PART IV

CARDIOVASCULAR PHYSIOLOGY

CHAPTER

11

An Overview of the Cardiovascular System and Hemodynamics

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LEARNING OBJECTIVES

Upon mastering the material in this chapter you should be able to:

- Explain how the performances of the right and left heart are interconnected because of their anatomic arrangement in series.
- Explain how the parallel arrangement of arteries in the systemic organ systems allows the blood flow of each organ to be controlled independently.
- Explain the effects of the primary physiological vasodilator and vasoconstrictor agents on vascular resistance and vascular compliance.
- Explain how the magnitude of vascular transmural pressure and vascular smooth muscle contraction affect vascular compliance; describe how aging affects these relationships.
- Explain why changes in total blood volume affect volume in the venous side of the circulation more than on the arterial side of the circulation.
- Explain how gravity, pressure, and venous compliance interact to affect pooling of blood in the lower extremities upon standing.
- Explain why a blood vessel with a large internal diameter has more difficulty contracting than a vessel with a small diameter, even though both are exposed to the same transmural pressure. Apply this principle to the ability of capillaries to withstand high intravascular pressure.
- Explain how vascular wall thickness affects this principle.
- Explain how changes in arterial pressure and vascular resistance theoretically affect blood flow.
- Explain how blood flow and vascular resistance affect arterial pressure.
- Predict how vasodilator and vasoconstrictor agents directly affect blood pressure or organ blood flow.
- Predict how vasodilators, vasoconstrictors, changes in hematocrit, and changes in the number of vessels arranged in parallel affect vascular resistance.
- Determine the pressure profile along any point of a vascular tree composed of multiple series and parallel vascular elements of various given resistances.
- Explain the hemodynamic mechanism that increases workload on the heart following dehydration.
- Explain why flow resistance increases when flow velocity decreases.
- Predict how changes in blood flow velocity will affect endothelial shear stress, intravascular pressure, blood viscosity, and resistance to flow caused by blood.
- Predict what changes in the output of the heart and blood composition will create heart murmurs.

The cardiovascular system is commonly described as a fluid transport system that delivers substances to the tissues of the body while removing the byproducts of metabolism. This bland definition is technically correct but fails to convey how essential the cardiovascular system is for human survival. It also hides the fact that no living organism can exist in a form much larger than a microbe if it does not have a cardiovascular system.

Oxygen and the CO_2 produced by oxidative metabolism enter or exit, respectively, the cells of our body through passive diffusion. Transporting substances using passive diffusion is a benefit to the cell because it does not require any expenditure of energy. However, transporting substances to and from cells by diffusion does come with a drawback. Unfortunately, the distance needed to be traveled significantly affects the time required for any molecule to randomly diffuse from one point to another. For example, it takes approximately 5 seconds for an O_2 molecule to diffuse 100 µm, a distance that is compatible with the size of our cells, their nearest source of O_2, and the rate of O_2 usage by cells during human oxidative metabolism. However, the physics of random molecular motion are such that each 10-fold increase in the distance required to travel by passive random diffusion increases the average time required to traverse that distance by a factor of 100. Therefore, should the diffusion distance in the example just given increase from 100 µm to 1,000 µm (1 mm), the average time a molecule would take to traverse that distance would increase to 500 seconds. A further increase from 1 mm to 1 cm would increase the average time to 50,000 seconds or almost 14 hours!

There are two important consequences of diffusion limitations for cellular transport. First, as living organisms, we could not exist in a body larger than a microbe were it not for the existence of some sort of transport system to at least bring oxygen in close proximity to every cell of the body. In this manner, each cell can get the oxygen it needs by simple diffusion in a time compatible with its O_2 consumption. This is the ultimate function of any circulatory system and why even the tiniest multicellular organisms have one. Without such a system, large multicellular organisms could not exist. When such a system malfunctions, the organism as a whole malfunctions; if the system fails, the organism fails. The physics of passive diffusion place another constraint on our body. If for any reason a cell becomes separated by more than 100 µm from its nearest source of oxygen, as arranged by the existing cardiovascular system, that cell will become ischemic (insufficient O_2). In such a state, the cell will malfunction and likely die. As shall be seen later in this text, such conditions do occur in various human cardiovascular diseases.

In addition to its essential role in maintaining overall health and survival, the cardiovascular system is also exploited for other tasks in the body. For example, the body uses hormones for the control of important physiological functions, and these hormones are transported from the site of their production to their target organs in the bloodstream by the cardiovascular system. In addition, bloodserves as a reservoir for heat. The cardiovascular system plays an important role in the control of heat exchange between the body and external environment by controlling the amount of blood flowing through the skin, which is in contact with the environment surrounding the body as a whole.

A REVIEW OF THE FUNCTIONAL ORGANIZATION OF THE CARDIOVASCULAR SYSTEM

Students in medical physiology should be familiar with the anatomic organization of the heart and blood vessels from their courses in gross anatomy and histology. A brief overview is contained in this section. The cardiovascular system is a fluid transport system for the movement of blood throughout the body. This is represented in simplistic form in Figure 11.1. Blood is driven through the cardiovascular system through the actions of a hollow muscular pump called the **heart**. The heart is a four-chambered muscular organ that contracts and relaxes in a regular repeating cycle to pump blood. The period of time the heart spends in

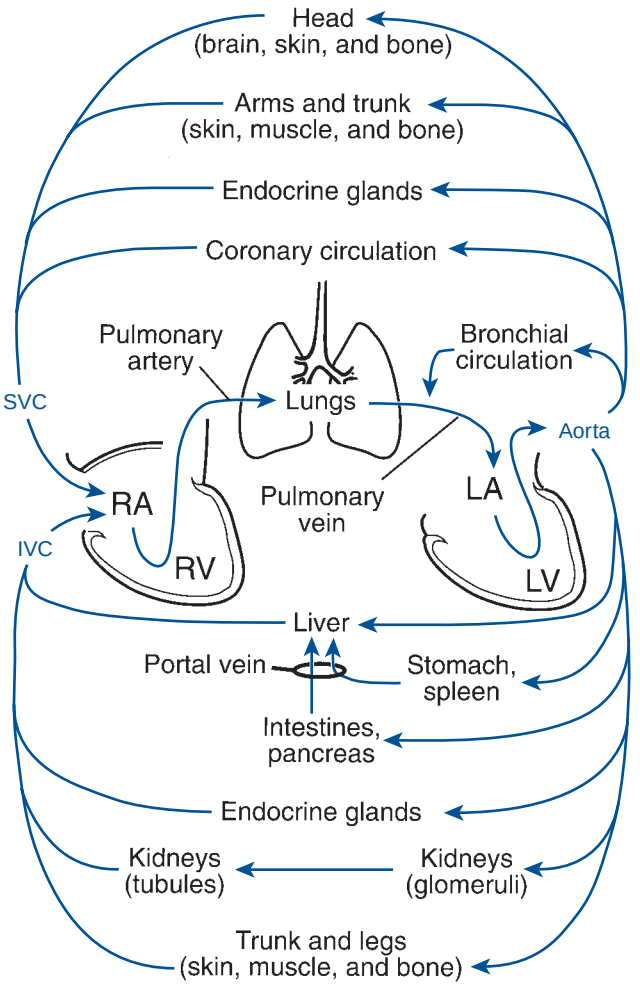

FIGURE 11.1 A model of the cardiovascular system. The right and left sides of the heart are aligned in series, as are the systemic circulation and the pulmonary circulation. In contrast, the circulations of the organs other than the lungs are in parallel. Each organ receives blood from the aorta and returns it to the vena cava. Exceptions are the series arrangements between the splanchnic veins and portal circulation of the liver as well as the glomerular and tubular capillary networks of the kidney. SVC, superior vena cava; IVC, inferior vena cava; RA, right atrium; RV, right ventricle; LA, left atrium; LV, left ventricle.

contraction is called **systole**, and the time it spends in relaxation is called **diastole**.

