The Blood Vessels and Blood Pressure

INTRODUCTION

Most body cells are not in direct contact with the external environment, yet these cells must make exchanges with this environment, such as picking up O_2 and nutrients and eliminating wastes. Furthermore, chemical messengers must be transported between cells to accomplish integrated activity. To achieve these long-distance exchanges, the cells are linked with each other and with the external environment by vascular (blood vessel) highways. Blood is transported to all parts of the body through a system of vessels that brings fresh supplies to the vicinity of all cells while removing their wastes.

To review, all blood pumped by the right side of the heart passes through the pulmonary circulation to the lungs for O_2 pickup and CO_2 removal. The blood pumped by the left side of the heart into the systemic circulation is distributed in various proportions to the systemic organs through a parallel arrangement of vessels that branch from the aorta (Figure 10-1). This arrangement ensures that all organs receive blood of the same composition; that is, one organ does not receive "left-over" blood that has passed through another organ. Because of this parallel arrangement, blood flow through each systemic organ can he independently adjusted as needed.

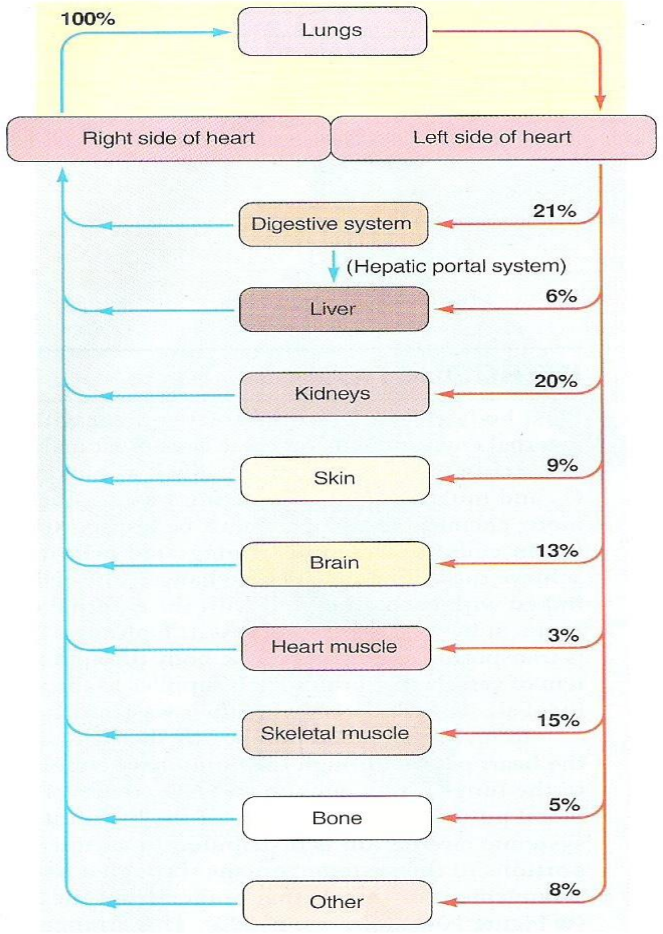


FIGURE 10-1

Distribution of cardiac output at rest. The lungs receive all the blood pumped out by the right side of the heart, whereas the systemic organs each receive some of the blood pumped out by the left side of the heart. The percentage of pumped blood received by the various organs under resting conditions is indicated. This distribution of cardiac output can be adjusted as needed.

Reconditioning Organs

Blood is constantly "reconditioned" so that its composition remains relatively constant despite an ongoing drain of supplies to support metabolic activities and despite the continual addition of wastes from the tissues. The organs that recondition the blood normally receive much more blood than is necessary to meet their basic metabolic needs, so they can adjust the extra blood to achieve homeostasis, For example, large percentages of the

cardiac output are distributed to the digestive tract (to pick up nutrient supplies), to the kidneys (to eliminate metabolic wastes and adjust water and electrolyte composition), and to the skin (to eliminate heat). Blood flow to the other organs-heart, skeletal muscles, and so on-is solely for filling these tissues' metabolic needs and can be adjusted according to their level of activity. For example, during exercise additional blood is delivered to the active muscles to meet their increased metabolic needs.

Because reconditioning organs-digestive organs, kidneys, and skin-receive blood flow in excess of their own needs, they can withstand temporary reductions in blood flow much better than can other organs that do not have this extra margin of blood supply. The brain in particular suffers irreparable damage when transiently deprived of blood supply. After only four minutes without O_2, permanent brain damage occurs. Therefore, a high priority in the overall operation of the circulatory system is the constant delivery of adequate blood to the brain, which can least tolerate disrupted blood supply.

Blood flow

The flow rate of blood through a vessel (that is, the volume of blood passing through per unit of time) is directly proportional to the pressure gradient and inversely proportional to vascular resistance:

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

where

F = flow rate of blood through a vessel
ΔP = pressure gradient
R = resistance of blood vessels

PRESSURE GRADIENT

The pressure gradient is the difference in pressure between the beginning and end of a vessel. Blood flows from an area of higher pressure to an area of lower pressure down a pressure gradient. Contraction of the heart imparts pressure to the blood, which is the main driving force for flow through a vessel. Because of frictional losses (resistance), the pressure drops as it flows throughout the vessel's length. Accordingly, pressure is higher at the beginning than at the end of the vessel, establishing a pressure gradient for forward flow of blood through the vessel. The greater the pressure gradient forcing blood through a vessel, the greater the rate of flow through that vessel.

RESISTANCE

The other factor influencing flow rate through a vessel is the resistance, which is a measure of the hindrance or opposition to blood flow through a vessel, caused by friction between the moving fluid and the stationary vascular walls. As resistance to flow increases, it is more difficult for blood to pass through the vessel, so flow decreases.

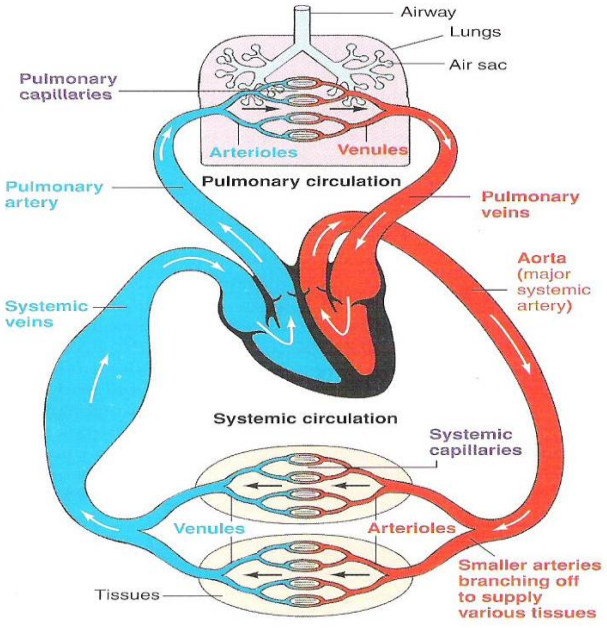
Resistance to blood flow depends on three factors: (1) viscosity of the blood, (2) vessel length, and (3) vessel radius, which is by far the most important. The term viscosity refers to the friction developed between the molecules of a fluid as they slide over each other during flow of the fluid. The greater the viscosity, the greater the resistance to flow. In general, the thicker a liquid, the more viscous it is. Blood viscosity is determined primarily by the number of circulating red blood cells. Surface area is determined by both the length *(L)* and radius (r) of the vessel. At a constant radius, the longer the vessel the greater the surface area and the greater the resistance to flow. Because vessel length remains constant in the body, it is not a variable factor in the control of vascular resistance.

