

Capillary blood pressure declines as blood flows from the arterial end to the venous end of a capillary. As a result, the rates of filtration and reabsorption gradually change as blood passes along the length of a capillary. The factors involved are diagrammed in **Figure 21–13**.

Net hydrostatic pressure is the difference between the pressure inside the capillary wall and the hydrostatic pressure outside

the capillary. The *net capillary hydrostatic pressure* tends to push water and solutes out of capillaries and into the interstitial fluid. Factors that contribute to the net hydrostatic pressure include:

1. the *capillary hydrostatic pressure (CHP)*, which ranges from 35 mm Hg at the arterial end of a capillary to 18 mm Hg at the venous end, and
2. the *interstitial fluid hydrostatic pressure (IHP)*. Measurements of IHP have yielded very small values that differ from tissue to tissue—from +6 mm Hg in the brain to −6 mm Hg in subcutaneous tissues. A positive IHP opposes CHP, and the tissue hydrostatic pressure must be overcome before fluid can move out of a capillary. A negative IHP assists CHP, and additional fluid will be pulled out of the capillary. However, under normal circumstances the average IHP is 0 mm Hg, and we can assume that the net hydrostatic pressure is equal to CHP. (For this reason, IHP is not included in **Figure 21–13**.)

Plasma proteins in capillary blood create capillary colloid osmotic pressure. The *net capillary colloid osmotic pressure* tends to pull water and solutes into a capillary from the interstitial fluid. The net colloid osmotic pressure is the difference between

1. the *blood colloid osmotic pressure (BCOP)*, which is roughly 25 mm Hg, and
2. the *interstitial fluid colloid osmotic pressure (ICOP)*. The ICOP is as variable and low as the IHP, because the interstitial fluid in most tissues contains negligible quantities of suspended proteins. Reported values of ICOP are from 0 to 5 mm Hg, within the range of pressures recorded for the IHP. It is thus safe to assume that under normal circumstances the net colloid osmotic pressure is equal to the BCOP. (For this reason, ICOP is not included in **Figure 21–13**.)

The **net filtration pressure (NFP)** is the difference between the net hydrostatic pressure and the net osmotic pressure. In terms of the factors just listed, this means that

$$\begin{array}{ccccc} \text{net filtration} & = & \text{net hydrostatic} & - & \text{net colloid} \\ \text{pressure} & & \text{pressure} & & \text{osmotic pressure} \\ \text{NFP} & = & (\text{CHP} - \text{IHP}) & - & (\text{BCOP} - \text{ICOP}) \end{array}$$

At the arterial end of a capillary, the net filtration pressure can be calculated as follows:

$$\text{NFP} = (35 - 0) - (25 - 0) = 35 - 25 = 10 \text{ mm Hg}$$

Because this value is positive, it indicates that fluid will tend to move *out of* the capillary and into the interstitial fluid. At the venous end of the capillary, the net filtration pressure will be

