The route taken by the blood after it leaves the heart was a point of much confusion until the seventeenth century. Chinese emperor Huang Ti (2697–2597 B.C.E.) correctly believed that it flowed in a complete circuit around the body and back to the heart. But in the second century, Roman physician Claudius Galen (129–c. 199) argued that it flowed back and forth in the veins, like air in the bronchial tubes. He believed that the liver received food from the small intestine and converted it to blood, the heart pumped the blood through the veins to all other organs, and those organs consumed the blood.

Huang Ti was right, but the first experimental demonstration of this did not come until the seventeenth century. English physician William Harvey (1578–1657) studied the filling and emptying of the heart in snakes, tied off the vessels above and below the heart to observe the effects on cardiac filling and output, and measured cardiac output in a variety of living animals. He concluded that (1) the heart pumps more blood in half an hour than there is in the entire body, (2) not enough food is consumed to account for the continual production of so much blood, and (3) since the planets orbit the sun and (as he believed) the human body is modeled after the solar system, it follows that the blood orbits the body. So for a peculiar combination of experimental and superstitious reasons, Harvey argued that the blood returns to the heart rather than being consumed by the peripheral organs. He could not explain how, since the microscope had yet to be developed and he did not know of capillaries—later discovered by Antony van Leeuwenhoek and Marcello Malpighi.

Harvey published his findings in 1628 in a short but elegant book entitled *Exercitio Anatomica de Motu Cordis et Sanguinis in Animalibus (Anatomical Studies on the Motion of the Heart and Blood in Animals).* This landmark in the history of biology and medicine was the first experimental study of animal physiology. But so entrenched were the ideas of Aristotle and Galen in the medical community, and so strange was the idea of doing experiments on living animals, that Harvey's contemporaries rejected his ideas. Indeed, some of them regarded him as a crackpot because his conclusion flew in the face of common sense—if the blood was continually recirculated and not consumed by the tissues, they reasoned, then what purpose could it possibly serve?

Harvey lived to a ripe old age, served as physician to the kings of England, and later did important work in embryology. His case is one of the most interesting in biomedical history, for it shows how empirical science overthrows old theories and spawns better ones, and how common sense and blind allegiance to authority can interfere with acceptance of the truth. But most importantly, Harvey's contributions represent the birth of experimental physiology—the method that generated most of the information in this book.

General Anatomy of the Blood Vessels

Objectives

When you have completed this section, you should be able to

- trace the route usually taken by the blood from the heart and back again;
- describe some variations on this route;
- describe the structure of a blood vessel; and
- describe the different types of arteries, capillaries, and veins.

Circulatory Routes

At its simplest, the usual route of blood flow is heart → arteries → arterioles → capillaries → venules → veins → heart. Blood usually passes through only one network of capillaries from the time it leaves the heart until the time it returns (fig. 20.1*a*). But there are exceptions, notably portal systems and anastomoses. In a **portal system** (fig. 20.1*b*), blood flows through two consecutive capillary networks before returning to the heart. One portal system connects the hypothalamus and anterior pituitary (see chapter 17). Others are found in the kidneys and between the intestines and liver; the latter system is detailed in table 20.13.

An **anastomosis** is a point where two blood vessels merge. In an **arteriovenous anastomosis (shunt),** blood flows from an artery directly into a vein and bypasses the capillaries (fig. 20.1*c*). Shunts occur in the fingers, palms, toes, and ears, where they reduce heat loss in cold weather by allowing warm blood to bypass these exposed surfaces. Unfortunately, this makes these poorly perfused areas more susceptible to frostbite. In an **arterial anastomosis,**

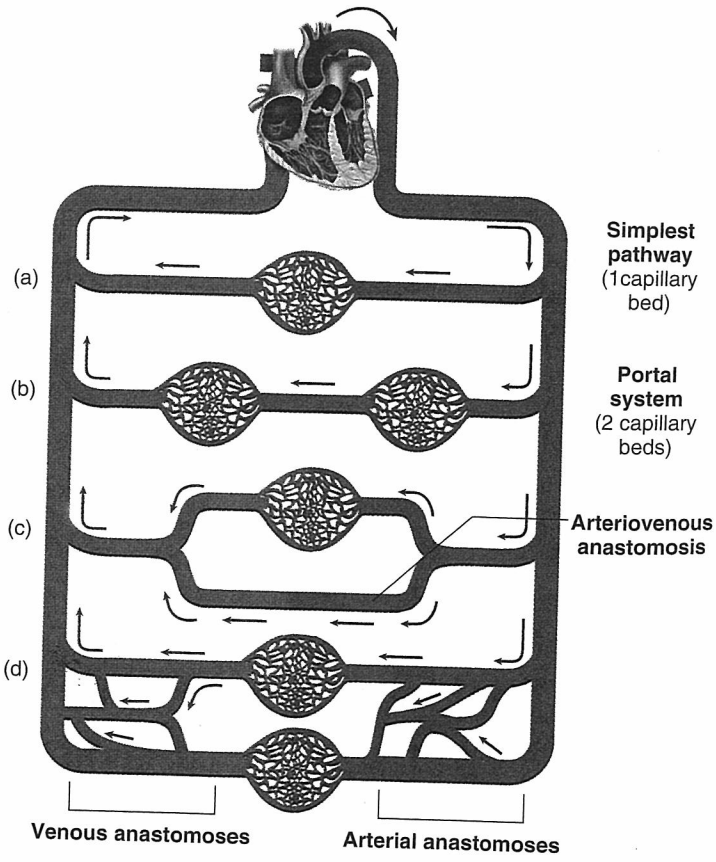


Figure 20.1 Variations in Circulatory Pathways.

two arteries merge and provide *collateral* (alternative) routes of blood supply to a tissue (fig. 20.1*d*). Those of the coronary circulation were mentioned in chapter 19. They are also common around joints where movement may temporarily obstruct one pathway. **Venous anastomoses** are more common. They provide several alternative routes of drainage from an organ, so blockage of a vein is rarely as life-threatening as blockage of an artery. Several arterial and venous anastomoses are described later in this chapter.

The Vessel Wall

The walls of the arteries and veins have three layers called *tunics* (figs. 20.2 and 20.3):

1. The **tunica externa (tunica adventitia**[1]) is the outermost layer. It consists of loose connective

[1] *advent* = added to

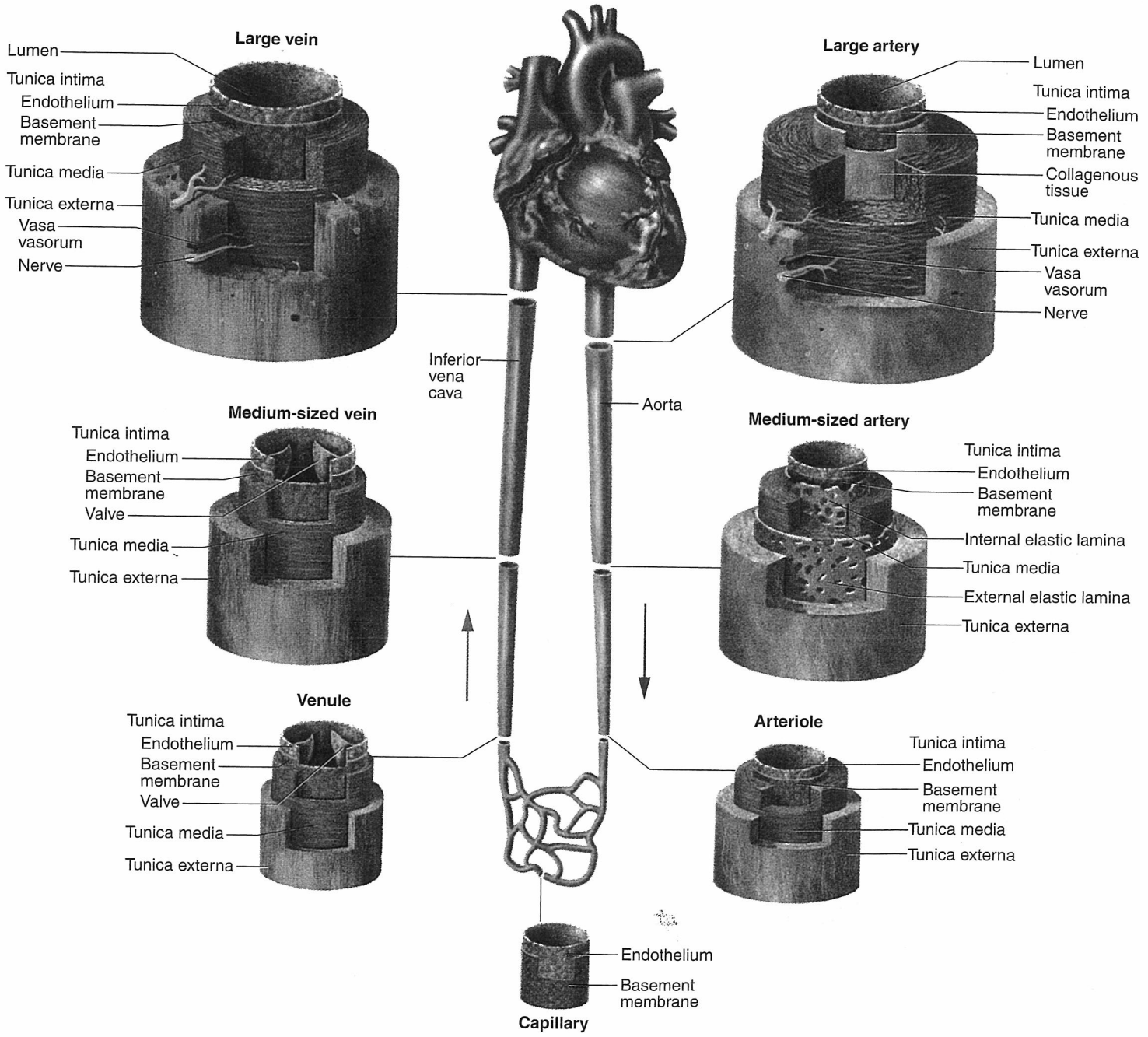


Figure 20.2 The Structure of Arteries and Veins.
Why are elastic laminae found in arteries but not in veins?

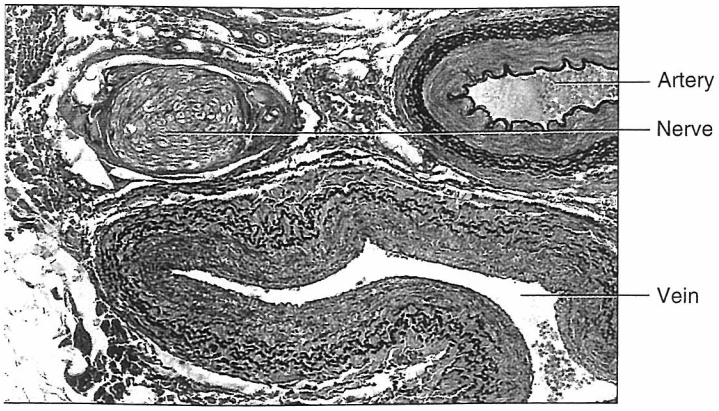


Figure 20.3 A Neurovascular Bundle. A small artery, small vein, and nerve traveling together in a common sheath of connective tissue.

tissue that often merges with that of neighboring blood vessels, nerves, or other organs. It anchors the vessel and provides passage for small nerves, lymphatic vessels, and smaller blood vessels. Small vessels called the **vasa vasorum**[2] (VAY-za vay-SO-rum) supply blood to at least the outer half of the wall of a larger vessel. Tissues of the inner half of the wall are thought to be nourished by diffusion from blood in the lumen.

2. The **tunica media,** the middle layer, is usually the thickest. It consists of smooth muscle, collagen, and sometimes elastic tissue. The smooth muscle is responsible for the vasoconstriction and vasodilation of blood vessels.
3. The **tunica intima (tunica interna),** the inner layer, is exposed to the blood. It consists of a simple squamous **endothelium** overlying a basement membrane and a sparse layer of fibrous tissue. The endothelium acts as a selectively permeable barrier to blood solutes, and it secretes vasoconstrictors and vasodilators to be considered later. It also provides a smooth inner lining that normally repels blood cells and platelets. However, platelets may adhere to a damaged endothelium. During inflammation, leukocytes also adhere loosely to it by means of *cell-adhesion molecules* produced by the endothelial cells (see chapter 21).