The heart is really two pumps connected in series. The left heart is composed of the **left atrium** and **left ventricle**, separated by the **mitral valve**. Contraction of the left ventricle is responsible for pumping blood to all systemic organs except the lungs. Blood exits the ventricle through the **aortic valve** into a single tubular conduit called the **aorta**. The aorta is classified as an **artery**, which by definition is any blood vessel that carries blood away from the heart and to the tissues of the body. The aorta branches into successively smaller arteries, many of which are given anatomic names. These arteries in turn branch into millions of smaller vessels of ~10 to 1,000 μm in external diameter, called **arterioles**. Arterioles in turn terminate into billions of **capillaries**, which are the main site of transport of water, gases, electrolytes, substrates, and waste products between the bloodstream and the extracellular fluid. Blood from the capillaries of all the systemic organs coalesces into thin-walled **venules**, which merge into **veins**. By definition, a vein is any blood vessel that returns blood from the tissues back into the heart. Small veins eventually merge to form two large single veins called the **superior vena cava** (SVC) and the **inferior vena cava** (IVC). The SVC collects blood from the head and upper extremities above the level of the heart, whereas the IVC collects blood from all regions below the level of the heart. Both of these large veins empty into the **right atrium**. The right atrium is the upper chamber of the right heart. It is separated from the **right ventricle** by the **tricuspid valve.** The right ventricle pumps blood through the **pulmonic valve** into the **pulmonary artery** and thence into the lungs. Blood exiting the lungs is returned to the **left atrium** where it passes through the **mitral valve** and into the left ventricle, completing the circulatory loop.

The Output of the Right and Left Heart Are Interdependent Because Their Chambers Are Connected in Series

Imagine a bucket of water interposed between two pumps. One pump removes water from the bucket and pumps it into the inflow of the second pump. The second pump takes this inflow and returns it into the bucket for the first pump to remove again. It is obvious that if the outputs of the two pumps are not matched identically the level of water in the bucket will change; the bucket could be drained dry or overflow. This is analogous to the situation in the pulmonary circulation that is interposed between the right and left heart. The right and left heart are said to be arranged *in series,* or in line, one after the other, right to left.

There are multiple consequences of this series arrangement of the two pumps in the heart. First, should the output of the left heart exceed that of the right by as little as 2%, the pulmonary circulation would be drained of blood in less than ten minutes! Conversely, if right heart output exceeded the left by a similar amount, the pulmonary circulation would overflow and a person would drown in his or her own body fluids. Clearly, neither of these situations arises in a healthy person. The implication of this arrangement is that some mechanism must function to closely match the outputs of the right and left heart. Such a mechanism exists at the level of the muscle cell itself and is based on the same principles of skeletal muscle cell mechanics you have read about in earlier chapters. Details of these principles as they apply to the heart will be discussed in Chapter 13.

The series arrangement of the right and left heart also implies that malfunctions in the left heart will be transmitted back into the pulmonary circulation and the right heart, potentially causing the respiratory system to malfunction. Indeed, one of the first clinical signs of left heart failure is respiratory distress. Conversely, problems originating on the right side of the circulation affect the output of the left heart and imperil the blood supply to all systemic organs. Large blood clots can form in the major veins of the leg and abdomen following surgery. These clots can break away and slip through the tricuspid valve into the right ventricle and thence into the pulmonary artery, where they eventually lodge, to form what is called a **pulmonary embolus**. Pulmonary emboli compromising about 75% of the pulmonary circulation can block enough flow into the left heart to kill a person.

Blood Flow to Individual Organs Can Be Controlled Primarily Independently Because Circulations to Individual Organs Are Arranged in Parallel

The arterial system delivers blood to organ systems that are arranged in a *parallel,* or side-by-side, network. Therefore, in most cases, blood flow into one organ system is not dependent on blood flow through another organ upstream. The metabolic demands of our muscles, digestive system, brain, etc., may be different relative to one another and relative to their own resting values depending on the activity in the organ at a given time. The parallel arterial distribution system of organ blood supply allows adjustment of blood flow to an individual organ to meet its own needs without creating major disturbances in the blood supply to other organs. A notable exception to this arrangement, however, is seen in the portal circulation. Venous outflow from the intestines and other splanchnic organs drains into the liver through the **portal vein** before being emptied into the IVC. The liver obtains blood from the portal vein as well as its own arterial supply (see Fig. 11.1) and can be considered to be arranged in series with much of the splanchnic circulation.

The Lumen Diameter of All Arteries and Veins Can Be Actively Changed by Contraction or Relaxation of the Circular Layers of Smooth Muscle Contained Within Their Walls

All blood vessels, except capillaries, have a similar basic structure. All arteries and veins are lined with a single layer of epithelial cells called the **endothelium**. The media of vessels contain circular layers of smooth muscle cells, whereas the outermost layer, called the **adventitia**, is composed of collagen and elastin fibers that add flexible structural integrity to arteries and veins. Because the smooth muscle within blood vessels is arranged in circular layers, contraction or relaxation of these muscles will either, respectively, reduce

or widen the lumen diameter of arteries and veins. The changing of the diameter of blood vessels has a profound effect on the physical factors that determine blood flow and distribution in the cardiovascular system. These effects will be discussed later in this chapter.

There are literally scores of normal physiological, pathological, and clinical pharmacological agents that can alter the contraction and relaxation of arterial and venous smooth muscle. These take the form of direct physical forces and chemical agents, hormones, paracrine substances, and receptor-mediated hormonal and neurotransmitter agonists. For example, the contraction of arteries and veins is modified by transmitters released from sympathetic nerve endings that enter these vessels through their adventitial layer and act on specific receptors on the smooth muscle membrane. The endothelium, which stands at the interface between blood plasma and the rest of the vessel wall, is the source of important paracrine agents that have major, receptor-independent, direct effects on blood vessel contraction. A simplified, partial list of factors that contract or relax vascular smooth muscle is provided in Table 11.1.

TABLE 11.1 A Simplified List of Direct (Non–Receptor-Mediated) and Smooth Muscle Membrane Receptor-Mediated Factors That Contract or Relax Vascular Smooth Muscle

Vasoconstrictor/Vasodilator	Mechanism of Action
Vasoconstrictors: Non–receptor-mediated	
Ca^{++}	Enters cells through membrane channels or is released from the SR by IP_3; binds to calmodulin, which activates myosin light chain kinase to initiate crossbridge attachment and cycling
Ba^{++}	Substitutes for calcium in the contraction cascade
K^+	Membrane depolarization resulting in activation of L-type Ca^{++} channels
O_2 (normoxia)	Maintenance of contraction
Membrane depolarization	Activation of L-type Ca^{++} channels
Decreased transmembrane sodium gradient	Decreased activation of plasma membrane Na^+/Ca^{++} exchange and increased intracellular Ca^{++}
Increased transmural pressure	Activation of stretch-activated plasma membrane calcium channels
Action potentials	Membrane depolarization resulting in activation of L-type calcium channels
Vasoconstrictors: Receptor-mediated	
Norepinephrine	Activation of α adrenoreceptors to open receptor-operated plasma membrane calcium channels, activation of phospholipase C, formation of IP_3 and DAG, and release of calcium from the SR
Epinephrine	Same as norepinephrine
Acetylcholine	Activation of muscarinic M_2 receptors to open receptor-operated plasma membrane calcium channels, activation of phospholipase C, formation of IP_3 and DAG, and release of calcium from the SR; inhibits cAMP formation
Serotonin	Activation of 5-HT_2 receptors to open receptor-operated plasma membrane calcium channels
Vasopressin	Activation of V receptors to open receptor-operated plasma membrane calcium channels
Endothelin	Activation of ET_A receptors with stimulation of phospholipase C, formation of IP_3, and release of calcium from the SR
ATP	Activation of P_{2x} receptor to open receptor-operated plasma membrane channels
Vasodilators: Direct	
Nitric oxide (NO)	Activation of guanylate cyclase, formation of cGMP, and calcium removal
Hyperpolarization	Inhibition of voltage-gated Ca^{++} channels
Decreased transmural pressure	Inhibition of stretch-operated Ca^{++} channels
Hypoxia	Likely a result of decreased ATP supply and formation of adenosine
Hypercapnia	Likely from acidosis
Acidosis	Unknown
Hyperosmolarity	Unknown
cAMP	Activation of cAMP-dependent kinase resulting in a phosphorylation cascade that reduces intracellular calcium concentration
cGMP	Activation of cGMP-dependent kinase resulting in a phosphorylation cascade that reduces intracellular calcium concentration
Hyperkalemia (low levels)	Membrane hyperpolarization resulting from activation of the Na^+/K^+ pump
Vasodilators: Receptor-mediated	
Epinephrine	β_2 receptor-mediated activation of adenyl cyclase resulting in the formation of cAMP
Adenosine	A_1, A_{2A}, and A_{2B} receptor activation of ATP-dependent K^+ channels leading to membrane hyperpolarization and closure of voltage-gated calcium channels
Histamine	H_2 receptor activation of adenyl cyclase with formation of cAMP
PGI_2	Activation of adenyl cyclase with formation of cAMP

5-HT, 5-hydroxytryptamine; ATP, adenosine triphosphate; cAMP, cyclic adenosine monophosphate; cGMP, cyclic guanosine monophosphate; DAG, diacylglycerol; IP_3, inositol 1,4,5-triphosphate; PGI_2, prostacyclin; SR, sarcoplasmic reticulum.