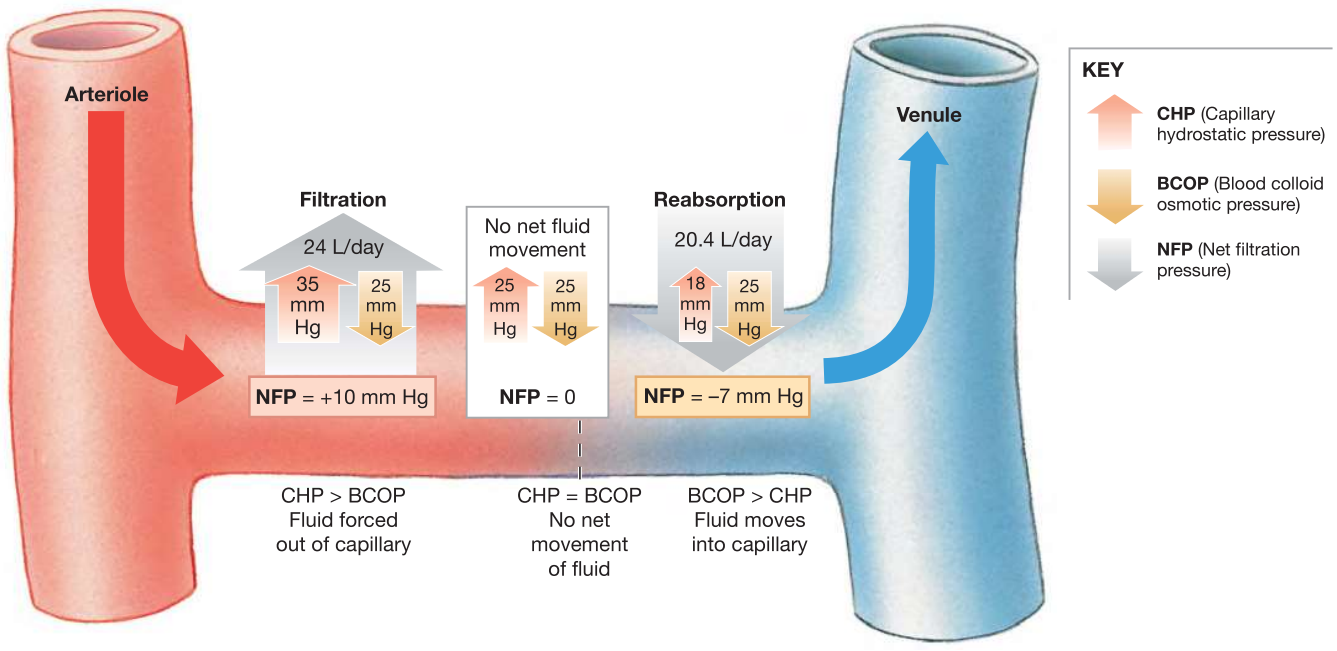
$$\text{NFP} = (18 - 0) - (25 - 0) = 18 - 25 = -7 \text{ mm Hg}$$

The minus sign indicates that fluid tends to move *into* the capillary; that is, reabsorption is occurring.

The transition between filtration and reabsorption occurs where the CHP is 25 mm Hg, because at that point the hydro-

21

Figure 21–13 Forces Acting across Capillary Walls. At the arterial end of the capillary, capillary hydrostatic pressure (CHP) is greater than blood colloid osmotic pressure (BCOP), so fluid moves out of the capillary (filtration). Near the venule, CHP is lower than BCOP, so fluid moves into the capillary (reabsorption). In this model, interstitial fluid colloid osmotic pressure (ICOP) and interstitial fluid hydrostatic pressure (IHP) are assumed to be 0 mm Hg and so are not shown.



Clinical Note Edema

It's not a good time but a swell time

Edema (e-DĒ-muh) is an abnormal accumulation of interstitial fluid. Edema has many causes, and we will encounter specific examples in later chapters. The underlying problem in all types of edema is a disturbance in the normal balance between hydrostatic and osmotic forces at the capillary level. For instance:

- When a capillary is damaged, plasma proteins can cross the capillary wall and enter the interstitial fluid. The resulting rise in the interstitial fluid colloid osmotic pressure (ICOP) reduces the rate of capillary reabsorption and produces a localized edema. This is why you usually have swelling at a bruise.
- In starvation, the liver cannot synthesize enough plasma proteins to maintain normal concentrations in the blood. Blood colloid osmotic pressure (BCOP) declines, and fluids begin moving from the blood into peripheral tissues. In children, fluid builds up in the abdominopelvic cavity, producing the swollen bellies typical of starvation victims. A reduction in BCOP also takes place after severe burns and in several types of liver and kidney diseases.
- In the U.S. population, most serious cases of edema result from increases in arterial blood pressure, venous pressure, or total circulatory pressure. The increase may result from heart problems such as heart failure, venous blood clots that elevate venous pressures, or other cardiovascular abnormalities. The net result is an increase in capillary hydrostatic pressure (CHP) that accelerates fluid movement into the tissues.

static and osmotic forces are equal—that is, the NFP is 0 mm Hg. If the maximum filtration pressure at the arterial end of the capillary were equal to the maximum reabsorption pressure at the venous end, this transition point would lie midway along the length of the capillary. Under these circumstances, filtration would occur along the first half of the capillary, and an identical amount of reabsorption would occur along the second half. However, the maximum filtration pressure is higher than the maximum reabsorption pressure, so the transition point between filtration and reabsorption normally lies closer to the venous end of the capillary than to the arterial end. As a result, more filtration than reabsorption occurs along the capillary. Of the roughly 24 liters of fluid that move out of the plasma and into the interstitial fluid each day, 20.4 liters (85 percent) are reabsorbed. The remainder (3.6 liters) flows through the tissues and into lymphatic vessels, for eventual return to the venous system.