Arteries and Metarterioles

Arteries are constructed to withstand the surges of blood pressure generated by ventricular systole. They are more muscular than veins and appear relatively round in tissue sections. They are divided into three categories by size, but of course there is a smooth gradation from one category to the next:

1. **Conducting (elastic) arteries** are the largest. Some examples are the pulmonary arteries, aorta, and common carotid arteries. Their tunica media consists of numerous sheets of elastic tissue, perforated like slices of Swiss cheese, alternating with thin layers of smooth muscle, collagen, and elastic fibers. Conducting arteries expand when the ventricles pump blood into them during systole, and recoil during diastole. This lessens the fluctuations in blood pressure exerted on smaller arteries downstream.
2. **Distributing (muscular) arteries** are smaller branches farther away from the heart that distribute blood to specific organs. You could compare a conducting artery to an interstate highway and distributing arteries to the exit ramps and state highways that serve specific towns. Distributing arteries typically have 25 to 40 layers of smooth muscle cells constituting about three-quarters of the wall thickness. Most arteries to which we give names are in these first two size classes. The brachial, femoral, and splenic arteries are examples of distributing arteries.
3. **Resistance (small) arteries** are usually too variable in number and location to be given names. They exhibit up to 25 layers of smooth muscle cells and relatively little elastic tissue. Their tunica media is thicker in proportion to the lumen than that of larger arteries. The smallest of these arteries, about 40 to 200 μm in diameter and with only one to three layers of smooth muscle, are the **arterioles.** For reasons discussed later, they are the primary points at which the body controls the relative amounts of blood directed to various organs.

Metarterioles[3] are short vessels that link arterioles and capillaries. Instead of a continuous tunica media, they have individual muscle cells spaced a short distance apart, each forming a **precapillary sphincter** that encircles the entrance to a capillary.

Capillaries

Capillaries (fig. 20.4) are the "business end" of the circulatory system. All the rest of the system exists to serve them, because capillaries are almost the only point in the circulatory system where materials are exchanged between the blood and tissue fluid. Capillaries are ideally suited to their role. They consist only of endothelium and a basement membrane. Capillaries have walls as thin as 0.2 to 0.4 μm. They average about 5 μm in diameter at the prox-

[2] *vasa* = vessels + *vasorum* = of the vessels

[3] *meta* = beyond, next in a series

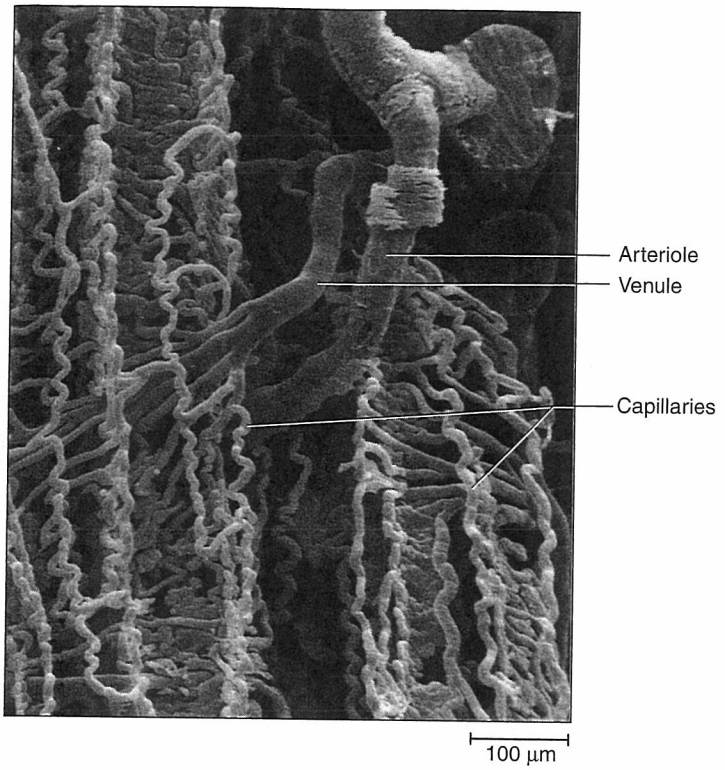


Figure 20.4 Vascular Cast of Blood Vessels in Human Skeletal Muscle. This was prepared by injecting the vessels with a polymer, digesting away all tissue to leave a replica of the vessels, and photographing the cast through the SEM. From R. G. Kessel and R. H. Kardon, *Tissues and Organs: A Text-Atlas of Scanning Electron Microscopy* (W. H. Freeman & Co., 1979).

imal (arterial) end, widen to about 9 μm in diameter at the distal (venous) end, and often branch along the way. (Recall that an erythrocyte is about 7 μm in diameter.) The number of capillaries has been estimated at a billion and their total surface area at 6,300 m^2. But a more important point is that scarcely any cell in the body is more than 60 to 80 μm away from the nearest capillary. There are a few exceptions. Capillaries are scarce in tendons and ligaments and absent from cartilage, epithelia, and the cornea and lens of the eye.

Capillary Beds

Capillaries are organized in groups called **capillary beds**—usually 10 to 100 capillaries supplied by a single metarteriole (fig. 20.5). The metarteriole continues through the bed as a **thoroughfare channel** leading directly to a venule. Capillaries arise from the proximal end of the metarteriole and lead into its distal end or directly into the venule.

There is a precapillary sphincter at the entrance to each capillary. When the sphincters are open, the capillaries are well perfused with blood and they engage in exchanges

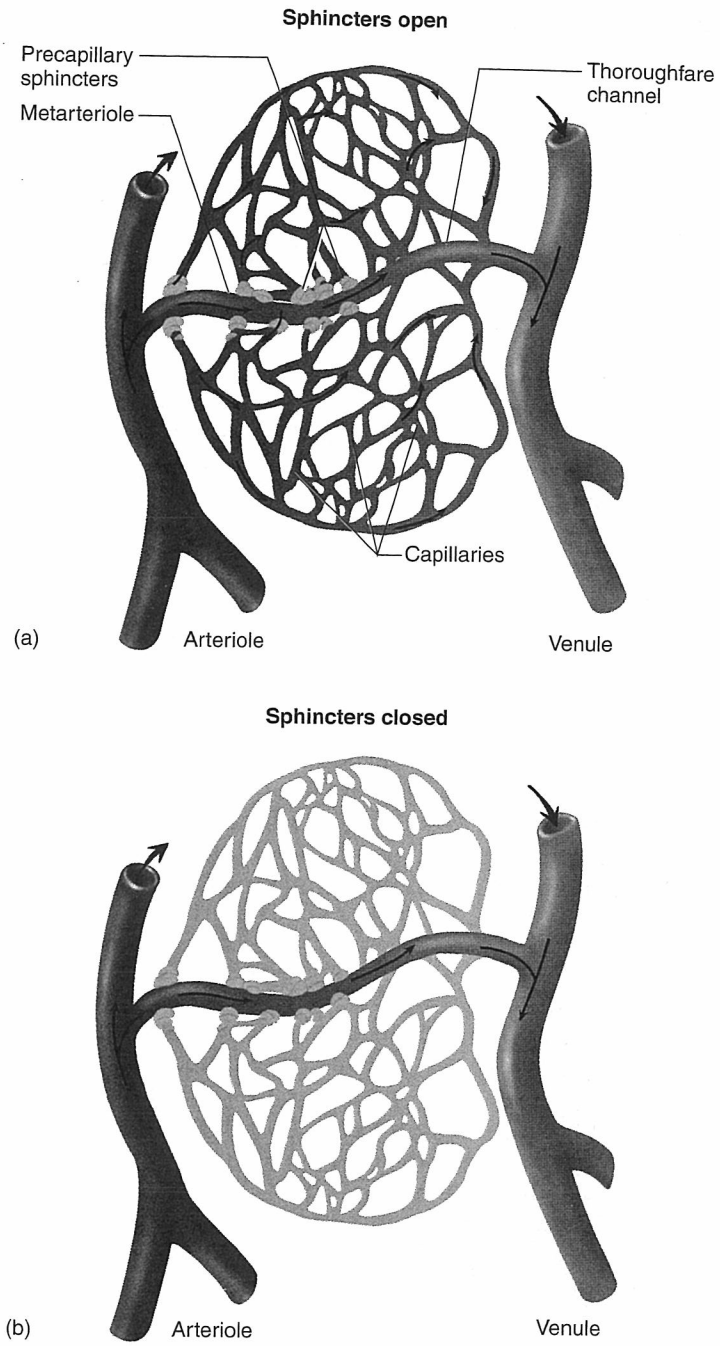


Figure 20.5 Control of Perfusion of a Capillary Bed. (*a*) Precapillary sphincters dilated and capillaries well perfused. (*b*) Precapillary sphincters closed, with blood bypassing the capillaries.

with the tissue fluid. When the sphincters are closed, blood bypasses the capillaries, flows through the thoroughfare channel to a venule, and does not engage in significant fluid exchange. There is not enough blood in the body to fill the entire vascular system at once; consequently, about three-quarters of the body's capillaries are closed at any given time. The shifting of blood flow from one capillary bed to another is discussed later in the chapter.

Types of Capillaries

Two types of capillaries are distinguished by the ease with which they allow substances to pass through their walls and by structural differences that account for their greater or lesser permeability:

1. **Continuous capillaries** occur in most tissues, such as skeletal muscle. Their endothelial cells, held together by tight junctions, form an uninterrupted tube. The cells usually have narrow **intercellular clefts** about 4 nm wide between them. Small solutes, such as glucose, can pass through these clefts, but plasma proteins, other large molecules, and formed elements are held back. The continuous capillaries of the brain lack intercellular clefts and have more complete tight junctions that form the blood-brain barrier discussed in chapter 14.
2. **Fenestrated capillaries** have endothelial cells that are riddled with holes called **fenestrations**[4] **(filtration pores)** (fig. 20.6). Fenestrations are about 20 to 100 nm in diameter and are usually covered by a thin mucoprotein diaphragm. They allow for the rapid passage of small molecules but still retain proteins and larger particles in the bloodstream. Fenestrated capillaries are important in organs that engage in rapid absorption or filtration—the kidneys, endocrine glands, small intestine, and choroid plexuses of the brain, for example.

Sinusoids are irregular blood-filled spaces in the liver, bone marrow, spleen, and some other organs. They are twisted, tortuous passageways that conform to the shape of the surrounding tissue. Some of them are continuous capillaries with very thin walls; others are fenestrated capillaries with extraordinarily large pores that allow the blood plasma to come into direct contact with the perivascular cells. Even proteins and blood cells can pass through these pores; this is how albumin, clotting factors, and other proteins synthesized by the liver enter the blood and how newly formed blood cells enter the circulation from the bone marrow and lymphatic organs.

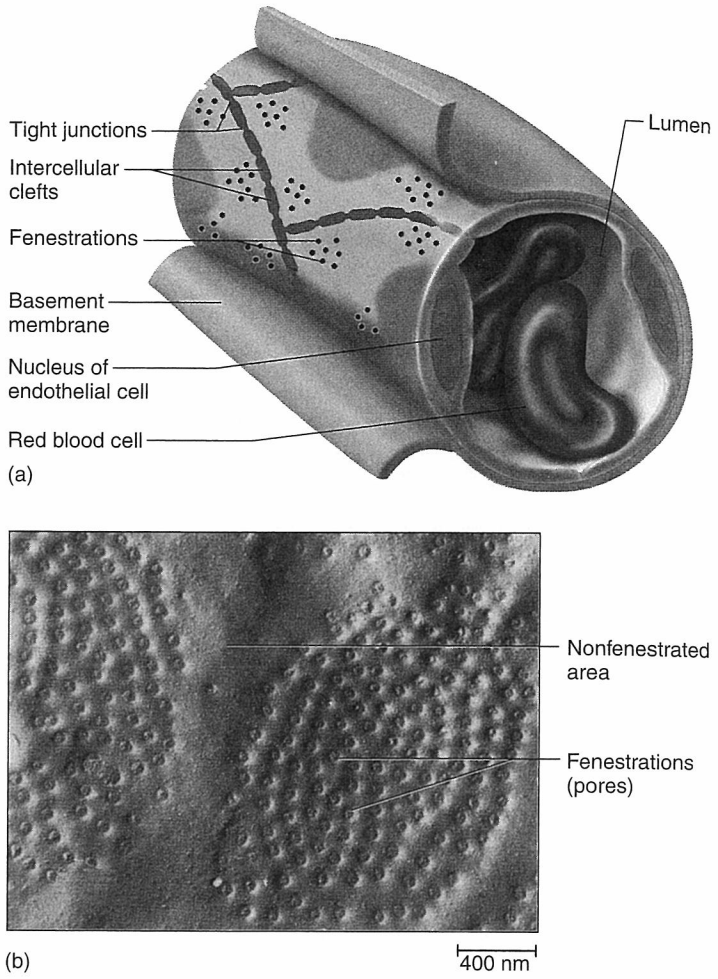


Figure 20.6 A Fenestrated Capillary. (*a*) Structure of the capillary wall. (*b*) Surface view of a fenestrated endothelial cell. The cell has patches of fenestrations separated by nonfenestrated areas.

Veins

After flowing through the capillaries, blood collects in the distal end of the thoroughfare channel and flows into a venule. In the venous circulation, blood flows from smaller vessels into progressively larger ones; hence, instead of giving off *branches* as arteries do, veins receive smaller *tributaries,* just as a river receives water from the many streams that form its tributaries.

Venules range from about 15 to 100 μm in diameter. The proximal part of a venule has only a few fibroblasts around it and is quite porous; therefore venules, like capillaries, exchange fluid with the surrounding tissues. Farther along, a venule acquires a tunica media of smooth muscle. Even the largest veins, however, have relatively sparse muscular and elastic tissue compared to arteries.

Venous sinuses are veins with especially thin walls, large lumens, and no smooth muscle. Examples include the coronary sinus of the heart and the dural sinuses of the brain.

