4

CIRCULATORY SYSTEM

The circulatory system contains several very different components, including the ***heart***, a hollow muscular pump that stands at the operational center of the system that pumps liquid ***blood*** throughout the body through three types of flexible tubes, the ***blood vessels*** (Fig. 4.1). The ***arteries*** channel blood from the heart to all parts of the body needing service. Once there, the blood passes through narrow arteries and enters the ***capillaries***, which are the narrowest blood vessels. Many substances and some blood cells pass into and out of the blood by moving through the thin porous capillary walls. The blood is then carried through the ***veins***, which return the blood to the heart. The passage of blood through the vessels in a part of the body is called ***perfusion*** of that part.

Some materials that are carried away from a region of the body do not pass into the blood but are collected by vessels called ***lymph capillaries*** (Fig. 4.2). The materials in these vessels make up a liquid called ***lymph***, which is carried through the ***lymph vessels*** toward the heart. Along the way, the lymph passes through ***lymph nodes*** where harmful chemicals and microbes that might have entered it are removed. The lymph is finally added to the blood in the veins shortly before the blood enters the heart.

MAIN FUNCTIONS FOR HOMEOSTASIS

Transportation

One main function of the circulatory system is transportation of materials within the body. Transportation helps maintain homeostasis by ensuring that the concentrations of substances surrounding body cells are kept at proper and fairly steady levels. Materials consumed by the cells are immediately replenished, and materials produced by the cells are swept away before their concentrations become too high.

The flowing blood also transports useful materials from their point of entry into the body to the organs that need them. For example, oxygen from the lungs and nutrients from the digestive system are delivered to the muscles. Furthermore, some cells manufacture substances (e.g., hormones) needed by cells in other organs, and the circulatory system provides the delivery service for them.

FIGURE 4.1 The circulatory system, showing the pathway for blood flow.

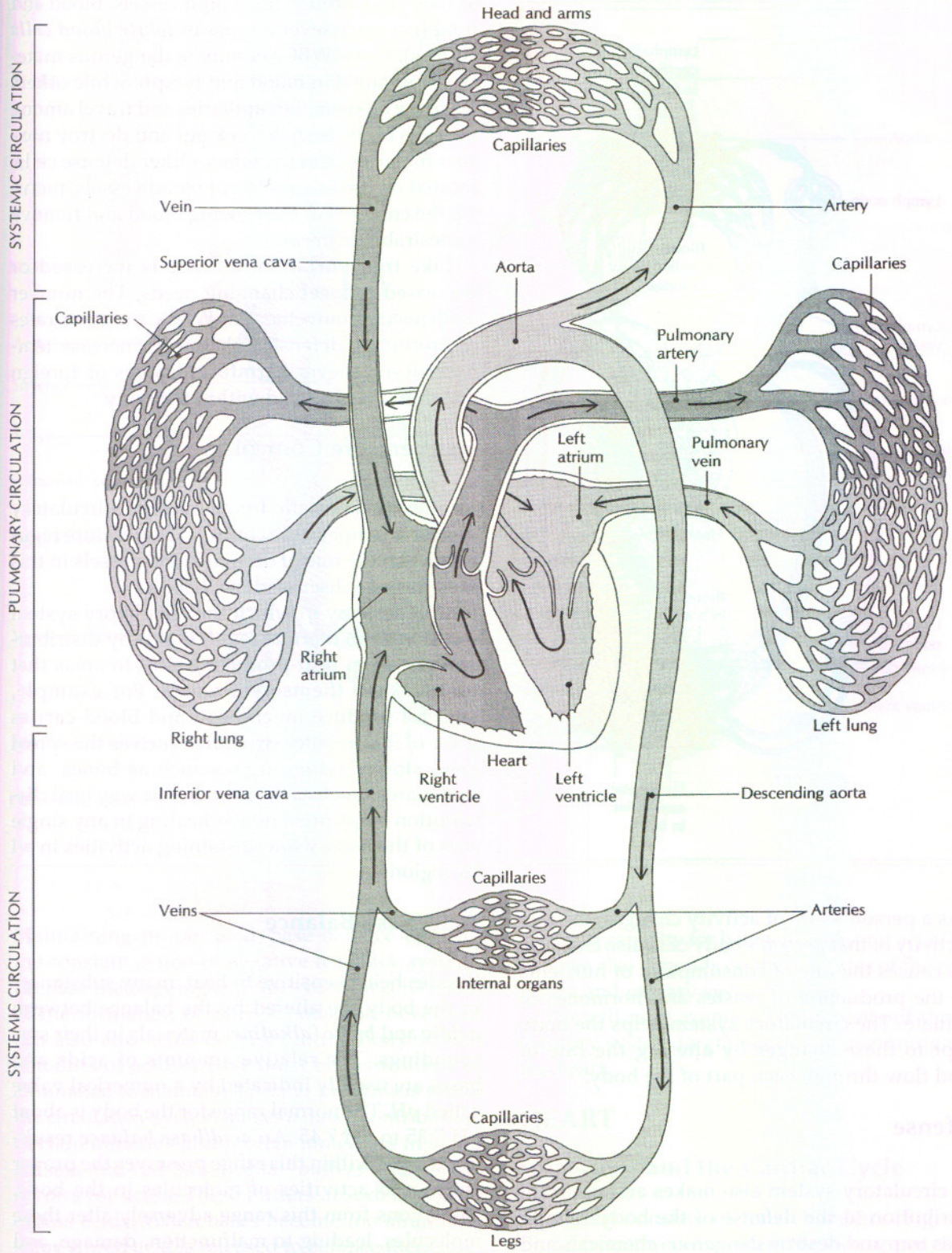
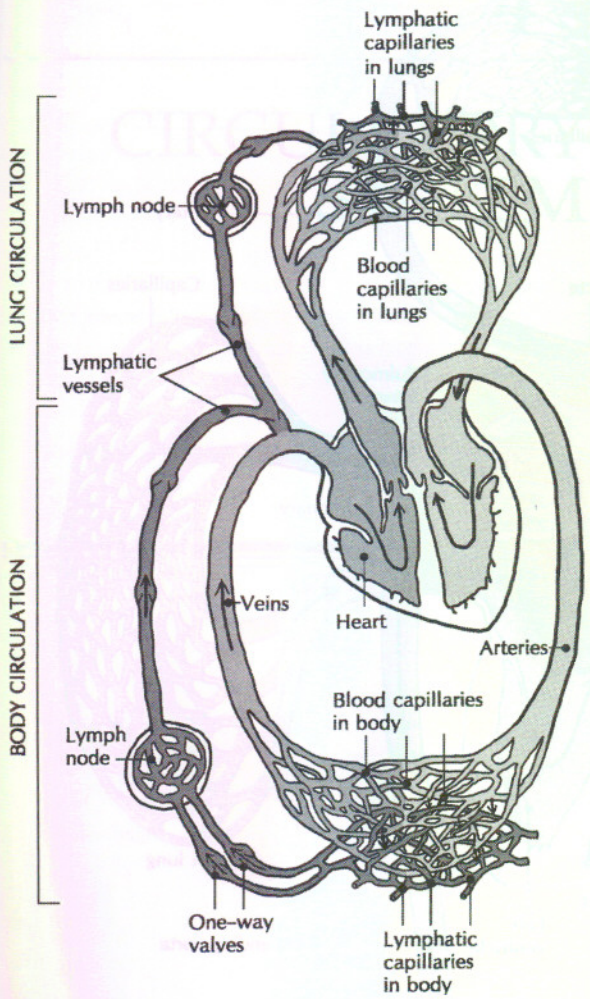


FIGURE 4.2 The circulatory system showing pathways for blood flow and lymph flow.



As a person's rate of activity changes, the rate of activity of that person's body cells also changes. This causes the rate of consumption of nutrients and the production of wastes and hormones to fluctuate. The circulatory system helps the body adapt to these changes by altering the rate of blood flow through each part of the body.

Defense

The circulatory system also makes an important contribution to the defense of the body. Lymph nodes trap and destroy dangerous chemicals and microbes before they can spread throughout the body. For example, toxins and bacteria that enter the lymph from an infected wound are inactivated as they pass through the lymph vessels. Blood and lymph contain several types of ***white blood cells*** (***WBCs***). Some WBCs eliminate dangerous materials contained in blood and lymph, while others leave the blood in the capillaries and travel among the cells of the body to seek out and destroy noxious materials and microbes. Other defense cells, located on the inner walls of blood vessels, monitor the contents of the flowing blood and remove undesirable materials.

Like transportation, defense is increased or decreased to meet changing needs. The number and speed of movement of WBCs and their rates of producing defensive chemicals increase temporarily whenever harmful microbes or foreign materials are detected within the body.

Temperature Control

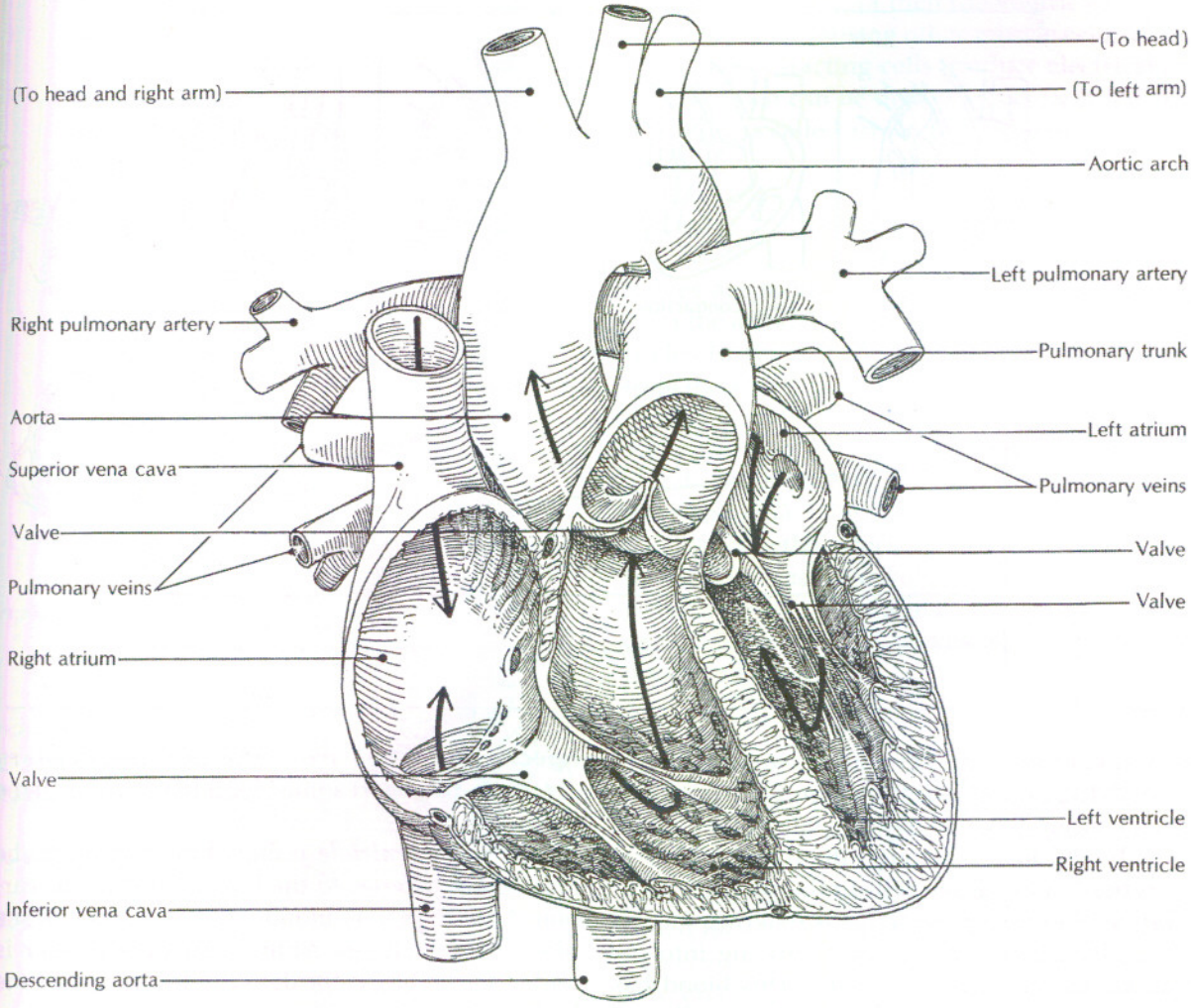
Another homeostatic function of the circulatory system is temperature control. Temperature regulation and the role of dermal blood vessels in this process were discussed in Chap. 3.

