The SA node generates electrical impulses much like those produced by nerve cells. Because cardiac muscle cells are electrically coupled (by the intercalated disks between adjacent cells), impulses from the SA node spread rapidly through the walls of the atria, causing both atria to contract in unison **(Figure 42.8)**. The impulses also pass to another region of specialized cardiac muscle tissue, a relay point called the **atrioventricular (AV) node**, located in the wall between the right atrium and right ventricle. Here the impulses are delayed for about 0.1 second before spreading to the walls of the ventricles. The delay ensures that the atria empty completely before the ventricles contract. Specialized muscle fibers called bundle branches and Purkinje fibers then conduct the signals to the apex of the heart and throughout the ventricular walls.

The impulses that travel through cardiac muscle during the heart cycle produce electrical currents that are conducted through body fluids to the skin, where the currents can be detected by electrodes and recorded as an **electrocardiogram** (ECG or EKG).

The SA node sets the tempo for the entire heart, but is influenced by a variety of physiological cues. Two sets of nerves affect heart rate: one set speeds up the pacemaker, and the other set slows it down. Heart rate is a compromise regulated by the opposing actions of these two sets of nerves. The pacemaker is also influenced by hormones secreted into the blood by glands. For example, epinephrine, the "fight-or-flight" hormone secreted by the adrenal glands, increases heart rate (see Chapter 45). Body temperature is another factor that affects the pacemaker. An increase of only 1°C raises the heart rate by about 10 beats per minute. This is the reason your pulse increases substantially when you have a fever. Heart rate also increases with exercise, an adaptation that enables the circulatory system to provide the additional O_2 needed by muscles hard at work.

Concept Check 42.2

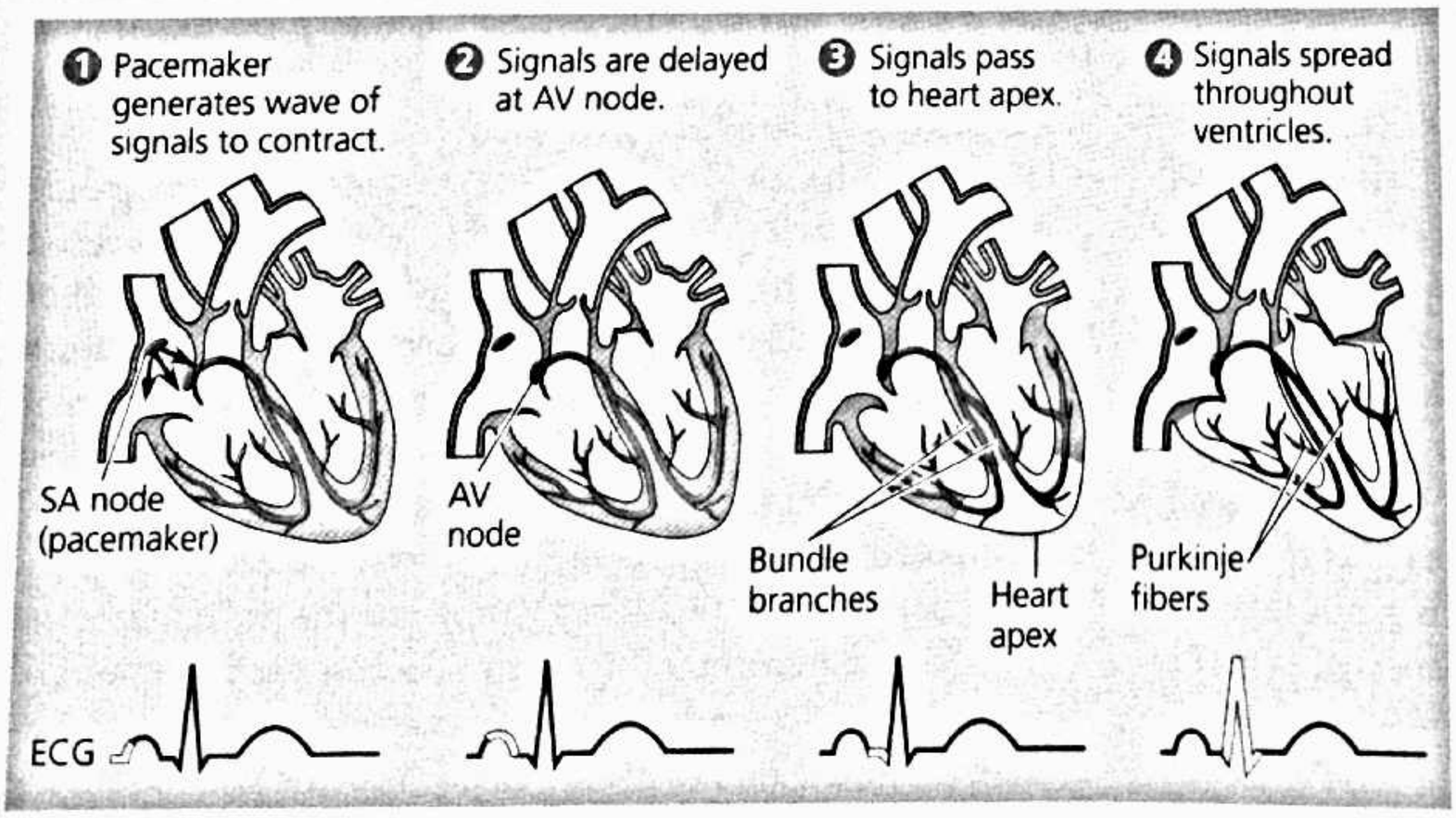
1. Some babies are born with a small hole between their left and right ventricles. Explain how, if not surgically corrected, this hole would affect the O_2 content of the blood entering the systemic circuit from the heart.
2. Why is it important that the AV node of the heart slow or delay the electrical impulse moving from the SA node and the atrial walls to the ventricles?

For suggested answers, see Appendix A.

Concept 42.3

Physical principles govern blood circulation

Blood delivers nutrients and removes wastes throughout an animal's body. These functions are made possible by the circulatory system, a branching network of vessels similar in some ways to the plumbing system that delivers fresh water to a city and removes the city's wastes. The same physical principles that govern the operation of such plumbing systems also influence the functioning of animal circulatory systems.