PHYSICAL FACTORS INVOLVED WITH THE CONTAINMENT AND MOVEMENT OF BLOOD THROUGH THE CARDIOVASCULAR SYSTEM

The study of the physical variables related to the containment and movement of blood in the cardiovascular system is called **hemodynamics**. From an engineering standpoint, an accurate description of all the hemodynamic phenomena in the cardiovascular system is complex. Fortunately, the human body deals with these phenomena and their control in a considerably simplified manner. The cardiovascular system behaves much as if the heart were producing an average steady flow through a series of solid pipes, similar to the flow of water through a city's water distribution system. Thus, basic principles of fluid dynamics can be applied to the understanding of cardiovascular phenomena.

Fluid cannot move through a system unless some energy is applied to it. In fluid dynamics, this energy is in the form of a difference in **pressure**, or pressure gradient, between two points in the system. Pressure is expressed as units of force, or weight, per unit area. A familiar example of this is in the pounds per square inch (psi) recommendation stamped on the side of tires. The psi indicates the pressure to which a tire should be inflated with air above atmospheric pressure. Inflating a tire to 32 psi signifies that 32 more pounds press against every square inch of the inner tire surface than against the outside of the tire.

The pressure exerted at any level within a column of fluid reflects the collective weight of all the fluid above that level as it is pulled down by the acceleration of gravity. It is defined as

$$P = \rho g h \qquad (1)$$

where P = pressure, ρ = the density of the fluid, g = the acceleration of gravity, and h = the height of the column of fluid above the layer where pressure is being measured. The force represented by pressure in a fluid system is often described as the force that is able to push a column of fluid in a tube straight up against gravity. In this way the magnitude of the force resulting from fluid pressure can be measured by how high the column of fluid rises in the tube (Fig. 11.2A). In physiological systems, this manner of expressing pressure is designated as centimeters H_2O, or the more convenient mm Hg, because mercury is much denser than water and therefore will not be pushed upward as far by typical pressures seen within the cardiovascular system.

Without going into mechanistic details at this time, arterial pressure peaks shortly after the heart contracts and pumps blood into the aorta and falls to a lower value when the heart relaxes between beats and is therefore not pumping blood into the aorta. The peak pressure during contraction of the heart is called the **systolic pressure** and is typically about 120 mm Hg in humans, whereas the minimum arterial pressure value during relaxation of the heart is called the **diastolic pressure** and is about 80 mm Hg. Thus, if one end of a tube were to be inserted into the aorta with the other end connected to a column of mercury sitting perpendicular to the ground at the level of the heart, that column of mercury would rise 120 mm during systole and fall to 80 mm during diastole. In clinical practice, human arterial pressure is

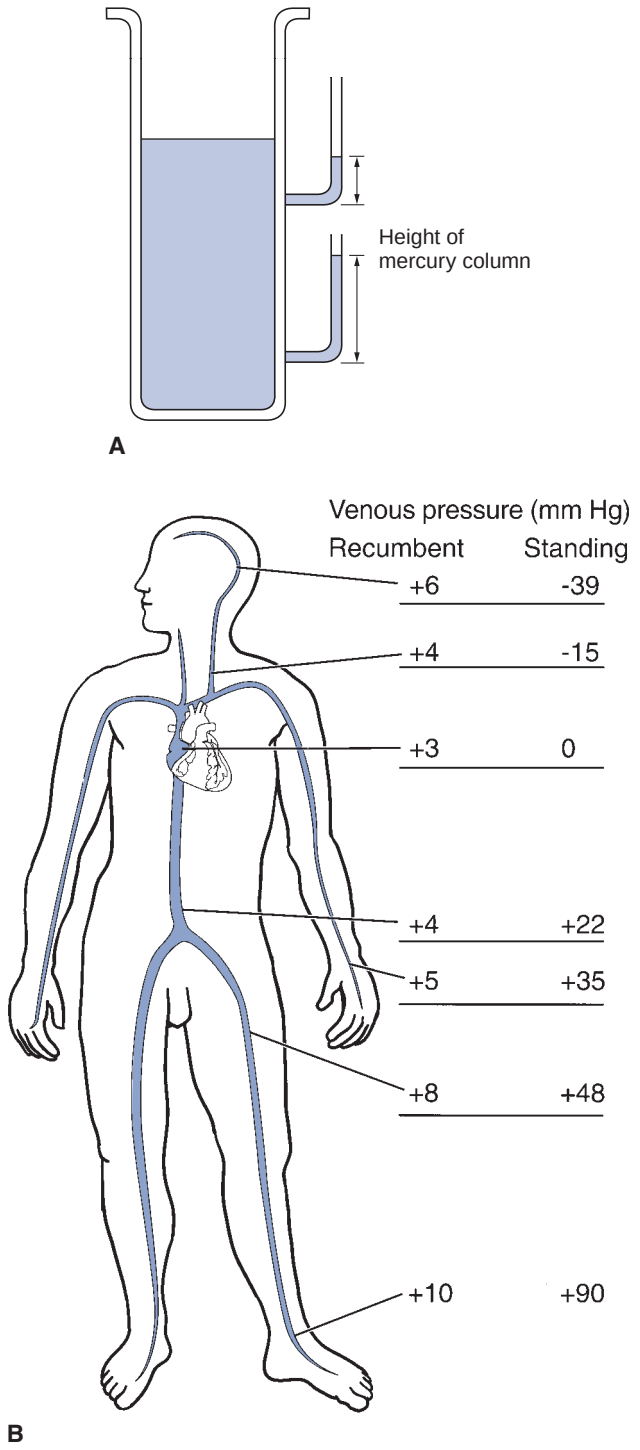

FIGURE 11.2 The effect of the height on pressure at different levels within a column of fluid. A, Fluid pressure is proportional to the height of the column of fluid above the point of measurement. It is often convenient to express pressure as the force capable of raising a column of mercury vertically against gravity; higher pressure raises the column of mercury higher. Pressure in the cardiovascular system is commonly reported in units of mm Hg. **B,** The effect of gravity on pressure within veins. Blood is pulled down by the effect of gravity, subtracting pressure from veins in the head and adding pressure to veins in the lower extremities.

reported as systolic over diastolic pressure or, in this example, 120/80. (Our mean arterial pressure is not the arithmetic mean of systolic and diastolic pressure but is instead about 93 mm Hg, because the time the heart spends relaxing is longer than the time it spends contracting and ejecting blood into the aorta.)

The pressure outside the body or on the outside of any hollow structure within the body other than the intrapleural space is about the same as atmospheric pressure. Technically, atmospheric pressure at sea level is equivalent to 760 mm Hg. In reality, therefore, our average blood pressure is 93 + 760 mm Hg, or 863 mm Hg. However, pressures within our body are never expressed in this technically exact manner. Instead, the effect of atmospheric pressure is simply ignored and taken as a *zero reference point.* The pressure reported in our systems then is really the difference of pressure within that system relative to atmospheric pressure.

The effect of gravity on pressure within the veins is significant when we are standing, as shown in Figure 11.2B. In a recumbent position, pressure in the veins is between 2 and 10 mm Hg. However, when one stands, the influence of gravity subtracts approximately 40 mm Hg of pressure from the arteries and veins in the head and adds about 90 mm Hg of pressure to those in the feet. If human veins were rigid tubes, this would not have a profound effect on the circulation and distribution of blood within sections of the cardiovascular system. However, veins are flexible structures. Therefore, when one stands, blood tends to pool in the veins of the lower extremities. This is responsible for the swelling and aching of the feet after standing for long periods of time and can even result in such extensive pooling that fainting will occur from an inability of enough blood to return to the heart to be pumped to the brain.

The Volume Contained Within an Artery or Vein Is a Function of the Flexibility of the Vessel Wall and the Difference in Pressure Between the Inside and the Outside of the Vessel

The volume of fluid within a container made of inflexible walls, such as a glass bottle, is the same no matter what the pressure difference is between the inside and the outside of the bottle. In such a container the walls cannot move, or flex, when any difference in pressure is applied across them. Arteries and veins are more like rubber balloons in that their walls are flexible. Consequently, the volume contained within them is a function of both the pressure difference across their wall, called the **transmural pressure**, and the degree of flexibility within the vascular wall. Transmural pressure, or P_T, is always defined as the difference in pressure *inside versus outside* a hollow structure. Large transmural pressures within flexible vessels create large intravascular volumes; small transmural pressures in stiff-walled vessels produce small intravascular volumes.