Another way in which the circulatory system contributes to thermal regulation is by distributing heat from heat-producing sites to areas that cannot keep themselves warm. For example, muscles produce much heat, and blood carries some of it to smaller structures such as the spinal cord, slower-acting organs such as bones, and cooler areas such as the skin. In this way heat distribution helps prevent overheating in any single area of the body while sustaining activities in all its regions.

Acid/Base Balance

Besides being sensitive to heat, many substances in the body are altered by the balance between ***acidic*** and ***basic*** (***alkaline***) materials in their surroundings. The relative amounts of acids and bases are usually indicated by a numerical value called ***pH.*** The normal range for the body is about pH 7.35 to pH 7.45. An ***acid/base balance*** resulting in a pH within this range preserves the proper shape and activities of molecules in the body. Deviations from this range adversely alter these molecules, leading to malfunction, damage, and even the death of cells.

FIGURE 4.3 The internal structure of the heart and adjoining blood vessels.



Maintaining proper acid/base balance requires the constant action of negative feedback systems because the ongoing activities of most cells result in the formation of acids. Foods and beverages can also add acids or bases to the body. Excess amounts of acid or base must be neutralized or eliminated to maintain a proper pH. This is where the circulatory system makes a major contribution. Certain minerals and protein molecules in blood plasma and red blood cells—***buffers***—act as reservoirs for acids. These buffers absorb and store excess acids. When bases become too abundant, some stored acid is released to balance them, preserving the acid/base balance. These buffers have a limited capacity for balancing pH, and acid/base balance also depends on the activities of the respiratory and urinary systems.

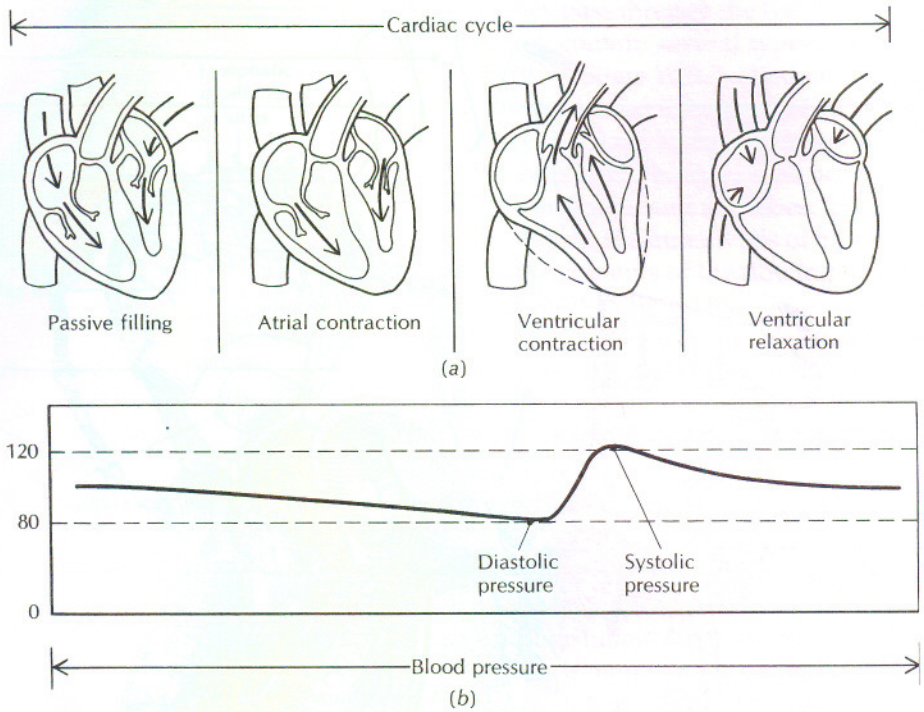
We will now examine components of the circulatory system in greater detail, beginning with the heart.

HEART

Chambers and the Cardiac Cycle

The heart consists of four chambers (Fig. 4.3). Blood from the veins enters the two upper chambers, called ***atria***. Blood from the lungs returns

FIGURE 4.4 (a) Cardiac cycle and (b) blood pressure.



to the heart through several ***pulmonary veins***, which deliver it to the ***left atrium***. This blood has a high concentration of oxygen, which was added as the blood passed through the lungs. The oxygen is needed by all the cells in the body.

While blood from the lungs is entering the left atrium, blood from the body is flowing into the ***right atrium*** via two large veins. This blood has had most of its oxygen removed by body cells and contains a high concentration of a waste product called ***carbon dioxide***, which was produced by body cells. It also carries many useful substances (e.g., nutrients and hormones) added by various organs.

The blood flows easily from each atrium into the ***ventricle*** just below it because the ventricles relax and tend to widen at this time (Fig. 4.4*a*). The flow is aided by a relatively weak contraction of the atria. Once the ventricles have been filled, they contract powerfully, squeezing the blood and pumping it into the arteries. The ventricles contract for a fraction of a second and then relax again.

The blood from the ***left ventricle*** is pushed very forcefully into a large artery, the ***aorta***. Branches from the aorta deliver this oxygen-rich and nutrient-rich blood to all parts of the body except the lungs. Special branches from the aorta—***coronary arteries***—transport some blood to the walls of the heart.

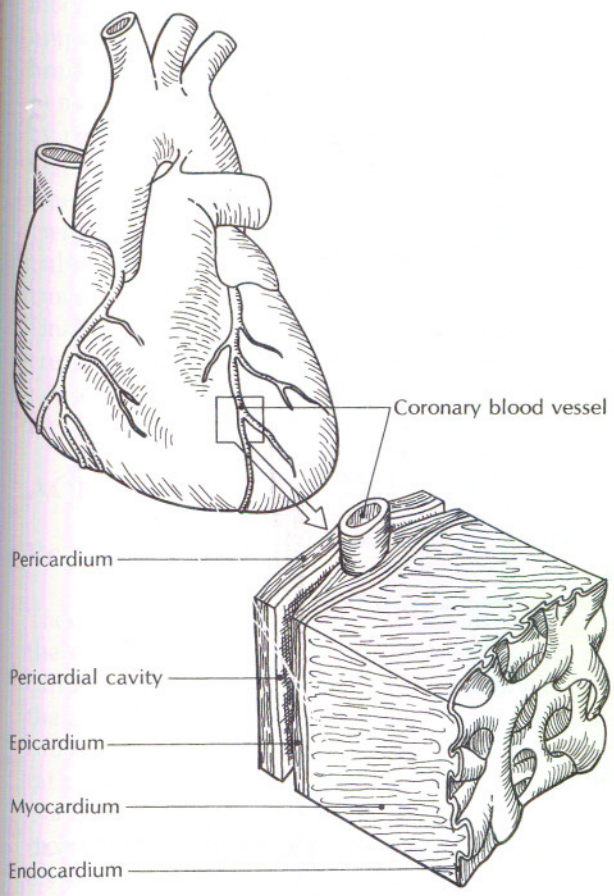
The ***right ventricle*** pumps blood through the ***pulmonary arteries*** to the lungs. Most of the carbon dioxide in this blood is removed while the blood is in the lungs. At the same time, oxygen is added to the blood for delivery to the rest of the body.

When the ventricles contract and force blood into the arteries, the blood pressure rises quickly to a peak value called ***systolic pressure*** (Fig. 4.4*b*). When the ventricles relax and blood in the arteries flows into the capillaries, the arterial blood pressure drops to a low value called ***diastolic pressure***. Diastolic pressure does not reach zero because the ventricles remain relaxed for only a fraction of a second before contracting again. Also, as will be described later, the elasticity of large arteries helps prevent it from falling too low.

While the ventricles are contracting, the atria relax and then begin to fill with the next volume of blood that will enter the ventricles and be pumped to the body.

This completes one heartbeat, or ***cardiac cycle***. By repeating this process over and over, the heart

FIGURE 4.5 Layers of the heart.



keeps the blood circulating. The blood must pass through the heart twice to make one complete circuit around the body (Fig. 4.1). The rate of flow depends on the amount pumped per minute: the ***cardiac output*** (***CO***). Cardiac output equals the amount pumped by each beat of either the left or the right ventricle [***stroke volume*** (***SV***)] times the number of beats per minute [***heart rate*** (***HR***)]. Therefore, CO = SV × HR.

The highly coordinated and well-timed operation of the heart chambers is controlled by special muscle cells. A patch of these cells in the right atrium signals when each beat is to begin. For this reason, the patch of cells is called the ***pacemaker***, a name shared by the artificial electronic devices sometimes used to restore the proper heart rate to a diseased heart. Other cells send the signal through the atria and then the ventricles. As the signal spreads, causing other muscle cells to contract, the contracting cells produce electrical impulses which can be detected and recorded. The recording is called an ***electrocardiogram*** (***ECG*** or ***EKG***).

Valves

Valves are located within the openings leading from the atria to the ventricles and from the ventricles to the arteries. The movement of blood from the atria into the ventricles and from the ventricles into the arteries pushes the valves open. When the ventricles begin to contract, some of the blood within them begins to move backward toward the atria. Similarly, when the ventricles relax, blood in the arteries starts to flow back into them. This causes the valves to swing shut, stopping the backward flow of blood. Thus, the valves ensure that the blood moves only in the correct direction (Fig. 4.4*a*).

Layers

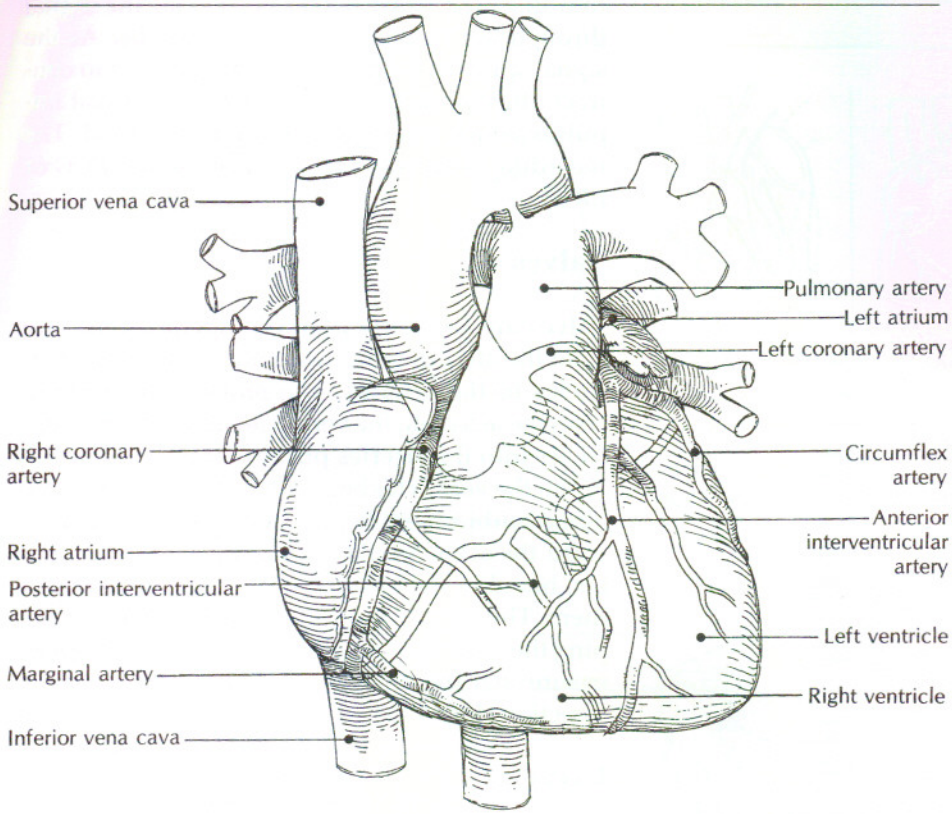
The heart wall is composed of three layers: the endocardium, myocardium, and epicardium.