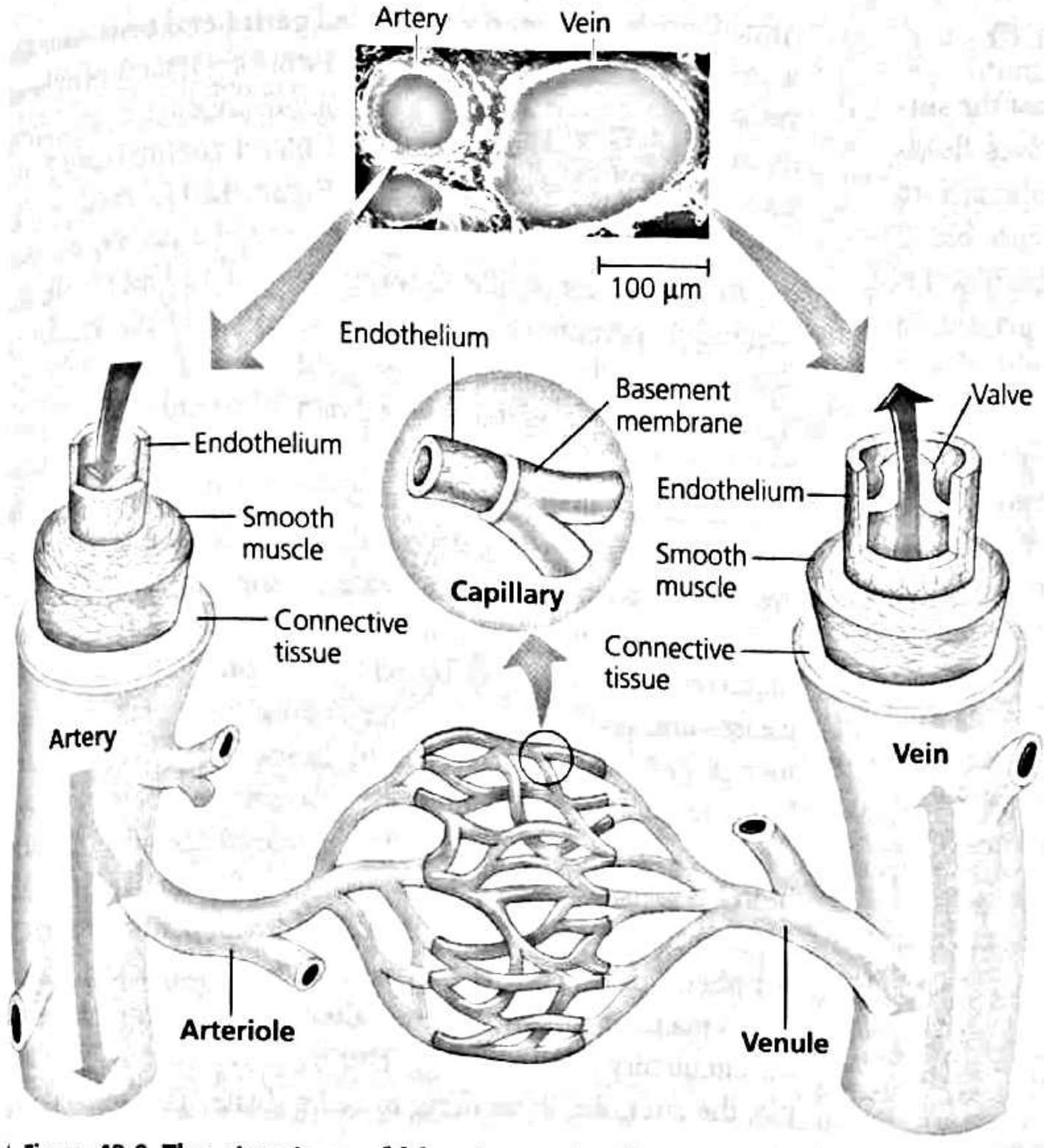


▲ **Figure 42.8 The control of heart rhythm.** The gold portions of the graphs at the bottom indicate the components of an electrocardiogram (ECG) corresponding to the sequence of electrical events in the heart. In step 4, the black portion of the ECG to the right of the gold "spike" represents electrical activity after the ventricles contract; during this phase, the ventricles become electrically re-primed and thus able to conduct the next round of contraction signals.

Blood Vessel Structure and Function

The "infrastructure" of the circulatory system consists of its network of blood vessels. All blood vessels are built of similar tissues. The walls of both arteries and veins, for instance, have three similar layers **(Figure 42.9)**. On the outside, a layer of connective tissue with elastic fibers allows the vessel to stretch and recoil. A middle layer contains smooth muscle and more elastic fibers. Lining the lumen of all blood vessels, including capillaries, is an **endothelium**, a single layer of flattened cells that provides a smooth surface that minimizes resistance to the flow of blood.

Structural differences correlate with the different functions of arteries, veins, and capillaries. Capillaries lack the two



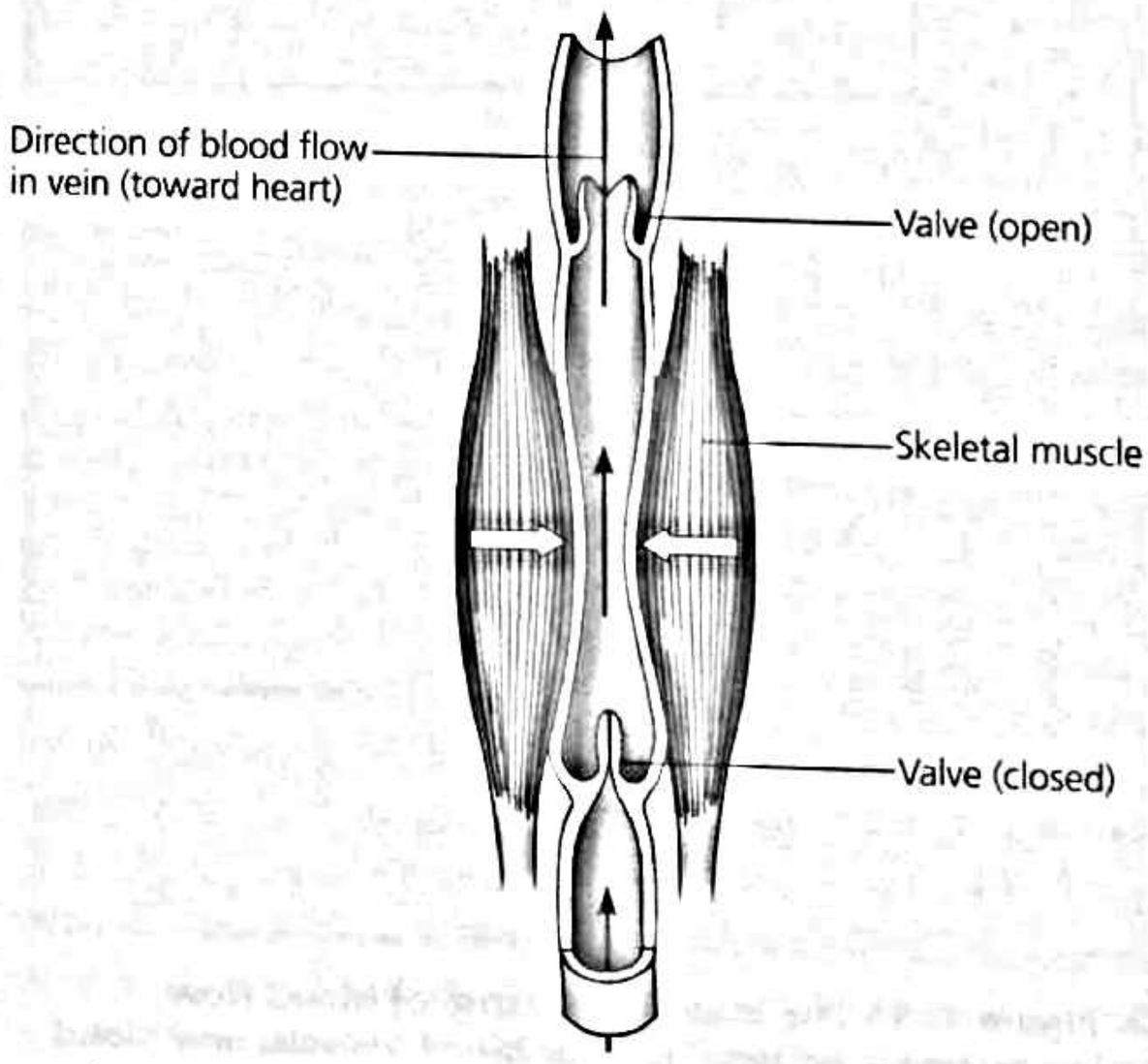
▲ **Figure 42.9 The structure of blood vessels.** This micrograph (SEM) shows an artery next to a thinner-walled vein.

outer layers, and their very thin walls consist only of endothelium and its basement membrane. This facilitates the exchange of substances between the blood and the interstitial fluid that bathes the cells. Arteries have thicker middle and outer layers than veins. Blood flows through the vessels of the circulatory system at uneven speeds and pressures. The thicker walls of arteries provide strength to accommodate blood pumped rapidly and at high pressure by the heart, and their elasticity helps maintain blood pressure even when the heart relaxes between contractions. The thinner-walled veins convey blood back to the heart at low velocity and pressure. Blood flows through the veins mainly as a result of muscle action; whenever you move, your skeletal muscles squeeze your veins and push blood through them. Within large veins, flaps of tissue act as one-way valves that allow blood to flow only toward the heart **(Figure 42.10)**.