Any condition that affects hydrostatic or osmotic pressures in the blood or tissues will shift the balance between hydrostatic and osmotic forces. We can then predict the effects on the basis of an understanding of capillary dynamics. For example,

- If hemorrhaging occurs, both blood volume and blood pressure decline. This reduction in CHP lowers the NFP and increases the amount of reabsorption. The result is a reduction in the volume of interstitial fluid and an increase in the circulating plasma volume. This process is known as a *recall of fluids*.
- If dehydration occurs, the plasma volume decreases due to water loss, and the concentration of plasma proteins increases. The increase in BCOP accelerates reabsorption and a recall of fluids that delays the onset and severity of clinical signs and symptoms.
- If the CHP rises or the BCOP declines, fluid moves out of the blood and builds up in peripheral tissues, a condition called *edema*.

Checkpoint

5. **Identify the factors that contribute to total peripheral resistance.**
6. **In a healthy individual, where is blood pressure greater: at the aorta or at the inferior vena cava? Explain.**
7. **While standing in the hot sun, Sally begins to feel light-headed and faints. Explain what happened.**
8. **Mike's blood pressure is 125/70. What is his mean arterial pressure?**

See the blue Answers tab at the back of the book.

21-3 Cardiovascular regulatory mechanisms involve autoregulation, neural mechanisms, and endocrine responses

Homeostatic mechanisms regulate cardiovascular activity to ensure that blood flow through tissues, called **tissue perfusion,** meets the demand for oxygen and nutrients. The factors

that affect tissue perfusion are (1) cardiac output, (2) peripheral resistance, and (3) blood pressure. We discussed cardiac output in Chapter 20 (p. 697). We considered peripheral resistance and blood pressure earlier in this chapter.

Most cells are relatively close to capillaries. When a group of cells becomes active, the circulation to that region must increase to bring the necessary oxygen and nutrients, and to carry away the waste products and carbon dioxide they generate. The purpose of cardiovascular regulation is to ensure that these blood flow changes occur (1) at an appropriate time, (2) in the right area, and (3) without drastically changing blood pressure and blood flow to vital organs.

The regulatory mechanisms focus on controlling cardiac output and blood pressure to restore adequate blood flow after blood pressure drops. We can group these mechanisms as follows:

- *Autoregulation.* Local factors change the pattern of blood flow within capillary beds as precapillary sphincters open and close in response to chemical changes in interstitial fluids. This is an example of autoregulation at the tissue level. Autoregulation causes immediate, localized homeostatic adjustments. If autoregulation fails to normalize conditions at the tissue level, neural mechanisms and endocrine factors are activated.
- *Neural Mechanisms.* Neural mechanisms respond to changes in arterial pressure or blood gas levels sensed at specific sites. When those changes occur, the cardiovascular centers of the autonomic nervous system adjust cardiac output and peripheral resistance to maintain blood pressure and ensure adequate blood flow.
- *Endocrine Mechanisms.* The endocrine system releases hormones that enhance short-term adjustments and that direct long-term changes in cardiovascular performance.

Now let's see how each of these regulatory mechanisms responds to inadequate perfusion of skeletal muscles. The regulatory relationships are diagrammed in **Figure 21–14**.

Autoregulation of Blood Flow within Tissues

Under normal resting conditions, cardiac output remains stable, and peripheral resistance within individual tissues is adjusted to control local blood flow.

Factors that promote the dilation of precapillary sphincters are called **vasodilators. Local vasodilators** act at the tissue level to accelerate blood flow through their tissue of origin. Examples of local vasodilators include the following:

- Decreased tissue oxygen levels or increased CO_2 levels.
- Lactic acid or other acids generated by tissue cells.
- Nitric oxide (NO) released from endothelial cells.
- Rising concentrations of potassium ions or hydrogen ions in the interstitial fluid.
- Chemicals released during local inflammation, including histamine and NO. ↩ p. 138
- Elevated local temperature.

These factors work by relaxing the smooth muscle cells of the precapillary sphincters. All of them indicate that tissue conditions are in some way abnormal. An increase in blood flow, which brings oxygen, nutrients, and buffers, may be sufficient to restore homeostasis.

As noted in Chapter 19, aggregating platelets and damaged tissues produce compounds that stimulate precapillary sphincters to constrict. These compounds are **local vasoconstrictors.** Examples include prostaglandins and thromboxanes released by activated platelets and white blood cells, and the endothelins released by damaged endothelial cells.

