Chapter 50

The Circulatory System

Chapter Outline

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50.5 Characteristics of Blood Vessels
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Enhancer

Introduction

In all multicellular organisms, oxygen obtained by the respiratory system and nutrients processed by the digestive system must be transported to cells throughout the body. Conversely, carbon dioxide and other waste products produced within the cell must be removed by the respiratory system, and waste products must be transported from the body. The transport of these materials is the primary function of the circulatory system. All multicellular organisms have a heart that pumps fluid through the body. Many invertebrates have an open system in which fluids move through the body cavity. Vertebrates also have a system that moves lymph through the body, whereas the primary circulatory fluid is blood, which means that circulation of blood is involved.

50.1 The Components of Blood

Learning Outcomes

1. Describe the functions of circulating blood.
2. Distinguish between the types of formed elements.
3. Describe the process of blood clotting.

Blood is a connective tissue composed of a fluid matrix, called plasma, and several different kinds of cells and other formed elements that circulate within that fluid (Figure 50.1). Blood participate in many processes in the body, including:

1. Regulation. The cardiovascular system transports regulatory hormones from the endocrine glands and also transports regulatory hormones from the endocrine glands and also participates in temperature regulation. Contraction and dilation of blood vessels helps maintain the body temperature.
2. Nutrients, wastes, and hormones. Dissolved within the plasma are all the nutrients resulting from digestive breakdown that can be used by cells, including glucose, amino acids, and vitamins. Also dissolved in the plasma are wastes such as nitrogen compounds and CO2 produced by metabolizing cells. Endocrine hormones released from glands are also carried through the blood to target cells.
3. Protection. The cardiovascular system provides blood to all tissues in the body. Blood contains antibodies that fight infection and toxins introduced into the body. Blood clotting helps prevent blood loss when vessels are damaged. Wastes, such as carbon dioxide, are transported by the blood to the lungs for removal.

Formed elements include circulating cells and platelets. The formed elements of blood cells include red blood cells, white blood cells, and platelets. Each element has a specific function in maintaining the body's health and homeostasis.

Erythrocytes

Each microliter of blood contains about 5 million red blood cells, or erythrocytes. The fraction of the total blood volume occupied by red cells is expressed as the hematocrit.

Leukocytes

Less than 1% of the cells in human blood are white blood cells, or leukocytes. Leukocytes are larger than erythrocytes and have more functions. Leukocytes are not confined to the blood as erythrocytes are, but can migrate out of capillaries through the intercellular spaces into the interstitial (tissue) fluid.

Leukocytes

B. Monocytes

C. Lymphocytes

Figure 50.1 Composition of blood.

Blood plasma is a fluid matrix

Blood plasma is the matrix in which blood cells and platelets are suspended. Interstitial (extracellular) fluids originate from the fluid present in plasma.

Although plasma is 92% water, it also contains the following:

1. Nutrients, waste, and hormones. Dissolved within the plasma are all the nutrients resulting from digestive breakdown that can be used by cells, including glucose, amino acids, and vitamins. Also dissolved in the plasma are wastes such as nitrogen compounds and CO2 produced by metabolizing cells. Endocrine hormones released from glands are also carried through the blood to their target cells.
2. Ions. Blood plasma is a dilute salt solution. The predominant plasma ions are Na+, Cl-, and bicarbonate ions (HCO3-). In addition, plasma contains trace amounts of other ions such as Ca2+, Mg2+, Ca2+, K+, and Zn2+.
3. Proteins. As mentioned earlier, the liver produces most of the plasma proteins, including albumin, which constitutes most of the plasma protein; the alpha (a) and beta (b) globulins, which serve as carriers of lipids and steroid hormones; and fibrinogen, which is required for blood clotting. Blood plasma with the fibrinogen removed is called serum.
Platelets
Platelets are cell fragments that pinch off from larger cells in the bone marrow. They are approximately 1 μm in diameter, and following an injury to a blood vessel, the liver releases prothrombin into the blood. In the presence of this clotting factor, fibrinogen is converted into insoluble threads of fibrin. Fibin then aggregates to form the clot.

Formed elements arise from stem cells
The formed elements of blood each have a finite life span and therefore must be constantly replaced. Many of the old cell fragments are digested by phagocytic cells of the spleen, however, many products from the old cells, such as iron and amino acids, are incorporated into new formed elements. The creation of new formed elements begins in the bone marrow (see chapter 47).

All of the formed elements develop from pluripotent stem cells (see chapter 49). The production of blood cells occurs in the bone marrow and is called hematopoiesis. This process generates two types of stem cell with a more restricted fate: a lymphoid stem cell that gives rise to lymphocytes and a myeloid stem cell that gives rise to the rest of the blood cells (figure 50.2).

When the oxygen available in the blood decreases, the kidney converts a plasma protein into the hormone erythropoietin. Erythropoietin then stimulates the production of erythrocytes from the myeloid stem cells through a process called erythropoiesis. In mammals, maturing erythrocytes lose their nuclei prior to release into circulation. In contrast, the mature erythrocytes of all other vertebrates remain nucleated.

