

The systemic circulation

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CHAPTER OUTLINE

- DETERMINANTS OF ARTERIAL PRESSURE
- THE MEASUREMENT OF ARTERIAL PRESSURE
- THE NORMAL RANGE OF ARTERIAL PRESSURE

- SYSTEMIC VASCULAR RESISTANCE (SVR)
- BLOOD VOLUME
- THE COUPLING OF VENOUS RETURN AND CARDIAC OUTPUT

KEY CONCEPTS

1. Cardiac output and systemic vascular resistance determine mean arterial pressure.
2. Stroke volume and arterial compliance are the main determinants of pulse pressure.
3. Arterial compliance decreases as arterial pressure increases.
4. Systolic and diastolic arterial pressure can be measured noninvasively.

5. Systemic vascular resistance is most influenced by the radius of arterioles.
6. The venous side of the systemic circulation contains a large fraction of the systemic blood volume.
7. Venous return and cardiac output are equal at a unique right atrial pressure.
8. Shifts in blood volume between the periphery (extrathoracic blood volume) and chest (central blood volume) influence preload and cardiac output.

An understanding of the major systemic hemodynamic variables—arterial pressure, systemic vascular resistance, and blood volume—is a prerequisite to understanding the regulation of arterial pressure and blood flow to individual tissues. The purpose of this chapter is to consider these variables in detail, in preparation for discussions of blood flow to specific regions of the body as well as the regulation of the circulation.

DETERMINANTS OF ARTERIAL PRESSURE

The key measures of systemic arterial pressure are mean arterial pressure, systolic and diastolic arterial pressures, and pulse pressure. These terms were introduced in Chapter 12 and, now that cardiac output, stroke volume, and heart rate have been discussed in Chapter 14, we can discuss them in more depth. For simplicity, mean arterial pressure, systolic pressure, and diastolic pressure are often presented as constant from moment-to-moment. Nothing could be further from the truth. Arterial pressures vary around average values from heartbeat to heartbeat and from minute to minute.

Mean Arterial Pressure Is Determined by Cardiac Output and Systemic Vascular Resistance

Mean arterial pressure (\bar{P}_a) is determined mathematically as indicated in Figure 15.1, but is often approximated from the equation,

$$\bar{P}_a = \bar{P}_d + (\bar{P}_s - \bar{P}_d)/3 \text{ or } \bar{P}_a = (2\bar{P}_d + \bar{P}_s)/3 \quad (1)$$

where \bar{P}_d is the diastolic pressure, \bar{P}_s is the systolic pressure, and $\bar{P}_s - \bar{P}_d$ is the pulse pressure. \bar{P}_a is closer to \bar{P}_d , instead of halfway between \bar{P}_s and \bar{P}_d , because the duration of diastole is about twice as long as systole.

The difference between mean arterial pressure and right atrial pressure (P_{ra}) is equal to the product of cardiac output (CO) and systemic vascular resistance (SVR):

$$\bar{P}_a - P_{ra} = CO \times SVR \quad (2)$$

Because right atrial pressure is small compared to mean arterial pressure, cardiac output and SVR are usually considered to be the physiologically important determinants of mean arterial pressure.

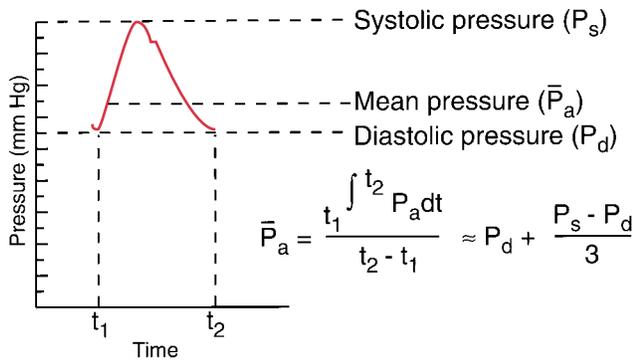


FIGURE 15.1 Definition of mean arterial pressure. Mean pressure is the area under the pressure curve divided by the time interval. This can be approximated as the diastolic pressure plus one-third pressure.

Pulse Pressure Is Determined Largely by Stroke Volume and Arterial Compliance

Arterial compliance is a nonlinear variable that depends on the volume of the aorta and major arteries. The volume of the aorta and major arteries is dependent on mean arterial pressure, meaning that pulse pressure is indirectly dependent on mean arterial pressure. Figure 15.2A shows the effect of a change in aortic volume on aortic pressure if aortic compliance were not a function of aortic volume. No matter what initial volume is present, the same change in volume causes the same change in pressure. In real life, however, aortic compliance decreases as aortic volume is increased, as shown in Figure 15.2B. Because of this, a given change in aortic volume at a low initial volume causes a relatively small change in pressure, but the same change in volume at a high initial volume causes a much larger change in pressure. The large arteries behave in an analogous manner.

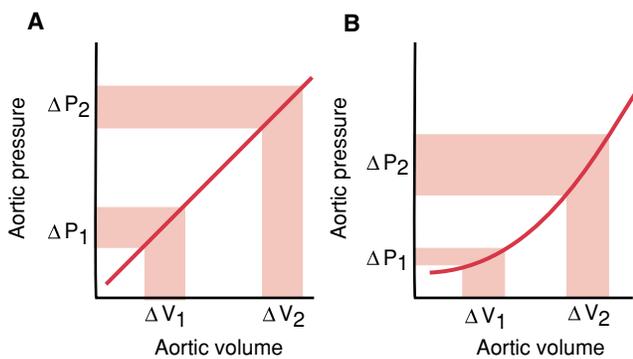


FIGURE 15.2 Relationship between aortic volume and pressure. A, aortic compliance is independent of aortic volume. The change in volume (ΔV_1) causes the change in pressure (ΔP_1). The same change in volume (ΔV_2) at a higher initial volume causes a change in pressure (ΔP_2) equal to ΔP_1 . B, aortic compliance decreases as aortic volume increases. The change in volume (ΔV_1) causes the change in pressure (ΔP_1). The same change in volume (ΔV_2) at a higher initial volume causes a much larger change in pressure (ΔP_2).