Therefore, the major determinant of resistance to flow is the vessel's radius. A slight change in the radius of a vessel brings about a notable change in flow, because the resistance is inversely proportional to the fourth power of the radius.

$$R \ \alpha \ \frac{1}{r^4}$$

Arteries, arterioles, capillaries, venules and veins

The systemic and pulmonary circulations each consist of a closed system of vessels (Figure 10-4). Looking specifically at the systemic circulation, **arteries**, which carry blood from the heart to the organs, branch into a "tree" of progressively smaller vessels, with the various branches delivering blood to different regions of the body. When a small artery reaches the organ it is supplying, it branches into numerous **arterioles**. The volume of blood flowing through an organ can be adjusted by regulating the caliber (internal diameter) of the organ's arterioles. Arterioles branch further within the organs into capillaries, the smallest of vessels, across which all exchanges are made with surrounding cells. Capillary exchange is the entire purpose of the circulatory system; all other activities of the system are directed toward ensuring an adequate distribution of replenished blood to capillaries for exchange with all cells. Capillaries rejoin to form small **venules**, which further merge to form small **veins** that leave the organs. The small veins progressively unite to form larger veins that eventually empty into the heart. The



For simplicity, only two capillary beds within two organs are illustrated.

FIGURE 10-4

Basic organization of the cardiovascular system. Arteries progressively branch as they carry blood from the heart to the organs. A separate small arterial branch delivers blood to each of the various organs. As a small artery enters the organ it is supplying, it branches into arterioles, which further branch into an extensive network of capillaries. The capillaries rejoin to form venules, which further unite to form small veins that leave the organ. The small veins progressively merge as they carry blood back to the heart.

arterioles, capillaries, and venules are collectively referred to as the microcirculation, because they are only visible through a microscope. The pulmonary circulation consists or the same vessel types, except that all the blood in this loop goes between the heart and lungs.

ARTERIES

The consecutive segments of the vascular tree are specialized to perform specific tasks (Table 10-1). **Arteries** are specialized (1) to serve as rapid-transit passageways for blood from the heart to the organs (because of their large radius, arteries offer little resistance to blood flow) and (2) to act as a **pressure reservoir** to provide the driving force for blood when the heart is relaxing.

TABLE 10-1
Features of Blood Vessels

	VESSEL TYPE			
FEATURE	Arteries	Arterioles	Capillaries	Veins
Number	Several hundred*	Half a million	Ten billion	Several hundred*
Special Features	Thick, highly elastic, walls; large radii*	Highly muscular, well-innervated walls; small radii	Thin walled; large total cross-sectional area	Thin walled; highly distensible; large radii*
Functions	Passageway from heart to organs; serve as pressure reservoir	Primary resistance vessels; determine distribution of cardiac output	Site of exchange; determine distribution of extracellular fluid between plasma and interstitial fluid	Passageway to heart from organs; serve as blood reservoir

The heart alternately contracts to pump blood into the arteries and then relaxes to refill from the veins. When the heart is relaxing and refilling, no blood is pumped out. However, capillary flow does not fluctuate between cardiac *sys*tole and diastole; that is, blood flow is continuous through the capillaries supplying the organs. The driving force for the continued flow of blood to the organs during cardiac relaxation is provided by the elastic properties of the arterial walls.

All vessels are lined with a thin layer of smooth, flat endothelial cells that are continuous with the endothelial lining of the heart. A thick wall made up of smooth muscle and connective tissue surrounds the arteries' endothelial lining. Arterial connective tissue contains an abundance of two types of connective tissue fibers*; collagen fibers*, which provide tensile strength against the high driving pressure of blood ejected from the heart, and *elastin fibers,* which give the arterial walls elasticity so that they behave much like a balloon.

As the heart pumps blood into the arteries during ventricular systole, a greater volume of blood enters the arteries from the heart than leaves them to flow into smaller vessels downstream, because the smaller vessels have a greater resistance to flow. The arteries' elasticity enables them to expand to temporarily hold this excess volume of ejected blood, storing some of the pressure energy imparted by cardiac contraction in their stretched walls-just as a balloon expands to

accommodate the extra volume of air you blow into it (Figure 10-5a). When the heart relaxes and ceases pumping blood into the arteries, the stretched arterial walls passively recoil, like an inflated balloon that is released. This recoil pushes the excess blood contained in the arteries into the vessels downstream, ensuring continued blood flow to the organs when the heart is relaxing and not pumping blood into the system **(**Figure 10-5b).