Endocardium The inner lining of the heart is called the ***endocardium*** (Fig. 4.5). This layer must be very smooth and must have no gaps that allow blood to contact the underlying collagen. Blood that contacts rough spots or collagen will clot, and clots formed in the heart can move into arteries and block blood flow.

Myocardium The middle layer of the heart—the ***myocardium***—is a thick layer that constitutes most of the wall of the heart. The myocardium consists mostly of heart muscle (***cardiac muscle***), though it may also contain fat tissue and collagen fibers. Contraction of the cardiac muscle provides the force that pumps the blood.

The myocardium in the atria is thin because the atria pump blood only into the neighboring ventricles. The myocardium of the right ventricle is of moderate thickness because it must pump blood somewhat farther through the lungs. The myocardium of the left ventricle is much thicker because it pumps blood farther and through many

FIGURE 4.6 Coronary arteries.



vessels in all other regions of the body.

Epicardium The outer layer of the heart—the ***epicardium***—contains some connective tissue coated with a smooth, slippery layer of epithelial cells. This coating allows the beating heart to move easily within the pericardial cavity. At the top of the heart, the epicardium tethers the heart to other structures in the chest so that it does not shift out of position.

Coronary Blood Flow

The heart muscle must have a steady supply of energy to pump blood continuously. It gets this energy through a complicated series of chemical reactions that combine oxygen with nutrients such as blood sugar. These materials must be delivered to the myocardial cells by the blood flowing through the ***coronary arteries*** (Fig. 4.6). The heart muscle cannot get materials directly from the blood inside the heart chambers because molecules do not pass easily through the thick wall of the heart.

In addition to producing useful energy, the reactions in heart cells produce wastes such as water and carbon dioxide, which are removed from the heart by blood in the coronary capillaries and veins. These wastes are finally eliminated by the lungs and kidneys.

If myocardial cells do not get enough oxygen for their energy requirements, they malfunction and the heart cannot pump blood adequately. People in this condition get out of breath easily. They feel weak and lethargic, tire quickly, may become dizzy and faint, and can suffer heart attacks. Therefore, the coronary arteries must deliver plenty of oxygen-rich blood to the myocardium.

Cardiac Adaptability

Recall that as the rate of activity of body cells changes, the amount of blood flow around the cells must also change to provide for their vary-

ing needs. This is especially important when levels of physical activity change because active muscles use materials and produce wastes much faster than resting muscles do. One way in which blood flow is adjusted is an alteration in cardiac output caused by changes in stroke volume or heart rate. Since alterations in CO must be made to maintain homeostasis, the heart is controlled by negative feedback systems. The nervous system detects changes in internal body conditions when exercise begins or ends. Cardiac output is then adjusted through changes in the nerve impulses sent to control the heart. Levels of hormones that influence the heart are also adjusted. Finally, the heart has intrinsic mechanisms to increase or decrease its own stroke volume as needed. As a result, the parts of the body receive the right amount of blood.

AGE CHANGES IN THE HEART

Resting Conditions

Though aging causes several changes in the heart, these age changes do not result in an alteration in cardiac output when a person is at rest. This is the case because the changes are slight and because adjustments that compensate for detrimental changes occur. These adjustments include changes in the atria and the myocardium that increase heart strength and increases in blood levels of ***norepinephrine***, which stimulates the heart.

Cardiac Adaptability

As aging occurs, changes occur in the way the heart adjusts CO to meet the varying demands of the body. However, as with resting conditions, the changes are not very great, and most detrimental changes in the heart are overshadowed by compensatory changes. For example, the heart compensates for an age-related decrease in maximum heart rate by increasing the amount it pumps per beat. Therefore, the maximum cardiac output which can be achieved when a person is exercising as vigorously as possible (cardiac reserve capacity) remains essentially unchanged. The compensatory change that seems most important involves norepinephrine: As age increases, its blood level rises faster and reaches a higher peak value after vigorous activity begins.

An adverse age change in the heart for which there is no compensatory adjustment is an increase in the amount of blood remaining in the left ventricle after contraction. This residual blood causes a slight inhibition of blood flow from the lungs, resulting in an accumulation of blood in the lungs—***pulmonary congestion***—which raises the blood pressure in lung capillaries and forces extra fluid out through the capillary walls. This fluid accumulation (***pulmonary edema***) reduces respiratory functioning and causes people to feel out of breath sooner and more intensely when they exercise strenuously.

Another important age change involves the declining efficiency of the heart. A stiffer, dilated and thickened older heart consumes more oxygen to pump the same amount of blood pumped by a younger heart. This is not important as long as the coronary arteries remain completely normal because these arteries widen and allow blood to flow adequately when the heart needs more oxygen. However, most people do not have completely normal coronary arteries. In these cases, the decreased efficiency of the heart and the resultant increased demand for oxygen can become serious. In fact, individuals who show even slightly low coronary blood flow when exercising are very likely to have a heart attack.

In summary, because there are both positive and negative age changes in the normal heart, its ability to adjust the pumping of blood to supply the varying needs of the body remains essentially unchanged. However, the maximum rate of exercise people can perform normally declines with advancing age. This chapter and Chaps. 5, 6, 8, and 9 will show how this is due to a variety of factors outside the heart, including age changes in other parts of the circulatory system and in the respiratory, nervous, muscle, and skeletal systems. The maximum rate of physical activity decreases even more when diseases of the heart, blood vessels, or other body systems are present.

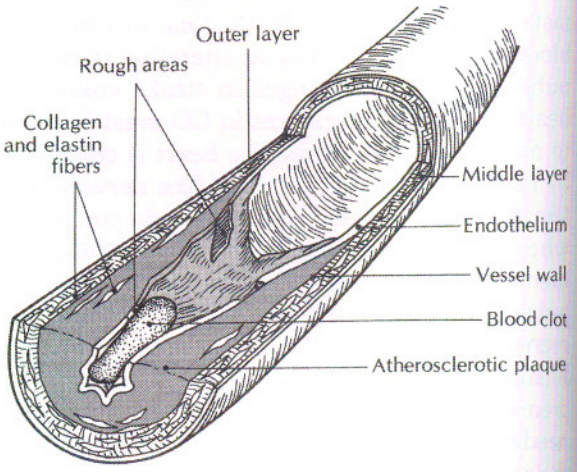
Exercise and the Aging Heart

Though the effects of exercise programs on the hearts of younger people have been well studied, only a few of the effects of training on the older heart have been elucidated. For the older heart, these effects include lack of change in the resting heart rate and the maximum heart rate attainable, decreases in the maximum heart rate required for maximum activity, and increases in stroke volume

and cardiac efficiency. However, it is expected that other beneficial effects of regular exercise on the older heart will be discovered. We will see later in this chapter that regular exercise has beneficial effects on other parts of the circulatory system.

To affect an older heart, an exercise program must involve fairly vigorous exercise performed for an extended period during each session. The sessions must occur frequently, at least once every few days. The degree of improvement is proportional to the intensity, duration, and frequency of activity. Exercise at a low level, performed for a short time, or conducted infrequently has no effect on the aged heart. Beneficial changes in cardiac output can be observed within days to a few weeks after beginning an exercise program, and regressive detrimental changes in CO occur within the same time frame when a person ends the program.

FIGURE 4.7 Atherosclerosis.



DISEASES OF THE HEART

Thus far we have seen that aging of the heart does not significantly alter its ability to meet the needs of the body. However, few adults have a completely normal heart, and in most individuals some degree of disease adversely affects the heart. Both the incidence and seriousness of such disease increase with age.

The reasons for these increases are the same as the reasons for those which lead to an age-related rise in other diseases: higher chances for exposure to disease-producing factors, increasing occasions and durations of exposure to such factors, more time for the development of slowly progressing diseases.

Heart disease is the fourth leading chronic disease among people between the ages of 45 and 64 and ranks second among those over age 64. It is the leading cause for seeking medical care among those over age 64 and is a major cause of disability and altered lifestyle. Though the incidence of death from heart disease among the elderly has been declining for decades, this is still by far the leading cause of death for people 65 and over.

Coronary Artery Disease

Though several different heart diseases become more common and more serious with age, disease of the coronary arteries stands out as the most common of these disorders.

Functions of Coronary Arteries When a person is at rest, the coronary arteries are normally wide enough to allow ample blood to pass through to the cardiac muscle cells. However, the demand of cardiac muscle for oxygen goes up and down as the amount of work performed by the heart rises and falls. Conditions requiring more work and higher amounts of oxygen include increases in heart rate, stroke volume, width, and thickness and in blood pressure. Such increases occur when a person becomes physically active and as part of aging. The heart normally accommodates these increases by dilating its arteries to allow more blood to flow through them.

Effects of Atherosclerosis The coronary arteries are prevented from supplying adequate blood flow to the heart by a disease called ***atherosclerosis***. Atherosclerosis, which is described in greater detail later in this chapter, involves the formation and enlargement of a weak scar-like material called ***plaque*** in the walls of arteries. Plaque causes coronary arteries to become narrower and thus reduces blood flow (Fig. 4.7). It also stiffens the arteries, reducing their ability to dilate when more oxygen is needed by the heart muscle. Finally, plaque causes roughening of the inner lining of the arteries and exposure of the underlying collagen. Roughness and collagen cause the blood in arteries to form clots; clots clog

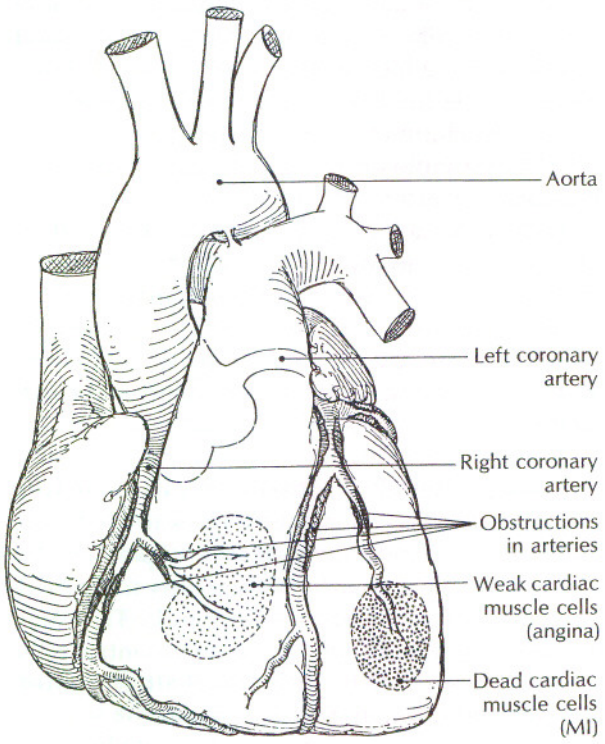
arteries and can stop blood flow quickly and completely.

Whenever the amount of oxygen needed by the heart is lower than the amount supplied, the cardiac muscle cells become weak and cannot pump enough blood to body organs. In addition, the muscle cells begin to produce a waste product called ***lactic acid***, which upsets the normal acid/base balance. This imbalance injures the muscle cells, which become even weaker, and blood flow to the body drops further. All the organs begin to perform less well. The brain, kidneys, lungs, and heart are especially in danger because these organs require high levels of blood flow. A person in this condition often feels weak and out of breath and frequently experiences chest pain as injury to the heart cells develops. In mild cases the pain will subside if the person rests because the oxygen demand of the heart drops back to the level being supplied. Such temporary pain is called ***angina***.