Blood clotting is an example of an enzyme cascade
When a blood vessel is broken or cut, smooth muscle in the vessel walls contracts, causing the vessel to constrict. Platelets then accumulate at the injured site and form a plug by sticking to one another and to the surrounding tissues (figure 50.3). A cascade of enzymatic reactions is triggered by the platelets, plasma factors, and molecules released from the damaged tissue.

One of the results of this cascade is that fibrinogen, normally dissolved in the plasma, comes out of solution in a reaction that forms fibrin. The platelet plug is then reinforced by fibrin threads, which contract to form a tighter mass. The tightening plug of platelets, fibrin, and other trapped erythrocytes constitutes a blood clot.

Once the tissue damage is healed, the careful process of dissolving the blood clot begins. This process is significant because if a clot were to loosen and travel in the circulatory system, it may end up blocking a blood vessel in the brain, causing a stroke, or in the heart, causing a heart attack.

Learning Outcomes Review 50.1
- Be able to identify a system function in transport of materials, regulation of temperature, and endocrine, and protection of the body. Formed elements include red blood cells, white blood cells, and platelets.
- Blood clotting is a cascade of enzymatic reactions triggered by platelets and plasma factors to produce insoluble fibrin from fibrinogen.
- How does a blood clot form?

Figure 50.3 Blood clotting. Fibrin is formed from a soluble protein, fibrinogen, in the plasma. This reaction is catalyzed by the enzyme thrombin, which is formed from an inactive enzyme called prothrombin. The activation of thrombin is the last step in a cascade of enzymatic reactions that produces a blood clot when a blood vessel is damaged.
Invertebrate Circulatory Systems

Learning Outcomes
1. Distinguish between open and closed circulatory systems.
2. Define hemolymph.

The nature of the circulatory system in multicellular invertebrates is directly related to the size, complexity, and lifestyle of the organism in question. Sponges and most cnidarians utilize water from the environment as a circulatory fluid. Sponges pass water through a series of channels in their bodies, and Hydra and other cnidarians circulate water through a gastrovascular cavity (figure 50.4). Because the body wall in Hydra species is only two cell layers thick, each cell layer is in direct contact with the external environment or the gastrovascular cavity. Pseudocoelomate invertebrates (roundworms, rotifers) use the fluids of the body cavity for circulation. Most of these invertebrates are quite small or are long and thin, and therefore adequate circulation is accomplished by movements of the body against the fluid, which is in direct contact with the internal tissues and organs. Larger animals, however, have tissues that are several cell layers thick, so that many cells are too far away from the body surface or digestive cavity to directly exchange materials with the environment. Instead, oxygen and nutrients are transported from the environment and digestive cavity to the body cells by an internal fluid within a circulatory system.

Open circulatory systems move fluids in a one-way path

The two main types of circulatory systems are open and closed. In an open circulatory system, such as that found in most mollusks and in arthropods (figure 50.4), there is no distinction between the circulating fluid and the extracellular fluid of the body tissues. This fluid is thus called hemolymph. In insects, a muscular tube, or heart, pumps hemolymph through a network of channels and cavities in the body. The fluid then drains back into the central cavity.

Closed circulatory systems move fluids in a loop

In a closed circulatory system, the circulating fluid, blood, is always enclosed within blood vessels that transport it away from and back to the heart (figure 50.4). In vertebrates, such as cephalopod mollusks and annelids (see chapter 34), and all vertebrates have a closed circulatory system. In annelids such as earthworms, a dorsal vessel contracts rhythmically to function as a pump. Blood is pushed through five small connecting arteries, which branch as capillaries into a network of capillaries in a ventral vessel, which transports the blood back to the body, eventually recovers the dorsal vessel. Smaller vessels branch from each artery to supply the tissues of the earthworm with oxygen and nutrients and to remove waste products.

Vertebrate Circulatory Systems

Learning Outcomes
1. Trace the evolution of the chambered heart from lampreys to birds and mammals.
2. Define the flux of blood through the circulatory system in birds and mammals.

In vertebrates, open circulatory systems pump hemolymph into tissues, from which it drains into a central cavity. Closed circulatory systems move fluid in a loop, from a muscular pumping region such as a heart. Hemolymph (hemocytes) is identical to the extracellular fluid in the tissues.

In the open circulatory system of insects, how does hemolymph get back to the heart? Compare the hemolymph system of most vertebrates to the open circulatory system of insects.

The evolution of large and complex hearts and closed circulatory systems put a premium on efficient circulation. In response, many vertebrates have evolved a remarkable set of adaptations that inevitably link circulation and respiration, which has facilitated diversification throughout aquatic and terrestrial habitats and permitted the evolution of large body size.

In fishes, more efficient circulation developed concurrently with gills. Chordates ancestral to the vertebrates are thought to have had simple tubular hearts, similar to those now seen in crinoids, sea cucumbers, and sea urchins. The heart and circulation of a fish. Diagram of a fish heart, showing the structures in series with each other (sinus venosus, atrium, ventricles, conus arteriosus) that form two pumping chambers. Blood is pumped by the ventricle through the gills and then to the body. Blood rich in oxygen (oxygenated) is shown in red; blood low in oxygen (deoxygenated) is shown in blue.