There are a couple of ways of depicting pressure/volume interrelationships in blood vessels. The volume of blood contained in the vessel for a given transmural pressure is called the **vascular capacitance** and is calculated as

$$\text{Capacitance} = \text{Volume}/P_T \text{ mm Hg} \quad (2)$$

where volume and pressure are generally given the units of mL and mm Hg, respectively. However, physiologists are interested in how volume changes in a distensible blood vessel for a given change in pressure. The change in volume for a given change in transmural pressure is called the **compliance** and is given by the equation,

$$C = \Delta V/\Delta P \quad (3)$$

where the Δ signifies the before/after change of volume or pressure. (Note that for this equation the pressure outside the vessel is taken to be atmospheric pressure, which is always given the baseline value of zero in physiological systems.) This equation can be rearranged to yield two useful relationships relating changes in either volume or pressure as a function of the other in a blood vessel. For example, one can write $\Delta V = C \Delta P_T$. This equation indicates that the change in volume contained within a vascular segment will be great in a vessel with high compliance and a large change in intravascular pressure. One can also write $\Delta P_T = \Delta V / C$, which indicates that adding volume into a vascular segment will produce a large increase in pressure within the vessel if the volume added is large and the vascular compliance is low.

Both capacitance and compliance can be used as measures of the distensibility, or flexibility, of a blood vessel; highly distensible vessels have a higher capacitance and compliance than vessels of the same dimensions with stiff walls. For this reason, veins have a higher capacitance and compliance than arteries of similar size. However, use of these variables to measure vessel flexibility fails when vessels of significantly different sizes are compared. For example, a large stiff-walled vessel may have a higher capacitance value than a tiny flexible vessel. For this reason, one should use the *percentage* increase in volume for a given increase in pressure as a means of comparing distensibility between vessels and segments of the vasculature of different sizes. This value is sometimes called vascular distensibility. As explained in later chapters, vascular capacitance, compliance, and distensibility are critical determinants of the performance of the heart, the stress and workload placed on the heart, and the amount of oxygen the heart must receive to function properly. All of these factors are important parameters in understanding the consequences of heart diseases and their treatments.

Even within a given artery or vein, capacitance, distensibility, and compliance are not constants in the cardiovascular system. For example, as transmural pressure increases, compliance decreases (Fig. 11.3). In addition, as shown in Figure 11.3, arterial compliance decreases with age at any given transmural pressure. Finally, contraction of the smooth muscle within either arteries or veins makes the vessel less distensible and compliant while reducing its capacitance (effect not shown in Fig. 11.3). This active control over pressure/volume interrelationships in the vascular tree is an important component of the moment-to-moment control of cardiac performance in a person.

Blood Vessels Must Overcome Wall Stress to Be Able to Contract

Any transmural pressure within an artery or a vein exerts a force on the vessel wall that would tend to rip the wall apart

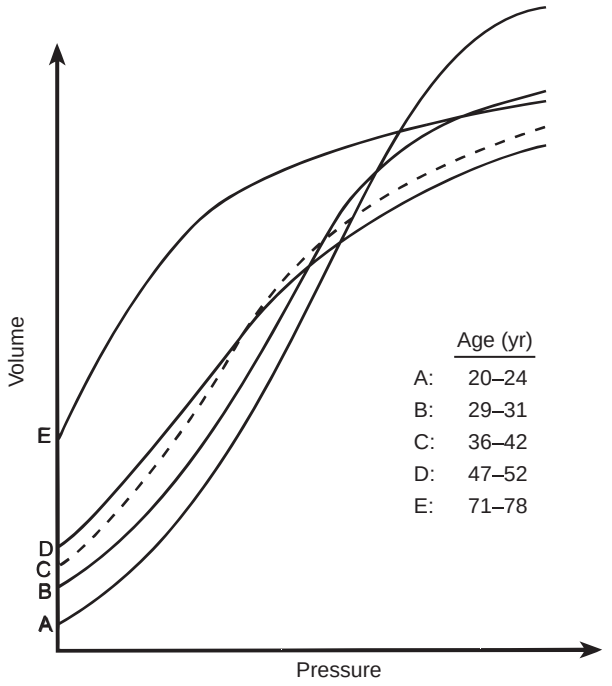

FIGURE 11.3 The relationship between volume and transmural pressure in arteries. Volume within an artery increases with an increase in transmural pressure because the arterial wall is flexible. In normal healthy people, the artery is stiffest when it is first filled and when it is near the limit of its volume capacity (i.e., at low and high transmural pressure, respectively). The slope of this arterial volume:pressure relationship at any point is a measure of arterial compliance. Arterial compliance tends to diminish when pressure increases in the high transmural pressure range. Arterial compliance decreases with aging as can be seen by comparing volume:pressure curves at different ages. (Modified from Hallock P, Benson JC. Studies on the elastic properties of human isolated aorta. J Clin Invest 1937;16:595–602.)

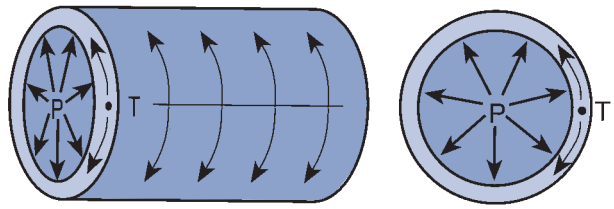

FIGURE 11.4 Pressure and tension in a cylindrical blood vessel. The tension is the force that would pull the vessel apart along an imaginary line along the length of the vessel. Tension in the vessel wall is related by the law of LaPlace, as described by the text. P, pressure; T, tension.

were it not for opposing forces supplied by the muscle and connective tissue of the vessel wall, as shown in Figure 11.4. This force is called **tension** and is equal to the product of the transmural pressure and the vessel radius. This relationship is called the **Law of LaPlace**. However, this relationship applies directly only to cylinders with thin walls. Blood vessel walls are sufficiently thick so that, in reality, this force is equal to a **wall stress** (the product of pressure (P) and the radius (r) divided by the wall thickness (w), or $S = P \times r / w$). There are many consequences of this relationship in distensible tubes. First, because tension and stress are related to vessel radius, small vessels are able to withstand higher pressures than vessels of larger diameters. For this reason capillaries (inner diameter ~10 μm) can withstand relatively high intravascular pressure even though they are only composed of a single cell layer of endothelial cells. In arteries and veins, vessels with thick walls relative to their radius are able to withstand higher pressure than vessels with small r/w ratios because wall stress is lower in the former. Finally, tension and stress, not simply pressure, are the true forces that must be overcome to contract any hollow organ such as a blood vessel or the heart. As will be discussed later, tension and stress are important determinants of energy requirements for contraction of hollow organs.

THE PHYSICAL DETERMINANTS OF THE MOVEMENT OF BLOOD IN THE CIRCULATION

An understanding of the physical factors and laws that govern the movement of blood in the cardiovascular system is critically important to the overall understanding of its function. The amount of blood that flows through any segment of the cardiovascular system is a function of blood pressure, vascular geometry, and the dynamic fluid characteristics of blood. In any tube of given diameter, the amount of flow through the tube is proportional to the *difference* in pressure between one end of the tube and the other (Fig. 11.5); doubling the pressure difference doubles the flow, whereas halving the difference halves the flow. Flow through a cylindrical tube is related to the length of the tube in an inverse proportion. For example, keeping all other determinants of flow unchanged, doubling only the length of a cylindrical tube reduces flow through the tube by half. However, as shown in Figure 11.5, flow through a tube is profoundly affected by the tube radius in that flow varies with the 4th power of the tube radius, or flow ∞radius^4). Consequently, doubling the tube radius results in a 16-fold increase in flow! Finally, flow through a tube is affected by the viscosity, or the "thickness and stickiness," of the fluid. Thick, sticky fluids will not flow as easily as thinner, watery-like fluid. The units of viscosity are given in poise, named after Louis Poiseuille. Water has a viscosity of approximately 0.01 poise, or 1 centipoise, which is a handy reference point for comparing the viscosity of body fluids. Blood is a suspension of proteins and cells in a salt solution. As such it is more viscous than water. Blood plasma has a viscosity of 1.7 centipoise, and whole blood a viscosity of approximately 4 centipoise.