The above discussion shows that the influence of stroke volume on pulse pressure depends on the mean arterial pressure. As mean arterial pressure increases, arterial compliance decreases. As arterial compliance decreases, a given stroke volume causes a larger pulse pressure.

Stroke Volume, Heart Rate, and Systemic Vascular Resistance Interact in Affecting Mean Arterial and Pulse Pressures

When cardiac changes in the face of a constant SVR, mean arterial pressure is influenced according to the formula $\bar{P}_a = CO \times SVR$. The influence of a change in cardiac output on mean arterial pressure is independent of the cause of the change—heart rate or stroke volume (remember that $CO = SV \times HR$). In contrast, the effect of a change in cardiac output on pulse pressure greatly depends on whether stroke volume or heart rate changes. Below we consider the effects of changes in heart rate, stroke volume, cardiac output, SVR, and arterial compliance on pulse pressure and mean arterial pressure.

Effect of Changes in Heart Rate and Stroke Volume With No Change in Cardiac Output. If an increase in heart rate is balanced by a proportional and opposite change in stroke volume, *mean* arterial pressure does not change because cardiac output remains constant. However, the decrease in stroke volume that occurs in this situation results in a diminished pulse pressure; the diastolic pressure increases, while the systolic pressure decreases around an unchanged mean arterial pressure. An increase in stroke volume with no change in cardiac output likewise causes no change in mean arterial pressure. The increased stroke volume, however, produces a rise in pulse pressure; systolic pressure increases and diastolic pressure decreases.

Another way to think about these events is depicted in Figure 15.3A. The first two pressure waves have a diastolic pressure of 80 mm Hg, systolic pressure of 120 mm Hg, and mean arterial pressure of 93 mm Hg. Heart rate is 72 beats/min. After the second beat, the heart rate is slowed to 60 beats/min, but stroke volume is increased sufficiently to maintain the same cardiac output. The longer time interval between beats allows the diastolic pressure to fall to a new (lower) value of 70 mm Hg. The next systole, however, produces an increase in pulse pressure because of the ejection of a greater stroke volume, so systolic pressure rises to 130 mm Hg. The pressure then falls to the new (lower) diastolic pressure, and the cycle is repeated. Mean arterial pressure does not change because cardiac output and SVR are constant. The increased pulse pressure is distributed evenly around the same mean arterial pressure.

If an increase in heart rate is balanced by a decrease in stroke volume so that there is no change in cardiac output, the result is no change in mean arterial pressure but a decrease in pulse pressure. Systolic pressure decreases and diastolic pressure increases.

Effect of Changes in Cardiac Output Balanced by Changes in Systemic Vascular Resistance. Mean arterial pressure may remain constant despite a change in cardiac output because of an alteration in SVR. A good exam-

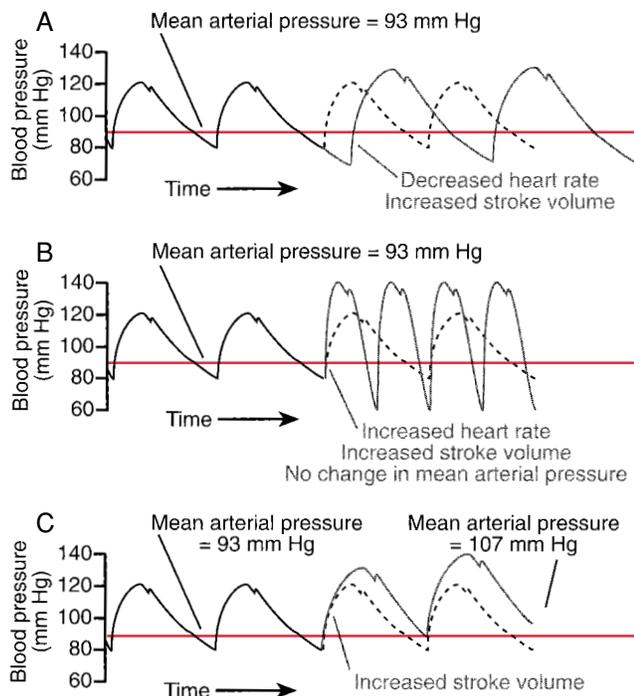


FIGURE 15.3 Effects of A, Effect of increased stroke volume on arterial pressure with constant cardiac output and SVR. When cardiac output is held constant by lowering heart rate, there is no change in mean arterial pressure (93 mm Hg) and systolic pressure increases while diastolic pressure decreases. B, Effect of increased heart rate and stroke volume with no change in mean arterial pressure because of decreased SVR. After the first two beats, stroke volume and heart rate are increased. Pulse pressure increases around an unchanged mean arterial pressure, and systolic pressure is higher and diastolic pressure is lower than the control. C, Effect of increased stroke volume, with constant heart rate and SVR. Cardiac output, mean arterial pressure, systolic pressure, diastolic pressure, and pulse pressure are all increased.

ple of this is **dynamic exercise** (e.g., running or swimming). Dynamic exercise often produces little change in mean arterial pressure because the increase in cardiac output is balanced by a decrease in SVR. The increase in cardiac output is caused by increases in both heart rate and stroke volume. The elevated stroke volume results in a higher pulse pressure. Systolic pressure is higher because of the elevated stroke volume. Diastolic pressure is lower because the fall in SVR increases flow from the aorta during diastole (Figs. 15.3B and 15.4). These examples demonstrate that when mean arterial pressure remains constant, moment-to-moment changes in pulse pressure can be predicted from changes in stroke volume.

