

GLOBAL
EDITION



Human Biology

Concepts and Current Issues

EIGHTH EDITION

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CURRENT ISSUE

How Should Comparative Effectiveness Research Be Used?

Mr. Reynolds has a heart problem. An angiogram shows that a short section of one of the main arteries supplying the left ventricle of his heart is narrowed, restricting blood flow to his heart muscle. His doctor tells him that he is at serious risk of a heart attack. The doctor explains that there are at least three techniques that could be used to restore blood flow to his heart: (1) balloon angioplasty, (2) a coronary artery stent, or (3) a coronary artery bypass graft (CABG). Which technique would be best for Mr. Reynolds? The doctor and Mr. Reynolds go over the options together, but the differences between the techniques are difficult for Mr. Reynolds to understand. He leaves the decision to his physician, whom he has known for 25 years. The physician chooses a coronary artery stent because it has worked best for his previous patients with heart disease.

The body of medical literature is now so vast and expanding so rapidly that even the best physicians can't know it all. This is where a relatively new field of medical science called Comparative Effectiveness Research (CER) comes in. CER focuses on analysis of the medical literature available to date, in order to reach scientifically sound judgments about the value (or lack thereof)



Doctoring, 1948.

of specific medical tests, treatments, and disease prevention strategies. In essence, CER seeks to determine the best practices in medicine based on our current knowledge.

Changing How Medicine Is Practiced

Consider how CER might benefit Mr. Reynolds's physician (and Mr. Reynolds, of course). By reviewing CER data, Mr. Reynolds's physician learns that a stent tends to be most effective for middle-aged

Questions to Consider

1 Who do you want to help you decide which treatment options would be best for you? If not a specific professional (doctor, patient representative, health insurance specialist), what other information would you like to have available to you?

2 Do you think cost-effectiveness should be a part of any comparative effectiveness analysis of treatment or diagnostic options? Why or why not?

white males with heart disease. However, the research shows that there's an age-related tipping point on the effectiveness of the technique and that the best treatment option depends on the severity of the narrowing: If the patient is over 55, the data indicates that balloon angioplasty is the best option. (Hmmm, how old is Mr. Reynolds this year?) If the degree of narrowing of a coronary artery is greater than 80%, for example, then the best option (again, for a middle-aged white male) would be a coronary artery bypass graft. (What is the degree of narrowing in Mr. Reynolds, anyway?) Toss in other factors like gender, race, physical condition, body weight, smoker-versus-nonsmoker, and you can begin to see the full power of CER. In theory, CER could analyze multiple factors at once to arrive at the best treatment option for patients who are described by a particular combination of factors. Even the most experienced physicians can't carry *that* much information around in their heads!

Some politicians believe that the federal government should invest in CER, because any money spent on the research now would be offset by reduced health care expenditures in the future. To jump-start a national CER program, Congress passed the Comparative Effectiveness Research Act of 2009 and funded it with \$1.1 billion as part of the economic stimulus package. To keep the program free of bias, the prestigious Institute of Medicine of the National Academies of Science was asked to come up with a list of 100 top priority topics for CER funding. Among the topics are comparisons of the most effective practices to treat or prevent a number of cardiovascular diseases and risk factors, including high blood pressure, coronary artery disease, heart failure, →



Doctoring in the twenty-first century.

and abnormalities of heart electrical rhythm. This is not surprising because cardiovascular diseases are the number one cause of death in the United States (cancer is second).

Who Will Make Health Care Decisions?

CER could become a powerful tool for improving health care quality and lowering costs. Nevertheless, the CER Act of 2009 has stirred strong feelings among physicians, patients, politicians, and the health care industry because of the ways it could change how medicine is practiced. Physicians and patient advocacy groups worry that if “best practices” become defined by CER, doctors and patients could begin to lose the right to make decisions regarding treatment options. They fear that health care decisions may be dictated primarily by bureaucrats and insurance companies. In recognition of this concern, the CER Act includes language to the effect that the findings of CER research shall “not be construed as mandates for practice guidelines, coverage recommendations, payment, or policy recommendations.” In other words, physicians and patients can still use their judgment in deciding the appropriate treatment option. But by the same token, neither private insurers nor

our primary public health care system (Medicare) are required by law to pay for it.