Because they are farther away from the heart, veins have much lower blood pressure than arteries. In large arteries, it averages 90 to 100 mmHg and surges to 120 mmHg during systole, whereas in veins it averages about 10 mmHg and fluctuates very little with the heartbeat. This has significant implications for the form and function of veins:

- Since they need not withstand high pressure, veins have thinner walls than arteries, with less muscular and elastic tissue. They collapse when empty and look

[4] *fenestra* = window

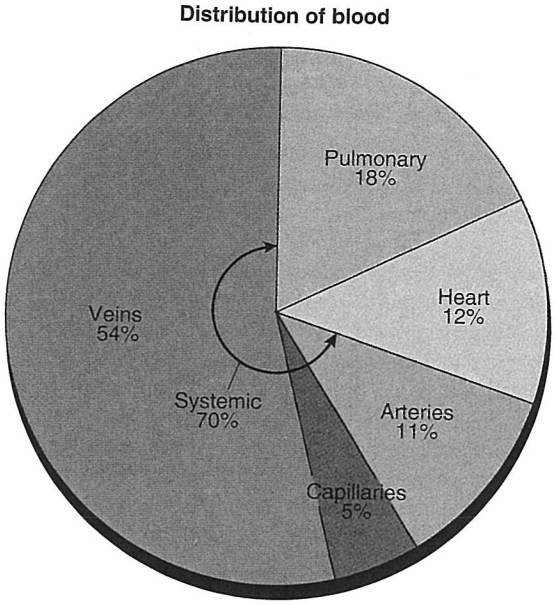


Figure 20.7 **Average Distribution of Blood in a Resting Adult.**

relatively flattened or irregular in histological sections (see fig. 20.3).

- Since their walls are so thin, veins expand more easily and accommodate more blood than arteries do. About 54% of the blood is found in the systemic veins at rest (fig. 20.7); veins are therefore called *capacitance vessels.*
- The pressure in the veins is not high enough to push blood upward against the pull of gravity to the heart. The upward flow of blood depends in part on the massaging action of skeletal muscles and the presence of one-way **venous valves** that keep the blood from dropping down again when the muscles relax (see fig. 20.2). These valves, similar to the semilunar valves of the heart, occur especially in medium veins of the arms and legs; they are absent from very small and very large veins, veins of the ventral body cavity, and veins of the brain. Varicose veins result in part from the failure of these valves (see insight 20.1).

Insight 20.1 Clinical Application

Varicose Veins

In people who stand for long periods, such as dentists and hairdressers, blood tends to pool in the lower limbs and stretch the veins. This is especially true of superficial veins, which are not surrounded by supportive tissue. Stretching pulls the cusps of the venous valves farther apart until the valves become incompetent to prevent the backflow of blood. As the veins become further distended, their walls grow weak and they develop into *varicose veins* with irregular dilations and twisted pathways. Obesity and pregnancy also promote development of varicose veins by putting pressure on large veins of the pelvic region and obstructing drainage from the legs. Varicose veins sometimes develop because of hereditary weakness of the valves. With less drainage of blood, tissues of the leg and foot may become edematous and painful. *Hemorrhoids* are varicose veins of the anal canal.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

1. Explain how an anastomosis and a portal system differ from the simple artery → capillary → vein scheme of circulation.
2. Name the three tunics of a typical blood vessel and explain how they differ from each other.
3. Describe the route of blood flow through a capillary bed.
4. Contrast the two types of capillaries.
5. Explain why many veins have valves but arteries do not.

Blood Pressure, Resistance, and Flow

Objectives

When you have completed this section, you should be able to

- explain the relationship between blood pressure, resistance, and flow;
- describe how blood pressure is expressed and how pulse pressure and mean arterial pressure are calculated;
- describe three factors that determine resistance to blood flow;
- explain how vasomotion influences blood flow; and
- describe some local, neural, and hormonal influences on vasomotion.

Blood flow is the amount of blood flowing through an organ, tissue, or blood vessel in a given time (such as mL/min). **Perfusion** is the flow per given volume or mass of tissue (such as mL/min/g). Perfusion governs the speed of oxygen and nutrient delivery to a tissue and the speed of waste removal. If flow does not keep pace with the metabolic rate of a tissue, the likely result is tissue necrosis and possibly death of the individual. In a resting individual, *total* flow is quite constant and is equal to cardiac output (typically 5.25 L/min). Flow through individual organs, however, varies from minute to minute as blood is redirected from one organ to another. Great variations in regional flow can occur with little or no change in total flow.

Hemodynamics, the physical principles of blood flow, are based mainly on pressure and resistance. The greater the pressure difference (ΔP) between two points, the greater the flow; the greater the resistance (R), the less the flow—in summary, $F \propto \Delta P/R$. Therefore, to understand

the flow of blood, we must consider the factors that affect pressure and resistance.

Blood Pressure

Blood pressure (BP) is the force that the blood exerts against a vessel wall. It can be measured within a blood vessel or heart chamber by inserting a catheter or needle connected to an external manometer (pressure-measuring device). For routine clinical purposes, however, the measurement of greatest interest is the systemic arterial BP at a point close to the heart. As mentioned in chapter 19, we customarily measure it with a sphygmomanometer at the brachial artery of the arm. It is easy to encircle the arm with a pressure cuff, and this artery is sufficiently close to the heart to reflect the maximum arterial BP found anywhere in the systemic circuit.

Two pressures are recorded: **systolic pressure** is the peak arterial BP attained during ventricular systole, and **diastolic pressure** is the minimum arterial BP between heartbeats. For a healthy person aged 20 to 30, these pressures are typically about 120 and 75 mmHg, respectively. Arterial BP is written as a ratio of systolic over diastolic pressure: 120/75.

The difference between systolic and diastolic pressure is called **pulse pressure** (not to be confused with pulse *rate*). For the preceding BP, pulse pressure would be 120 − 75 = 45 mmHg. This is an important measure of the stress exerted on small arteries by the pressure surges generated by the heart. Another measure of stress on the blood vessels is the **mean arterial pressure (MAP)**—the mean pressure you would obtain if you took measurements at several intervals (say every 0.1 sec) throughout the cardiac cycle. Since diastole lasts longer than systole, MAP is not simply the average of systolic and diastolic pressures. The best estimate of MAP is the sum of diastolic pressure and one-third of the pulse pressure. For a blood pressure of 120/75, MAP ≈ 75 + 45/3 = 90 mmHg, a typical value for vessels at the level of the heart. MAP varies, however, with the influence of gravity. In a standing adult, it is about 62 mmHg in the major arteries of the head and 180 mmHg in major arteries of the ankle.

Hypertension (high BP) is commonly considered to be a chronic resting blood pressure higher than 140/90 (see insight 20.4, p. 792). (*Transient* high BP resulting from emotion or exercise is not hypertension.) Among other effects, it can weaken the small arteries and cause **aneurysms**[5] (AN-you-rizms) (see insight 20.2). **Hypotension** is chronic low resting BP. It may be a consequence of blood loss, dehydration, anemia, or other factors and is normal in people approaching death.

[5] *aneurysm* = widening

Insight 20.2 Clinical Application

Aneurysm

An aneurysm is a weak point in a blood vessel or in the heart wall. It forms a thin-walled, bulging sac that pulsates with each beat of the heart and may eventually rupture. In a *dissecting aneurysm,* blood pools between the tunics of a vessel and separates them, usually because of degeneration of the tunica media. The most common sites of aneurysms are the abdominal aorta, the renal arteries, and the arterial circle at the base of the brain. Even without hemorrhaging, aneurysms can cause pain or death by putting pressure on brain tissue, nerves, adjacent veins, pulmonary air passages, or the esophagus. Other consequences include neurological disorders, difficulty in breathing or swallowing, chronic cough, or congestion of the tissues with blood. Aneurysms sometimes result from congenital weakness of the blood vessels and sometimes from trauma or bacterial infections such as syphilis. The most common cause, however, is the combination of atherosclerosis and hypertension.

The ability of the arteries to distend and recoil during the cardiac cycle is important in modulating arterial BP. If the arteries were rigid tubes, pressure would rise much higher in systole and drop to nearly zero in diastole. Blood throughout the circulatory system would flow and stop, flow and stop, thus putting great stress on the small vessels. But when the conducting arteries are healthy, they expand with each systole and absorb some of the force of the ejected blood. Then, when the heart is in diastole, their elastic recoil exerts pressure on the blood and prevents the BP from dropping to zero. The combination of expansion and recoil in the arteries maintains a steady flow of blood downstream, in the capillaries, throughout the cardiac cycle. Thus, the elastic arteries "smooth out" the pressure fluctuations and reduce stress on the smaller arteries.

Nevertheless, blood flow in the arteries is *pulsatile.* Blood in the aorta rushes forward at 120 cm/sec during systole and an average speed of 40 cm/sec over the cardiac cycle. When measured at points farther away from the heart, systolic and diastolic pressures are lower and there is less difference between them (fig. 20.8). In capillaries and veins, the blood flows at a steady speed without pulsation because the pressure surges have been damped out by the distance traveled and the elasticity of the arteries. This is why an injured vein exhibits relatively slow, steady bleeding, whereas blood spurts intermittently from a severed artery. In the inferior vena cava near the heart, however, venous flow fluctuates with the respiratory cycle for reasons explained later, and there is some fluctuation in the jugular veins of the neck.

Think About It

Explain how the histological structure of large arteries relates to their ability to stretch during systole and recoil during diastole.

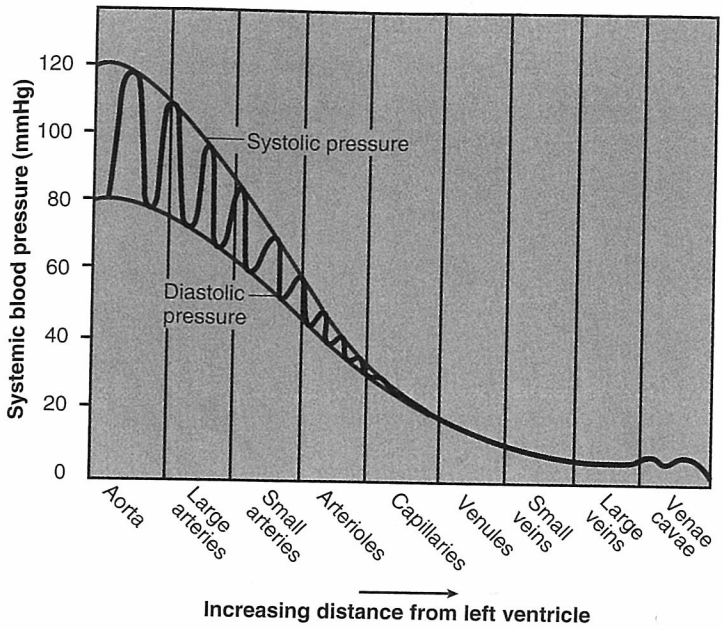


Figure 20.8 Changes in Blood Pressure Related to Distance from the Heart. Because of arterial elasticity and the effect of friction against the vessel wall, all measures of blood pressure decline with distance—systolic pressure, diastolic pressure, pulse pressure, and mean arterial pressure. There is no pulse pressure beyond the arterioles, but there are slight pressure oscillations in the venae cavae caused by the respiratory pump.

Blood pressure rises with age (table 20.1) as the arteries become less distensible and absorb less systolic force. Atherosclerosis also stiffens the arteries and leads to a rise in BP.

Blood pressure is determined mainly by cardiac output, blood volume, and peripheral resistance. The regulation of cardiac output and blood volume are discussed in chapters 19 and 24, respectively. Here, we turn our attention to peripheral resistance.

Resistance

A moving fluid has no pressure unless it encounters at least some resistance. Thus, pressure and resistance are not independent factors in blood flow—rather, pressure is affected by resistance, and flow is affected by both. **Peripheral resistance** is the resistance that the blood encounters in the vessels as it travels away from the heart. It results from the friction of blood against the walls of the vessels and is proportional to three variables: *blood viscosity, vessel length,* and *vessel radius.*

Blood Viscosity

Blood viscosity ("thickness" of the blood) is due mainly to erythrocytes and albumin. A deficiency of erythrocytes (anemia) or albumin (hypoproteinemia) decreases peripheral resistance and speeds up blood flow. If viscosity increases (as a result of polycythemia or dehydration, for example), resistance increases and flow declines.

Table 20.1 Normal Arterial Blood Pressure at Various Ages*

Age (years)	Male	Female
1	96/66	95/65
5	92/62	92/62
10	103/69	103/70
15	112/75	112/76
20	123/76	116/72
25	125/78	117/74
30	126/79	120/75
40	129/81	127/80
50	135/83	137/84
60	142/85	144/85
70	145/82	159/85
80	145/82	157/83

*Average for healthy individuals

Vessel Length

The farther a liquid travels through a tube, the more cumulative friction it encounters; thus, pressure and flow decline with distance. Partly for this reason, if you were to measure MAP in a reclining person, you would obtain a higher value in the arm, for example, than in the ankle. (This would not be true in a standing person because of the influence of gravity, explained earlier.) A strong pulse in the dorsal pedal artery of the foot is a good sign of adequate cardiac output. If perfusion is good at that distance from the heart, it is likely to be good elsewhere in the systemic circulation.