Blood Flow Velocity

Blood travels over a thousand times faster in the aorta (about 30 cm/sec on average) than in capillaries (about 0.026 cm/sec). This velocity change follows from the *law of continuity*, which describes fluid movement through pipes. If a pipe's diameter changes over its length, a fluid flows through narrower segments of the pipe faster than it flows through wider segments. Since the *volume* of flow per second must be constant through the entire pipe, the fluid must flow faster as the cross-sectional area of the pipe narrows (think of the velocity of water squirted by a hose with and without a nozzle).

Based on the law of continuity, you might think that blood should travel faster through capillaries than through arteries, because the diameter of capillaries is very small. However, it is the *total* cross-sectional area of capillaries that determines flow rate. Each artery conveys blood to such an enormous number of capillaries that the total cross-sectional area is much greater in capillary beds than in any other part of the circulatory system. For this reason, the blood slows substantially as it enters the arterioles from arteries, and slows further still in the capillary beds. Capillaries are the only vessels with walls thin enough to permit the transfer of substances between the blood and interstitial fluid, and the slower flow of blood through these tiny vessels enhances this exchange. As blood leaves the capillaries and enters the venules and veins, it speeds up again as a result of the reduction in total cross-sectional area (**Figure 42.11**, on the next page).

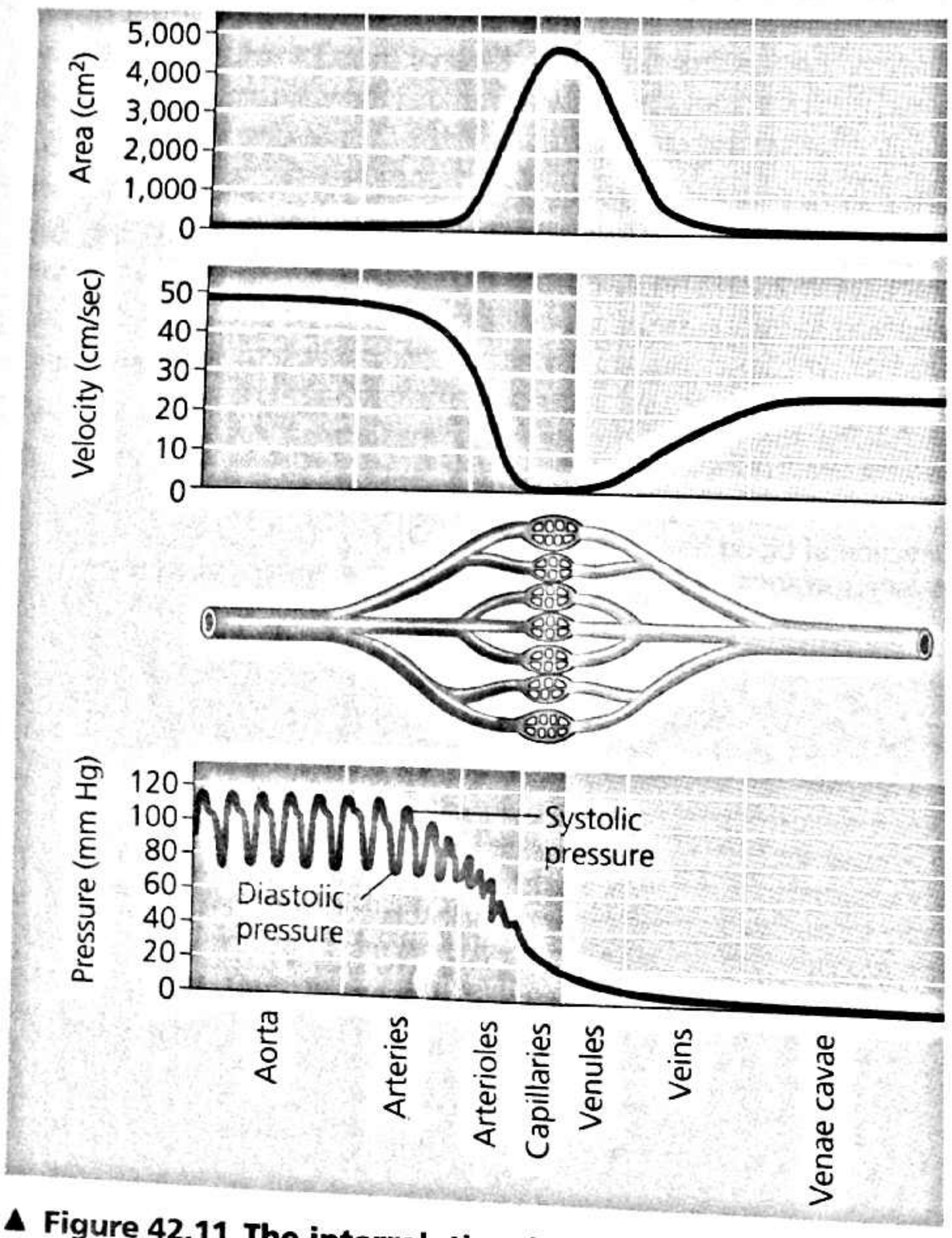


▲ **Figure 42.10 Blood flow in veins.** Contracting skeletal muscles squeeze the veins. Flaps of tissue within the veins act as one-way valves that keep blood moving only toward the heart. If we sit or stand too long, the lack of muscular activity causes our feet to swell with stranded blood unable to return to the heart.

Blood Pressure

Fluids exert a force called hydrostatic pressure against the surfaces they contact, and it is that pressure that drives fluids through pipes. Fluids flow from areas of higher pressure to areas of lower pressure. The hydrostatic pressure that blood exerts against the wall of a vessel and that propels the blood is called blood pressure. Blood pressure is much greater in arteries than in veins and is highest in arteries when the heart contracts during ventricular systole (**systolic pressure;** see Figure 42.11).

When you take your pulse by placing your fingers on your wrist, you can feel an artery bulge with each heartbeat. The surge of pressure is partly due to the narrow openings of arterioles impeding the exit of blood from the arteries. Thus, when the heart contracts, blood enters the arteries faster than it can leave, and the vessels stretch from the pressure. The elastic walls of the arteries snap back during diastole, but the heart contracts again before enough blood has flowed into the arterioles to completely relieve pressure in the arteries. This



▲ **Figure 42.11 The interrelationship of blood flow velocity, cross-sectional area of blood vessels, and blood pressure.** Blood flow velocity decreases markedly in the arterioles and is lowest in the capillaries, owing to an increase in total cross-sectional area. Blood pressure, the main force driving blood from the heart to the capillaries, is highest in the arteries.

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Blood pressure is determined partly by cardiac outpu partly by peripheral resistance. Contraction of smooth cles in the walls of the arterioles reduces the diameter tiny vessels, increases peripheral resistance, and therefo creases blood pressure upstream in the arteries. Whe smooth muscles relax, the arterioles dilate (increase diameter). Consequently, blood flow through the arterio creases and pressure in the arteries falls. Nerve impulses mones, and other signals control these arteriole wall mu Stress, either physical or emotional, can raise blood pr by triggering nervous and hormonal responses that co blood vessels.