If oxygen demand is brought back into balance with oxygen supply soon enough, the heart begins to function normally again. Of course, the arteries are still diseased and the problem will most likely recur. The incidents may become more severe as the degree of coronary artery disease increases.

If the oxygen supply is very low for just a few minutes, the cardiac muscle cells begin to die. This condition is a true ***heart attack***, also called a ***myocardial infarction*** (***MI***) (Fig. 4.8). The heart becomes much weaker, and the pumping of blood drops precipitously. Cells in the brain and other organs deteriorate, and the person is in danger of dying. In fact, first-time heart attacks are fatal 65 percent of the time. Individuals who survive the initial effects of a heart attack still face many problems. The heart attack can cause damage to the heart valves or may produce a hole between the left and right ventricles, in which case the blood will flow in the wrong direction within the heart. Incorrect blood flow tends to overwork the heart, causing more heart disease and often preventing the lungs from functioning properly. An MI can also cause blood clots to form inside the heart chambers and then be pumped to other organs. If clots travel to the brain, they can cause a stroke. Finally, the heart can become so weak that the person may require lengthy medical treatment and face long-term disability. The person's social contacts, sense of well-being, normal daily routines, and employment often undergo radical undesirable changes.

FIGURE 4.8 Coronary artery disease.



Risk Factors All that has been said thus far about coronary atherosclerosis may seem like bad news, but there is also good news about this disease. Most of the factors contributing to the development of atherosclerosis have been identified, and many of them can be avoided or greatly reduced. This is the main reason for the dramatic decline since 1950 in the incidence of deaths from heart disease. Furthermore, reducing or eliminating one or more of the risk factors reduces the chances of being affected by this disease regardless of the age at which the decrease in risk factors occurs. Of course, the earlier the risk-reducing steps are taken, the greater is the benefit.

Another important fact regarding risk factors must be highlighted here. Having two or more risk factors drastically boosts one's chances of developing coronary atherosclerosis because the detrimental effects of each risk factor are multiplied by the effects of the others. For example,

smoking almost doubles the risk. Having high blood pressure multiplies the risk four times. A person who smokes and has high blood pressure has an eightfold greater risk. Adding high blood lipoproteins, which increases the risk threefold, increases the total risk to 24-fold. Therefore, reducing or eliminating even one risk factor can cause a manyfold decrease in the risk of developing coronary artery disease.

Some risk factors create more problems than others do. The following six factors provide the highest levels of risk. The actual amount of increase in risk from each one depends on when the risk factor first existed; its intensity, frequency, and duration; and its interaction with other risk factors.

Smoking Inhaling tobacco smoke increases blood pressure and adds substances to the blood that seem to promote the formation of plaque. The effect of smoking on arteries is greatly magnified in women who take birth control pills. The combination of smoking and taking birth control pills increases the risk of having a heart attack almost 18-fold. The solution is to not smoke.

High Blood Pressure High blood pressure seems to cause repeated minor injuries to the arteries. As the arteries try to repair the damage, they form scar tissue and plaque. High blood pressure also makes the heart work harder, increasing the amount of oxygen it needs, and eventually weakens the heart.

Having blood pressure checked regularly and, if it is high, seeking professional advice on how to reduce it are especially important as people get older. Blood pressure tends to rise with age and an abnormal increase has more of an effect on the arteries as a person ages.

High Blood LDLs Blood contains a variety of lipoprotein molecules. The lipids in these lipoproteins are obtained from the diet and made by the body. Most of the lipid in blood lipoproteins is cholesterol and triglycerides (fats), and lipoproteins containing predominately cholesterol are called ***low-density lipoproteins*** (***LDLs***). When LDLs are in high concentrations, the cholesterol can accumulate in the walls of arteries and contribute to the formation of plaque. The accumulation of cholesterol is reduced by other lipoproteins called ***high-density lipoproteins*** (***HDLs***). As age increases, many individuals have an increase in the concentrations of LDLs with a simultaneous decrease in HDLs.

To reduce the risk of developing high blood LDLs, the amounts of cholesterol and saturated fats in the diet should be kept low. Foods containing high amounts of these lipids include egg yolks, dairy products containing milk fat or cream, red meats such as beef and pork, solid shortening, and oils such as palm oil and coconut oil. High alcohol consumption should be avoided since it promotes the formation of LDLs. However, consuming low or moderate levels of alcohol, eating foods containing certain dietary oils (e.g., safflower oil), and exercise can reduce blood LDLs while increasing HDLs. Blood lipoprotein levels should be checked, and professional guidance should be followed if the ratio of LDLs to HDLs is found to be too high.

Diabetes Mellitus *Diabetes mellitus* is a disease that alters many aspects of the body, including blood glucose levels and the maintenance and repair of arterial walls. In so doing, it promotes the formation of plaque.

Individuals should be aware of the warning signs of diabetes mellitus, which include excessive hunger and thirst, fatigue, unusual weight gain or loss, excessive formation and elimination of urine, and slow healing of wounds. Suspected cases require diagnosis and treatment by a qualified professional.

Family History Several unidentified genes increase the chances of developing coronary atherosclerosis. The mechanism by which these genes act is not known.

Individuals from families with a history of atherosclerosis may have inherited the genes that predispose them to this disease. Though these individuals cannot alter their genes, they should try to reduce or eliminate as many other risk factors as possible. They should also inform their health care providers of their family history so that problems can be detected and necessary treatments can be initiated early.

Advancing Age Advancing age increases the risk of problems from coronary artery disease in several ways. First, aging causes arterial stiffening. Second, there is an increase in the heart's oxygen demand because the heart becomes less efficient.

Third, aging is associated with higher blood pressure, elevated blood cholesterol and LDLs, lowered blood HDLs, an increased incidence of diabetes, and decreased physical activity. Fourth, increasing age provides more time for other risk factors to take effect and for the slow process of plaque formation to progress significantly.

Though nothing can be done to alter the passage of time, people of advanced age should reduce other risk factors as much as possible.

Other risk factors are of moderate importance compared with the six just discussed. They include the following.

High Blood Homocysteine *Homocysteine* (*Hcy*) is produced and released into the blood when the body breaks down an amino acid called ***methionine***. Having high blood levels of Hcy increases the risk of developing atherosclerosis. Blood levels of Hcy rise with increasing age and when women pass through menopause. High blood levels of Hcy also develop in people with deficiencies in ***vitamin B6*** or the ***vitamin B12*** (***cobalamin***). These vitamins are essential for adequate disposal of Hcy. Finally, some people are born with a metabolic abnormality that causes them to produce excess Hcy.

Usually blood levels of Hcy can be kept low by eating a diet with adequate vitamin B6 and vitamin B12. Since there is little vitamin B12 in plants, vegetarians are at risk for vitamin B12 deficiency. People with abnormalities of the stomach may be unable to absorb adequate vitamin B12. Vitamin supplements can help people who do not get adequate vitamin B6 or vitamin B12 from foods.

Physical Inactivity The cells of people who are physically inactive require less blood flow, and the heart therefore gets less exercise because it does not have to work hard. Like every other muscle, heart muscle that gets little exercise becomes weaker and less efficient and loses some of its blood vessels. Such a heart is unprepared to increase the pumping of blood when a person suddenly begins strenuous activity. When such activity begins, an imbalance in the oxygen demand and supply of the heart occurs. In addition, lack of exercise promotes increases in blood pressure and in the ratio of LDLs to HDLs; both changes promote the development of atherosclerosis.

Engaging in a regular program of vigorous physical activity or in an occupation or hobby that includes such activity greatly reduces or eliminates this risk factor. This occurs because the heart is strengthened and develops more blood vessels, blood pressure is kept low, blood levels of HDLs are increased, body weight is less likely to become excessive, and psychological stress is minimized. All these effects reduce the risk of coronary artery disease. Planning involvement in physical activity is especially important for persons of advanced age because of the tendency toward age-related reductions in physical activity.

Obesity Being very overweight weakens the heart and makes it less efficient because the heart is being overworked and tends to become invaded with fat. Obesity also promotes high blood pressure, high levels of blood cholesterol and LDLs, diabetes mellitus, and low levels of physical activity. Obesity can be prevented or reduced by participation in a planned program of diet modification and regular exercise.

Stress A sustained high level of emotional tension or stress promotes atherosclerosis by causing prolonged periods of high blood pressure.

Emotional stress can be reduced in many ways. One way is to avoid stress-inducing situations. When this is not possible, taking breaks or vacations from such situations helps. Exercise, hobbies, and other diversions can also provide relief. Talking with a trusted confident can help, and some individuals can benefit from professional counseling.

Menopause The decline in estrogen and progesterone that occurs at menopause ends the protective effect those hormones have on the arteries. Surgical removal of the ovaries has the same effect.

Some women can benefit from hormone replacement therapy. Such therapy should be conducted only on the advice and under the continued direction of a physician knowledgeable in this area.

Male Gender Coronary artery disease occurs more frequently in men than in women, probably because the lifestyle of men generally includes more and higher levels of the risk factors associated with this disease. The incidence rate for women has been approaching that for men as women have become more involved in the same activities. Furthermore, the incidence among women approaches that of men as the age of a

population increases because of losing the protective effects of female hormones after menopause.

Personality Individuals with certain personality characteristics seem to be at higher risk for developing coronary atherosclerosis. These characteristics include being highly competitive, striving for perfection, and feeling that there is never enough time to accomplish one's goals. These characteristics indicate a high level of stress. Recent evidence suggests that stress is the key feature and that personality contributes little if any risk.

High Blood Iron Levels Another possible risk factor, which some scientists think provides a risk exceeded only by that from smoking, is having higher than average levels of iron in the blood. The iron may promote atherosclerosis by increasing the accumulation of LDLs in arteries and causing cell damage by promoting the formation of free radicals. If having relatively high blood levels of iron is shown conclusively to be a significant risk factor, steps to lower these levels might include reducing the consumption of foods high in iron (e.g., red meat, liver, spinach, iron-fortified foods); not drinking water with a high iron content; taking iron supplements only when absolutely necessary; and giving blood regularly.

Periodontal Disease Periodontal disease is associated with increased risk of atherosclerosis, heart attack, and stroke. The mechanism by which periodontal disease contributes to atherosclerosis is not known. They may involve a genetic predisposition to both periodontal disease and atherosclerosis; toxins and chemical signals produced at the teeth; and effects from bacteria spreading from the teeth throughout the body. Some of these mechanisms may affect endothelial function.

Congestive Heart Failure

Congestive heart failure (*CHF*) is another disease that becomes more common and serious with age. Approximately three million people in the U.S. have CHF, and there are approximately 400,000 new cases each year. More than 75 percent of cases are in people age 65 and over. Incidence rates double for each decade over age 45, and approximately 10 percent of elders over age 80 have CHF. Congestive heart failure is the leading cause of hospital admissions for people 65 and over, and it is a major cause of disability, reduced independence, and death. The number of cases is expected to double by the year 2040.

Main causes of CHF are factors that weaken the heart. The most frequent causes are coronary artery disease, high blood pressure, disease of the heart valves, obesity, and kidney disease. The underlying problem is years of overworking the heart. An overworked heart tends to strengthen itself by dilating and thickening. At first these changes increase heart strength, but if the heart continues to be overworked, it continues to dilate and thicken. Excessive amounts of these changes weaken the heart. Then the heart chambers contain a great deal of blood but cannot pump it effectively. The flow of blood diminishes, and organs begin to malfunction.

In addition, fluid accumulates in the lungs (pulmonary edema). Affected individuals have difficulty breathing and may feel out of breath after the slightest exertion or even when resting. Poor circulation in other areas, especially the legs, causes swelling and discomfort and promotes the formation of varicose veins. Many ordinary activities become difficult or impossible.