Local vasodilators and vasoconstrictors control blood flow within a single capillary bed (**Figure 21–5**). In high concentrations, these factors also affect arterioles, increasing or decreasing blood flow to all the capillary beds in a given area.

Neural Mechanisms

The nervous system adjusts cardiac output and peripheral resistance in order to maintain adequate blood flow to vital tissues and organs. Centers responsible for these regulatory activities include the *cardiac centers* and the *vasomotor center* of the medulla oblongata. ↩ p. 458

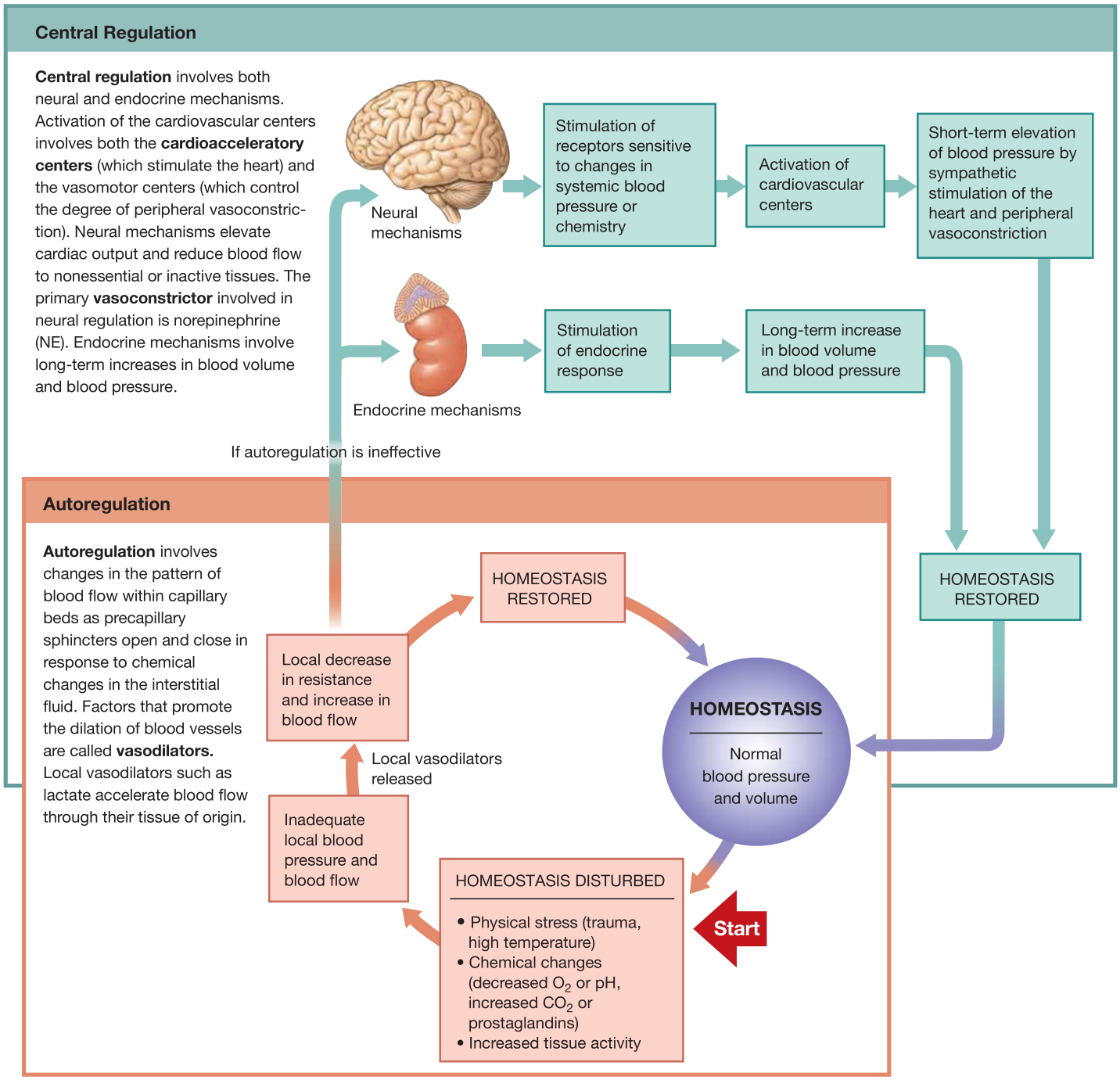
It is difficult to distinguish the cardiac and vasomotor centers anatomically. They are often considered to form complex **cardiovascular (CV) centers.** In functional terms, however, the cardiac and vasomotor centers often act independently.