Therein lie the big questions: Will physicians and patients continue to be the decision makers in medical treatment decisions? Or is it inevitable that the old way of practicing medicine is going to change? Do we really believe that health insurance companies, group health plans, and even Medicare/Medicaid will *not* find a way to use CER data to influence reimbursement policies and hence treatment decisions? Would it be a good thing or a bad thing if they did?


Flash forward 25 years. You’re in the doctor’s office, and the doctor is telling you that a scan of your heart shows a 63% narrowing of a section of your left-anterior

descending coronary artery. She swings around to her computer, taps a few keys, and turns back to you to report that according to the latest data from the Comparative Effectiveness Research Institute, the most effective method for repair of your coronary artery is Robotic Artificial Vessel Extension (RAVE). A few more taps on her computer keyboard informs her that your government-supported health insurance will pay for the procedure and that there is an opening on the hospital’s surgical schedule on Tuesday. Data further reveals that 99.7% of Dr. Sloan’s RAVE surgeries have been successful and that 94% of all patients with your condition who undergo RAVE are discharged from the hospital on the same day as their surgery. You go ahead and book that vacation to London next month.

SUMMARY

- The medical literature is expanding so rapidly that even the best physicians can no longer keep up with it.
- Recognizing this, the government will spend \$1.1 billion on Comparative Effective Research (CER) to determine the best practices in medicine based on our current knowledge and make that information available to everyone.
- CER could slow down rising health-care costs.
- A concern is that CER recommendations will eventually influence third-party payer reimbursement policies, so that patients and doctors will lose the ability to make treatment choices.

The heart and blood vessels play a critical role in the maintenance of homeostasis. Collectively known as the **cardiovascular system** (from the Greek *kardia*, heart, and the Latin *vasculum*, small vessel), the heart and blood vessels function as a centrally controlled blood distribution network. The heart provides the power to move the blood, and the vascular system represents the network of branching conduit vessels through which the blood flows. Central control (oversight and management, if you will) is provided by the nervous system. By controlling the rate at which the heart pumps and the resistance to flow through blood vessels, the nervous system apportions blood flow to the various tissues and organs according to need.

 Homeostasis is not maintained by just the cardiovascular and nervous systems, however; other organ systems are also involved. The digestive system delivers nutrients to the blood passing through its blood vessels. The kidneys of the urinary system remove excess salt, water, and the waste products of cellular metabolism. Glands of the endocrine system secrete

hormones into the blood. The respiratory system provides life-sustaining oxygen and removes the waste by-product carbon dioxide. Even the skin is involved in homeostasis, by adjusting the amount of heat lost from the body. ■

We’ll start the chapter by considering the blood vessels and the structure and function of the heart. Then we’ll describe how the cardiovascular system is regulated. Finally, we’ll take a look at some major cardiovascular disorders.

8.1 Blood vessels transport blood

A branching network of blood vessels transports blood to all parts of the body. The network is so extensive that if our blood vessels were laid end to end, they would stretch 60,000 miles!

We classify the body’s blood vessels into three major types: *arteries*, *capillaries*, and *veins*. Thick-walled arteries transport blood to body tissues under high pressure. Microscopic capillaries exchange solutes and water with the

cells of the body. Thin-walled veins store blood and return it to the heart. **Figure 8.1** illustrates the structures of each type of blood vessel, described in more detail below.

Arteries transport blood away from the heart

As blood leaves the heart, it is pumped into large, muscular, thick-walled **arteries**. Arteries transport blood away from the heart. The larger arteries have a thick layer of muscle because they must be able to withstand the high pressures generated by the heart. Arteries branch again and again, so the farther blood moves from the heart, the smaller in diameter the arteries become.

Large- and medium-sized arteries are like thick garden hoses, stiff yet somewhat elastic (distensible). Arteries stretch a little in response to high pressure but are strong enough to withstand high pressures year after year. The ability to stretch under pressure is important because a function of arteries is to store the blood that is pumped into them with each beat of the heart and then provide it to the capillaries (at high pressure) even between heartbeats. The elastic recoil of arteries is the force that maintains the blood pressure between beats. Think of the arteries as analogous to a city's water system of branching, iron or steel pipes that provide nearly constant water pressure to nearly every building in the vicinity.