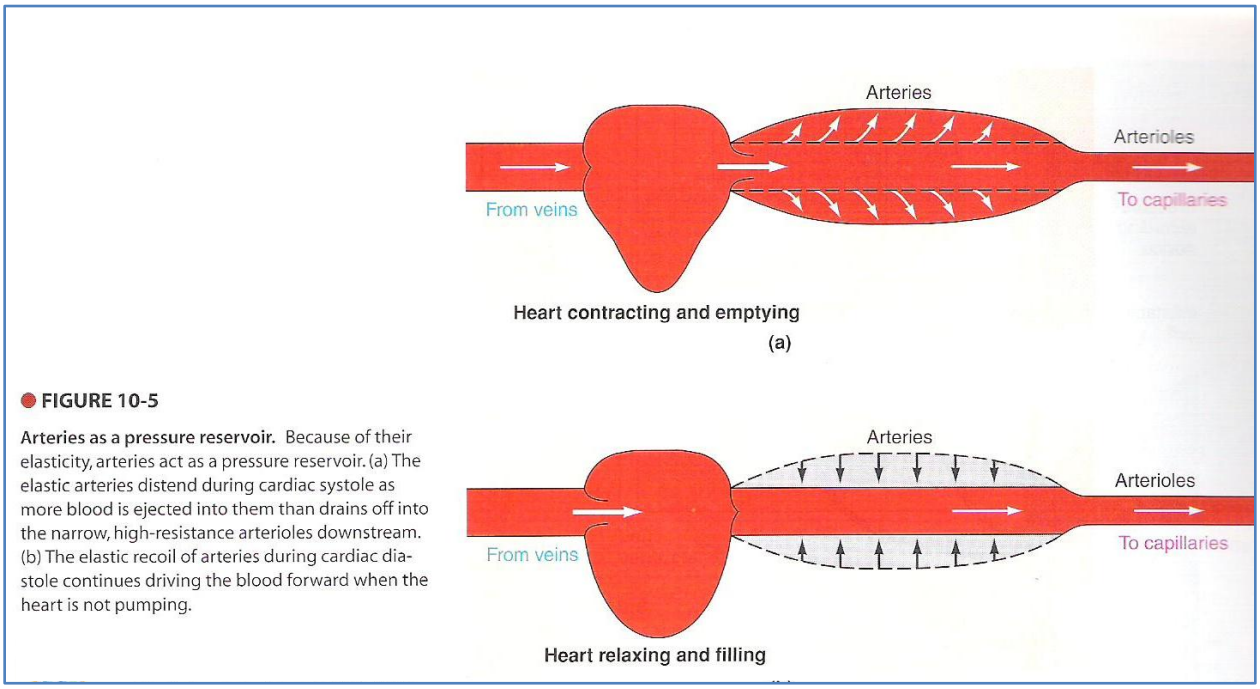


FIGURE 10-5

Arteries as a pressure reservoir. Because of their elasticity, arteries act as a pressure reservoir. (a) The elastic arteries distend during cardiac systole as more blood is ejected into them than drains off into the narrow, high-resistance arterioles downstream. (b) The elastic recoil of arteries during cardiac diastole continues driving the blood forward when the heart is not pumping.

Arterial pressure

Blood pressure, the force exerted by the blood against a vessel wall, depends on the volume of blood contained within the vessel and the **compliance**, or **distensibility**, of the vessel walls (how easily they can be stretched). During ventricular systole, a stroke volume of blood enters the arteries from the ventricle while only about one third as much blood leaves the arteries to enter the arterioles. During diastole, no blood enters the arteries, while blood continues to leave, driven by elastic recoil. The maximum pressure exerted in the arteries when blood is ejected into them during systole, the **systolic pressure**, averages 120 mm Hg. The minimum pressure within the arteries when blood is draining off into the rest of the vessels during diastole, the **diastolic pressure**, averages 80 mm Hg.

PULSE PRESSURE

The pulse that can be felt in an artery lying close to the surface of the skin is due to the difference between systolic and diastolic pressures. This pressure difference is known as the **pulse pressure**. When blood pressure is 120/80, pulse pressure is 40 mm Hg (120 mm Hg - 80 mm Hg).

Mean arterial pressure

The mean arterial pressure is the ave*rage pressure* driving blood forward into the tissues throughout the cardiac cycle. Contrary to what you might expect, mean arterial pressure is not the halfway value between systolic and diastolic pressure (for example, with a blood pressure of 120/80, mean pressure is not 100 mm Hg). The reason is that arterial pressure remains closer to diastolic than to systolic pressure for a longer portion of each cardiac cycle. At resting heart rate, about two thirds of the cardiac cycle is spent in diastole and only one third in systole. A good approximation of the mean arterial pressure can be determined using the following formula:

Mean arterial pressure = diastolic pressure + 1/3 pulse pressure

At 120/80, mean arterial pressure = 80 mm Hg + (1/3) 40 mm Hg = 93 mm Hg

The mean arterial pressure, not the systolic or diastolic pressure, is monitored and regulated by blood pressure reflexes described later. Because arteries offer little resistance to flow, only a negligible amount of pressure energy is lost in them because of friction. Therefore, arterial pressure -systolic, diastolic, pulse, or mean- is essentially the same throughout the arterial tree (Figure 10-8).

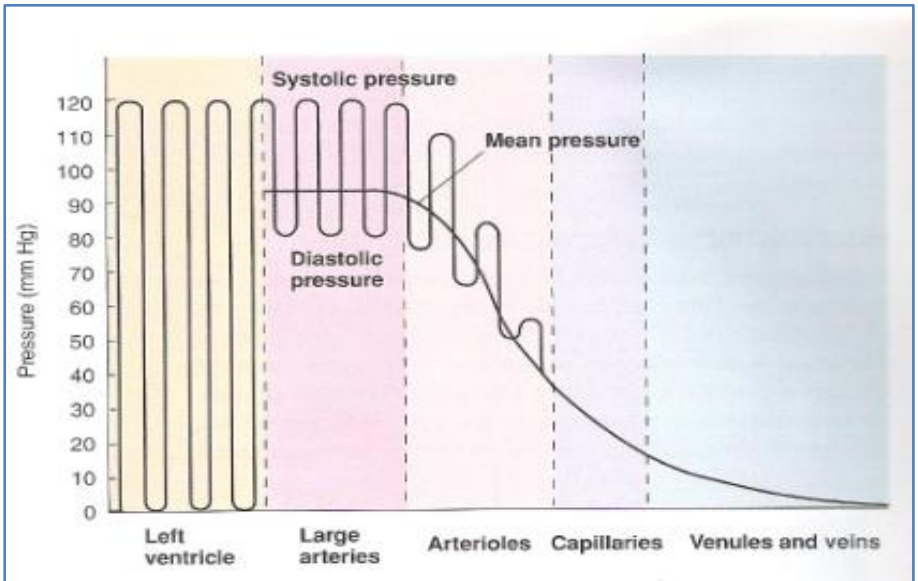


FIGURE 10-8

Pressures throughout the systemic circulation. Left ventricular pressure swings between a low pressure of 0 mm Hg during diastole to a high pressure of 120 mm Hg during systole. Arterial blood pressure, which fluctuates between a peak systolic pressure of 120 mm Hg and a low diastolic pressure of 80 mm Hg each cardiac cycle, is of the same magnitude throughout the large arteries. Because of the arterioles' high resistance, the pressure drops precipitously and the systolic-to-diastolic swings in pressure are converted to a nonpulsatile pressure when blood flows through the arterioles. The pressure continues to decline but at a slower rate as blood flows through the capillaries and venous system.

ARTERIOLES

When an artery reaches the organ it is supplying, it branches into numerous arterioles within the organ.

Arterioles are the major resistance vessels.

Arterioles are the major resistance vessels in the vascular tree because their radius is small enough to offer considerable resistance to flow. (Even though the capillaries have a smaller radius than the arterioles, you will see later how collectively the capillaries do not offer as much resistance to flow as the arteriolar level of the vascular tree does.) In contrast to the low resistance of the arteries, the high degree of arteriolar resistance causes a marked drop in mean pressure as blood flows through these vessels. On average, the pressure falls from 93 mm Hg, the mean arterial pressure (the pressure of the blood entering the arterioles), to 37 mm Hg, the pressure of the blood leaving the arterioles and entering the capillaries (Figure 10-8). This decline in pressure helps establish the pressure differential that encourages the flow of blood from the heart to the various organs downstream.