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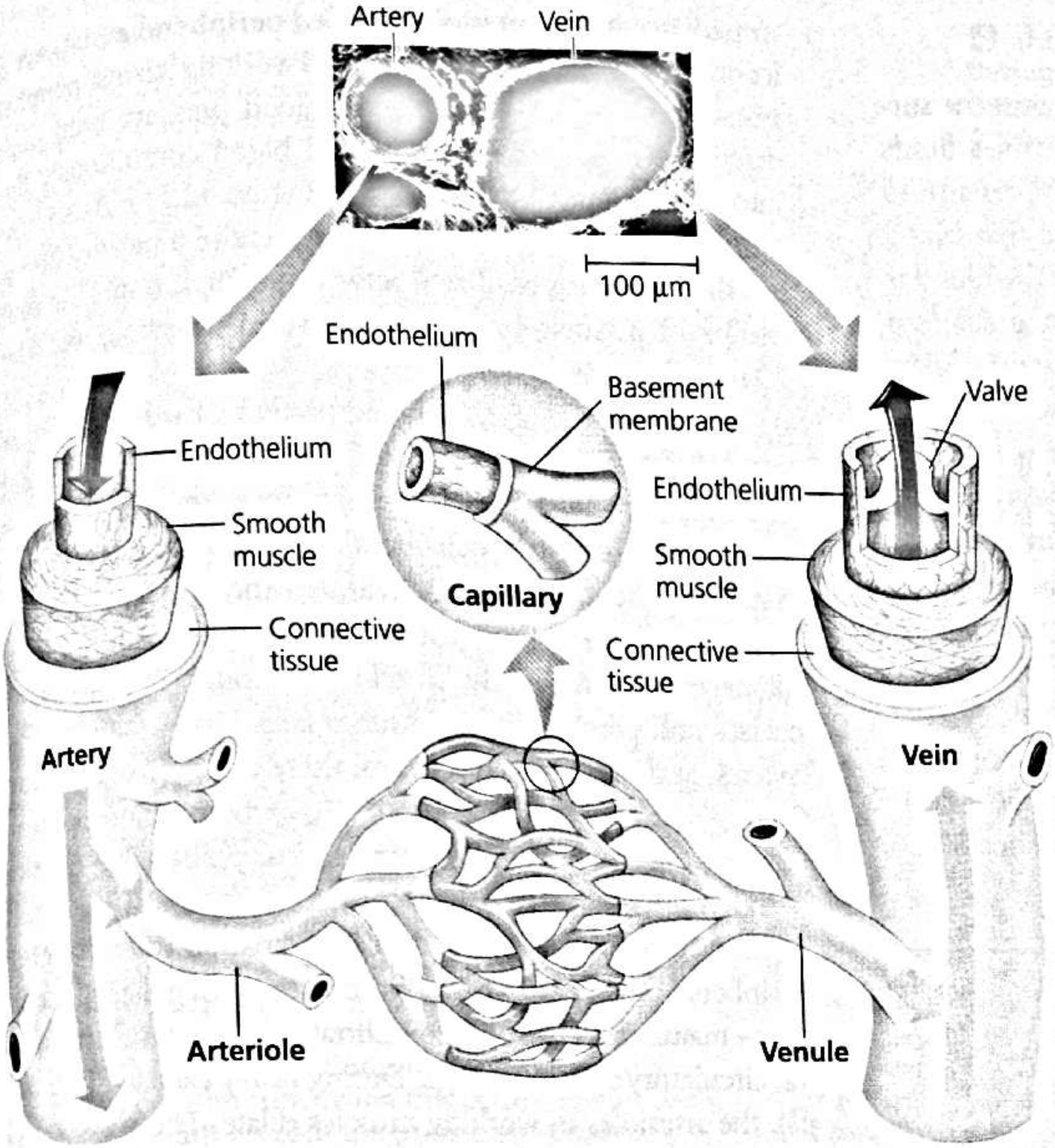
In large land animals, another factor that affects bloo sure is gravity. Besides the force needed to overcome per resistance, additional pressure is necessary to push above the level of the heart. In a standing human, bloo rise about 0.35 m to get from the heart to the brain. T mands an extra 27 mm Hg of pressure, which requi heart to expend more energy in its contraction cycl pumping challenge is significantly greater for animal long necks. A standing giraffe, for example, needs to blood as much as 2.5 m above the heart. That requires 190 mm Hg of additional blood pressure in the left ve and a giraffe's normal systolic pressure near the heart 250 mm Hg. (Systolic pressure that high would be ext dangerous in a human.) Check valves and sinuses, alon feedback mechanisms that reduce cardiac output, preve high pressure from damaging the giraffe's brain when it its head to drink—a body position that causes blood downhill almost 2 m from the heart, adding an extra 1 Hg of blood pressure in the arteries leading to the brain iologists speculate about blood pressure and cardiov adaptations in di



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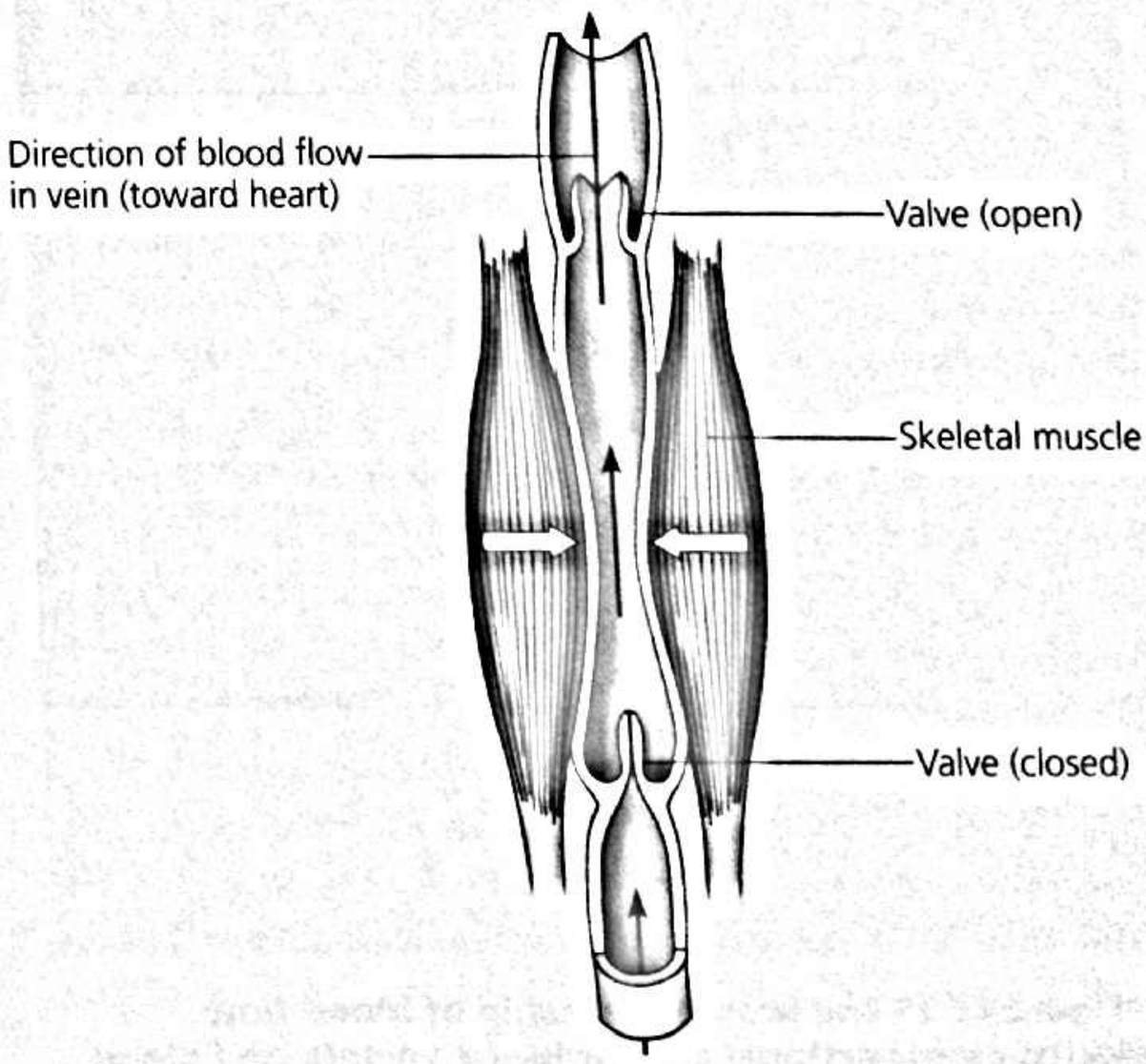