As noted in Chapter 20, each cardiac center has a *cardioacceleratory center*, which increases cardiac output through sympathetic innervation. Each cardiac center also has a *cardioinhibitory center*, which reduces cardiac output through parasympathetic innervation. ↩ p. 698

The vasomotor center contains two populations of neurons: (1) a very large group responsible for widespread vasoconstriction and (2) a smaller group responsible for the vasodilation of arterioles in skeletal muscles and the brain. The vasomotor center controls the activity of sympathetic motor neurons:

1. *Control of Vasoconstriction.* The neurons innervating peripheral blood vessels in most tissues are *adrenergic*; that is, they release the neurotransmitter norepinephrine (NE). NE stimulates smooth muscles in the walls of arterioles, producing vasoconstriction.
2. *Control of Vasodilation.* Vasodilator neurons innervate blood vessels in skeletal muscles and in the brain. The stimulation of these neurons relaxes smooth muscle cells in the walls of arterioles, producing vasodilation. This relaxation is triggered by the appearance of NO in the surroundings. The vasomotor center may control NO release indirectly or

Figure 21–14 Short-Term and Long-Term Cardiovascular Responses. This diagram indicates general mechanisms that compensate for a reduction in blood pressure and blood flow.



directly. The most common vasodilator synapses are *cholinergic*—their synaptic terminals release ACh. In turn, ACh stimulates endothelial cells in the area to release NO, causing local vasodilation. Other vasodilator synapses are *nitroxidergic*—their synaptic terminals release NO as a neurotransmitter. Nitric oxide has an immediate and direct relaxing effect on the vascular smooth muscle cells in the area.

Vasomotor Tone

In Chapter 16, we saw how autonomic tone sets a background level of neural activity that can increase or decrease on demand. ↩ p. 531 The sympathetic vasoconstrictor nerves are always active, producing a significant **vasomotor tone.** This vasoconstrictor activity normally keeps the arterioles partially

constricted. Under maximal stimulation, arterioles constrict to about half their resting diameter. To dilate fully, an arteriole increases its resting diameter by about 1.5 times.

Constriction has a large effect on resistance, because, as we saw earlier, resistance increases sharply as luminal diameter decreases. The resistance of a maximally constricted arteriole is roughly 80 *times* that of a fully dilated arteriole. Because blood pressure varies directly with peripheral resistance, the vasomotor center can control arterial blood pressure very effectively by making modest adjustments in vessel diameters. Extreme stimulation of the vasomotor centers also produces venoconstriction and mobilizes the venous reserve.

Reflex Control of Cardiovascular Function

The cardiovascular centers detect changes in tissue demand by monitoring arterial blood, especially its blood pressure, pH, and concentrations of dissolved gases. The *baroreceptor reflexes* (*baro-*, pressure) respond to changes in blood pressure, and the *chemoreceptor reflexes* monitor changes in the chemical composition of arterial blood. These reflexes are regulated through a negative feedback loop: The stimulation of a receptor by an abnormal condition leads to a response that counteracts the stimulus and restores normal conditions.

Baroreceptor Reflexes. Baroreceptors are specialized receptors that monitor the degree of stretch in the walls of expandable organs. ↩ p. 501 The baroreceptors involved in cardiovascular regulation are found in the walls of (1) the **carotid sinuses,** expanded chambers near the bases of the *internal carotid arteries* of the neck (**Figure 21–23**); (2) the **aortic sinuses,** pockets in the walls of the ascending aorta adjacent to the heart (**Figure 20–8b**, p. 679); and (3) the wall of the right atrium. These receptors are part of the **baroreceptor reflexes,** which adjust cardiac output and peripheral resistance to maintain normal arterial pressures.

Aortic baroreceptors monitor blood pressure within the ascending aorta. Any changes trigger the **aortic reflex,** which adjusts blood pressure to maintain adequate blood pressure and blood flow through the systemic circuit. Carotid sinus baroreceptors trigger reflexes that maintain adequate blood flow to the brain. The carotid sinus receptors are extremely sensitive because blood flow to the brain must remain constant. **Figure 21–15** presents the basic organization of the baroreceptor reflexes triggered by changes in blood pressure at the carotid and aortic sinuses.