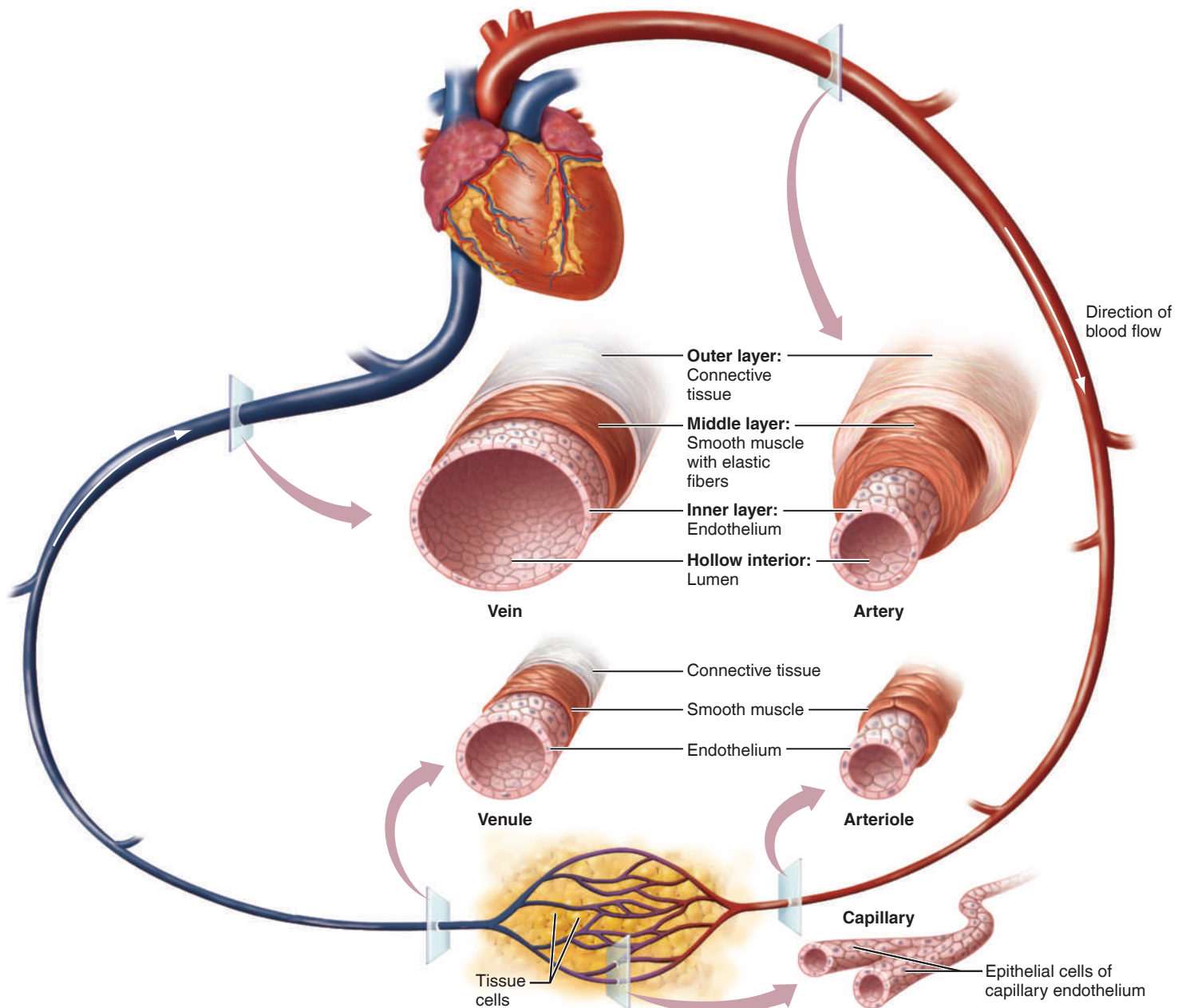


Figure 8.1 The structures of blood vessels in the human body.