The radius (and, accordingly, the resistances) of arterioles supplying individual organs can be adjusted independently to accomplish two functions: (1) to variably distribute the cardiac output among the systemic organs, depending on the body's momentary needs, and (2) to help regulate arterial blood pressure.

VASOCONSTRICTION AND VASODILATION

Unlike arteries, arteriolar walls contain very little elastic connective tissue. However, they do have a thick layer of smooth muscle that is richly innervated by sympathetic nerve fibers. The smooth muscle is also sensitive to many local chemical changes and to a few circulating hormones. The smooth muscle layer runs circularly around the arteriole (Figure 10-9a), so when it contracts the vessel's circumference (and its radius) becomes smaller, increasing resistance and decreasing the flow through that vessel. Vasoconstriction is the term applied to such narrowing of a vessel (Figure10-9c). The term vasodilation refers to enlargement in the circumference and radius of a vessel as a result of its smooth muscle layer relaxing (Figure 10-9d). Vasodilation leads to decreased resistance and increased flow through that vessel.

VASCULAR TONE

Arteriolar smooth muscle normally displays a state of partial constriction known as vascular tone, which establishes a baseline of arteriolar resistance **(**Figure 10-9b). Two factors are responsible for vascular tone. First, arteriolar smooth muscle has considerable myogenic activity; that is, it shows self-induced contractile activity independent of any neural or hormonal influences. Second, the sympathetic fibers supplying most arterioles continually release norepinephrine, which further enhances muscle tone.

This ongoing tonic activity makes it possible to either increase or decrease the level of contractile activity to accomplish vasoconstriction or vasodilation, respectively.