When blood pressure climbs, the increased output from the baroreceptors alters activity in the CV centers and produces two major effects (**Figure 21–15**):

1. *A decrease in cardiac output*, due to parasympathetic stimulation and the inhibition of sympathetic activity.
2. *Widespread peripheral vasodilation*, due to the inhibition of excitatory neurons in the vasomotor center.

The decrease in cardiac output reflects primarily a reduction in heart rate due to the release of acetylcholine at the sinoatrial (SA) node. ↩ p. 698 The widespread vasodilation lowers peripheral resistance, and this effect, combined with a reduction in cardiac output, leads to a decline in blood pressure to normal levels.

When blood pressure falls below normal, baroreceptor output is reduced accordingly (**Figure 21–15**). This change has two major effects working together to raise blood pressure:

1. *An increase in cardiac output*, through the stimulation of sympathetic innervation to the heart. This results from the stimulation of the cardioacceleratory center and is accompanied by an inhibition of the cardioinhibitory center.
2. *Widespread peripheral vasoconstriction*, caused by the stimulation of sympathetic vasoconstrictor neurons by the vasomotor center.

The effects on the heart result from the release of NE by sympathetic neurons innervating the SA node, the atrioventricular (AV) node, and the general myocardium. In a crisis, sympathetic activation occurs, and its effects are enhanced by the release of both NE and epinephrine (E) from the adrenal medullae. The net effect is an immediate increase in heart rate and stroke volume, and a corresponding rise in cardiac output.

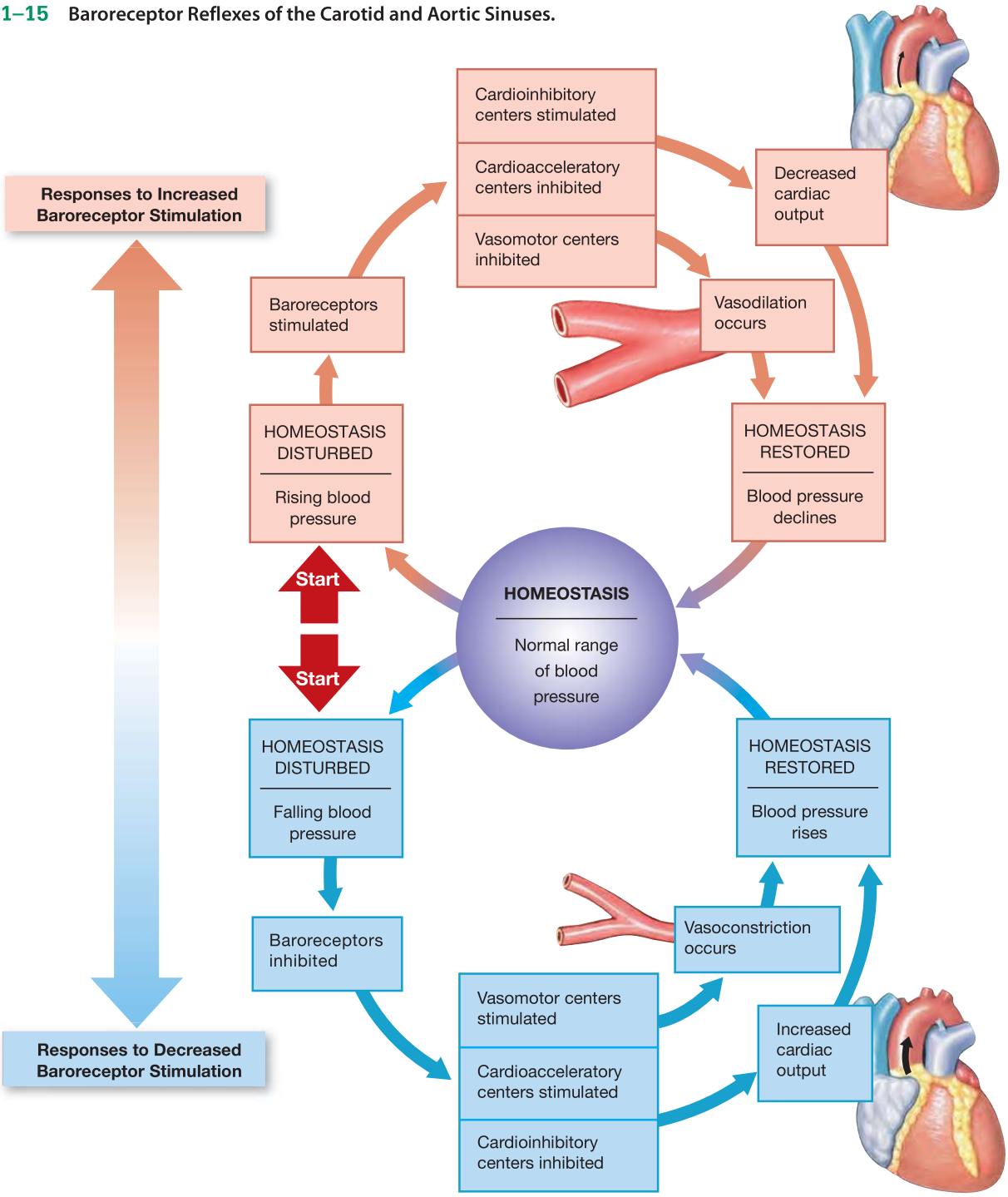
The vasoconstriction, which also results from the release of NE by sympathetic neurons, increases peripheral resistance. These adjustments—increased cardiac output and increased peripheral resistance—work together to elevate blood pressure.