Vessel Radius

In a healthy individual, blood viscosity is quite stable, and of course vessel lengths do not change in the short term. Therefore, the only significant way of controlling peripheral resistance from moment to moment is by adjusting the radius of the blood vessels. A change in vessel radius is called **vasomotion.** This includes **vasoconstriction,** the narrowing of a vessel, and **vasodilation,** the widening of a vessel. Vasoconstriction occurs when the smooth muscle of the tunica media contracts. Vasodilation occurs when this muscle relaxes and allows the blood pressure within the vessel to push its walls outward.

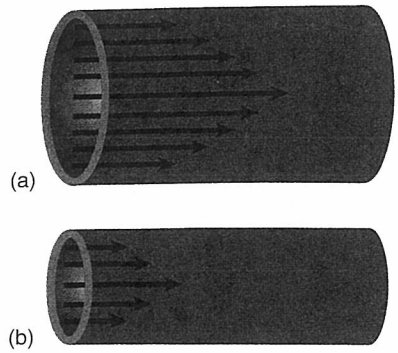


Figure 20.9 Laminar Flow and the Effect of Vessel Radius. Blood flows more slowly near the vessel wall, as indicated by shorter arrows, than it does near the center of the vessel. (*a*) When vessel radius is large, the average velocity of flow is high. (*b*) When the radius is less, the average velocity is lower because a larger portion of the blood is slowed down by friction against the vessel wall.

The effect of vessel radius on blood flow is related to the friction of the moving blood against the walls of the vessel. Blood normally exhibits smooth, silent **laminar**[6] **flow.** That is, it flows in "layers"—faster near the center of a vessel, where it encounters less friction, and slower near the walls, where it drags against the vessel. You can observe a similar effect from the vantage point of a riverbank. The current may be very swift in the middle of a river but quite sluggish near shore, where the water encounters more friction against the riverbank and bottom. When a blood vessel dilates, a greater portion of the blood is in the middle of the stream and the average flow may be quite swift. When the vessel constricts, more of the blood is close to the wall and the average flow is slower (fig. 20.9).

Thus the radius of a vessel markedly affects blood velocity. Indeed, blood flow is proportional not merely to vessel radius but to the *fourth power* of radius—that is, $F \propto r^4$. This makes vessel radius a very potent factor in the control of flow. Arterioles can constrict to as little as one-third of their fully relaxed radius (fig. 20.10). For the sake of simplicity, consider a hypothetical blood vessel with a 1 mm radius when maximally constricted and a 3 mm radius when completely relaxed. At a 1 mm radius, suppose the blood travels 1 mm/sec. By the formula $F \propto r^4$, consider how the velocity would change as radius changed:

$r = 1$ mm	$r^4 = 1^4 = 1$	$F = 1$ mm/sec (given)
$r = 2$ mm	$r^4 = 2^4 = 16$	$F = 16$ mm/sec
$r = 3$ mm	$r^4 = 3^4 = 81$	$F = 81$ mm/sec

These actual numbers do not matter; what matters is that a mere 3-fold increase in radius has produced an 81-fold increase in velocity—a demonstration that vessel radius exerts a very powerful influence over flow; moreover, it is the most adjustable of all variables that govern peripheral resistance.

[6] *lamina* = layer

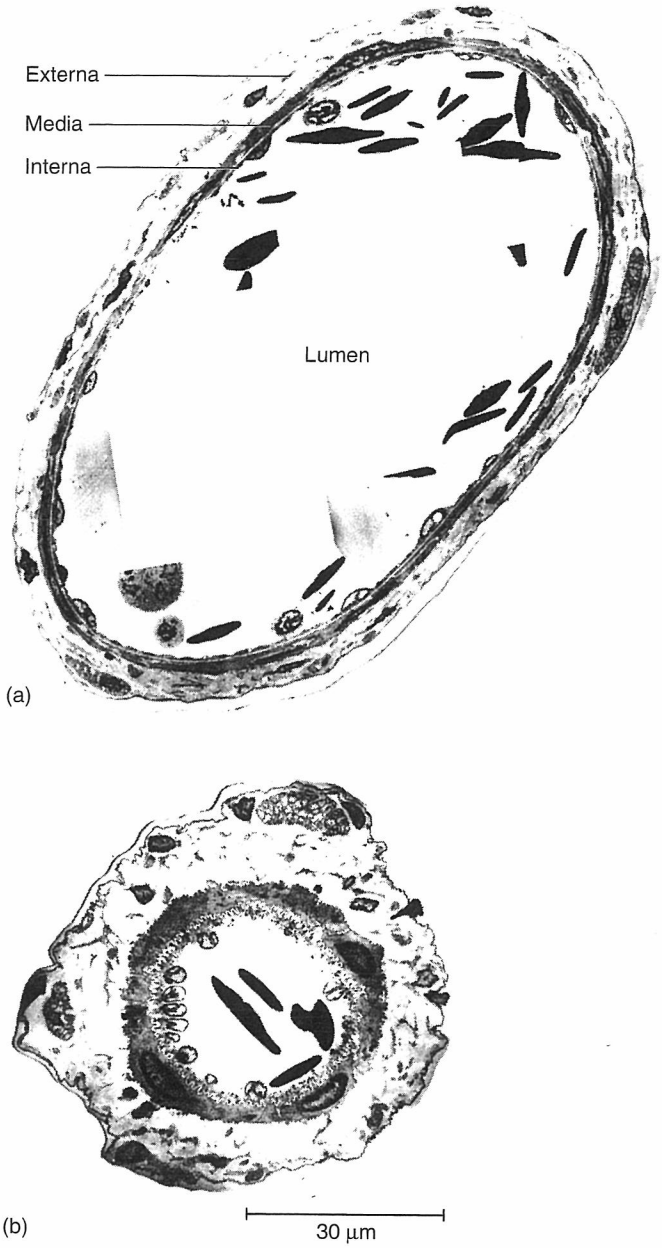


Figure 20.10 The Capacity for Vasoconstriction in an Arteriole. (*a*) A dilated arteriole. (*b*) The same arteriole, at a point just 1 mm from the area photographed in *a*, stimulated by a single drop of epinephrine. The diameter of the dilated region is about three times that of the constricted region.

Think About It

Suppose a vessel with a radius of 1 mm had a flow of 5 mm/sec, and then the vessel dilated to a radius of 5 mm. What would be the new flow rate?

Table 20.2 Blood Velocity in the Systemic Circuit

Vessel	Typical Lumen Diameter	Velocity*
Aorta	2.5 cm	1,200 mm/sec
Arterioles	20–50 μm	15 mm/sec
Capillaries	5–9 μm	0.4 mm/sec
Venules	20 μm	5 mm/sec
Inferior vena cava	3 cm	80 mm/sec

*Peak systolic velocity in the aorta; mean or steady velocity in other vessels

To integrate this information, consider how the velocity of blood flow differs from one part of the systemic circuit to another (table 20.2). Flow is fastest in the aorta because it is a large vessel close to the pressure source, the left ventricle. From aorta to capillaries, velocity diminishes for three reasons: (1) The blood has traveled a greater distance, so friction has slowed it down. (2) The arterioles and capillaries have smaller radii and therefore put up more resistance. (3) Even though the radii of individual vessels become smaller as we progress farther from the heart, the number of vessels and their *total* cross-sectional area becomes greater and greater. The aorta has a cross-sectional area of 3 to 5 cm^2, while the total cross-sectional area of all the capillaries is about 4,500 to 6,000 cm^2. Thus, a given volume of aortic blood is distributed over a greater total area in the capillaries, which *collectively* form a wider path in the bloodstream. Just as water slows down when a narrow mountain stream flows into a lake, blood slows down as it enters pathways with a greater total width.

From capillaries to vena cava, velocity rises again. One reason for this is that the veins have larger diameters than the capillaries, so they create less resistance. Furthermore, since many capillaries converge on one venule, and many venules on a larger vein, a large amount of blood is being forced into a progressively smaller channel—like water flowing from a lake into an outlet stream and thus flowing faster again. Note, however, that blood in the veins never regains the velocity it had in the large arteries. This is because the veins are farther from the heart and the pressure is much lower.

Regulation of Blood Pressure and Flow

Blood pressure is subject to local, neural, and hormonal controls over vasomotion. We now consider each of these three influences in turn.

Local Control

Autoregulation is the ability of tissues to regulate their own blood supply. According to the *metabolic theory of autoregulation,* if a tissue is inadequately perfused, it becomes hypoxic and its metabolites (waste products) accumulate—CO_2, H^+, K^+, lactic acid, and adenosine, for example. These factors stimulate vasodilation, which increases perfusion. As the bloodstream delivers oxygen and carries away the metabolites, the vessels constrict. Thus, a homeostatic dynamic equilibrium is established that adjusts perfusion to the tissue's metabolic needs.

Blood platelets, endothelial cells, and the perivascular tissues secrete a variety of **vasoactive chemicals**—substances that stimulate vasomotion. Histamine, bradykinin, and prostaglandins stimulate vasodilation under such conditions as trauma, inflammation, and exercise. Endothelial cells secrete prostacyclin and nitric oxide, which are vasodilators, and polypeptides called *endothelins,* which are vasoconstrictors.

If a tissue's blood supply is cut off for a time and then restored, it often exhibits **reactive hyperemia**—an increase above the normal level of flow. This may be due to the accumulation of metabolites during the period of ischemia. Reactive hyperemia can be seen when the skin flushes after a person comes in from the cold. It also occurs in the forearm if a blood pressure cuff is inflated for too long and then loosened.

In the long run, a hypoxic tissue can increase its own perfusion by **angiogenesis**[7]—the growth of new blood vessels. (This term also refers to embryonic development of blood vessels.) Three situations in which this is important are the regrowth of the uterine lining after each menstrual period, the development of a higher density of blood capillaries in the muscles of well-conditioned athletes, and the growth of arterial bypasses around obstructions in the coronary circulation. Several growth factors and inhibitors control angiogenesis, but physiologists are not yet sure how it is regulated. Malignant tumors secrete growth factors that stimulate a dense network of blood vessels to grow into them and provide nourishment to the cancer cells. Oncologists are interested in finding a way to block tumor angiogenesis, which would choke off a tumor's blood supply and perhaps shrink or kill it.

Neural Control

In addition to local control, the blood vessels are under remote control by hormones and the autonomic nervous system. The **vasomotor center** of the medulla oblongata exerts sympathetic control over blood vessels throughout the body. (Precapillary sphincters have no innervation, however, and respond only to local and hormonal stimuli.)

[7] *angio* = vessels + *genesis* = production of

Sympathetic nerve fibers stimulate most blood vessels to constrict, but they dilate the vessels of skeletal and cardiac muscle in order to meet the metabolic demands of exercise. The role of sympathetic tone and vasomotor tone in controlling vessel diameter is explained in chapter 15.

The vasomotor center is an integrating center for three autonomic reflexes—*baroreflexes, chemoreflexes,* and the *medullary ischemic reflex.* A **baroreflex** is an autonomic, negative feedback response to changes in blood pressure. The changes are detected by stretch receptors called **baroreceptors.**[8] These occur in all of the large arteries above the heart but are especially concentrated in the aortic arch, the *aortic sinuses* behind the aortic valve cusps, and the *carotid sinus* at the base of each internal carotid artery near the angle of the mandible (fig. 20.11). They are branched, knobby nerve fibers somewhat resembling Golgi tendon organs (see p. 508). The baroreceptors transmit signals continually to the brainstem. When the blood pressure rises, their signaling rate rises. This input inhibits the sympathetic cardiac and vasomotor neurons and reduces sympathetic tone, and it *excites* the vagal fibers to the heart. Thus, it reduces the heart rate and cardiac output, dilates the arteries and veins, and reduces the blood pressure (fig. 20.12). When BP drops below normal, on the other hand, the opposite reactions occur and BP rises back to normal.

Baroreflexes are important chiefly in short-term regulation of BP, for example in adapting to changes in posture. Perhaps you have jumped quickly out of bed and felt a little dizzy for a moment. This occurs because gravity draws the blood into the large veins of the abdomen and lower limbs when you stand, which reduces venous return to the heart and cardiac output to the brain. Normally, the baroreceptors respond quickly to this drop in pressure and restore cerebral perfusion. Baroreflexes are not effective in correcting chronic hypertension, however. Apparently they adjust their set point to the higher BP and maintain dynamic equilibrium at this new level.