The heart tends to solve these problems by dilating and thickening even more, but this exacerbates the situation. Unless steps are taken to strengthen the heart and reduce its workload, the heart gradually becomes so weak that it fails completely and the individual dies.

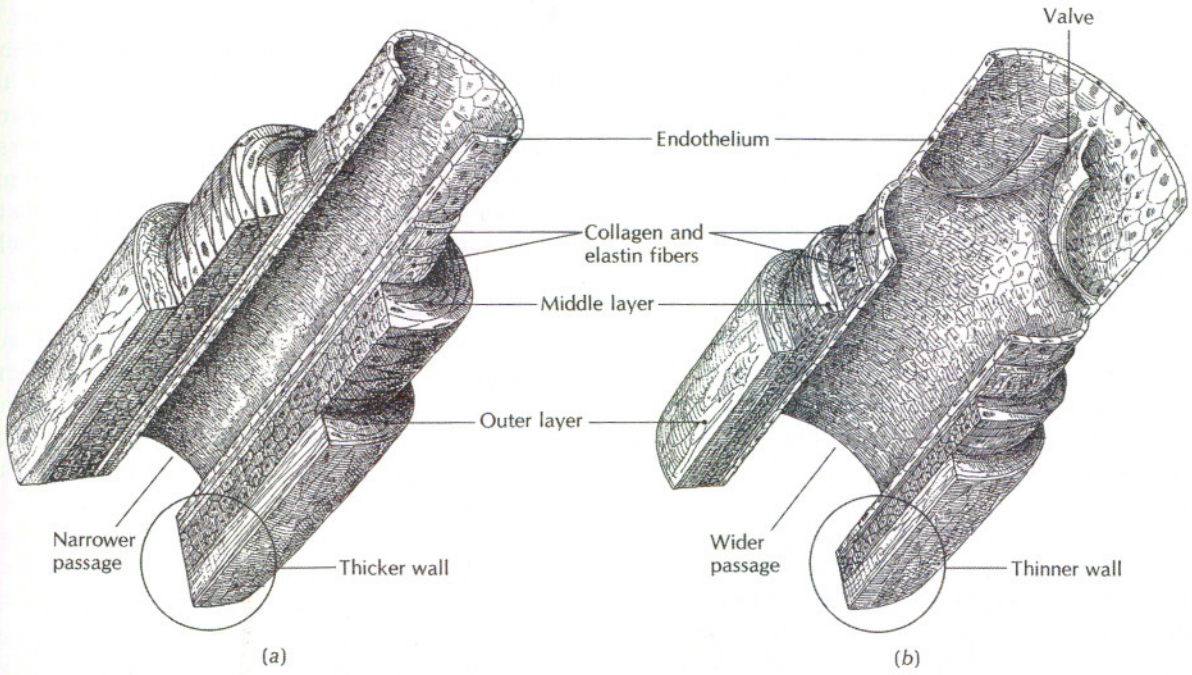
Valvular Heart Disease

Untreated serious *valvular heart disease* causes detrimental changes similar to those resulting from congestive heart failure. This disease usually develops after coronary artery disease or rheumatic fever, which can prevent the valves from closing properly. Then some of the blood in the heart flows backward during each beat. Rheumatic fever can also prevent the valves from opening properly, and so blood does not flow forward as easily as it should. In either case the heart is overworked.

ARTERIES

Arteries are flexible tubes that carry blood from the heart to every region of the body. Arteries have special properties that ensure that they perform this task effectively. These properties derive from the three layers composing the arterial wall.

FIGURE 4.9 Structure of (a) arteries and (b) veins.



Inner Layer

The innermost layer of an artery is called the ***endothelium***. It is supported by a thin underlying layer that contains collagen and a mat of elastin fibers (Fig. 4.9*a*). Like the endocardium in the heart, the endothelium provides smoothness by forming a continuous glistening layer that coats the collagen and other materials in the arterial wall. In so doing, it permits blood to flow easily without clotting.

The endothelium also secretes several signaling materials including ***nitric oxide*** (***NO**). ***endothelin, prostacyclin,*** and ***angiotensin converting enzyme*** (***ACE***). Nitric oxide and prostacyclin promote vasodilation in many arteries. Nitric oxide also limits vessel thickening by inhibiting the growth of smooth muscle, and it inhibits clot formation and plaque formation. Endothelin and ACE stimulate vasoconstriction. The effects of *NO usually dominate, keeping vessels adequately dilated.

Middle Layer: Large Arteries

The middle layer in the largest arteries consists mostly of a thick layer of elastic fibers that make the arteries strong. Most of the elastic fibers in the aorta are produced before birth or during childhood, but some new elastin is produced throughout life. Since these arteries are closest to the heart, strength is necessary to withstand the high blood pressure produced by each heartbeat.

This layer also provides elasticity, which allows the arteries to be stretched outward somewhat each time the ventricles pump blood into them. The extra space provided by the stretching prevents the systolic pressure from rising too high, and the work the heart must perform is kept reasonably low, just as it is easier to blow up an easily stretched balloon than a stiff one. Preventing excessive pressure also keeps the arteries from being injured by the accompanying extreme forces.

The elasticity of large arteries helps to prevent blood pressure from rising too high in yet another way. Unusually high blood pressure immediately causes normal arteries to be stretched outward excessively. Nerve cells in the walls of arteries detect this abnormal stretching and send signaling impulses to the blood pressure control center in the brain. Other factors from the artery that influence the sensory neurons include prostacyclin, which increases the signals, and reactive oxygen species, which reduce them. The brain

then sends impulses to the heart telling it to pump less blood. It also tells blood vessels in various areas of the body to dilate to provide more space for the blood coming from the heart. As a result, blood pressure decreases and the large arteries return to their normal size. The nerve cells are then no longer activated, and blood pressure stabilizes at the normal level. Note that this is a negative feedback system that maintains proper and fairly stable conditions in the body.

The nerves in blood vessels send different impulses to the brain when blood pressure is too low and arteries are not stretched enough. The result is the sending of norepinephrine and related substances to the heart and vessels. These substances raise blood pressure by several means, including stimulating the heart and causing the smaller arteries to constrict.

Elasticity also causes the arteries to snap back to their original diameters when the ventricles are relaxing. This elastic recoil helps maintain diastolic pressure between beats by squeezing the blood. Diastolic pressure keeps the blood moving forward steadily while the heart rests briefly after each beat. Thus, elastic recoil serves the same purpose as the spring that keeps a watch ticking between windings.

Middle Layer: Smaller Arteries

The middle layer of smaller arteries contains some elastic fibers but is composed mostly of smooth muscle. When the muscle contracts, it causes the arteries to constrict, reducing the flow of blood.

As a rule, the smooth muscle in most smaller arteries contracts weakly, providing some resistance to flow while allowing ample blood flow through the arteries. This resistance is important because without it, blood would flow from the arteries into the capillaries so quickly that blood pressure would drop too low, especially between heartbeats. The same effect is observed with tires. A tire with a tiny hole loses pressure so slowly that it can be reinflated before any harm is done, while a tire with a large leak loses all its pressure and goes flat very quickly.

In normal situations the constriction of small arteries increases whenever blood pressure begins to drop too far. This additional constriction increases resistance and raises blood pressure back to the proper level. Conversely, if blood pressure rises too high, the smooth muscle relaxes, the arteries dilate, resistance drops, and blood pressure decreases back to normal levels.

In addition to regulating blood pressure by constricting or dilating as a group, individual arteries can constrict to reduce blood flow to organs that need little flow while others dilate to increase flow to more active organs. Thus, the smaller arteries act like a set of valves or traffic signals to make sure that each part of the body receives only as much blood flow as it needs.

The constriction and dilation of smaller arteries are controlled by negative feedback systems. The arteries respond to several factors, including nerve impulses, hormones, temperature, and chemical conditions in their vicinity. These mechanisms help maintain normal blood pressure and blood flow to each body structure.

Outer Layer

The outer layer of arteries consists largely of loose connective tissue containing soft gel and scattered fibers. This layer loosely attaches arteries to other structures, enabling arteries to be shifted as parts of the body move while preventing the arteries from moving too far out of position.

AGE CHANGES IN ARTERIES

There are no important age changes in the endothelial structure, its supporting layer, or the outer layer of arteries. These layers function well regardless of age with one major exception. There is an age-related decline in the ability of the endothelium to regulate blood vessels and blood pressure. The cause is not clear. It may be due to aging of endothelial cells, to free radical damage, or to age-related increases in blood pressure. Nitric oxide reacts with superoxide radicals ($*O_2$), producing toxic $ONOO^-$ (peroxynitrite). This reaction reduces the amount of *NO available to regulate vessels and blood clotting, and the $ONOO^-$ can slow *NO production further by injuring endothelial cells. These changes may contribute to high blood pressure and to atherosclerosis.

Middle Layer: Large Arteries

Numerous age changes occur in the middle layer

of large arteries. Age changes in elastic fibers include breakage, glycation, accumulation of calcium and lipid deposits, and faster breakdown by enzymes. Old damaged elastic fibers accumulate. The increase in many substances, including smooth muscle, collagen, calcium deposits, and cholesterol and other fatty materials, causes thickening and stiffening of the arteries. These changes amplify the decline in elasticity caused by the altered elastic fibers. Since the arteries are less able to be stretched by each pulse of blood, systolic pressure tends to rise.

Since much elastin in the aorta is produced before birth, children with low birth weights may have less aortic elastin, resulting in less aortic strength and elasticity. This can speed up aortic thickening and stiffening during childhood and adulthood, resulting in a greater risk of high blood pressure and related diseases (e.g., atherosclerosis, congestive heart failure). These effects highlight the importance of events in youth or even before birth to age-related changes and disease later in life.

At the same time the arteries are stiffening, years of containing blood under high pressure causes them to gradually widen and lengthen. This is especially evident in the aorta. These changes provide more space for blood. At first this compensates for the declining ability of large arteries to be stretched, and consequently it keeps the tendency toward increases in systolic pressure in check. Eventually, however, the elastic fibers are stretched so much that they can yield no further. Then each contraction of the heart produces a rapid and dramatic rise in systolic blood pressure. This can increase cardiac oxygen demand by almost 30 percent. At the same time, the high blood pressure and thickening of the heart reduce the amount of *NO in coronary vessels. This limits the vessel dilation required to increase oxygen supply to the heart muscle.

Once the arteries no longer stretch much with each heartbeat, sensory nerve cells that detect vessel stretching are not activated as much. Age changes in the endothelium that reduce prostacyclin and increase reactive oxygen species (ROS) also reduce the nerve cell activation. The reflex to prevent abnormal increases in blood pressure is suppressed, and the pressure remains high. In most cases sensory nerve cells are fooled and respond as though blood pressure were too low. Age changes in the brain's blood pressure control center amplify this effect. The final result is the release of norepinephrine, which augments the high pressure but also stimulates the heart. In this way, the extra norepinephrine seems to be compensatory because it helps the aging heart maintain cardiac output.

As with all age changes, there is much variation among individuals with respect to the rise in systolic pressure. While the elevations are modest in most people, about 40 percent of the elderly have systolic pressures above the safe maximum for those of advanced age (160 mmHg). Recall that elevated blood pressure increases the heart's workload and oxygen needs and the risk of developing atherosclerosis. Therefore, it is important for the elderly to have their blood pressure checked and, when necessary, receive therapy to keep it within safe limits. However, elevated blood pressure in older individuals must not be lowered too quickly or too far, since the result can be weakness, fainting, or more serious damage to the heart, the brain, and other parts of the body.

In addition to restricting stretching, stiffening of the arteries diminishes their elastic recoil. The slow decline in recoil does not cause a substantial change until about age 60, after which diastolic pressure declines slightly. The result is a slowing of blood flow through coronary arteries and other small arteries between heart beats. Normally, this decline is not large enough to cause significant effects, though it brings a person closer to having inadequate blood flow during each diastole.