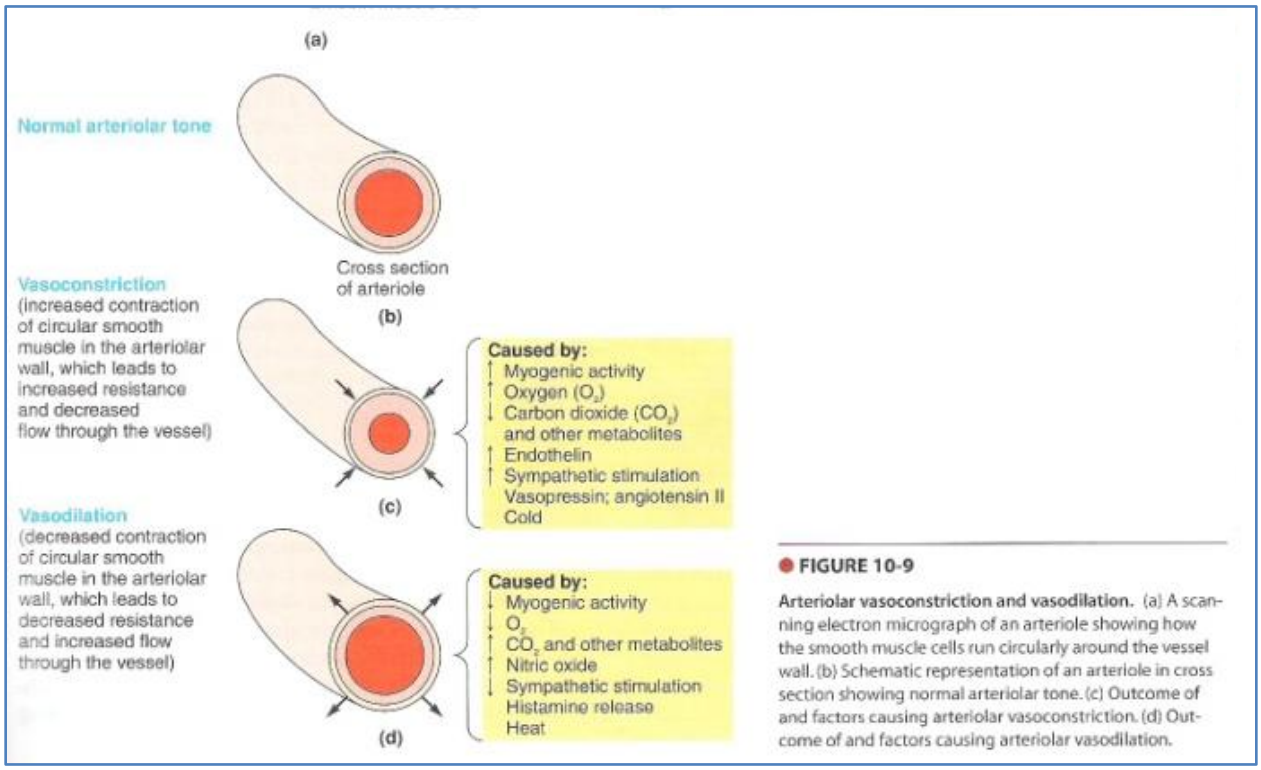


FIGURE 10-9

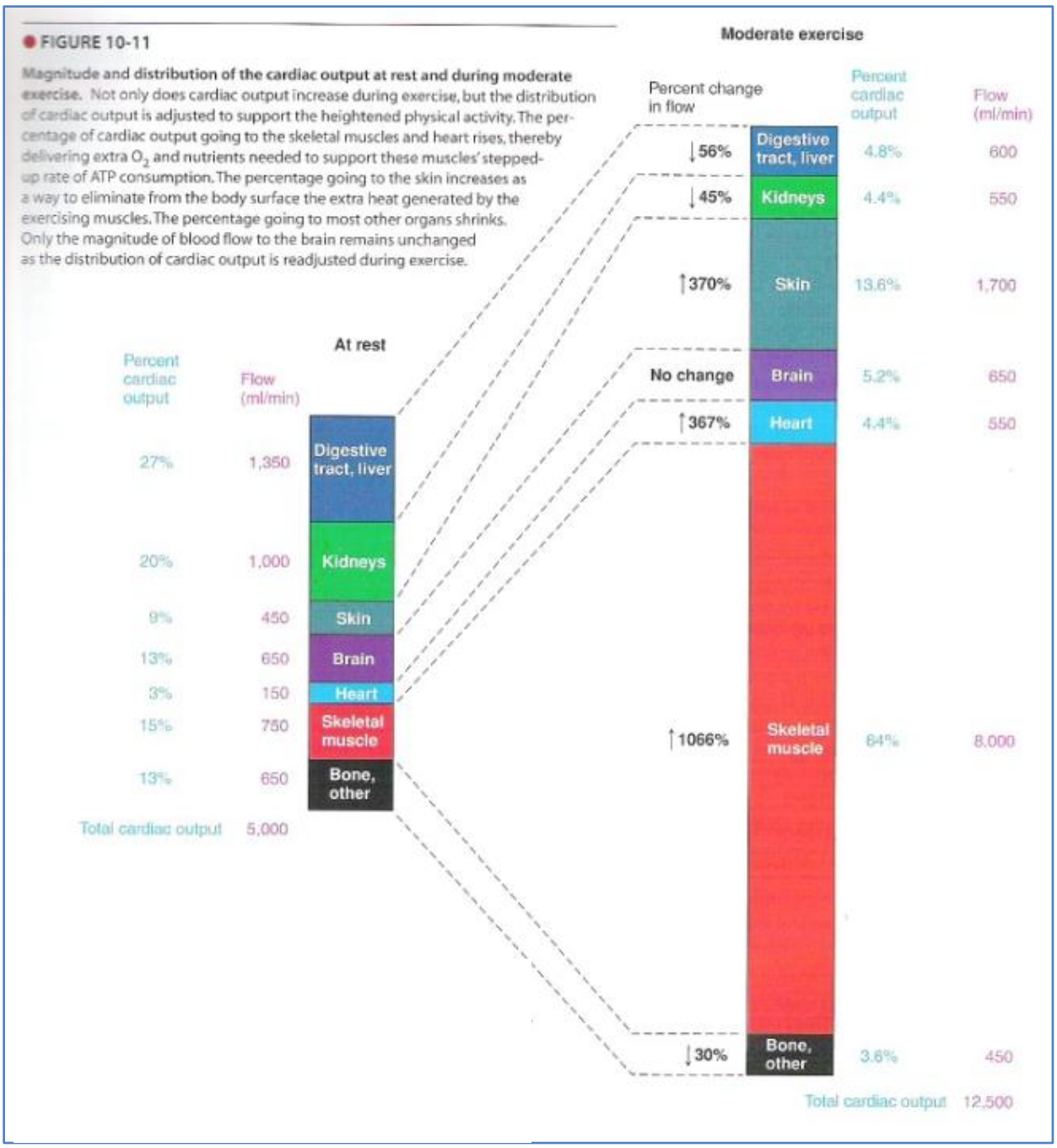
Arteriolar vasoconstriction and vasodilation. (a) A scanning electron micrograph of an arteriole showing how the smooth muscle cells run circularly around the vessel wall. (b) Schematic representation of an arteriole in cross section showing normal arteriolar tone. (c) Outcome of and factors causing arteriolar vasoconstriction. (d) Outcome of and factors causing arteriolar vasodilation.

A variety of factors can influence the level of contractile activity in arteriolar smooth muscle, thereby substantially changing resistance to flow in these vessels. These factors fall into two categories: local (intrinsic) controls, which are important in determining the distribution of cardiac output; and extrinsic controls, which are important in blood pressure regulation.

Local control of arteriolar radius

The fraction of the total cardiac output delivered to each organ is not always constant; it varies, depending on the demands for blood at the time. The amount of the cardiac output received by each organ is determined by the number and caliber of the arterioles supplying that area. Recall that $F = \Delta P/R$. Because blood is delivered to all organs at the same mean arterial pressure, the driving force for flow is identical for each organ. Therefore, differences in flow to various organs are completely determined by differences in the extent of vascularization and by differences in resistance offered by the arterioles supplying each organ. On a moment-to-moment basis, the distribution of cardiac output can be varied by differentially adjusting arteriolar resistance in the various vascular beds.

Similarly, more blood flows to areas whose arterioles offer the least resistance to its passage. During exercise, for example, not only is cardiac output increased, but also, because of vasodilation in skeletal muscle and in the heart, a greater percentage of the pumped blood is diverted to these organs to support their increased metabolic activity. Simultaneously, blood flow to the digestive tract and kidneys is reduced, as a result of arteriolar vasoconstriction in these organs (Figure 10-11).



Only the blood supply to the brain remains remarkably constant no matter what the person is doing, be it vigorous physical activity, intense mental concentration, or sleep. Although the total blood flow to the brain remains constant, new imaging techniques demonstrate that regional blood flow varies within the brain in close correlation with local neural activity patterns.

Local (intrinsic) controls are changes within an organ that alter the radius of the vessels and hence adjust blood flow through the organ by directly affecting the smooth muscle of the organ's arterio1es. Local influences may be either chemical or physical. Local chemical influences on

arteriolar radius include (1) local metabolic changes and (2) histamine release. Local physical influences include (1) local application of heat or cold and (2) myogenic response to stretch.

Local metabolic influences on arteriolar radius

The most important local chemical influences on arteriolar smooth muscle are related to metabolic changes within a given organ. The influence of these local changes on arteriolar radius is important in matching blood flow through an organ with the organ's metabolic needs. Local metabolic controls arc especially important in skeletal muscle and in the heart, the organs whose metabolic activity and need for blood supply normally vary most.

ACTIVE HYPEREMIA

Arterioles lie within the organ they are supplying and can be acted on by local factors within the organ. During increased metabolic activity, such as when a skeletal muscle is contracting during exercise, local concentrations of a number of the organ's chemicals change. For example, the local O_2 concentration decreases as the actively metabolizing cells use up more O_2 to support oxidative phosphorylation for ATP production. This and other local chemical changes (such as increased CO_2 and other metabolites) produce local arteriolar dilation by triggering relaxation of the arteriolar smooth muscle in the vicinity. Local arteriolar vasodilation then increases blood flow to that particular area, a response called active hyperemia (*hyper* means "above normal"; *emia* means "blood"). When cells are more active metabolically, they need more blood to bring in O_2 and nutrients and to remove metabolic wastes. The increased blood flow meets these increased local needs.

LOCAL VASOACTIVE MEDIATORS

Among the best studied of these local vasoactive mediators is **nitric oxide (NO),** which causes local arteriolar vasodilation by inducing relaxation of arteriolar smooth muscle in the vicinity. It does so by inhibiting the entry of contraction-inducing Ca^{2+} into these smooth muscle cells. NO is a small, highly reactive, short-lived gas molecule that once was known primarily as a toxic air pollutant. Yet studies have revealed an astonishing number of biological roles for NO, which is produced in many other tissues besides endothelial cells. In fact, it appears that NO serves as one of the body's most important messenger molecules, as endothelial cells release other important chemicals besides NO. **EndotheIin**, another endothelial vasoactive substance, causes arteriolar smooth-muscle contraction and is one of the most potent vasoconstrictors yet identified.

Local histamine release pathologically dilates arterioles

Histamine is another local chemical mediator that influences arteriolar smooth muscle, but it is not released in response to local metabolic changes and is not derived from endothelial cells. Although histamine normally does not participate in controlling blood flow, it is important in certain pathological conditions. Histamine is synthesized and stored within special connective tissue cells in many organs and in certain types of circulating white blood cells. When organs are injured or during allergic reactions, histamine is released and acts as a paracrine in the damaged region. By promoting relaxation of arteriolar smooth muscle,

histamine is the major cause of vasodilation in an injured area. The resultant increase in blood flow into the area produces the redness and contributes to the swelling seen with inflammatory responses.