The structure of the walls of large and medium-sized arteries is ideally suited to their functions. The vessel wall is a sandwich of three distinct layers surrounding the *lumen*, or hollow interior of the vessel:

1. The thin inner layer, the *endothelium*, is a layer of flattened, *squamous* epithelial cells. It is a continuation of the lining of the heart. The flattened cells fit closely together, creating a slick surface that keeps friction to a minimum and promotes smooth blood flow.
2. Just outside the endothelium is a layer composed primarily of smooth muscle with interwoven elastic connective tissue. In most arteries this is the thickest of the three layers. Steady partial contraction of the smooth muscle of large and medium-sized arteries stiffens the arteries and helps them resist the high pressures within, but it does not constrict them enough to alter blood flow. The elastic tissue makes large and medium-sized arteries slightly distensible so they can stretch passively to accommodate the blood that enters with each heartbeat.
3. The outermost layer of large and medium-sized arteries consists of a tough supportive layer of connective tissue, primarily collagen. This sturdy casing anchors vessels to surrounding tissues and helps protect them from injury.

The fact that arteries are constantly under high pressure places them at risk of injury. If the endothelium becomes damaged, blood may seep through the injured area and work its way between the two outer layers, splitting them apart. The result is an *aneurysm*, or ballooning of the artery wall. Some aneurysms cause the smooth muscle and endothelial layers to bulge inward as they develop, narrowing the lumen enough to reduce blood flow to an organ or region of the body. Others force the outer connective tissue layer to bulge outward. Sometimes aneurysms cause severe chest pain, but in other cases they are completely symptomless until they rupture or “blow out,” causing massive internal bleeding and often death. If you’ve ever seen a water line burst, you know how quickly it can be devastating. Aneurysms of the aorta (see section 8.2) kill an estimated 25,000 Americans every year. Actor John Ritter’s sudden death in 2003 was caused by a ruptured aneurysm.

Aneurysms often take years to develop. During this time, many can be detected and repaired surgically. Some physicians recommend that anyone with a family history of aneurysm should be examined, even if there are no symptoms. Doctors can sometimes detect inward-bulging aneurysms with a stethoscope (an instrument for listening to sounds inside the body) because flowing blood produces characteristic sounds as it passes through a narrowed arterial lumen. A computerized tomography (CT) scan may also locate aneurysms before they rupture.

Arterioles and precapillary sphincters regulate blood flow

Eventually blood reaches the smallest arteries, called **arterioles** (literally, “little arteries”). The largest artery in the body, the *aorta*, is about 2.5 centimeters (roughly 1 inch)

wide. In contrast, arterioles have a diameter of 0.3 millimeter or less, about the width of a piece of thread.

By the time blood flows through the arterioles, blood pressure has fallen considerably. Consequently, arterioles can be simpler in structure. Generally, they lack the outermost layer of connective tissue, and their smooth muscle layer is not as thick. In addition to blood transport and storage, arterioles have a third function not shared by the larger arteries: They help regulate the amount of blood that flows to each capillary. They do this by contracting or relaxing the smooth muscle layer, altering the diameter of the arteriole lumen.

Right where an arteriole joins a capillary is a band of smooth muscle called the **precapillary sphincter** (Figure 8.2). The precapillary sphincters serve as gates that control blood flow into individual capillaries.

Relaxation of vascular smooth muscle is called *vasodilation*. Vasodilation of arterioles and precapillary sphincters increases their diameter and thus increases blood flow to the capillaries. Conversely, contraction of vascular smooth muscle is called *vasoconstriction*. Vasoconstriction of arterioles and precapillary sphincters reduces their diameter and thus reduces blood flow to the capillaries.

A wide variety of external and internal factors can produce vasodilation or vasoconstriction, including nerves, hormones, and conditions in the local environment of the arterioles and precapillary sphincters. If you go outside on a cold day, you may notice that your fingers start to look pale. This is because vasoconstriction produced by nerves is narrowing your vessels