Effect of Changes in Cardiac Output With Constant SVR. Figure 15.3C shows what happens if stroke volume is increased with no change in heart rate (cardiac output is increased). The increased stroke volume occurs at the time of the next expected beat, and the diastolic pressure is, as for previous beats, 80 mm Hg. After a transition beat, the increased stroke volume results in an elevation in systolic

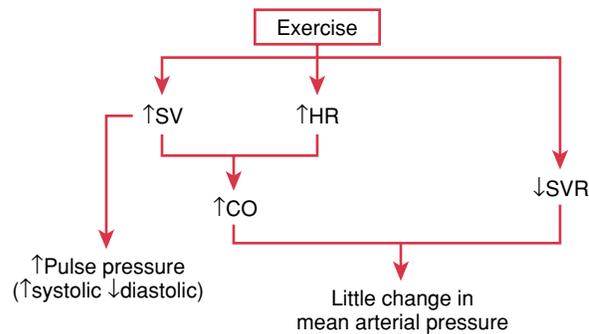


FIGURE 15.4 Effect of dynamic exercise on mean arterial pressure and pulse pressure. Heart rate (HR) and stroke volume (SV) increase, resulting in an increase in cardiac output (CO). However, dilation of resistance vessels in skeletal muscle lowers systemic vascular resistance (SVR), balancing the increase in cardiac output and causing little change in mean arterial pressure.

pressure to 140 mm Hg, after which the pressure falls to a new diastolic pressure of 90 mm Hg. In this new steady state, systolic, diastolic, and mean arterial pressures are all higher. The increase in mean arterial pressure (to 107 mm Hg) results in a decrease in arterial compliance (see Fig 15.2). The increase in pulse pressure results from both higher stroke volume and decreased arterial compliance.

Effect of Increased SVR. When SVR increases, flow out of the larger arteries transiently decreases. If cardiac output is unchanged, the volume in the aorta and large arteries increases (Fig. 15.5). Mean arterial pressure also increases, until it is sufficient to drive the blood out of the larger vessels and into the smaller vessels at the same rate as it enters from the heart (i.e., cardiac output). At a higher volume (and mean arterial pressure) arterial compliance is lower, and therefore pulse pressure is greater for a given stroke volume (see Fig. 15.2). The net result is an increase in mean arterial, systolic, and diastolic pressures. The extent of the increase in pulse pressure depends on how much arterial compliance decreases with the rise in mean arterial pressure and arterial volume.

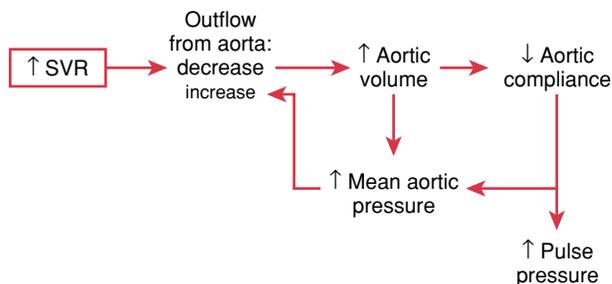


FIGURE 15.5 Effect of increased SVR on mean arterial and pulse pressures. Increased SVR impedes outflow from the aorta and large arteries, increasing their volume and pressure. The increase in aortic pressure brings the outflow from the aorta back to its original value, but at a higher aortic volume. The larger volume lowers aortic compliance and, thereby, raises pulse pressure at a constant stroke volume. The word “increase” in smaller type indicates a secondary change.

The compliance of the aorta decreases with age. The fall in compliance for a given increase in mean arterial pressure is greater in older than in younger individuals (Fig. 15.6). This explains the higher pulse and systolic pressures often observed in older individuals with modest elevations in SVR.

THE MEASUREMENT OF ARTERIAL PRESSURE

Arterial blood pressure can be measured by direct or indirect (noninvasive) methods. In the laboratory or hospital setting, a cannula can be placed in an artery and the pressure measured directly using electronic transducers. In clinical practice, however, blood pressure is usually measured indirectly.

The Routine Method for Measuring Human Blood Pressure Is by an Indirect Procedure Using a Sphygmomanometer

The **sphygmomanometer** uses an inflatable cuff that is wrapped around the patient’s arm and inflated so that the pressure in it exceeds systolic blood pressure (Fig. 15.7). The external pressure compresses the artery and cuts off blood flow into the limb. The external pressure is measured by the height of a column of mercury in the manometer connected to the cuff or by means of a me-

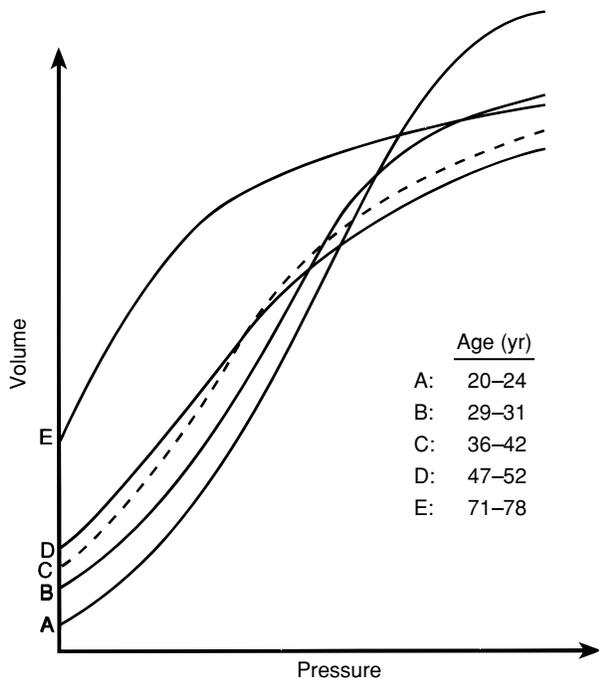


FIGURE 15.6 Effect of aging on vascular compliance. The curves illustrate the relationship between pressure and volume for aortas of humans in different age groups. In older aortas, because of decreased compliance, a given increase in volume causes a larger increase in pressure. (Modified from Hallock P, Benson IC. Studies on the elastic properties of human isolated aorta. *J Clin Invest* 1937;16:595–602.)