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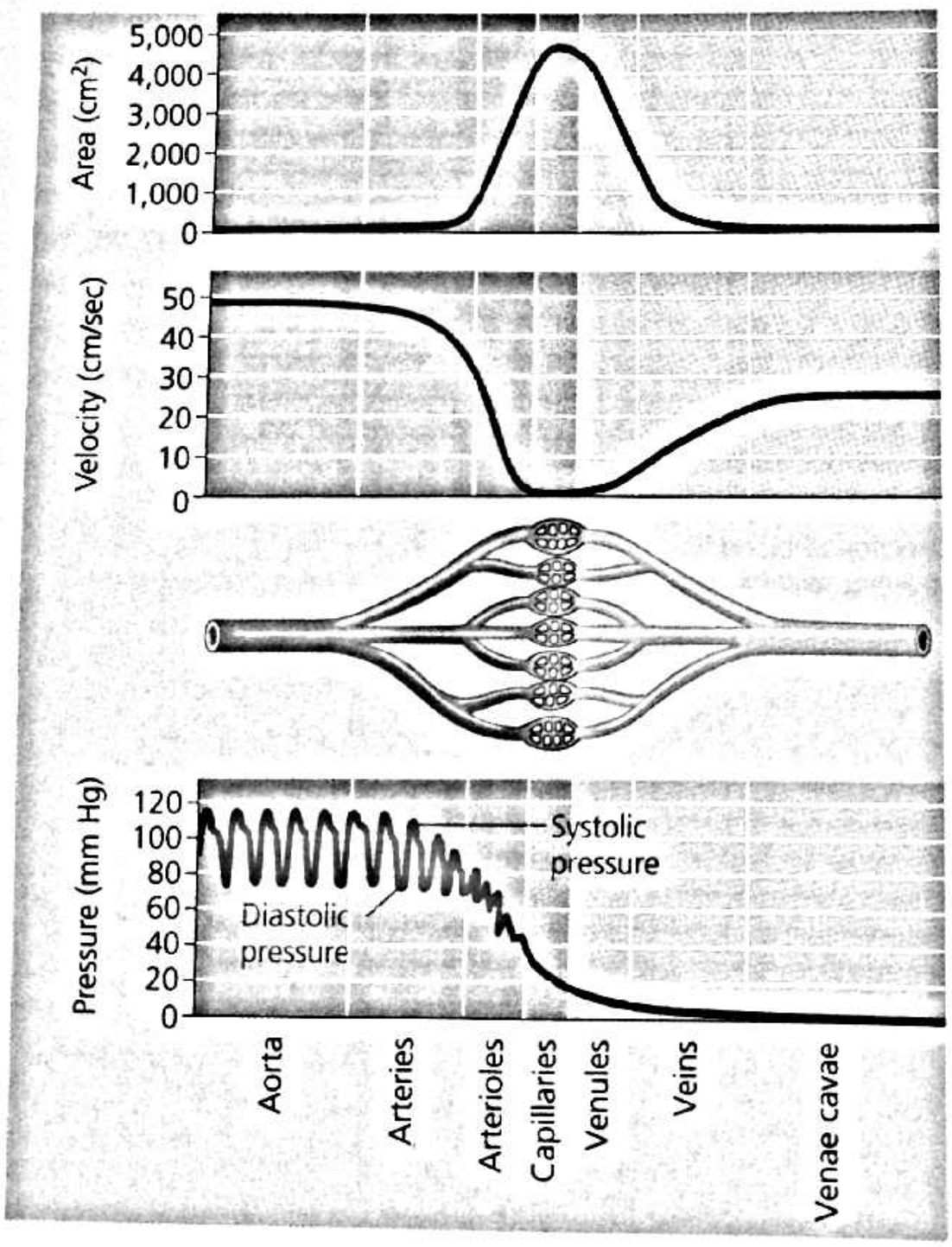

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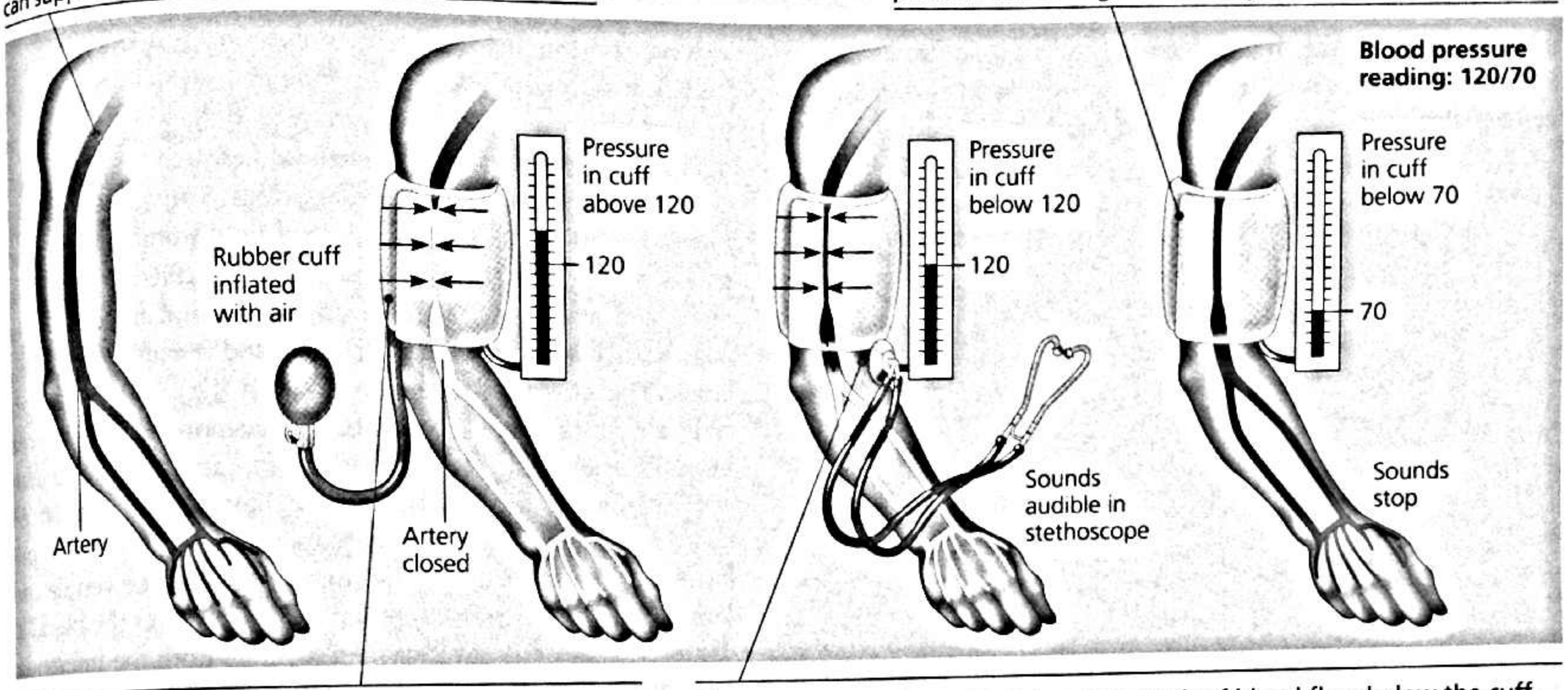
Blood pressure is determined partly by cardiac output and partly by peripheral resistance. Contraction of smooth muscles in the walls of the arterioles reduces the diameter of the tiny vessels, increases peripheral resistance, and therefore increases blood pressure upstream in the arteries. When the smooth muscles relax, the arterioles dilate (increase their diameter). Consequently, blood flow through the arterioles increases and pressure in the arteries falls. Nerve impulses, hormones, and other signals control these arteriole wall muscles. Stress, either physical or emotional, can raise blood pressure by triggering nervous and hormonal responses that constrict blood vessels.