A **chemoreflex** is an autonomic response to changes in blood chemistry, especially its pH and concentrations of O_2 and CO_2. It is initiated by chemoreceptors within small organs called **aortic bodies** and **carotid bodies,** located in the aortic arch, subclavian arteries, and external carotid arteries. The primary role of chemoreflexes is to adjust respiration to changes in blood chemistry, but they have a secondary role in stimulating vasomotion. Hypoxemia (O_2 deficiency), hypercapnia (CO_2 excess), and aci-

[8] *baro* = pressure

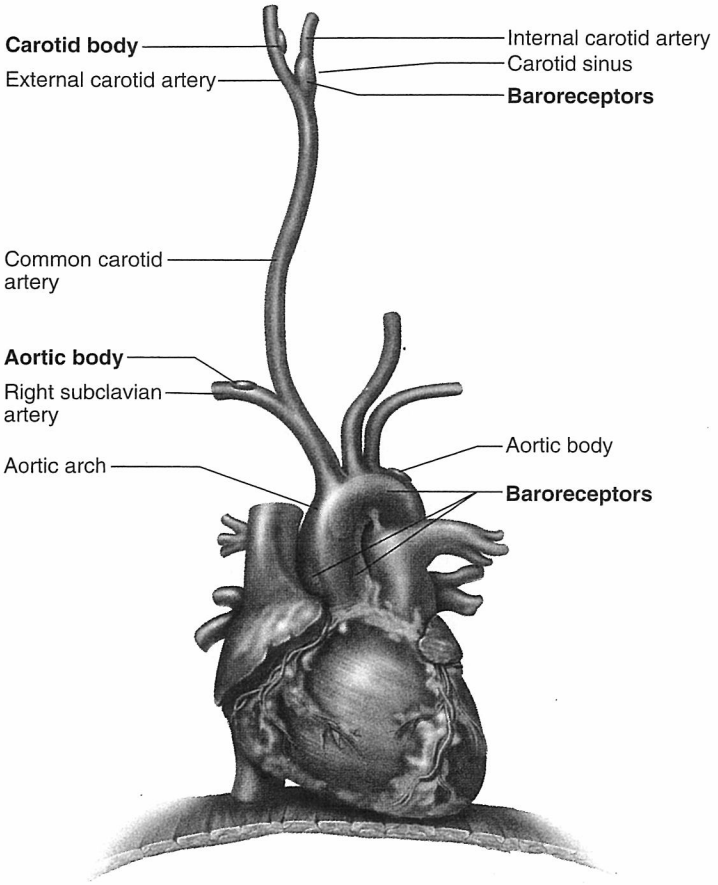


Figure 20.11 Locations of Arterial Baroreceptors and Chemoreceptors. Chemoreceptors are located in the carotid bodies and aortic bodies. Baroreceptors are located in the ascending aorta, aortic arch, and carotid sinus. The structures shown here in the *right* carotid arteries are repeated in the *left* carotids.

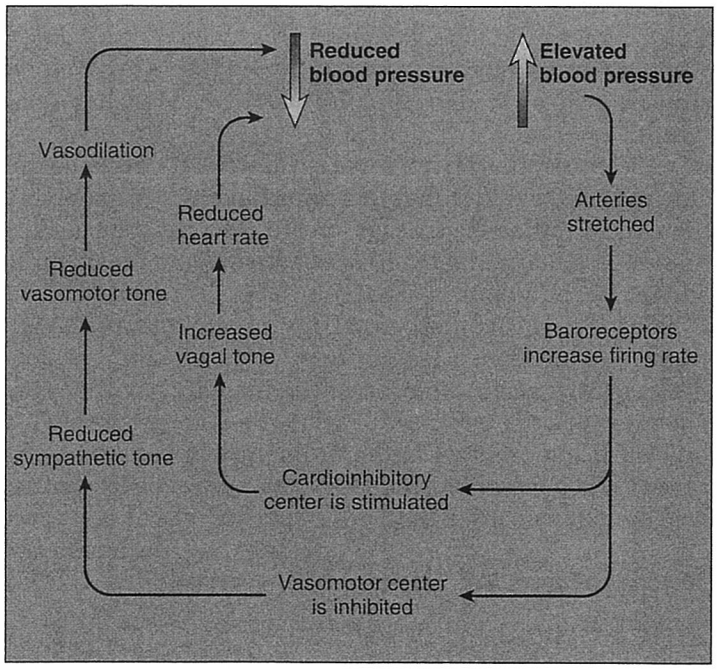


Figure 20.12 Negative Feedback Control of Blood Pressure. The reactions here occur in response to a rise in blood pressure.

dosis (low blood pH) stimulate the chemoreceptors and act through the vasomotor center to cause widespread vasoconstriction. This increases overall BP, thus increasing perfusion of the lungs and the rate of gas exchange. Chemoreceptors also stimulate one's breathing, so increased ventilation of the lungs matches their increased perfusion. Increasing one without the other would be of little use.

The **medullary ischemic** (iss-KEE-mic) **reflex** is an autonomic response to a drop in perfusion of the brain. Within seconds, the cardiac and vasomotor centers of the medulla oblongata send sympathetic signals to the heart and blood vessels that induce (1) an increase in heart rate and contraction force and (2) widespread vasoconstriction. These actions raise the blood pressure and, ideally, restore normal perfusion of the brain. The cardiac and vasomotor centers also receive input from other brain centers. Thus stress, anger, and arousal can also raise the blood pressure. The hypothalamus acts through the vasomotor center to redirect blood flow in response to exercise or changes in body temperature.

Hormonal Control

All of the following hormones influence blood pressure:

- **Angiotensin II.** This is a potent vasoconstrictor that raises the blood pressure. Its synthesis and action are detailed in chapter 23 (see fig. 23.13). One of the enzymes required for its synthesis is *angiotensin-converting enzyme (ACE).* Hypertension is often treated with drugs called *ACE inhibitors,* which block the action of this enzyme, thus lowering angiotensin II levels and blood pressure.
- **Aldosterone.** This "salt-retaining hormone" primarily promotes Na^+ retention by the kidneys. Since water follows sodium osmotically, Na^+ retention promotes water retention, thus promoting a higher blood volume and pressure.
- **Atrial natriuretic peptide.** ANP, secreted by the heart, antagonizes aldosterone. It increases Na^+ excretion by the kidneys, thus reducing blood volume and pressure. It also has a generalized vasodilator effect that contributes to lowering the blood pressure.
- **Antidiuretic hormone.** ADH primarily promotes water retention, but at pathologically high concentrations it is also a vasoconstrictor—hence its alternate name, *vasopressin.* Both of these effects raise blood pressure.
- **Epinephrine and norepinephrine.** These adrenal and sympathetic catecholamines bind to α-adrenergic receptors on the smooth muscle of most blood vessels. This stimulates the muscle to contract, thus producing vasoconstriction and raising the blood pressure. In the coronary blood vessels and blood vessels of the skeletal muscles, however, these chemicals bind to β-adrenergic receptors and cause vasodilation, thus increasing blood flow to the myocardium and muscular system during exercise.

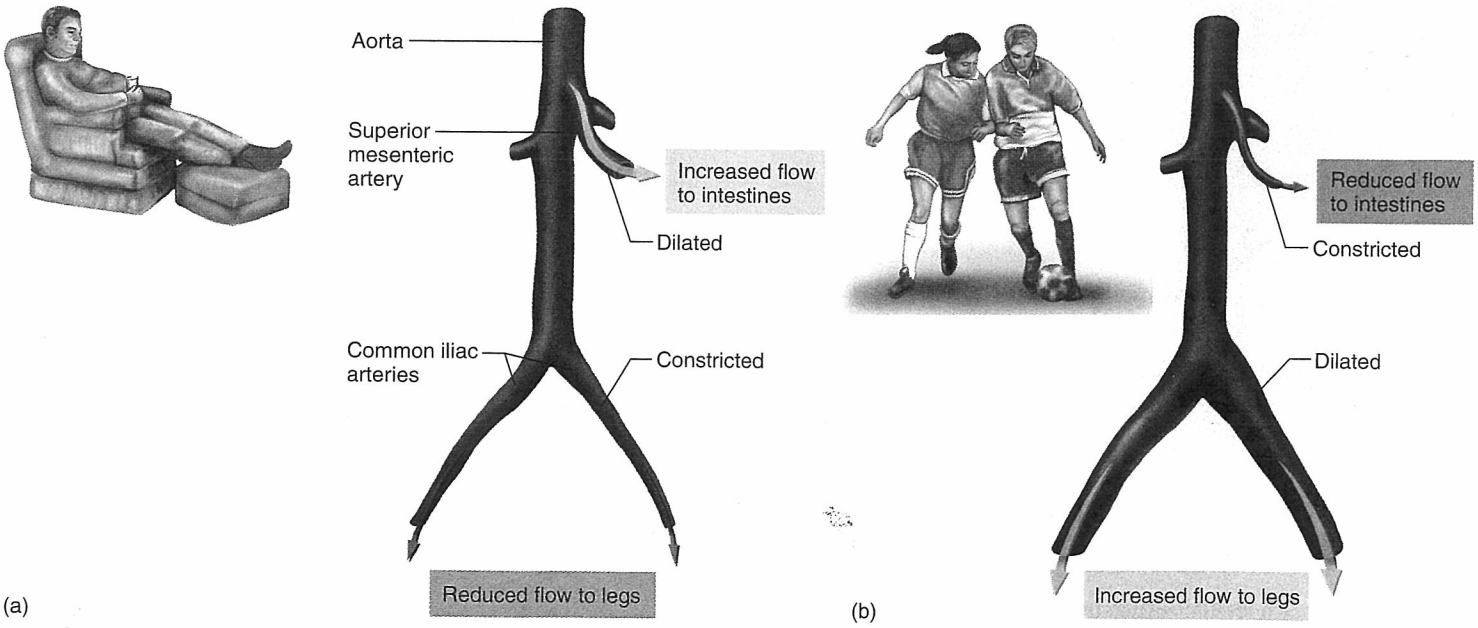
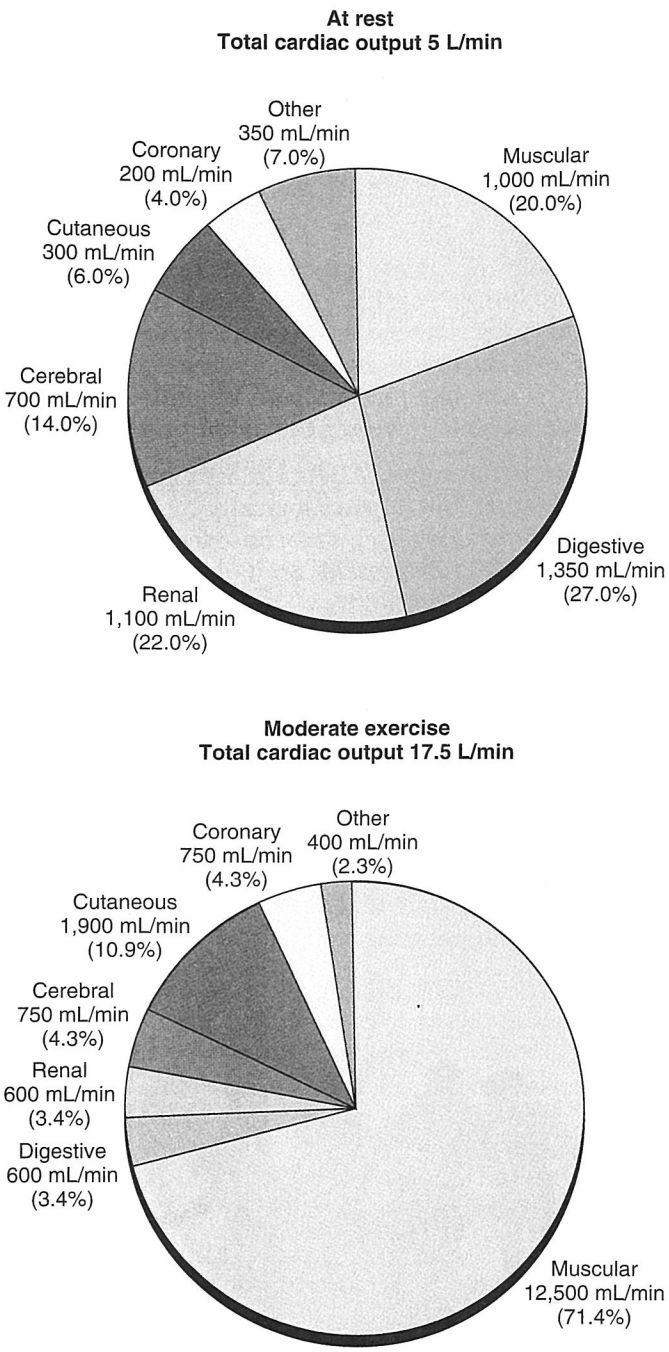


Figure 20.13 Redirection of Blood Flow in Response to Changing Metabolic Needs. (*a*) After a meal, the intestines receive priority and the skeletal muscles receive relatively little flow. (*b*) During exercise, the muscles receive higher priority. Although vasodilation and vasoconstriction are shown here in major arteries for illustration purposes, most control occurs at a microscopic level in the arterioles.



igure 20.14 Changes in Systemic Blood Flow During Rest nd Exercise.

Vasomotion and Routing of Blood Flow

f a chemical such as epinephrine causes widespread vasoonstriction, or if it causes vasoconstriction in a large sysem such as the integumentary or digestive system, it can roduce an overall rise in blood pressure. Localized vasoonstriction, however, has a very different effect. If a particular artery constricts, pressure downstream from the constriction drops and pressure upstream from it rises. If blood can travel by either of two routes and one route puts up more resistance than the other, most blood follows the path of least resistance. This mechanism enables the body to redirect blood from one organ to another.