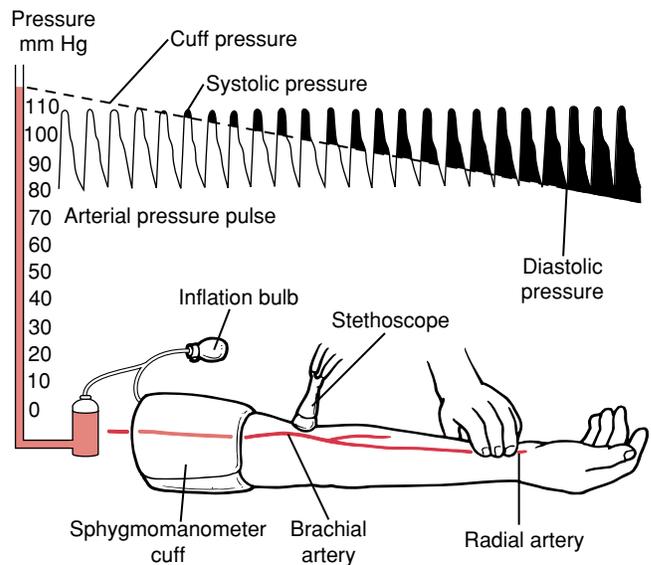


FIGURE 15.7 The relationship between true arterial pressure and blood pressure as measured with a sphygmomanometer. When cuff pressure falls just below systolic pressure, turbulent blood squirting through the partially occluded artery under the cuff produces the first Korotkoff sound, which can be heard via a stethoscope bell placed over the brachial artery (auscultatory method). Systolic pressure can also be estimated by palpating the radial artery and noting the cuff pressure at which the pulse is first felt at the wrist (palpatory method). When the cuff pressure falls just below diastolic pressure, the artery stays open, flow is no longer turbulent, and the sounds cease. The arterial pressure tracing is simplified in that systolic, diastolic, and mean arterial pressures vary around average values from moment-to-moment. For this reason, the production of sounds may vary from heartbeat to heartbeat. (From Rushmer RF. *Cardiovascular Dynamics*. 4th Ed. Philadelphia: WB Saunders, 1970;155.)

chanical manometer calibrated by a column of mercury. The air in the cuff is slowly released until blood can leak past the occlusion at the peak of systole. Blood spurts past the point of partial occlusion at high velocity, resulting in turbulence. The vibrations associated with the turbulence are in the audible range, enabling a stethoscope (placed over the brachial artery) to detect noises caused by the turbulent flow of the blood pushing under the cuff; the noises are known as **Korotkoff sounds**. The pressure corresponding to the first appearance of blood pushing under the cuff is the systolic pressure. As pressure in the cuff continues to fall, the brachial artery returns toward its normal shape and both the turbulence and Korotkoff sounds cease. The pressure at which the Korotkoff sounds cease is the diastolic pressure.

Indirect Methods of Measuring Arterial Pressure May Be Subject to Artifacts

The width of the inflatable cuff is an important factor that can affect pressure measurements. A cuff that is too narrow will give a falsely high pressure because the pressure in the cuff is not fully transmitted to the underlying artery. Ideally, cuff width should be approximately 1.5 times the diameter of

the limb at the measurement site. In older adults (or those who have “stiff” or hard-to-compress blood vessels from other causes, such as arteriosclerosis), additional external pressure may be required to compress the blood vessels and stop the flow. This extra pressure gives a falsely high estimate of blood pressure. Obesity may contribute to an inaccurate assessment if the cuff used is too small.

THE NORMAL RANGE OF ARTERIAL PRESSURE

As with all physiological variables, values for individuals are distributed around a mean value. Although the range of blood pressures in the population as a whole is rather broad, changes in a given patient are of diagnostic importance. Normal arterial blood pressure in adults is approximately 120 mm Hg systolic and 80 mm Hg diastolic (usually written 120/80).

Age, Race, Gender, Diet and Body Weight, and Other Factors Affect Blood Pressure

In Western societies, arterial pressure is dependent on age. Systolic blood pressure rises throughout life, while diastolic blood pressure rises until the sixth decade of life after which it stays relatively constant. Blood pressure is higher among African Americans than Caucasian Americans. Blood pressure is higher among men than among women with functional ovaries. Dietary fat and salt, as well as obesity, are associated with higher blood pressures. Other factors that affect blood pressure are excessive alcohol intake, physical activity, psychosocial stress, potassium and calcium intake, and socioeconomic status.

Hypertension Is a Sustained Elevation in Blood Pressure

Epidemiological data show that chronically elevated blood pressure is associated with excess cardiovascular morbidity and mortality. In adults, hypertension is defined as sustained systolic blood pressure of 140 mm Hg or higher, sustained diastolic blood pressure of 90 mm Hg or higher, or taking antihypertensive medication. Hypertension causes damage to the arterial system, the myocardium, the kidneys, and the nervous system, including the retinas. Medical treatment that lowers blood pressure to normal values significantly reduces the risk of damage of these target tissues.

SYSTEMIC VASCULAR RESISTANCE (SVR)

SVR is the frictional resistance to blood flow provided by all of the vessels between the large arteries and right atrium, including the small arteries, arterioles, capillaries, venules, small veins, and veins.

Small Arteries, Arterioles, and Capillaries Account for 90% of Vascular Resistance

The relative importance of the various segments contributing to the systemic vascular resistance is appreciated by ob-

serving a profile of the pressure drop along the vascular tree (Fig. 15.8). Little change in pressure occurs in the aorta and large arteries. Approximately 70% of the pressure drop occurs in the small arteries and arterioles, and another 20% occurs in the capillaries. Contraction and relaxation of the smooth muscle in the walls of small arteries and arterioles cause changes in vessel diameter, which, in turn, influence blood flow.

When medium and large arteries are affected by disease, they may become major sources of increased resistance and significantly reduce blood flow to regions of the body (see Clinical Focus Box 15.1).

Blood Viscosity, Vessel Length, and Vessel Radius Affect Resistance

To understand the importance of smooth muscle in the control of SVR, we will consider the role of each factor expressed in Poiseuille’s law (see Chapter 12):

$$R = 8\eta L/\pi r^4 \quad (3)$$

Viscosity (η) increases with hematocrit, especially when the hematocrit is above the normal range of 38 to 54% (Fig. 15.9). An increase in viscosity raises vascular resistance and, thereby, limits flow. Because oxygen delivery depends on blood flow as well as blood oxygen content, a limited flow can negate the increase in oxygen content resulting from the increased number of red blood cells. In individuals with polycythemia (an increased number of red blood cells), less oxygen may actually be delivered to tissues because of increased viscosity; this occurs despite the enhanced oxygen-carrying capacity provided by the extra red blood cells. A normal hematocrit reflects a good balance between sufficient red blood cells for oxygen transport and the viscosity caused by red blood cells.