Learning Outcomes Review 50.2
1. Invertebrates, open circulatory systems pump hemolymph into tissues, from which it then drains into a central cavity. Closed circulatory systems move fluid in a loop, from a muscular pumping region such as a heart. Hemolymph (hemocytes) is identical to the extracellular fluid in the tissues.

Ventral vessels

Figure 50.5 The heart and circulation of a fish. Diagram of a fish heart, showing the structure in series with each other (sinus venosus, atrium, ventricles, conus arteriosus) that form two pumping chambers. Blood is pumped by the ventricle through the gills and then to the body. Blood rich in oxygen (oxygenated) is shown in red; blood low in oxygen (deoxygenated) is shown in blue.
In amphibians and most reptiles, lungs required a separate circulation

The heart and circulation of an amphibian. a. The frog has a three-chambered heart with two atria but only one ventricle, which pumps blood both to the lungs and to the body. b. Despite the potential for mixing, the oxygenated and deoxygenated bloods (red and blue lines, respectively) mix little as they are pumped to the body and lungs. Oxygenation of blood also occurs by gas exchange through the skin.

Learning Outcomes Review 50.3

What is the physiological advantage of having separated ventricles?

Amphibians and crocodilians have two completely separated circulatory systems

Mammals, birds, and crocodilians have a four-chambered heart with two separate atria and two separate ventricles (figure 50.7). The hearts of birds and crocodilians exhibit some differences, but overall are quite similar, which is not surprising given their close evolutionary relationship (figure 50.8). However, the extreme simplicity of the hearts of birds and mammals—so alike that a single illustration can suffice for both (see figure 50.7)—is a remarkable case of convergent evolution (see figure 50.8).

In a four-chambered heart, the right atrium receives deoxygenated blood from the lungs and delivers it to the right ventricle, which pumps the blood to the lungs. The left atrium receives oxygenated blood from the lungs and delivers it to the left ventricle, which pumps the oxygenated blood to the rest of the body (see figure 50.7).

The heart in these vertebrates is a two-cycle pump. Both atria fill with blood and simultaneously contract, emptying the blood into the ventricles. Both ventricles also contract at the same time, pushing blood simultaneously into the pulmonary and systemic circulations.

The increased efficiency of the double circulatory system in mammals and birds is thought to have been important in the evolution of endothermy. More efficient circulation is necessary to support the high metabolic rate required for maintenance of internal body temperature about a set point.

Throughout the evolutionary history of the vertebrate heart, the sinus venosus has served as a pacemaker, the site where the impulses that initiate the heartbeat originate. Although the sinus venosus constitutes a major chamber in the fish heart, it is reduced in size in amphibians and is further reduced in reptiles. In mammals and birds, the sinus venosus is no longer present as a separate chamber, although some of its tissue remains in the wall of the right atrium. This tissue, the sinus nodal (SA) node, is still the site where each heartbeat originates as detailed later in the chapter.
Despite their similarity, the four-chambered hearts of mammals and birds evolved convergently.

Learning Outcomes
1. Explain the cardiac cycle and how it is measured.
2. Describe the structure and function of the heart.
3. Define blood pressure and how it is measured.

The cardiac cycle begins with the atria contracting and pushing blood into the ventricles. The ventricles then contract, propelling blood out of the heart. This cycle is repeated continuously.

Figure 50.9 The cardiac cycle. A. Contraction and relaxation of the heart muscle results in blood volume changes through the circulatory system. B. Blood moves from the atria to the ventricles, the left atrium, and the right atrium, and the right ventricle and left ventricle. C. The readiness of the heart muscle is increased by an action potential, resulting in increased blood pressure. D. The heart muscle is relaxed, and the ventricles and atria are filled with blood. E. The heart muscle is contracted, and the ventricles pump blood into the systemic and pulmonary circulatory systems.

The cardiac cycle is divided into two phases: systole and diastole. Systole is the contraction phase, and diastole is the relaxation phase. The electrical activity of the heart is regulated by the sinoatrial (SA) node, which generates an action potential. This potential spreads through the atria, causing the atrial muscles to contract. The action potential then travels to the atrioventricular (AV) node, where it is delayed before passing to the ventricles. This delay ensures that the atria and ventricles contract simultaneously, preventing backflow of blood. The ventricles then contract, propelling blood into the systemic and pulmonary circulatory systems.

Blood pressure is measured by the systolic and diastolic pressures. Systolic pressure is the maximum pressure during ventricular contraction, and diastolic pressure is the minimum pressure during ventricular relaxation. Blood pressure is influenced by several factors, including age, gender, lifestyle, and medical conditions.

Contraction of the heart muscle is initiated by autonomic nervous cells. These cells respond to changes in the body's needs, such as increased physical activity or stress, by regulating the heart's rate and force of contraction.
removed from the cytoplasm by a pump in the sarcomplasmic reticulum similar to skeletal muscle, and an additional carrier in the plasma-membrane pumps Ca²⁺ into the interstitial space.