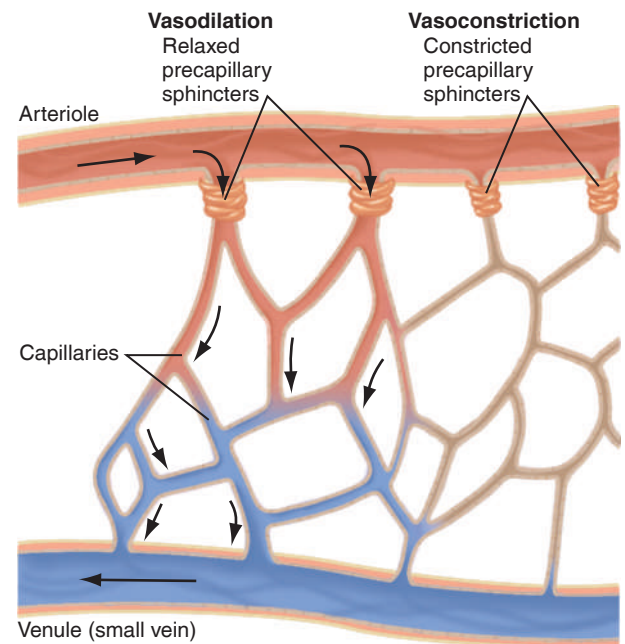


Figure 8.2 Precapillary sphincters control the flow of blood into individual capillaries. In this diagram, the two precapillary sphincters on the right are vasoconstricted, reducing flow in that region. Arrows indicate direction of blood flow.

to reduce heat loss from your body. On the other hand, hot weather will make your skin appear flushed as vasodilation occurs to speed up heat loss and cool you off. Emotions can also have an impact: Vasodilation is partly responsible for the surge in blood flow that causes the penis or clitoris to become erect when we are sexually aroused. Later in this chapter, we will talk more about how the cardiovascular system is regulated to maintain homeostasis.

Capillaries: where blood exchanges substances with tissues

Arterioles connect to the smallest blood vessels, called **capillaries** (Figure 8.3a). Capillaries are thin-walled vessels that average only about one-hundredth of a millimeter in diameter—not much wider than the red blood cells that travel through them. In fact, they are so narrow that red blood cells (RBCs) often have to pass through them in single file or even bend to squeeze through (Figure 8.3b).

Extensive networks of capillaries, called *capillary beds*, can be found in all areas of the body, which is why you are likely to bleed no matter where you cut yourself. The branching design of capillaries and their thin, porous walls allow blood to exchange oxygen, carbon dioxide, nutrients, and waste products with tissue cells. Capillary walls consist of a single layer of squamous epithelial cells (Figure 8.3c). Microscopic pores pierce this layer, and the cells are separated by narrow slits. These openings are large enough to allow the exchange of fluid and other materials between blood and the interstitial fluid (the fluid that surrounds every living cell), yet small enough to retain RBCs and most plasma proteins in the capillary. Some white blood cells

(WBCs) can also squeeze between the cells in capillary walls and enter the tissue spaces.

In effect, capillaries function as biological strainers that permit selective exchange of substances with the interstitial fluid. In fact, capillaries are the *only* blood vessels that can exchange materials with the interstitial fluid.

Figure 8.4 illustrates the general pattern of how water and substances move across a capillary. At the beginning of a capillary, fluid is filtered out of the vessel into the interstitial fluid, accompanied by oxygen, nutrients, and raw materials needed by the cell. The filtered fluid is essentially like plasma except that it contains very little protein because most protein molecules are too large to be filtered. Filtration of fluid is driven by the blood pressure generated by the heart. Waste materials such as carbon dioxide and urea (a nitrogen-containing substance) diffuse out of the cells and back into the blood.

Most of the filtered fluid is reabsorbed by diffusion back into the last half of the capillary before it joins a vein. The force for this reabsorption is the presence of protein in the blood but not in the interstitial fluid. In other words, fluid diffuses from an area of high water concentration (interstitial fluid) to an area of lower water concentration (blood plasma). However, the diffusional reabsorption of fluid does not quite match the pressure-induced filtration of fluid, so a small amount of filtered fluid remains in the interstitial space as excess interstitial fluid.

✓ Why doesn't exchange of gases and nutrients with the interstitial fluid occur in arteries and arterioles too, instead of just in capillaries? Put another way, what about the structure of an artery or an arteriole prevents such exchange from occurring?