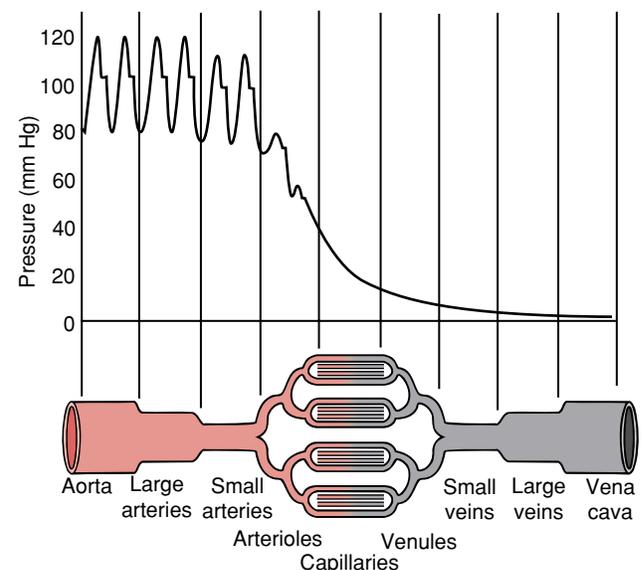


FIGURE 15.8 Pressures in different vessels of the systemic circulation. Pulse pressure is greatest in the aorta and large arteries. The greatest drop in pressure occurs in the arterioles.

CLINICAL FOCUS BOX 15.1

Arterial Disease

Disease processes such as **atherosclerosis** can reduce the diameter of most medium and large arteries, causing an increase in arterial resistance and a subsequent decrease in blood flow. The signs and symptoms resulting from atherosclerotic disease depend on which arteries are **stenotic** (narrowed) and the severity of the reduction in blood flow. Regions commonly affected by atherosclerosis include the heart, brain, and legs.

Coronary artery disease is the most common serious manifestation of atherosclerosis. When the stenotic lesions are relatively mild, blood flow may be inadequate only when the myocardial demand is high, such as during exercise. If blood flow is inadequate to meet the metabolic needs of a particular tissue, the tissue is said to be **ischemic**. In the heart, short periods of **ischemia** may produce chest pain known as **angina**. As the disease progresses and the coronary stenosis becomes more severe, ischemia tends to occur at increasingly lower cardiac workloads, eventually resulting in angina at rest. In cases of severe stenosis and/or complete occlusion of the coronary arteries, blood flow may become inadequate to maintain myocardial viability, resulting in **infarction** (cell or tissue death). Millions of people in the United States are affected by coronary disease, with more than 1 million experiencing myocardial infarction each year and 700,000 ultimately

dying from infarction, making this the leading cause of death in the nation.

Stenoses in the carotid or vertebral arteries can lead to ischemia and infarction—**stroke** or **cerebrovascular accident**—involving the brain. Strokes are the third leading cause of death in the United States and a leading cause of significant disability.

As with the heart, mild arterial disease involving the legs usually becomes symptomatic only when the demand for blood flow is high, such as during exercise involving the lower extremities. Muscle ischemia produces pain called **claudication**, which typically resolves rapidly when the patient rests. As the disease becomes more severe, symptoms may progress to include **rest pain** and, ultimately, limb infarction with gangrene.

In all of these cases, blood flow to the affected organ may be preserved by the development of collateral arteries, which can carry blood around the stenotic or occluded segments of arteries. When collateral flow is inadequate to meet needs, blood flow may be improved with **angioplasty** (using a balloon catheter, laser, etc.) or **bypass surgery** (using autologous vein or synthetic material to route blood around a blockage). More than 1 million revascularization procedures using these techniques are performed in the United States annually.

Returning to equation 3, despite the potential effect of blood viscosity on resistance, hematocrit normally does not change much and is usually not an important cause of changes in vascular resistance. Likewise, the length (L) of blood vessels does not change significantly (except with

growth) and is, therefore, not important as a physiological determinant of vascular resistance. *The remaining influence, vessel radius (r), is the major determinant of changes in SVR.* Since resistance is inversely proportional to r^4 , small changes in the radius cause relatively large changes in vascular resistance. For example, the vascular resistance to skeletal muscle during exercise may decrease 25-fold. This fall in resistance results from a 2.2-fold increase in resistance vessel radius (i.e., $2.2^4 = \sim 25$). Vessel radius is determined primarily by the contractile activity of smooth muscle in the vessel wall (see Chapter 16).

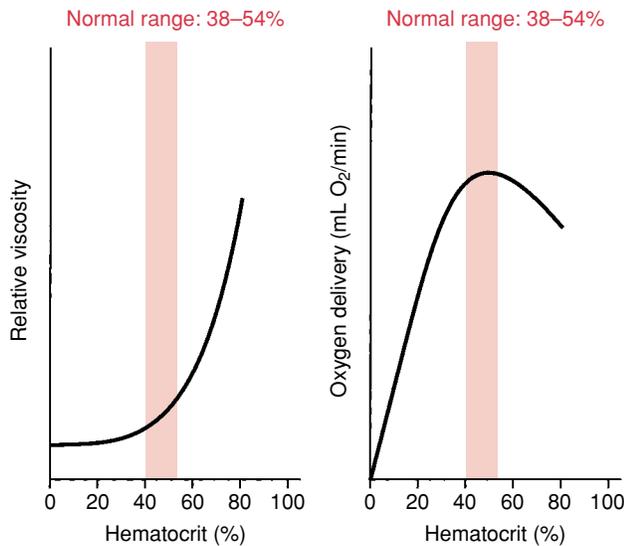


FIGURE 15.9 Effect of hematocrit on blood viscosity. Above-normal hematocrits produce a sharp increase in viscosity. Because increased viscosity raises vascular resistance, hemoglobin and oxygen delivery may fall when the hematocrit rises above the normal range.