The Relationship Between Pressure, Flow, and the Determinants of Vascular Resistance Are Mathematically Quantified by Poiseuille Law

In the 1840s Louis Poiseuille conducted experiments that resulted in a mathematical relationship to describe flow in

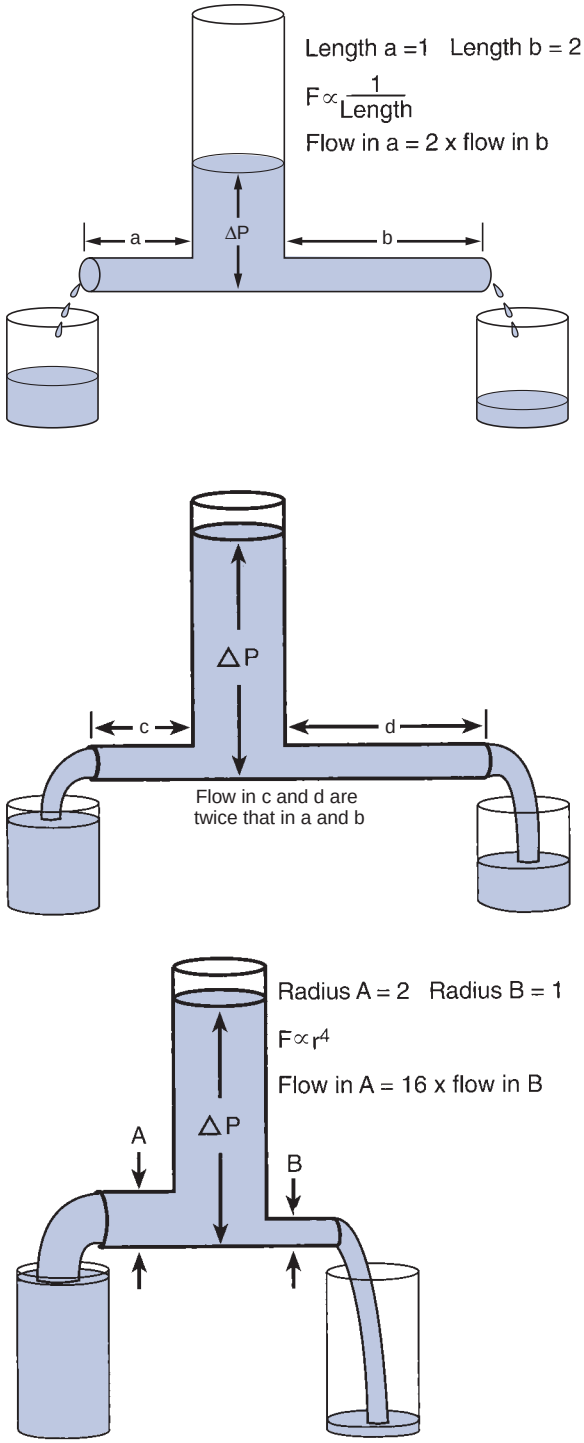

FIGURE 11.5 The influence of pressure difference, tube length, and tube radius on flow. The pressure difference (Δ P) driving flow is the result of the height of the column of fluid above the openings of tubes A and B. Increasing the pressure *difference* increases flow; if pressure was the same at the opening of the tubes as at the bottom of the column of fluid, there would be no flow. Flow is reduced in direct proportion to the length of the tube through which it flows; doubling the length reduces flow to ½ its original value, tripling the length reduces it to ⅓, etc. Because flow is determined by the fourth power of the radius, small changes in radius have a much greater effect than small changes in length. F, flow; P, pressure.

a cylindrical tube. This has become known as **Poiseuille's law**. Poiseuille's law states:

$$Q = (P_1 - P_2)\pi r^4 / 8\eta l \qquad (4)$$

where Q = flow, $(P_1 - P_2)$ = the pressure difference between the beginning and the end of the tube, r = the tube radius, l = the tube length, η = viscosity, and π and 8 are constants of proportionality. This relationship can also be written as $(P_1 - P_2) = Q\ 8\eta l / \pi r^4$. In this form, the term $8\eta l / \pi r^4$ is the resistance to blood flow and is sometimes simply designated as, R. Flow resistance is a measure of how easily the fluid can pass through a tube for any given pressure difference. In physiology, it is easier to calculate resistance as $(P_1 - P_2) / Q$ and to express it in units of mm Hg/mL per minute with the name of peripheral resistance unit (PRU).

Poiseuille law gives two of the most fundamentally important relationships used to describe flow and pressure in the cardiovascular system, which are

$$Q = (P_1 - P_2)/R \quad \text{and} \quad (P_1 - P_2) = Q \times R \qquad (5)$$

These equations indicate that flow is proportional to the pressure difference between the entrance and exit points of the tube and inversely proportional to the resistance (i.e., as resistance increases, flow decreases). It also tells us that at any given flow, the pressure drop along any two points down the length of the tube is proportional to resistance. In the cardiovascular system, the final "end of the tube" is considered the right atrium. Pressure in the right atrium is about 2 mm Hg. This is sufficiently close to zero and thus is ignored. Therefore $(P_1 - P_2)$ becomes simply P. Furthermore, for the purposes of understanding basic hemodynamics, P is usually taken as the mean pressure within an artery or vein. Consequently, Poiseuille law reduces to

$$Q = P/R \quad \text{or} \quad P = Q \times R \qquad (6)$$

Applied to the whole cardiovascular system, this law indicates that arterial pressure is the product of the flow output of the heart, called the **cardiac output**, and the resistance to flow provided by all the blood vessels in the circulation. This resistance is termed the **total peripheral vascular resistance** (TPR).

Strictly speaking, Poiseuille law applies only to nonpulsatile flow of a homogenous fluid in uniform, rigid, nonbranching cylindrical tubes. Because none of these characteristics is met in the cardiovascular system, one might imagine that Poiseuille's law cannot be applied to blood flow. However, Poiseuille's law can be and is applied to the cardiovascular system. Note that this application is not used as a simplified expedient that ignores some of the complex realities of the physics of blood flow. Rather, Poiseuille law can be used in the manner expressed in equation 6 because the cardiovascular system truly does behave as if the heart pumped blood at a steady flow, producing a mean arterial pressure as the result of a single total peripheral vascular resistance. Thus, equation 6 predicts that mean arterial pressure will increase if the cardiac output, TPR, or both increase, whereas it will decrease if TPR and/or cardiac output decrease. It also predicts that at a constant mean

arterial pressure, blood flow through any portion of the vascular tree will increase if TPR decreases and will decrease if TPR increases. These simple cause-and-effect relationships are the critical determinants of arterial pressure and organ blood flow in the cardiovascular system and will be described more fully in the context of cardiovascular control mechanisms in Chapter 17.

The Total Resistance of Multiple Vascular Segments Summed Together Is Different for Series Versus Parallel Additions of the Segments

The cardiovascular system is composed of millions of vessels of different sizes. There are two simple rules used to determine how many vessels of different sizes combine to give a single resistance to flow. In a system composed of different-sized tubes arranged in series (i.e., sequentially, or end-to-end), the total resistance of that system is simply the sum of the individual resistances. Or,

$$R_{total} = \Sigma R_{individual} \quad (7)$$

For example, if one were to examine the resistance of a segment of a tapering artery where the proximal 1 cm of length had an R = 1 PRU, the next 1 cm had an R = 2 PRUs, and the 1 cm after that an R = 5 PRUs, the resistance across the entire 3-cm length of that artery would be 1 + 2 + 5 = 8 PRUs. Nevertheless, the arterial portion of the cardiovascular system is not a single long blood vessel; the aorta branches into thousands of arteries and capillaries, which are arranged in parallel. The total resistance in a system of parallel tubes is given by

$$1/R_{total} = \Sigma 1/R_{individual} \quad (8)$$

That is, the reciprocal of the total resistance in vessels arranged in parallel is the sum of the reciprocals of the individual resistances. Using the arterial segments mentioned above but arranged in parallel, one would arrive at $1 / R_{total} = 1/1 + 1/2 + 1/8 = 13/8$, or $R_{total} = 8/13$, or ~0.62 PRUs. In this case the total resistance of the system of the three arteries arranged in parallel is not only less than it would have been if they were arranged in series but actually less than the resistance of any one segment in the circuit. In most cases, this is a *general* rule of thumb; losing similar-size vessels in parallel in the arterial system raises vascular resistance, whereas adding similar-size vessels in parallel reduces resistance. This latter case is seen following long-term aerobic training, such as distance running, in which the arteriolar and capillary network increase their numbers in parallel, thereby reducing resistance to blood flow.

The effect of summed series and parallel elements in the cardiovascular system is a bit more complicated than can be described solely by equations 7 and 8. In the cardiovascular system, vessels get smaller as they proceed from arteries down to arterioles and capillaries, which tends to increase resistance to flow. However, the number of vessels arranged in parallel also increases dramatically in this direction, which tends to decrease resistance. The effect of these two phenomena on the relative resistances of individual sections of the vasculature depends on whether the number of vessels added in parallel can compensate for the resistance effects of adding vessels that individually have a high resistance resulting from small radii. This interplay between series and parallel elements is a primary factor in creating the form of the pressure profile, or ΔP, along the arterial side of the circulation, as will be explained later in this chapter.