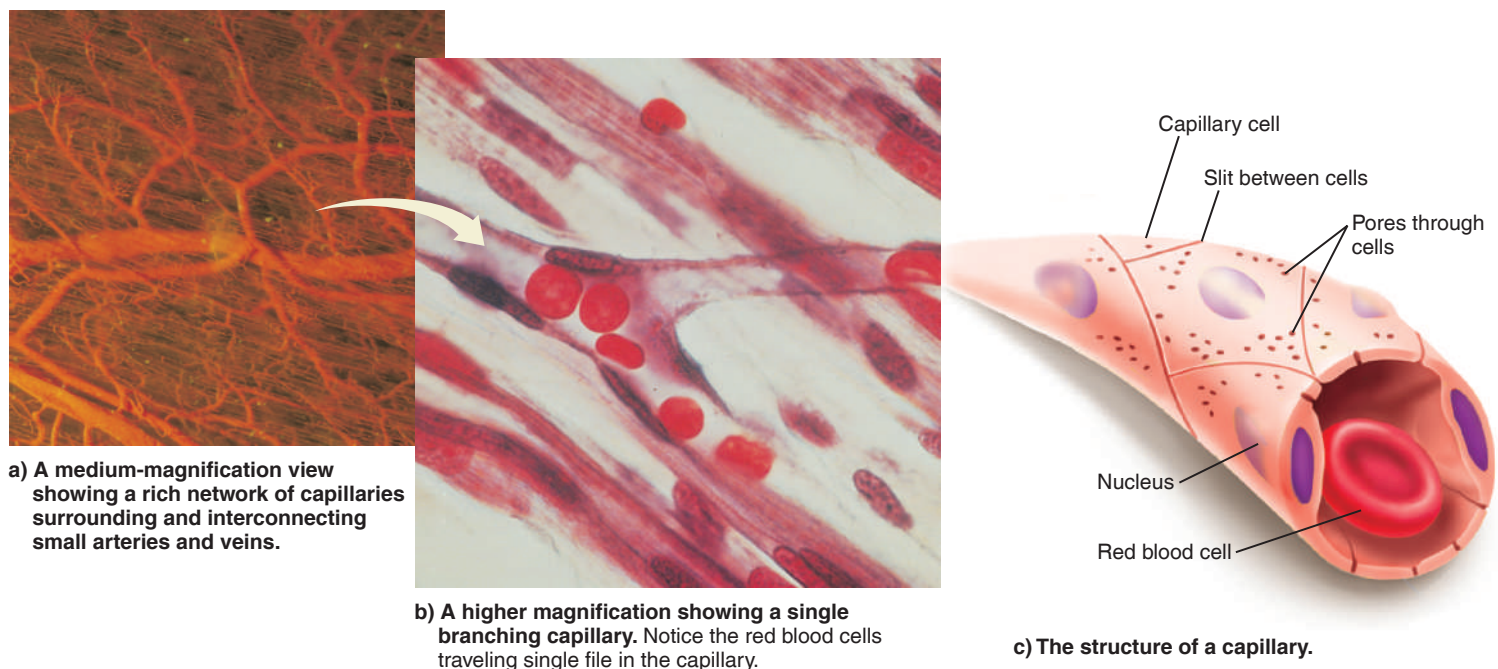


Figure 8.3 Capillaries.

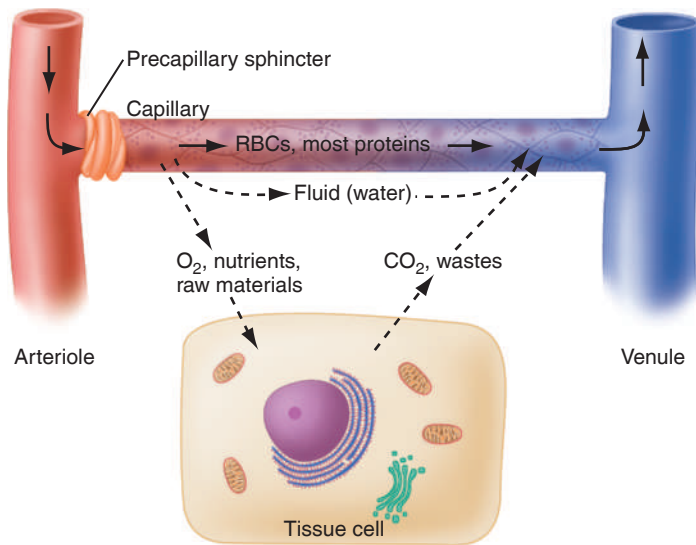


Figure 8.4 The general pattern of fluid movement between capillaries, the interstitial fluid, and cells. For simplicity, only a single tissue cell is shown, but a single capillary may supply many nearby cells.