The electrical activity of the heart can be recorded from the surface of the body with electrodes placed on the chest and back. The recording, called an electrocardiogram (ECG or EKG), shows how the cells of the heart depolarize and repolarize during the cardiac cycle (see figure 50.10). Depolarization causes contraction of the heart, and repolarization causes relaxation.

The first peak in the recording, P, is produced by the depolarization of the atria, and is associated with atrial systole.

The second, larger peak, QRS, is produced by ventricular depolarization, during this time, the ventricles contract (ventricular systole). The last peak, T, is produced by ventricular repolarization; at this time, the ventricles begin diastole.

Arteries and veins branch to and from all parts of the body

The right and left pulmonary arteries deliver oxygen-depleted blood from the right ventricle to the right and left lungs. As previously mentioned, the pulmonary veins return oxygenated blood from the lungs to the left atrium of the heart.

The aorta and all its branches are systemic arteries, carrying oxygen-rich blood from the left ventricle to all parts of the body. The coronary arteries are the first branches of the aorta, which supply oxygenated blood to the heart muscle itself (see figure 50.16). Other systemic arteries branch from the aorta as it makes an arch above the heart and descends and traverses the thoracic and abdominal cavities.

The blood from the body’s organs, now lower in oxygen, returns to the heart in the systemic veins. These eventually empty into two major veins: the superior vena cava, which drains the upper body, and the inferior vena cava, which drains the lower body. These veins empty into the right atrium, completing the systemic circulation.

The flow of blood through the arteries, capillaries, and veins is driven by the pressure generated by ventricular contraction. The ventricles must contract forcefully enough to move the blood through the entire circulatory system.

**Arterial blood pressure can be measured**

As the ventricles contract, great pressure is generated within them and transmitted through the arteries once the aortic valve opens. The pulse that you can detect in your wrist or neck results from changes in pressure as elastic arteries expand and contract with the periodic blood flow. Doctors use blood pressure as an general indicator of cardiovascular health because a variety of conditions can cause increases or decreases in pressure.

A physical examination measures the blood pressure in the brachial artery found on the side of the arm, above the elbow (figure 50.11). A cuff wrapped around the upper part of the arm is tightened enough to stop the flow of blood to the lower part of the arm. As the cuff is slowly loosened, eventually the blood pressure produced by the heart is greater than the constraining pressure of cuff and blood begins pulsating through the artery, producing a sound that can be detected using a stethoscope. The point at which this pulsing sound begins marks the peak pressure, or systolic pressure, at which the ventricles are contracting. As the cuff is loosened further, the point is reached where the pressure of the cuff is lower than the blood pressure throughout the cardiac cycle, at which time the blood vessel is no longer distorted and the pulsing sound stops. This point marks the minimum pressure between heartbeats or diastolic pressure, at which the ventricles are relaxed.

The blood pressure is written as a ratio of systolic over diastolic pressure, and for a healthy person in his or her twenties, a typical blood pressure is 120 / 70 (measured in millimeters

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**Figure 50.10 The path of electrical excitation in the heart.** The event occurring during contraction of the heart are correlated with the measurement of electrical activity by an electrocardiogram (EGG also called EKG). The depolarization/contraction of the atrium is shown in green above and corresponds to the P wave of the ECG (also in green). Depolarization/contraction of the ventricles is shown in red and corresponds to the QRS wave of the ECG (also in red). The T wave on the ECG corresponds to the repolarization of the ventricles. The atrial repolarization is marked by the QRS wave.

**Figure 50.11 Measurement of blood pressure.** The blood pressure of cuff is tightened to stop the flow of blood through the brachial artery. As the cuff is loosened, the maximal systolic pressure increases greater than cuff pressure and blood can momentarily pass through, producing a pulse that can be heard with a stethoscope. The pressure at this point recorded as the systolic pressure. As the cuff pressure continues to drop, blood pressure is greater than cuff pressure for larger portions of the cardiac cycle. Eventually, even the minimum pressure during the cardiac cycle is greater than the cuff pressure, at which time the blood vessel is no longer distorted and silent lumina flow returns, replacing the pulsing sound. The diastolic pressure is recorded as the pressure at which the sound is no longer heard.

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The rate of blood flow through vessels is governed by the frictional resistance to flow. In a vessel that is half the diameter of another, the flow is reduced by a factor of 16 times the frictional resistance to flow. In fact, a vessel that is half the diameter has a resistance to flow that is 16 times greater than the other. Therefore, the smaller vessels have a greater resistance to flow and are more likely to be constricted by the smooth muscle layer in the walls of the vessels. This would not be ideal for diffusion, and is actually not the case. Although each capillary is very narrow, so many of them exist that the capillaries have the greatest total cross-sectional area of any other type of vessel. Consequently, blood moving through capillaries goes more slowly and has more time to exchange materials with the surrounding extracellular fluid. By the time the blood reaches the end of a capillary, it has released some of its oxygen and nutrients and picked up carbon dioxide and other waste products. Blood loses pressure and velocity as it moves through the arterioles and capillaries, but as cross-sectional area decreases in the venous side, velocity increases.