Sources of Resistance in the Systemic Circulation Are Arranged in Series and in Parallel

Systemic vascular resistance is the net result of the resistance offered by many vessels arranged both in series and in parallel, and it is worth considering the effects of vessel arrangement on total resistance. Resistances in series are simply summed; for example:

$$SVR = R_{\text{small arteries}} + R_{\text{arterioles}} + R_{\text{capillaries}} + R_{\text{venules}} + R_{\text{small veins}} \quad (4)$$

For resistances in parallel, the reciprocals of the parallel resistances are summed (Fig. 15.10); for example, for the various parallel blood flows in the body:

$$1/SVR = 1/R_{\text{cerebral}} + 1/R_{\text{coronary}} + 1/R_{\text{splanchnic}} + 1/R_{\text{renal}} + 1/R_{\text{muscle}} + 1/R_{\text{skin}} + 1/R_{\text{other}} \quad (5)$$

Resistances in hemodynamic circuits are treated the same way as in the analysis of electrical circuits.

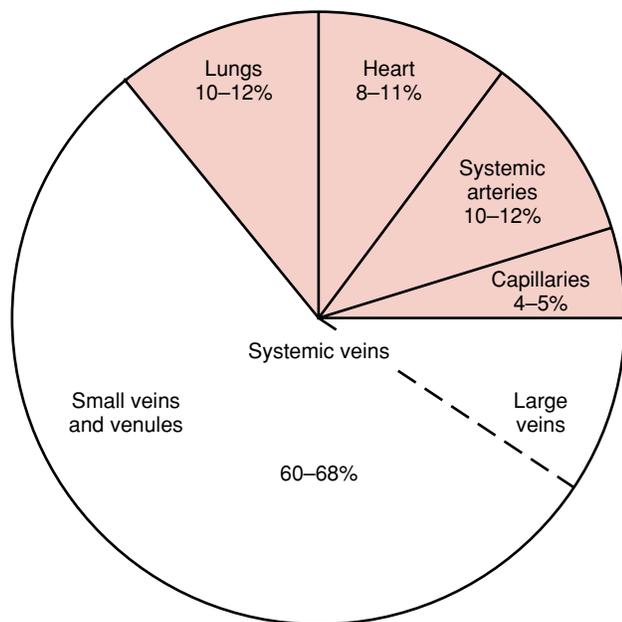


FIGURE 15.10 Blood volumes of various elements of the circulation in a person at rest.

BLOOD VOLUME

The blood volume is distributed among the various portions of the circulatory system according to the pattern shown in Figure 15.10. Total blood volume in a 70-kg adult is 5.0 to 5.6 L.

Three Fourths of the Blood in the Systemic Circulation Is in the Veins

Approximately 80% of the total blood volume is located in the **systemic circulation** (i.e., the total volume minus the volume in the heart and lungs). About 60% of the total blood volume (or 75% of the systemic blood volume) is located on the venous side of the circulation. The blood present in the arteries and capillaries is only about 20% of the total blood volume. Because most of the systemic blood volume is in veins, it is not surprising that changes in systemic blood volume primarily reflect changes in venous volume.

Small Changes in Systemic Venous Pressure Can Cause Large Changes in Venous Volume

Systemic veins are approximately 20 times more compliant than systemic arteries; small changes in venous pressure are, therefore, associated with large changes in venous volume. If 500 mL of blood is infused into the circulation, about 80% (400 mL) locates in the systemic circulation. This increase in systemic blood volume raises mean circulatory filling pressure by a few mm Hg. This small rise in filling pressure, distributed throughout the systemic circulation has a much larger effect on the volume of systemic veins than systemic arteries. Because of the much higher compliance of veins than arteries, 95% of the 400 mL (or 380 mL) is found in veins, and only 5% (20 mL) is found in arteries.

Central Blood Volume Is About One Fourth of Total Blood Volume

In considering the role of distribution of blood volume in filling the heart, it is useful to divide the blood volume into central (or intrathoracic) and extrathoracic portions. The **central blood volume** includes the blood in the superior vena cava and intrathoracic portions of the inferior vena cava, right atrium and ventricle, pulmonary circulation, and left atrium; this constitutes approximately 25% of the total blood volume. The central blood volume can be decreased or increased by shifts in blood to and from the extrathoracic blood volume. From a functional standpoint, the most important components of the **extrathoracic blood volume** are the veins of the extremities and abdominal cavity. Depending on several factors to be discussed below, blood shifts readily between these veins and the vessels containing the central blood volume. Although a part of the extrathoracic blood volume, the blood in the neck and head is less important because there is far less blood in these regions, and the blood volume inside the cranium cannot change much because the skull is rigid. Blood in the central and extrathoracic arteries can be ignored because the low compliance of these vessels means that little change in their volume occurs. The volume of blood in the veins of the abdomen and extremities is about equal to the central blood volume; therefore, about half of the total blood volume is involved in shifts in distribution that affect the filling of the heart.

The Measurement of Central Venous Pressure Provides Information on Central Blood Volume

Central venous pressure can be measured by placing the tip of a catheter in the right atrium. Changes in central venous pressures are a good indicator of central blood volume because the compliance of the intrathoracic vessels tends to be constant. In certain situations, however, the physiological meaning of central venous pressure is changed. For example, if the tricuspid valve is incompetent, right ventricular pressure is transmitted to the right atrium during ventricular systole. In general, the use of central venous pressure to assess changes in central blood volume depends on the assumption that the right heart is capable of pumping normally. Also, central venous pressure does not necessarily reflect left atrial or left ventricular filling pressure. Abnormalities in right or left heart function or in pulmonary vascular resistance can make it difficult to predict left atrial pressure from central venous pressure.

Unfortunately, measurements of the peripheral venous pressure, such as the pressure in an arm or leg vein, are subject to too many influences (e.g., partial occlusion caused by positioning or venous valves) to be helpful in most clinical situations.

Cardiac Output Is Sensitive to Changes in Central Blood Volume

Consider what happens if blood is steadily infused into the inferior vena cava of a normal individual. As this occurs, the volume of blood returning to the chest—venous return—is transiently greater than the volume leaving it—the cardiac

output. This difference between the input and output of blood produces an increase in central blood volume. It will occur first in the right atrium where the accompanying increase in pressure enhances right ventricular filling, end-diastolic fiber length, and stroke volume. Increased flow into the lungs increases pulmonary blood volume and filling of the left atrium. Left cardiac output will increase according to Starling's law, so that the output of the two ventricles exactly matches. Cardiac output will increase until it equals the sum of the previous venous return to the heart plus the infusion of new blood.

Central Blood Volume Is Influenced by Total Blood Volume and Its Distribution.