Atrial baroreceptors monitor blood pressure at the end of the systemic circuit—at the venae cavae and the right atrium. Recall from Chapter 20 that the **atrial reflex** responds to a stretching of the wall of the right atrium. ↩ p. 699

Under normal circumstances, the heart pumps blood into the aorta at the same rate at which blood arrives at the right atrium. When blood pressure rises at the right atrium, blood is arriving at the heart faster than it is being pumped out. The atrial baroreceptors correct the situation by stimulating the CV centers to increase cardiac output until the backlog of venous blood is removed. Atrial pressure then returns to normal.

A procedure known as the Valsalva maneuver is a simple way to check for normal cardiovascular responses to changes in arterial pressure and venous return. The *Valsalva maneuver* involves trying to exhale forcefully with closed lips and nostrils so that no air can leave the lungs and pressure in the thoracic cavity rises sharply. This action causes reflexive changes in blood pressure and cardiac output due to increased intrathoracic pressure, which impedes venous return to the right atrium. When internal pressures rise, the venae cavae collapse, and the venous return decreases. The resulting drop in cardiac output and blood pressure stimulates the aortic and carotid baroreceptors, causing a reflexive increase in heart rate and peripheral vasoconstriction. When the glottis opens and pressures return to normal, venous

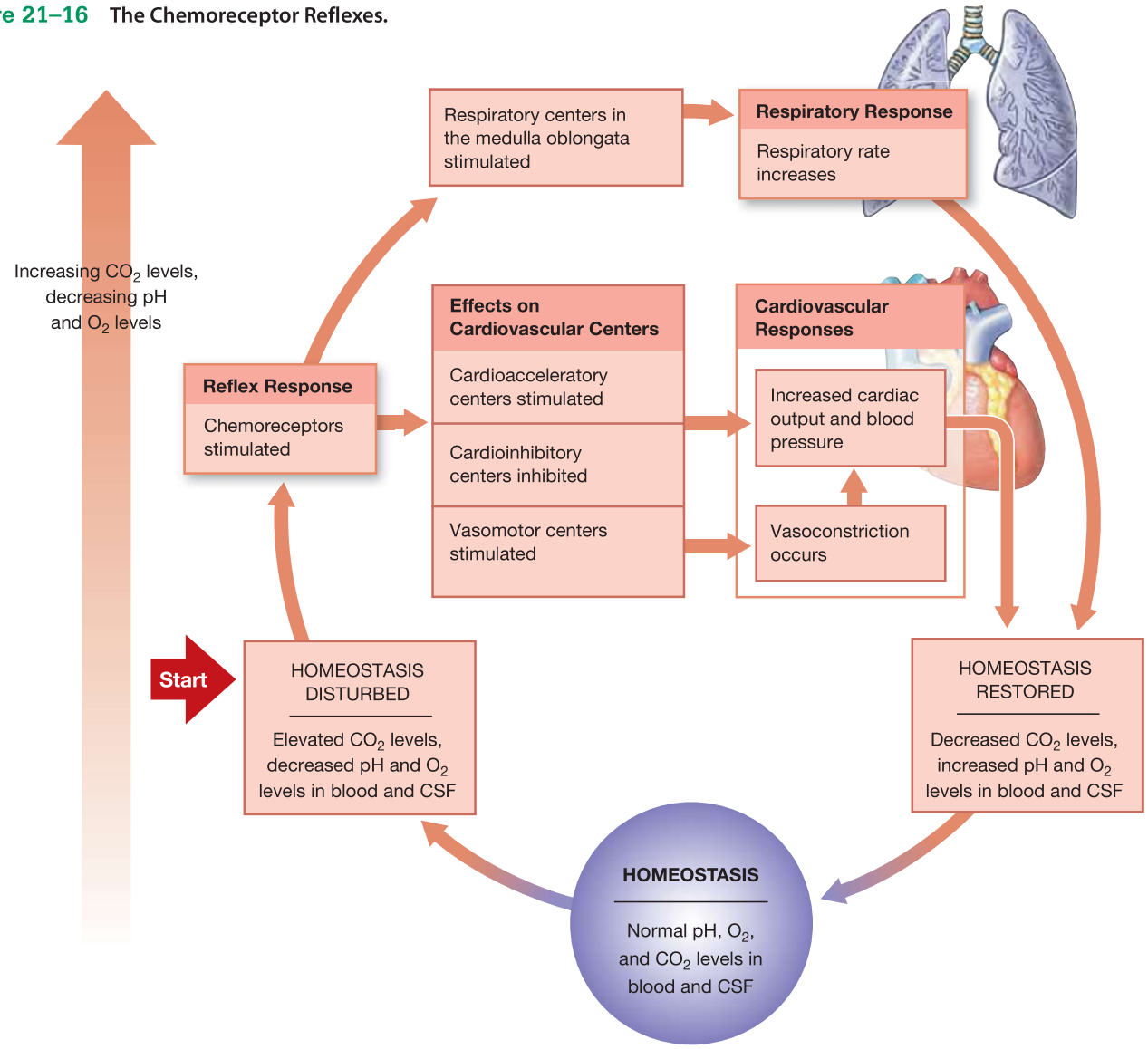
Figure 21–15 Baroreceptor Reflexes of the Carotid and Aortic Sinuses.



return increases suddenly and so does cardiac output. Because vasoconstriction has occurred, blood pressure rises sharply, and this inhibits the baroreceptors. As a result, cardiac output, heart rate, and blood pressure quickly return to normal levels.