**50.5 Characteristics of Blood Vessels**

**Learning Outcomes Review 50.4**
- Describe the four tissue layers in blood vessels.
- Explain the distinctions among arteries, capillaries, and veins.
- Describe how the lymphatic system operates.

You already know that blood leaves the heart through vessels known as arteries. These continually branching, forming a hollow "tree" that enters each organ of the body. The finest, microscopic branches of the arterial tree are the arterioles. Blood from the arteries enters the capillaries, an elaborate network of very many, thin-walled tubes. After traversing the capillaries, the blood is collected into microscopic venules, which lead to larger vessels called veins, and these carry blood back to the heart.

**Figure 50.12 The structure of blood vessels.** Arteries (a) and veins (b) have the same tissue layers, but the smooth muscle layer in arteries is much thicker and there are two elastic layers. c. Capillaries are composed of a single layer of endothelial cells. (Not to scale)

Larger vessels are composed of four tissue layers:

- Arteries, arterioles, veins, and venules all have the same basic structure (figure 50.12). The innermost layer is an epithelial sheet called the endothelium. Covering the endothelium is a thin layer of elastic fibers, a smooth muscle layer, and a connective tissue layer. The walls of these vessels, therefore, are thick enough to significantly reduce exchange of materials between the blood and the tissues outside the vessels.

- The walls of capillaries, in contrast, are composed only of endothelium, so molecules and ions can leave the blood plasma by diffusion, by filtration through pores between the cells of the capillary walls, and by transport through the endothelial cells. Therefore, exchange of gases and metabolites between the blood and the intracellular fluids and cells of the body takes place through the capillaries.

**Arteries and arterioles have evolved to withstand pressure.** The larger arteries contain more elastic fibers in their walls than other blood vessels, allowing them to recoil each time they receive a volume of blood pumped by the heart. Smaller arteries and arterioles are less elastic, but their relatively thick smooth muscle layer enables them to resist bursting.

The narrower the vessel, the greater the frictional resistance to flow. In fact, a vessel that is half the diameter of another has 1/16th the frictional resistance. Resistance to blood flow is proportional to the fourth power of the radius of the vessel. Therefore, within the arterial tree, the small arteries and arterioles provide the greatest resistance to blood flow.

- Contraction of the smooth muscle layer of the arterioles results in vasoconstriction, which greatly increases resistance and decreases flow. Relaxation of the smooth muscle layer results in vasodilation, decreasing resistance and increasing blood flow to an organ. Chronic vasoconstriction of the arteriolar resistance increases in hypertension, or high blood pressure.

- Venous valves are important means of regulating body heat in both ectotherms and endotherms (figure 50.13). By increasing blood flow to the skin, an animal can increase the rate of heat exchange, which is beneficial for gaining or losing heat. Conversely, shutting blood away from the skin is effective when an animal needs to minimize heat exchange, as might happen in cold weather.

**Figure 50.13 Regulation of heat exchange.** The amount of heat gained or lost at the body's surface can be regulated by controlling the flow of blood to the surface. a. Constriction of surface blood vessels limits flow and heat loss when the animal is warmer than the surrounding air (not shown here), constriction minimizes heat loss; b. dilation of these vessels increases flow and heat exchange.

**Capillaries form a vast network for exchange of materials.** The huge number and extensive branching of the capillaries ensure that every cell in the body is within 100 micrometers (μm) of a capillary. On the average, capillaries are about 1 μm long and 9 μm in diameter, this diameter is only slightly larger than a red blood cell (5 to 7 μm in diameter). Despite the close fit, normal red blood cells are flexible enough to squeeze through capillaries without difficulty.

The rate of blood flow through vessels is governed by hydrodynamics. The smaller the cross-sectional area of a vessel, the faster fluid moves through it. Given this, flow in the capillaries would be expected to be fastest in the system. This would not be ideal for diffusion, and is actually not the case. Although each capillary is very narrow, so many of them exist that the capillaries have the greatest total cross-sectional area of any other type of vessel. Consequently, blood moving through capillaries goes more slowly and has more time to exchange materials with the surrounding extracellular fluid. By the time the blood reaches the end of a capillary, it has released some of its oxygen and nutrients and picked up carbon dioxide and other waste products. Blood loses pressure and velocity as it moves through the arterioles and capillaries, but as cross-sectional area decreases in the venous side, velocity increases.

**Venes and veins have less muscle in their walls.** Venules and veins have the same tissue layers as arteries, but they have a thinner layer of smooth muscle. Less muscle is needed because the pressure in the veins is only about one-tenth that in the arteries. Most of the blood in the cardiovascular system is contained within veins, which can expand to hold additional amounts of blood. You can see the expanded veins in your feet when you stand for a long time.