Changes in central blood volume initiate changes in filling of the ventricles, and therefore, central blood volume is an important influence on cardiac output. Central blood volume is altered by two events: changes in total blood volume and changes in the distribution of total blood volume between central and extrathoracic regions.

Changes in Total Blood Volume. An increase in total blood volume can occur as a result of an infusion of fluid, the retention of salt and water by the kidneys, or a shift in fluid from the interstitial space to plasma. A decrease in blood volume can occur as a result of hemorrhage, losses through sweat or other body fluids, or the transfer of fluid from plasma into the interstitial space. In the absence of compensatory events, changes in blood volume result in proportional changes in both central and extrathoracic blood volume. For example, a moderate hemorrhage (10% of blood volume) with no distribution shift would cause a 10% decrease in central blood volume. The reduced central blood volume would, in the absence of compensatory events, lead to decreased filling of the ventricles and diminished stroke volume and cardiac output.

Redistribution of Blood Volume. Central blood volume can be altered by a shift in blood volume to or away from the periphery. Shifts in the distribution of blood volume occur for two reasons: a change in transmural pressure or a change in venous compliance.

Changes in the transmural pressure of vessels in the chest or periphery enlarge or diminish their size. Because there is a finite volume of blood, it shifts in response to changes in transmural pressure in one or the other of these regions. Imagine a long balloon filled with water: If it is slowly turned end over end, the lower end of the balloon has the greatest transmural pressure because of the weight of the water pressing from above. As it is turned, the lower end of the balloon will bulge and the upper end will shrink.

The best physiological example of a change in transmural pressure occurs when a person stands up. Standing increases the transmural pressure in the blood vessels of the legs because it creates a vertical column of blood between the heart and the blood vessels of the legs. The arterial and venous pressures at the ankles during standing can easily be increased by 130 cm (4.3 ft) of water (blood), which is almost 100 mm Hg higher than in the recumbent position. The increased transmural pressure (outside pressure is still

atmospheric) results in little distention of arteries because of their low compliance, but results in considerable distention of veins because of their high compliance. In fact, approximately 550 mL of blood is needed to fill the stretched veins of the legs and feet when an average person stands up. Filling of the veins of the buttocks and pelvis also increases, but to a lesser extent, because the increase in transmural pressure is less.

Blood is redistributed to the legs from the central blood volume by the following sequence of events. When a person stands, blood continues to be pumped by the heart at the same rate and stroke volume for one or two beats. However, much of the blood reaching the legs remains in the veins as they become passively stretched to their new size by the increased venous (transmural) pressure, decreasing the return of blood to the chest. As cardiac output exceeds venous return for a few beats, the central blood volume falls (as does the end-diastolic fiber length, stroke volume, and cardiac output). Once the veins of the legs reach their new steady-state volume, the venous return again equals cardiac output. The equality between venous return and cardiac output is reestablished even though the central blood volume is reduced by 550 mL. However, the new cardiac output and venous return are decreased (relative to what they were before standing) because of the reduction in central blood volume. Without compensation, the resulting decrease in systemic arterial pressure would cause a drop in brain blood flow and loss of consciousness. Compensatory events, including increased activity of the sympathetic nervous system, to be discussed in Chapter 18, are required to maintain arterial pressure in the face of decreased cardiac output.

When the smooth muscle of the systemic veins contracts, the compliance of the systemic veins decreases. This results in a redistribution of blood volume toward the central blood volume. Ven constriction is an important compensatory mechanism following hemorrhage. The redistribution of blood toward the central blood volume helps to maintain ventricular filling and cardiac output.

THE COUPLING OF VENOUS RETURN AND CARDIAC OUTPUT

Because the blood moves in a closed circuit, **venous return**—the flow of blood from the periphery back to the right atrium—must equal cardiac output. The interplay between venous return and cardiac output can be analyzed from the viewpoint of the heart or the systemic circulation. From the viewpoint of the heart, venous return is kept equal to cardiac output by Starling's law. An increase in venous return raises diastolic filling of the ventricles and cardiac output rises to match the new venous return. The relation between cardiac output and right atrial pressure, shown in Figure 15.11, was presented earlier (see Fig. 14.2).

From the viewpoint of the systemic circulation, venous return to the heart is driven by the pressure gradient created by contractions of the left ventricle. The relationship between venous return and right atrial pressure is shown in Figure 15.11. If, in the absence of any reflex compensations, the heart fails and cardiac output falls below venous return, right atrial pressure rises. In Figure 15.11, the por-

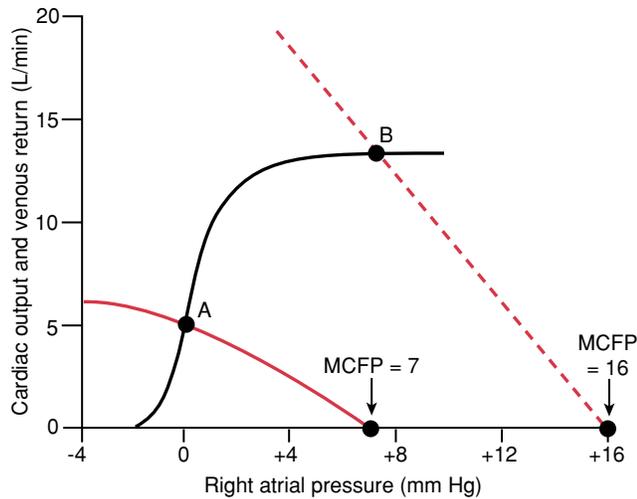


FIGURE 15.11 Interplay between venous return and cardiac output. The Starling curve relating cardiac output to right atrial pressure is shown in black. The normal curve showing venous return as a function of right atrial pressure is shown in solid red. Note that venous return is zero when right atrial pressure equals the mean circulatory filling pressure (7 mm Hg). The two curves intersect at point A where cardiac output and venous return are equal; the right atrial pressure in this case is 0 mm Hg. The dashed red line shows the venous return curve after transfusion of 1 L of blood. Filling of the cardiovascular system by the extra volume of blood raises mean circulatory filling pressure to 16 mm Hg. The slope of the venous return curve is also changed by the transfusion. The Starling curve is unchanged by the transfusion. The unique right atrial pressure that gives equal venous return and cardiac output (point B) is now 8 mm Hg. The transfusion raises cardiac output and venous return from 5 to 13 L/min. (From Guyton AC, Hall JE. *Medical Physiology*. Philadelphia: WB Saunders, 2000;219).

tion of the venous return curve for right atrial pressures above 0 mm Hg shows this. In this example, when right atrial pressure reaches 7 mm Hg, venous return stops. Generally, when right atrial pressure reaches the mean circulatory filling pressure, venous return stops. This is under-

standable because right atrial pressure and all other circulatory pressures will equal mean circulatory filling pressure when the heart stops (see Chapter 12 to review this point).