✓ Why does most of the fluid that was filtered out of the proximal (beginning) end of the capillary move back into the distal (far) end?

The lymphatic system helps maintain blood volume

Although the imbalance between the amount of plasma fluid filtered by the capillaries and the amount reabsorbed is not large, over the course of a day it would amount to about 2 or 3 liters. This excess plasma fluid must be returned to the cardiovascular system somehow, or all the plasma would end up in the interstitial fluid.

The excess plasma fluid is absorbed by blind-ended capillaries that join together into a collection system of larger vessels, collectively called the *lymphatic system*. The lymphatic system is somewhat similar to (and nearly parallel to) the venous system of blood vessels, except that the fluid of the lymphatic system (called *lymph*) does not contain plasma proteins or RBCs. In addition to absorbing excess interstitial fluid, the capillaries of the lymphatic system also pick up objects in the interstitial fluid that are too large to diffuse into the blood capillaries, such as lipid droplets absorbed during digestion and invading microorganisms. The lymphatic system transports the lymph back to veins near the heart, where the lymph rejoins the venous blood.

Aside from its role in returning excess fluid and large objects to the blood, the lymphatic system also plays a major role in our immune defenses. You'll hear more about the lymphatic system when we discuss the immune system. For now, just be aware that the lymphatic system, though technically not part of the cardiovascular system, plays a vital role in maintaining the proper volumes of blood and interstitial fluid.

✓ There are certain parasitic worms that can enter the lymphatic system and completely block the lymphatic capillaries draining an arm or a leg. Predict what would happen to the arm or leg if this occurs.

Veins return blood to the heart

From the capillaries, blood flows back to the heart through *venules* (small veins) and **veins** (see Figures 8.1 and 8.4). Like the walls of arteries, the walls of veins consist of three layers of tissue. However, the outer two layers of the walls of veins are much thinner than those of arteries. Veins also have a larger diameter lumen than arteries.

The anatomical differences between arteries and veins reflect their functional differences. As blood moves through the cardiovascular system, blood pressure becomes lower and lower. The pressure in veins is only a small fraction of the pressure in arteries, so veins do not need nearly as much wall strength as arteries. The larger diameter and high distensibility of veins allows them to stretch like thin balloons to accommodate large volumes of blood at low pressures.

In addition to their transport function, then, veins serve as a blood volume reservoir for the entire cardiovascular system. Nearly two-thirds of all the blood in your body is in your veins. Thanks to their blood reservoir function, even if you become dehydrated or lose a little blood, your heart will still be able to pump enough blood to keep your blood pressure fairly constant.

The distensibility of veins, however, can lead to problems in returning blood to the heart against the force of gravity. When you stand upright, blood tends to collect in the veins of your legs and feet. People who spend a lot of time on their feet may develop *varicose veins*, permanently swollen veins that look twisted and bumpy from pooled blood. Varicose veins can appear anywhere, but they are most common in the legs and feet. In severe cases, the skin surrounding veins becomes dry and hard because the tissues are not receiving enough blood. Often, varicose veins can be treated by injecting an irritating solution that shrivels the vessels and makes them less visible. This should not affect blood flow because surrounding undamaged veins take over and return blood to the heart.

Fortunately, three mechanisms assist the veins in returning blood to the heart: (1) contractions of skeletal muscles, (2) one-way valves inside the veins, and (3) movements associated with breathing. Let's look at each in turn.

Skeletal muscles squeeze veins On their path back to the heart, veins pass between many skeletal muscles. As we move and these muscles contract and relax, they press against veins and collapse them, pushing blood toward the heart. You may have noticed that you tire more easily when you stand still than when you walk around. This is because walking improves the return of blood to your heart and prevents fluid accumulation in your legs. It also increases blood flow and the supply of energy to your leg muscles.

One-way valves permit only one-way blood flow Most veins contain valves consisting of small folds of the inner layer that protrude into the lumen. The structure of these valves allows blood to flow in one direction only: toward the heart. They open passively to permit blood to move toward the heart and then close whenever blood begins to flow backward. Together, skeletal muscles and valves form