The venous pressure alone is not sufficient to return blood to the heart from the feet and legs, but several other sources of pressure provide help. Most significantly, skeletal muscle activity squeezing the veins can contract to move blood by squeezing the veins, a mechanism called the venous pump. Blood moves in one direction through the veins back to the heart with the help of valves (figure 50.14). When a
The lymphatic system handles fluids that leave the cardiovascular system

The cardiovascular system is considered a closed system because all its vessels are connected with one another—none are simply open-ended. But a significant amount of water and solutes in the blood plasma filter through the walls of the capillaries to form the interstitial (tissue) fluid. Most of the fluid leaves the capillaries near their arteriolar ends, where the blood pressure is higher; it is returned to the capillaries near their venular ends (figure 50.15).

Fluid returns by osmosis (see chapter 5). Most of the plasma proteins cannot escape through the capillary pores because of their large size, and so the concentration of proteins in the plasma is greater than the protein concentration in the interstitial fluid. The difference in protein concentration produces an osmotic pressure gradient that causes water to move into the capillaries from the interstitial space.

High capillary blood pressure makes this too much interstitial fluid to accumulate. In pregnant women, for example, the enlarged uterus, carrying the fetus, compresses veins in the abdominal cavity, thereby adding to the capillary blood pressure in the woman's lower limbs. The increased interstitial fluid can cause swelling of the tissues, or edema, of the feet. Edema may also result if the plasma protein concentration is too low. Fluids do not return to the blood vessels as interstitial fluid. Low protein concentration in the plasma may be caused either by liver disease, because the liver produces most of the plasma proteins, or by insufficient dietary protein intake, such as occurs in starvation.

Even under normal conditions, the amount of fluid filtered out of the capillaries is greater than the amount that returns to the capillaries by osmosis. The remainder does eventually return to the cardiovascular system by way of an open circulatory system called the lymphatic system.

The lymphatic system consists of lymphatic capillaries, lymphatic vessels, lymph nodes, and lymphatic organs, including the spleen and thymus. Faces fluid in the tissue spaces into blind-ended lymph capillaries with highly permeable walls. This fluid, now called lymph, passes into progressively larger lymphatic vessels, which resemble veins and have one-way valves (similar to figure 50.14). The lymph eventually enters two major lymphatic vessels, which drain into the left and right subclavian veins located under the clavicles.

Movement of lymph in mammals is due to skeletal muscle contraction. As the skeletal muscle fibers contract, they compress the lymphatic vessels, forcing lymph into the veins. In some cases, the lymphatic vessels contract rhythmically. In many fishes, all amphibians and reptiles, bird embryos, and some adult birds, movement of lymph is propelled by lymph hearts. As the lymph moves through lymph nodes and lymphatic organs, it is modified by phagocytic cells (see chapter 4) that line the channels of these organs. In addition, the lymph nodes and lymphatic organs contain germinal centers, where the activation and proliferation of lymphocytes occurs.

Cardiovascular diseases affect the delivery system

Cardiovascular diseases are the leading cause of death in the United States, more than 80 million people have some form of cardiovascular disease. Many disease conditions result from problems in arteries, such as blockage or rupture.

Atherosclerosis, or hardening of the arteries, is an accumulation within the arteries of fatty materials, abnormal accumulation of smooth muscle, deposits of cholesterol or fibrin, or various kinds of cellular debris. These accumulations cause an increase in vascular resistance, which impedes blood flow (figure 50.16). The lumen (interior) of the artery may be further narrowed by a clot that forms as a result of the atherosclerosis. In the severest cases, the artery becomes completely blocked.

The accumulation of cholesterol in vessels is affected by a number of factors including total serum cholesterol, the levels of different cholesterol carrier proteins. Because cholesterol is not very water-soluble, it is carried in blood in the form of lipoprotein complexes. Two main forms are observed that differ in density: low-density lipoproteins (LDL) and high-density lipoproteins (HDL)—often called "bad cholesterol" and "good cholesterol," respectively. The reason for this is that HDLs tend to take cholesterol out of circulation, transporting it to the liver for elimination, and LDL is the carrier that brings cholesterol to all cells in the body. The transport of cholesterol just discussed. Stopping smoking is the single most effective action a smoker can take to reduce the risk of atherosclerosis.

Arteriosclerosis occurs when calcium is deposited in arterial walls. It tends to occur whentherosclerosis is severe. Not only do such arteries have reduced blood flow, but they also lack the ability to expand as normal arteries do. This decrease in flexibility forces the heart to work harder because blood pressure increases to maintain flow.

Heart attacks (myocardial infarctions) are the main cause of cardiovascular deaths in the United States, accounting for about one-fifth of all deaths. Heart attack result from an insufficient supply of blood to one or more parts of the heart muscle, which causes myocardial cells in those parts to die. Heart attacks may be caused by a blood clot forming somewhere in the coronary arteries and may also result if an artery is blocked by atherosclerosis. Recovery from a heart attack is possible if the portion of the heart that was damaged is small enough that the heart can still contract as a functional unit.

Angina pectoris, which literally means "chest pain," occurs for reasons similar to those that cause heart attacks, but it is not as severe. The pain may occur in the heart and often also in the left arm and shoulder. Angina pectoris is a warning sign that the blood supply to the heart is inadequate but is still sufficient to avoid myocardial cell death.