For example, if you are dozing in an armchair after a big meal, vasoconstriction shuts down blood flow to 90% or more of the capillaries in the muscles of your lower limbs. This raises the BP above the limbs, where the aorta gives off a branch, the superior mesenteric artery, supplying the small intestine. High resistance in the circulation of the legs and low resistance in the superior mesenteric artery routes blood to the small intestine, where it is needed to absorb digested nutrients (fig. 20.13*a*).

On the other hand, during vigorous exercise, the arteries in your muscles dilate. To make blood available to the muscles, flow must be reduced elsewhere—notably in the skin, kidneys, and digestive tract (fig. 20.13*b*). Thus, changes in peripheral resistance can shift blood flow from one organ system to another to meet the changing metabolic priorities of the body. Physical exertion increases perfusion of the lungs, myocardium, and skeletal muscles while reducing perfusion of the kidneys and digestive tract (fig. 20.14).

The arterioles are the most significant point of control over peripheral resistance and blood flow because (1) they are on the proximal sides of the capillary beds, so they are best positioned to regulate flow into the capillaries; (2) they greatly outnumber any other class of arteries and thus provide the most numerous control points; and (3) they are more muscular in proportion to their diameters than any other class of blood vessels and are highly capable of vasomotion. Arterioles alone account for about half of the total peripheral resistance of the circulatory system. However, larger arteries and veins are also capable of considerable vasomotion and control of peripheral resistance.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

6. For a healthy 15-year-old girl at rest, what would be typical readings for systolic pressure, diastolic pressure, pulse pressure, and mean arterial pressure?
7. Explain why arterial blood flow is pulsatile and venous flow is not.
8. What three variables affect peripheral resistance to blood flow? Which of these is most able to change from one minute to the next?
9. What are the three primary mechanisms for controlling vessel radius? Briefly explain each.
10. Explain how the baroreflex serves as an example of homeostasis and negative feedback.
11. Explain how the body can shift the flow of blood from one organ system to another.

Capillary Exchange

Objectives

When you have completed this section, you should be able to

- describe how materials get from the blood to the surrounding tissues;
- describe and calculate the forces that enable capillaries to give off and reabsorb fluid; and
- describe the causes and effects of edema.

Only 250 to 300 mL of blood is in the capillaries at any given time. This is the most important blood in the body, however, for it is mainly across capillary walls that exchanges occur between the blood and surrounding tissues. **Capillary exchange** refers to this two-way movement of fluid.

Substances pass between the blood and tissue fluid by three routes: (1) through the intercellular clefts between endothelial cells, (2) through the fenestrations (pores) of fenestrated capillaries, and (3) through the endothelial cell cytoplasm (fig. 20.15). The mechanisms involved are *diffusion, transcytosis, filtration,* and *reabsorption,* which we examine in that order.

Diffusion

The most important mechanism of exchange is diffusion. Glucose and oxygen, being more concentrated in the systemic blood than in the tissue fluid, diffuse out of the blood. Carbon dioxide and other wastes, being more concentrated in the tissue fluid, diffuse into the blood. (Oxygen and carbon dioxide diffuse in the opposite directions in the pulmonary circuit.) Such diffusion is only possible if the solute can either permeate the plasma membranes of the endothelial cells or find passages large enough to pass through—namely, the fenestrations and intercellular clefts. Such lipid-soluble substances as steroid hormones, O_2, and CO_2 diffuse easily through the plasma membranes. Substances insoluble in lipids, such as glucose and electrolytes, must pass through membrane channels, fenestrations, or intercellular clefts. Large molecules such as proteins are usually held back by the small size of these passages.

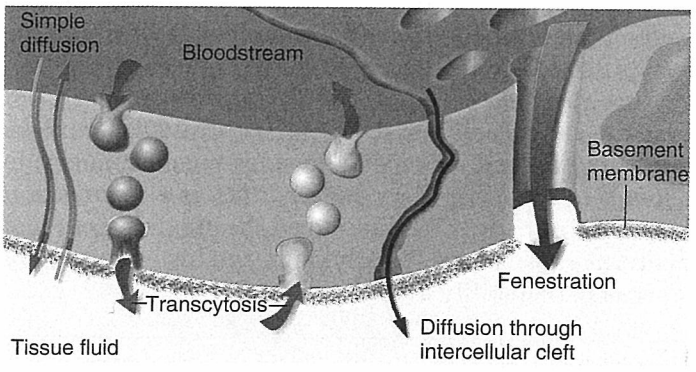


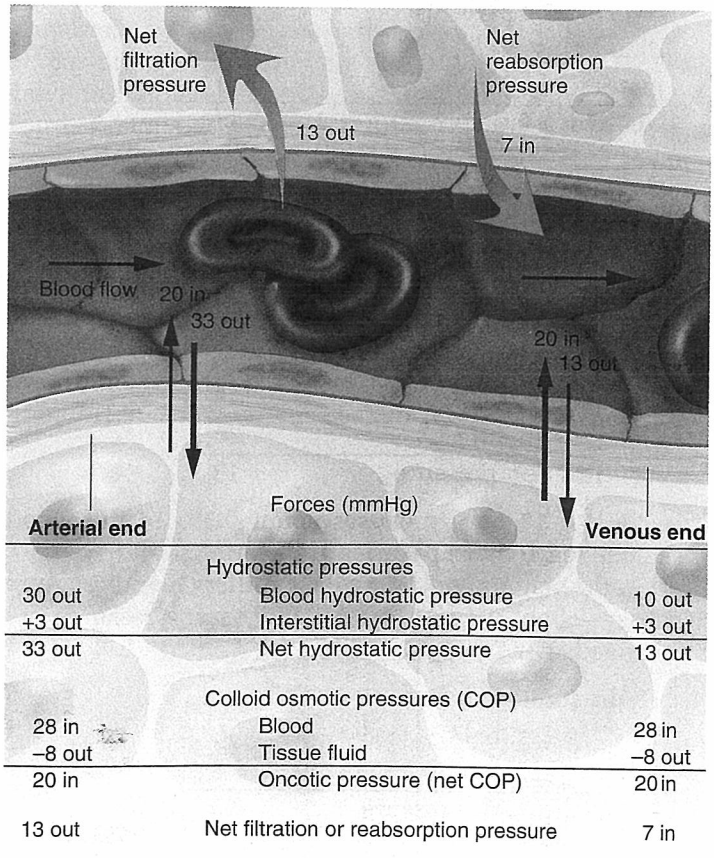
Figure 20.15 Pathways of Capillary Fluid Exchange.

Transcytosis

Transcytosis is a process in which endothelial cells pick up droplets of fluid on one side of the plasma membrane by pinocytosis, transport the vesicles across the cell, and discharge the fluid on the other side by exocytosis (see fig. 3.23, p. 114). This probably accounts for only a small fraction of solute exchange across the capillary wall, but fatty acids, albumin, and some hormones such as insulin move across the endothelium by this mechanism.

Filtration and Reabsorption

The equilibrium between filtration and osmosis discussed in chapter 3 becomes particularly relevant when we consider capillary fluid exchange. Typically, fluid filters out of the arterial end of a capillary and osmotically reenters it at the venous end (fig. 20.16). This fluid delivers materials to the cells and removes their metabolic wastes.



	Hydrostatic pressures	
30 out	Blood hydrostatic pressure	10 out
+3 out	Interstitial hydrostatic pressure	+3 out
33 out	Net hydrostatic pressure	13 out
	Colloid osmotic pressures (COP)	
28 in	Blood	28 in
−8 out	Tissue fluid	−8 out
20 in	Oncotic pressure (net COP)	20 in
13 out	Net filtration or reabsorption pressure	7 in

Figure 20.16 The Forces of Capillary Filtration and Reabsorption. Note the shift from net filtration at the arterial (*left*) end to net reabsorption at the venous (*right*) end.

It may seem odd that a capillary could give off fluid at one point and reabsorb it at another. This comes about as the result of a shifting balance between hydrostatic and osmotic forces. A typical capillary has a blood (hydrostatic) pressure of about 30 mmHg at the arterial end. The hydrostatic pressure of the interstitial space has been difficult to measure and remains a point of controversy, but a typical value accepted by many authorities is −3 mmHg. The negative value indicates that this is a slight suction, which helps draw fluid out of the capillary. (This force will be represented hereafter as 3_{out}.) In this case, the positive hydrostatic pressure within the capillary and the negative interstitial pressure work in the same direction, creating a total outward force of about 33 mmHg.

These forces are opposed by **colloid osmotic pressure (COP),** the portion of the blood's osmotic pressure due to its plasma proteins. The blood has a COP of about 28 mmHg, due mainly to albumin. Tissue fluid has less than one-third the protein concentration of blood plasma and has a COP of about 8 mmHg. The difference between the COP of blood and COP of tissue fluid is called **oncotic pressure:** $28_{in} - 8_{out} = 20_{in}$. Oncotic pressure tends to draw water into the capillary by osmosis, opposing hydrostatic pressure. These opposing forces produce a **net filtration pressure (NFP)** of 13 mmHg out, as follows:

Hydrostatic pressure	
Blood pressure	30_{out}
Interstitial pressure	$+ 3_{out}$
Net hydrostatic pressure	33_{out}

Colloid osmotic pressure	
Blood COP	28_{in}
Tissue fluid COP	$- 8_{out}$
Oncotic pressure	20_{in}

Net filtration pressure	
Net hydrostatic pressure	33_{out}
Oncotic pressure	$- 20_{in}$
Net filtration pressure	13_{out}

The NFP of 13 mmHg causes about 0.5% of the blood plasma to leave the capillaries at the arterial end.

At the venous end, however, capillary blood pressure is lower—about 10 mmHg. All the other pressures are unchanged. Thus, we get:

Hydrostatic pressure	
Blood pressure	10_{out}
Interstitial pressure	$+ 3_{out}$
Net hydrostatic pressure	13_{out}

Net reabsorption pressure	
Oncotic pressure	20_{in}
Net hydrostatic pressure	$- 13_{out}$
Net reabsorption pressure	7_{in}

The prevailing force is inward at the venous end because osmotic pressure overrides filtration pressure. The **net reabsorption pressure** of 7 mmHg inward causes the capillary to reabsorb fluid at this end.

Now you can see why a capillary gives off fluid at one end and reabsorbs it at the other. The only pressure that changes from the arterial end to the venous end is the capillary blood pressure, and this change is responsible for the shift from filtration to reabsorption. With a reabsorption pressure of 7 mmHg and a net filtration pressure of 13 mmHg, it might appear that far more fluid would leave the capillaries than reenter them. However, since capillaries branch along their length, there are more of them at the venous end than at the arterial end, which partially compensates for the difference between filtration and reabsorption pressures. They also typically have nearly twice the diameter at the venous end that they have at the arterial end, so there is more capillary surface area available to reabsorb fluid than to give it off. Consequently, capillaries reabsorb about 85% of the fluid they filter. The other 15% is absorbed and returned to the blood by way of the lymphatic system, as described in chapter 21.

Of course, water is not the only substance that crosses the capillary wall by filtration and reabsorption. It carries along many of the solutes dissolved in it. This process is called **solvent drag.**

Variations in Capillary Filtration and Reabsorption

The figures used in the preceding discussion serve only as examples; circumstances differ from place to place in the body and from time to time in the same capillaries. Capillaries usually reabsorb most of the fluid they filter, but this is not always the case. The kidneys have capillary networks called *glomeruli* in which there is little or no reabsorption; they are entirely devoted to filtration. Alveolar capillaries of the lungs, by contrast, are almost entirely dedicated to absorption so that fluid does not fill the air spaces.

Capillary activity also varies from moment to moment. In a resting tissue, most precapillary sphincters are constricted and the capillaries are collapsed. Capillary BP is very low (if there is any flow at all), and reabsorption predominates. When a tissue becomes metabolically active, its capillary flow increases. In active muscles, capillary pressure rises to the point that it overrides reabsorption along the entire length of the capillary. Fluid accumulates in the muscle, and exercising muscles increase in size by as much as 25%. Capillary permeability is also subject to chemical influences. Traumatized tissue releases such chemicals as substance P, bradykinin, and histamine, which increase permeability and filtration.

Edema

Edema is the accumulation of excess fluid in a tissue. It often shows as swelling of the face, fingers, abdomen, or

ankles but also affects internal organs, where its effects are hidden from view. Edema occurs when fluid filters into a tissue faster than it is reabsorbed. It has three fundamental causes:

1. **Increased capillary filtration.** This results from increases in capillary BP or permeability. Poor venous return, for example, causes pressure to back up into the capillaries. Congestive heart failure and incompetent heart valves can impede venous return from the lungs and cause pulmonary edema. Systemic edema is a common problem when a person is confined to a bed or wheelchair, with insufficient muscular activity to promote venous return. Kidney failure leads to edema by causing water retention and hypertension. Histamine causes edema by dilating the arterioles and making the capillaries more permeable. Capillary permeability also increases with age, which puts older people at risk of edema.
2. **Reduced capillary reabsorption.** Capillary reabsorption depends on oncotic pressure, which is proportional to the concentration of blood albumin. A deficiency of blood albumin (hypoproteinemia) produces edema because the capillaries osmotically reabsorb even less of the fluid that they give off. Since blood albumin is produced by the liver, liver diseases such as cirrhosis tend to lead to hypoproteinemia and edema. Edema is commonly seen in regions of famine due to dietary protein deficiency. Hypoproteinemia also commonly results from severe burns, radiation sickness, and kidney diseases that allow protein to escape in the urine.
3. **Obstructed lymphatic drainage.** The lymphatic system, described in detail in chapter 21, is a system of one-way vessels that collect fluid from the tissues and return it to the bloodstream. Obstruction of these vessels or the surgical removal of lymph nodes can interfere with fluid drainage and lead to the accumulation of tissue fluid distal to the obstruction.