Cardiac output is adjusted in coordination with changes in peripheral resistance. This coordination of regulatory mechanisms maintains adequate blood flow as the body's demands on the circulatory system change. During heavy exercise, for example, the arterioles in working muscles dilate. This response admits a greater flow of oxygen-rich blood to the muscles and also decreases peripheral resistance. By itself, this would cause a drop in blood pressure (and therefore blood flow) in the body as a whole. However, cardiac output increases, maintaining blood pressure and supporting the necessary increase in blood flow.

In large land animals, another factor that affects blood pressure is gravity. Besides the force needed to overcome peripheral resistance, additional pressure is necessary to push blood above the level of the heart. In a standing human, blood must rise about 0.35 m to get from the heart to the brain. This demands an extra 27 mm Hg of pressure, which requires the heart to expend more energy in its contraction cycle. This pumping challenge is significantly greater for animals with long necks. A standing giraffe, for example, needs to pump blood as much as 2.5 m above the heart. That requires about 190 mm Hg of additional blood pressure in the left ventricle, and a giraffe's normal systolic pressure near the heart is over 250 mm Hg. (Systolic pressure that high would be extremely dangerous in a human.) Check valves and sinuses, along with feedback mechanisms that reduce cardiac output, prevent this high pressure from damaging the giraffe's brain when it lowers its head to drink—a body position that causes blood to flow downhill almost 2 m from the heart, adding an extra 150 mm Hg of blood pressure in the arteries leading to the brain. Physiologists speculate about blood pressure and cardiovascular adaptations in dinosaurs—some of which had necks almost



❶ A typical blood pressure reading for a 20-year-old is 120/70. The units for these numbers are mm of mercury (Hg); a blood pressure of 120 is a force that can support a column of mercury 120 mm high.

❹ The cuff is loosened further until the blood flows freely through the artery and the sounds below the cuff disappear. The pressure at this point is the diastolic pressure remaining in the artery when the heart is relaxed.

❷ A sphygmomanometer, an inflatable cuff attached to a pressure gauge, measures blood pressure in an artery. The cuff is wrapped around the upper arm and inflated until the pressure closes the artery, so that no blood flows past the cuff. When this occurs, the pressure exerted by the cuff exceeds the pressure in the artery.

❸ A stethoscope is used to listen for sounds of blood flow below the cuff. If the artery is closed, there is no pulse below the cuff. The cuff is gradually deflated until blood begins to flow into the forearm, and sounds from blood pulsing into the artery below the cuff can be heard with the stethoscope. This occurs when the blood pressure is greater than the pressure exerted by the cuff. The pressure at this point is the systolic pressure.

▲ **Figure 42.12 Measurement of blood pressure.** Blood pressure is recorded as two numbers separated by a slash. The first number is the systolic pressure; the second is the diastolic pressure.

10 m long, which would have required a systolic pressure of nearly 760 mm Hg to pump blood to the brain when the head was fully raised. But evidence indicates that dinosaurs probably did not have hearts powerful enough to generate such pressures. Based on this analysis and on studies of neck-bone structure, some biologists have concluded that the long-necked dinosaurs fed close to the ground rather than raising their head to feed on high foliage.

By the time blood reaches the veins, its pressure is not affected much by the action of the heart. This is because the blood encounters so much resistance as it passes through the millions of tiny arterioles and capillaries that the pressure generated by the pumping heart has been dissipated and can no longer propel the blood through the veins. How does blood return to the heart, especially when it must travel from the lower extremities against gravity? Rhythmic contractions of smooth muscles in the walls of venules and veins account for some movement of the blood. More importantly, the activity of skeletal muscles during exercise squeezes blood through the veins (see Figure 42.10). Also, when we inhale, the change in pressure within the thoracic (chest) cavity causes the venae cavae and other large veins near the heart to expand and fill with blood.

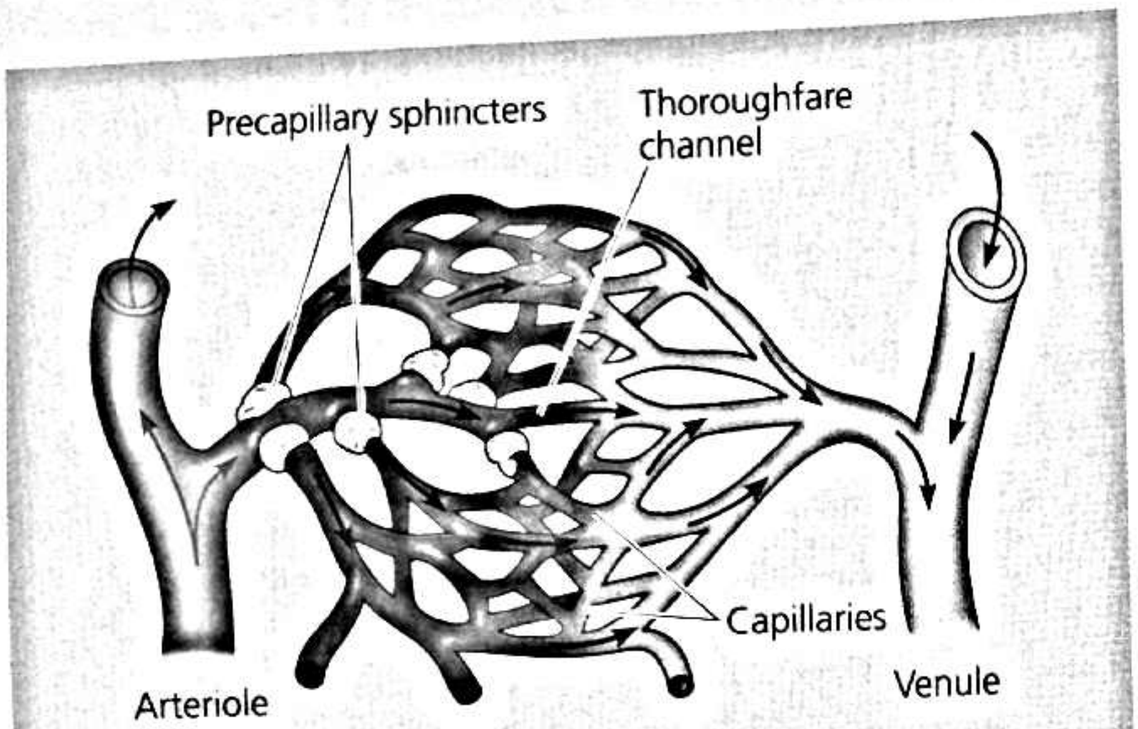
Capillary Function

At any given time, only about 5–10% of the body's capillaries have blood flowing through them. However, each tissue has many capillaries, so every part of the body is supplied with blood at all times. Capillaries in the brain, heart, kidneys, and liver are usually filled to capacity, but in many other sites, the blood supply varies over time as blood is diverted from one destination to another. After a meal, for instance, blood supply to the digestive tract increases. During strenuous exercise, blood is diverted from the digestive tract and supplied more generously to skeletal muscles and skin. This is one reason that exercising heavily immediately after eating a big meal may cause indigestion.

Two mechanisms regulate the distribution of blood in capillary beds. Both depend on smooth muscles controlled by nerve signals and hormones. In one mechanism, contraction of the smooth muscle layer in the wall of an arteriole constricts the vessel, reducing its diameter and decreasing blood flow through it to a capillary bed. When the muscle layer relaxes, the arteriole dilates, allowing blood to enter the capillaries. In the other mechanism, rings of smooth muscle—called precapillary sphincters because they are located at the

entrance to capillary beds—control the flow of blood between arterioles and venules **(Figure 42.13)**.