Local physical influences on arteriolar radius include temperature changes and stretch.

Among the physical influences on arteriolar smooth muscle, the effect of temperature changes is exploited clinically but the myogenic response to stretch is most important physiologically.

Heat application, by causing localized arteriolar dilation, is a useful therapeutic agent for promoting increased blood flow to an area. Conversely, applying ice packs to an inflamed area produces vasoconstriction which reduces swelling by counteracting histamine-induced vasodilation.

Arteriolar smooth muscle responds to being passively stretched by myogenically increasing its tone, thereby acting to resist the initial passive stretch. Converse1y, a decrease in arteriolar stretching induces a reduction in myogenic vessel tone.

Extrinsic sympathetic control of arteriolar radius

Extrinsic control of arteriolar radius includes both neural and hormonal influences, the effects of the sympathetic nervous system being the most important. Sympathetic nerve fibers supply arteriolar smooth muscle everywhere in the systemic circulation except in the brain.

The medullary cardiovascular control center

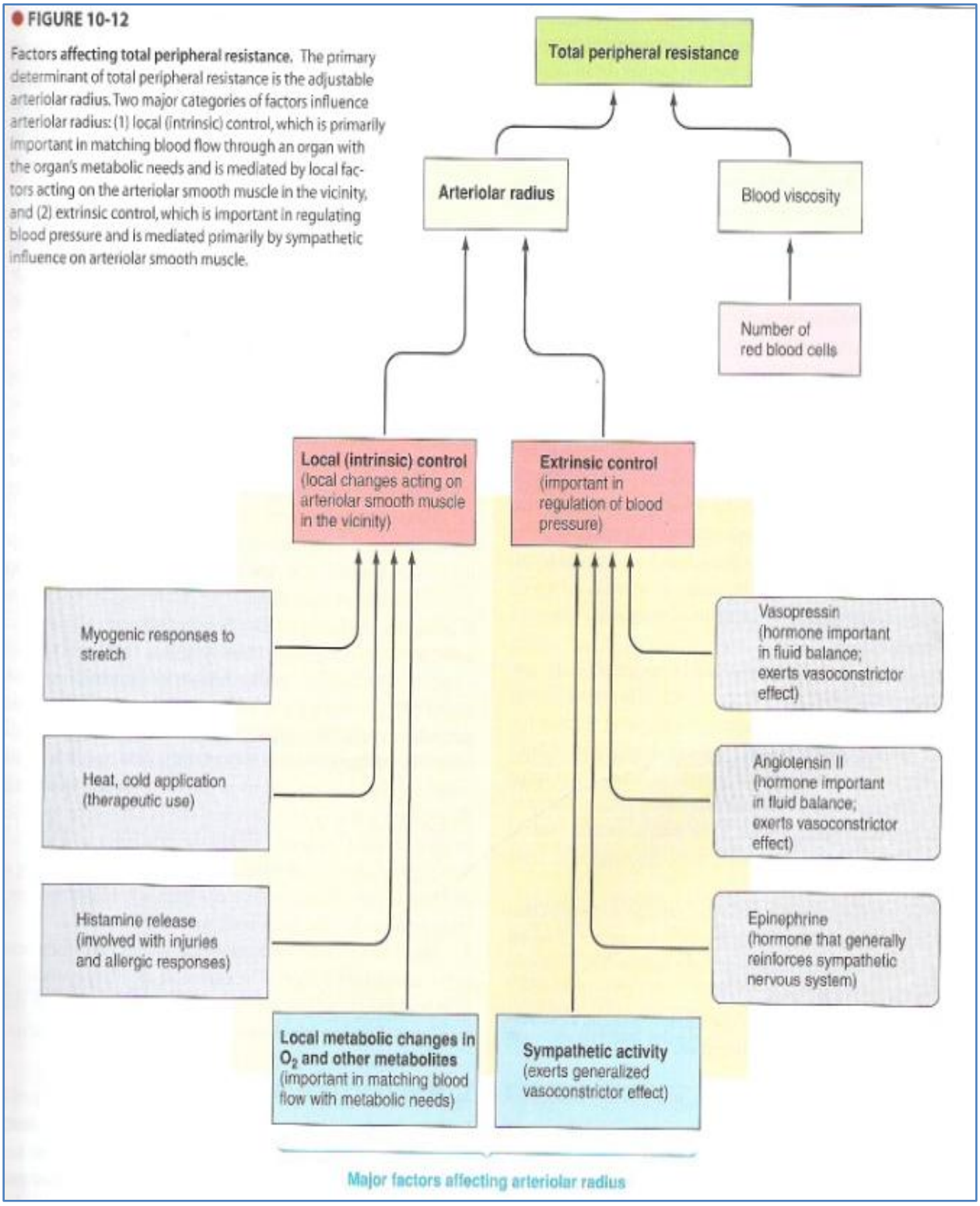
The main region of the brain that adjusts sympathetic output to the arterioles is the cardiovascular control center in the medulla of the brain stem. This is the integrating center for blood pressure regulation. Several other brain regions also influence blood distribution, the most notable being the hypothalamus, which, as part of its temperature-regulating function, controls blood flow to the skin to adjust heat loss to the environment.

In addition to neural reflex activity, several hormones also extrinsically influence arteriolar radius. These hormones include the major adrenal medullary hormone epinephrine, which generally reinforces the sympathetic nervous system in most organs, as well as vasopressin and angiotensin II, which are important in controlling fluid balance. Vasopressin is primarily involved in maintaining water balance by regulating the amount of water the kidneys retain for the body during urine formation. Angiotensin II is part of a hormonal pathway, the renin-angiotensin-aldosterone pathway, which is important in regulating the body's salt balance. Both vasopressin and angiotensin II are potent vasoconstrictors.

The most important factors that affect total peripheral resistance are summarized in Figure 10-12.

FIGURE 10-12

Factors affecting total peripheral resistance. The primary determinant of total peripheral resistance is the adjustable arteriolar radius. Two major categories of factors influence arteriolar radius: (1) local (intrinsic) control, which is primarily important in matching blood flow through an organ with the organ's metabolic needs and is mediated by local factors acting on the arteriolar smooth muscle in the vicinity, and (2) extrinsic control, which is important in regulating blood pressure and is mediated primarily by sympathetic influence on arteriolar smooth muscle.



CAPILLARIES

Capillaries, the sites for exchange of materials between blood and tissue cells, branch extensively to bring blood within the reach of every cell. There are no carrier-mediated transport systems across capillaries, with the exception of those in the brain that plays a role in the blood-brain barrier. Materials are exchanged across capillary walls mainly by diffusion.