In severe edema, so much fluid may transfer from the blood vessels to the tissue spaces that blood volume and pressure drop so low as to cause circulatory shock (described later in this chapter). Furthermore, as the tissues become swollen with fluid, oxygen delivery and waste removal are impaired and tissue necrosis may occur. Pulmonary edema presents a threat of suffocation, and cerebral edema can produce headaches, nausea, and sometimes seizures and coma.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

12. List the three mechanisms of capillary exchange and relate each one to the structure of capillary walls.
13. What forces favor capillary filtration? What forces favor reabsorption?
14. How can a capillary shift from a predominantly filtering role at one time to a predominantly reabsorbing role at another?
15. State the three fundamental causes of edema and explain why edema can be dangerous.

Venous Return and Circulatory Shock

Objectives

When you have completed this section, you should be able to

- explain how blood in the veins is returned to the heart;
- discuss the importance of physical activity in venous return;
- discuss several causes of circulatory shock; and
- name and describe the stages of shock.

Hieronymus Fabricius (1537–1619) discovered the valves of the veins and argued that they would allow blood to flow in only one direction, not back and forth as Galen had thought. One of his medical students was William Harvey, who performed simple experiments on the valves that you can easily reproduce. In figure 20.17, from Harvey's book, the experimenter has pressed on a vein at point *H* to block flow from the wrist toward the elbow. With another finger, he has milked the blood out of it up to point *O,* the first valve proximal to *H.* When he tries to force blood downward, it stops at that valve. It can go no farther, and it causes the vein to swell at that point. Blood can flow from right to left through that valve but not from left to right.

You can easily demonstrate the action of these valves in your own hand. Hold your hand still, below waist level, until veins stand up on the back of it. (Do not apply a tourniquet!) Press on a vein close to your knuckles, and while holding it down, use another finger to milk that vein toward the wrist. It collapses as you force the blood out of it, and if you remove the second finger, it will not refill.

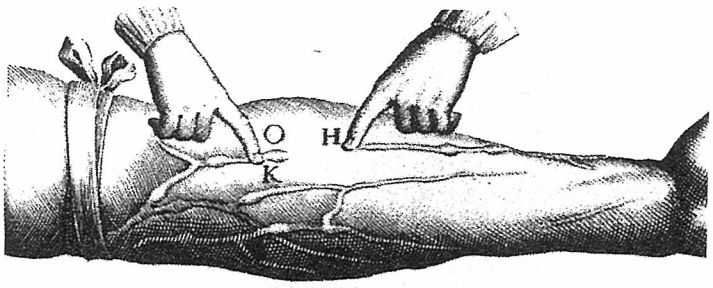


Figure 20.17 An Illustration from William Harvey's *De Motu Cordis* (1628). These experiments demonstrate the existence of one-way valves in veins of the arms. See text for explanation.
In the space between *O* and *H,* what (if anything) would happen if the experimenter lifted his finger from point *O?* What if he lifted his finger from point *H?* Why?

e valves prevent blood from flowing back into it from ove. When you remove the first finger, however, the vein s from below.

echanisms of Venous Return

e flow of blood back to the heart, called **venous return,** achieved by five mechanisms:

1. **The pressure gradient.** Pressure generated by the heart is the most important force in venous flow, even though it is substantially weaker in the veins than in the arteries. Pressure in the venules ranges from 12 to 18 mmHg, and pressure at the point where the venae cavae enter the heart, called **central venous pressure,** averages 4.6 mmHg. Thus, there is a venous pressure gradient (ΔP) of about 7 to 13 mmHg favoring the flow of blood toward the heart. The pressure gradient and venous return increase when blood volume increases. Venous return decreases when the veins constrict *(venoconstriction)* and oppose flow, and it increases when they dilate and offer less resistance. However, it increases if *all* the body's blood vessels constrict, because this reduces the "storage capacity" of the circulatory system and raises blood pressure and flow.
2. **Gravity.** When you are sitting or standing, blood from your head and neck returns to the heart simply by "flowing downhill" by way of the large veins above the heart. Thus the large veins of the neck are normally collapsed or nearly so, and their venous pressure is close to zero. The dural sinuses, however, have more rigid walls and cannot collapse. Their pressure is as low as −10 mmHg, creating a risk of *air embolism* if they are punctured (see insight 20.3).
3. **The skeletal muscle pump.** In the limbs, the veins are surrounded and massaged by the muscles. They squeeze the blood out of the compressed part of a vein, and the valves ensure that this blood can go in only one direction—toward the heart (fig. 20.18).
4. **The thoracic (respiratory) pump.** This mechanism aids the flow of venous blood from the abdominal to the thoracic cavity. When you inhale, your thoracic cavity expands and its internal pressure drops, while downward movement of the diaphragm raises the pressure in your abdominal cavity. The *inferior vena cava (IVC),* your largest vein, is a flexible tube passing through both of these cavities. If abdominal pressure on the IVC rises while thoracic pressure on it drops, then blood is squeezed upward toward the heart. It is not forced back into the lower limbs because the venous valves there prevent this. Because of the thoracic pump, central venous pressure fluctuates from 2 mmHg when you inhale to 6 mmHg when you exhale, and blood flows faster when you inhale.

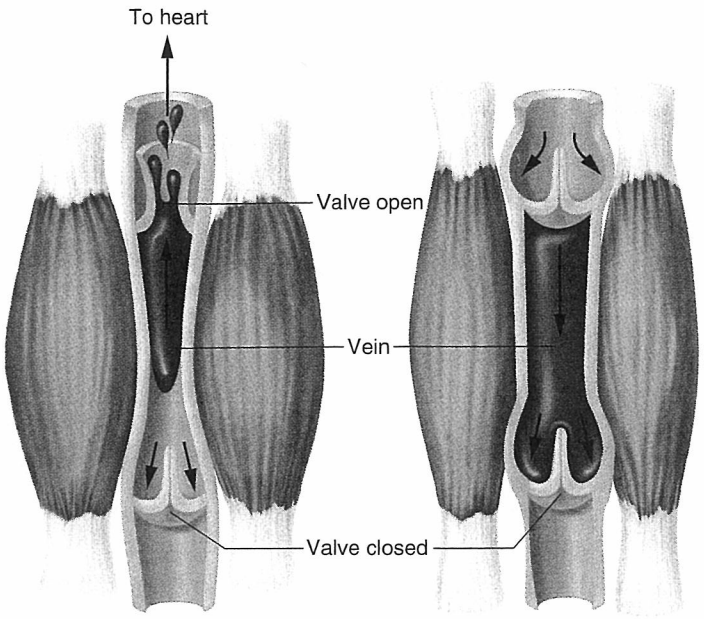


Figure 20.18 The Skeletal Muscle Pump. (*a*) When the muscles contract and compress a vein, blood is squeezed out of it and flows upward toward the heart; valves below the point of compression prevent backflow of the blood. (*b*) When the muscles relax, blood flows back downward under the pull of gravity but can only flow as far as the nearest valve.

5. **Cardiac suction.** During ventricular systole, the chordae tendineae pull the AV valve cusps downward, slightly expanding the atrial space. This creates a slight suction that draws blood into the atria from the venae cavae and pulmonary veins.

Insight 20.3 Clinical Application

Air Embolism

Injury to the dural sinuses or jugular veins presents less danger from loss of blood than from air sucked into the circulatory system. The presence of air in the bloodstream is called *air embolism.* This is an important concern to neurosurgeons, who sometimes operate with the patient in a sitting position. If a dural sinus is punctured, air can be sucked into the sinus and accumulate in the heart chambers, which blocks cardiac output and causes sudden death. Smaller air bubbles in the systemic circulation can cut off blood flow to the brain, lungs, myocardium, and other vital tissues.

Venous Return and Physical Activity

Exercise increases venous return for many reasons. The heart beats faster and harder, increasing cardiac output and

blood pressure. Blood vessels of the skeletal muscles, lungs, and heart dilate, increasing flow. The increase in respiratory rate and depth enhances the action of the thoracic pump. Muscle contractions increase venous return by the skeletal muscle pump mechanism. Increased venous return increases cardiac output, which is important in perfusion of the muscles just when they need it most.

Conversely, when a person is still, blood accumulates in the limbs because venous pressure is not high enough to override the weight of the blood and drive it upward. Such accumulation of blood is called **venous pooling.** To demonstrate this effect, hold one hand above your head and the other below your waist for about a minute. Then, quickly bring your two hands together and compare the palms. The hand held above your head usually appears pale because its blood has drained out of it; the hand held below the waist appears redder than normal because of venous pooling in its veins and capillaries. Venous pooling is troublesome to people who must stand for prolonged periods. If enough blood accumulates in the limbs, cardiac output may become so low that the brain is inadequately perfused and a person may experience dizziness or **syncope** (SIN-co-pee) (fainting). This can usually be prevented by periodically tensing the calf and other muscles to keep the skeletal muscle pump active. Military jet pilots often perform maneuvers that could cause the blood to pool in the abdomen and lower limbs, causing partial loss of vision or loss of consciousness. To prevent this, they wear pressure suits that inflate and tighten on the lower limbs during these maneuvers; in addition, they sometimes must tense their abdominal muscles to prevent venous pooling and blackout.

Think About It

Why is venous pooling not a problem when you are sleeping and the skeletal muscle pump is inactive?

Circulatory Shock

Circulatory shock (not to be confused with electrical or spinal shock) is any state in which cardiac output is insufficient to meet the body's metabolic needs. All forms of circulatory shock fall into two categories: (1) **cardiogenic shock,** caused by inadequate pumping by the heart usually as a result of myocardial infarction, and (2) **low venous return (LVR) shock,** in which cardiac output is low because too little blood is returning to the heart.

There are three principal forms of LVR shock:

1. **Hypovolemic shock,** the most common form, is produced by a loss of blood volume as a result of hemorrhage, trauma, bleeding ulcers, burns, or dehydration. Dehydration is a major cause of death from heat exposure. In hot weather, the body produces as much as 1.5 L of sweat per hour. Water transfers from the bloodstream to replace lost tissue fluid, and blood volume may drop too low to maintain adequate circulation.
2. **Obstructed venous return shock** occurs when a growing tumor or aneurysm, for example, compresses a nearby vein and impedes its blood flow.
3. **Venous pooling (vascular) shock** occurs when the body has a normal total blood volume, but too much of it accumulates in the limbs. This can result from long periods of standing or sitting or from widespread vasodilation. **Neurogenic shock** is a form of venous pooling shock that occurs when there is a sudden loss of vasomotor tone, allowing the vessels to dilate. This can result from causes as severe as brainstem trauma or as slight as an emotional shock.

Elements of both venous pooling and hypovolemic shock are present in certain cases, such as septic shock and anaphylactic shock, which involve both vasodilation and a loss of fluid through abnormally permeable capillaries. **Septic shock** occurs when bacterial toxins trigger vasodilation and increased capillary permeability. **Anaphylactic shock,** discussed more fully in chapter 21, results from exposure to an antigen to which a person is allergic, such as bee venom. Antigen-antibody complexes trigger the release of histamine, which causes generalized vasodilation and increased capillary permeability.

Responses to Circulatory Shock

In **compensated shock,** several homeostatic mechanisms act to bring about spontaneous recovery. The hypotension resulting from low cardiac output triggers the baroreflex and the production of angiotensin II, both of which counteract shock by stimulating vasoconstriction. Furthermore, if a person faints and falls to a horizontal position, gravity restores blood flow to the brain. Even quicker recovery is achieved if the person's feet are elevated to promote drainage of blood from the legs.

If these mechanisms prove inadequate, **decompensated shock** ensues and several life-threatening positive feedback loops occur. Poor cardiac output results in myocardial ischemia and infarction, which further weakens the heart and reduces output. Slow circulation of the blood can lead to disseminated intravascular coagulation (DIC) (see chapter 18). As the vessels become congested with clotted blood, venous return grows even worse. Ischemia and acidosis of the brainstem depress the vasomotor and cardiac centers, causing loss of vasomotor tone, further vasodilation, and further drop in BP and cardiac output. Before long, damage to the cardiac and brain tissues may be too great to be undone.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

16. Explain how respiration aids venous return.
17. Explain how muscular activity and venous valves aid venous return.
18. Define *circulatory shock.* What are some of the causes of low venous return shock?