As you have read, the critical exchange of substances between the blood and the interstitial fluid that bathes the cells takes place across the thin endothelial walls of the capillaries. Some substances may be carried across an endothelial cell in vesicles that form by endocytosis on one side of the cell and then release their contents by exocytosis on the opposite side. Others simply diffuse between the blood and the interstitial fluid. Small molecules, such as O_2 and CO_2, diffuse down concentration gradients across the endothelial cells. Diffusion can also occur through the clefts between adjoining cells. However, transport through these clefts occurs mainly by bulk flow due to fluid pressure. Blood pressure within the capillary pushes fluid (consisting of water and small solutes such as sugars, salts, O_2, and urea) through the capillary clefts. The outward movement of this fluid causes a net loss of fluid from the upstream end of the capillary near an arteriole. Blood cells suspended in blood and most proteins dissolved in the blood are too large to pass readily through the endothelium and remain in the capillaries. The blood proteins remaining in the capillaries, especially albumin, create approximately constant osmotic pressure from the arteriole to the venule end of a capillary bed. In contrast, blood pressure drops sharply. This difference between blood pressure and osmotic pressure drives fluids out of capillaries at the arteriole end and into capillaries at the venule end **(Figure 42.14)**. About 85% of the fluid that leaves the blood at the arterial end of a capillary bed reenters from the interstitial fluid at the venous end, and the remaining 15% is eventually returned to the blood by the vessels of the lymphatic system.



▲ **Figure 42.13 Blood flow in capillary beds.** Precapillary sphincters regulate the passage of blood into capillary beds. Some blood flows directly from arterioles to venules through capillaries called thoroughfare channels, which are always open.

Fluid Return by the Lymphatic System

So much blood passes through the capillaries that the cumulative loss of fluid adds up to about 4 L per day. There is also some leakage of blood proteins, even though the capillary wall is not very permeable to large molecules. The lost fluid and proteins return to the blood via the **lymphatic system.** Fluid enters this system by diffusing into tiny lymph capillaries intermingled among capillaries of the cardiovascular system. Once inside the lymphatic system, the fluid is called **lymph;** its composition is about the same as that of interstitial fluid. The lymphatic system drains into the circulatory system near the junction of the venae cavae with the right atrium (see Figure 43.5).

Lymph vessels, like veins, have valves that prevent the backflow of fluid toward the capillaries. Rhythmic contractions of the vessel walls help draw fluid into lymphatic capillaries. Also like veins, lymph vessels depend mainly on the movement of skeletal muscles to squeeze fluid toward the heart.

Along a lymph vessel are organs called **lymph nodes.** By filtering the lymph and attacking viruses and bacteria, lymph nodes play an important role in the body's defense. Inside each lymph node is a honeycomb of connective tissue with spaces filled by white blood cells specialized for defense. When the body is fighting an infection, these cells multiply rapidly, and the lymph nodes become swollen and tender (which is why your doctor checks your neck for swollen lymph nodes when you feel sick).

The lymphatic system helps defend against infection and maintains the volume and protein concentration of the blood

pluripotent stem cells may soon provide an effective treatment for a number of human diseases, including leukemia. A person with leukemia has a cancerous line of the stem cells that produce leukocytes. The cancerous stem cells crowd out cells that make erythrocytes and produce an unusually high number of leukocytes, many of which are abnormal. One experimental treatment for leukemia involves removing pluripotent stem cells from a patient, destroying the bone marrow, and restocking it with noncancerous stem cells. As few as 30 of these cells can completely repopulate the bone marrow.

Blood Clotting

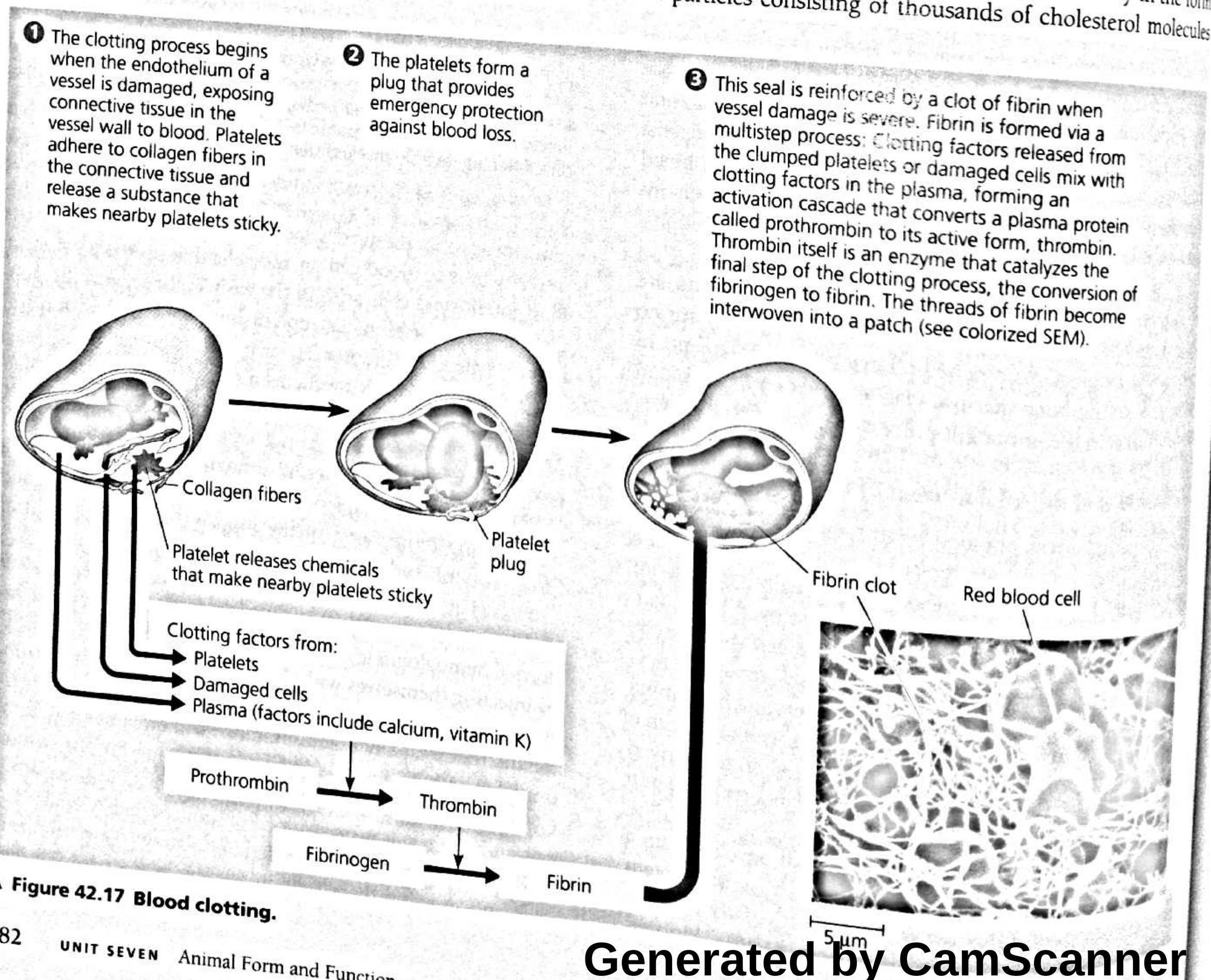
Most people get cuts and scrapes from time to time, yet we do not bleed to death because blood contains a self-sealing material that plugs leaks. The sealant is always present in an inactive form called **fibrinogen.** A clot forms only when this plasma protein is converted to its active form, **fibrin,** which aggregates into threads that form the framework of the clot. The clotting mechanism usually begins with the release of clotting factors from platelets and involves a complex chain of reactions that ultimately transforms fibrinogen to fibrin **(Figure 42.17)**. More than a dozen clotting factors have been discovered, and the mechanism is still not fully understood. A genetic mutation that affects any step of the clotting process causes **hemophilia,** a disease characterized by excessive bleeding from even minor cuts and bruises.

Anticlotting factors in the blood normally prevent spontaneous clotting in the absence of injury. Sometimes, however, platelets clump and fibrin coagulates within a blood vessel, blocking the flow of blood. Such a clot is called a **thrombus.** These potentially dangerous clots are more likely to form in individuals with cardiovascular disease.