In a large longitudinal study of people with no diseases of the circulatory system, systolic BP does not change until approximately age 40 in women and age 50 in men. Then BP increases approximately 5-8 mmHg per decade. In women, the systolic BP may stop rising and may even begin to decrease after age 70, while in men the systolic BP continues to rise throughout life. The overall increase in systolic pressure averages 21 mmHg in women and 15 mmHg in men. Diastolic pressure in women increases from ages 40 to 60, but then levels off or declines. Diastolic pressure in men increases 1 mmHg per decade. Overall, diastolic pressures increase 5 mmHg in women and 3.5 mmHg in men. Studies that include people with diseases or who take medications show greater changes in BP, and the women may not have the leveling and decline in BP after age 70.

Middle Layer: Smaller Arteries

Aging causes little if any change in the overall resistance provided by the smaller arteries. Their thickening seems to help prevent overstretching as systolic blood pressure increases with age. Older arteries do not respond quite as well when conditions such as chemical levels begin to change. This seems to be due in part to decreased functioning of the nervous system and altered levels of the hormones that control the vessels. The vessels also seem to have reduced sensitivity or a reduced ability to respond to control signals. Therefore, the arteries do not dilate as well when the areas they supply need more oxygen. This decrease in supply tends to reduce the maximum rate of work that certain organs (e.g., muscles) can perform.

The decreased ability of the arteries to respond to rising or falling body temperature is an even greater problem, leaving older people less able to prevent themselves from overheating or becoming chilled. For example, inadequate dilation of dermal vessels prevents the extra heat produced during exercise from leaving the body quickly. This can lead to excessively high body temperature, damage to body molecules and cell parts, malfunctioning of organs such as the brain, illness, or even death. Poor constriction by dermal vessels when a person is in a cold environment can cause excessive loss of body heat and a drop in body temperature. Not only will such an individual feel uncomfortably cold, but because of slowing cell activities and malfunctioning of organs such as the muscles and the heart, he or she may also become ill.

The declining ability to maintain normal body temperature as age increases is due not only to age changes in the middle layer of smaller arteries but also to age changes in the integumentary system (e.g., sweat glands, fat tissue), the nervous system (e.g., sensory neurons), and the muscle system (e.g., muscle mass).

Because of reduced thermal adaptability, older individuals should avoid environments and activities that tend to cause significant elevation or depression of body temperature. Hot weather or very warm indoor areas, hot baths or showers, the use of numerous blankets or electric blankets, and strenuous physical activity tend to cause overheating. Cold weather or cool rooms, cool water for swimming or bathing, exposure of the skin, inadequate clothing, and restricted physical activity increase the risk of developing hypothermia.

Number of Arteries

The number of larger arteries remains the same throughout life. The number of smaller arteries remains about the same or increases slightly in some areas of the body (e.g., heart and brain). This slight increase helps sustain normal blood flow by compensating for the development of somewhat irregular arteries. Other areas (e.g., skin, kidneys) have decreasing numbers of smaller arteries with age.

Fortunately, the adverse effects on blood flow caused by the aging of arteries can be largely overcome through steps such as receiving proper medical care, pacing activities, and avoiding situations that place a person in danger of overheating or chilling. Unfortunately, for most individuals, aging arteries are affected not only by age changes but also by arterial diseases.

ATHEROSCLEROSIS: AN ARTERIAL DISEASE

By far the most common arterial disease is ***atherosclerosis***, which is one of a group of arterial diseases called ***arteriosclerosis***. Because atherosclerosis is very common, some people mistakenly use these two terms interchangeably. The incidence of atherosclerosis and the serious difficulties it causes rise with age for the same reasons that cause the age-related increase in heart disease.

Importance

Some statistics on the importance of atherosclerosis were presented earlier in this chapter. In addition to causing most heart attacks, atherosclerosis causes most strokes. A ***stroke*** is injury to or death of brain cells caused by low blood flow or bleeding in the brain (Chap. 6). For those over age 65, strokes are now the third leading cause of death, days in the hospital, and days in bed. Strokes also cause many cases of dementia and other forms of disability.

Atherosclerosis is also a major contributor to kidney disease, problems in the legs (e.g., weakening of muscles and skin, pain during exertion),

and male impotence. Such outcomes not only affect an individual's health and survival but also have an impact on all other aspects of life. For example, dietary restrictions may become necessary, demanding occupational or recreational activities may have to be curtailed, and interpersonal relations between affected men and their spouses can suffer dramatically.

Development and Effects

Atherosclerosis begins as small streaks of fatty tissue within the inner layer of arteries. Gradually, the streaks widen and thicken as they accumulate a variety of other materials, including smooth muscle cells, collagen fibers, cholesterol, and calcium deposits. The resulting masses—***plaques***—protrude inward and narrow the passageway in the artery (Fig. 4.7). The plaques often grow completely through the endothelium and replace regions of it. Both the roughness and the collagen fibers of the plaques cause the blood to form clots. As a result, the narrowing of the artery leads to reductions in or complete blockage of blood flow. In addition, pieces of the plaque sometimes break off, move down the artery, and block the artery where it branches to form smaller arteries.

These plaques usually grow outward and infiltrate the middle layer of the artery, causing it to stiffen. When this occurs in larger arteries, they are less able to be stretched outward to accommodate pulses of blood from the heart, and systolic pressure can skyrocket. Since the arteries are also less able to spring back when the heart relaxes, diastolic pressure drops and the flow of blood becomes less regular. When plaque grows outward in smaller arteries, the stiffening and replacement of the smooth muscle prevent them from adjusting blood pressure and blood flow to suit body needs. The cells do not receive adequate oxygen and nutrients, and waste materials accumulate. The resulting loss of homeostasis injures or kills cells, and the organs they compose malfunction.

The outward growth of plaque also causes weakening of the middle layer, and affected arteries begin to bulge outward from blood pressure. The outpocketings, called ***aneurysms***, can disturb nearby structures by pressing on them (Fig. 4.10). Additionally, blood flowing past aneurysms tends to swirl and form clots. Some arteries become so weak that they rupture, causing severe internal bleeding that can lead to the most serious strokes.

Mechanisms Promoting Atherosclerosis

Several factors seem to cause atherosclerosis or to promote its development. These include endothelial dysfunction, free radicals, blood lipoproteins, elastase, glycation, heat shock proteins, and insulin-like growth factors (IGFs). Some of these may interact synergistically.

Endothelial Dysfunction Endothelial dysfunction may cause or result from endothelial aging, high blood pressure, or atherosclerosis. Endothelial dysfunction increases the adverse effects from high BP and from atherosclerosis. Part of the effect may be from an age-related increase in $^*O_2^-$, which reduces *NO by reacting with it to form $ONOO^-$. With less *NO, vessel dilation is reduced and vessel smooth muscle growth and clot formation increase. At the same time, $ONOO^-$ may initiate or promote plaque formation by injuring the vessel wall.

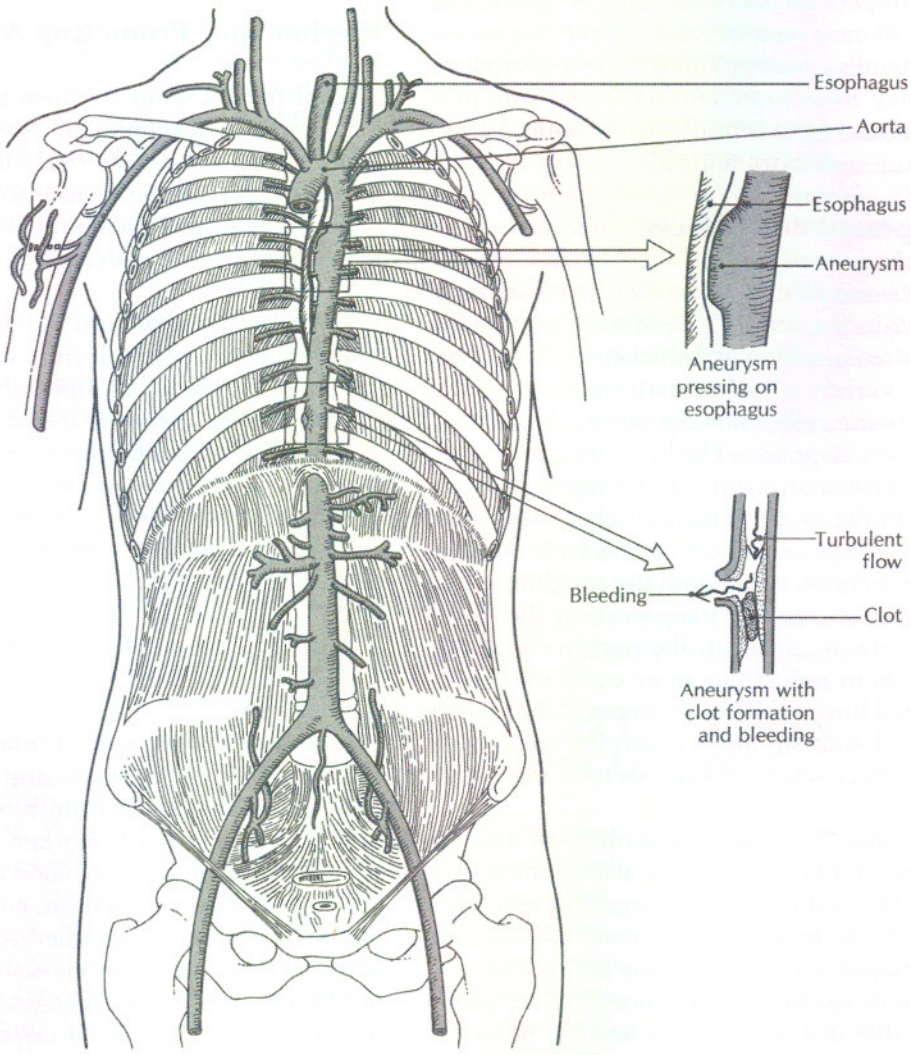
Free Radicals Free radicals may also contribute to atherosclerosis by increasing the formation of lipid peroxides (LPs) from blood lipoproteins. Blood LPs increase with age and after menopause, and also with increases in blood LDLs, blood pressure, stress, diabetes mellitus, and smoking. Lipid peroxides may promote atherosclerosis in several ways. Examples include increasing the absorption of LDLs by vessel macrophages, converting them to cholesterol-filled ***foam cells***; injuring vessel cells directly; attracting monocytes and macrophages into vessel walls, which promote inflammation and cell damage; promoting vessel constriction; and promoting blood clot formation.

Blood LDLs Blood LDLs may promote atherosclerosis by increasing LPs and by increasing elastase.

Elastase ***Elastase*** is an enzyme that breaks down elastic fibers into elastin peptides. Elastin peptides are also formed during elastin synthesis. Elastase increases with age and with higher LDL levels. Elevated levels of elastin peptides seem to promote more elastase production by promoting the binding of calcium and lipids to elastin fibers.

Elastase may increase atherosclerosis by

FIGURE 4.10 Aneurysms.



reducing elastic fibers in arteries, making vessels more susceptible to damage by blood pressure. The effects from the elastin peptides produced seem to increase *NO. Results include benefits such as vasodilation, and drawbacks such as vessel damage by stimulated monocytes. Research has provided contradictory results regarding the effects from elevated elastin peptides on promoting or reducing atherosclerosis.

Glycation Glycation of proteins in arteries produces age-related glycation end-products (AGEs) and *FRs. The *FRs may promote atherosclerosis directly. The AGEs bind in fatty streaks and stimulate inflammation and *FR formation by macrophages. Glycated collagen in arteries is distorted and stiffer causing adverse effects. These include reduced effectiveness of nitric oxide as a vasodilator; detachments of endothelium from the vessel wall; and increased clot formation.