Special Circulatory Routes

Objectives

When you have completed this section, you should be able to

- explain how the brain maintains stable perfusion;
- discuss the causes and effects of strokes and transient ischemic attacks;
- explain the mechanisms that increase muscular perfusion during exercise; and
- contrast the blood pressure of the pulmonary circuit with that of the systemic circuit, and explain why the difference is important in pulmonary function.

Certain circulatory pathways have special physiological properties adapted to the functions of their organs. Two of these are described in other chapters: the coronary circulation in chapter 19 and fetal and placental circulation in chapter 29. Here we take a closer look at the circulation to the brain, skeletal muscles, and lungs.

Brain

Total blood flow to the brain fluctuates less than that of any other organ (about 700 mL/min at rest). Such constancy is important because even a few seconds of oxygen deprivation causes loss of consciousness, and 4 or 5 minutes of anoxia is time enough to cause irreversible brain damage. While total cerebral perfusion is fairly stable, blood flow can be shifted from one part of the brain to another in a matter of seconds as different parts engage in motor, sensory, or cognitive functions.

The brain regulates its own blood flow in response to changes in BP and chemistry. The cerebral arteries dilate when the systemic BP drops and constrict when BP rises, thus minimizing fluctuations in cerebral BP. Cerebral blood flow thus remains quite stable even when mean arterial pressure (MAP) fluctuates from 60 to 140 mmHg. A MAP below 60 mmHg produces syncope and a MAP above 160 mmHg causes cerebral edema.

The main chemical stimulus for cerebral autoregulation is pH. Poor cerebral perfusion allows CO_2 to accumulate in the brain tissue. This lowers the pH of the tissue fluid and triggers local vasodilation, which improves perfusion. Extreme hypercapnia, however, depresses neural activity. The opposite condition, hypocapnia, raises the pH and stimulates vasoconstriction, thus reducing perfusion and giving CO_2 a chance to rise to a normal level. Hyperventilation (exhaling CO_2 faster than the body produces it) induces hypocapnia, which leads to cerebral vasoconstriction, ischemia, dizziness, and sometimes syncope.

Brief episodes of cerebral ischemia produce **transient ischemic attacks (TIAs),** characterized by temporary dizziness, light-headedness, loss of vision or other senses, weakness, paralysis, headache, or aphasia. A TIA may result from spasms of diseased cerebral arteries. It lasts from just a moment to a few hours and is often an early warning of an impending stroke.

A stroke, or **cerebrovascular accident (CVA),** is the sudden death (infarction) of brain tissue caused by ischemia. Cerebral ischemia can be produced by atherosclerosis, thrombosis, or a ruptured aneurysm. The effects of a CVA range from unnoticeable to fatal, depending on the extent of tissue damage and the function of the affected tissue. Blindness, paralysis, loss of sensation, and loss of speech are common. Recovery depends on the ability of neighboring neurons to take over the lost functions and on the extent of collateral circulation to regions surrounding the cerebral infarction.

Skeletal Muscles

In contrast to the brain, the skeletal muscles receive a highly variable blood flow depending on their state of exertion. At rest, the arterioles are constricted, most of the capillary beds are shut down, and total flow through the muscular system is about 1 L/min. During exercise, the arterioles dilate in response to epinephrine and norepinephrine from the adrenal medulla and sympathetic nerves. Precapillary sphincters, which lack innervation, dilate in response to muscle metabolites such as lactic acid, CO_2, and adenosine. Blood flow can increase more than 20-fold during strenuous exercise, which requires that blood be diverted from other organs such as the digestive tract and kidneys to meet the needs of the working muscles.

Muscular contraction compresses the blood vessels and impedes flow. For this reason, isometric contraction causes fatigue more quickly than intermittent isotonic contraction. If you squeeze a rubber ball as hard as you can without relaxing your grip, you feel the muscles fatigue more quickly than if you intermittently squeeze and relax.

Lungs

After birth, the pulmonary circuit is the only route in which the arterial blood contains less oxygen than the venous blood. The pulmonary arteries have thin distensible walls with less elastic tissue than the systemic arteries. Thus, they have a BP of only 25/10. Capillary hydrostatic

pressure is about 10 mmHg in the pulmonary circuit as compared with an average of 17 mmHg in systemic capillaries. This lower pressure has two implications for pulmonary circulation: (1) blood flows more slowly through the pulmonary capillaries, and therefore it has more time for gas exchange; and (2) oncotic pressure overrides hydrostatic pressure, so these capillaries are engaged almost entirely in absorption. This prevents fluid accumulation in the alveolar walls and lumens, which would interfere with gas exchange. In a condition such as mitral valve stenosis, however, BP may back up into the pulmonary circuit, raising the capillary hydrostatic pressure and causing pulmonary edema, congestion, and hypoxemia.

Think About It

What abnormal skin coloration would result from pulmonary edema?

Another unique characteristic of the pulmonary arteries is their response to hypoxia. Systemic arteries dilate in response to local hypoxia and improve tissue perfusion. By contrast, pulmonary arteries constrict. Pulmonary hypoxia indicates that part of the lung is not being ventilated well, perhaps because of mucous congestion of the airway or a degenerative lung disease. Vasoconstriction in poorly ventilated regions of the lung redirects blood flow to better ventilated regions.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

19. In what conspicuous way does perfusion of the brain differ from perfusion of the skeletal muscles?
20. How does a stroke differ from a transient ischemic attack? Which of these bears closer resemblance to a myocardial infarction?
21. How does the low hydrostatic blood pressure in the pulmonary circuit affect the fluid dynamics of the capillaries there?
22. Contrast the vasomotor responses of the lungs versus skeletal muscles to hypoxia.

Anatomy of the Pulmonary Circuit

Objective

When you have completed this section, you should be able to

- trace the route of blood through the pulmonary circuit.

The remainder of this chapter centers on the names and pathways of the principal arteries and veins. The pulmonary circuit is described here, and the systemic arteries and veins are described in the two sections that follow.

The pulmonary circuit (fig. 20.19) begins with the **pulmonary trunk,** a large vessel that ascends diagonally from the right ventricle and branches into the right and left **pulmonary arteries.** Each pulmonary artery enters a medial indentation of the lung called the *hilum* and branches into one **lobar artery** for each lobe of the lung: three on the right and two on the left. These arteries lead ultimately to small basketlike capillary beds that surround the pulmonary alveoli. This is where the blood unloads CO_2 and loads O_2. After leaving the alveolar capillaries, the pulmonary blood flows into venules and veins, ultimately leading to the **pulmonary veins,** which exit the lung at the hilum. The left atrium of the heart receives two pulmonary veins on each side.

The purpose of the pulmonary circuit is to exchange CO_2 for O_2. It does not serve the metabolic needs of the lung tissue itself; there is a separate systemic supply to the lungs for that purpose, the *bronchial arteries,* discussed later.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

23. Trace the flow of an RBC from right ventricle to left atrium and name the vessels along the way.
24. The lungs have two separate arterial supplies. Explain their functions.

Anatomy of the Systemic Arteries

Objectives

When you have completed this section, you should be able to

- identify the principal arteries of the systemic circuit; and
- trace the flow of blood from the heart to any major organ.

The systemic circuit supplies oxygen and nutrients to all the organs and removes their metabolic wastes. Part of it, the coronary circulation, was described in chapter 19. The other systemic arteries are described in tables 20.3 through 20.8 (figs. 20.20–20.30). The names of the blood vessels often describe their location by indicating the body region traversed (as in the *axillary* artery or *femoral* artery); an adjacent bone (as in *radial* artery or *temporal* artery); or the organ supplied or drained by the vessel (as in *hepatic* artery or *renal* vein). There is a great deal of anatomical variation in the circulatory system from one person to another. The remainder of this chapter describes the most common pathways.

Table 20.15 Some Disorders of the Arteries and Veins

Dissecting aneurysm	Splitting of the layers of an arterial wall from each other because of the accumulation of blood between layers. Results from either a tear in the tunica intima or rupture of the vasa vasorum.
Fat embolism	The presence of fat globules traveling in the bloodstream. Globules originate from bone fractures, fatty degeneration of the liver, and other causes and may block cerebral or pulmonary blood vessels.
Orthostatic hypotension	A decrease in blood pressure that occurs when one stands, often resulting in blurring of vision, dizziness, and syncope (fainting). Results from sluggish or inactive baroreflexes.

Disorders described elsewhere

Aneurysm 754	Embolism 707	Stroke 766
Atherosclerosis 741	Hypertension 792	Transient ischemic attack 766
Circulatory shock 765	Hypotension 754	Varicose veins 753
Edema 762		

Chapter 29 describes the effects of aging on the circulatory system, and table 20.15 lists some disorders of the blood vessels. Disorders of the blood and heart are tabulated in chapters 18 and 19.

Before You Go On

Answer the following questions to test your understanding of the preceding section:

28. If you were dissecting a cadaver, where would you look for the internal and external jugular veins? What muscle would help you distinguish one from the other?
29. How do the vertebral veins differ from the vertebral arteries in their superior terminations?
30. By what route does blood from the abdominal wall reach the superior vena cava?
31. Trace one possible path of an RBC from the fingertips to the right atrium and name the veins along the way.
32. State two ways in which the great saphenous vein has special clinical significance. Where is this vein located?

Insight 20.4 Clinical Application

Hypertension—The "Silent Killer"

Hypertension, the most common cardiovascular disease, affects about 30% of Americans over age 50 and 50% by age 74. It is a "silent killer" that can wreak its destructive effects for 10 to 20 years before its effects are first noticed. Hypertension is the major cause of heart failure, stroke, and kidney failure. It damages the heart because it increases the afterload, which makes the ventricles work harder to expel blood. The myocardium enlarges up to a point (the *hypertrophic response*), but eventually it becomes excessively stretched and less efficient. Hypertension strains the blood vessels and tears the endothelium, thereby creating lesions that become focal points of atherosclerosis. Atherosclerosis then worsens the hypertension and establishes an insidious positive feedback cycle.

Another positive feedback cycle involves the kidneys. Their arterioles thicken in response to the stress, their lumens become narrower, and renal blood flow declines. When the kidneys detect the resulting drop in blood pressure, they release renin, which leads to the formation of the vasoconstrictor angiotensin II and the release of aldosterone, a hormone that promotes salt retention (described in detail in chapter 24). These effects worsen the hypertension that already existed. If diastolic pressure exceeds 120 mmHg, blood vessels of the eye hemorrhage, blindness ensues, the kidneys and heart deteriorate rapidly, and death usually follows within 2 years.

Primary hypertension, which accounts for 90% of cases, results from such a complex web of behavioral, hereditary, and other factors that it is difficult to sort out any specific underlying cause. It was once considered such a normal part of the "essence" of aging that it continues to be called by another name, *essential hypertension.* That term suggests a fatalistic resignation to hypertension as a fact of life, but this need not be. Many risk factors have been identified, and most of them are controllable.

One of the chief culprits is obesity. Each pound of extra fat requires miles of additional blood vessels to serve it, and all of this added vessel length increases peripheral resistance and blood pressure. Just carrying around extra weight, of course, also increases the workload on the heart. Even a small weight loss can significantly reduce blood pressure. Sedentary behavior is another risk factor. Aerobic exercise helps to reduce hypertension by controlling weight, reducing emotional tension, and stimulating vasodilation.

Dietary factors are also significant contributors to hypertension. Diets high in cholesterol and saturated fat contribute to atherosclerosis. Potassium and magnesium reduce blood pressure; thus, diets deficient in these minerals promote hypertension. The relationship of salt intake to hypertension has been a very controversial subject. The kidneys compensate so effectively for excess salt intake that dietary salt has little effect on the blood pressure of most people. Reduced salt intake may, however, help to control hypertension in older people and in people with reduced renal function.

Nicotine makes a particularly devastating contribution to hypertension because it stimulates the myocardium to beat faster and harder; it also stimulates vasoconstriction and thus increases the afterload against which the myocardium must work. Just when the heart needs extra oxygen, nicotine causes coronary vasoconstriction and promotes myocardial ischemia.

Some risk factors cannot be changed at will—race, heredity, and sex. Hypertension runs in some families. A person whose parents or siblings have hypertension is more likely than average to develop it. The incidence of hypertension is about 30% higher, and the incidence of strokes about twice as high, among blacks as among whites. From ages 18 to 54, hypertension is more common in men, but above age 65, it is more common in women. Even people at risk from these factors, however, can minimize their chances of hypertension by changing risky behaviors.

Treatments for primary hypertension include weight loss, diet, and certain drugs. Diuretics lower blood volume and pressure by promoting urination. ACE inhibitors block the formation of the vasoconstrictor angiotensin II. Beta-blockers such as propranolol block the vasoconstrictive action of the sympathetic nervous system. Calcium channel blockers such as verapamil and nifedipine inhibit the inflow of calcium into cardiac and smooth muscle, thus inhibiting their contraction and promoting vasodilation and reduced cardiac workload.

Secondary hypertension, which accounts for about 10% of cases, is high blood pressure that is secondary to (results from) other identifiable disorders. These include kidney disease (which may cause renin hypersecretion), atherosclerosis, hyperthyroidism, Cushing syndrome, and polycythemia. Secondary hypertension is corrected by treating the underlying disease.