Strokes are caused by an interference with the blood supply to the brain. They may occur when a blood vessel bursts in the brain (hemorrhagic stroke), when blood flow in a cerebral artery is blocked by a blood clot or by atherosclerotic (ischemic stroke). The effects of a stroke depend on the severity of the damage and where in the brain the stroke occurs.

Learning Outcomes Review 50.5

The blood levels of blood vessels (a) endothelium, (b) smooth muscle, and (c) connective tissue. In contrast, capillaries have only endothelium. Arteries move more water than does veins to help offset the greater pressure in the arteries compared to the veins. Figure 50.15 Relationship between blood, lymph, and interstitial fluid. a. Vessels of the circulatory and lymphatic systems are shown indicating the direction of flow of fluid in the vessels. b. Plasma fluid, lymph, and interstitial fluid are shown indicating fluid flow. c. Figure 50.16 Atherosclerosis. a. The coronary artery shows only minor blockage. b. The artery exhibits severe atherosclerosis. c. Many of the blood vessels are blocked by buildup on the interior walls of the artery. c. The coronary artery is essentially completely blocked.
50.6 Regulation of Blood Flow and Blood Pressure

Learning Outcomes

1. Describe how exercise affects cardiac output.
2. Explain how hemodynamics regulate blood volume.

Although the autonomic nervous system does not initiate the heartbeat, it does modulate its rhythm and force of contraction. In addition, several mechanisms regulate characteristics of the cardiovascular system, including cardiac output, blood pressure, and blood volume.

The nervous system may speed up or slow down heart rate

Heart rate is under the control of the autonomic nervous system. The cardiac center of the medulla oblongata is part of the hypothalamus. It is made up of two neurones that modulate heart rate. The cardiac center receives signals from the sympathetic nervous system and the parasympathetic nervous system through the vagus nerve. The vagus nerve secretes acetylcholine, which increases the heart rate. Sympathetic nervous system stimulation can also increase contractility of the heart muscle itself, thus increasing more blood per contraction (stroke volume).

Cardiac output increases with exertion

Cardiac output is the volume of blood pumped by each ventricle per minute. It is calculated by multiplying the heart rate by the stroke volume, which is the volume of blood ejected by each ventricle per beat. For example, if the heart rate is 72 beats per minute and the stroke volume is 70 mL, the cardiac output is 5 L/min, which is about average for a resting human.

Cardiac output increases during exercise because of an increase in both heart rate and stroke volume. When exercise begins, such as running, the heart rate increases up to about 100 beats per minute to provide more oxygen to cells in the body. As movement becomes more intense, skeletal muscles squeeze on veins more vigorously, returning blood to the heart more rapidly. In addition, the veins contract more strongly, so they empty more completely with each beat. During exercise, the cardiac output increases to a maximum of about 25 L/min in an average young adult. Although the cardiac output has increased fivefold, no all organs receive five times the blood flow; some receive more, others less. Arterioles in some organs, such as the digestive system, contract, while the arterioles in the working muscles and heart dilate.

The baroreceptor reflex maintains homeostasis in blood pressure

The arterial blood pressure (BP) depends on two factors: the cardiac output (CO) and the resistance (R) to blood flow in the vascular system. This relationship can be expressed as

\[ BP = CO \times R \]

An increased blood pressure, therefore, could be produced by an increase in either heart rate or blood volume (because both increase the cardiac output), or by vasoconstriction, which increases the resistance to blood flow. Conversely, blood pressure falls if the heart rate slows or if the blood volume is reduced—for example, by dehydration or excessive bleeding (haemorrhage). Changes in arterial blood pressure are detected by baroreceptors located in the arch of the aorta and in the carotid arteries (see figure 50.16). These sensors are stretch receptors sensitive to expansion and contraction of arteries. When the baroreceptors detect a fall in blood pressure, the number of impulses to the cardiac center is decreased, resulting in increased sympathetic stimulation and decreased parasympathetic stimulation of the heart and other organs. This increases heart rate and stroke volume to amplify cardiac output. This also causes vasoconstriction of blood vessels in the skin and viscera, raising resistance. These combine to increase blood pressure, closing the feedback loop in this direction (figure 50.17, top).

When baroreceptors detect a rise in blood pressure, the number of impulses to the cardiac center is increased. This has the opposite effect of decreasing sympathetic stimulation and increasing parasympathetic stimulation of the heart. This lowers heart rate and stroke volume to reduce cardiac output. The cardiac center also sends signals causing vasodilation of blood vessels in the skin and viscera, lowering resistance. This permits the baroreceptor reflex to maintain blood pressure and return to the normal range.

Figure 50.17 Baroreceptor negative feedback loop controls blood pressure

Baroreceptors form the afferent portion of a feedback loop controlling blood pressure. The frequency of nerve impulses from these stretch receptors correlates with blood pressure. This information is processed in the cardiac center of the medulla. The effector portion of the loop involves sympathetic and parasympathetic nerves that innervate the heart. This control can raise or lower heart rate and stroke volume to move and lower blood pressure in response to homeostatic signals.