High Blood Flow Velocity Decreases Lateral Pressure and Increases Shear Stress on the Arterial Wall While Increasing the Probability of the Creation of Turbulent Flow in Arteries

In addition to the amount of blood flowing through a given vessel or organ system per minute, physiologists are often interested in how fast the bloodstream is flowing from one point to the next in the circulation. This variable is called **flow velocity** and is usually expressed in cm/sec. Fluid flow velocity is given simply by the volume of flow per second (cm^3/sec) divided by the cross-sectional area of the system through which the fluid is flowing (Fig. 11.6A). If a flow of 200 mL/sec in a tube is forced through another, narrower, tube, the flow must go through that smaller opening faster to maintain a volume flow at 200 mL/sec. Conversely, if this fluid is allowed to expand into a much larger cross-sectional area, it can move slower and still deliver 200 mL/sec. This relationship holds whether applied to a single tube or a composite cross-sectional area of many tubes arranged in parallel, such as a cross section of the vascular system. Thus, at a constant flow, a decrease in the cross-sectional area through which the flow is moving increases flow velocity, and an increase in area decreases flow velocity.

The blood pressure exerted against the walls of an artery and the energy required to move blood at a certain velocity are interrelated by the **Bernoulli principle**. The total energy of blood flow in a blood vessel is the sum of its potential energy (represented as pressure against the vascular wall) and its kinetic energy resulting from its velocity (kinetic energy equals ½ mass times velocity^2). The total of potential and kinetic energy at any given point in a system is constant. Consequently, any increase in one form of the energy has to come at the expense of the other. For example, as flow velocity increases, lateral pressure must decrease to keep the total energy of the system constant (see Fig. 11.6A). This principle is seen with flow in the aorta, where high velocity reduces lateral pressure relative to that measured directly facing the flow stream, which equals the total energy in the system. This phenomenon is exploited clinically to evaluate the severity of the hemodynamic consequences of a stenotic (narrowed) aortic valve. A catheter with two pressure sensors is placed in the heart such that one lies within the ventricle and the other just across the narrowed aortic valve. A high-velocity jet of blood moving through the narrowed valve causes a significant drop in lateral pressure detected by the aortic sensor compared with the ventricular sensor; the hemodynamic severity of the stenosis is proportional to this pressure difference.

All flowing fluids exert a "rubbing" force against the inner wall of the cylinder in which they flow. This force is

CLINICAL FOCUS

11.1

Vascular Abnormalities Associated With Chronic Primary Arterial Hypertension

Chronic arterial hypertension is a cardiovascular disease whose main manifestation is a consistent elevation of arterial pressure ≥140/90 mm Hg. Diagnosis of chronic arterial hypertension in a patient is established following documentation of elevated pressure in a clinical setting when measured at several time points over a period of many weeks or months. Even with this criterion, it is estimated that more than 65,000,000 people in the United States alone suffer from chronic arterial hypertension. It is the leading risk factor in stroke and a major contributor to morbidity and mortality associated with heart failure, coronary artery disease, atherosclerosis, and renal insufficiency.

Arterial hypertension is largely asymptomatic until it results in end-stage organ disease, which is a major reason it goes unrecognized and untreated by the patient. However, people with untreated hypertension have significantly higher levels of cardiovascular morbidity with a reduced life expectancy. Left untreated, arterial hypertension becomes more severe over time, as the result of progressive arterial and renal abnormalities resulting from exposure to high arterial pressure. People with untreated arterial hypertension do not get better on their own and must stay on medication throughout their lives to keep their arterial pressure down. Keeping pressure down in hypertension has been clinically established to provide definitive benefits to the patient, whereas failure to control hypertension results in definitive harm.

Chronic arterial hypertension is classified broadly as either primary or secondary hypertension. Secondary hypertension indicates that the elevated blood pressure is a secondary result of some other primary disease. Hypertension is a secondary consequence of renal artery stenosis, renal parenchymal disease, primary aldosteronism, pheochromocytoma, aortic coarctation, and thyrotoxicosis. Although there are several mechanisms known to cause secondary hypertension, only 5% to 15% of all cases of chronic arterial hypertension fall into that category. The remaining individuals with hypertension have what is called primary, or essential, hypertension, which indicates that the hypertension is a primary condition in its own right of unknown cause. Currently, the etiology of primary hypertension is believed to be the result of multiple initiating factors and regulatory dysfunctions with strong genetic predispositions involving both. Current attention is being directed at such factors as they relate to how the kidney manages salt and water balance.

Whatever the mechanisms may be, one thing is certain—chronic arterial hypertension is the result of elevated peripheral vascular resistance. For this reason, hypertension is considered a *vascular* disease involving the arterioles because these vessels are the major contributor to total peripheral vascular resistance. In hypertension, arteries have thickened vascular walls and narrowed lumens. This thickening increases the resistance of arteries, even in the absence of all vascular smooth muscle contraction, and acts as a structural, geometric amplifier of any vasoconstrictor stimuli. As a result, all arterial smooth muscle contraction, from maximum dilation to maximum contraction, results in exaggerated increases in arterial resistance in arteries from hypertensive, compared with normotensive, patients. In addition, the arterial smooth muscle cells in hypertensive patients are hypersensitive to vasoconstrictor stimuli and hyposensitive to vasodilators. This too, results in an exaggerated increase in vascular resistance with any vasoconstrictor stimuli and a reduced capacity of the arteries to counteract this exaggeration with any vasodilator stimuli. Lost production and bioavailability of arterial endothelial nitric oxide, which is a potent anticonstrictor agent, are also a consequence of hypertension and may be a contributing factor in the maintenance and inevitable progression of that disease.

analogous to what one feels by rubbing the palms of the hands together and is called **shear stress**. Shear stress on the inner walls of arteries increases proportionally as the velocity of flow near the wall increases. This has several medical implications. Release of paracrine substances from the endothelium as well as other transport phenomena is stimulated by increased shear stress on the endothelial cells that line arteries. These factors are instrumental in stimulating capillary growth and endothelial repair and may be the link between the growth of new blood vessels in skeletal muscle and periodic increases in muscle blood flow during aerobic exercise training. Conversely, the accumulation of atherosclerosis in arteries is enhanced in low shear areas of arteries, whereas it is diminished in high shear areas.

Flow velocity also affects the organization of fluid layers of blood in arteries. Normally, the cells in layers of fluid in arteries flow with a streamlined or bullet-shaped profile, as shown in Figure 11.6B. In three dimensions, this can be envisioned as a set of thin telescoping cylindrical layers projecting from the inner arterial wall out uniformly to the center of the vessel. Flow velocity is highest in the center of a streamline blood flow and lowest adjacent to the inner arterial wall. However, if total flow velocity becomes too high in an artery, the kinetic energy of the flow streams overcomes the tendency of the fluid layers to stick together from vis-