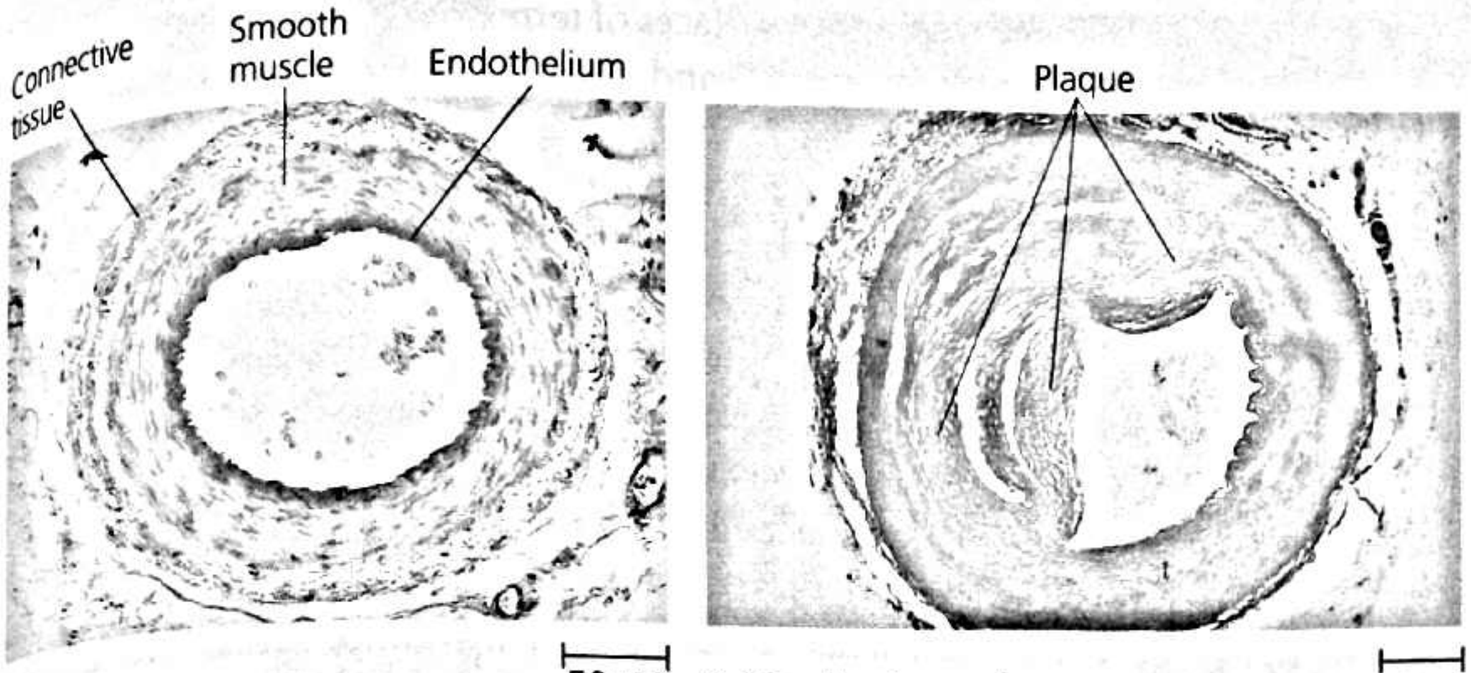
Cardiovascular Disease

More than half the deaths in the United States are caused by **cardiovascular diseases,** disorders of the heart and blood vessels. The tendency to develop cardiovascular disease is inherited to some extent, but lifestyle plays a large role, too. Nongenetic factors that increase the risk of cardiovascular problems include smoking, lack of exercise, a diet rich in animal fat, and high concentrations of cholesterol in the blood.

Cholesterol travels in the blood plasma mainly in the form of particles consisting of thousands of cholesterol molecules



▲ **Figure 42.17 Blood clotting.**



▲ **Figure 42.18 Atherosclerosis.** These light micrographs contrast a cross section of **(a)** a normal (healthy) artery with **(b)** an artery partially blocked by an atherosclerotic plaque. Plaques consist mostly of fibrous connective tissue and smooth muscle cells infiltrated with lipids.

and other lipids bound to a protein. One type of particle—**low-density lipoproteins (LDLs)**, often called the "bad cholesterol"—is associated with the deposition of cholesterol in arterial plaques, growths that develop on the inner walls of arteries. Another type—**high-density lipoproteins (HDLs)**, or "good cholesterol"—appears to reduce the deposition of cholesterol. Exercise increases HDL concentration, whereas smoking has the opposite effect on the LDL/HDL ratio.

Healthy arteries have smooth inner linings that promote unimpeded blood flow. The deposition of cholesterol thickens and roughens this smooth lining. A plaque forms at the site and becomes infiltrated with fibrous connective tissue and still more cholesterol. Such plaques narrow the bore of the artery, leading to a chronic cardiovascular disease known as **atherosclerosis (Figure 42.18)**. The rough lining of an atherosclerotic artery seems to encourage the adhesion of platelets, triggering the clotting process and interfering with circulation.

Hypertension (high blood pressure) promotes atherosclerosis and increases the risk of heart attack and stroke. Atherosclerosis tends to raise blood pressure by narrowing the vessels and reducing their elasticity. According to one hypothesis, chronic high blood pressure damages the endothelium that lines arteries, promoting plaque formation. Fortunately, hypertension is simple to diagnose and can usually be controlled by diet, exercise, medication, or a combination of these. A diastolic pressure above 90 may be cause for concern, and living with extreme hypertension—say, 200/120—is courting disaster.

As atherosclerosis progresses, arteries become narrower, and the threat of heart attack or stroke increases. There may be warning signs. For example, if a coronary artery is only partially blocked, the person may feel occasional chest pain, a condition known as angina pectoris. The pain is most likely to appear when the heart is laboring hard as a result of physical or emotional stress, and it signals that part of the heart is not receiving enough O_2. However, many people with atherosclerosis are completely unaware of their condition until catastrophe strikes.

The final blow is usually a heart attack or a stroke. A **heart attack** is the death of cardiac muscle tissue resulting from prolonged blockage of one or more coronary arteries, the vessels that supply oxygen-rich blood to the heart. Because they are small in diameter to begin with, the coronary arteries are particularly vulnerable. Such blockage can destroy cardiac muscle quickly, since the constantly beating heart muscle cannot survive long without oxygen. A **stroke** is the death of nervous tissue in the brain, usually resulting from rupture or blockage of arteries in the head.

Heart attacks and strokes frequently result from a thrombus, or blood clot, that clogs an artery. A key process leading to the clogging of an artery by a thrombus is an inflammatory response triggered by the accumulation of LDLs in the artery's inner lining. Such an inflammation, which is analogous to the body's response to a cut infected by bacteria (see Figure 43.6), can cause plaques to rupture, releasing fragments that form a thrombus. The thrombus may originate in a coronary artery or an artery in the brain, or it may develop elsewhere in the circulatory system and reach the heart or brain via the bloodstream. The transported clot, called an *embolus*, is swept along until it lodges in an artery too small for the clot to pass. An embolus is more likely to become trapped in a vessel that has been narrowed by plaques. The embolus blocks blood flow, and cardiac or brain tissue downstream from the obstruction may die from O_2 deprivation. If damage in the heart interrupts the conduction of electrical impulses through cardiac muscle, heart rate may change drastically or the heart may stop beating altogether. Still, the victim may survive if a heartbeat is restored by cardiopulmonary resuscitation (CPR) or some other emergency procedure within a few minutes of the attack. The effects of a stroke and the individual's chance of survival depend on the extent and location of the damaged brain tissue.

Concept Check 42.4

1. About how many red blood cells does the bone marrow of a human produce per day, assuming a total red blood cell count of 25 trillion (2.5×10^{13}) and an average longevity of 4 months for the cells?
2. Explain why a physician might order a white-cell count for a patient with symptoms of an infection.
3. How can a few dozen transplanted bone marrow stem cells replace the wide variety of cells that occur in bone marrow?

For suggested answers, see Appendix A.