FACTORS THAT ENHANCE DIFFUSION ACROSS CAPILLARIES

Capillaries are ideally suited to enhance diffusion, in accordance with Fick's law of diffusion. They minimize diffusion distances while maximizing surface area and time available for exchange, as follows:

1. Diffusing molecules have only a short distance to travel between blood and surrounding cells because of the thin capillary wall and small capillary diameter, coupled with the close proximity of every cell to a capillary. This short distance is important because the rate of diffusion slows down as the diffusion distance increases.
    a. Capillary walls are very thin (1 μm in thickness; in contrast, the diameter of a human hair is 100 μm). Capillaries consist of only a single layer of flat endothelial cells. No smooth muscle or connective tissue is present.
    b. Each capillary is so narrow (7 μm average diameter) that red blood cells (8 μm diameter) have to squeeze through. Consequently, plasma contents are either in direct contact with the inside of the capillary wall or are only a short diffusing distance from it.
    c. Researchers estimate that because of extensive capillary branching, no cell is farther than 0.01 cm from a capillary.
2. Because capillaries are distributed in such incredible numbers (estimates range from 10 to 40 billion capillaries), a tremendous total surface area is available for exchange (an estimated 600 m^2). Despite this large number of capillaries, at any point in time they contain only 5% of the total blood volume.
3. Blood flows more slowly in the capillaries than elsewhere in the circulatory system. The extensive capillary branching is responsible for this slow velocity of blood flow through the capillaries.

SLOW VELOCITY OF FLOW THROUGH CAPILLARIES

The velocity with which blood flows through the different segments of the vascular tree varies, because velocity of flow is inversely proportional to the total cross-section area of all the vessels at any given level of the circulatory system. Even though the cross-section area of each capillary is extremely small compared to that of the large aorta, the total cross-section area of all the capillaries added together is about 1300 times greater than the cross-section area of the aorta because there are so many capillaries. Accordingly, blood slows considerably as it passes through the capillaries (Figure 10-14). This slow velocity allows adequate time for exchange of nutrients and metabolic end products between blood and tissue cells, which is the sole purpose of the entire circulatory system.