The venous return curve for right atrial pressures below 0 mm Hg is not sensitive to right atrial pressure (see Fig. 15.11). Instead of continuing to increase as right atrial pressure falls, venous return levels off. Venous return does not increase because, when right atrial pressure drops below zero (atmospheric pressure), the large veins collapse as they enter the chest. This is because the pressure in the lungs surrounding the veins is close to atmospheric pressure and the transmural pressure gradient favors collapse of the veins. The suction imposed by further drops in right atrial pressure further collapses the large veins, instead of sucking more blood into the chest. No matter how low right atrial pressure gets, venous return hardly increases.

Figure 15.11 shows a unique right atrial pressure at which a specific cardiac output curve and a specific venous return curve intersect. This is the right atrial pressure that provides a level of ventricular filling adequate to produce cardiac output that exactly matches the venous return.

The relationship between right atrial pressure, venous return, and cardiac output is not fixed. For example, Figure 15.11 shows the effects of transfusion of a liter of blood on these variables. Central blood volume participates in the increased blood volume, and filling of the heart is increased. This increases cardiac output from point A to point B, along an unchanged cardiac output curve. The increase in blood volume further fills the cardiovascular system and increases mean circulatory filling pressure. This changes the relationship between right atrial pressure and venous return, as shown by the dashed line. The curve is shifted to the right so that there is zero venous return at the new, elevated mean circulatory filling pressure (16 mm Hg). It also changes the slope of the venous return curve for reasons not discussed here. The unique right atrial pressure at which venous return is equal to cardiac output is now 8 mm Hg. Other factors that influence the relationship between cardiac output, venous return, and right atrial pressure include venous resistance to venous return, changes in sympathetic nervous system activity, and changes in SVR.

REVIEW QUESTIONS

DIRECTIONS: Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the ONE lettered answer or completion that is BEST in each case.

- Mean arterial pressure equals
 - Arterial compliance times stroke volume
 - Heart rate times stroke volume
 - Cardiac output times systemic vascular resistance
 - Cardiac output times arterial compliance
- Mean arterial pressure changes if
 - Heart rate increases, with no changes in cardiac output or systemic vascular resistance
 - Stroke volume changes, with no changes in heart rate or systemic vascular resistance
 - Arterial compliance changes, with no changes in cardiac output or systemic vascular resistance
 - Heart rate doubles and systemic vascular resistance is halved, with no change in stroke volume
 - Arterial compliance doubles and systemic vascular resistance is halved, with no change in heart rate
- Blood pressure measured using a sphygmomanometer
 - May be falsely low with too narrow a cuff
 - May be falsely low in patients with badly stiffened arteries
 - May be falsely high in obese patients
 - Gives a direct reading of mean arterial pressure
 - Depends on the disappearance of sound to signal systolic pressure
- In the systemic circulation, vascular resistance
 - Increases with increased blood flow
 - Increases with increased blood viscosity
 - Increases with increased vessel length
 - Increases with increased vessel diameter
 - Increases with increased vessel branching

(continued)

- (A) Changes occur mainly in the aorta and large arteries
 (B) Is altered more by changes in blood viscosity than radius
 (C) Is altered more by changes in vessel radius than length
 (D) Is altered more by changes in vessel length than radius
5. Standing up causes
 (A) Decreased diameter of leg veins
 (B) Decreased blood volume within the cranium
 (C) Increased stroke volume
 (D) Increased right atrial volume
 (E) Decreased central blood volume
6. If a person has an arterial blood pressure of 125/75 mm Hg,
 (A) The pulse pressure is 40 mm Hg
 (B) The mean arterial pressure is 92 mm Hg
 (C) Diastolic pressure is 80 mm Hg
 (D) Systolic pressure is 120 mm Hg
 (E) The mean arterial pressure is 100 mm Hg
7. A person with an arterial blood pressure of 150/90 mm Hg and a right atrial pressure of 3 mm Hg develops an incompetent tricuspid valve, and right atrial pressure rises to 13 mm Hg with no change in arterial pressure. The pressure gradient forcing blood through the systemic circulation
 (A) Is unchanged
 (B) Decreased from 107 to 97 mm Hg
 (C) Increased from 103 to 113 mm Hg
 (D) Decreased from 147 to 137 mm Hg
 (E) Increased from 93 to 103 mm Hg
8. If mean arterial pressure increases (due to an increase in systemic vascular resistance) and stroke volume and heart rate remain constant, the pulse pressure
 (A) Increases
 (B) Decreases
 (C) Does not change
9. If the compliance of veins were equal to that of arteries, the change in central blood volume with standing would be

- (A) Less than normal
 (B) Greater than normal
 (C) The same as normal

SUGGESTED READING

- Coleman TC, Hall JE. Systemic hemodynamics and regional blood flow regulation. In: Izzo JL, Black HR, eds. *Hypertension Primer*. Baltimore: Lippincott Williams & Wilkins, 1999.
- Guyton AC, Hall JE. *Medical Physiology*. Philadelphia: WB Saunders, 2000, Chapter 20.
- Kaplan NM. Systemic hypertension: Mechanisms and diagnosis. In: Braunwald E, Zipes DP, Libby P, eds. *Heart Disease*. 6th Ed. Philadelphia: WB Saunders, 2001.
- O'Rourke MF. Arterial stiffness and hypertension. In: Izzo JL, Black HR, eds. *Hypertension Primer*. Baltimore: Lippincott Williams & Wilkins, 1999.
- Rowell LB. *Human Cardiovascular Control*. New York: Oxford University Press, 1993, Chapter 1.