Chemoreceptor Reflexes. The **chemoreceptor reflexes** respond to changes in carbon dioxide, oxygen, or pH levels in blood and cerebrospinal fluid (CSF) (**Figure 21–16**). The chemoreceptors involved are sensory neurons. They are located in the **carotid bodies,** situated in the neck near the carotid sinus, and the **aortic bodies,** near the arch of the aorta. ↩ p. 502 These receptors monitor the composition of arterial blood. Additional chemoreceptors located on the ventrolateral surfaces of the medulla oblongata monitor the composition of CSF.

Figure 21–16 The Chemoreceptor Reflexes.



When chemoreceptors in the carotid bodies or aortic bodies detect either a rise in the carbon dioxide content or a fall in the pH of the arterial blood, the cardioacceleratory and vasomotor centers are stimulated. At the same time, the cardioinhibitory center is inhibited. This dual effect causes an increase in cardiac output, peripheral vasoconstriction, and a rise in blood pressure. A drop in the oxygen level at the aortic bodies has the same effects. Strong stimulation of the carotid or aortic chemoreceptors causes widespread sympathetic activation, with more dramatic increases in heart rate and cardiac output.

The chemoreceptors of the medulla oblongata are involved primarily with the control of respiratory function, and secondarily with regulating blood flow to the brain. For example, a steep rise in CSF carbon dioxide levels triggers the vasodilation of cerebral vessels, but produces vasoconstriction in most other organs. The result is increased blood flow—and increased oxygen delivery—to the brain.

Coordination of cardiovascular and respiratory activities is vital, because accelerating blood flow in the tissues is useful only if the circulating blood contains an adequate amount of oxygen. Arterial CO_2 levels can be reduced and O_2 levels increased most effectively by coordinating cardiovascular and respiratory activities. Chemoreceptor stimulation also stimulates the respiratory centers, and the rise in cardiac output and blood pressure is associated with an increased respiratory rate. In addition, a rise in the respiratory rate accelerates venous return through the action of the respiratory pump. (We consider other aspects of chemoreceptor activity and respiratory control in Chapter 23.)