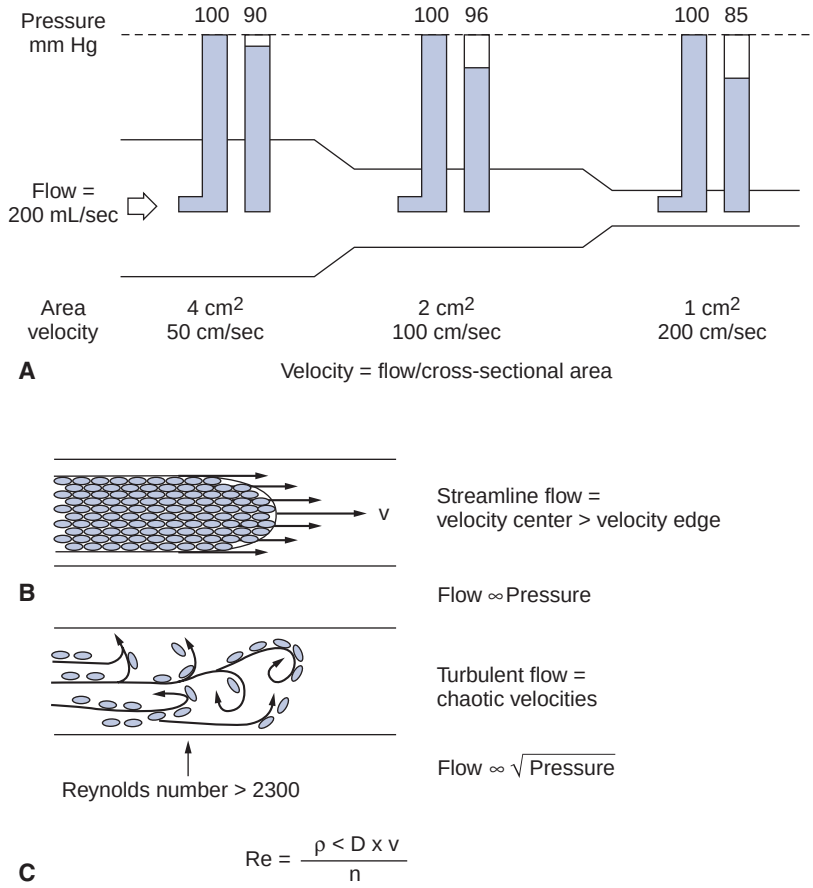

FIGURE 11.6 Effect of flow velocity on lateral intravascular pressure, axial streaming, and turbulent flow. A, If any given flow of blood is forced through progressively smaller cross-sectional areas, the velocity of blood flow must increase. The Bernoulli principle states that increased flow velocity reduces the lateral pressure of the flow stream exerted against the wall of the vessel. **B,** The distribution of red blood cells in a blood vessel depends on flow velocity. As flow velocity increases, red blood cells move toward the center of the blood vessel (axial streaming), where velocity is highest. Axial streaming of red blood cells creates a cell-free layer of plasma along the inner vessel wall. **C,** At high flow velocity, the kinetic forces of flowing fluid overcome the viscous forces holding layers of fluid together, resulting in turbulent flow.

cous forces. When this happens, the fluid layers break apart and become random and chaotic. This is a condition called **turbulence** (see Fig. 11.6C). Turbulence is a wasteful process that dissipates pressure energy in the cardiovascular system, which could otherwise be used to produce flow. The tendency to produce turbulent flow is expressed in a mathematical term called the **Reynolds number**, R_e. The Reynolds number is a measure of the ratio of kinetic energy in the system (which will pull fluid layers apart) and the viscous component of the system (which holds the fluid layers together) as given by

$$R_e = \rho D v / \eta \qquad (9)$$

where ρ = fluid density, D = inner vessel diameter, v = flow velocity, and η = blood viscosity. Generally a $R_e \geq 2{,}300$ indicates that turbulence will occur in the fluid stream. Clearly, large-diameter vessels, high flow velocity, and low blood viscosity favor turbulence in the cardiovascular system.

Whereas laminar flow in arteries is silent, turbulent flow creates sounds. These sounds are clinically known as **heart murmurs** or simply murmurs. Certain diseases, such as atherosclerosis and rheumatic fever, can scar the aortic or pulmonic valves, creating narrow openings and high flow velocities when blood is forced through them. A clinician can detect this problem by listening to the noise created by the resultant turbulence.

Because Blood Is a Suspension, Its Viscosity Is Dependent on Hematocrit and Is Higher at Low Flow Velocity than at High Flow Velocity

The fluid dynamic properties of blood are more complicated than they are for a simple homogenous fluid such as water because blood is really a suspension of proteins and cells in an aqueous medium. The study of the fluid dynamic properties of blood is called **rheology**. The presence of proteins and cells in blood has two important hemodynamic consequences. First, blood viscosity increases exponentially as the blood hematocrit increases (Fig. 11.7A). Thus, as the hematocrit increases, the flow resistance against which the heart must pump increases, which substantially increases the cardiac workload. Although there are some pathological instances in which a patient's hematocrit can increase because of overproduction of red blood cells (e.g., polycythemia vera), an abnormally increased hematocrit can come from the loss of blood plasma without a proportional loss of red blood cells. This can occur in severe dehydration, loss of plasma from severe burns, or inappropriate loss of water through the renal system as a consequence of kidney disease. Second, red blood cells tend to clump if blood flow velocity is sluggish (see Fig. 11.7B). This clumping raises blood viscosity, which can be a negative complicating factor in any condition that adversely diminishes the overall flow output of the heart, such as circulatory shock or heart failure.

CLINICAL FOCUS

11.2

Hemodynamic Localization of Atherosclerosis

Atherosclerosis is a chronic inflammatory response of the walls of large arteries that is initiated by injury to the endothelium. The exact cause of this injury is unknown. However, exposure to high serum lipid levels in the form of low-density lipoprotein (LDL) cholesterol and triglycerides is considered a prime culprit, with contributions from hypertension, the chemicals in cigarette smoke, viruses, toxins, and homocysteinemia. With injury, the normal endothelium barrier becomes compromised. Leukocytes, primarily monocytes, adhere and infiltrate the arterial intima. These cells and the intima itself accumulate large quantities of lipoproteins, mainly LDL, which, when oxidized, further damage the artery, stimulate the production of damaging reactive oxygen species, and set up a more aggressive local arterial inflammatory response. This results in mitotic activation of arterial smooth muscle cells, which migrate into the intima, and the activation of monocytes, which transform into macrophages that engulf lipid to become foam cells. These factors create an inwardly directed growth of the arterial wall, which encroaches on the arterial lumen and creates the appearance of fatty streaks on the inner arterial wall. Over time this streak grows with the accumulation of extracellular matrix proteins, the development of a fibrous cap over the atheroma, and the development of a lipid-laden necrotic core containing debris, foam cells, crystallized cholesterol, and calcium deposits. This creates what is often called an atherosclerotic plaque.

Atherosclerotic plaques usually only develop in a portion of the circumference of the arterial wall. The wall opposite the plaque can actively contract in response to vasoconstrictor stimuli, whereas the wall beneath the plaque becomes weakened, creating an arterial aneurysm that can rupture. Atherosclerotic plaques stimulate platelet aggregation and blood clot formation that can totally occlude an artery. Furthermore, the plaque is friable and can rupture, spilling debris into the arterial lumen which further stimulate clot formation. Plaque rupture in the arteries of the heart is a primary cause of death from heart attack.

Branch points and curvatures alter flow velocity and shear stress at the arterial wall; it is less along the inner curvature of a flow stream and at the upstream edge of branch points. It is well known that plaque formation in the vascular system does not occur either uniformly or totally randomly in the vascular tree. Instead, it develops at branch points and bifurcations and along the inner curvature of arteries. All these areas contain regions of low flow velocity and low shear stress. The anatomic characteristics of the coronary arteries, the bifurcation of the common carotid arteries, and the entry to the renal arteries make these regions especially susceptible to the accumulation of atherosclerotic plaques and thus place the blood supply to the heart, brain, and kidney at risk.

Axial Streaming of Red Blood Cells Allows for Application of Poiseuille Law to the Cardiovascular System

Application of Poiseuille law to fluid dynamics assumes that the fluid is homogeneous, i.e., it is made of one element of uniform composition, such as water. Although all suspensions are nonhomogeneous fluids, the properties of blood cells flowing in arteries are such that blood behaves hemodynamically as if it were a homogeneous fluid. Blood cells tend to compact densely in the center of the flow stream, leaving a thin layer of cell-free plasma against the vascular wall. This is called **axial streaming**. As such, blood flows more as a compact bulk fluid than as a mixed conglomeration of particles in suspension. For this reason Poiseuille law can be applied to the cardiovascular system as it was written. However, axial streaming of blood does tend to separate this bulk flow into two components of different viscosities. The fluid near the vessel wall is essentially cell-free plasma and has a viscosity of only 1.7 centipoise, as opposed to 4 centipoise for whole blood. In large vessels, such as the aorta, this low-viscosity layer is only a small percentage of the viscosity of the flow stream. Thus, for all practical purposes, the viscosity of the blood flowing through the entire aortic cross section can be considered to be 4 centipoise. However, in small arterioles (<300 μm interior diameter) and capillaries, this thin layer becomes a greater percentage of the total volume contained within the vessel and thus contributes a greater percentage to the total viscosity of the blood traveling through those vessels. When fluid flows through these smaller vessels, fluid viscosity as a whole decreases. This is called the Fahraeus-Lindqvist effect, and it is responsible for reducing blood viscosity and therefore flow resistance when blood flows through extremely small vessels such as capillaries. This makes it easier for blood to flow through vessels that otherwise have extremely high resistances.