Learning Outcomes Review 50.6

Cardiac output: the heart's rate times stroke volume. A decrease in cardiac output, cardiac output increases to meet body demands. Blood pressure decreases on opening an arteriole and the resistance to blood flow due to constriction of the arteries. The blood volume is regulated by antidiuretic hormone, aldosterone, and serotonin. The renin-angiotensin-aldosterone system increases blood pressure.

What are the connections between regulation of heart rate and breathing rate?
A sphygmomanometer measures the peak (systolic) and minimum (diastolic) blood pressure. Blood pressure is expressed as the ratio of systolic to diastolic.

Arterial blood pressure can be measured.

Arteries and arterioles carry oxygenated blood to the body; veins and venules return deoxygenated blood to the heart (see figure 50.7). Arteries and veins branch to and from all parts of the body.

Upon initiation of clotting, fibrinogen, normally dissolved in the plasma, is turned into fibrin, an insoluble protein, via an enzyme cascade. As a wound heals, the clot must be dissolve.

Blood clotting is an example of an enzyme cascade.

Blood cells are derived from pluripotent stem cells in bone marrow by hematopoiesis (see figure 50.2). Formed elements arise from stem cells.

Blood cells include erythrocytes (red cells), leukocytes (white cells), and platelets. Erythrocytes contain hemoglobin for oxygen transport, and leukocytes are part of the immune system. Platelets help initiate blood clotting (see figure 50.3).

Plasma is 92% water plus nutrients, hormones, ions, plasma proteins, and wastes (see figure 50.1).

Blood plasma is a fluid matrix.

Characteristics of Blood Vessels

Arteries and arterioles have evolved to withstand pressure.

Arteries and veins consist of endothelium, elastic fibers, smooth muscle, and connective tissues (see figure 50.12). Capillaries have only one layer of endothelium.

Larger vessels are composed of four tissue layers.

Atherosclerosis is an accumulation of fatty materials in arteries; it is one cause of a heart attack, which results from an insufficient supply of blood to heart muscle. Strokes are caused by blockage of the blood supply to the brain.

Cardiovascular diseases affect the delivery system.

Fluid from plasma filters out of capillaries, then returns via the separate, one-way lymphatic system (see figure 50.15). The lymphatic system connects with the blood circulation at the subclavian veins.

The lymphatic system handles fluids that leave the cardiovascular system.

The return of blood to the heart through veins is facilitated by skeletal muscle contractions and one-way valves (see figure 50.14). Venules and veins have less muscle in their walls.

Capillaries are the region of the circulatory system where exchange takes place with the body's tissues (see figure 50.13). Capillaries form a vast network for exchange of materials.

Arteries and arterioles have thicker muscular layer and more elastic fibers to control blood flow and to recoil with changes in blood pressure.

50.2 Invertebrate Circulatory Systems

Closed systems have a distinct circulatory fluid, such as blood, enclosed in vessels and transported in a loop.

Closed circulatory systems move fluids in a loop.

Sponges pass water through channels, and cnidarians circulate water through a gastrovascular cavity. Small animals can use body cavity fluids for circulation.

Open circulatory systems move fluids in a one-way path.

50.3 Vertebrate Circulatory Systems

The four-chambered heart has two ventricles (see figure 50.7). The extreme similarity between the heart of mammals and birds is an example of convergent evolution.

Mammals, birds, and crocodilians have two completely separated circulatory systems.

Pulmonary circulation pumps blood to the lungs, and systemic circulation pumps blood to the body. Amphibian hearts have ... The heart of most reptiles has a septum that partially divides the ventricle, reducing mixing of blood from the atria.

In amphibians and most reptiles, lungs required a separate circulation.

Fishes have a linear heart with two pumping chambers to increase efficiency of blood flow through the gills; from the gills, the blood moves into the rest of the body (see figure 50.5).

In fishes, more efficient circulation developed concurrently with gills.

50.4 The Four-Chambered Heart and the Blood Vessels

Contraction is initiated by the SA node, a natural pacemaker, and impulses then travel to the AV node (see figure 50.10). Contraction of heart muscle is initiated by autorhythmic cells.

The unidirectional flow of blood through the heart is maintained by two atrioventricular valves (see figure 50.9). During diastole ventricles relax and atria contract; during systole ventricles contract.

The cardiac cycle drives the cardiovascular system.

50.6 Regulation of Blood Flow and Blood Pressure

The baroreceptor reflex maintains homeostasis in blood pressure.

Both heart rate and stroke volume increase with exertion.

Cardiac output increases with exertion.

Norepinephrine from sympathetic neurons increases heart rate; acetylcholine from parasympathetic neurons decreases heart rate.

The nervous system may speed up or slow down heart rate.

Blood volume regulation and arterial resistance involves the effects of four hormones: (1) antidiuretic hormone, (2) aldosterone, (3) atrial natriuretic hormone, and (4) nitric oxide.

Blood volume is regulated by hormones.

Arterial blood pressure is monitored by baroreceptors in the aortic arch and carotid arteries, which relay impulses to the cardiac center (see figure 50.17).