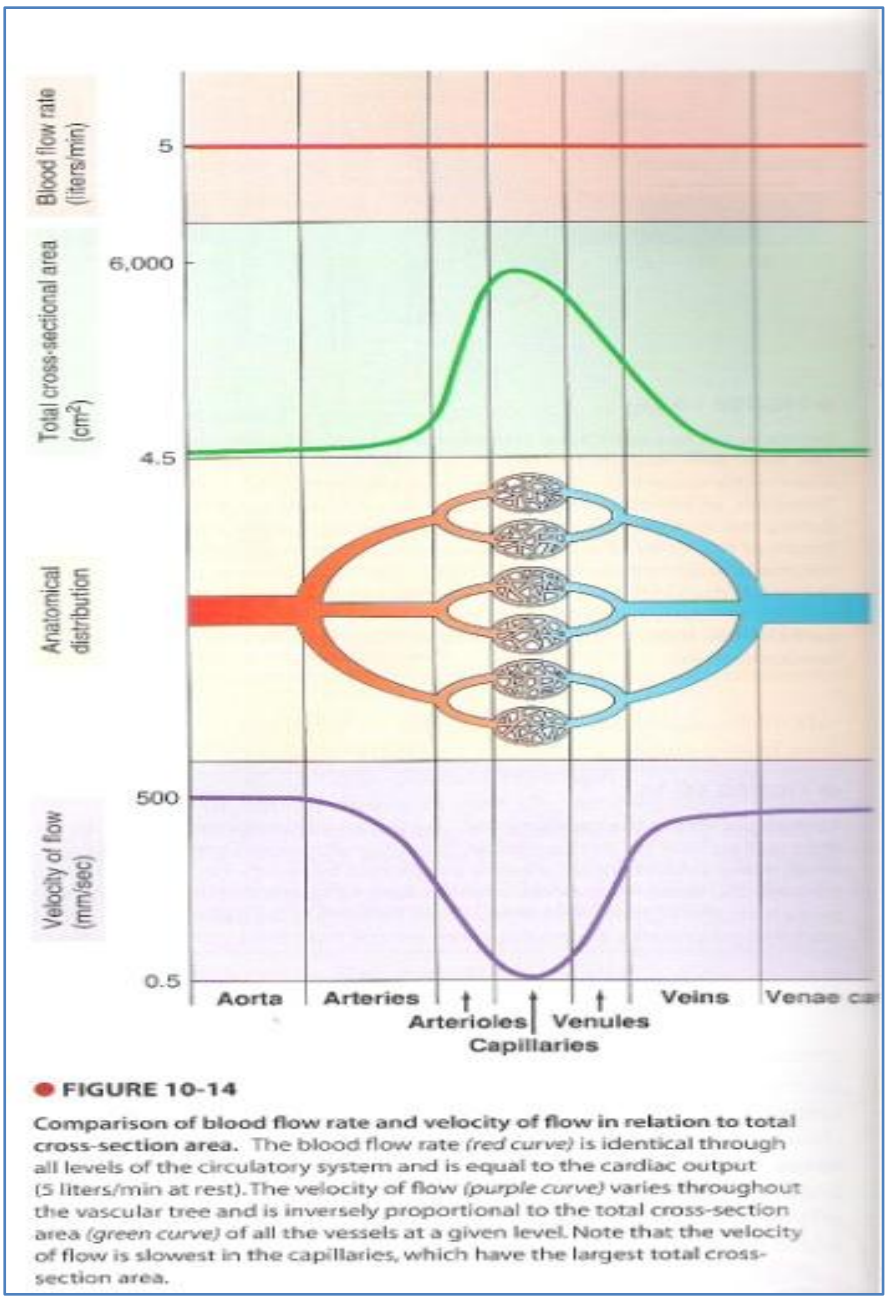


FIGURE 10-14

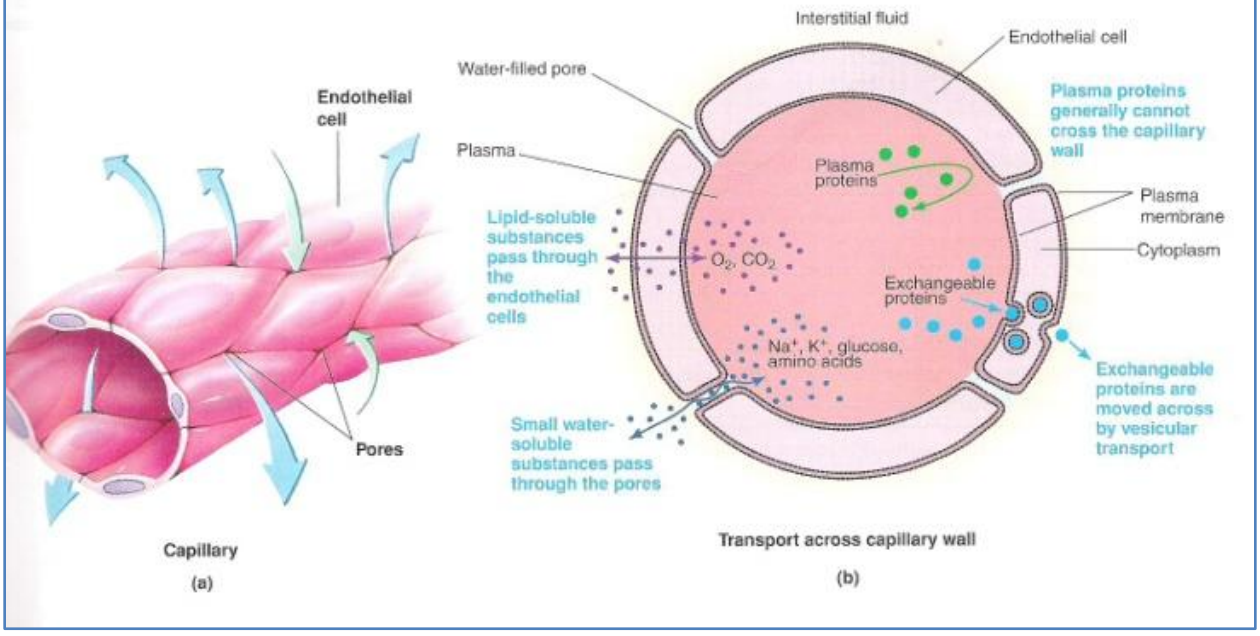
Comparison of blood flow rate and velocity of flow in relation to total cross-section area. The blood flow rate *(red curve)* is identical through all levels of the circulatory system and is equal to the cardiac output (5 liters/min at rest). The velocity of flow *(purple curve)* varies throughout the vascular tree and is inversely proportional to the total cross-section area *(green curve)* of all the vessels at a given level. Note that the velocity of flow is slowest in the capillaries, which have the largest total cross-section area.

Water-filled capillary pores permit passage of small, water-soluble substances.

Diffusion across capillary walls also depends on the walls' permeability to the materials being exchanged. In most capillaries, narrow, water-filled gaps, or pores, lie at the junctions between the cells (Figure 10-16). These pores permit passage of water-soluble substances. Lipid-soluble substances, such as O_2 and CO_2, can readily pass through the endothelial cells themselves by dissolving in the lipid bilayer barrier. Large, non-lipid-soluble materials that cannot fit through the pores, such as plasma proteins, are kept from passing.

● FIGURE 10-16

Exchanges across the capillary wall. (a) Slitlike gaps between adjacent endothelial cells form pores within the capillary wall. (b) As depicted in this schematic representation of a cross section of a capillary wall, small water-soluble substances are exchanged between the plasma and the interstitial fluid by passing through the water-filled pores, whereas lipid-soluble substances are exchanged across the capillary wall by passing through the endothelial cells. Proteins to be moved across are exchanged by vesicular transport. Plasma proteins generally cannot escape from the plasma across the capillary wall.



Thus the degree of leakiness does not necessarily remain constant for a given capillary bed. For example, histamine increases capillary permeability by triggering contractile responses in endothelial cells to widen the intercellular gaps. This is not a muscular contraction, because no smooth muscle cells are present in capillaries. It is due to an actin-myosin contractile apparatus in the nonmuscular capillary endothelial cells. Because of these enlarged pores, the affected capillary wal1 is leakier. As a result, normally retained plasma proteins escape into the surrounding tissue, where they exert an osmotic effect. Along with histamine-induced vasodilation, the resulting additional local fluid retention contributes to inflammatory swelling.

Vesicular transport also plays a limited role in the passage of materials across the capillary wall. Large non-lipid-soluble molecules such as protein hormones that must be exchanged between blood and surrounding tissues are transported from one side of the capillary wall to the other in endocytotic-exocytotic vesicles.

Interstitial fluid is a passive intermediary between blood and cells.

Exchanges between blood and tissue cells are not made directly. Interstitial fluid, the true internal environment in immediate contact with the cells, acts as the go-between. Only 20% of the ECF circulates as plasma. The remaining 80% consists of interstitial fluid, which bathes all the cells in the body. Cells exchange materials directly with interstitial fluid, with the type and extent of exchange being governed by the properties of cellular plasma membranes. Movement across the plasma membrane may be either passive (that is, by diffusion down electrochemical

gradients or by facilitated diffusion) or active (that is, by active carrier-mediated transport or by vesicular transport).

In contrast, exchanges across the capillary wall between plasma and interstitial fluid are largely passive. The only transport across this barrier that requires energy is the limited vesicular transport. Because capillary walls are highly permeable, exchange is so thorough that the interstitial fluid takes on essentially the same composition as incoming arterial blood, with the exception of the large plasma proteins that usually do not escape from the blood.

Exchanges between blood and surrounding tissues across the capillary walls arc made in two ways: (1) passive diffusion down concentration gradients, the primary mechanism for exchanging individual solutes; and (2) bulk flow, a process that fills the totally different function of determining the distribution of the ECF volume between the vascular and interstitial fluid compartments.

Diffusion across the capillary walls is important in solute exchange.

Because there are no carrier-mediated transport systems in most capillary walls, solutes cross primarily by diffusion down concentration gradients. The chemical composition of arterial blood is carefully regulated to maintain the concentrations of individual solutes at 1evels that will promote each solute's movement in the appropriate direction across the capillary walls. The reconditioning organs continuously add nutrients and O_2 and remove CO_2 and other wastes as blood passes through them. Meanwhile, cells constantly use up supplies and generate metabolic wastes. As cells use up O_2 and glucose, the blood constantly brings in fresh supplies of these vital materials, maintaining concentration gradients that favor the net diffusion of these substances from blood to cells. Simultaneously, ongoing net diffusion of CO_2 and other metabolic wastes from cells to blood is maintained by the continual production of these wastes at the cell level and by their constant removal by the circulating blood.

Bulk flow across the capillary walls is important in extracellular fluid distribution.

The second means by which exchange is accomplished across capillary walls is bulk flow. A volume of protein-free plasma actually filters out of the capillary, mixes with the surrounding interstitial fluid, and then is reabsorbed. This process is called bulk flow, because the various constituents of the fluid are moving together in bulk, or as a unit, in contrast to the discrete diffusion of individual solutes down concentration gradients.

The capillary wall acts like a sieve, with fluid moving through its water-filled pores. When pressure inside the capillary exceeds pressure on the outside, fluid is pushed out through the pores in a process known as **ultrafiltration**. Most plasma proteins are retained on the inside during this process because of the pores' filtering effect, although a few do escape. Because all other constituents in plasma are dragged along as a unit with the volume of fluid leaving the capillary, the filtrate is essentially a protein-free plasma. When inward-driving pressures exceed outward pressures across the capillary wall net inward movement of fluid from the interstitial fluid compartment into the capillaries takes place through the pores, a process known as reabsorption.