DISTRIBUTION OF PRESSURE, FLOW, VELOCITY, AND BLOOD VOLUME IN THE CARDIOVASCULAR SYSTEM

Meaningful insights into characteristics of the cardiovascular system can be obtained by examination of the

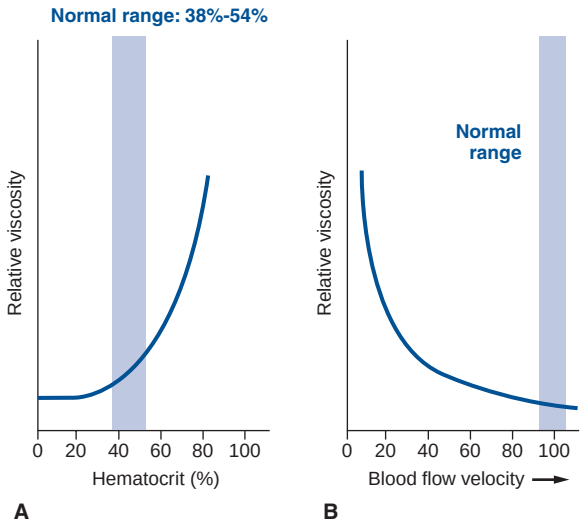

FIGURE 11.7 Effect of hematocrit and flow velocity on blood viscosity. A, Increases in hematocrits above normal values produce a sharp increase in viscosity, causing marked increase in resistance to flow. **B,** Blood viscosity in arteries increases dramatically whenever flow velocity slows to low levels. Thus, the resistance to flow is higher in a slow-moving arterial stream than in one that moves with high velocity.

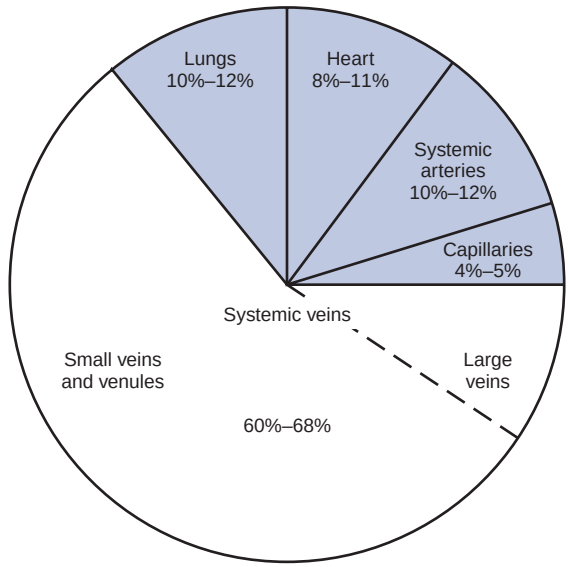

FIGURE 11.8 Blood volumes of various elements of the circulation in a person at rest. The majority of the blood volume is in systemic veins.

distribution of flow, velocity, pressure, and volume within the system. For example, because veins are more compliant than arteries, one would expect that more of the total volume of blood in the cardiovascular system would reside in the venous rather than the arterial side of the circulation. This is precisely the case as shown in Figure 11.8. Also, because cross-sectional area increases greatly from arteries to the arterioles and to the capillaries, the lowest blood flow velocity occurs through the capillary network (Fig. 11.9). This slow velocity through this exchange segment of the vascular system has the beneficial effect of allowing more time for exchange of material between the cardiovascular system and the extracellular fluid.

The heart is an intermittent pump; it generates high pressure within the ventricles when it contracts during systole, which then drops to near zero during diastole. However, because arteries are compliant, some of the ejected blood into the arteries distends these vessels, like the expansion of a water-filled balloon. During diastole, recoil of the arteries pushes blood forward against the downstream vascular resistance, generating a significant diastolic pressure. For this reason, diastolic pressure drops to only about 80 mm Hg in the aorta as compared with near zero in the ventricles.

Examination of the pressure profile across the cardiovascular system (see Fig. 11.9) shows that the largest drop of pressure occurs across the arterioles, indicating that this is the site of greatest vascular resistance in the cardiovascular system. Although there are many more arterioles than arterioles in the cardiovascular system (resistances in parallel), this large pressure drop indicates that their reduction in individual size dominates over the addition of parallel vessels. Similarly, although individual capillaries are small, so many of these lie in parallel that resistance across the capil-

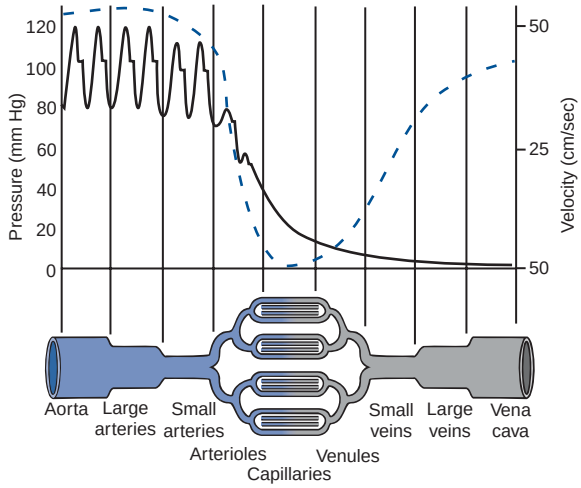

FIGURE 11.9 Pressure and flow velocity profile in the systemic circulation. The arterial portion of the circulation is characterized by high, pulsatile pressure and high flow velocity. This profile changes to one of low pressure and velocity without pulsatile character in the veins. The largest drop in mean arterial pressure occurs across the arteriolar segment of the circulation, indicating that this is the sight of highest vascular resistance in the cardiovascular system.

FROM BENCH TO BEDSIDE

11.1 Developments in the Prevention and Analysis of Atherosclerotic Plaques

Rupture of unstable atherosclerotic plaques is the underlying cause of sudden myocardial ischemia and heart attack. Statins and fibrates are classes of drugs that were designed to control the development of atherosclerosis by lowering plasma lipid concentration. However, use of these drugs has revealed that they may have additional unexpected benefits. One of these includes the stabilization of atherosclerotic plaques. Recent clinical investigations have used DNA microarray analysis to evaluate the effects of statins and fibrates on transcriptional regulation and expression profiles in stable and unstable plaques. This work provides insight into factors leading to the destabilization of plaques and whether pharmacological intervention can prevent this potentially dangerous situation from occurring in patients with atherosclerosis.

The difficulty with most investigations into characteristics of plaques is that they are often restricted to analysis "after the fact," using samples from arterectomies or obtained during autopsies. Polarization-sensitive optical coherence tomography (PSOCT) is a new technology that is being examined as a minimally invasive means for examining the detailed structure of plaques in situ. PSOCT is analogous to ultrasound imaging except that it uses infrared light instead of sound. This technique holds the promise that details of the cross-sectional structure of plaques can be evaluated in living tissue in a patient and observed over time. This could prove to be a valuable tool in helping physicians intervene in patients before plaques rupture.

laries is actually lower than that across the arterioles; hence, the pressure drop across the capillary segment of the circulation is less than that across the arterioles.

Pressures within the arteries of the pulmonary circulation are not the same as those in the systemic circulation. Pulmonary arterial pressure is about 25 mm Hg during systole and 8 mm Hg during diastole. Because the outputs of the right and left heart are the same, the low pressure in the pulmonary circulation must indicate, according to Poiseuille law, that vascular resistance is much lower in the pulmonary circulation than in all the organs combined that make up the systemic circulation.

CHAPTER SUMMARY

- The cardiovascular system is a fluid transport system that delivers substances to the tissues of the body while removing the byproducts of metabolism. It also is responsible for the delivery of blood through the pulmonary circulation for the uptake of oxygen from and release of carbon dioxide into the lungs.
- The heart is composed of two pumps connected in series. The right heart pumps blood into the lungs. The left heart pumps blood through the rest of the body.
- Pressure is created within the atria and ventricles of the heart by contraction of cardiac muscle. The directional opening of valves, which prevent back flow between chambers, ensures forward movement of blood through the heart.
- Arteries transport blood from the heart to organs. Veins transport blood from organs to the heart. The vascular supplies to the systemic organs are arranged anatomically in parallel.
- Capillaries are the primary site of transport between blood and the extracellular fluid.
- Altering contraction or relaxation of its smooth muscle layer can change the radius of any artery or vein.
- The volume contained within any vascular segment is a function of transmural pressure and the flexibility of the vascular wall.
- Transmural pressure in blood vessels produces wall tension and stress that must be overcome for the vessel to contract.
- Blood flow and pressure throughout the vascular system is created in accordance with the principles of Poiseuille's law; flow moves in proportion to the pressure gradient divided by vascular resistance between points in the circulation.
- The velocity of blood flow in an artery affects lateral pressure and inner wall shear stress in arteries as well as transport across the capillary wall. It is also a factor in the creation of turbulence in the arterial flow stream.
- The viscous nature of blood as a suspension affects flow resistance in arteries and is influenced by hematocrit and blood flow velocity.
- The hemodynamic profile in the cardiovascular system is the result of the combined effects of all the relationships and laws governing the containment and movement of blood in the cardiovascular system.