Heat Shock Proteins ***Heat shock proteins*** are produced when cells are stressed or injured. These proteins received their name because they were first discovered in cells subjected to abnormally high temperatures. Heat shock proteins seem to protect cells from a variety of harmful environmental factors. An immune response to heat shock

FIGURE 4.11 Capillary exchange and lymph formation.

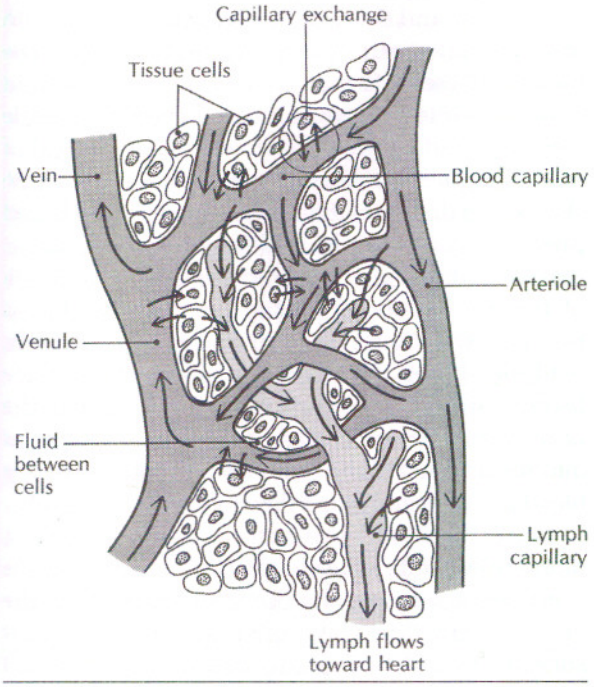
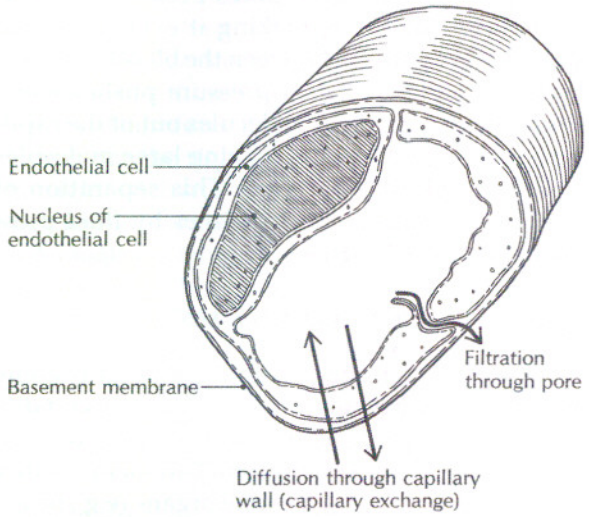


FIGURE 4.12 Capillary structure and capillary exchange.



protein in damaged arteries may be the initial event in atherosclerosis.

Insulin-like Growth Factors ***Insulin-like growth factors*** **(*IGFs*)** from cells stimulate growth and regulate other cell activities. The distribution and effectiveness of IGFs are altered when they bind to ***insulin-like growth factor binding proteins*** **(*IGFBPs*)**. Research suggests that different ratios of IGFs and IGFBPs influence the development of atherosclerosis, possibly by altering blood levels of lipoproteins and *NO and by affecting the growth of vessel smooth muscle.

Prevention

The incidence and seriousness of atherosclerosis can be greatly lowered by avoiding or reducing the known risk factors, which were discussed in the section on coronary artery disease.

CAPILLARIES

The ***capillaries***, which receive blood from the smallest arteries, are often no more than 1 mm in length. They are so narrow that blood cells can pass through only in single file and often must actually fold to pass through. The capillaries run among the body cells and are so numerous and so close together that no cell is very far from a capillary (Fig. 4.11).

Capillaries are porous vessels through which materials in the blood move out to the surrounding body cells and many of the materials produced by body cells (e.g., wastes, hormones) move back into the blood. Since materials are moving in both directions, this process is called ***capillary exchange***. However, a portion of the material that moves out of the capillaries and some of the material produced by the cells do not travel back into the capillaries. This material passes instead into ***lymph capillaries***, where it is known as ***lymph***. The lymph then passes through lymph vessels, which deliver it into large veins near the heart.

The structure of capillaries is well suited for capillary exchange (Fig. 4.12). The wall of each capillary is composed of a single layer of thin cells that are supported by a thin layer of material they secrete (***basement membrane***). Many small atoms and molecules pass through the capillary wall quickly and easily by the process of ***diffusion***, which involves the movement of materials from an area of higher concentration to an area of lower concentration. Therefore, substances that are

abundant in the blood diffuse outward to the cells, while other substances diffuse from the cells into the blood.

Capillary walls have pores between the cells that constitute them, making it even easier for substances to diffuse between the blood and body cells. In addition, blood pressure pushes many atoms, ions, and small molecules out of the capillaries through the pores, leaving large molecules and cells within the blood. This separation of small substances from large ones by fluid pressure is called ***filtration***.

Age Changes in Capillaries

With increasing age, many capillaries become narrower and irregular in shape, and this retards the flow of blood. Some capillaries become so narrow that blood cells get stuck in them, further inhibiting blood flow. In some organs (e.g., heart, muscles) blood supply is further reduced because of a decrease in the number of capillaries. Finally, capillary walls become thicker and have a decrease in the number of pores; both changes inhibit capillary exchange.

Age changes reduce the ability of capillaries to meet the needs of body cells quickly. Therefore, while the cells may be able to function well at low levels of activity, both the ability to sustain vigorous activity and the maximum rate of physical activity may be lowered. This becomes evident when people tire more quickly while performing vigorous work or experience a gradual drop in the maximum speed of activity they can attain while performing vigorous activities such as running or riding a bicycle.

VEINS

Blood passing through capillaries flows into very small ***veins***. The small veins join to form larger veins as they transport the blood back to the heart (Fig. 4.1).

Veins are made up of the same three layers found in smaller arteries (Fig. 4.9*b*). The layers in veins are thinner and weaker, however, since venous blood pressure is much lower than arterial pressure; therefore, there is no need for thick strong walls in veins. Veins also tend to be somewhat larger in diameter than arteries in the same area of the body. This extra internal space, along with the greater ability of veins to expand outward, allows the veins to serve as a reservoir for storing blood.

The inner layer provides smoothness to prevent blood clots, and the middle layer contains smooth muscle that regulates the diameter. When the muscle relaxes and the veins dilate, they can hold a considerable amount of blood. When the muscle contracts and constricts the veins, a great deal of blood is squeezed out and sent to the heart. These changes in diameter are useful in regulating blood pressure. For example, if blood pressure rises excessively, dilation allows the veins to store much of the extra blood from the arteries. The blood pressure will then return to normal. Conversely, if higher blood pressure is needed, the muscle layer contracts, squeezing more blood back to the heart. The heart immediately pumps this extra blood into the arteries, filling them further and increasing blood pressure and blood flow to the desired levels.

Since the blood pressure in veins is so low, blood flow tends to be sluggish. Gravity increases this tendency by pulling blood in veins below the heart downward, away from the heart. To prevent such backward flow, veins below the heart and in the arms contain ***valves***. These valves consist of flaps of tissue extending from the walls of the veins into the blood (Fig. 4.9b). The valves operate in the same way as do those in the heart.

The movement of blood in veins is greatly aided by the alternating contraction and relaxation of nearby muscles, such as occurs during exercise involving body movement. During contraction, muscles widen and press on neighboring veins, forcing blood to move along the veins. During relaxation, the muscles become thinner, allowing the veins to expand and fill with blood from below. Therefore, exercise promotes blood flow in veins.

Age Changes in Veins

Several age changes occur in veins, including accumulations of patchy thickenings in the inner layer and fibers in the middle layer and valves. However, these changes do not alter the functioning of veins because veins have such a large diameter to begin with that slight narrowing is unimportant. Veins have thin walls and are able to expand easily and compensate for narrowing, and there are often several veins draining blood from each area of the body, which can provide ample alternative routes for blood.

Diseases of Veins

Some disease changes in veins occur with increasing frequency and severity as age increases. One of the most common is varicose veins, which now ranks as the tenth leading chronic condition among people above age 64.

Varicose Veins A ***varicose vein*** is a vein that has developed a much larger diameter than normal because blood has accumulated in the vein, stretching it outward. If the vein is stretched frequently and for prolonged periods, it loses its elasticity and remains permanently distended.

Varicose veins frequently develop in the legs. Conditions promoting their development in this area include standing still for long periods, sitting in a posture that reduces circulation, wearing tight clothing, and having certain diseases (e.g., congestive heart failure). Varicose veins are also found inside the abdomen; for example, cirrhosis of the liver is a common cause of varicose veins in the digestive system.

Varicose veins cause several problems. Affected veins close to the skin can be cosmetically undesirable because they appear as irregular bluish vessels. When veins remain engorged with blood for long periods or become inflamed, they can be very painful. They can even become sites of infection and, in extremely serious cases, sites of bleeding. Bleeding is the main problem when a person has varicose veins from cirrhosis. Very wide varicose veins also prevent the valves from stopping backward blood flow, since the valve flaps are too far apart to meet and blood slips back through the opening that remains between them. The blood backs up into the capillaries, slowing flow there. When this happens in the legs, swelling in the area below the varicose vein develops. Slow flow also prevents the capillaries from serving the needs of body cells, and the cells become weak and injured and may even die. Infection often adds to the resulting skin, nerve, and muscle problems.

Another undesirable result from varicose veins occurs because blood flow through these veins is fairly sluggish and the blood tends to clot. A stationary blood clot inside a vessel is called a ***thrombus***. As in arteries, a thrombus in a vein can block blood flow. Frequently, blood flow propels the thrombus within the vein, in which case it is called a ***thromboembolus*** or simply an ***embolus***. An embolus can cause serious problems when it moves to the heart and is pumped into the arteries, because as the arteries branch into narrower ones, the embolus will finally reach an artery through which it cannot pass and will block blood flow through that artery.

Almost all varicose veins develop in systemic veins such as those in the legs and the digestive system. Therefore, most emboli from varicose veins enter the right atrium and are pumped by the right ventricle into the pulmonary arteries. Such emboli are called ***pulmonary emboli***.

A small pulmonary embolus causes death of the area of the lung normally serviced by the artery that has become blocked. If only a very small artery is blocked, the area that dies may be so small as to go unnoticed. However, repetition of this type of event or blockage of a larger pulmonary artery by a more substantial embolus may kill a considerable portion of the lung, significantly reducing the ability of the lung to serve the needs of the body. Dead lung tissue can become infected and form a pocket of pus called a ***pulmonary abscess***. These infections and abscesses can make a person ill and can even be fatal.

A large pulmonary embolus can obstruct blood flow from the right ventricle to the lungs to such an extent that the right ventricle can no longer empty adequately and becomes overfull. This overfilling, coupled with the high pressure developed as the right ventricle attempts to pump blood through the blocked arteries, causes the heart to fail completely. The result can be sudden death.

Since varicose veins cause such a variety of undesirable and serious consequences, slowing or preventing their formation can help maintain the quality and length of life. When possible, people who stand or sit for long periods of time should move about or change position frequently. When one is standing, alternately tensing and relaxing the leg muscles periodically can help pump blood out of the veins. Support stockings or tights that apply an even pressure over the legs also help prevent the expansion of veins. Elevating the legs for short periods allows accumulated blood to drain out of the veins. In addition, certain situations should be avoided. For example, sitting for long periods with the legs crossed or in a tightly bent position inhibits blood flow out of the veins. Clothing that is tight in the upper regions of the legs should be avoided for the same reason. Excessive habitual consumption of alcoholic bever-

ages should be avoided because this is the most common cause of liver cirrhosis. Individuals who have a weak heart or are developing congestive heart failure should pay particular attention to these suggestions.

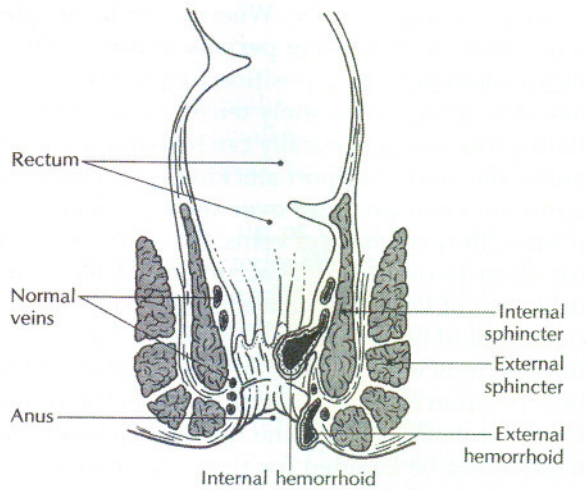
Hemorrhoids One type of varicose vein is singled out here because of its location; it is found in the area of the anus and is called a ***hemorrhoid*** (Fig. 4.13). Hemorrhoids may remain small for long periods, may enlarge slowly, or may become large in a short time. Some may reach the size of Ping-Pong balls.

Like other types of varicose veins, hemorrhoids can be painful and may bleed, become infected, develop thrombi, and require surgery. These consequences can cause substantial disability.

Factors that promote the formation of hemorrhoids include chronic constipation, forced bowel movements, chronic cough, and cirrhosis of the liver. The first two factors are often found among disabled individuals and people whose occupations limit the availability of toilet facilities. Chronic cough is associated with smoking and other forms of air pollution, chronic bronchitis, and emphysema.

Several strategies can be used to decrease the chance of developing hemorrhoids. Adequate amounts of fiber and water in the diet help because these substances promote regular and relatively easy bowel movements, as does exercise. Adequate access to toilet facilities and timely use of those facilities are important.

FIGURE 4.13 Hemorrhoids.



Smoking, breathing polluted air, and consuming alcohol habitually should be avoided.

LYMPHATICS AND THE SPLEEN

The structure and valves of lymph vessels are very much like those of veins. Lymph flowing through lymph vessels passes through ***lymph nodes***, which are spongy structures ranging up to the size of a large bean (Fig. 4.2). Lymph nodes contain defense cells that neutralize or remove harmful chemicals and microorganisms. By acting like purifying filters, lymph nodes reduce the risk of spreading dangerous materials from a site of injury or infection in one area of the body to another region.

Much lymph passes through the ***spleen***, which is toward the back of the abdominal cavity near the lowest rib on the left side of the body. The spleen serves as a very large lymph organ, stores blood, and removes old and damaged red blood cells from the circulation.

Some defense cells in the lymph nodes and spleen are called ***macrophages*** because they ingest substances. Others are called ***lymphocytes***. Macrophages and lymphocytes are parts of the immune system.

Age Changes in Lymphatics and the Spleen

Aging seems to cause little significant change in the structure and functioning of lymph vessels, lymph nodes, and the spleen. However, there are important age changes in the ***immune system***.

BLOOD

Blood is a complex fluid containing many different types of substances and cellular components. Approximately 55 percent of the blood consists of a pale yellow liquid called ***plasma***; the other 45 percent is made up of the blood cells and platelets, which are suspended in the plasma (Fig. 4.14). A person maintains normal numbers of RBCs and platelets by balancing their rapid destruction with rapid production in the red bone marrow.

Plasma

About 90 percent of blood plasma consists of water. The properties of water allow it to dissolve most substances and flow easily through the cir-

culatory system, transporting materials and blood cells. Water also provides an excellent medium for distributing heat from warmer to cooler areas. The water and buffers in the plasma help maintain proper acid/base balance in body cells. Finally, plasma contains defense substances (e.g., antibodies). Therefore, plasma contributes to all four functions of the circulatory system.

Red Blood Cells

Red blood cells (***RBCs***) are the most numerous blood cells. They contain a great deal of a red material called ***hemoglobin***. Because hemoglobin can bind oxygen and carbon dioxide and can act as a buffer, RBCs can transport much oxygen from the lungs to body cells, transport some carbon dioxide from body cells to the lungs, and help regulate acid/base balance.

Platelets

Platelets are cell fragments that form when small pieces break off from large parent cells in the red bone marrow. Platelets start the formation of blood clots.

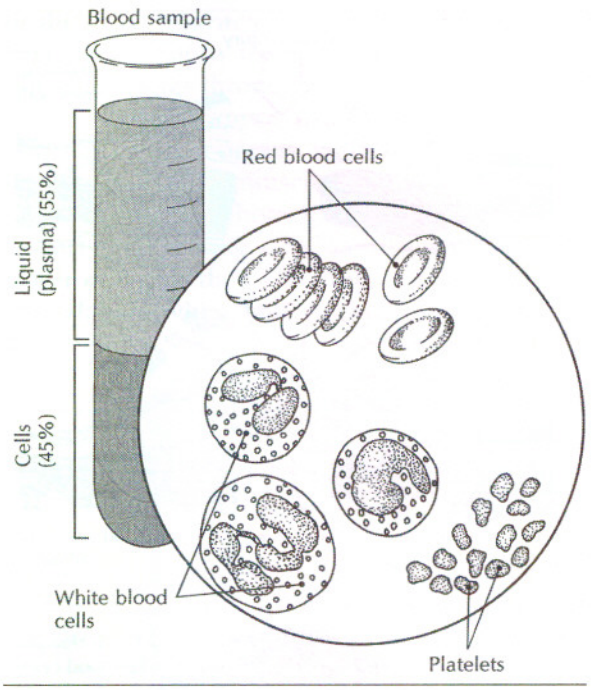
Because platelets are fragments of cells, they are fragile and burst open when they come into contact with rough spots, collagen, or unusual chemicals. This occurs, for example, when blood leaks out of a damaged vessel (Fig. 4.15). The bursting platelets release substances that help form a sticky fibrous material called ***fibrin***, which begins to plug the hole in the vessel. As blood cells become trapped in the fibrin mesh, the spaces among the fibrin threads are filled. The resulting blood clot forms a leakproof seal, stopping the bleeding.

Unfortunately, platelets burst open and start the clotting mechanism whenever roughness, collagen, or unusual chemicals are encountered. When this happens on an atherosclerotic plaque, the resulting clot may block the artery and lead to a heart attack or stroke. In addition, since some platelets are bursting at all times, slow blood flow, as occurs in varicose veins, permits the substances released by platelets to accumulate at that location. When enough platelet material builds up, a thrombus forms.

White Blood Cells

The ***white blood cells*** (***WBCs***) are also called ***leukocytes***, which means "white cells." Blood contains only 1 WBC for every 500 RBCs.

FIGURE 4.14 Components of blood.



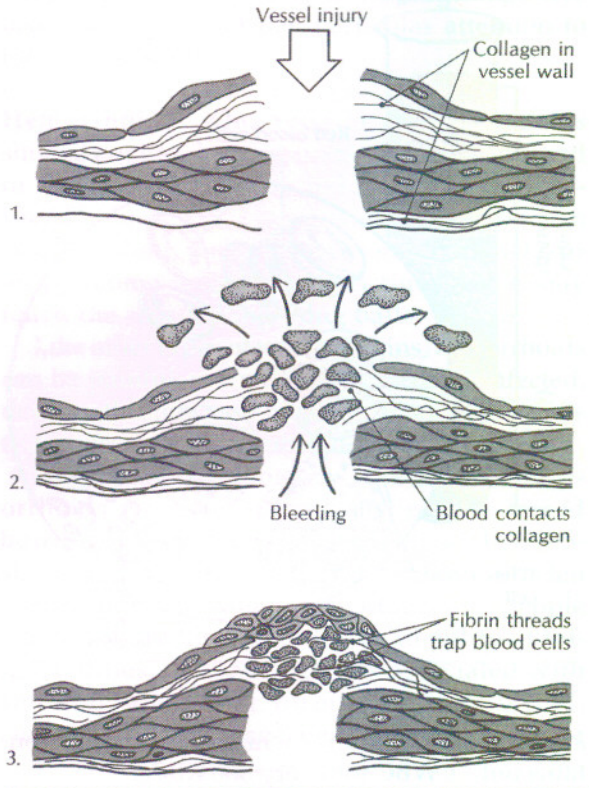
WBCs can be divided into two main groups. The cells in one group are called ***polymorphonuclear leukocytes*** ("many structured nucleus, white cell") (***PMNs***) or ***granulocytes*** ("granular cells"). The other main group of WBCs consists of the ***agranulocytes*** ("cells without granules").

There are three types of PMNs. The most numerous type by far are ***neutrophils***, which are important defense cells because they ***phagocytize*** (ingest) undesirable materials. Because they can move about like amoebas and can travel through capillary walls, they are found not only in the circulating blood but also among body cells. These and other phagocytic WBCs resemble vacuum cleaners as they move into every area of the body, sucking up debris.

Many neutrophils are stored within blood vessels, especially in the bone marrow. Stored neutrophils are mobilized into the circulating blood when there is a need for additional defense activity, as occurs when an infection develops.

The other two types of PMNs are ***basophils*** and ***eosinophils***. Basophils produce histamine, which initiates inflammation whenever body cells are injured or killed. Eosinophils seem to help mod-

FIGURE 4.15 Formation of blood clots. (See text for explanation.)



erate inflammation. Eosinophils seem to be defense cells too, because their number increases in certain situations, such as during an allergic reaction or when small parasites invade the body. Eosinophils and basophils are thought to have several additional functions.

There are only two types of agranulocytes in the blood. ***Lymphocytes*** are the more numerous and function as part of the immune system. ***Monocytes*** function like neutrophils and participate in immune responses. Lymphocytes and monocytes are discussed in Chap. 15.

Age Changes in Blood

The total amount of blood per unit of body mass and the relative amounts of plasma and cellular components remain constant regardless of age. Though some of the reserve capacity of the bone marrow to produce blood cells and platelets declines with aging, the marrow always retains enough power to supply as many blood cells and platelets as needed. Information about aging and blood components follows.

Plasma Negligible changes occur in the chemical composition of plasma, though there is an increase in certain waste products (e.g., urea, creatinine). Increases in these wastes are probably due to the decline in the ability of the kidney to remove them from the blood.

There is an age-related increase in the viscosity or "thickness" of blood. Reasons for the increased viscosity include an increase in clotting factors and broken fibrin strands; elevated norepinephrine, which promotes clot formation; and stiffening of RBCs, especially in blood with high blood cholesterol. Certain clotting factors increase dramatically at menopause, causing a rapid rise in blood viscosity. Other factors that increase blood viscosity include reduced blood oxygen; inadequate exercise; stress; and smoking, including secondhand smoke. These factors can be reduced or eliminated. Effects from higher blood viscosity include slower blood flow, increased risk of clot formation, and more rapid development of atherosclerosis.

Red Blood Cells No substantial changes occur in RBCs, though there are some indications of a decrease in the concentration of hemoglobin in men over age 65. Overall, however, aging causes no changes in the ability of the RBCs to function.

Platelets The number of platelets circulating in the blood remains essentially unchanged, and the platelets retain the ability to initiate clot formation. An age-related increase in the tendency of platelets to clump together may cause a slight increase in the risk of thrombus formation.

White Blood Cells Age changes in PMNs include decreases in the number and rate of release of stored cells, rate of movement, ability to be chemically attracted to areas, and proportion of cells capable of performing phagocytosis. The number of PMNs capable of performing phagocytosis seems to decline especially rapidly after age 60. The net effect of age changes in PMNs is a decrease in their ability to defend the body against infection, which helps explain the age-related increase in susceptibility to infections in areas such as the respiratory, urinary, and integumentary systems.

Little has been reported on age changes in monocytes that circulate in the blood. Age changes in lymphocytes are discussed in Chap. 15.